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**Regulation of members of the
angiopoietin family by Kaposi
sarcoma herpesvirus**

by Richard James Vart BSc

Thesis submitted to the University of London,
University College London for the degree of Doctor
of Philosophy

2008

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Declaration

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Richard James Vart

Abstract

Kaposi sarcoma herpesvirus (KSHV) is the causative agent of Kaposi sarcoma (KS), a vascular tumour of endothelial cells. The angiopoietin family are a group of secreted glycoproteins whose members play important roles in tumour vascularisation. The primary aim of this work was to investigate how KSHV regulated members of the angiopoietin family through the construction of a selected KSHV lentiviral expression library.

Angiopoietin-2 (Ang2) is an important angiogenic factor which binds to the receptor Tie2 and is up-regulated in KS. Using a constructed KSHV lentiviral library, viral interleukin-6 (vIL6) and viral G-protein-coupled receptor (vGPCR) were found to up-regulate *Ang2* in lymphatic endothelial cells (LEC). Both vIL6 and vGPCR up-regulated *Ang2* in a paracrine manner and caused an up-regulation of *Ang2* through the mitogen-activated protein kinase pathway. Gene expression microarray analysis identified how other factors important for *Ang2* function, and other members of the angiopoietin family, were regulated by KSHV infection of LEC.

Angiopoietin-like 2 (Angptl2) has been shown to be important for proper vascularisation. My aim was to investigate the regulation of Angptl2 by KSHV and to start to investigate the function of Angptl2 in KS and cancer in general. *Angptl2* is up-regulated in KS and in KSHV-infected LEC and is expressed in a variety of other neoplasms; however, its expression profile did not correlate with expected angiogenic factors. The KSHV encoded viral interferon regulatory factor-1 (vIRF1) up-regulated *Angptl2* expression in LEC and vIRF1 increased *Angptl2* promoter activity using the first 1 kb of the *Angptl2* promoter. Over-expression of Angptl2 in a mouse tumorigenesis model affected tumour growth resulting in smaller and more necrotic tumours.

Ang2 and Angptl2 are likely to play important roles in KS pathogenesis. These angiopoietins along with the molecular mechanisms regulating their expression might present future targets for anti-KS therapeutics.

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Publications

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Abbreviations

ADM	adrenomedullin
AIDS	acquired immune deficiency syndrome
Ang	angiopoietin
Angptl	angiopoietin-like
AP1	activator protein 1
AP4	activator protein 4
ARE	AU-rich element
ARP2	angiopoietin-related protein 2
ATM	ataxia telangiectasia-mutated
BAC	bacterial artificial chromosome
BEC	blood vascular endothelial cells
BSA	bovine serum albumin
bFGF	basic fibroblast growth factor
CAM	chorioallantoic membrane
CBP	cAMP response element binding protein binding protein
c/c	lentiviral copies per cell
ChIP	chromatin immunoprecipitation
CMV	cytomegalovirus
CREB	cAMP response element binding protein
CR-UK	Cancer Research UK
Ct	threshold cycle
DEDs	death effector domains
dH ₂ O	distilled water
ddH ₂ O	double distilled water
DMEM	Dulbecco's modified Eagle medium
DMSO	dimethyl sulphoxide
EBV	Epstein-Barr virus
EDTA	ethylene diamino tetraacetic acid
EGF	epidermal growth factor
ERK	extracellular signal-regulated kinase
FADD	Fas-associated death domain

FAK	focal adhesion kinase
FBN1	fibrillin 1
FBS	foetal bovine serum
FLICE	Fas-associated death domain-like interleukin-1 β - converting enzyme
GEM	gene expression microarray
GFP	green fluorescent protein
GRIM19	retinoid-IFN-induced mortality-19
GRO α	growth-related oncogene α
GSK-3 β	glycogen synthase kinase 3 β
GorRHV1	gorilla rhadinoherpesvirus 1
GPCR	G-protein-coupled receptor
HAT	histone acetyltransferase
hIL6	human interleukin-6
HIV	human immunodeficiency virus
HHV8	human herpesvirus 8
HIF-1 α	hypoxia inducible factor 1- α
HPV-16	human papillomavirus type 16
HRP	horseradish peroxidase
hTERT	catalytic subunit of human telomerase
HUVEC	human umbilical vein endothelial cells
HVS	herpesvirus saimiri
IFN	interferon
IL8	interleukin-8
ISREs	interferon-stimulated response elements
IU	infectious unit
JNK	c-jun-NH ₂ -kinase
kapA	kaposin A
kapB	kaposin B
kapC	kaposin C
KBEC	KSHV-infected BEC
KLEC	KSHV-infected LEC
KS	Kaposi sarcoma

KSHV	Kaposi sarcoma herpesvirus
LAMP	latency-associated membrane protein
LANA-1	latent nuclear antigen
LEC	lymphatic endothelial cells
LOX	lysyl oxidase
LTR	long terminal repeat
MAPK	mitogen-activated protein kinase
MEK	mitogen-activated protein / extracellular signal-regulated kinase kinase
MCD	multicentric Castleman's disease
MCS	multiple cloning site
MHC-I	major histocompatibility complex class I
MHV68	murine herpesvirus 68
MK2	mitogen-activated protein kinase-associated protein kinase 2
MSC	mesenchymal stem cells
miRNA	microRNA
NF-AT	nuclear factor of activated T cells
NF1	nuclear factor 1
ORF	open reading frame
PanRHV1a	panrhadinovirus 1a
PanRHV1b	panrhadinovirus 1b
PBS	phosphate buffered saline
p.i.	post-infection
pCAF	CBP/p300-associated factor
PCR	polymerase chain reaction
PDGF	platelet derived growth factor
PEL	primary effusion lymphoma
PI3-K	phosphatidylinositol 3-kinase
PIC	pre-integration complex
PP2A	protein phosphatase 2A
pSIN	pSIN-MCS empty vector
PRDI1	positive regulatory domain 1-binding factor 1
qPCR	quantitative polymerase chain reaction

qRT-PCR	quantitative reverse transcriptase-polymerase chain reaction
RCL	replication competent lentiviruses
RPE	R-phycoerythrin
rhAng2	recombinant human Ang2
RIPA	radioimmunoprecipitation assay
RLU	relative light units
RNAi	RNA interference
RRV	rhesus monkey rhadinovirus
RT-PCR	reverse transcriptase-polymerase chain reaction
SDS	sodium dodecyl sulfate
SDS-PAGE	SDS-polyacrylamide gel electrophoresis
SE	standard error
SIN	self inactivating
Sp1	specificity protein 1
ST	SV40 small T antigen
STAT	signal transducers and activators of transcription
SV40	simian virus 40
TBS	Tris buffered saline
TGF- β	transforming growth factor- β
tMSC	transformed mesenchymal stem cells
TNF- α	tumour necrosis factor- α
TPA	12-O-tetradecanoyl phorbol-13-acetate
TR	terminal repeat
UTR	untranslated region
vBcl-2	viral Bcl-2
vcyclin	viral cyclin
VEGF	vascular endothelial growth factor
VEGFR	vascular endothelial growth factor receptor
vFLIP	viral Fas-associated death domain-like interleukin-1 β -converting enzyme inhibitory protein
vGPCR	viral G-protein-coupled receptor
vIL6	viral interleukin-6

vIRF	viral interferon regulatory factor
VSV-G	vesicular stomatitis virus glycoprotein
v/v	volume / volume
WPRE	woodchuck hepatitis virus post-transcriptional regulatory
w/v	weight / volume

(Abbreviations used only in figures and not in the main text of the thesis are shown in the appropriate figure legends.)

Chapter 1. Introduction

1.1 Kaposi sarcoma herpesvirus

The epidemiologist Patrick Moore, his wife Yuan Chang and their team in 1994 used representational difference analysis to identify DNA sequences of a novel herpesvirus in Kaposi sarcoma (KS) tissues (Chang et al., 1994). This virus is known as Kaposi sarcoma herpesvirus (KSHV) or human herpesvirus 8 (HHV8) and is a γ_2 -herpesvirus which is part of the *Rhadinovirus* genus and is related to the Epstein-Barr virus (EBV) (Moore et al., 1996b). Since its initial discovery, KSHV has been shown to be essential in the development of KS, as well as certain lymphoproliferations. The sequencing of the KSHV genome in 1996 revealed that KSHV not only encodes genes important for viral replication, but also encodes numerous cellular gene homologues (Russo et al., 1996). These cellular homologues and other KSHV encoded genes are likely to play important roles in both transformation and creating the necessary environment for the growth of KS and KSHV-associated lymphoproliferations.

1.1.1 Kaposi sarcoma

1.1.1.1 Clinico-epidemiologic forms

Moritz Kaposi, in 1872, first described an “idiopathic multiple pigmentar sarcoma of the skin” in five clinical cases and this is now known as KS (Kaposi, 1872). From its original identification, four clinico-epidemiologic forms of the neoplasm with differing degrees of severity have been recognised.

1.1.1.1.1 Classical KS

Classical KS is an indolent form of KS generally causing skin lesions at the extremities. Classical KS occurs predominately in men from Southern and Eastern Europe and the Middle East (Franceschi and Geddes, 1995). This is the original form of KS observed by Moritz Kaposi.

1.1.1.1.2 Endemic KS

A more aggressive form of KS occurring in Sub-Saharan Africa is known as endemic KS. This form of KS affects children, as well as the elderly, and often affects lymph nodes. Children can die of the disease and its occurrence is higher in males compared to females (D'Oliveira and Torres, 1972; Bayley, 1984).

1.1.1.1.3 Post-transplant KS

Post-transplant KS (also called iatrogenic KS) occurs in patients who receive immunosuppressive therapy which is often given to organ transplant patients (Harwood et al., 1979). Patients from certain populations such as from Mediterranean or Jewish ancestry are over-represented in organ transplant patients who acquire post-transplant KS (Harwood et al., 1979; Franceschi and Geddes, 1995). This is also the case for patients from endemic areas (Boshoff and Weiss, 2002).

1.1.1.1.4 Acquired immune deficiency syndrome (AIDS)-KS

The most aggressive form of KS is acquired immune deficiency syndrome (AIDS)-KS and if left untreated progresses from a few skin lesions to it affecting various internal organs such as the lungs and gut (Boshoff and Weiss, 1998). AIDS-KS marked the beginning of the AIDS epidemic and is not only the most common form of KS but is also the most common cause of cancer among human immunodeficiency virus (HIV)-infected individuals (Centers for Disease Control, 1981; Beral et al., 1990; Rabkin and Yellin, 1994; Martin, 2007).

1.1.1.2 KSHV the transmissible cause of KS

Before the discovery of KSHV, a sexual transmittable agent of KS was suspected (Beral et al., 1990). The occurrence of AIDS-KS appeared to be linked to sexual practices with AIDS-KS being over-represented in gay or bisexual men (Beral et al., 1990). Since KSHV has been discovered, KSHV DNA or RNA has been found in all stages of KS and has been found in the vast majority of lesions in the different forms of KS (Boshoff et al., 1995; Cathomas et al., 1996; Staskus et al., 1997; Boshoff and Weiss, 2001). KSHV is rarely detected in various other

tumours (Cathomas et al., 1996; Staskus et al., 1997). Furthermore, KSHV DNA can be detected in the peripheral blood cells of HIV-infected individuals prior to the appearance of KS lesions and could predict which HIV-infected individuals would develop AIDS-KS (Whitby et al., 1995). Similarly, seroconversion to being positive for antibodies against KSHV antigens often occurs prior to the appearance of KS (Gao et al., 1996a). All these support that KSHV is the transmissible agent of KS.

1.1.1.3 Histogenesis

KS lesions are vascular tumours which normally appear on the skin although can also disseminate to the viscera and lymph nodes (Fig. 1.1). KS lesions start as various small irregular endothelial-lined spaces among normal dermal blood vessels and these early lesions (patch stage) have a variable inflammatory infiltrate. This is followed by a growth of spindle cells in the dermis where they form slit-like vascular channels containing erythrocytes (plaque stage). Late stage lesions (nodular stage) contain sheets of proliferating spindle cells with abnormal, leaky, slit-like blood vessels and an inflammatory infiltrate (Boshoff and Weiss, 1998).

The spindle cells are thought to be the KS tumour cells, as they make up the bulk of the KS lesion. In early KS lesions, under 10% of the spindle cells are positive for KSHV, while in nodular lesions over 90% of spindle cells are positive (Dupin et al., 1999). Due to the percentage of KSHV positive cells increasing between early and late KS lesions, this suggests that KSHV infection provides a growth advantage to the cells (Dupin et al., 1999).

The KS spindle cells have recently been shown to have a gene expression microarray (GEM) profile closest to that of lymphatic endothelial cells (LEC) (Wang et al., 2004a). This is supported by the spindle cells expressing LEC markers such as vascular endothelial growth factor receptor (VEGFR)-3 (VEGFR3), LYVE-1 and podoplanin. (Wang et al., 2004a; Pyakurel et al., 2006). However, GEM analysis revealed that both LEC and blood vascular endothelial cells (BEC) markers are present in the KS expression signature (Wang et al.,

2004a). Suggesting that the KS spindle cell could originate in two ways. Either KSHV infects LEC directly and reprograms the cell to its own needs or infects endothelial precursor cells which can differentiate to either BEC or LEC but KSHV directs their differentiation towards a lymphatic endothelial type cell (Boshoff and Weiss, 2002; Wang et al., 2004a). However this still needs further investigation.

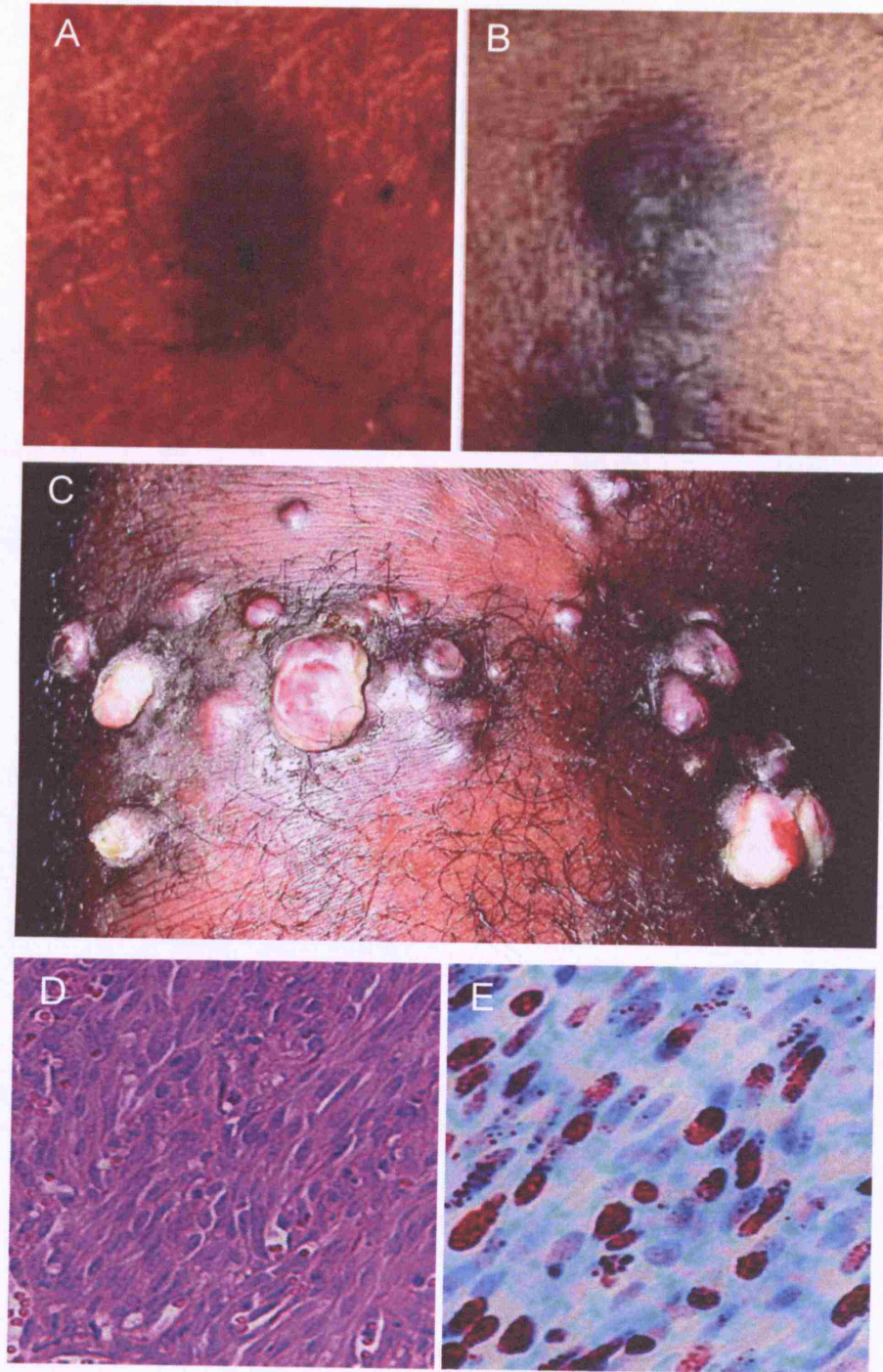


Figure 1.1. KS lesions and histology. *A*, Patch stage KS lesion. *B*, Plaque stage KS lesion. *C*, Nodular stage KS lesions. *D*, Haematoxylin and Eosin staining of a nodular KS lesion. *E*, LANA-1 staining of KS spindle cells in a nodular KS lesion. Pictures and staining from Duprez et al., 2007.

1.1.1.4 Clonality

An important question regarding KS is whether individual KS lesions and the various disseminated lesions arise from the proliferation and expansion of a single KSHV-infected cell or whether KS arises from multiple cellular proliferation events. The majority of human malignancies arise from the proliferation and expansion of a single cell. The most recent and preferred technique to study the clonality of KS lesions is to examine the fusion of the terminal repeat (TR) sequences at the end of the KSHV genome, which occurs when the virus enters latency. The fused TR region has a unique size for each infected cell and its subsequent descendents. From the latest and most in depth study it was found that most KS lesions are oligoclonal and arise from several different KSHV infected cells undergoing proliferation (Duprez et al., 2007), which is in contrast to a previous study which suggests that most KS lesions are monoclonal (Rabkin et al., 1997). In addition, from the latest study, it was found that disseminated lesions in an individual never all arose from the same single KSHV-infected cell clone (Duprez et al., 2007). However, a few individual lesions were monoclonal indicating that KSHV was present before the proliferation and expansion of spindle cells supporting that KSHV has an important role in promoting the proliferation and expansion of the spindle cells (Duprez et al., 2007). It can be concluded that KS is usually an oligoclonal or polyclonal neoplasm.

1.1.1.5 Cytokines and the tumour microenvironment

The vascular and inflammatory nature of KS lesions means it has been suggested that KS lesions are cytokine driven and it is likely that cytokines play an important role in the development of KS. KS cells produce a wide range of cytokines that cause autocrine, paracrine and angiogenic effects (Ensoli et al., 1989). These cytokines include factors such as basic fibroblast growth factor (bFGF), vascular endothelial growth factor (VEGF)-A (VEGFA), human interleukin-6 (hIL6) and oncostatin M (Ensoli et al., 1989; Miles et al., 1990; Ensoli et al., 1992; Nair et al., 1992; Samaniego et al., 1995). hIL6 promotes the proliferation of KS cells (Miles et al., 1990). Both bFGF and VEGFA promote

angiogenesis and also enhances the proliferation of KS cells (Ensoli et al., 1992). KSHV itself directly contributes to the cytokine environment by encoding genes with cytokine activity. These include genes such as the viral macrophage inflammatory proteins which are likely to contribute to the angiogenesis and the inflammatory infiltrate seen in KS (Boshoff et al., 1997).

The more aggressive nature of AIDS-KS compared to other forms of KS has led to speculation that HIV may play a further role in KS than only causing severe immunosuppression in patients. Extracellular HIV Tat, which is produced from acute HIV infection of T cells, can promote the growth of KS cells and induce angiogenesis (Ensoli et al., 1993; Albin et al., 1996). Tat can also enhance KSHV infection of endothelial cells (Aoki and Tosato, 2004).

1.1.1.6 Epidemiology and transmission

The epidemiology of KSHV is complex and many studies using a wide variety of serologic assays have been performed. A comprehensive review of the latest KSHV epidemiology is presented by Jeffrey Martin (Martin, 2007).

The worldwide seroprevalence of KSHV can be divided into three groups; non-endemic, intermediate-level endemic and high-level endemic. Firstly Northern Europe, North, Central and Southern America and Asia are non-endemic areas and have a seroprevalence of KSHV less than 10% in the general population. However, like with KS in these areas KSHV antibodies were found often in HIV positive gay men with seroprevalences over 30% (Gao et al., 1996b; Kedes et al., 1996). In the Mediterranean area, KSHV seroprevalence is generally between 10 - 25% and is an intermediate-level endemic area. Southern Italy and Sicily interestingly have particularly high KSHV seroprevalences at 24.6% and 35.0% respectively (Whitby et al., 1998). Through-out many parts of Sub-Saharan Africa and the Middle East KSHV seroprevalence ranges between 30 - 70% and are high-level endemic areas. The HIV epidemic in some of these high endemic KSHV areas has resulted in KS being the most common cancer overall in countries like Uganda and Malawi (Wabinga et al., 2000; Banda et al., 2001).

There is evidence of various routes for KSHV transmission with strong evidence for sexual transmission especially between gay men, non-sexual horizontal transmission in children, transmission through organ transplantation and transmission through injection drug use (Martin, 2007). KSHV seroprevalence was found to increase linearly with the number of male sexual partners among gay men (Martin et al., 1998). Although there is evidence for acquiring KSHV through injection drug use, the risk is low and KSHV seroprevalence among intravenous drug users is much less than in gay men (Renwick et al., 1998; Cannon et al., 2001). This is consistent with the finding that there is a low amount of KSHV DNA in the blood compared to the saliva (Pauk et al., 2000).

1.1.2 KSHV associated lymphoproliferative disorders

In addition to KS, KSHV has also been associated with two types of lymphoproliferations. These are primary effusion lymphoma (PEL) and multicentric Castleman's disease (MCD).

PEL is a post germinal centre B-cell lymphoma which usually presents as neoplastic effusions in the pleural, peritoneal or pericardial cavities but without having a significant tumour mass (Cathomas, 2003; Mate et al., 2004). PEL, lacks typical B cell markers, is positive for CD45 and unlike Burkitt's lymphoma, does not have any c-myc gene rearrangements (Nador et al., 1996; Mate et al., 2004). KSHV is present in all cases of PEL (Cesarman et al., 1995; Nador et al., 1996). PEL is a clonal malignancy and most PEL cells are positive for EBV, however, the fact that not all cases contain EBV DNA indicates that EBV is not essential for PEL formation (Fassone et al., 2000; Jenner and Boshoff, 2002). The majority of patients with PEL are HIV positive (Jenner and Boshoff, 2002). KSHV is latent in the majority of PEL cells, like in KS (Boshoff et al., 1998). Cellular and viral IL6 (vIL6) as well as other KSHV encoded genes are likely to play important roles in the pathogenesis of PEL (see Section 1.2).

MCD is an unusual polyclonal lymphoproliferation which involves multiple lymphoid organs and is more common in HIV infected individuals (Soulier et al., 1995; Du et al., 2001). KSHV has been shown to associated with a specific form

of MCD known as plasmablastic MCD (Soulier et al., 1995; Dupin et al., 2000). In plasmablastic MCD large plasmablastic cells all of which are positive for KSHV are present mostly in the mantle zone of B cell follicles (Dupin et al., 2000). These plasmablastic cells originate from naive B-cells (Du et al., 2001). hIL6 and vIL6, like in PEL, are likely to play a role in the development of plasmablastic MCD (Du et al., 2001).

1.1.3 Related herpesviruses

The main criterion for inclusion of a virus into the family of herpesviridae is the morphology of the virion. All herpesviruses contain a single copy of double stranded DNA present in an icosahedral capsid surrounded by tegument which itself is surrounded by a lipid envelope (Davison, 2007). All herpesviruses are classified within three subgroups *Alphaherpesvirinae*, *Betaherpesvirinae* and *Gammaherpesvirinae* based on biological properties and more recently genomic attributes (McGeoch et al., 2000). In general *Alphaherpesvirinae* show latency in neurons, *Betaherpesvirinae* show latency in the monocyte lineage and *Gammaherpesvirinae* show latency in lymphocytes. The *Gammaherpesvirinae* has two genera *Lymphocryptovirus* and *Rhadinovirus*.

KSHV is a gammaherpesvirus part of the *Rhadinovirus* genus and is the eighth human herpesvirus to be discovered. KSHV is closely related to rhadinoviruses discovered in old world primates and KSHV is most closely related to panrhadinovirus 1a (PanRHV1a) and gorilla rhadinoherpesvirus 1 (GorRHV1) (Fig. 1.2). Some of these old world primate herpesviruses may prove useful to investigate KSHV. Currently the best and most investigated old world primate *Rhadinovirus* herpesvirus is the rhesus monkey rhadinovirus (RRV). In the presence of simian immunodeficiency virus RRV can cause the development of an arteriopathy which is similar to what is seen in KS lesions (Mansfield et al., 1999).

Another *Rhadinovirus* closely related to KSHV is the murine herpesvirus 68 (MHV68). This gammaherpesvirus infects murid rodents and can cause lymphoproliferative disease, lymphomas and in certain conditions vascular

disease (Sunil-Chandra et al., 1994; Weck et al., 1997). MHV68 has been used as a mouse model to study and investigate KSHV. EBV (*Lymphocryptovirus* genera) is the most closely related human herpesvirus to KSHV, as KSHV is the only human rhadinovirus. EBV infects and establishes latency in B-cells and EBV infection is associated with various diseases such as Burkett's lymphoma and Hodgkin's lymphoma.

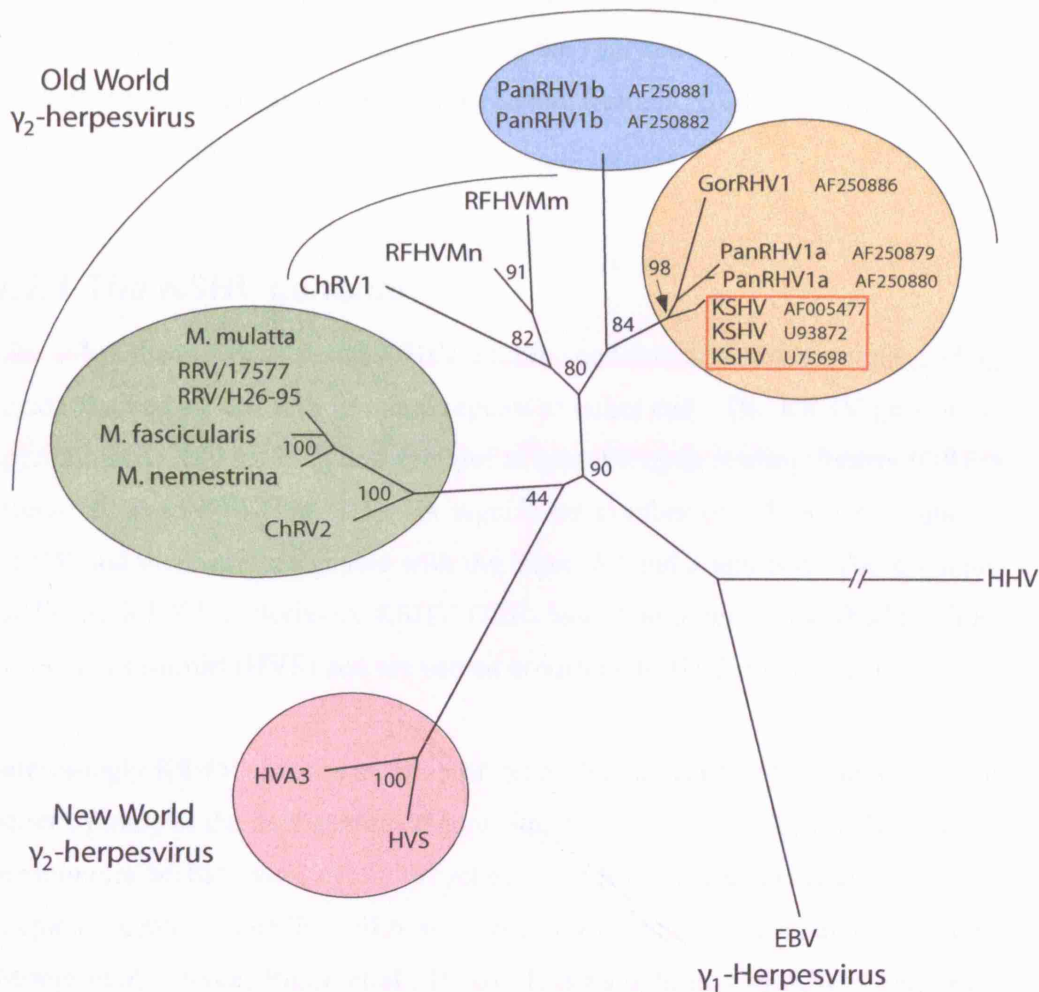


Figure 1.2. Phylogenetic tree of primate herpesviruses closely related to KSHV. The analysis was performed using the amino acid sequence of a particular 151 amino acid fragment of the herpesvirinae DNA polymerase gene. The relative evolutionary distance between herpesvirinae is shown by the branch lengths. The numbers on the tree indicate the number of times (as a percentage) out of a 100 replicates of analysis that the particular branch appeared. GenBank accession numbers are shown. ChRV, Chlorocebus rhadinovirus; EBV, Epstein-Barr virus; GorRHV1, gorilla rhadinovirus 1; HVA3, ateline herpesvirus 3; HVS, herpesvirus saimiri. PanRHV, panrhadinovirus; RFHVMm, retroperitoneal fibromatosis-associated herpesvirus of rhesus macaques; RFHVMn, retroperitoneal fibromatosis-associated herpesvirus-Macaca nemestrina; RRV, rhesus monkey rhadinovirus. Adapted from (Lacoste et al., 2000).

1.2 KSHV molecular virology

KSHV infection is now well established as a necessary factor for the development of KS. Key to understanding the role and contribution of KSHV to KS is through the genes and epigenetic factors (microRNAs) it encodes and how these interact with factors in the host.

1.2.1 The KSHV genome

Like other rhadinoviruses, the KSHV genome consists of a single unique coding region flanked by GC rich terminal repeats at either end. The KSHV genome is approximately 140 kb long and encodes at least 90 open reading frames (ORFs) (Russo et al., 1996) (Fig. 1.3). A significant number of ORFs are unique to KSHV and these are designated with the letter 'K' and a number. These unique ORFs are K1-K15. Sixty-six KSHV ORFs have homology to the rhadinovirus, herpesvirus saimiri (HVS) and are named according to HVS nomenclature.

Interestingly KSHV encodes an array of genes that appear to be acquired through genetic piracy of the host genome (Moore and Chang, 1998). These cellular gene homologues include viral cyclin (vcyclin), viral Bcl-2 (vBcl-2), viral G-protein-coupled receptor (vGPCR), vIL6 and various viral interferon regulatory factors (Moore et al., 1996a; Russo et al., 1996). It is thought that by KSHV acquiring these cellular genes it enables KSHV to hijack cellular processes (Moore and Chang, 1998). These cellular homologues are likely to play important roles in KSHV pathogenesis (Neipel et al., 1997b). KSHV encoded genes also have critical roles in viral replication, propagation and the establishment of latent infection.

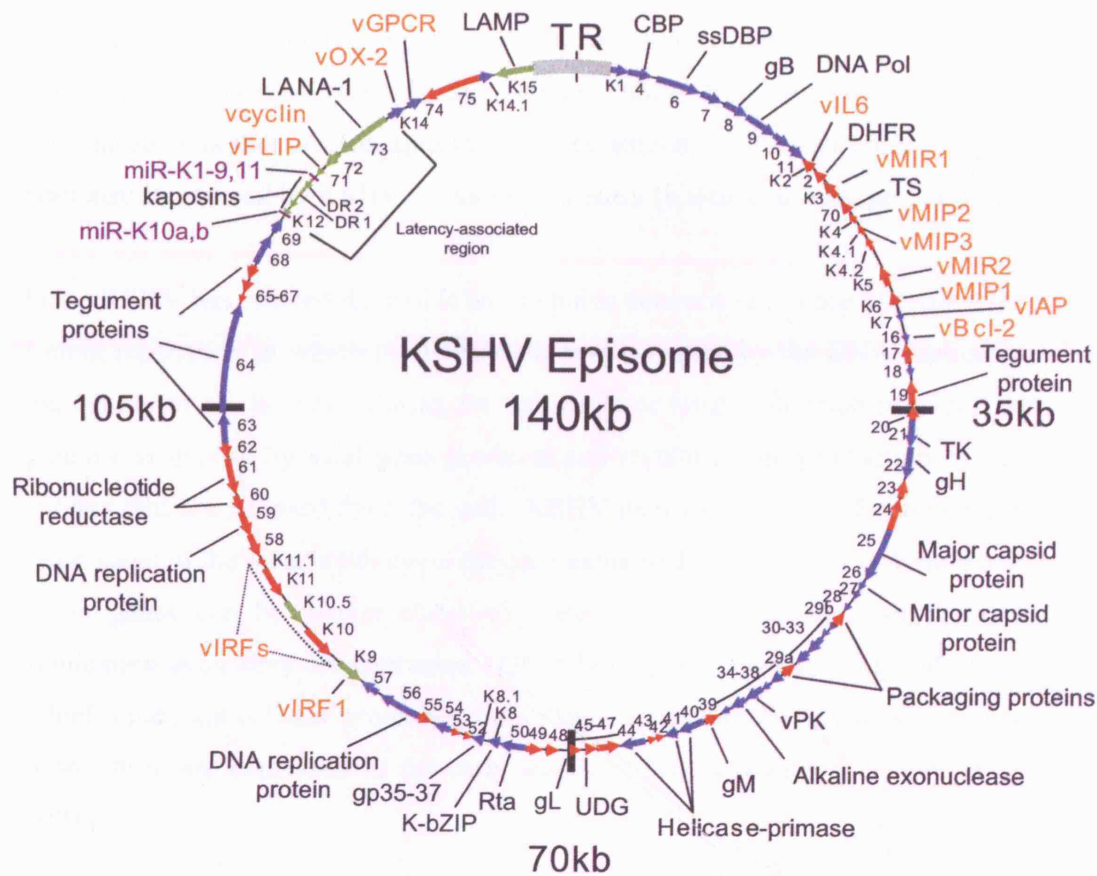


Figure 1.3. The KSHV genome as a viral episome. The KSHV-encoded ORFs are shown as numbers on the inside of the episome with those ORFs unique to KSHV being designated K1 to K15. Green arrows indicate ORFs expressed during latency, blue arrows indicate ORFs encoded in a 5' to 3' positive polarity, red arrows indicate ORFs encoded in a 3' to 5' negative polarity. KSHV encoded miRNAs are shown in purple and cellular homologues are labelled in orange. TR, terminal repeat; CBP, complement binding protein; ssDBP, single-stranded DNA binding protein; gB, glycoprotein B; DNA Pol, DNA polymerase; vIL6, viral interleukin-6; DHFR, dihydrofolate reductase; vMIR, viral modulators of immune responses; TS, thymidylate synthase; vMIP, viral macrophage inflammatory protein; vIAP, viral inhibitor-of-apoptosis protein; vBcl-2, viral Bcl-2; TK, thymidine kinase; gH, glycoprotein H; vPK, viral protein kinase; gM, glycoprotein M; UDG, uracil DNA glucosidase; gL, glycoprotein L; gp35-37, glycoprotein 35-37; vIRF, viral interferon regulatory factor; vFLIP, viral Fas-associated death domain interleukin-1 β -converting enzyme inhibitory protein; vcyclin, viral cyclin; LANA-1, latent nuclear antigen; vOX-2, viral OX-2; vGPCR, viral G-protein-coupled receptor; LAMP, latency-associated membrane protein. Adapted from Sharp and Boshoff, 2000.

1.2.2 Latent and lytic replication

KSHV *in vivo* can be detected in B- and endothelial cell lineages and *in vitro* KSHV can infect a wide variety of cell types (Renne et al., 1998; Dupin et al., 1999; Bechtel et al., 2003). KSHV can enter susceptible cells through direct fusion of the virion and target cell membrane using the cystine transporter xCT as a fusion entry receptor (Kaleeba and Berger, 2006). xCT expression correlates with those cells that are susceptible to KSHV infection although other receptors may also be utilised by KSHV for target cell entry (Kaleeba and Berger, 2006).

Once KSHV has entered the cell it has a choice between two types of replication. Latent replication in which the KSHV genome is copied by the DNA replication machinery of the host cell during the cell cycle or lytic replication in which the genome is copied by viral gene products and results in the production of new virions that are released from the cell. KSHV genes are classified depending at what stage in the virus's life cycle they are expressed, either latent or lytic genes. Lytic genes can be further classified depending at which stage of the lytic replication cycle they are expressed. Often lytic genes, such as vIL6 and vBcl2, which modulate cellular processes, rather than being directly involved in virion production, are expressed in the early stages of lytic replication (Jenner et al., 2001).

The large majority of KSHV infections results in the establishment of latent replication (Bechtel et al., 2003). Here the KSHV genome is maintained as a circular episome in cells tethered to the host chromatin through the KSHV encoded latent nuclear antigen (LANA-1) (Renne et al., 1996; Ballestas et al., 1999; Cotter and Robertson, 1999). Only a small fraction of latently infected cells undergo spontaneous lytic replication (Bechtel et al., 2003). Lytic replication from latently infected cells can be stimulated by the expression of the KSHV Rta (ORF 50) or by the use of chemicals such as 12-O-tetradecanoyl phorbol-13-acetate (TPA) and sodium butyrate (Lukac et al., 1998; Yu et al., 1999).

1.2.3 Latent proteins and microRNAs

During latency only a small fraction of KSHV genes are expressed which minimises the potential viral epitopes that are presented to immune cells (Zhong et al., 1996). However, as KSHV is latent in the majority of cells it infects it is likely that these latent genes play important roles in KSHV pathogenesis and oncogenesis.

Most of the KSHV latent genes are transcribed from the latency-associated region in the KSHV genome (Fig. 1.3). These latent genes encode for LANA-1 (ORF 73), vcyclin (ORF 72), viral FLICE [Fas-associated death domain (FADD)-like interleukin-1 β -converting enzyme] inhibitory protein (vFLIP) (ORF 71) and the kaposins. Transcripts encoding these proteins are present in latent infected cells and LANA-1, vcyclin and vFLIP have been shown to be expressed in all infected cells (Li et al., 2002; Jenner and Boshoff, 2002; Pearce et al., 2005; Cai and Cullen, 2006). KSHV also encodes microRNAs (miRNAs) within the latency-associated region and these miRNAs are present within transcripts present in latency (Pearce et al., 2005; Cai and Cullen, 2006). In addition, KSHV has latent genes in other areas of the genome and these encode for: latency-associated membrane protein (LAMP) (K15), viral interferon (IFN) regulatory factor-1 (vIRF1) (K9) which is latent in KS and viral interferon regulatory factor-3 (vIRF3) (K10.5) which is latent in PEL and MCD (Cathomas, 2003).

1.2.3.1 Latent nuclear antigen (LANA-1)

LANA-1 is a large versatile protein that has a range of functions in addition to tethering the viral episome to the host chromatin. LANA-1 can bind to the tumour suppressors p53 and pRb (Friborg, Jr. et al., 1999; Radkov et al., 2000). By binding to p53, LANA-1 inhibits p53 induced apoptosis and suppresses p53 dependent transcription (Friborg, Jr. et al., 1999). By binding to pRb, LANA-1 prevents pRb binding to E2F, resulting in E2F activating genes involved in cell cycle progression (Radkov et al., 2000). LANA-1 can also activate the Wnt- β -catenin pathway (Fujimuro et al., 2003). It does this by binding to glycogen synthase kinase 3 β (GSK-3 β) and transporting it to the nucleus where GSK-3 β is

unable to phosphorylate β -catenin and therefore mark β -catenin for degradation (Boshoff, 2003; Fujimuro et al., 2003). This causes the stabilisation of β -catenin which results in the up-regulation of genes involved in cell proliferation such as cyclin D1 (Fujimuro et al., 2003). Therefore, it is likely that LANA-1 contributes to KSHV persistence and oncogenesis, which is supported by LANA-1 being able to extend the life span of endothelial cells and transform primary rat embryo cells in the presence of *Hras* (Radkov et al., 2000; Watanabe et al., 2003).

1.2.3.2 Viral cyclin (vcyclin)

The KSHV viral cyclin is a cyclin D homologue and like vFLIP is expressed at the same time as LANA-1 (Chang et al., 1996). vcyclin is able to associate and activate Cdk6 and to a lesser extent also Cdk4 (Li et al., 1997). vcyclin is a functional cyclin and is able to phosphorylate pRb and stimulates cell cycle progression (Chang et al., 1996; Swanton et al., 1997). Unlike cellular cyclins the vcyclin/Cdk6 complexes are insensitive to inhibition by CDK inhibitors such as p16 and p21 (Swanton et al., 1997). Therefore, vcyclin in KS may result in cell cycle deregulation and contribute to KSHV oncogenesis. Interestingly, vcyclin when expressed on its own in primary cells causes growth arrest and sensitises cells to apoptosis (Verschuren et al., 2002). This is prevented by the loss of p53 and illustrates that vcyclin probably needs other KSHV genes, such as LANA-1, to achieve its oncogenic potential (Verschuren et al., 2002).

1.2.3.3 Viral FLICE inhibitory protein (vFLIP)

vFLIP is a viral homologue of cellular FLIP and viral FLIPs are also present in other gammaherpesvirus (Thome et al., 1997). FLIPs are inhibitors of death receptor signalling from receptors such as FAS ligand receptors. Through their death effector domains (DEDs) they prevent the recruitment of caspase 8 to death receptor signalling complexes and therefore prevent apoptosis. vFLIP has been shown to act in this way (Djerbi et al., 1999). vFLIP can also inhibit apoptosis by activating NF- κ B (Chaudhary et al., 1999). vFLIP activates this transcription factor through its direct interaction with IKK γ which thereby results in I κ B

kinase activation and hence NF- κ B activation through the subsequent loss of I κ B protein from NF- κ B (Field et al., 2003).

1.2.3.4 Kaposins

The kaposins consist of three proteins kaposin A (kapA), kaposin B (kapB) and kaposin C (kapC) all of which are translated from a single mRNA transcript (Sadler et al., 1999). The kaposins have been shown to be latently expressed in KS lesion and in PEL derived cells (Staskus et al., 1997; Sturzl et al., 1997). KapA is encoded by the small ORF K12 and is a transmembrane protein (Kliche et al., 2001). KapB instead is encoded immediately 5' to kapA and is encoded by GC -rich tandem 23 nucleotide repeats of two types termed DR1 and DR2 (Sadler et al., 1999; McCormick and Ganem, 2005). KapC, whose function has not been investigated, is encoded by the tandem repeats of kapB and the ORF K12 of kapA and therefore contains the amino acid sequence of kapA and kapB (Sadler et al., 1999; McCormick and Ganem, 2005).

KapA can transform immortalised rodent fibroblasts causing vascular sarcomas, although the mechanism for this transformation has not been thoroughly investigated (Muralidhar et al., 1998). KapA activates extracellular signal-regulated kinase (ERK) and interacts and activates cytohesin-1 (Kliche et al., 2001). Cytohesin-1 is a guanine nucleotide exchange factor that is involved in integrin signalling and a dominant negative cytohesin-1 inhibits ERK activation (Kliche et al., 2001). In contrast, kapB acts by inhibiting the degradation of AU-rich element (ARE) containing cytokines, such as hIL6, and therefore contributes to the ability of KSHV to up-regulate an array of cytokines (McCormick and Ganem, 2005). KapB achieves this by binding and activating mitogen-activated protein kinase-associated protein kinase 2 (MK2) via a mechanism requiring p38 (McCormick and Ganem, 2005). MK2 is an inhibitor of ARE-containing mRNA degradation.

1.2.3.5 KSHV encoded microRNAs

KSHV encodes 12 latently expressed miRNAs (Pfeffer et al., 2005; Cai et al., 2005; Samols et al., 2005). 10 miRNAs are encoded in the intron between ORF 71 and K12 while 2 other miRNAs are encoded within the ORF of K12 (Fig. 1.3). miRNAs are ~22 nucleotide long non-coding RNA molecules which regulate gene expression. miRNAs regulate gene expression by binding to complementary mRNAs resulting in either the mRNA being directed for degradation or the translation of the mRNA being inhibited. The functions of the KSHV encoded miRNAs are largely unknown, although progress is being made. KSHV encoded miRNAs have been found to down regulate the expression of the anti-angiogenic factor thrombospondin-1 in 293 cells (Samols et al., 2007).

1.2.3.6 Viral interferon regulatory factor 1 (vIRF1)

vIRF1 is one of four proteins encoded by KSHV that have homology to the interferon (IFN) regulatory factor (IRF) family of transcription factors. Cellular IRFs mediate bacteria- virus- and IFN-induced signalling and play critical roles in antiviral defences (Paun and Pitha, 2007). The cellular IRFs are reviewed in Paun and Pitha, 2007. The vIRF1 protein is encoded by K9 and is a 449 amino acid protein with a DNA binding domain at its N-terminal region (Russo et al., 1996; Cunningham et al., 2003; Park et al., 2007). vIRF1 has been shown to be latently expressed in KS and in the PEL derived cell line BCBL-1 (Dittmer, 2003; Pozharskaya et al., 2004). However, vIRF1 expression is increased during lytic replication (Dittmer, 2003; Pozharskaya et al., 2004).

vIRF1 is the most studied of the KSHV encoded vIRFs; it affects a variety of factors and pathways and this is summarised in Figure 1.4. One important role of vIRF1 is preventing the host antiviral defences against KSHV by inhibiting IFN signalling. vIRF1 has been shown to inhibit the responses of type 1 IFN α and IFN β and type 2 IFN γ and inhibit the transcription of IFN α and IFN β (Zimring et al., 1998; Li et al., 1998; Lin et al., 2001). Although vIRF1 has been shown to bind to DNA, vIRF1 achieves many of its effects, such as those on IFN signalling, by binding to coactivator proteins cAMP response element binding

protein (CREB) binding protein (CBP) and p300 (Seo et al., 2000; Li et al., 2000; Lin et al., 2001; Park et al., 2007). Binding of vIRF1 to CBP/p300 prevents these coactivators from binding to transcription factors. In this way, for example, vIRF1 prevents cellular IRF3 from activating transcription of certain IFN responsive genes such as RANTES (Lin et al., 2001). Binding of vIRF1 to CBP/p300 and preventing them from associating to transcription factors can also inhibit major histocompatibility complex class I (MHC-I) expression in LEC (Lagos et al., 2007). CBP and p300 have histone acetyltransferase (HAT) activity and associate with CBP/p300-associated factor (pCAF) (Chan and La Thangue, 2001). HAT activity is important for opening up the chromatin and allowing transcription to occur. Binding of vIRF1 to p300 prevents it from associating with pCAF and inhibits p300 HAT activity and this for example inhibits the expression of certain cytokines (Li et al., 2000).

In addition to binding to CBP/p300 vIRF1 also interacts with a variety of other factors. vIRF1 can bind directly to the central region of p53 and prevent p53 dependent transcription and apoptosis (Seo et al., 2001; Nakamura et al., 2001). By interacting with ataxia telangiectasia-mutated (ATM) kinase vIRF1 also reduces the amount of p53 present in the cell (Shin et al., 2006). vIRF1 inhibits ATM kinase activity resulting in decreased p53 phosphorylated at serine 15 and therefore increased p53 ubiquitination and degradation (Shin et al., 2006). By binding to Smad3 and Smad4 vIRF1 inhibits transforming growth factor- β (TGF- β) signalling and therefore prevents TGF- β signalling from inhibiting cell proliferation (Seo et al., 2005). Also vIRF1 binds to retinoid-IFN-induced mortality-19 (GRIM19) and thereby inhibits IFN/retinoic acid-induced cell death (Seo et al., 2002). vIRF1 is able to induce malignant transformation in mouse cells supporting the ability of vIRF1 to affect factors such as p53 which are important for tumorigenesis (Gao et al., 1997; Li et al., 1998).

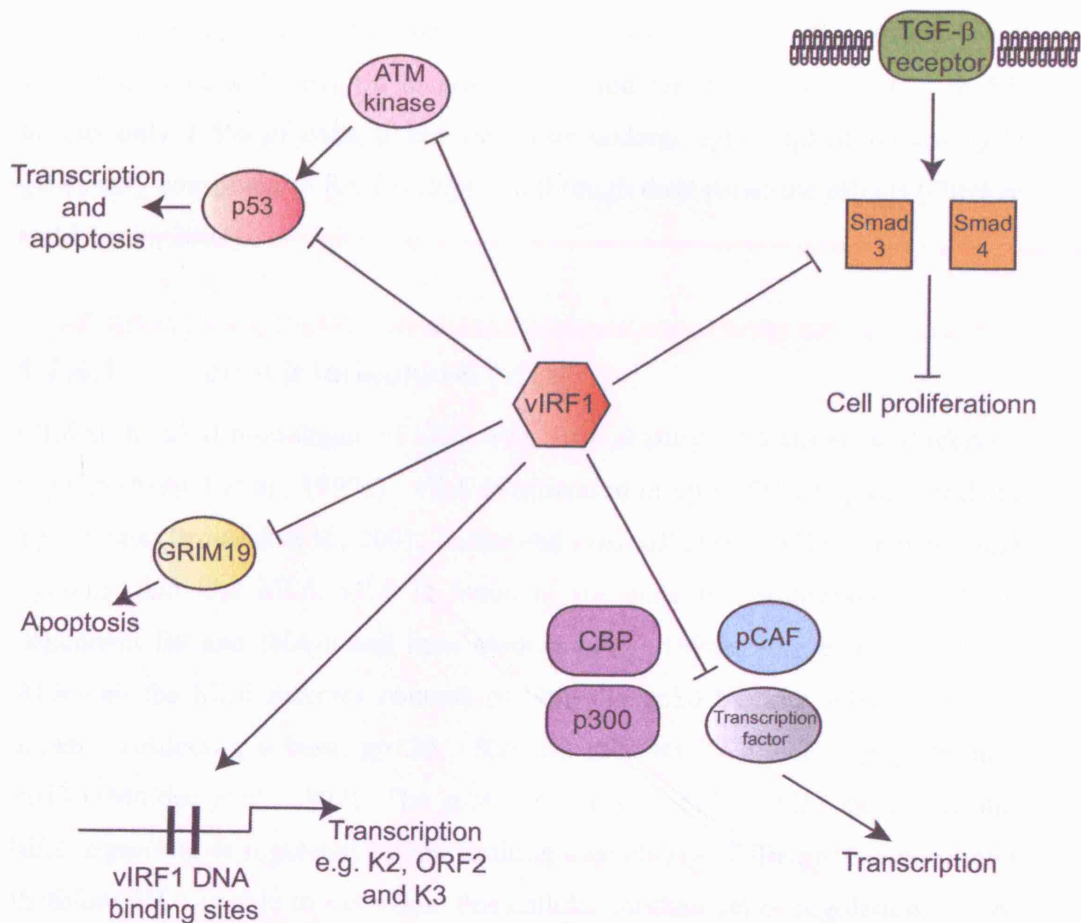


Figure 1.4. vIRF1 signalling. vIRF1 unlike cellular IRFs exerts most of its signalling by binding and inhibiting the activity of proteins such as coactivators and transcription factors. vIRF1, however, like cellular IRFs has been found also to bind directly to DNA and activate the promoter of K2, ORF2 and K3. The vIRF1 DNA binding site consensus sequence is: 5'- GCGTCnnGACGC-3' (Park et al., 2007). ATM, ataxia telangiectasia-mutated; TGF- β , transforming growth factor- β ; pCAF, CBP/p300-associated factor; CBP, cAMP response element binding protein (CREB) binding protein; GRIM19, retinoid-IFN-induced mortality-19.

1.2.4 Lytic proteins

The majority of lytic genes are involved directly with the production of new virions. However, a significant proportion of lytic genes have cellular gene homologues and are involved in modulating cellular processes to KSHV's advantage during lytic replication (Moore and Chang, 1998). These lytic genes are often expressed early on in lytic replication (Jenner et al., 2001). In KS lesions only 1-5% of cells at any one time undergo lytic replication and lytic genes may contribute to KS development through their paracrine effects (Direkze and Laman, 2004).

1.2.4.1 Viral interleukin-6 (vIL6)

vIL6 is the viral homologue of hIL6 with vIL6 sharing 25% amino acid identity to hIL6 (Neipel et al., 1997a). vIL6 is expressed in up to 5% of spindle cells in KS lesions (Brousset et al., 2001; Jenner and Boshoff, 2002). vIL6 is a functional cytokine and like hIL6, vIL6 is found to stimulate the proliferation of hIL6 dependent B9 and INA-6 cell lines (Moore et al., 1996a; Burger et al., 1998). Although the hIL6 receptor consists of both the gp80 binding subunit and the signal transducing subunit gp130, vIL6 can mediate its effects solely through gp130 (Molden et al., 1997). The gp80 subunit is needed for hIL6 signalling and hIL6 signalling is regulated by the limiting availability of the gp80 subunit and therefore vIL6 is able to overcome this cellular mechanism of regulation. vIL6, like hIL6, can activate, both Janus-activated kinase (JAK)/signal transducers and activators of transcription (STAT) signalling and the mitogen-activated protein kinase (MAPK) pathway (Molden et al., 1997; Osborne et al., 1999; Hideshima et al., 2000). vIL6 also increases hIL6 expression, further enhancing the amount of gp130 signalling (Mori et al., 2000). *In vivo*, vIL6 promotes tumour angiogenesis and increases VEGFA expression (Aoki et al., 1999).

1.2.4.2 Viral G-protein-coupled receptor (vGPCR)

vGPCR is a constitutively active G-protein-coupled receptor (GPCR), which is related to the human interleukin-8 (IL8) receptors CXCR1 and CXCR2

(Cesarman et al., 1996; Arvanitakis et al., 1997). Like vIL6, vGPCR is expressed in only a small fraction (0.5-3%) of spindle cells in late stage KS lesions (Chiou et al., 2002). Although vGPCR is a constitutively active receptor, ligands bind to vGPCR and affect vGPCR signalling; for example, IL8 and growth-related oncogene α (GRO α) activate vGPCR above its constitutive levels (Gershengorn et al., 1998; Geras-Raaka et al., 1998). vGPCR, like other G-protein coupled receptors, signals through G-proteins that comprise of an α subunit and a $\beta\gamma$ -heterodimer. When G-proteins are activated by vGPCR it results in GDP being exchanged for GTP releasing active α -subunits and $\beta\gamma$ -heterodimers which activate downstream signalling proteins. vGPCR, through its activation of a variety of α -subunits and the $\beta\gamma$ -heterodimer subunit, activates multiple pathways, (some of which may be cell specific) transcription factors and induces the expression of angiogenic and proinflammatory factors, such as VEGFA, IL8, IL2 and IL4 (Bais et al., 1998; Shepard et al., 2001; Montaner et al., 2001; Smit et al., 2002; Pati et al., 2003). The signalling pathways and factors vGPCR activate include the mitogen-activated protein /ERK kinase (MEK), c-jun-NH₂-kinase (JNK) and p38 MAPK pathways, the antiapoptotic serine-threonine kinase AKT pathway, as well as NF- κ B and nuclear factor of activated T cells (NF-AT) (Bais et al., 1998; Shepard et al., 2001; Smit et al., 2002; Cannon et al., 2003; Pati et al., 2003). vGPCR also activates the small G protein Rac1 resulting in the up-regulation of angiogenic factors such as IL8 and GRO α (Montaner et al., 2004). Angiogenic factors, such as VEGFA, are also up-regulated by vGPCR through the activation of the hypoxia inducible factor 1- α (HIF-1 α) via p38 activation (Sodhi et al., 2000).

It is not surprising with vGPCR being able to constitutively activate pathways involved in proliferation and cell survival that vGPCR is able to cause malignant transformation of mouse NIH3T3 cells (Bais et al., 1998). Transgenic mice expressing vGPCR form vascular tumours which resemble morphologically KS lesions (Yang et al., 2000; Guo et al., 2003). vGPCR also causes the immortalisation of human umbilical vein endothelial cells (HUVEC) with constitutive up-regulation of both VEGFR2 and VEGFA (Bais et al., 2003). With vGPCR being expressed in only a small percentage of cells in KS it is likely

that vGPCR through its constitutive up-regulation of angiogenic and inflammatory cytokines contributes to the tumour environment needed for KS development.

1.2.4.3 Viral macrophage inflammatory proteins (vMIPs)

KSHV encodes three viral chemokines, vMIP1 (K6), vMIP2 (K4) and vMIP3 (K4.1) that are expressed during lytic replication. These viral chemokines can attract inflammatory cells such as eosinophils, monocytes and TH2-type T cells and interact with chemokine receptors such as CCR3, CCR4 and CCR8, although each of the vMIPs have different chemokine receptor specificities (Boshoff et al., 1997; Sozzani et al., 1998; Stine et al., 2000). Interestingly, all the vMIPs induce angiogenesis in the chorioallantoic membrane (CAM) assay unlike their cellular homologues MIP-1 α and RANTES (Boshoff et al., 1997; Stine et al., 2000). vMIP1 induces VEGFA expression in PEL cell lines and, through its interaction with CCR8, can induce the chemotaxis of HUVEC (Haque et al., 2001; Liu et al., 2001). Therefore, the expression of vMIPs in KS may contribute to the angiogenesis and inflammatory infiltrate seen in KS lesions.

1.3 Tumour vasculature

Tumour vascularisation is a critical process for KS and other neoplasms as it is important for tumour growth and development. Blood vessels supply oxygen and nutrients to the tumour and act as a route for tumour metastasis and as a route for the infiltration of immune cells to the tumour. Lymphatic vessels act as a conduit for fluid extravasated from blood vessels and play important roles for tissue homeostasis, immune surveillance and tumour metastasis (Sundar and Ganesan, 2007).

1.3.1 Tumour angiogenesis

The adult vasculature originates from the initial process of vasculogenesis that occurs in the embryo. During vasculogenesis, angioblasts differentiate to form a primitive tubular network in a previously avascular tissue. This primitive tubular

network then undergoes remodelling through pruning and enlargement and maturation to form the mature vascular system (Risau, 1997). Most of the human vasculature in adults is quiescent with angiogenesis normally only occurring during the menstrual cycle in the female reproductive tissue, during wound healing or during pathological conditions such as in tumours. Tumour angiogenesis can occur through the sprouting of new blood vessels from pre-existing vessel, the intussusception of pre-existing vessels and by the recruitment of circulating endothelial cell precursors (Carmeliet and Jain, 2000).

Cells for their survival need to be within 100 to 200 μm of blood vessels and as the human vasculature is normally quiescent the induction of angiogenesis by tumours is a rate limiting step in tumour development (Carmeliet and Jain, 2000). It is thought that the normal quiescent vasculature is maintained by a balance of pro-angiogenic and anti-angiogenic factors and that this balance is pushed towards angiogenesis by tumours. This angiogenic switch by tumours can be triggered, for example, by hypoxia due to tumour size, the activation of oncogenes and inhibition / mutation of tumour suppressors (Bergers and Benjamin, 2003). KSHV regulates pathways and encodes a number of genes, such as vGPCR, which are likely to play a critical role in the angiogenesis seen in KS. Although in tumour angiogenesis there is an up-regulation of pro-angiogenic factors rather than anti-angiogenic factors, tumour angiogenesis is not as well controlled and coordinated as in physiological angiogenesis. This results that tumour vessels are leaky, fail to mature and can even have tumour cells rather than endothelial cells lining parts of the vessels (Carmeliet and Jain, 2000).

There are many pro-angiogenic factors which are regulated in tumours. Some of the most important factors for angiogenesis are VEGFA and members of the angiopoietin family which regulate vessel stabilisation (discussed in Section 1.4). VEGFA binds to the tyrosine kinase receptors VEGFR1 and VEGFR2 and stimulates endothelial cell proliferation and migration, inhibits endothelial cell apoptosis and stimulates *in vivo* angiogenesis (Connolly et al., 1989; Gerber et al., 1998; Dimmeler et al., 2000). Other pro-angiogenic factors include adrenomedullin (ADM), bFGF, epidermal growth factor (EGF) and platelet

derived growth factor (PDGF). ADM, bFGF and EGF stimulate endothelial cell proliferation and *in vivo* angiogenesis (Papetti and Herman, 2002; Nikitenko et al., 2006). Anti-angiogenic factors include angioarrestin, endostatin and thrombospondin-1 (Bergers and Benjamin, 2003). Thrombospondin-1 inhibits endothelial cell proliferation, survival and migration and inhibits tumour angiogenesis (Lawler, 2002).

1.3.2 Tumour lymphangiogenesis

Lymphatic capillaries are LEC connected together with loose junctions and have little or no basement membrane and no smooth muscles cells which normally surround blood vessels (Makinen et al., 2007). Lymphatic capillaries typically surround and follow blood vessels. LEC originate from vein endothelial cells during embryo development (Makinen et al., 2007). The critical regulator for LEC development and distinguishes LEC from BEC is the transcription factor Prox1 which is expressed in LEC. Mice which lack Prox1 fail to develop lymphatics but still develop a blood vessel system (Wigle and Oliver, 1999).

Tumours are typically characterised with large lymphatics vessel around the tumour periphery with some tumours having intratumoral lymphatics and others not (Stacker et al., 2002). The lack of intratumoral lymphatics in some tumours may be due to the pressure of the growing tumour (Padera et al., 2002). Unlike other tumours, cells of lymphatic origin are the tumour cell of KS and therefore these cells make up most of the tumour mass in KS (Wang et al., 2004a).

Factors important to lymphangiogenesis are VEGFC, VEGFD, ADM and the angiopoietins (Discussed in section 1.4). Both VEGFC and VEGFD interact with and activate VEGFR2 and VEGFR3 although both VEGFC and VEGFD mainly signal through VEGFR3 (Joukov et al., 1996; Achen et al., 1998; Adams and Alitalo, 2007). VEGFR3 is mostly expressed on LEC while VEGFR2 is expressed on both LEC and BEC. VEGFR3 activation leads to *in vivo* lymphangiogenesis and induces LEC proliferation, survival and migration (Makinen et al., 2001; Veikkola et al., 2001). ADM signalling, through

calcitonin receptor-like receptor, is important for lymphatic vasculature development and induces LEC proliferation (Fritz-Six et al., 2008).

Tumours often over-express VEGFC, and less often VEGFD, and higher levels of these factors correlate with increased lymph node metastasis (Sundar and Ganesan, 2007). VEGFC over-expression in tumours results in increased lymphangiogenesis and intratumoral lymphatics or / and increased size of the lymphatic vessels surrounding the tumours (Skobe et al., 2001; Padera et al., 2002).. In both cases, however, the increase in VEGFC expression increases tumour metastasis (Skobe et al., 2001; Padera et al., 2002).

1.4 The angiopoietins

The human angiopoietin family contains ten members all of which are secreted glycoproteins with a characteristic coiled-coil domain and a C-terminal fibrinogen-like domain (Katoh and Katoh, 2006). The classical angiopoietins are angiopoietin-1 (Ang1), angiopoietin-2 (Ang2) and angiopoietin-4 (Ang4) of which Ang1 and Ang2 are the most studied members of the angiopoietin family and have important roles in angiogenesis, lymphangiogenesis and other processes (Maisonpierre et al., 1997; Gale et al., 2002; Lee et al., 2004). The classical angiopoietins bind to Tie2, a receptor tyrosine kinase that is expressed on endothelial cells (Davis et al., 1996; Maisonpierre et al., 1997; Valenzuela et al., 1999). The other members of the angiopoietin family are the angiopoietin-like (Angptl) proteins of which there are seven (Angptl1-7). The angiopoietin-like proteins, except Angptl3, are orphan ligands with no known receptors. These protein have been shown to be involved in angiogenesis, stem cell growth and various metabolic processes (Kim et al., 1999; Oike et al., 2005; Zhang et al., 2006). A summary of the functions of the members of the angiopoietin family is shown in Table 1.1. The most relevant angiopoietins are discussed in more detail in the following sections.

Member	Other names	Expression pattern in adults	Function
Ang1	N/A	- Widely expressed although barely expressed in liver and heart	- Agonist to the Tie2 receptor - Vessel maturation and stabilisation - Chemotactic factor for endothelial cells and inhibits endothelial cell apoptosis
Ang2	N/A	- Sites of vessel remodelling e.g. female reproductive tissue	- Conditional antagonist to the Tie2 receptor - Promotes vessel destabilisation - Promotes angiogenesis in the presence of other angiogenic factors - Important for proper lymphatic development
Ang4	N/A	- Highly expressed in lung	- Agonist to the Tie2 receptor - Promotes the survival of endothelial cells, might be angiogenic
Angpt1	ARP1, Angioarrestin	- Widely expressed especially in vascularised glandular tissue e.g. thyroid glands	- Important for proper vasculature development - Anti-angiogenic factor - Inhibits endothelial cell proliferation, migration, adhesion and <i>in vitro</i> tube formation
Angpt2	ARP2, HARP	- Widely expressed especially in muscle tissue such as the heart	- Important for proper vasculature development - Promotes endothelial cell survival and sprouting - Hematopoietic stem cell growth factor
Angpt3	N/A	- Primarily expressed in the liver	- Regulates fat metabolism, hematopoietic stem cell growth factor - Angiogenic <i>in vivo</i> and promotes endothelial cell migration and adhesion - Binds to an integrin receptor
Angpt4	ARP4, FIAF, HFARP, PGAR	- Primarily expressed in liver and adipose tissue	- Regulates fat metabolism - Anti-angiogenic factor <i>in vivo</i> - Inhibits endothelial cell proliferation, migration and vessel formation
Angpt5	N/A	- Mainly expressed in the heart	- Hematopoietic stem cell growth factor
Angpt6	ARP5, AGF	- Primarily expressed in the liver	- Effects gluconeogenesis, prevents obesity and the related insulin resistance
Angpt7	CDT6, AngX	- Expressed exclusively in the cornea	- Anti-angiogenic factor <i>in vivo</i> - Hematopoietic stem cell growth factor

Table 1.1. Summary of the human angiopoietin family. All the human angiopoietin family members are shown with a summary of their expression pattern and function. The information presented in the table was obtained from references in the Introduction and the following additional references: Angpt11, (Dhanabal et al., 2002; Dhanabal et al., 2005); Angpt3, (Camenisch et al., 2002; Hattada et al., 2007; Shimamura et al., 2007); Angpt5, (Zeng et al., 2003); Angpt6, (George, 2006); Angpt7, (Peek et al., 1998; Peek et al., 2002).

1.4.1 Angiopoietin-1

Ang1 has critical roles in angiogenesis and Ang1 exerts its effects by binding and activating its receptor Tie2 (Davis et al., 1996; Suri et al., 1996; Suri et al., 1998). Tie2 knock-out mice are embryonically lethal, showing a low vascular complexity and knock-down of Tie2 expression in endothelial cells leads to apoptosis (Dumont et al., 1994; Jones et al., 2001). Similarly, Ang1 knock-out mice have an abnormal vascular network with defects in the vascular organisation and a reduction in the number of large vessels (Suri et al., 1996). Ang1 over-expressing mice have increased number, size and branching of blood vessels (Suri et al., 1998). Ang1 is thought to be important for the maturation and stabilisation of blood vessels with Ang1 affecting the junctions between endothelial cells and the recruitment of the underlying support cells of the blood vessels (Suri et al., 1996; Gamble, 2000). This results that mice over-expressing Ang1 have vessels resistant to leakage caused, for example, by inflammatory agents (Thurston et al., 1999; Mei et al., 2007).

Through Ang1 activating Akt, via Tie2, Ang1 inhibits the apoptosis of endothelial cells (Papapetropoulos et al., 2000). Activated Tie2, in addition to Akt, has been shown to activate focal adhesion kinase (FAK) and Nck both of which promote cell migration (Jones and Dumont, 2000). Ang1 is a chemotactic factor for endothelial cells (Witzenbichler et al., 1998). Activated Tie2 also activates STATs (Korpelainen et al., 1999). Whether activated Tie2 activates the MAPK pathway is uncertain (Jones and Dumont, 2000; Kanda et al., 2005).

Although Ang1 is expressed in tumours its effects are generally counteracted by a higher expression of Ang2 (Tait and Jones, 2004). Over-expression of Ang1 in tumours causes reduced tumour size and increases the number of mature vessels (Bach et al., 2007).

1.4.2 Angiopoietin-2

Both Ang1 and Ang2 bind with similar efficiencies to Tie2, however, while Ang1 acts as agonist, Ang2 often acts as antagonist resulting they can have different

roles in angiogenesis (Fig. 1.5) (Maisonpierre et al., 1997). Ang2 over-expressing mice are embryonically lethal and have a defective abnormal vascular network similar to that seen in Ang1 or Tie2 knock-out mice (Maisonpierre et al., 1997). This supports the antagonist role of Ang2. Ang2 knock-out mice demonstrate that Ang2 is critical for post-natal angiogenesis and that Ang2 is not required for normal blood vessel formation during embryonic development (Gale et al., 2002). By acting as an antagonist to the Tie2 receptor, Ang2 is thought to destabilize endothelial cells and vessels causing them to enter a more plastic state and therefore allowing them to respond to other pro-angiogenic stimuli such as VEGFA (Maisonpierre et al., 1997; Gale et al., 2002; Visconti et al., 2002; Scharpfenecker et al., 2005). Ang2 in the presence of endogenous VEGFA increases the proliferation and migration of endothelial cells *in vivo*, as well as increase vessel diameter and promote new vessel sprouting (Lobov et al., 2002; Visconti et al., 2002). While in the absence of endogenous VEGFA, Ang2 causes endothelial cell death and vessel regression (Lobov et al., 2002). In certain conditions, however, Ang2 can promote angiogenesis by acting as an agonist to the Tie2 receptor and in this way Ang2 can prevent apoptosis, stimulate endothelial cell proliferation and promote tube formation (Kim et al., 2000a; Teichert-Kuliszewska et al., 2001; Mochizuki et al., 2002; Bogdanovic et al., 2006). Ang2 acts as an agonist to Tie2 in endothelial progenitor cells (Kim et al., 2006). Whether Ang2 acts as an antagonist or agonist to Tie2 may depend on whether Tie2 is physically associated with Tie1 or not on the endothelial cell surface (Kim et al., 2006).

Ang2 also plays a critical role in lymphangiogenesis, since Ang2 knock-out mice have a defective, leaky lymphatic system (Gale et al., 2002). Interestingly, Ang2 is thought to act predominantly as an agonist to Tie2 in the lymphatic system, with Tie2 being expressed on LEC (Gale et al., 2002).

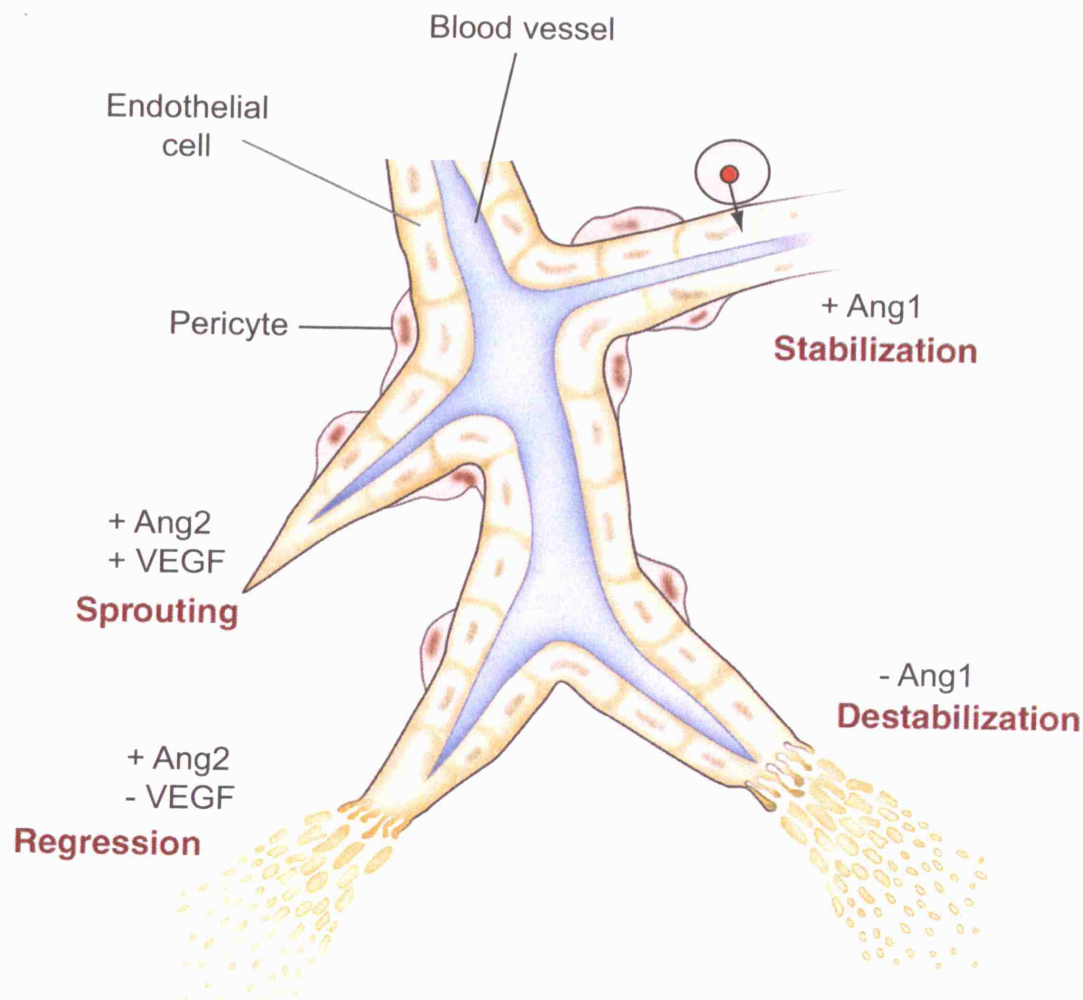


Figure 1.5. Effects of Ang1 and Ang2 on blood vessels. By acting as an agonist to Tie2, Ang1 promotes endothelial cell maturation and stabilisation. While by acting as an antagonist to Tie2 Ang2 promotes vessel destabilisation and primes vessels to other angiogenic factors. The actions of Ang1 and Ang2 are based on *in vivo* experiments. The effects of Ang2 may change in certain conditions in which it acts as an agonist to the Tie2 receptor. Adapted from Ramsauer and D'Amore, 2002.

1.4.2.1 Ang2 in tumour angiogenesis and inflammation

Relative to Ang1, Ang2 is over-expressed in a large array of tumours (Tait and Jones, 2004). Ectopic expression of Ang2 in cancer cells increases angiogenesis, thereby promoting tumour growth in experimental models (Tanaka et al., 1999; Ahmad et al., 2001; Etoh et al., 2001). Although increased Ang2 expression in certain cases inhibits tumour growth causing aberrant angiogenesis, leading to endothelial cell and tumour cell death (Yu and Stamenkovic, 2001; Cao et al., 2007). The importance of Ang2 for tumour angiogenesis is illustrated with the use of Ang2 specific inhibitors. Such inhibitors, inhibit tumour growth by directly inhibiting angiogenesis (Oliner et al., 2004; Sarraf-Yazdi et al., 2007). Increased Ang2 expression in cancer cells also increases tumour metastasis including metastasis of tumour cells to the lymph nodes (Etoh et al., 2001; Imanishi et al., 2007).

Ang2 is also involved in causing *in vivo* vascular leakage and inflammation. Ang2 destabilises interactions between endothelial cells resulting in increased vasculature permeability and Ang2 is directly involved in promoting inflammatory responses such as those induced by *Staphylococcus aureus* and tumour necrosis factor- α (TNF- α) (Roviezzo et al., 2005; Fiedler et al., 2006; Parikh et al., 2006). Therefore, Ang2 is not only involved in tumour angiogenesis, but also in tumour-associated inflammation. This is further supported by the finding that Ang2 attracts Tie2-expressing monocytes to tumours where they promote angiogenesis and affect tumour-associated inflammation (Murdoch et al., 2007; Venneri et al., 2007; Lewis et al., 2007).

1.4.2.2 Regulation of Ang2

The regulation of Ang2 in endothelial cells is affected by a wide range of factors with hypoxia, VEGFA, bFGF and TNF- α increasing Ang2 mRNA levels, while Ang1, Ang2 and TGF- β reducing Ang2 mRNA levels (Mandriota and Pepper, 1998; Kim et al., 2000c). The activation of the MAPK pathway up-regulates Ang2 expression and Ang2 expression is up-regulated by members of the Ets family of transcription factors, which are some of the effectors of the MAPK

pathway (Oh et al., 1999; Hasegawa et al., 2004; Hegen et al., 2004). While the phosphatidylinositol 3-kinase (PI3-K)/Akt pathway down regulates Ang2 expression (Tsigkos et al., 2006). Ang2 is stored in Weibel-Palade bodies in endothelial cells where it released by for example stimulation with histamine or thrombin (Fiedler et al., 2004).

1.4.3 Angiopoietin-4

Ang4 like Ang1 binds and activates the Tie2 receptor and Ang4 is significantly expressed in some cancers (Valenzuela et al., 1999; Currie et al., 2001; Nakayama et al., 2004; Nakayama et al., 2005). Ang4 leads to the phosphorylation of Akt and promotes the survival of endothelial cells (Lee et al., 2004). However, there are conflicting reports on whether Ang4 promotes angiogenesis and the migration of endothelial cells (Lee et al., 2004; Olsen et al., 2006).

1.4.4 Angiopoietin-like 2

Angptl2 which is also called angiopoietin-related protein 2 (ARP2), was first isolated from cDNA from the adult heart and found to share 34% amino acid identity to either Ang1 or Ang2 (Kim et al., 1999). Angptl2 is widely expressed in adult tissues like Ang1, although Angptl2 is highly expressed in muscle tissue such as the heart, unlike Ang1 (Maisonpierre et al., 1997; Kim et al., 1999). This is in contrast to Ang2 which is only expressed in the adult at sites of vessel remodelling such as in the female reproductive tissue. (Maisonpierre et al., 1997). Unlike Ang1 and Ang2, Angptl2 does not bind to Tie2 although data suggests that Angptl2 does bind to an unknown receptor which is present on HUVEC (Kim et al., 1999; Kubota et al., 2005). Angptl2 knock-down zebrafish are embryonically lethal due to pericardial effusion and these embryos have vascular defects which are made worse by also knocking-down Angptl1 (Kubota et al., 2005). The pro-angiogenic effects of Angptl2 are also apparent, with Angptl2 being able to induce *in vitro* endothelial cell sprouting and prevent endothelial cell apoptosis through Akt phosphorylation (Kim et al., 1999; Kubota et al.,



2005). Angptl2 also causes a transient ERK activation although it does not stimulate endothelial cell proliferation (Kim et al., 1999; Kubota et al., 2005).

Angptl2 along with Angptl3, Angptl5 and Angptl7 have been shown to promote the *in vitro* expansion of haematopoietic stem cells (Zhang et al., 2006). Findings suggest that Angptl2 is also involved in diabetic nephropathy which may be due, at least in part, to its effects on endothelial cells (Sun et al., 2007).

1.4.5 Angiopoietin-like 4

A particularly interesting angiopoietin-like protein is Angptl4. As well as regulating fat metabolism, Angptl4 is an anti-angiogenic factor which is up-regulated by hypoxia in endothelial cells (Le et al., 2003; Ito et al., 2003; Oike et al., 2005). Angptl4 inhibits *in vivo* angiogenesis and *in vitro* Angptl4 inhibits endothelial cell proliferation, migration, vessel sprouting and tube formation (Ito et al., 2003; Cazes et al., 2006). Although perhaps in certain conditions Angptl4 may act as a pro-angiogenic factor (Le et al., 2003). Over-expression of Angptl4 results in an inhibition of tumour growth and metastasis (Li et al., 2004; Galaup et al., 2006).

Angptl4 is necessary for proper lymphatic vasculature with Angptl4 knock-out mice having blood filled lymphatics and Angptl4 may regulate the expression of Prox1 in LEC (Backhed et al., 2007).

1.5 Lentiviral vectors

Primary cells are often difficult to transfect and as we move to more relevant *in vitro* and *in vivo* biological models the ability to introduce genes and other elements into primary cells or other cells difficult to transfect becomes ever more important. The use of viruses as vehicles to introduce foreign genetic materials are often employed as viruses have evolved mechanisms to enter host cells and express their genes. There are a wide variety of viral vector systems currently used one of which are retrovirus including a class of retroviruses called lentiviruses. Retroviruses are unique in their ability to efficiently integrate the

viral construct into the host genome. The adeno-associated virus only integrates in 10-20% of infected cells (Huser et al., 2002). The integration of the retroviral construct in the host cell genome results in the construct being maintained in all subsequent daughter cells unlike transient transfection.

1.5.1 Retrovirus biology

The retroviral genome is present as two identical single stranded RNA molecules packaged within the viral protein core along with other enzymes needed for replication. The viral core is surrounded by the viral envelope made up of the cellular plasma membrane and viral glycoproteins. Retroviruses generally infect cells by first binding to a cell surface receptor with the subsequent fusion of the host cell and viral membranes. This results in the release of the viral core into the host cell cytoplasm. Here through the action of a reverse transcriptase the RNA is transcribed into DNA and is transported into the nucleus where it permanently integrates into host genome (now referred to as a provirus). The viral RNA, DNA and proteins altogether are called the preintegration complex (PIC) until viral integration in the host genome occurs. The provirus replicates along with the cell cycle or gets transcribed into RNA which is translated and packaged into new virions that are released from the host cells through budding.

The genomes of all retroviruses contain *gag*, *pol* and *env* genes with long terminal repeats (LTRs) at either end of the genome. *Gag* encodes the core proteins, *pol* encodes the reverse transcriptase, integrase and protease while *env* encodes the envelope glycoprotein. Retroviruses can also encode other genes. Lentiviruses, such as HIV-1 for example, encode various accessory genes and regulatory genes, such as *tat* and *rev*. The retroviral genome is transcribed as one long RNA transcript with the viral promoter in the 5' LTR and the polyadenylation signal in the 3' LTR.

1.5.2 Lentiviral vector mediated gene delivery

Retroviral vector systems are often based on the Moloney murine leukemia virus (MoMLV) while lentiviral vector systems are mainly based on HIV-1. The

advantage of lentiviral vectors compared to retroviral vectors is that lentiviruses can infect both dividing and non-dividing cells while retroviruses can only infect dividing cells (Lewis and Emerman, 1994). This is because retroviruses need the breakdown of the nuclear envelope, which occurs during mitosis, to gain access to the cell nucleus, while lentiviruses use active nuclear transport, which is independent of cell division, to transport the PIC into the nucleus (Bukrinsky et al., 1992). Although the exact mechanism for this nuclear transport is unknown it involves the matrix protein from *gag* and the integrase protein (Bukrinsky et al., 1993; Gallay et al., 1995). This ability of lentivirus allows lentiviral vectors to be introduced into a wider range of cell types, compared to retroviral vectors, and to be delivered into slow dividing primary cells more efficiently. Lentiviral vectors can be introduced into non-proliferating macrophages and terminally differentiated neurones unlike retroviral vectors (Naldini et al., 1996).

The HIV-1 based lentiviral vector system will be discussed as this is the most common system and is used for this thesis. Lentiviral vector systems generally involve transfecting several plasmids into 293T cells to produce lentiviral virions containing the lentiviral vector (Fig. 1.6). These lentiviral virions can then be used to infect the target cells. In the target cell the lentiviral vector integrates and expresses the cloned gene but is unable to produce new lentiviral virions to infect other cells.

The very first lentiviral vectors were nearly whole HIV genomes with foreign genes and promoters cloned into these backbones (Buchschaecher, Jr. and Wong-Staal, 2000). Safer lentiviral vector systems have now been achieved. Firstly, the accessory virulence genes of HIV-1 (*nef*, *vif*, *vpr* and *vpu*) which are not necessary for virus production have been removed (Zufferey et al., 1997). As lentiviruses transcribe their genome as a single RNA transcript, lentiviral vector systems distribute the various HIV-1 genome components between at least three different plasmids as is shown for the pSIN-MCS lentiviral vector system (Fig 1.6) (Naldini et al., 1996; Dull et al., 1998). These different plasmids are: the lentiviral vector containing plasmid, which is the only plasmid whose RNA is packaged into the lentiviral virions, the one or more packaging plasmids encoding the *gag*, *pol*, *rev* and *tat* genes, and the envelope plasmid containing the *env* gene.

All these plasmids are transfected together into cells to produce lentiviruses. By distributing the lentiviral genome between several different plasmids it minimises the possibility of generating replication competent lentiviruses (RCL).

The lentiviral vector itself contains no HIV-1 genes. However, in addition to the cloned foreign gene and promoter the lentiviral vector has other necessary *cis*-acting elements (Fig. 1.6). Importantly the lentiviral vector has the packaging signal which is required for packaging the lentiviral vector RNA into the lentiviral virions. For self inactivating (SIN) lentiviral vectors the 3'LTR is mutated so that once the lentiviral vector is integrated into the target cell there is a loss of LTR-directed transcription of the integrated lentiviral vector (Miyoshi et al., 1998; Zufferey et al., 1998) (Fig. 1.6). This minimises transcriptional interference of the internal promoter for transgene expression and minimises the risk of producing RCL.

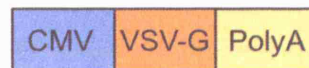
The *rev* gene is present in the packaging plasmid, in addition to the *gag* and *pol* genes, as *rev* is a post-transcriptional regulator of gene expression allowing for efficient expression of the lentiviral vector (Coffin et al., 1997; Trono, 2000). Rev by binding to the Rev response element (RRE) promotes the export of the lentiviral vector mRNA from the nucleus to the cytoplasm where the lentiviral vector can be packaged into virions (Coffin et al., 1997). The *tat* gene, which is not always present in lentiviral vector systems, is a strong activator of LTR-directed transcription causing efficient transcription of the lentiviral vector (Coffin et al., 1997; Kim and Sharp, 2001). In lentiviral vector systems which lack *tat* a constitutive promoter, such as the cytomegalovirus (CMV) promoter, is inserted into the 5'LTR to promote the transcription of the lentiviral vector (Dull et al., 1998). The HIV *env* gene is normally replaced with a different envelope glycoprotein gene in lentiviral vector systems. This is often the vesicular stomatitis virus glycoprotein (VSV-G) gene. VSV-G allows lentiviruses to infect a wide range of cell types although the receptor which VSV-G binds to on the cell surface is unknown (Coil and Miller, 2004). VSV-G increases the stability of the lentiviruses resulting in higher viral titres and being able to concentrate viral preparations by centrifugation (Burns et al., 1993).

Retroviral vector systems are similar to lentiviral vector systems except packaging cell lines are often used. These packaging cell lines have constitutive expression of the *gag*, *pol* and *env* genes and only the retroviral vector itself has to be transfected into these cells to produce retroviral virions.

pSIN-MCS with a gene of interest (Lentiviral vector)



pMD.G (Envelope plasmid)



pCMV-8.91 (Packaging plasmid)

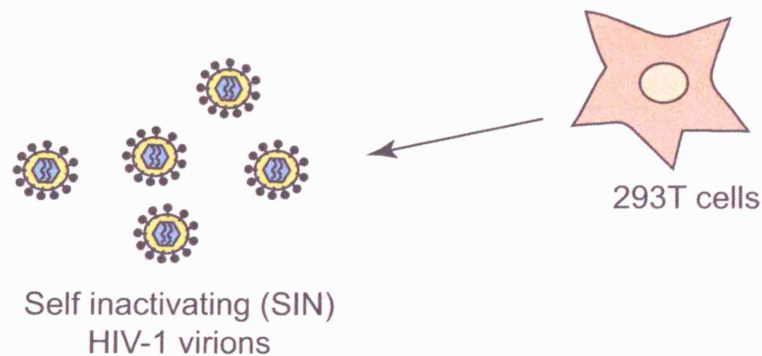
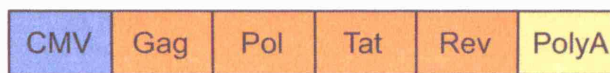


Figure 1.6. The pSIN-MCS lentiviral vector system. The pSIN-MCS lentiviral vector along with the envelope and packaging plasmids are transfected simultaneously into 293T cells. After 48 hours the media of the 293T cells is harvested. This harvested media contains self inactivating HIV-1 virions with RNA encoding the lentiviral part of the pSIN-MCS construct packaged inside and these virions can be used to infect target cells. The cloned gene in the pSIN-MCS construct is under the control of the spleen focus forming virus promoter (SFFV). The woodchuck hepatitis virus post-transcriptional regulatory element (WPRE) is present in the pSIN-MCS construct to increase the levels of expression of the cloned gene by increasing mRNA stability. Each long terminal repeat (LTR) consists of three regions named U3, R and U5. The U3 region in the 3' LTR is mutated in the pSIN-MCS construct causing the production of self inactivating lentiviruses. The central polypurine tract (cPPT) is needed for the synthesis of the plus strand of lentiviral DNA during the synthesis of lentiviral DNA from RNA. ψ , packaging signal; RRE rev-response element; CMV, cytomegalovirus promoter; VSV-G, vesicular stomatitis virus glycoprotein; PolyA, polyadenylation signal.

1.5.3 Biosafety of lentiviral vectors

Due to the various safety modifications that have been made to lentiviral vector systems the latest generation of lentiviral vector systems are handled in containment level 2 laboratories.

The main concern when working with lentiviruses is the generation of RCL. However, this is minimised by separating the components necessary for virion production on several different constructs and ensuring that sequences between the constructs are different from each other to prevent recombination. Despite this some low level recombination does occur between the *gag* gene and the lentiviral vector but no RCL have yet been associated with lentiviral vectors (Sastry et al., 2003; Sinn et al., 2005). It is still unknown, however, whether recombination could occur with other viruses that are present in the lentivirus producing cells (due to, for example, contamination) or with endogenous retroviral sequences, although this is unlikely (Buchsacher, Jr. and Wong-Staal, 2000).

1.6 Aims of this thesis

The aim of this work was to investigate the mechanisms by which KSHV modulates angiogenesis in KS lesions. For this investigation a selected KSHV lentiviral library was developed to enable individual KSHV gene expression in LEC. The regulation by KSHV of the angiogenesis associated factors Ang2 and Angptl2 was studied along with an initial investigation of the biological consequences of this regulation.

Chapter 2. Materials and Methods

2.1 Cell culture

2.1.1 Primary lymphatic endothelial cells

Primary LEC were obtained from TCS Cellworks. The LEC identity of these cells was confirmed by GEM profiling and staining cells with endothelial (CD31, von Willebrand factor and VCAM) and lymphatic markers (PROX-1) as described in Lagos et al., 2007. LEC were cultured on fibronectin (Marathon) coated flasks or wells in Endothelial Cell Growth Medium MV (PromoCell) supplemented with 10 ng/ml of VEGFC (R&D systems). Surfaces were coated with fibronectin by incubation with 1-5 $\mu\text{g}/\text{cm}^2$ of fibronectin in phosphate buffered saline (PBS) for 1 hour at room temperature after which the fibronectin was removed and the surfaces were washed with PBS. Media was changed every 1-2 days. LEC were supplied at passage 0 and were expanded before being used for experiments. LEC were used for experiments at passage 5 to 8.

LEC were split typically 1 in 3 when the cultures were 70-80% confluent. LEC were washed with PBS and incubated in 0.05% trypsin-ETDA (Invitrogen) diluted 1 in 5 in PBS for 5 min at 37°C. An equal volume of LEC media was then added and trypsin was removed by centrifugation at 1200 rpm for 5 min. LEC were resuspended in LEC media and seeded at a density of about 5×10^5 cells per T75 flask. All cell types cultured were counted using a haematocytometer before seeding.

The following procedure was used to cryogenically store all cell types used including LEC. Live cell pellets were resuspended in foetal bovine serum (FBS) with 10% dimethyl sulphoxide (DMSO). The cell suspension was aliquoted into cryotubes, which were placed at -80°C overnight insulated in paper towels to slow the freezing process. The next day the cryotubes were transferred into liquid nitrogen for long term storage.

Frozen LEC were recovered by placing the frozen cryotube into a 37°C water bath until thawed. The thawed cell suspension was placed into a T75 flask containing 10 ml of LEC media. 5 to 6 hours later the media was removed and 10 ml of fresh LEC media was added. The next day the media was changed and the LEC were cultured as normal.

Supernatants (conditioned media) from LEC, KSHV-infected LEC (KLEC) or lentiviral infected LEC were obtained by incubating cells for 24 to 48 hours with LEC media (overnight for LEC media with only 0.5% FBS and no other supplements) and passing the media through a 0.1µm filter to remove any cell debris and KSHV virions. The filtered supernatant was either added to LEC or stored at -80°C for later use.

2.1.2 Transformed mesenchymal stem cells

Mesenchymal stem cells (MSC) isolated from bone marrow were previously transformed using retroviruses to introduce the catalytic subunit of human telomerase (hTERT), E6 and E7 from human papillomavirus type 16 (HPV-16), simian virus 40 (SV40) small T antigen (ST) and H-Ras^{V12} (Funes et al., 2007). These transformed mesenchymal stem cells (tMSC) were cultured in 10 cm tissue culture plates in Mesencult medium with 10% human serum (StemCell Technologies) supplemented with 1 ng/ml of bFGF (R&D systems). tMSC were split every 2-3 days keeping cells sub-confluent at all times. tMSC were split 1 in 12 seeding about 1.3×10^5 cells in each 10 cm plate containing 8 ml of media. tMSC were split in the same way as LEC using undiluted 0.05% trypsin-ETDA. Cell lines, such tMSC, were routinely given to Mycoplasma Experience for mycoplasma testing.

tMSC were recovered from a frozen state by placing the frozen cryotube into a 37°C water bath until thawed. The thawed cell suspension was placed into 3 ml of tMSC media and spun at 1200 rpm for 5 min. The supernatant was poured off and the cell pellet was resuspended in tMSC media and placed into a 10 cm plate containing tMSC media. The tMSC were then cultured as normal.

2.1.3 293T cells

293T cells were cultured in Dulbecco's modified Eagle medium (DMEM) (Invitrogen), containing 10% FBS (Sigma), 100 units/ml penicillin G and 100 µg/ml streptomycin (Invitrogen). 293T cells were split 1 in 8 every 2 days seeding about 1×10^6 cells in a 10 cm plate with 10 ml of media. 293T cells were thawed in the same way as tMSC.

2.1.4 LinX cells

For retrovirus production the LinX packaging cell line (David Beach, Institute for Cell and Molecular Sciences, London, U.K.) was used. This is a 293 cell line containing the *gag pol* and *env* genes needed for retrovirus production. LinX cells were cultured in the same way as 293T cells.

2.1.5 PEL derived cell lines

BC-3 cells (KSHV-positive, EBV-negative cell line) and BCBL-1 cells containing a green fluorescent protein (GFP)-expressing KSHV (EBV-negative cell line) (Vieira et al., 2001) were grown in suspension in RPMI 164 medium (Invitrogen) containing 10% FBS. BCBL-1 cells in addition had 400 ng/ml of geneticin (Invitrogen) added to their media. Cells were normally grown in T75 flasks in 25ml of media at densities in the range of $2.5-6 \times 10^5$ cells / ml. Cells were split 1 in 5 every 2 to 3 days by transferring a proportion of the suspension culture into fresh media. Cells were thawed according to the tMSC protocol.

2.1.6 Cell culture conditions

Cells were normally grown at 37°C, 5% CO₂ in a humid atmosphere. cDNA of HUVEC grown in hypoxia and the control cDNA of HUVEC grown at the same time in normoxia was provided by Leonid Nikitenko [Cancer Research UK (CR-UK) Viral Oncology Group]. For this experiment HUVEC were incubated for 16

hours in either normoxia or hypoxia (0.1% O₂). A Napco 7001 incubator (Precision Scientific) was used to generate the hypoxic conditions.

2.2 Transfection and virus production and infection

2.2.1 DNA transfection of 293T cells

Transfections of 293T cells were performed with FuGENE (Roche) according to the manufacturer's protocol. FuGENE is a lipid-based transfection reagent and although the amount and composition of DNA varied between the different transfections performed the overall procedure carried out was the same. Whether a well was from a 12 well or 6 well plate or 10 cm plate was transfected the following procedure was used. The DNA to be transfected, which was present in double distilled water (ddH₂O), was placed into a 1.5 ml Eppendorf tube and the total volume in the tube was made up to 50 µl with serum free OPTI-MEM (Invitrogen). To another tube FuGENE was added to OPTI-MEM to give a total volume of 50 µl and this was incubated at room temperature for 5 min. The volume of FuGENE in microlitres added to the OPTI-MEM was 3× that of the amount of DNA in micrograms that was being transfected. The FuGENE mix was added to the DNA mix to give a total volume of 100 µl and was incubated at room temperature for 15-30 min. The 100 µl FuGENE/ DNA mix was then added dropwise to the well or plate. Five or ~16 hours (overnight) after the transfection the media was changed. When more than one plate or well was transfected, FuGENE master mixes were produced and volumes were scaled up appropriately. Prior to transfection the media was changed to fresh 293T cell media. For lentivirus production prior to transfection the media was changed to serum free OPTI-MEM rather than normal 293T cell media. This was performed for lentivirus production to maximise the amount of DNA taken up by cells and was performed to increase the amount of lentiviral particles produced. After the transfection the media was changed back to normal 293T cell media. For 12 well transfections performed for luciferase assay analysis the total volume of the FuGENE mix and DNA mix was halved by reducing the amount of OPTI-MEM in each. Therefore 50µl, rather than 100µl, was added to each well in this case.

293T cells were seeded in wells or plates the day before the transfection such that they were 50-70% confluent on the day of transfection.

For retrovirus production the calcium phosphate method of transfection was used to transfect LinX cells and this is described in section 2.2.4.

2.2.2 KSHV production and infection of LEC

GFP-expressing KSHV was produced as previously described (Vieira et al., 2001). For KSHV production BCBL-1 cultures were expanded to ~2.5 litres for each batch of KSHV. Geneticin was omitted from the media during the expansion of the BCBL-1 cultures. KSHV in the BCBL-1 cells was induced into lytic replication when a cell density of $\sim 1.2 \times 10^5$ cells/ml in ~2.5 litres of fresh media was achieved. Lytic replication was induced by adding 12-O-tetradecanoyl phorbol-13-acetate (TPA) (Sigma) to the media at a concentration of 20 ng/ml. After 3-4 day of the cells being cultured with TPA the KSHV was harvested. For each batch of KSHV this involved first centrifuging the ~2.5 litre culture at 400 g for 15 min using a JLA-10.500 rotor. The supernatant containing the virus was then poured into new centrifuge tubes and spun at 12500 g for 3 hours. The supernatant was poured off and the virus pellets were all resuspended in the same 12 ml of LEC media. The LEC media containing KSHV was passed through a 0.45 μ m filter to remove cell debris and aliquoted in tubes and stored at -80°C.

To test each 12 ml batch of KSHV, 500 μ l of the KSHV preparation was used to infect 1×10^5 293T cells seeded in wells of a 6 well plate in a total volume of 2 ml. The KSHV preparation was added to cells while they were still in suspension. Three days after adding the virus the cells were detached from the plate and resuspended in PBS and were subjected to flow cytometry using a FACSCalibur flow cytometer (BD Biosciences). KSHV batches were used to infect LEC if over 20% of 293T cells expressed GFP.

For KSHV infection of LEC, normally 1×10^5 LEC in 500 μ l of LEC media were seeded in wells of a six well plate. 2 ml of KSHV preparation was added to each well while the seeded LEC were still in suspension. The cells were incubated with the KSHV preparation overnight after which the media was changed. KSHV infections involving smaller wells were performed in a similar way with the amount of virus preparation added to the cells and total volume being decreased appropriately. Infections typically resulted in about 35% of LEC expressing GFP 3 to 4 days post-infection (p.i.). GFP expression in KSHV-infected cells was assessed by fluorescent microscopy using an Axiovert 100 fluorescent microscope (Carl Zeiss) and by flow cytometry using a FACSCalibur flow cytometer. Cells were lifted from the plates and resuspended in PBS before being subjected to flow cytometry. GFP-positive KLEC were isolated by passing detached cells through the cell sorter Moflo (Dako).

2.2.3 Lentivirus production and infection of LEC and 293T cells

Vesicular stomatitis virus-G (VSV-G) envelope-pseudotyped lentiviral virions were produced by cotransfecting 2 μ g lentiviral (pSIN-MCS or pCSGW) construct, 1.5 μ g p8.91 and 1.5 μ g pMD.G [Both packaging plasmids were obtained from Andrew Godfrey (Godfrey et al., 2005)] into a 10 cm plate of \sim 70% confluent 293T cells using the FuGENE (Roche) protocol. Five hours after transfection, the media was changed, and 48 hours after transfection, the media containing the lentiviral virions was collected, passed through a 0.45 μ m filter and either aliquoted directly and stored at -80°C or was first concentrated and then stored at -80°C . Lentiviral preparations were concentrated by centrifugation for 5 hours at 48000 g using a JA-25.50 rotor. After centrifugation the supernatant was poured off and the viral pellet was resuspended in LEC media. Typically 30ml of lentiviral preparation was concentrated and the subsequent viral pellet was resuspended in 3 ml of LEC media.

Lentiviral infections were performed by incubating the desired amount of virus preparation with LEC in culture, typically 1 ml per 1×10^5 LEC, for 5 hours after which the media was changed. The extent of infection and titration of the lentiviral preparations was determined by performing quantitative PCR (qPCR) 2

-3 days after infection. The expression of the lentiviral constructs was confirmed by reverse transcriptase-PCR (RT-PCR). 293T cells were infected with lentiviral preparations in the same way as LEC. GFP expression in pCSGW-infected cells was assessed by fluorescent microscopy using an Axiovert 100 fluorescent microscope and flow cytometry using a FACSCalibur flow cytometer. Cells were lifted from the plates and resuspended in PBS before being subjected to flow cytometry.

2.2.4 Retrovirus production and infection of tMSC

Retroviruses were used to produce the empty vector tMSC cell line and the *Angptl2* over-expressing tMSC cell line (*Angptl2* tMSC cell line). The *Angptl2* ORF was cloned into the retroviral vector pWZL-hygro (David Beach, Institute for Cell and Molecular Sciences, London, U.K.).

Retroviral virions were produced by transfecting 30 µg of retroviral vector (pWZL-hygro construct) into a ~ 60% confluent 10 cm plate of LinX cells using the calcium phosphate transfection method. For the calcium phosphate transfection 50 µl of 2.5 M CaCl₂ was added to 450 µl of ddH₂O containing 30 µg of plasmid DNA and was mixed. 500 µl of 2× HBS (50 mM Hepes pH 7, 1.5 mM Na₂HPO₄, 280 mM NaCl) was added dropwise to the solution while mixing. The mixture was left at room temperature for 20-30 min after which it was added dropwise to the cells. The day after the transfection the media was changed for 8 ml of fresh media and the cells were then grown at 32°C, 5% CO₂. 72 hours after transfection the retrovirus preparation was harvested by removing the media from the plates and passing it through a 0.45 µm filter. This produced ~7.5 ml of retrovirus preparation. The retrovirus preparation was then immediately used to infect tMSC.

tMSC infections were performed in 10 cm plates that were ~ 50% confluent. To infect a plate of tMSC the media from the tMSC was removed and 15 ml of retrovirus preparation containing 8 µg/ml of polybrene (Sigma) was added to the plate. The tMSC plate was then spun at 1500 rpm for 1 hour after which the cells

were placed at 32°C, 5% CO₂ overnight. The next day the media was changed and the cells were placed back at 37°C, 5% CO₂.

2.3 Molecular biology techniques

2.3.1 Plasmid preparation and purification

Plasmid DNA was prepared using Qiagen's miniprep or maxiprep according to the manufacturer's protocol. Minipreps normally yielded about 20 µg of plasmid DNA. Minipreps were mainly used during cloning to screen colonies for those containing the desired inserts. Maxipreps normally yielded about 500 µg using the 500 Qiagen-tips.

Bacteria containing the desired plasmid were first grown overnight on LB^{amp} agar [LB agar (Sigma) with 100 µg/ml ampicillin (Sigma)] plates. All the plasmids used contained ampicillin resistance. Colonies from plates were picked and inoculated into LB^{amp} [LB (Sigma) with 100 µg/ml ampicillin].

For minipreps, picked colonies were inoculated into 5 ml of LB^{amp} and incubated overnight (~16 hours) at 37°C (30°C for retroviral vectors) with vigorous shaking. The bacterial culture was then spun at 3000 rpm for 15 min using an ALC centrifuge PK120. The bacteria pellet was resuspended and lysed and neutralised through an alkaline lysis method according to Qiagen's protocol. The resulting solution was centrifuged at 13000 rpm in a desktop centrifuge so that the genomic DNA could be pelleted. The clear solution was pipetted into a miniprep column and spun at 13000 rpm in a desktop centrifuge for 1 min. The wash steps were performed according to the manufacturer's protocol. The plasmid DNA was eluted in 50 µl of ddH₂O.

For maxipreps picked colonies were inoculated into 2 ml of LB^{amp} to produce a starter culture. The starter culture was incubated at 37°C (30°C for retroviral vectors) for 8 hours with vigorous shaking. 1ml of starter culture was then added

to 500 ml of LB^{amp} and incubated with vigorous shaking at 37°C (30°C for retroviral vectors) overnight. The bacterial culture was then spun at 6000 g using a JLA-10.500 rotor. The bacteria pellet was resuspended, lysed and neutralised according to the manufacturer's protocol. The resulting solution was centrifuged twice at 20000 g using a JA-25.50 rotor to pellet the genomic DNA. The supernatant was added to an equilibrated 500 Qiagen tip (column). The subsequent wash steps and elution of the DNA was performed according to the manufacturer's instructions. The eluted DNA was precipitated using isopropanol and was washed using 70% ethanol. The final DNA pellet was resuspended in 500 µl of ddH₂O.

Plasmid DNA concentration and purity was quantified by measuring the absorbance at 260 nm and the absorbance at 260 nm / absorbance at 280 nm respectively using a NanoDrop UV spectrophotometer.

2.3.2 Restriction enzyme digestion

Restriction enzyme digestion was performed on polymerase chain reaction (PCR) products for cloning or PCR production validation and was performed on plasmid DNA for cloning and checking for the presence of a cloned insert.

Restriction enzyme digestions were performed at 37°C with 5-10 units of each enzyme used in a total volume of 15 to 25 µl. All restriction enzyme digestions used the appropriate amount of 10× restriction enzyme buffer and about 1 µg or less of DNA. The restriction enzyme buffer used was determined by consulting Promega's enzyme buffer compatibility chart and when multiple enzymes were used the most appropriate buffer was selected. The restriction enzyme digestions were normally performed for 1 to 2 hours except for PCR products containing certain restriction enzyme sites (such as *NotI*) at their ends in which case an overnight restriction enzyme digestion was performed.

After restriction enzyme digestion either an appropriate amount of 6× DNA loading buffer (Fermentas) was added and the product was electrophorised on an

agarose gel or for purified PCR products that underwent restriction enzyme digestion the digested product was then purified using the QIAquick Gel Extraction kit (Qiagen), see Section 2.3.4.

2.3.3 Agarose gel electrophoresis

To visualise or gel purify different DNA products agarose gel electrophoresis was performed. Generally 1% weight / volume (w/v) agarose (Sigma) in TAE (tris-acetate 0.4 M, ethylene diamino tetraacetic acid (EDTA) 0.01 M) gels were used except for DNA fragments under 200 bp where 2 – 4% agarose gels were used. Gels were made containing 0.04 mg/ml of ethidium bromide (Sigma). Agarose gels were electrophorised in TAE buffer at a constant voltage of 100 V. The DNA bands on the gels were visualised using a UV transilluminator and pictures were taken using the VersaDoc imaging system (Bio-Rad). Molecular weight markers [FastRuler DNA ladder middle range (Fermentas); 25 bp DNA ladder (Invitrogen)] were loaded to estimate the size of the DNA molecules.

2.3.4 Agarose gel extraction

For PCR products or digested plasmids run on an agarose gel, agarose gel extraction was performed when these DNA fragments were used for ligation or sequencing. Agarose gel extraction was performed using the QIAquick Gel Extraction kit (Qiagen). 500 µl of QG buffer was added to gel pieces (100-400 mg) containing the appropriate DNA band excised from an agarose gel. The solution was then incubated at 50°C for 10 min to dissolve the agarose gel. 100 µl of isopropanol was added and the samples were then loaded on to the QIAquick spin column and processed according to the manufacturer's protocol. The DNA was eluted from the column in 30 µl of ddH₂O.

The QIAquick Gel Extraction kit was also used to clean up PCR products which after being agarose gel purified underwent restriction enzyme digestion. After restriction enzyme digestion, 300 µl of QG buffer was added to the digested PCR product followed by 100 µl of isopropanol. The sample was then loaded on to

the QIAquick spin column and processed according to the manufacturer's protocol. The DNA was eluted from the column in 30 μ l of ddH₂O.

2.3.5 Ligation

The ligation reactions were performed in a total volume of 20 μ l using 1 μ l (20 units) of T4 DNA ligase and 2 μ l of 10 \times T4 DNA ligase buffer (New England Biolabs). Between 50 to 200 ng of vector was used along with variable amounts of insert starting off with 8 times the number of molecules of insert compared to vector. In addition, to varying the amount insert compared to vector to produce successful ligated products the length and temperature of the ligation reaction were varied. The ligation reaction was normally incubated at room temperature for an hour. However, certain ligation reactions often involving large inserts (>1.5 kb) were performed at 4°C or 16°C overnight.

Most ligation reactions involved cloning with different sticky ends at either end of the vector (and insert). This had the benefit of preventing the vector from self ligating and also allowed for directional cloning. However, in some cases the vector had to have complementary sticky ends and therefore to prevent self ligation the vector was subjected to alkaline phosphatase treatment before ligation. This was performed by adding 2 μ l (2 units) of shrimp alkaline phosphatase (Promega) along with an appropriate amount of its 10 \times buffer (Promega) to 200-1000 ng of gel purified vector restriction enzyme digestion product. The alkaline phosphatase containing mixture was incubated at 37°C for 15 min after which the mixture was heated at 65°C for 15 min. The digested vector was then used for the ligation reaction.

For cloning the K15-P PCR product generated using the *PfuTurbo* DNA polymerase (see Section 2.3.7) into the PCR-Script Amp SK(+) vector (Stratagene) blunt end ligation was performed using the PCR-Script Amp Cloning kit (Stratagene). The blunt end ligation was performed according to the manufacturer's protocol. The ligation reaction was performed in a total volume of 10 μ l with 10 ng (1 μ l) of PCR-Script Amp SK(+) vector, 1 μ l of PCR-Script

10× reaction buffer, 0.5 µl of 10 mM rATP, 4 µl of K15-P PCR product, 1 µl of *SrfI*, 1 µl of T4 DNA ligase and 1.5 µl of ddH₂O. The ligation reaction was incubated at room temperature for 1 hour and then incubated for 10 min at 65°C. 5 µl of the ligation mixture was then used for chemical bacterial transformation.

2.3.6 Bacterial transformation

Chemical transformation was generally used for bacterial transformation. However, electrical transformation was used to transform some ligation reactions and has the advantage of increased transformation efficiency. Chemical transformation was performed by placing 1-5 µl of ligation reaction or intact plasmid (~100 ng) into a vial containing 50 µl of One Shot TOP10 chemically competent *E.coli* (Invitrogen). The bacteria were then incubated on ice for 30 min and then placed in a 42°C water bath for 30 sec after which they were placed on ice. 250 µl of pre-warmed S.O.C media (Invitrogen) was then added to each vial and the bacteria were incubated at 37°C for 1 hour. 200 µl of the bacterial culture was spread or streaked across an LB^{amp} agar plate. The plates were incubated overnight at 37°C before colonies were picked.

Electrical transformation was performed by placing 20 µl of One Shot TOP10 Electrocomp *E.coli* (Invitrogen) into a chilled 1 mm electroporation cuvette (EquiBio) after which 1 µl of ligation reaction was added to the cells. Electroporation was performed using a Bio-Rad 100 electroporator set at 200 ohms, 1.25 kV and 2.5 µF. Successful electroporations had time constants between 4 and 5 ms. After electroporation 250 µl of pre-warmed S.O.C media was added to the cuvette and the bacterial culture was incubated at 37°C for 1 hour. 200 µl of the bacterial culture was then spread or streaked across an LB^{amp} agar plate. The plates were incubated overnight at 37°C before colonies were picked.

2.3.7 PCR for cloning

Most of the KSHV ORFs cloned and the *Angptl2* gene and promoter were cloned using a PCR cloning strategy (Fig. 3.2). Primers used for PCR cloning contained restriction enzyme digestion sites at their 5' ends with some junk DNA to aid restriction enzyme digestion. The primers used to clone the KSHV ORFs into the pSIN-MCS vector are shown in Table 3.3. Primers used to clone the *Angptl2* gene and promoter are displayed in Table 2.1 along with the names of the vectors used and constructs created. PCR was performed with 2 μ l each of 10 μ M forward and reverse primers, 1 μ l of 10 mM dNTPs (Invitrogen), 5 μ l *PfuTurbo* 10 \times reaction buffer (Stratagene) or 10 μ l HotStar HiFidelity 5 \times PCR Buffer (Qiagen), 1 μ l *PfuTurbo* DNA polymerase (2.5 units) (Stratagene) or 1 μ l HotStar HiFidelity DNA Polymerase (2.5 units) (Qiagen), 1 μ l of template DNA in a total volume of 50 μ l made up with ddH₂O. The typical PCR conditions used were as follows: 95°C for 2 min (or for HotStar HiFidelity DNA Polymerase 95°C for 5 min) then 40 cycles of 95°C for 1 min, 55°C for 1 min and 72°C for 1 min followed by 1 cycle of 72°C for 7 min. The different cycling conditions used for the different PCRs are shown in Table 2.1 and Table 3.3. PCR for KSHV ORFs used genomic DNA or cDNA from BC-3 cells (KSHV-positive, EBV-negative cell line) or plasmid DNA. cDNA from KLEC and genomic DNA from LEC were used to clone the *Angptl2* ORF and promoter respectively. Non-template controls were used when performing PCRs. The amplification of the correct DNA sequence was verified by running the PCR product on an agarose gel and checking its size and then sending the agarose gel extracted PCR product for sequencing.

Target cloned	Construct created	Vector used	Restriction enzymes used	Forward primer	Reverse primer	Cycling conditions for PCR	Origin of cloned DNA
<i>Angptl2</i> ORF	<i>Angptl2</i> -pWZL-hygro	pWZL-hygro	<i>EcoRI</i> / <i>SalI</i>	CCGGAATTCTGC AAGGACCATGAG GCCACTGTGCGT GAC	ACGCGTCGACTTA GTGGAAGGTGTTG GGG	35 cycles of 95°C for 1min, 57°C for 1min, 72°C for 2min	KLEC cDNA
First 1kb of the <i>Angptl2</i> promoter with 395bp of the first exon	pGL3-1kb- <i>Angptl2</i>	pGL3-basic	<i>MluI</i> / <i>XhoI</i>	CGACGGGTGCTG CCAGTGCTGACG TGTC	CCGCTCGAGAGCG GGGCAGCCTGTCC ATG	35 cycles of 95°C for 1min, 57°C for 1min, 72°C for 2min	LEC genomic DNA
First 500bp of the <i>Angptl2</i> promoter with 395bp of the first exon	pGL3-500bp- <i>Angptl2</i>	pGL3-basic	<i>MluI</i> / <i>XhoI</i>	CGACGGTTAAG CCACTGCCCTCCT GCTAAC	CCGCTCGAGAGCG GGGCAGCCTGTCC ATG	35 cycles of 95°C for 1min, 57°C for 1min, 72°C for 1min	LEC genomic DNA
First 319bp of the <i>Angptl2</i> promoter with 395bp of the first exon	pGL3-319bp- <i>Angptl2</i>	pGL3-basic	<i>MluI</i> / <i>XhoI</i>	CGACGGTAGTG CCCAACGAGGCA TCCAG	CCGCTCGAGAGCG GGGCAGCCTGTCC ATG	35 cycles of 95°C for 1min, 57°C for 1min, 72°C for 1min	LEC genomic DNA

Table 2.1. *Angptl2* ORF and promoter cloning details. The pWZL-hygro vector was supplied by David Beach at the Institute for Cell and Molecular Sciences, London, U.K. The pGL3-basic vector was obtained from Promega. Purple, junk DNA; green, restriction enzyme digestion site used for cloning.

2.3.8 Site directed mutagenesis

Site directed mutagenesis was performed using the QuikChange Site-Directed Mutagenesis Kit (Stratagene) to mutate the CREB2 binding site in the *Angptl2* promoter. The primers used are: 5'-CTGGGGCCGGAGCTCGTTCCTACACACCGGGCGGCCCGCC-3' and 5'-GGCGGGCCCGCCGGTGTGTAGGAACGAGCTCCGGCCCCAG-3'. Both primers are complementary to each other with the mutated sequence in the middle (shown underlined) surrounded by unchanged *Angptl2* promoter sequence. Firstly, the mutated plasmid DNA is generated by performing PCR using the high fidelity *PfuTurbo* DNA polymerase according to manufacturer's instructions. The PCR was performed with 125 ng of each of the primers and using 50 or 10 ng of pGL3-1kb-Angptl2 plasmid which contains the first 1 kb of the *Angptl2* promoter. The PCR conditions used were as follows: 95°C for 30 sec followed by 18 cycles of 95°C for 30 sec, 55°C for 1 min and 68°C for 7 min.

After the PCR, the non-mutated parent plasmid DNA in the PCR mixture was digested by incubating the PCR reaction mixture for 1 hour at 37°C with 1 µl of *DpnI* (10 units). After digestion with *DpnI*, 5 µl of the reaction was used for chemical bacterial transformation. The next day colonies were picked and minipreps were performed. The plasmids obtained were sent for sequencing, to check for the presence of the mutation, and run on an agarose gel, to check for any recombination.

2.3.9 Genomic DNA extraction

Genomic DNA was extracted from LEC, 293T cells and BC-3 cells using the QIAamp DNA Mini Kit (Qiagen). Cell pellets, containing approximately 1×10^5 cells, stored at -80°C were resuspended in 200 µl of PBS. To lyse the cells and release the genomic DNA 20 µl of Protease K followed by 200 µl of buffer AL were added to the cells and were mixed by pulse-vortexing. The samples were then incubated at 56°C for 10 min. 200 µl of ethanol was then added to each sample and again the samples were mixed by pulse vortexing. The samples were then loaded on to a QIAamp spin column and spun at 13000 rpm on a desktop

centrifuge for 1 min. The columns were washed according to the manufacturer's protocol and the genomic DNA was eluted in 80 μ l of buffer AE (10 mM Tris-Cl, 0.5 mM EDTA, pH 9). The DNA concentrations of the samples were then measured using the NanoDrop UV spectrophotometer.

2.3.10 Quantitative PCR (qPCR) for the quantification of lentiviral infections

To determine the number of lentiviral copies per cell (c/c) qPCR was performed for the *glyceraldehyde 3-phosphate dehydrogenase (GAPDH)* gene and the lentiviral packaging signal. Genomic DNA (2-3 days p.i.) was extracted as described in Section 2.3.9. *GAPDH* primers and probes and their concentrations used for qPCR were previously described (Bourboulia et al., 2004). The *GAPDH* primers and probes and their concentrations used for qPCR were as follows: forward primer 5'-GGAGTCAACGGATTTGGTCGTA-3', 0.7 μ M; reverse primer 5'-GGCAACAATATCCACTTTACCAGAGT-3', 0.7 μ M; the TaqMan probe 5'-FAM-CGCCTGGTCACCAGGGCTGC-3' TAMRA, 0.15 μ M. Primers and probes for the lentiviral packaging signal were designed using the Primer Express software (Applied Biosystems). The primers for the lentiviral packaging signal and their concentrations used in qPCR were as follows: forward primer 5'-GCACGGCAAGAGGCGA-3', 0.3 μ M; reverse primer 5'-CGCACCCATCTCTCTCCTTCTA-3', 0.3 μ M; the TaqMan probe 5'-FAM-CGGCGACTGGTGAGTACGCCAAAAT-3' TAMRA, 0.15 μ M. Real time PCR was performed using a Perkin-Elmer 7700 sequence detector (Perkin-Elmer Applied Biosystems). Reactions were performed in a total volume of 50 μ l using the Absolute QPCR ROX and dUTP mix (ABgene) and 0.01 units/ μ l AmpErase (Applied Biosystems). 10 μ l of genomic DNA at a concentration of 50-100 ng/ μ l was added to the reactions. The qPCR conditions used were as follows: 50°C for 2 min followed by 95°C for 15 min and 40 cycles of 95°C for 15 sec and 60°C for 1 min. DNA mixtures containing known number of copies of linearized pSIN-MCS plasmid and known number of copies of linearized pcDNA3.1/V5-His-TOPO *GAPDH* plasmid (Bourboulia et al., 2004) containing part of the *GAPDH* gene were used as standards. c/c were determined by adjusting the number of

lentiviral constructs present to the number of cells analyzed (using *GAPDH*). For each sample, two dilutions were run for both the lentiviral packaging signal and *GAPDH* reactions. Uninfected LEC, AE buffer and ddH₂O negative control reactions were performed for all qPCRs.

To titrate lentiviral preparations 0.8-1×10⁵ LEC were infected with set volumes of virus and 2-3 days p.i the cells were harvested for qPCR analysis. The c/c from these infections could then be used to titre the lentiviral preparations for future infections. To determine the number of integrating virions present per microlitre of virus preparation (IU/μl) the following equation was used.

$$\text{IU}/\mu\text{l} = (\text{c}/\text{c} \times \text{number of cells present during infection}) / \mu\text{l of virus preparation add})$$

IU/μl can also be called infectious units per microlitre. Once the lentiviral preparation was titered it could be determined what c/c would be present when a lentiviral infection was performed.

2.3.11 RNA extraction

Total RNA from LEC or other cells were extracted using TRIzol reagent (Invitrogen) and subjected to DNase I digestion (Invitrogen). The RNA was subsequently purified using the RNEasy Mini Kit (Qiagen). When handling RNA all work surfaces and instruments were cleaned with RNaseZAP (Ambion) or autoclaved to prevent RNase contaminating RNA samples.

For the initial RNA extraction with TRIzol, cells were lysed either directly on plates or from cell pellets which were stored at -80°C. For PBS washed wells of a six well plate or for cell pellets, the cells (~1×10⁵ cells) were lysed in 1ml of TRIzol reagent. The TRIzol reagent with the cells was then transferred into a 1.5 ml Eppendorf tube if cells were from a plate. For many mRNA studies LEC were grown in 24 well plates (~1×10⁴ cells). Here cells were harvested by adding 250 μl of TRIzol reagent to each PBS washed well. The resulting lysate was then

transferred into a 1.5 ml Eppendorf tube after which 550 μ l of fresh TRIzol reagent was added to the tube to give a total volume of 800 μ l. Once the cells were lysed in TRIzol and the lysates placed in 1.5 ml Eppendorf tubes the samples were stored at -80°C until RNA extraction could be continued. The RNA was extracted according to the manufacturer's protocol. Briefly, chloroform was first added to the TRIzol sample after which the sample was mixed and centrifuged. The aqueous layer was then collected and the RNA was precipitated by the addition of isopropanol. After centrifugation the resulting RNA pellet was washed with 75% ethanol. After removing the ethanol the pellet was stored at -80°C . For samples extracted from 24 well plates due to the low number of cells 6 μ g of RNase-free glycogen (Invitrogen) was added to the aqueous layer prior to the addition of isopropanol. The glycogen acts as a carrier for the RNA and aids in precipitating the RNA from the aqueous layer.

The RNA pellet obtained using TRIzol was resuspended in 34 μ l of sterile RNase free ddH₂O (Ambion). To remove any genomic DNA contamination, DNase I digestion was performed by adding 4 μ l of 10 \times DNase I reaction buffer and 2 μ l of DNase I (2 units) to the sample. The reaction was incubated for 15 min at room temperature. The DNase I reaction was then stopped by adding 4 μ l of 25 mM EDTA. The sample volume was then made up to 100 μ l using sterile RNase free ddH₂O and the RNA was cleaned up using the RNEasy Mini Kit. To clean up the RNA 350 μ l of RLT buffer was added to the sample. After mixing, 250 μ l of ethanol was added and again the solution was mixed. The sample was then loaded onto an RNEasy mini column and the RNA was cleaned up according to the manufacturer's protocol. The RNA was eluted from the column in 28 μ l of sterile RNase free ddH₂O. The concentration and purity of the RNA was quantified by measuring the absorbance at 260 nm and the absorbance at 260 nm / absorbance at 280 nm respectively using a NanoDrop UV spectrophotometer.

2.3.12 cDNA synthesis

Between 50 to 1000 ng of RNA from samples was used for cDNA synthesis. cDNA synthesis was performed using the SuperScript II reverse transcriptase

(Invitrogen). The cDNA synthesis reaction was performed with 11 μ l of total RNA, 1 μ l of 100 μ M oligo(dT)18, 4 μ l of 5 \times first strand buffer (Invitrogen), 2 μ l of 0.1 M DTT (Invitrogen), 1 μ l of 10 mM dNTPs and 1 μ l (200 units) of SuperScript II reverse transcriptase in a total volume of 20 μ l. The cDNA synthesis reaction was incubated at 42°C for 50 min and the reaction was inactivated by subsequently heating the samples at 70°C for 15 min. The cDNA was stored at -20°C until needed.

2.3.13 Reverse transcriptase-polymerase chain reaction (RT-PCR)

RT-PCR was used to detect whether mRNA was present for particular viral or cellular genes in various cells in tissue culture. RT-PCR was performed with 1 μ l each of 10 μ M forward and reverse primers, 0.5 μ l of 10 mM dNTPs (Invitrogen), 5 μ l 10 \times PCR buffer (Qiagen), 0.2 μ l HotStarTaq DNA polymerase (1.5 units) (Qiagen), 1 μ l of cDNA in a total volume of 25 μ l made up with ddH₂O. The typical PCR conditions used were as follows: 95°C for 15 min then 25-37 cycles of 95°C for 30 sec, 55°C for 30 sec and 72°C for 30 sec followed by a single cycle of 72°C for 1min. The RT-PCR primers used are displayed in Table 2.2. The primers used were designed using Primer3 (Rozen and Skaletsky, 2000) or are previously described (Favy et al., 2000; Bourboulia et al., 2004). The sizes of the RT-PCR products were between 78 bp to 400 bp. *GAPDH* or *18S* were used as positive controls for RT-PCRs. Non-template and minus reverse transcriptase controls were performed for all RT-PCRs. Minus reverse transcriptase controls used template generated from cDNA synthesis reactions performed without the reverse transcriptase. The minus reverse transcriptase controls were used to check for any genomic DNA contamination.

ORF	Protein product	Forward primer	Reverse primer	Product size
K1		GCAACGATACTCGGCTTCTC	TGATGGTTGTCCACACAAGG	158bp
K2	vIL6	ATGGGTGATCGATGAATGCT	ATCGGCGAGCTTTTAAGG	169bp
K3	vMIR1	GAGAGCTCGAGAACGTCCAT	TTCCAGACCCTCCTGGTAAG	164bp
K4.1	vMIP3	GAGAATTCCTGTCCAGTGC	ATCTCCGTGTGCTTCTCCAT	179bp
K5	vMIR2	GGTGACCGTACTGCCATACC	CGTCACGTTCTTTGTCTCCA	158bp
K6	vMIP1	CTGCGTTAGCGTACTGCTTG	TCAGCTGCCTAACCCAGTTT	239bp
ORF28		CTGCGTCTACTGCTGCATTC	AGGGCTCCTGGGTAGCTATG	158bp
ORF33		GTCGCCGGGTCTATCTAACA	GGGGTTGGGTGGCTAGTTAT	159bp
ORF36	vPK	TGGGAGCAAGTGGACTAACC	GTGTAGCCCAACGAGGACAT	234bp
ORF45		CATGGGATGGGTTAGTCAGG	GGGTGCTGTATGGTGAAGT	177bp
ORF49		GCACGTCCCTAACTCTCCTG	AATGGTGTAGGTGGGAGCAG	177bp
ORF50	Rta	CAAGGTGTGCCGTGTAGAGA	TCCCAAAGAGGTACCAGGTG	168bp
K8	K-bZIP	AAGCTCGCTGTTGTCAACCT	ATCTGCGAGTTGGAAGCTGT	227bp
K8.1	gp35-37	CACCACAGAACTGACCGATG	GTAGTGCGCGTCTCTTCCTC	184bp
K9	vIRF1	GCGTCAATCAAGGATTGGAT [#]	CTTGCAAGAGACGTGCCATA [#]	400bp
K11.1	vIRF2	GGAATGGCTCACGGACTTTA	CTCAGTCTCCGGGATTCTG	202bp
ORF58		GCCGCCAATAGTACACAGGT	TGCCTAAATGCCAAAAGTCC	150bp
K12	KapA	AGGCTTAACGGTGTGTTGTGG	CTCGTGCCTGAATGCTACG	155bp
ORF71	vFLIP	AGCTGTGTGCGAGGGATATT	GGCGATAGTGTGGGAGTGT	246bp
ORF72	vcyclin	ACGAGGTCAACACCCTGATT	CGCCTGTAGAACGAAACAT	191bp
ORF73	LANA-1	TTGCCACCCACGCAGTCT*	GGACGCATAGGTGTTGAAGA GTCT*	89bp
K14	vOX2	CCAGGAGCAGTTCACCTGACA	TAGGCCACCAGAGTAATGG	217bp
ORF74	vGPCR	CGCTGCACTGTTAATTGCAT	GTCGCCTTAGCAGAGTGCC	341bp
K15-P	LAMP	CCTATGCTTGCTTAATCACCA C	GGACCAGCATGTTTGCATC	150bp
GAPDH	GAPDH	GGAGTCAACGGATTTGGTCG TA*	GGCAACAATATCCACTTTACC AGAGT*	78bp
18S		CGGCTACCACATCCAAGGAA [§]	GCTGGAATTACCGCGGCT [§]	187bp

Table 2.2. Primers used for RT-PCR to detect the expression of viral and cellular genes in cells. All RT-PCR primers were designed using Primer3 (Rozen and Skaletsky, 2000) except * which are previously described in Bourbouli et al., 2004 and [§] which are previously described in Favy et al., 2000. [#] Same primers used to detect the expression of vIRF1 Δ 1-82.

2.3.14 Quantitative reverse transcriptase-polymerase chain reaction (qRT-PCR)

Real-time qRT-PCR was performed for *Ang2*, *Angptl2* and *GAPDH* using SYBR green. *GAPDH* primers and their concentrations were previously described (Bourboulia et al., 2004) and were as follows: forward primer 5'-GGAGTCAACGGATTTGGTCGTA-3', 0.3 μ M; reverse primer 5'-GGCAACAATATCCACTTTACCAGAGT-3', 0.3 μ M. *Ang2* and *Angptl2* qRT-PCR primers were designed using the Primer Express software. *Ang2* primers and their concentrations used were as follows: forward primer 5'-GTTTGCTACTGGAAAAAGAGGAAAGAG-3', 0.3 μ M; reverse primer 5'-AGGGCTGCTACGCTGCC-3', 0.9 μ M. *Angptl2* primers and their concentrations used were as follows: forward primer 5'-ACCTGGTGAAGCCGGAGAA-3', 0.9 μ M; reverse primer 5'-GGTCGTGTCTCTGGTCGCA-3', 0.3 μ M. qRT-PCRs were performed in a total volume of 25 μ l using the SYBR Green PCR mix (Applied Biosystems). 5 μ l of template was added to each reaction. The template DNA was 1 in 50 to 1 in 1000 diluted cDNA from the cDNA synthesis reaction. The cDNA was diluted in ddH₂O. The qRT-PCR conditions used were as follows: 50°C for 2 min followed by 95°C for 10 min and 40 cycles of 95°C for 15 sec and 60°C for 1 min. Relative *Ang2* or *Angptl2* expression was quantitated using the comparative C_T method using *GAPDH* as a house-keeping control gene, except for hypoxia experiments in which *actin* was used as the house keeping control gene. Negative control reactions using ddH₂O as template were performed for all qRT-PCRs.

Real time qRT-PCR for *VEGFA*, *VEGFC*, *ADM* and *actin* were performed using TaqMan Gene Expression assays (Applied Biosystems) according to the manufacturer's instructions. Reactions were performed in a total volume of 25 μ l using the TaqMan universal PCR master mix and 20 \times TaqMan probe and primer mix. 5 μ l of diluted cDNA template was added to each reaction. The qRT-PCRs were performed and analysed in the same way as *Ang2* and *Angptl2*.

2.4 Protein analysis

A summary of the primary antibodies used to detect protein in the various techniques described in this section along with the dilutions at which these antibodies were used at is displayed in Table 2.3.

Antigen	Antibody	Species and isotype	Dilution	Source
Ang2	180102	Mouse monoclonal IgG _{2B}	WB: 1 / 500 IFA: 1 / 500 IHC: 1 / 500	R&D Systems
Angptl2	239829	Mouse monoclonal IgG _{2B}	WB: 1 / 500	R&D Systems
ERK1/2		Rabbit polyclonal IgG	WB: 1 / 5000	Millipore
GAPDH	6C5	Mouse monoclonal IgG ₁	WB: 1 / 2000	Advanced ImmunoChemical
IgG _{2B} isotype control		Mouse monoclonal IgG _{2B}	IFA: 1 / 500 IHC: 1 / 500	BD Biosciences
K8.1A	2A3	Mouse monoclonal IgG _{2A}	IFA: 1 / 1000	Advanced Biotechnologies
LANA-1	LN53	Rat monoclonal IgG _{2C}	WB: 1 / 1000 IFA: 1 / 500	CR-UK Viral Oncology Group
LANA-1	Human KSHV seropositive serum with high LANA-1 titer	Human serum	IFA: 1 / 100	CR-UK Viral Oncology Group
LANA-1 staining human serum control	Human serum seronegative for KSHV	Human serum	IFA: 1 / 100	CR-UK Viral Oncology Group
MHC-I (HLA-A, -B, -C)	G46-2.6	Mouse monoclonal IgG ₁ , RPE labeled	FC: 1 / 30	BD Pharmingen
Phospho-ERK1/2		Rabbit polyclonal	WB: 1 / 1000	Cell Signaling Technology
vcyclin		Sheep polyclonal IgG	WB: 1 / 500	Exalpa Biologicals

Table 2.3. Details of the primary antibodies used. The dilutions of the antibodies used in various applications are shown. FC, flow cytometry; IFA, immunofluorescence assay; IHC, immunohistochemistry; WB, Western blotting. The anti-Ang2 antibody and the IgG_{2B} isotype control antibody were used at the same concentration (1 µg / ml) for immunohistochemistry and for immunofluorescence assay.

2.4.1 Western blotting

Protein lysates were prepared using radioimmunoprecipitation assay (RIPA) buffer containing protease inhibitor and phosphatase inhibitor cocktails (Sigma). The composition of the lysis buffer is described below.

Lysis buffer

150 mM NaCl

50 mM Tris-HCl pH 7.5

1% [volume / volume (v/v)] NP40

0.5% (w/v) Deoxycholic acid

0.1% (w/v) Sodium dodecyl sulfate (SDS)

1/100 Protease inhibitor cocktail

1/100 Phosphatase inhibitor cocktail I

1/100 Phosphatase inhibitor cocktail II

50-100 μ l of lysis buffer was added either to cell pellets (1×10^5 to 1×10^6 cells) in 1.5 ml Eppendorf tubes and then mixed by pipetting or to cells in wells of a six well plate that had been washed twice with PBS. After the addition of the lysis buffer to wells the cells were retrieved using a cell scraper and placed into 1.5 ml Eppendorf tubes. The lysates were incubated on ice for 30 min and then centrifuged at 13000 rpm for 20 min at 4°C. The pellets were discarded and supernatants containing the protein were stored at -80°C until needed.

The concentration of the protein lysates were measured using the Bradford assay (Bio-Rad). 1-2 μ l of lysate was diluted in 500 μ l of distilled water (dH₂O) to which 500 μ l of Bradford assay reagent was added and then the absorbance at 595 nm was measured using a UV-visible spectrophotometer (Camspec). The absorbance readings were compared to a standard curve produced with dilutions of a bovine serum albumin (BSA) solution (10 mg/ml) (Promega) to obtain the protein concentration of the lysates. Lysates and standards were assayed in duplicate.

The desired amount of protein lysate needed for Western blotting was mixed with 4× sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) sample loading buffer and the appropriate amount of dH₂O after which the lysate was heated at 99°C for 5 min and allowed to cool. The sample was then ready to be run on an SDS-PAGE gel. The composition of the 4× SDS-PAGE sample loading buffer is described below.

4× SDS-PAGE sample loading buffer

250 mM Tris-HCl pH 6.8

8% (w/v) SDS

10% (v/v) Glycerol

5% (v/v) β-mercaptoethanol

0.05% (w/v) Bromophenol blue

Prepared protein lysates were run on 10% (for ERK1/2 and LANA-1) or 12% (for Ang2, Angptl2 and vcyclin) SDS-PAGE gels which comprised a stacking gel with a 10 or 12% resolving gel. The SDS-PAGE gels were produced as described on the next page.

Stacking gel

1.4 ml, dH₂O
0.33 ml, 30% (w/v) acrylamide
0.25 ml, 1.0 M Tris pH 6.8
0.02 ml, 10% (w/v) SDS
0.02 ml, 10% (w/v) ammonium persulfate
0.002 ml, TEMED

10% Resolving gel

4 ml, dH₂O
3.3 ml, 30% (w/v) acrylamide
2.5 ml, 1.5 M Tris pH 8.8
0.1 ml, 10% (w/v) SDS
0.1 ml, 10% (w/v) ammonium persulfate
0.004 ml, TEMED

12% Resolving gel

3.3 ml, dH₂O
4 ml, 30% (w/v) acrylamide
2.5 ml, 1.5 M Tris pH 8.8
0.1 ml, 10% (w/v) SDS
0.1 ml, 10% (w/v) ammonium persulfate
0.004 ml, TEMED

10-50 µg of lysate was loaded on SDS-PAGE gels along with 10 µl of Rainbow colour protein molecular weight ladder (Bio-Rad). Gels were electrophorised at 100 V in SDS-PAGE running buffer (National Diagnostics) until the bromophenol blue marker ran off the gel. The protein was then transferred onto immobilon P membranes (Millipore) at 15 V for 1 hour using a semi-dry transfer apparatus (Bio-Rad) and transfer buffer (National Diagnostics). Membranes were then blocked with blocking solution [5% (w/v) milk, 0.05% (v/v) Tween20 (Sigma) in PBS] for 1 hour at room temperature and were then incubated overnight at 4°C with the primary antibody diluted in blocking solution. The membranes were then washed 4 times for 15 min each wash with PBS-Tween (0.05% (v/v) Tween20 in PBS) at room temperature and then incubated for 1 hour at room temperature with the appropriate horseradish peroxidase (HRP) conjugated secondary antibody diluted in blocking solution. The secondary antibodies used and the dilution at which they were used at is described on the next page.

Secondary antibodies used for Western blotting

Goat anti-mouse IgGs-HRP (Dako): Diluted 1/10000

Goat anti-rabbit IgGs-HRP (Dako): Diluted 1/5000

Rabbit anti-rat IgGs-HRP (Dako): Diluted 1/5000

Rabbit anti-sheep IgGs-HRP (Dako): Diluted 1/5000

After incubation with the secondary antibodies the membranes were then washed 4 times for 15 min each wash with PBS-Tween at room temperature and then developed using either ECL or ECL Plus (GE healthcare) according to the manufacturer's protocol. The produced chemi-luminescence signal was detected using Hyperfilm (GE healthcare). When using anti-phospho-ERK1/2 antibody the blocking solution used was [5% (w/v) milk, 0.05% (v/v) Tween20 in Tris buffered saline (TBS) (Sigma)] and the wash buffer used was TBS-Tween (0.05% (v/v) Tween20 in TBS).

To visualise total protein present on the immobilon P membranes Ponceau S staining solution (Sigma) was used. Membranes washed in PBS-Tween were incubated for 5 min with Ponceau S staining solution after which the membranes were rinsed in dH₂O to remove background staining. The membranes were then allowed to dry and pictures of the stained membranes were obtained using the VersaDoc imaging system.

2.4.2 Ang2 ELISA

Media from uninfected LEC, lentiviral infected LEC and KLEC were collected after 48 hours in culture to obtain supernatants (conditioned media) and stored at -80°C. Ang2 levels in the supernatants were measured using a 96 well plate format Ang2 ELISA kit (R&D Systems) according to the manufacturer's protocol. Samples were diluted 1 in 5 in calibrator diluent RD5-5 before being used in the ELISA. Ang2 standards with 3000 pg/ml to 46.9 pg/ml of recombinant human Ang2 (rhAng2) diluted in calibrator diluent RD5-5 were run along side the samples in the Ang2 ELISA to produce a standard curve. Calibrator diluent RD5-5 with no sample or standard added was used as a negative control in ELISAs.

For the Ang2 ELISA firstly 100 μ l of assay diluent RD1-76 was added to each well followed by 50 μ l of sample or standard. The plate was then incubated at room temperature for 2 hours on a rocking platform. The wells were then washed several times with wash buffer after which 200 μ l of Ang2 conjugate solution (containing anti-Ang2 antibody conjugated to horseradish peroxidase) was added to each well and incubated at room temperature for 2 hours on a rocking platform. The wells were then washed again several times with wash buffer after which 200 μ l of substrate solution was added to each well and incubated at room temperature for 30 min in the dark on the bench top. 50 μ l of stop solution (2 N sulphuric acid) was then added to the wells and the absorbance at 450 nm (A_{450}) and 650 nm (A_{650}) was measured using the SpectraMAX plus spectrophotometer (Molecular devices). The sample A_{450} - A_{650} values were compared to the standard curve produced from A_{450} - A_{650} values of the standards to determine the amount of Ang2 present in the samples.

2.4.3 Immunofluorescence assay

LEC, lentiviral infected LEC or KLEC to be analysed by immunofluorescence assay were seeded and grown in tissue culture on fibronectin coated glass coverslips (Scientific Laboratory Supplies). For the immunofluorescence assay, cells on the coverslips were washed twice with PBS after which they were fixed by being incubated for 10-15 min with 4% paraformaldehyde (Sigma). The cells were subsequently washed with PBS and then permeabilised by incubating the cells for 15 min with 0.2% (v/v) Triton X-100 (Sigma) in PBS after which the cells were washed again with PBS. The cells were then blocked with blocking solution (5% FBS in PBS) for 30 min and then exposed to the primary antibodies diluted in blocking buffer for 60 min. The cells were then washed with PBS and then incubated for 45 min in the dark with the appropriate R-phycoerythrin (RPE)-conjugated or FITC-conjugated secondary antibodies diluted in blocking solution. The secondary antibodies and the dilutions at which they were used are described on the next page.

Secondary antibodies used for immunofluorescence assay

Rabbit anti-human IgGs-FITC (Dako): Diluted 1/60

Goat anti-mouse IgGs-RPE (Molecular Probes): Diluted 1/500

Rabbit anti-Rat IgGs-FITC (Dako): Diluted 1/120

After incubation with the secondary antibodies the cells were washed with PBS and the coverslips were then mounted using VECTASHIELD mounting medium with 4',6-diamidino-2-phenylindole (DAPI) (Vector) or Prolong Gold antifade reagent (Molecular Probes). Visualization was performed with the use of a Nikon Eclipse E800 microscope and photographs taken with a Nikon DS-fi1 camera. For the quantification of the percentage of LANA-1 or K8.1A-positive cells in a population, between 5 and 14 fields were counted, resulting in between 300 and 1,100 cells being analysed. All the PBS washes carried out unless otherwise stated were performed by incubating the slides in fresh PBS three times for 5 min each time. All incubations were performed at room temperature.

2.4.4 Immunohistochemistry

Formalin-fixed, paraffin-embedded specimens of KS lesions ($n = 8$) were obtained from archival biopsies in the Department of Histopathology, University College London Hospitals. 4 μm paraffin sections were cut using a microtome and mounted onto glass slides, dewaxed in two changes of xylene (5 min each), rehydrated sequentially in absolute, 95% and 70% ethanol and dH_2O and then processed for immunohistochemistry. For immunohistochemistry primary anti-Ang2 antibody (R&D systems) and biotinylated goat anti-mouse IgG secondary antibody (Vector Laboratories) were used. After rinsing the hydrated sections with buffer 1 (100 mM, Tris-HCl 150 mM NaCl pH 7.5), sections were preincubated for 30 min with buffer 2 (buffer 1 + 2% horse serum + 0.1% Triton X-100) followed by an overnight incubation at 4°C with the primary antibody diluted in buffer 3 (buffer 1 + 1% horse serum + 0.1% Triton X-100) to a final concentration of 1 $\mu\text{g}/\text{ml}$. Sections were then washed twice for 5 min with buffer 1 and incubated for 60 min at room temperature with the secondary antibody diluted 1 in 750 in buffer 3. This procedure was followed by three 5 min washes with buffer 1 and then the application of the streptavidin-alkaline phosphatase

complex by the addition of Vectastain ABC-AP reagent (Vector Laboratories) for 30 min at room temperature. Slides were then washed three times with buffer 1 and then briefly in buffer 4 (100 mM, Tris-HCl, 100 mM NaCl, 50 mM MgCl₂ pH 9.5). Signal was revealed by colour development by incubating slides for 20-30 min with Vector Red alkaline phosphatase substrate solution (Vector Laboratories). Sections were then rinsed with water, counterstained with Mayer's hematoxylin for 1 min to reveal nuclei, and rinsed several times with water. The slides were then mounted using Hydromount (BDH). Visualization was performed with the use of a Nikon Eclipse E800 microscope and photographs taken with a Nikon CoolPIX900 digital camera. All incubations and washes unless otherwise stated were performed at room temperature.

Ang2 immunoreactivity was detected in all KS lesions studied. Consecutive sections were used for controls, which included substitution of the primary antibody with the isotype-matched mouse IgG antibody used at the same concentration (1µg / ml) or pre-incubation (preabsorption) of the primary antibody with rhAng2 (R&D systems, diluted to 5 µg/ml in buffer 3, for one hour prior to immunohistochemistry. These served as negative controls to indicate the specificity of the antibodies used.

The immunohistochemistry was performed with the help of Leonid Nikitenko.

2.4.5 Flow cytometry for MHC-I

To investigate cell surface expression of MHC-I flow cytometry was used. LEC in wells of 6 well plates were detached and pelleted ($\sim 2 \times 10^5$ cells) into 1.5 ml Eppendorf tubes. Each cell pellet to be stained was processed as follows. The pelleted cells were washed with 1 ml of PBS and pelleted again by centrifugation. The cells were then resuspended in 100 µl of PBS containing the diluted RPE conjugated anti-MHC-I antibody. The cells were incubated with the anti-MHC-I antibody for 30 min at 4°C after which the cells were washed with 700 µl of PBS and pelleted by centrifugation. The cell pellet was then resuspended in 400 µl of PBS and analysed by flow cytometry using a FACSCalibur flow cytometer. The

geomean fluorescence was used as a relative measure of MHC-I surface expression between samples.

2.5 Pharmacologic inhibition studies

For the VEGFR1 and VEGFR2 inhibition studies, LEC were seeded into wells of 24 well plates (1.1×10^4 cells per well) and, 24 hours later, exposed to supernatant (conditioned media) or supernatant with either 0.25% DMSO or 0.25% DMSO with 50 μ M VEGFR1 and VEGFR2 inhibitor, 4-[(4'-chloro-2'-fluoro)phenylamino]-6,7-dimethoxyquinazoline (Calbiochem). After 18 hours incubation, RNA from LEC was collected, and qRT-PCR was performed. Before the addition of the supernatant, LEC were preincubated for 5 hours with either standard media or media containing either 0.25% DMSO or 0.25% DMSO with 50 μ M VEGFR1 and VEGFR2 inhibitor. Supernatants from LEC, lentivirus infected LEC or KLEC were used.

For the MAPK inhibition studies, LEC, lentivirus infected LEC or KLEC were seeded into wells of 24 well plates (1.1×10^4 cells per well) and, 72 hours p.i., subjected to standard media or media with 0.1% DMSO, 0.25% DMSO, or different concentrations of the following inhibitors: mitogen-activated protein (MAP)/extracellular signal-regulated kinase (ERK) kinase (MEK) inhibitor, PD98059 and U0126 (Calbiochem), each with 0.1% DMSO or c-jun-NH₂-kinase (JNK) inhibitor, SP600125 (Calbiochem) with 0.25% DMSO. After 8.5 hours incubation, RNA was collected, and qRT-PCR was performed.

A summary of the pharmacologic inhibitors used is displayed in Table 2.4.

Inhibitor	Target	Concentrations used	% DMSO used in experiments	Supplier
PD98059	MEK	2.5 μ M, 12.5 μ M, 25 μ M	0.1%	Calbiochem
SP600125	JNK	2.5 μ M, 12.5 μ M, 25 μ M	0.25%	Calbiochem
U0126	MEK	1 μ M, 10 μ M, 20 μ M,	0.1%	Calbiochem
VEGFR1 and VEGFR2 inhibitor (4-[(4'-chloro-2'-fluoro)phenylamino]-6,7-dimethoxyquinazoline)	VEGFR1, VEGFR2	50 μ M	0.25%	Calbiochem

Table 2.4. Pharmacologic inhibitors used. The concentrations of inhibitors used are shown along with the percentage (v/v) of DMSO present when the inhibitors were used in tissue culture. Therefore, the percentages of DMSO shown were the percentages of DMSO present in the DMSO controls used in experiments with these inhibitors. The amount of DMSO present was determined by the solubility of the inhibitors in DMSO.

2.6 Cell viability studies

Studies were performed using the CellTiter96® AQueous One Solution Cell Proliferation Assay (Promega) according to the manufacturer's protocol to test whether the pharmacologic inhibitors and DMSO used caused a significant effect on LEC viability. LEC (1×10^4 LEC seeded the day before) in wells of 24 well plates were incubated for 24 hours with either normal media, media containing DMSO, or media containing the highest concentration of inhibitor used in inhibition studies. After the incubation with the inhibitors the media was removed and cells were washed with PBS. 250 μ l of fresh LEC media was then added to each well along with 50 μ l of CellTiter96® AQueous One Solution Cell Proliferation Assay reagent. The cells were then incubated for 1-2 hours at 37°C until a significant colour change in the media was observed and before the media was dark brown which would have resulted in an absorbance at 490 nm above 1. After the incubation with the CellTiter96® AQueous One Solution Cell Proliferation Assay reagent the reaction was stopped by adding 62.5 μ l of 10% (w/v) SDS in dH₂O. 150 μ l of solution from each well was then transferred into wells of a clear 96 well plate and the absorbance at 490 nm (A_{490}) and 650 nm (A_{650}) was measured using the SpectraMAX plus spectrophotometer. The A_{490} - A_{650} measured is directly proportional to the number of live cells in each well.

2.7 Interferon studies

For interferon studies, LEC or lentiviral infected LEC (60 h p.i.) present in 6 well plates were incubated overnight with either LEC media or LEC media containing 150 U/ml IFN α (R&D systems) or 1000 U/ml IFN γ (R&D systems). After the incubation, cells were processed for flow cytometry or qRT-PCR analysis.

2.8 Luciferase assays

Luciferase assays were performed to measure the amount of promoter activity present in luciferase reporter constructs transfected into 293T cells. Luciferase studies were performed by first seeding 0.75×10^5 293T cells in wells of 12 well

plates. The next day each well was transfected using FuGENE with 1 µg of pGL3 reporter construct and 20 ng of phRG-TK Renilla construct or 1 µg of pGL3 reporter constructs in total, 1 µg lentiviral construct and 20 ng of phRG-TK Renilla construct. Details of the reporter constructs and the phRG-TK Renilla construct used are displayed in Table 2.5. The transfections were performed overnight and the next day the media was changed. 48 hours after transfection the cells were analysed for luciferase expression by measuring the amount luminescence produced when the luciferase substrate was present. This was performed with the Dual-luciferase Reporter Assay System (Promega) based on the manufacturer's protocol. The 293T cells were first washed with PBS and then lysed by adding 250 µl of passive lysis buffer to each well and incubating the plate at room temperature on a rocking platform for 15 min. The lysates were then transferred into 1.5 ml Eppendorf tubes and centrifuged at 13000 rpm for 1 min on a bench top centrifuge to pellet any precipitate. 10 µl of each sample was then added to wells of a white non-transparent 96 well plate (Thermo). Each sample was assayed in duplicate. The plate was loaded into the Fluoroskan Ascent FL luminometer with dual injectors (Thermo). The luminometer automatically added 50 µl of luciferase assay reagent II (firefly luciferase substrate) to each well and measured the luminescence produced. The luminometer then automatically added 50 µl of Stop and Glo substrate (quenches the firefly luciferase reaction and contains the Renilla luciferase substrate) to each well and measured the luminescence produced. The luminometer was set up for a 2 sec pre-read delay followed by a 10 sec luminescence measurement time. The luminescence was recorded as relative light units (RLU).

For analysis, the firefly luciferase luminescence values were normalised to total protein present in 10 µl of each sample (i.e. the amount of sample run on the luminometer). This method of normalisation has been previously performed (Cannon et al., 2003). Total protein was measured using the BCA protein assay kit (Pierce) based on the manufacturer's protocol. For protein measurement 10 µl of each sample lysate was added to wells of transparent 96 well plates after which 10 µl of dH₂O was added to each well. Solution A was mixed with solution B at a ratio of 50 to 1 and 180 µl of this mixture was added to each well. The plate

was then incubated at room temperature for 30 min after which the absorbance at 562 nm was measured using the SpectraMAX plus spectrophotometer. BSA protein standards ranging from 2 mg/ml to 0.0625 mg/ml diluted in dH₂O were run at the same time as the samples to create a standard curve which was used to determine the amount of protein present in the samples. Samples were assayed in duplicate and dH₂O was used as a negative control in the assay.

Firefly luciferase luminescence values were normalised to total protein to account for any difference between samples due to differences in cell number or pipetting. However, originally it was planned to normalise the firefly luciferase luminescence values to the Renilla luciferase luminescence values. This is because it was predicted that while the firefly luciferase luminescence values would vary depending on what promoter was present in front of the firefly luciferase ORF (e.g. different *Angptl2* promoter lengths) or what lentiviral construct was transfected into the 293T cells (e.g. pSIN versus vIRF1) the Renilla luciferase luminescence values would remain constant. Therefore, it was predicted that Renilla luciferase luminescence could be used to normalise for differences between samples such as cell number and pipetting errors. However, it was found that despite transfecting the same amount of Renilla and total DNA into the same number of cells that the Renilla luciferase luminescence varied significantly between samples even when the Renilla luciferase luminescence was normalised to total protein (Fig. 2.1). The Renilla luciferase luminescence values were affected by which lentiviral construct was transfected into 293T cells at the same time as the Renilla expressing construct, phRG-TK. Renilla luciferase luminescence varies because the genes encoded in the lentiviral constructs appear to affect the activity of the Renilla luciferase promoter. In summary, although the phRG-TK construct was transfected in all luciferase assays performed the Renilla luciferase luminescence values were not used in the analysis of the results. Therefore, the addition of the phRG-TK construct to the luciferase assays is not discussed or mentioned further in the thesis and the Renilla luciferase data is not used in the generation of any Result chapter figures or tables.

Fluorescent microscopy visualisation and flow cytometry analysis of GFP expression in 293T cells transfected with luciferase constructs and pCSGW was performed in the same way as described in Section 2.2.3.

Plasmid	Promoter	Reporter	Supplier
pGL3-basic	No promoter	Firefly luciferase	Promega
pGL3-control	SV40 promoter	Firefly luciferase	Promega
phRG-TK	HSV-TK promoter	Renilla luciferase	Promega
pGL3-1kb-Angptl2	First 1kb of the <i>Angptl2</i> promoter	Firefly luciferase	n/a
pGL3-500bp-Angptl2	First 500bp of the <i>Angptl2</i> promoter	Firefly luciferase	n/a
pGL3-319bp-Angptl2	First 319bp of the <i>Angptl2</i> promoter	Firefly luciferase	n/a

Table 2.5. Plasmids used for luciferase assays. The promoters in the plasmids, which control the reporters present, are shown. HSV-TK, herpes simplex virus-thymidine kinase.

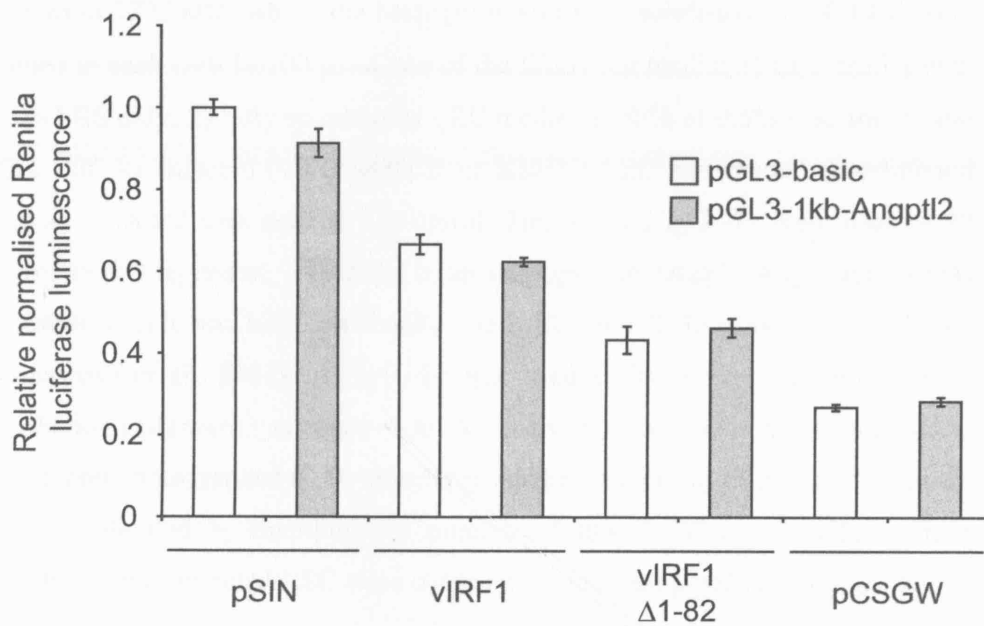


Figure 2.1. Variation of normalised Renilla luciferase luminescence with different reporter and lentiviral constructs. 0.75×10^5 293T cells were transfected with $1 \mu\text{g}$ of a lentiviral construct and 20ng of pRG-TK along with either $1 \mu\text{g}$ of pGL3-basic or pGL3-1kb-Angptl2. 48h later the cells were harvested and the Renilla luciferase activity was detected as luminescence which was measured as relative light units (RLU). The Renilla luciferase derived luminescence was normalised for total protein and then normalised to levels present in pSIN plus pGL3-basic transfected cells to give relative normalised Renilla luciferase luminescence. Experiment was performed in triplicate. vIRF1 Δ 1-82 lacks the first 82 amino acids of vIRF1 and was cloned into the pSIN-MCS vector. *Columns*, mean; *bars*, SE.

2.9 Functional assays

2.9.1 Matrigel tube formation assay

96 well plates were coated with 80 μ l of Matrigel Basement Membrane Matrix (Matrigel) (VWR International Ltd, Leicestershire, UK). This was performed by adding cold (<4°C) liquid Matrigel to each well and then incubating the plate for 30 min at 37°C after which the Matrigel would have solidified. 9000 LEC were seeded in each well in 100 μ l of one of the following media: 1) LEC media with 0.5% FBS only; 2) fully supplement LEC media; 3) 50% of 0.5% FBS media and 50% LEC or infected (vIL6, vGPCR or KSHV) LEC supernatant (conditioned media). rhAng2 was used at 220 ng/ml; Tie2-Fc and IgG₁-Fc were used at 20 μ g/ml (R&D systems). Tie2-Fc is an angiopoietin (Ang1, Ang2 and Ang4) inhibitor which has been previously used (Teichert-Kuliszewska et al., 2001; Yamakawa et al., 2003) and IgG₁-Fc was used as its control. 24 hours post-incubation cells were visualised on an Axiovert 100 fluorescent microscope (Carl Zeiss) and photographed (2.5 \times objective) using an AxioCam camera and software (Zeiss) followed by counting the number of tubes. The supernatants from infected or non-infected LEC were obtained by incubating cells in LEC media for 48 hours.

2.9.2 tMSC mice tumour studies

For tumour formation studies 4×10^6 Angptl2 tMSC or empty vector tMSC were injected subcutaneously into both flanks of 6-8 week old male athymic CD1 nude mice (Charles River Breeding Laboratories). Each mouse used had both flanks injected with the same tMSC cell line. Once tumours appeared, tumour size was measured about every three days. The tumour volume was calculated using the 'ellipsoidal' method (Singh et al., 2007) using the following formula:

$$V = L \times W \times H \left(\frac{\pi}{6} \right)$$

Where V is tumour volume, L is maximum tumour length, W is maximum tumour width and H is maximum tumour height.

At day 29 after inoculation the tumours were harvested and placed in liquid nitrogen. The mouse work was performed by Mathew Robinson (Royal Free University College Medical School, London, U.K.).

2.10 GEM analysis

2.10.1 Initial processing of Affymetrix microarray data

Raw gene expression microarray (GEM) data (Affymetrix CEL files) were obtained either from previous publications, the NCBI GEO database or from previous experiments performed by members of our lab. Bioinformatics Stephen Henderson and Matthew Trotter performed the initial processing of raw microarray data to obtain the microarray log expression values, p- and q-values. The processed GEM data were then used by me to perform further analysis with the help of Stephen Henderson and Matthew Trotter. Information on the GEM data used for my investigations on KSHV infection, skin versus KS experiments and MSC cell lines and tMSC tumours is described below.

2.10.1.1 LEC versus KLEC GEM data

GEM data from six LEC and six KLEC (3 or 4 days p.i. and at least 50% positive for GFP expression) hybridized to Affymetrix hg-u133+2 GeneChips were obtained from Lagos et al., 2007.

The raw GEM data were processed as described in Lagos et al., 2007. In summary the Bioconductor (<http://www.bioconductor.org>) 'affy' package for the R statistical programming language (<http://www.r-project.org>) was used to process the raw array data to obtain the microarray log expression values [also called the RMA log expression units (Irizarry et al., 2003)]. To assess the significance of differences between LEC and KLEC sample groups a moderated t-statistic was applied to the microarray log expression values (Smyth, 2004). The p-values obtained were corrected for the false discovery rate (FDR) to obtain q-values (Storey and Tibshirani, 2003). The statistical analysis performed on the

GEM data to obtain the t-statistic and q-values was performed using the limma and qvalue packages of Bioconductor and R statistical programming language respectively.

2.10.1.2 BEC versus KBEC GEM data

GEM data from six BEC and six KBEC (3 or 4 days p.i. and at least 50% positive for GFP expression) hybridized to Affymetrix hg-u133+2 GeneChips were obtained from Dimitrios Lagos (unpublished data, CR-UK Viral Oncology Group). The raw GEM data were processed as described in Section 2.10.1.1.

2.10.1.3 Skin versus KS GEM data

GEM data from five skin biopsies, from different individuals, and six nodular KS biopsies of the skin, from different individuals (five AIDS-KS and one classical KS), hybridized to Affymetrix hg-u133A GeneChips were obtained from Wang et al., 2004. The raw GEM data were processed as described in Wang et al., 2004.

2.10.1.4 GEM data of the MSC cell lines and tMSC tumours

GEM data of the MSC cell lines with different numbers of oncogenic hits and the GEM data of tMSC tumours in athymic CD1 nude mice were obtained from Funes et al., 2007. The GEM data were processed as described in Funes et al., 2007. For the *in vitro* cell lines with 0 – 5 oncogenic hits the microarray data are an average of 3 samples while the tumour microarray data are an average of 5 tumours (Funes et al., 2007).

2.10.2 Using LEC versus KLEC GEM data to investigate the regulation of angiogenic factors by KSHV

A subset of processed microarray data from the LEC versus KLEC GEM data was employed to visualize the effect of KSHV infection upon a selection of factors involved in angiogenesis. A list of genes related to angiogenesis was compiled based on publicly available databases (Gene Ontology, <http://www.geneontology.org>; Panther, <http://www.pantherdb.org>), a commercial website (SuperArray Biosciences, <http://www.superarray.com>) and recent

literature. The list was compiled prior to statistical analysis, to avoid any selection bias, and contained 240 genes (the gene list and corresponding GEM data are displayed in Appendix Table A1). The GEM data for this list were extracted from all the GEM data of LEC versus KLEC (Lagos et al., 2007).

The majority of genes in the ‘genes related to angiogenesis’ list are represented by more than one Affymetrix hg-u133+2 GeneChip probe-set (240 genes / 611 probe-sets). In order to facilitate visualization of gene expression in heat maps of ‘the genes related to angiogenesis’ list, the probe-set with the highest expression across all samples, regardless of sample group, was selected when more than one probe-set was available to measure the expression of a particular gene.

GEM data in the ‘genes related to angiogenesis’ list which displayed differential expression between LEC versus KLEC with a q-value < 0.001 (FDR threshold of 0.1%) were visualized in the heat map of Figure 4.11. While GEM data of genes in the ‘genes related to angiogenesis’ list which were related to *Ang2* or relevant for its function regardless of q-value were displayed in the heat map of Figure 4.12A.

2.10.3 GEM analysis of *Angptl2* in a selection of neoplasms

To investigate *Angptl2* expression in neoplasms and to investigate those genes whose expression profile cluster with *Angptl2* a dataset comprising 12 of the commonest types of carcinoma (see Appendix Table A2) was used. This dataset was a handpicked subset of the expO dataset from the NCBI GEO database (GSE2109, n = 168) (<https://expo.intgen.org/geo/home.do>) (Barrett et al., 2007). Raw GEM data (Affymetrix CEL files) were downloaded and processed according to Section 2.10.1.1.

In order to find genes that were functionally clustered with *Angptl2* and *Ang2* (for comparison) we used the highest expressed probe-set ‘213001_at’ and ‘205572_at’ as bait respectively. Using the selected carcinoma dataset we searched for the 100 probe-sets (including the bait itself) with highest correlation

to our bait probe-set using the R statistical programming language. The probe-sets pulled out for *Angptl2* and *Ang2* correlation analysis along with their microarray log expression values are shown in Appendix Tables A2 and A3 respectively. Heat maps (Fig. 5.1B and 5.2) were then generated to visualise the GEM data of the *Angptl2* and *Ang2* signatures.

2.10.4 Gene expression heat maps

Heat maps of differential gene expression were produced with dChip microarray analysis package (<http://www.biostat.harvard.edu>) using the relevant probe-sets microarray log expression values. Heat maps represent the expression of each probe-set in units of its standard deviation across all sample replicates. The scale at the bottom of all heat maps displays the relationship between colour and its intensity and the microarray log expression value's amount of standard deviation from the mean. In some heat maps (Fig. 4.11 and 4.12A) the gene expression is displayed in order of decreasing log₂ fold-change between conditions.

2.11 *Angptl2* promoter analysis

A cross species comparative *Angptl2* promoter analysis was performed using the DiAlignTF (using MatInspector) software from Genomatix (Cartharius et al., 2005). The promoter analysis performed was verified by Sascha Ott performing promoter analysis using another promoter analysis program which is the BiFa software using the ReMo database (University of Warwick). For the *Angptl2* promoter analysis 7 kb sequences from human, rhesus monkey, dog, mouse and rat were obtained from the NCBI database or UCSC genome bioinformatics site (<http://genome.ucsc.edu/>). The 7 kb sequences obtained from each species comprise of 5 kb of the *Angptl2* promoter, which is upstream of the predicted transcription start site, with the rest of the 7 kb sequence being down stream of the predicted transcription start site. The DiAlignTF software aligns the different sequences and then identifies transcription factor binding sites in the conserved regions. For the analysis only common promoter elements conserved between at least 3 species and other regulatory elements conserved between at least 4 species were investigated. All conserved transcription factor binding sites found had

100% similarity with one of their possible core sequences except for a GC box (-88) which had a similarity above 75% (87.6%) the cut off used for the analysis. Only conserved transcription factor binding sites before the transcription start site were investigated.

2.12 Statistical analysis

Standard error of the mean (SE) was used to calculate the error bars for *in vitro* and *in vivo* experiments, except where its calculation was difficult and not applicable to the measurements, in which case standard deviation was used to calculate the experimental error.

Standard error of the mean was calculated by the dividing the standard deviation (σ) by the square root of the number of samples (N).

$$SE = \frac{\sigma}{\sqrt{N}}$$

The standard deviation is the square root of the variance (σ^2) which is a measure of the spread of a particular distribution and therefore it can be used as a measure of variation between sample values.

$$\sigma = \sqrt{\sigma^2} \qquad \sigma^2 = \frac{\sum (X - \mu)^2}{N}$$

(Where X is a sample value and μ is the mean of the sample values)

To determine whether the difference between two conditions was significant (with the exception of GEM data) the Student's t test was performed and the difference was considered significant when $p < 0.05$.

Chapter 3. The construction of a selected KSHV lentiviral library

The aim of this chapter was to establish a lentiviral expression library of KSHV genes which are thought to be important for the pathogenesis of KSHV. A qPCR system for the titration of lentiviral preparations was developed and the ability of lentivirus to infect and express cloned KSHV genes in LEC was tested.

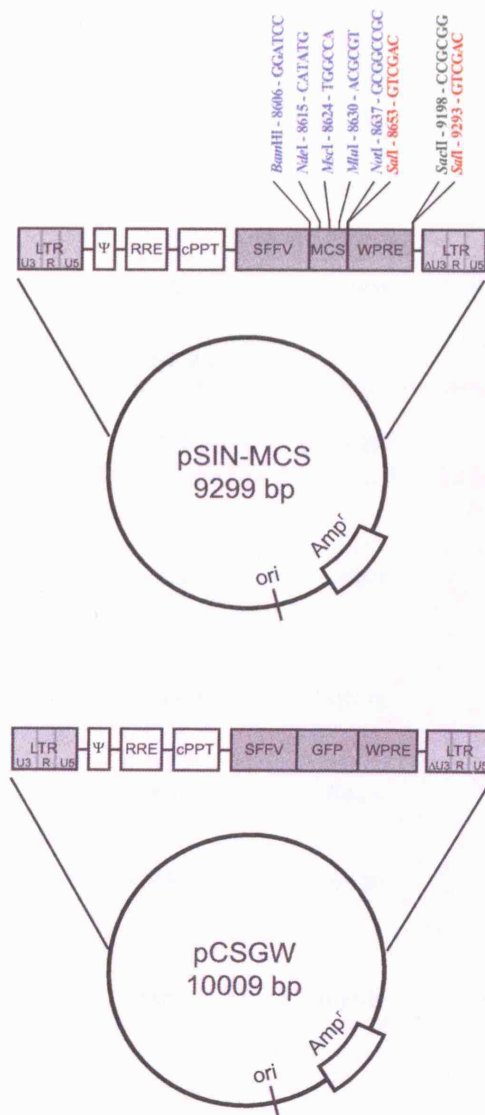
3.1 Background and planning of the KSHV lentiviral library

An expression library of individual KSHV genes was produced in which individual KSHV genes were cloned into the lentiviral vector pSIN-MCS. A library was produced to be able to screen for the ability of KSHV genes to cause effects seen in KS. This would allow the identification of gene(s) responsible for the different effects KSHV has and the subsequent identification of the cellular pathways responsible for these effects. KSHV expression libraries have previously been developed and used for screens, however, the constructs used for these libraries have to be transfected into cells (Coscoy and Ganem, 2000). This is unsuitable for primary LEC, the closest uninfected cell type to the KS spindle cell, as LEC are difficult to transfect with plasmids (Wang et al., 2004a). Therefore a KSHV lentiviral expression library was produced in which HIV-1 based lentiviral virions can deliver constructs efficiently to difficult-to-transfect primary cells such as endothelial cells (Naldini et al., 1996; De et al., 2003). The pSIN-MCS lentiviral vector system used for this KSHV lentiviral library is displayed in Figure 1.6.

The pSIN-MCS vector used for the KSHV lentiviral library is based on the pCSGW vector (Godfrey et al., 2005). Diagrams of the pSIN-MCS and pCSGW vectors are displayed in Figure 3.1 along with the functions of the various elements in the pSIN-MCS vector. To create the pSIN-MCS vector the GFP from the pCSGW vector was removed with *Bam*HI and *Not*I and a multiple cloning site (MCS) was inserted in its place (Andrew Godfrey, unpublished work,

CR-UK Viral Oncology Group) (Fig. 3.1). The pSIN-MCS vector has no protein tags or markers, such as GFP, meaning any effect of the cloned KSHV gene would not be altered. Also, the lack of markers or protein tags made this vector smaller and therefore easier to clone into.

Due to time constraints, I only produced a selected KSHV lentiviral library containing 13 KSHV genes. The genes cloned are shown in Table 3.1 and most were chosen for their importance in KSHV pathogenesis. The genes cloned include most of KSHV's latent genes, including LANA-1, vcyclin and vFLIP which are shown to be expressed in all infected cells, and a selection of lytic genes, three of which were previously shown to promote angiogenesis (vIL6, vMIP1 and vGPCR) (Jenner and Boshoff, 2002). ORF 28, a KSHV gene with no known function, was also cloned.



Element present in pSIN-MCS	Full name	Function
LTR	Long terminal repeat	5'LTR is the site of transcription initiation of the lentiviral vector. 3'LTR contains the polyadenylation signal. Both LTRs are involved in the reverse transcription of the lentiviral vector
Ψ	Packaging signal	Directs the lentiviral vector RNA to be packaged into virions
RRE	rev-response element	Promotes the export of lentiviral vector mRNA from the nucleus
cPPT	Central polypurine tract	Necessary for the synthesis of the plus strand of lentiviral DNA during reverse transcription
SFFV	Spleen focus forming virus promoter	Internal promoter for transgene expression
MCS	Multiple cloning site	Region containing multiple restriction enzyme digestion sites for cloning
WPRE	Woodchuck hepatitis virus post-transcriptional regulatory element	Stabilises mRNA resulting in enhanced transgene expression
ori	Origin of replication	Required for the replication of the plasmid in <i>E. coli</i>
Amp ^r	Ampicillin resistance gene	Allows bacteria containing the plasmid to be selected

Figure 3.1. The pSIN-MCS and pCSGW vectors. Schematic diagrams of the pSIN-MCS and pCSGW vectors are shown along with a table of the elements present in the pSIN-MCS vector and their function. For the pSIN-MCS vector, unique restriction enzyme digestion sites present in the MCS are shown in blue, *SalI* sites flanking the WPRE are shown in red and a unique *SacII* site after the WPRE is shown in green. Each LTR consists of three regions named U3, R and U5. The U3 region in the 3' LTR is mutated causing the production of self inactivating lentiviruses.

ORF cloned into pSIN-MCS	Protein product	Expression	Major functions
K2	vIL6	Lytic	<ul style="list-style-type: none"> - Activates gp130 independently of gp80 - Activates JAK/STAT and MAPK pathways - Angiogenic
K3	vMIR1	Lytic	<ul style="list-style-type: none"> - A viral ubiquitin ligase - Down regulates MHC-I and gamma interferon receptor 1
K6	vMIP1	Lytic	<ul style="list-style-type: none"> - Agonist of CCR8 - Chemotactic for endothelial cells - Angiogenic
ORF 28	-	Lytic	<ul style="list-style-type: none"> - No known function
K8	K-bZIP	Lytic	<ul style="list-style-type: none"> - Involved in lytic DNA replication - Transcription factor, regulates KSHV gene expression - Binds to and inhibits p53
K9	vIRF1	Latent	<ul style="list-style-type: none"> - Inhibits interferon and IRF-mediated responses - Inhibits p53 and TGF-β signalling - Oncogenic
K11.1	vIRF2	Lytic	<ul style="list-style-type: none"> - Inhibits interferon and IRF-mediated responses - Inhibits NF-κB signalling
K12	KapA	Latent	<ul style="list-style-type: none"> - Activates ERK and cytohesin-1 - Oncogenic
ORF 71	vFLIP	Latent	<ul style="list-style-type: none"> - Inhibits death receptor signalling - Activates NF-κB - Oncogenic
ORF 72	vcyclin	Latent	<ul style="list-style-type: none"> - Cyclin D homologue, binds to and activates Cdk6 and Cdk4 - Insensitive to inhibition by CDK inhibitors
ORF 73	LANA-1	Latent	<ul style="list-style-type: none"> - Tethers viral episome to host chromatin - Binds and inhibits p53 and pRb - Activates Wnt-β-catenin pathway - Oncogenic
ORF 74	vGPCR	Lytic	<ul style="list-style-type: none"> - Constitutively active GPCR - Oncogenic and angiogenic
K15-P	LAMP	Latent	<ul style="list-style-type: none"> - Activates MAPK and NF-κB - Interacts with the antiapoptotic factor HAX-1

Table 3.1. KSHV ORFs cloned into pSIN-MCS. The KSHV ORFs present in the selected KSHV lentiviral library are shown along with a summary of their expression and function. The information presented in the table was obtained from references in the Introduction and the following additional references: K3, (Ishido et al., 2000; Lorenzo et al., 2002; Li et al., 2007); K8, (Park et al., 2000; Liao et al., 2003; Lin et al., 2003; Wang et al., 2003; Wang et al., 2004b); K11.1, (Burysek et al., 1999); K15-P, (Glenn et al., 1999; Sharp et al., 2002; Brinkmann et al., 2003). HAX-1, HS1 associated protein X-1.

3.2 Cloning into the pSIN-MCS vector

Most of the KSHV ORFs were cloned using a PCR cloning strategy using BC-3 cDNA or genomic DNA as a template (Fig. 3.2). The advantage of this cloning technique is that it allows the precise cloning of each ORF without relying on restriction enzyme digestion sites in the KSHV genome. In PCR cloning, restriction enzyme digestion sites are added to the end of the primers used for PCR and by adding different restriction enzyme digestion sites on the forward and reverse primers it allows the PCR product to undergo directional cloning into the pSIN-MCS vector. Various problems were encountered during PCR cloning and various steps were employed to overcome these obstacles (Table 3.2).

A summary of how the 13 KSHV ORFs were cloned is shown in Table 3.3 along with the PCR primers and conditions used to amplify the KSHV ORFs. Interestingly, it was found that a number of ORFs contained previously unpublished coding polymorphisms (Table 3.3). These coding polymorphisms were confirmed by sequencing separate PCR products obtained from BC-3 cDNA or genomic DNA. Various silent mutations were also occasionally encountered; however, these were not investigated in detail as they did not affect the protein product produced. The silent polymorphisms therefore can be attributed to point mutations generated by the DNA polymerase during PCR or silent polymorphisms present in the BC-3 cells.

The novel coding polymorphisms found in the KSHV ORFs did not appear to affect the functions of the encoded proteins. vIL6 (K2) was found to activate the MAPK pathway (Section 4.5) as previously reported (Osborne et al., 1999). vMIR1 (K3) was still able to up-regulate MHC-I and vFLIP (ORF 71) activated NF- κ B (Lagos et al., 2007). While vcyclin (ORF 72), as previously reported (Verschuren et al., 2002), appeared in tissue culture to cause cells to undergo growth arrest as cells changed morphology and the cell culture slowed in growth (data not shown).

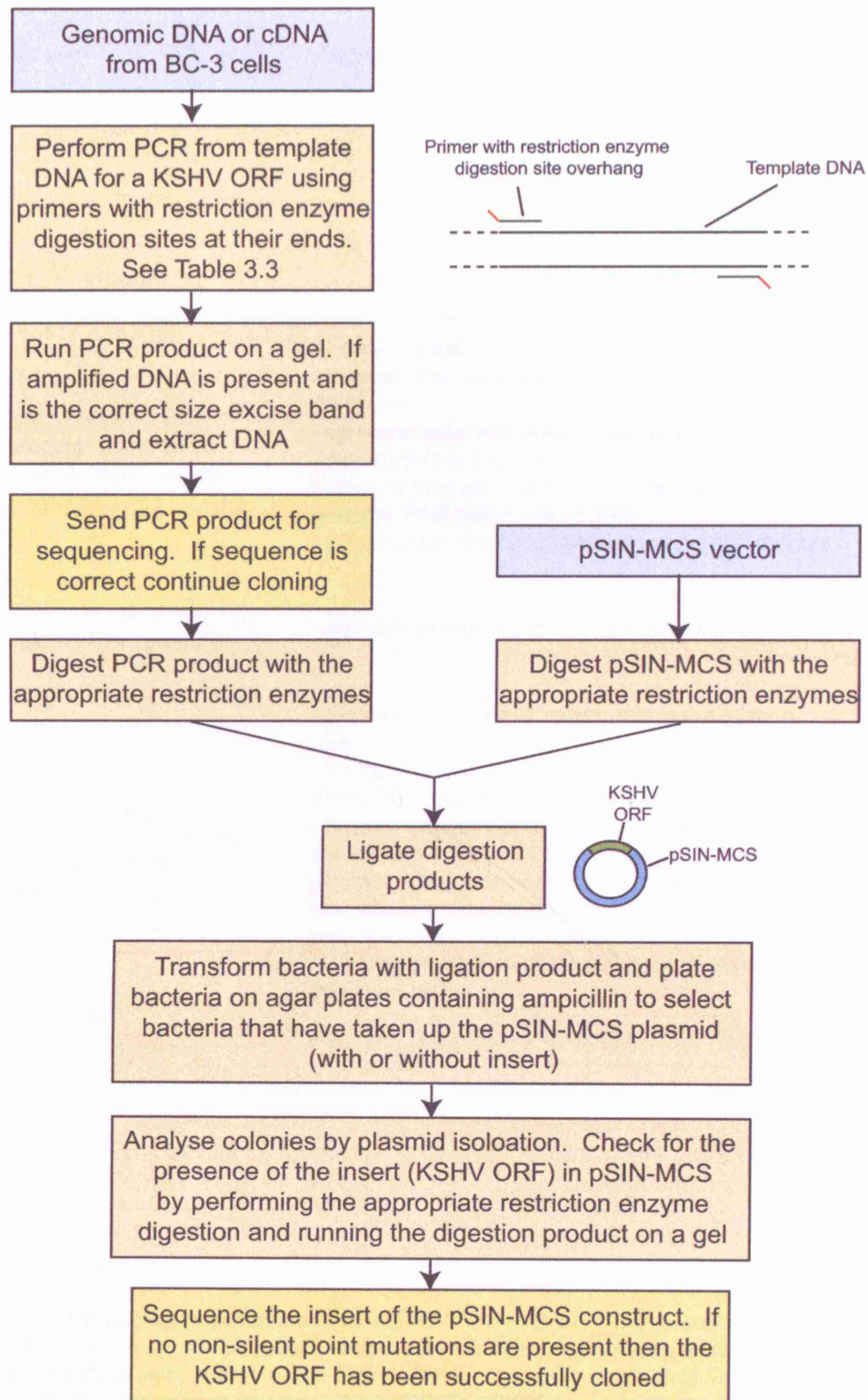


Figure 3.2. Overview of the PCR cloning strategy used to clone KSHV ORFs. PCR cloning was used to clone most of the KSHV ORFs cloned. If a consistent non-silent point mutation was present in a cloned KSHV ORF and in the PCRs of the particular KSHV ORF then this mutation was classified as a coding polymorphism and the KSHV ORF was considered to be successfully cloned.

Problem	Solution
Fail to obtain a PCR product / fail to obtain enough PCR product	<ul style="list-style-type: none"> - Lower annealing temperature of the PCR - Increase the number of cycles of the PCR (Up to 40 cycles) - Increase extension time of the PCR - Add DMSO to the PCR mixture - Change template used for PCR (e.g. Use BC-3 genomic DNA rather than cDNA) - Pool multiple PCRs to obtain enough PCR product
Obtain too many non-specific PCR products	<ul style="list-style-type: none"> - Increase annealing temperature of the PCR
Fail to get colonies containing the pSIN-MCS construct with the expected KSHV ORF	<ul style="list-style-type: none"> - Increase the insert to vector ratio in the ligation reaction - Perform ligation reaction overnight at 4°C or 16°C (Instead of room temperature for 1 hour) - Reduce the number of colonies caused by vector self ligation (caused by single cut plasmid or uncut plasmid). This was performed by increasing the restriction enzyme digestion time of pSIN-MCS before ligation - Perform electroporation rather than chemical transformation

Table 3.2. PCR cloning troubleshooting strategies. These troubleshooting strategies were used when cloning KSHV ORFs into the pSIN-MCS vector. The main difficulty in cloning was obtaining the PCR product although for some relatively large ORFs difficulties were also encountered for the ligation reaction and obtaining colonies containing the pSIN-MCS construct with the cloned KSHV ORF.

ORF	Size of ORF (bp)	Restriction enzymes used	Forward primer used for PCR cloning or vector subcloned from	Reverse primer used for PCR cloning	Cycling conditions for PCR	Origin of cloned gene	Coding polymorphisms present
K2	615	BamHI / NotI	CGCGGATCCATGTGCTGG TTCAAGTTGTGG	AAGGAAAAAAGCGCCGCTT ACTTATCGTGACGTCAGG	40 cycles of 95°C for 1min, 57°C for 1min 72°C for 1min 10sec	BC-3	G85A:E29K
K3	1002	BamHI / NotI	CGCGGATCCATGGAAGAT GAGGATGTTCCCTG	ATAAGAATGCGGCCGCTAAA CACCCACCAACACACAG	40 cycles of 95°C for 1min, 57°C for 1min 72°C for 1min 10sec	BC-3	G570T:Q190H
K6	288	BamHI / NotI	CGCGGATCCATGGCCCC CGTCCACGTTTTTA	AAGGAAAAAAGCGCCGCTT AAGCTATGGCAGGCAGC	40 cycles of 95°C for 1min, 50°C for 45sec 72°C for 1min	BC-3	
ORF 28	309	BamHI / NotI	CGCGGATCCATGAGCATG ACTTCCCCGCTC	ATAAGAATGCGGCCGCTT CACCCGTTCTAATCTGG	40 cycles of 95°C for 1min, 58°C for 1min 72°C for 30sec	BC-3	
K8	720	BamHI / NotI	CGCGGATCCATGCCCCAGA ATGAAGGACATACCTAC	ATAAGAATGCGGCCGCTT ACCTGCTGCAGCTGTC	40 cycles of 95°C for 1min, 54°C for 1min 72°C for 1min	BC-3	
K9	1350	BamHI / NotI	CGCGGATCCATGGACCCA GGCCAAAAGACCCGAAC	AAGGAAAAAAGCGCCGCTT ATTGCATGGCATCCCA	40 cycles of 95°C for 1min, 50°C for 1min 72°C for 2min 30sec	BC-3	
K11.1	492	BamHI / NotI	CGCGGATCCAAAGATGCCT CGCTACACGGAG	ATAAGAATGCGGCCGCTT CTCTGGGCTTTTTTCTAAG	40 cycles of 95°C for 1min, 56°C for 1min 72°C for 45sec	BC-3	
K12	183	BamHI / NotI	CGCGGATCCATGGATAGA GGCTTAACGGTG	ATAAGAATGCGGCCGCTT TGACACTCTTTGGAGGG	40 cycles of 95°C for 1min, 58°C for 1min 72°C for 30sec	BC-3	
ORF 71	567	BamHI / NotI	CGCGGATCCATGGCCACT TACGAGGTTCTC	AAGGAAAAAAGCGCCGCTT ATGGTGTATGGCGATAGTG	40 cycles of 95°C for 1min, 55°C for 1min 72°C for 1min	BC-3	G64A:V22I
ORF 72	774	MluI / NotI	CGCGACGGTATGGCAAC TGCCAAATAAC	AAGGAAAAAAGCGCCGCTT AATAGCTGTCCAGAAT	40 cycles of 95°C for 1min, 55°C for 1min 72°C for 1min	BC-3	G54T:E18D
ORF 73	3489	NotI / SacII / SalI	Derived from pcDNA3.1/His B (Rainbow et al., 1997)	Supplied by Ronit Sarid	N/A	BC-1	
ORF 74	1029	N/A	Sub-cloned from pckSHV vGPCR by Mark Cannon	(Anvanitakis et al., 1997)	N/A	BC-1	
K15-P	1470	BamHI / NotI	CGCGGATCCATGAAGACA CTCATATCTTCTGG	ATAAGAATGCGGCCGCTTAG TTCCTGGAAATAAAACCTC	35 cycles of 95°C for 1min, 58°C for 1min 72°C for 1min 35sec	BCBL-1	

Table 3.3. Summary of the KSHV lentiviral library cloning. The coding polymorphisms shown are those found in BC-3 cells that have not been previously recorded. The known sequences shown are from Russo et al., 1996. Purple, junk DNA; green, restriction enzyme digestion site used for cloning. The vGPCR clone was supplied by Mark Cannon (CR-UK Viral Oncology Group).

3.2.1 The cloning of LANA-1, vGPCR and LAMP

ORF 73, encoding LANA-1, is very large (over 3000 bp) and very GC rich and could potentially have presented difficulties with the PCR cloning strategy. ORF 73 was therefore sub-cloned from a pBluescript SK (+/-) plasmid produced by Juan Funes by sub-cloning LANA-1 from a pcDNA3.1/HisB plasmid supplied by Ronit Sarid (Rainbow et al., 1997). Unfortunately, ORF 73 was cloned into either pBluescript SK (+/-) or pcDNA3.1/HisB using restriction enzyme digestion sites not compatible with the MCS of pSIN-MCS. Therefore, ORF 73 was subcloned from pBluescript SK (+/-) into pSIN-MCS in two steps. Firstly, ORF 73 was inserted into pSIN-MCS from pBluescript using the *NotI* and *SacII* sites thereby removing the woodchuck hepatitis virus post-transcriptional regulatory element (WPRE) from the pSIN-MCS vector (Fig. 3.1). The WPRE from an empty pSIN-MCS vector was then inserted into the ORF 73 pSIN-MCS construct to replace the missing WPRE. This was achieved by using the *SalI* sites in pSIN-MCS followed by sequencing the ORF 73 pSIN-MCS construct to verify that the WPRE was inserted in the correct orientation.

vGPCR (ORF 74) was sub-cloned into the pSIN-MCS vector by Mark Cannon and the provided construct was then sequenced. K15-P, encoding LAMP, was PCR cloned using the pcR3 K15.15 plasmid supplied by Tyson Sharp (University of Nottingham, Nottingham, U.K.) (Sharp et al., 2002) as template DNA. However, a slightly different PCR cloning approach was used in cloning K15-P due to difficulty in obtaining enough PCR product to clone K15-P into the pSIN-MCS vector directly. Instead the PCR product was first cloned into a PCR cloning vector [PCR-Script Amp SK(+) vector (Stratagene)] using blunt end ligation and then sub-cloned into pSIN-MCS using the *BamHI* and *NotI* restriction enzyme digestion sites in the cloned PCR product.

3.3 KSHV gene expression of transfected pSIN-MCS constructs

A gel displaying the various KSHV ORFs cloned into the pSIN-MCS vector is shown in Figure 3.3. A selection of individual pSIN-MCS constructs were transfected into 293T cells to demonstrate that KSHV ORFs cloned into pSIN-MCS were expressed. RT-PCR analysis demonstrated that for the 6 pSIN-MCS constructs tested, KSHV ORF expression was detected in the transfected cells but not in empty vector transfected cells or in samples processed without reverse transcriptase in the cDNA synthesis step (Fig. 3.4A). Western blot analysis detected the expression of vcyclin and LANA-1 in transfected cells with LANA-1 having two bands due to alternative splicing as previously shown (Fig. 3.4B) (Godfrey et al., 2005). Therefore, the KSHV ORFs cloned into pSIN-MCS are expressed with KSHV ORFs being translated as well as transcribed.

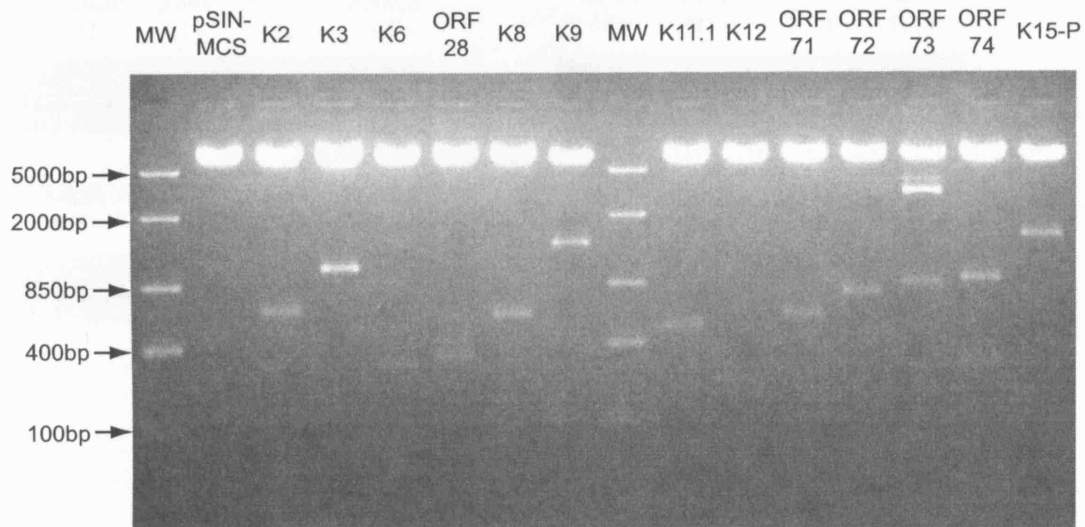
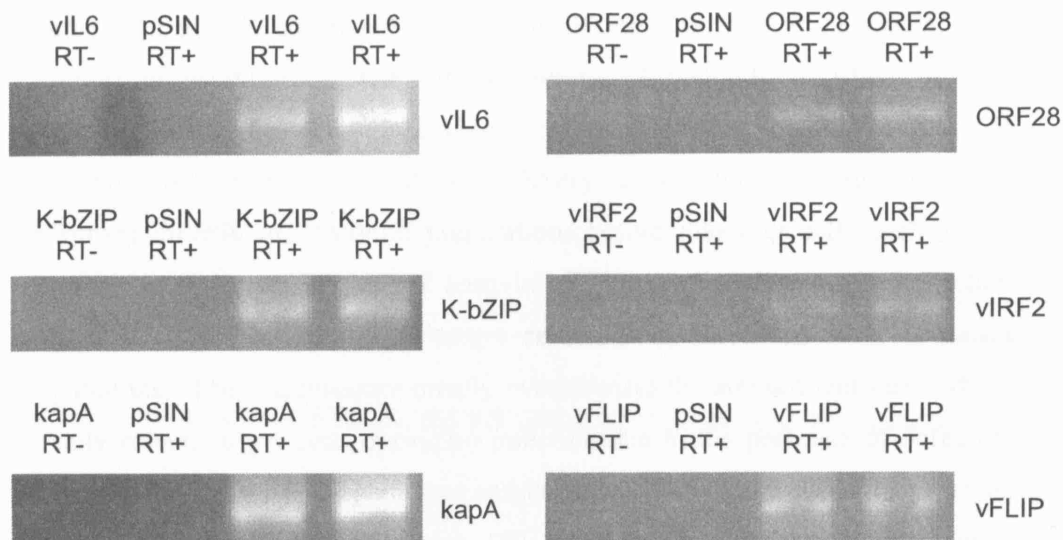


Figure 3.3. Restriction enzyme digestion of pSIN-MCS constructs. ~1 μg of the different pSIN-MCS constructs were digested with *Bam*HI and *Not*I to excise the cloned KSHV ORF from the pSIN-MCS vector. The top band is the empty pSIN-MCS vector and the lower band is the cloned KSHV ORF. ORF 73 and ORF 74 pSIN-MCS constructs have multiple lower bands due to these ORFs having internal *Bam*HI restriction enzyme digestion sites.

A



B

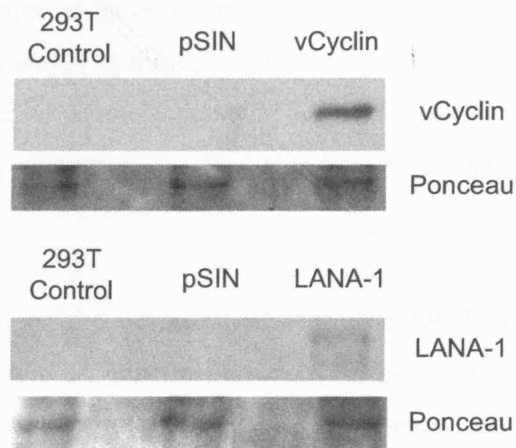


Figure 3.4. Expression of pSIN-MCS constructs in transfected 293T cells. *A*, RT-PCR analysis demonstrating the transcription of individual KSHV ORFs in the transfected 293T cells. The pSIN-MCS constructs transfected into 293T cells are shown on top of the gel images. PCR was carried out on samples processed with (RT+) or without (RT-) reverse transcriptase in the cDNA synthesis step. *B*, Western blot analysis demonstrating the translation of vCyclin and LANA-1 in transfected 293T cells. Ponceau, which stains all protein, was used as a loading control. pSIN, empty vector.

3.4 Quantification of lentiviral infections

To use lentiviral preparations effectively to express foreign genes into host cells it is important to be able to quantify the extent of infection and to be able to titre lentiviral preparations. There are a variety of methods to titre lentiviral preparations, however, the most accurate method is through the quantification of lentiviral DNA in the infected cells (Sastry et al., 2002). Other methods performed directly on lentiviral preparations before infecting cells such as the p24 ELISA or quantification of lentiviral RNA do not determine the actual amount of virus which infects target cells during infections with lentiviral preparations. These techniques greatly overestimate the amount of lentivirus which actually infects target cells during an infection due to the presence of defective virions in the lentiviral preparations and because some of the functional virions present in the lentiviral preparation will not infect target cells due to chance (Naldini et al., 1996; Sastry et al., 2002). Therefore, a lentivirus qPCR titration system was developed to quantify the extent cells were infected through the measurement of the amount of provirus present in cells 48-72 hours after a lentivirus preparation was added to the cells. The titre of lentiviral preparations can be determined by measuring the amount of integrated virus present after a defined amount of virus preparation is added to a known amount of cells (See Material and Methods).

A TaqMan assay system for the detection of lentiviral DNA was developed following a previously described general protocol (PE Biosystems, 2000). For the qPCR amplification of lentiviral DNA qPCR primers and probes were designed using the Primer Express software (Applied Biosystems) against the lentiviral packaging signal (Fig 3.5A). The lentiviral packaging signal was used as this sequence is the same in both pSIN-MCS and pCSGW as well as other lentiviral vectors and, like cloned KSHV genes, the packaging signal is integrated into the host genome in infected cells. A small amplicon size was chosen for qPCR as it promotes high efficiency PCRs. Genomic template DNA from 293T cells infected with a pCSGW lentivirus preparation was used for the optimisation and validation of the lentiviral qPCR. To confirm that the qPCR primers amplified the correct sequence a standard PCR was performed. The PCR product

was the correct size and its identity was confirmed by performing an *RsaI* digestion (Fig 3.5A).

Using standard TaqMan cycling conditions the concentrations of primers and probes were optimised to give the most sensitive [the lowest Ct (threshold cycle)] and most cost effective assay (Fig 3.5B and C). The optimised assay could be used to detect lentiviral DNA at a wide range of template DNA concentrations with no inhibition of the assay even when relatively high genomic DNA concentrations were used (Fig 3.5D). Lentiviral and *GAPDH* standards were produced using linearized pSIN-MCS vector and a pcDNA3.1/V5-His-TOPO *GAPDH* PCR product vector respectively. The *GAPDH* qPCR was previously optimised (Bourboulia et al., 2004). Standards were produced to be able to quantify the absolute number of integrated viruses in cells, without standards only relative levels of infection could be determined. Standard curves gave the expected linear plot with a slope close to the ideal slope of -3.33 and they had an intercept under 40 meaning potentially the assay could detect as low as one lentiviral- or *GAPDH*-containing DNA molecule per PCR reaction (Fig 3.5D). In summary, by performing qPCR on genomic DNA for the lentiviral packaging signal, to detect provirus, and *GAPDH*, to quantify cell number, the extent of infection can be measured and therefore the titre of lentiviral preparations can also be deduced.

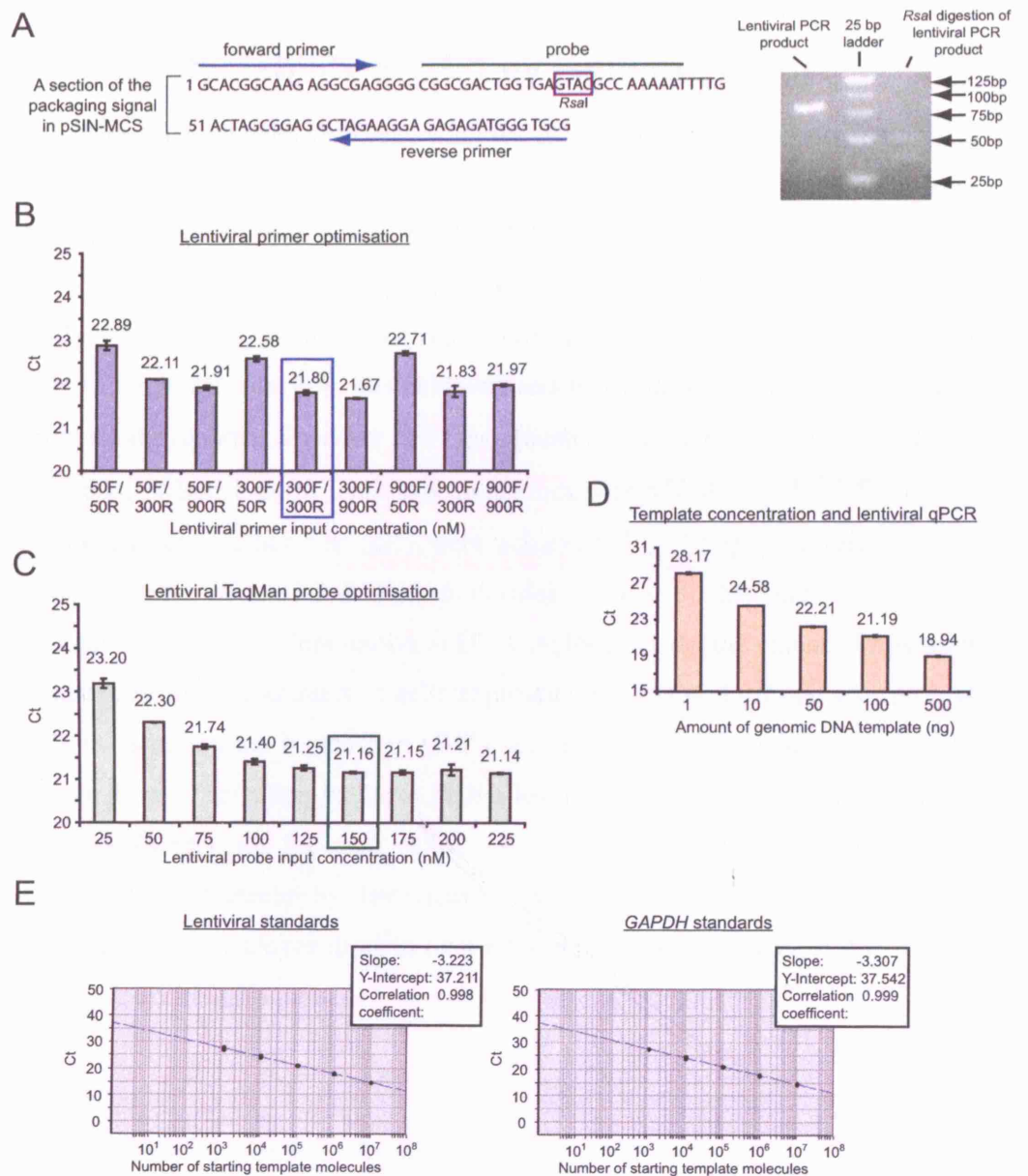


Figure 3.5. Development of a qPCR based lentivirus detection system. *A*, the lentiviral primers and probe used for qPCR and the section of lentiviral packaging signal amplified is shown. Standard PCR was performed using pCSGW infected 293T genomic DNA template and the lentiviral qPCR primers. The PCR product obtained and its *RsaI* digestion products run on an agarose gel is shown. *B*, optimisation of the concentration of lentiviral primers for qPCR. The concentration of lentiviral primers chosen [300 nM forward primer (F), 300 nM reverse primer (R)] was selected as they had the lowest Ct while using reasonable amounts of primers. The probe concentration used during this optimisation was 225 nM. *C*, optimisation of the concentration of lentiviral TaqMan probe for qPCR. The probe concentration chosen (150 nM) was the lowest concentration of probe necessary to achieve the lowest Ct while using the optimal primer concentration. *D*, different amounts of the same pCSGW infected 293T genomic DNA were analysed using the optimised lentiviral qPCR and the corresponding Ct values obtained are shown. *E*, standard curves obtained when the lentiviral and *GAPDH* plasmid standards were analysed by qPCR using the lentiviral or *GAPDH* qPCR set-ups respectively. The *GAPDH* qPCR set-up used was previously described (Bourbouliou et al., 2004). Samples were run in triplicate except for the standard curve where they were run in duplicate. For the optimisation of the lentiviral qPCR genomic template DNA from 293T cells infected with a pCSGW lentivirus preparation was used. Ct, threshold cycle. Columns, mean; bars, SE.

3.5 The infectability of LEC by lentiviruses

LEC were infected with different volumes of pCSGW lentivirus preparation to assess the ability of LEC to be infected by lentivirus. After 72 hours LEC were harvested and were subjected to qPCR and FACS to assess the extent of infection and to determine the percentage of cells expressing GFP respectively. It was found that as more pCSGW lentivirus preparation was added to cells higher levels of lentiviral infection was achieved and this followed a linear relationship as previously reported for other cell types (Sastry et al., 2002; Lizee et al., 2003) (Fig 3.6A). When 1 ml of lentivirus preparation was added to 1×10^5 LEC nearly 10 lentiviral copies per cell (c/c) were achieved (Fig 3.6A). c/c refers to the average number of lentiviral DNA molecules per cell in that population; some cells may have more or less lentiviral DNA molecules. As the extent of infection increased, so did the amount of cells expressing GFP (Fig 3.6B and C). At low levels of infection the increase in GFP expression appeared to increase linearly with the level of infection, while at higher levels of infection a plateau is reached as previously reported for other cell types (Lizee et al., 2003) (Fig 3.6C). LEC were readily infectable by lentiviruses with 1 ml of lentivirus preparation achieving nearly 10 c/c resulting in over 80% of LEC expressing GFP (Fig 3.6C).

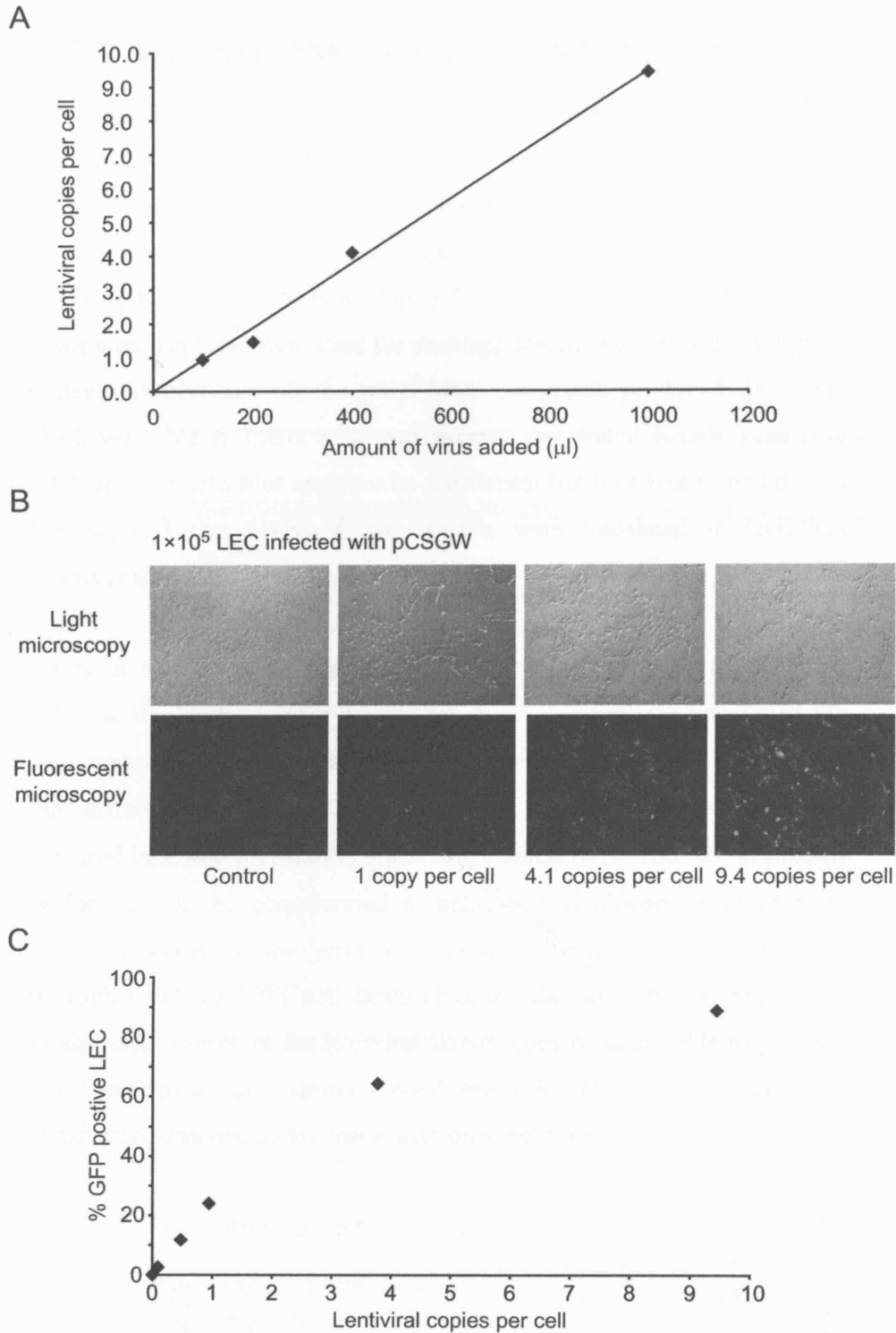


Figure 3.6. Assessing the infectability of LEC by lentiviruses. *A*, the lentiviral copies per cell (*c/c*) achieved when different amounts of pCSGW lentiviral preparation were added to 1×10^5 LEC. *B*, LEC infected with different amounts of pCSGW lentiviral preparation were visualised under a fluorescent microscope. *C*, correlation between percentage GFP positive cells determined by flow cytometry and *c/c* determined by qPCR on genomic DNA from the same population of cells. Experiments were performed 72h after infection.

3.6 KSHV gene expression in lentivirus infected LEC

Lentiviral preparations were produced for the various KSHV pSIN-MCS constructs and used to infect LEC. 1×10^5 LEC were infected with 1 ml of the different lentiviral preparations (except for vGPCR where a concentrated lentivirus preparation was used) and cells were harvested to check for the individual KSHV gene expression (Fig 3.7A). The supernatant from these experiments were kept and were used for an Ang2 screen (Section 4.2). RT-PCR analysis demonstrated that all the pSIN-MCS constructs produced functional virus which was able to infect LEC and express the cloned KSHV gene (Fig 3.7A). IFA and Western blot analyses on a different batch of lentivirus infected LEC demonstrated that LANA-1 and vcyclin were translated in lentivirus infected cells (Fig 3.7B).

Interestingly, it was observed that despite all the lentiviral preparations being produced in a similar way there was a significant variation in the c/c in the infections, indicating different amounts of functional lentiviruses were produced from the different pSIN-MCS constructs (Fig 3.7A). 1 ml of vGPCR unconcentrated lentiviral preparation gave 0.5 c/c when 1×10^5 LEC were infected and therefore had to be concentrated to achieve a significant level of LEC infection. The relatively low yield of vGPCR lentivirus may be due to the relatively high levels of 293T cell death observed during lentivirus production (data not shown). Therefore the lentiviral library constructs are able to produce functional lentiviruses and express cloned genes in lentivirus infected LEC although different lentiviruses are made with different levels of efficiency.

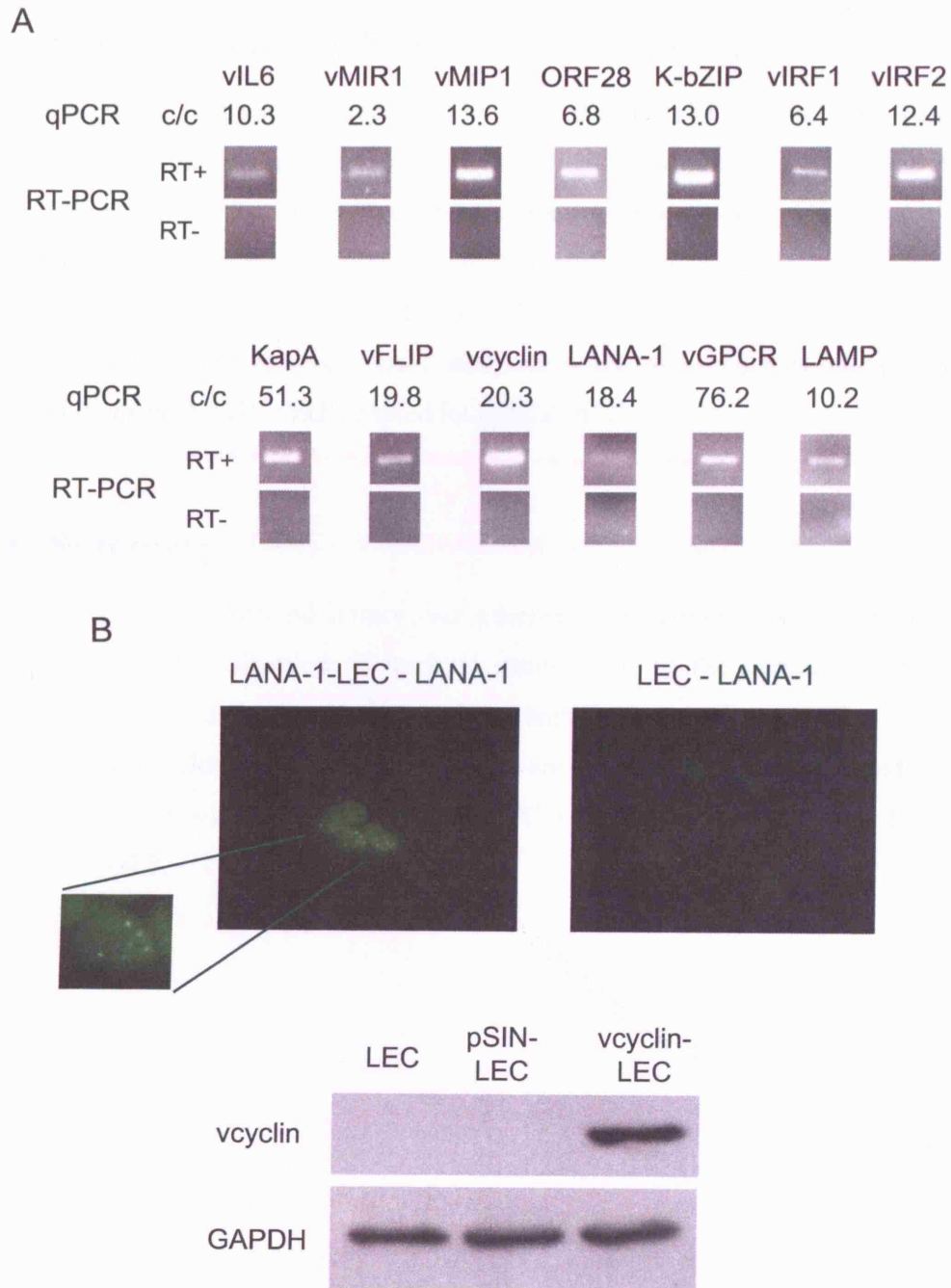


Figure 3.7. Expression of the pSIN-MCS constructs in lentivirus infected LEC. *A*, RT-PCR analysis of LEC infected with different lentivirus preparations containing pSIN-MCS constructs with KSHV ORF expression being detected in lentivirus infected LEC. Samples were processed with (RT+) or without (RT-) reverse transcriptase in the cDNA synthesis step. The c/c present in the different lentivirus infected LEC are shown. *B*, IFA for LANA-1 and Western blot analysis for vcyclin, in LEC or lentivirus infected LEC. LANA-1 positive cells had typical nuclear stippling, as previously shown (Rainbow et al., 1997; Kellam et al., 1997). Magnification, $\times 400$. A LANA-1 positive nucleus is shown enlarged from the original image. For IFA, LANA-1 infected LEC had 20 c/c, for Western blotting, vcyclin and empty vector (pSIN) infected LEC had 10 c/c. For Western blot analysis GAPDH was used as a loading control.

3.7 Expansion of the KSHV lentiviral library

The library was continuously expanded by other members of the lab, often with my help, after the initial development and validation of the 13 gene selected KSHV lentiviral library. Therefore when it came to perform the *Angptl2* screen, at a later point in my PhD, the screen was performed using 24 pSIN-MCS constructs (Section 5.2). Now a total of 31 KSHV genes as well as each of the KSHV encoded miRNA have been cloned into pSIN-MCS and it is planned to have all 90 of the KSHV ORFs cloned into pSIN-MCS.

3.8 Summary

A selected KSHV lentiviral library was generated containing most of KSHV's latent genes and a selection of its lytic genes. All of the lentiviral library constructs were found to produce functional lentivirus which could infect LEC and express the cloned KSHV gene. LEC were found to be easily infected by lentiviruses with ~10 c/c of pCSGW in LEC resulting in over 80% of LEC expressing GFP.

Chapter 4. KSHV-encoded interleukin-6 and G-protein-coupled receptor regulate angiopoietin-2 expression in lymphatic endothelial cells

Ang2 is a secreted angiogenic and lymphangiogenic molecule regulated by KSHV (Maisonpierre et al., 1997; Gale et al., 2002; Lobov et al., 2002; Wang et al., 2004a). Through the use of the selected KSHV lentiviral library the primary aim of this chapter was to investigate how KSHV regulated Ang2. GEM analysis was used to investigate how other angiopoietins and other angiogenic factors were regulated by KSHV and how this may affect the role of Ang2 in KS. Matrigel tube formation studies were performed in an attempt to investigate the functional role of Ang2 in KS.

By acting as an antagonist to the Tie2 receptor, Ang2 is critical for postnatal angiogenesis and acts to destabilise and prime endothelial cells to other proangiogenic factors such as VEGFA (Maisonpierre et al., 1997; Gale et al., 2002; Lobov et al., 2002). Ang2 is over-expressed in many cancers and ectopic expression of Ang2 increases tumour angiogenesis and tumour growth (Ahmad et al., 2001; Tait and Jones, 2004). Ang2 also plays important roles in lymphangiogenesis and inflammation (Gale et al., 2002; Fiedler et al., 2006).

Earlier work from our laboratory demonstrated through GEM analysis that *Ang2* mRNA was up-regulated in KS lesions (Wang et al., 2004a). Furthermore, it was shown that Ang2 levels increased in the plasma of individuals with KS, correlated with the number of lesions and declined during antiretroviral therapy when KS resolved (Wang et al., 2004a). This work supported earlier work demonstrating through *in situ* hybridisation that *Ang2* mRNA was present in KS lesions (Brown et al., 2000). How KSHV affects angiogenesis and how the KS tumour environment responds to angiogenic factors may depend on Ang2 up-regulation by KSHV in KS. In addition, Ang2 could play a critical role in KS by contributing to KSHV-infected endothelial cell proliferation and to the tumour-associated inflammation. Here I investigate the mechanism(s) by which KSHV up-regulates Ang2.

4.1 Ang2 expression in Kaposi sarcoma and KLEC

Previous studies demonstrated that *Ang2* mRNA is present in KS lesions and is up-regulated in KS compared to normal tissue, however, the presence of Ang2 protein in KS lesions had not been shown (Brown et al., 2000; Wang et al., 2004a). Immunohistochemistry was performed to investigate whether Ang2 protein is present in KS and, therefore, relevant to the pathogenesis of this neoplasm (Fig. 4.1). Immunostaining for Ang2 was observed in all the KS lesions studied and Ang2 staining was particularly strong in patch stage lesions showing areas of intense staining.

The KS spindle cells have a GEM profile that is closest to that of LEC making KSHV-infected LEC (KLEC) a relevant *in vitro* model to study KS pathogenesis (Wang et al., 2004a). To confirm that KLEC up-regulated Ang2 (Wang et al., 2004a), a GFP –expressing recombinant KSHV (Vieira et al., 2001) was used to infect LEC (Fig. 4.2A). KSHV infection of LEC typically resulted in about 35% of LEC expressing GFP 3 to 4 days after infection (Fig. 4.2A). It is likely that the actual percentage of LEC infected with KSHV is higher than this due to the presence of wild type KSHV in the viral preparations resulting in non-fluorescent KLEC that are not detected by flow cytometry.

Using an Ang2 ELISA, the KSHV infection of LEC was found to increase Ang2 secretion in accordance with a previous study (Wang et al., 2004a). Western blot analysis showed that intracellular Ang2 protein was also up-regulated in KLEC compared with LEC (Fig. 4.2B). The two distinct bands seen in the Ang2 Western blot are most likely due to alternative splice variants previously reported (Kim et al., 2000b). GFP-positive KLEC isolated by cell sorting up-regulated *Ang2* mRNA determined by performing qRT-PCR analysis for *Ang2* (Fig. 4.2C). This demonstrated that LEC infected with KSHV up-regulated *Ang2* expression.

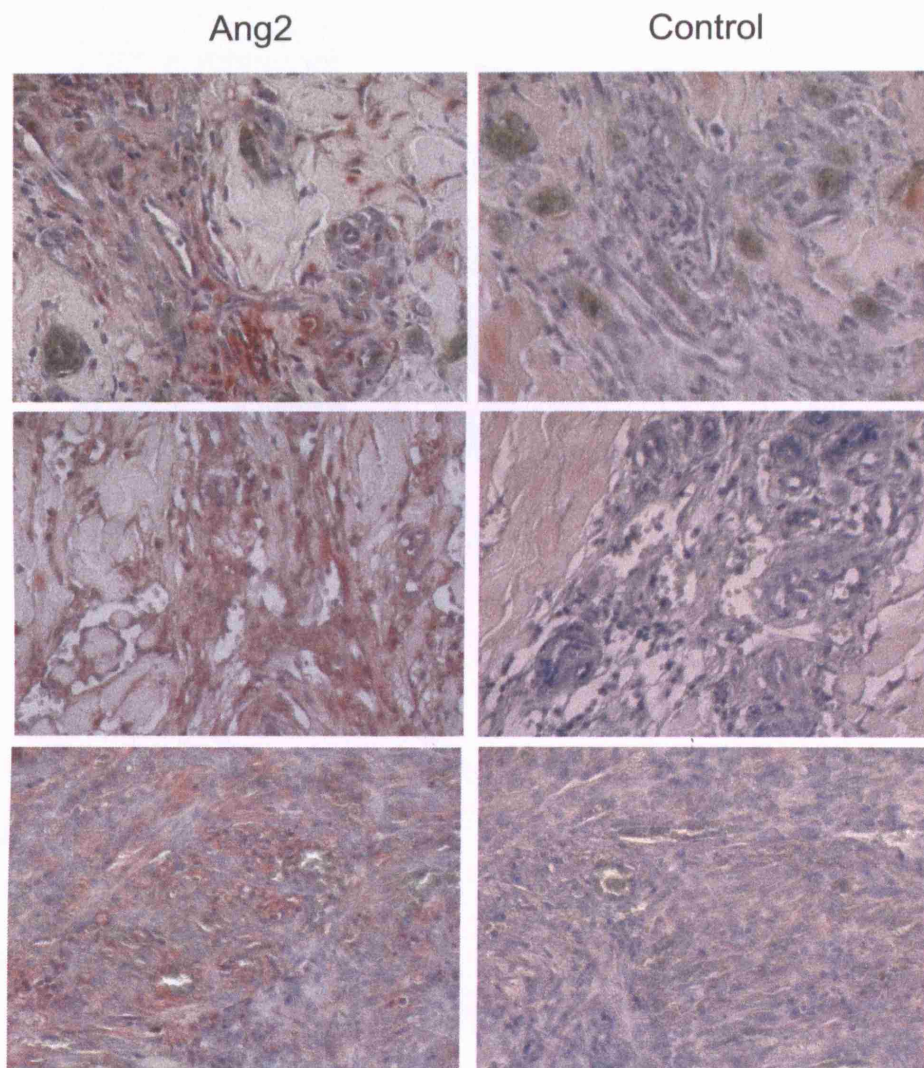


Figure 4.1. Ang2 expression in KS. Ang2 was detected in patch (*top and middle*) and nodular (*bottom*) lesions of KS by immunohistochemistry. Isotype-matched control antibody (*right*) was used to validate the specificity of the anti-Ang2 monoclonal antibody (*left*). Secondary alkaline phosphatase-conjugated antibodies were detected with Vector Red (*red*). Cell nuclei were counterstained with haematoxylin (*blue*). Magnification, $\times 200$.

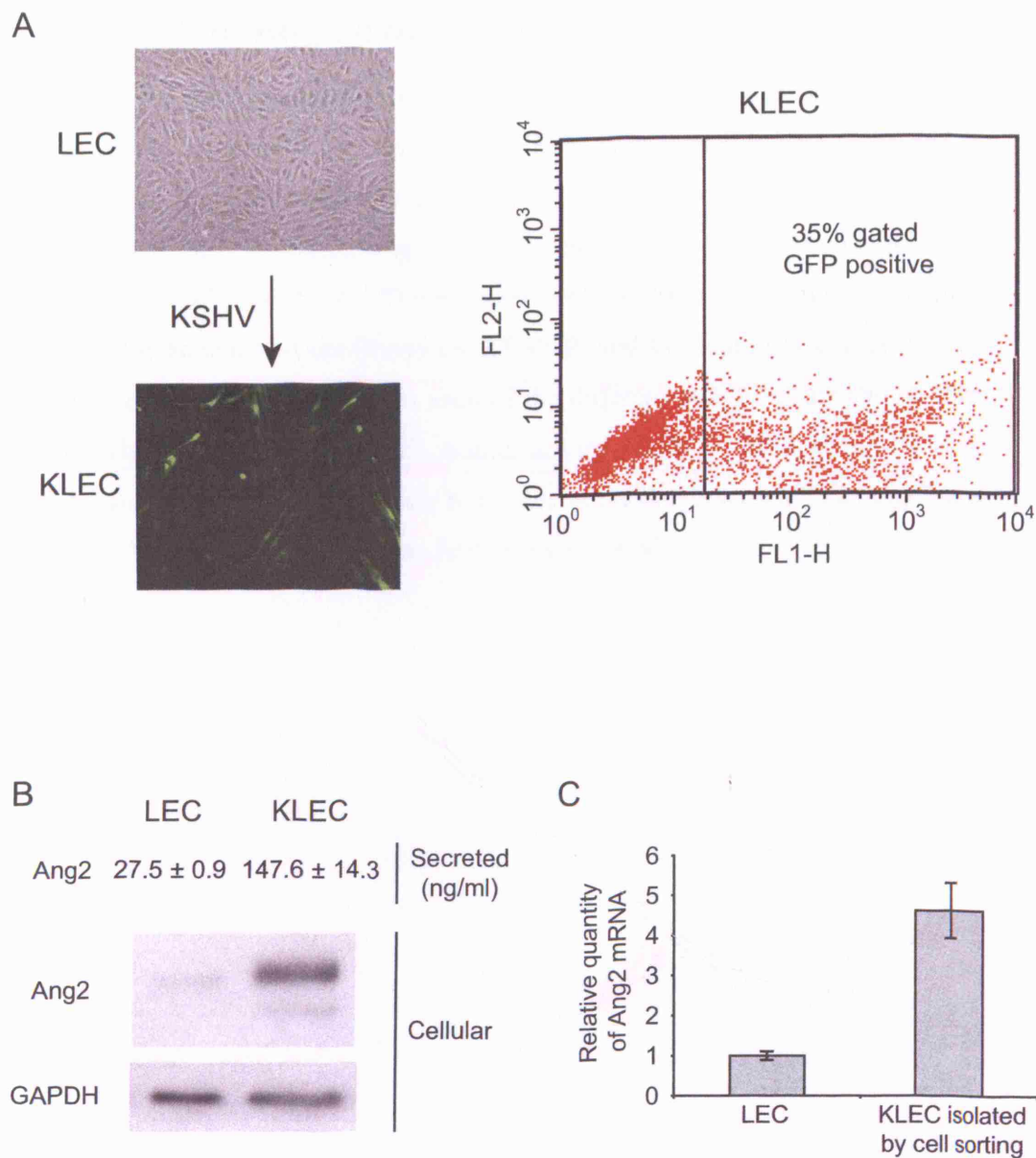


Figure 4.2. Ang2 expression in LEC and KLEC. *A*, LEC and LEC infected with a GFP-expressing recombinant KSHV (KLEC). A flow cytometry dot plot of KLEC 3 d p.i. is shown and 35% of KLEC were found to express GFP from gates made from uninfected LEC. *B*, concentrations of Ang2 (3 d p.i.) in the media (*Secreted*) of LEC and KLEC and the relative amounts of Ang2 total protein in the cell lysates (*Cellular*) of such cells detected by Western blotting. Ang2 levels in culture medium were assayed in duplicate and were measured using an Ang2 ELISA. *C*, relative Ang2 mRNA levels for LEC versus GFP-expressing KLEC (4 d p.i. isolated by cell sorting) determined by qRT-PCR. mRNA levels were normalized to LEC, and assays were done in quadruplicate. *Columns*, mean; *bars*, SE.

4.2 KSHV library screen identified genes that up-regulate Ang2 expression

A screen for the up-regulation of Ang2 was performed using the selected KSHV lentiviral library (Fig. 4.3). Ang2 levels in the culture media were measured 72 hours after infection with the different lentiviral preparations of the library. vGPCR and vIL6 increased Ang2 secretion, compared to empty vector (pSIN) or uninfected LEC (Fig. 4.3A). The expression of the different lentiviral constructs used in the screen was confirmed by RT-PCR, and the lentiviral copies per cell (c/c), as determined by qPCR, in each of the different infections are shown (Fig. 4.3). These RT-PCR and qPCR results are the same as those shown in (Fig. 3.7A), and shown here due to their relevance in the Ang2 screen. The regulation of Ang2 by vIL6 and vGPCR was further investigated.

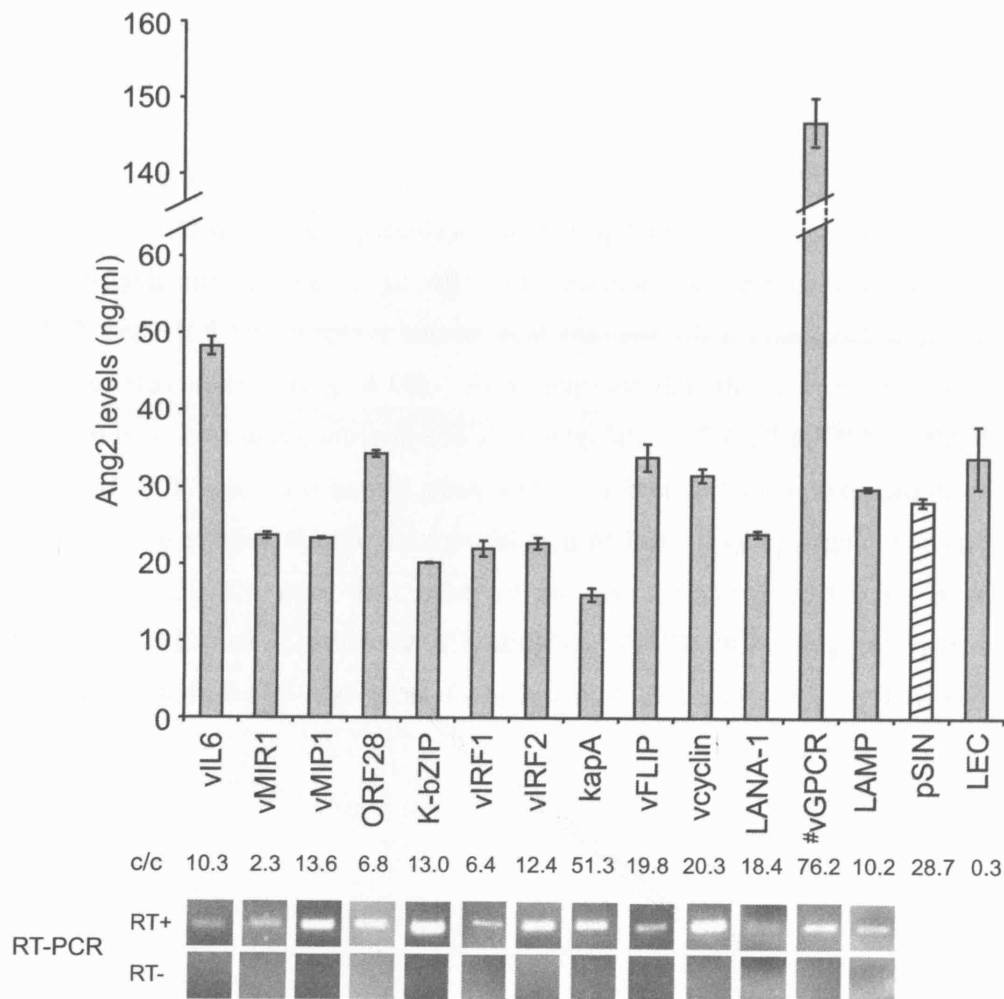


Figure 4.3. The KSHV lentiviral library screen for Ang2. Ang2 levels in the culture media of lentiviral infected LEC. Approximately 1×10^5 LEC were infected with 1 ml of lentivirus preparations encoding particular KSHV genes, and culture media of infected cells were collected 72h p.i. to determine Ang2 levels. Empty vector (pSIN) Ang2 levels were used as a guide for comparison. The lentiviral copies per cell (c/c) present in the infected LEC are shown along with RT-PCR analysis confirming the expression of individual KSHV genes in these cells. #, 0.6×10^5 LEC were infected with 1 ml of concentrated lentiviral preparation. PCR was performed using samples processed with (RT+) or without (RT-) reverse transcriptase in the cDNA synthesis step. Ang2 levels in culture media were assayed in duplicate and measured using an Ang2 ELISA. Columns, mean; bars, SE.

4.3 vGPCR and vIL6 up-regulate Ang2

Increasing amounts of vGPCR and vIL6 were delivered to LEC, and the cell lysates were subjected to Western blot analysis to confirm that vGPCR and vIL6 up-regulate Ang2 (Fig. 4.4A). Ang2 total cellular protein was up-regulated by both vGPCR and vIL6, with vIL6 strongly up-regulating Ang2 total protein in LEC even at low levels of expression. At about 9 c/c, vGPCR and vIL6 expressing LEC yielded comparable levels of Ang2 secretion (Fig. 4.4B). qRT-PCR analysis showed that *Ang2* mRNA expression was up-regulated by both vGPCR and vIL6 and displays similar fold changes when compared with the Ang2-secreted protein (Fig. 4.4B). This indicates that the increase in Ang2 secretion is at least partly attributed to an up-regulation of *Ang2* mRNA by these genes. vGPCR and vIL6 have a weak additive effect in their up-regulation of Ang2; when expressed together in a population of LEC, they up-regulated Ang2 total protein slightly more than either of the genes alone (Fig. 4.4C). Both vGPCR and vIL6 were expressed in KLEC (Fig. 4.4D), further suggesting that both contribute to the up-regulation of Ang2 upon KSHV infection (Fig. 4.2B and C).

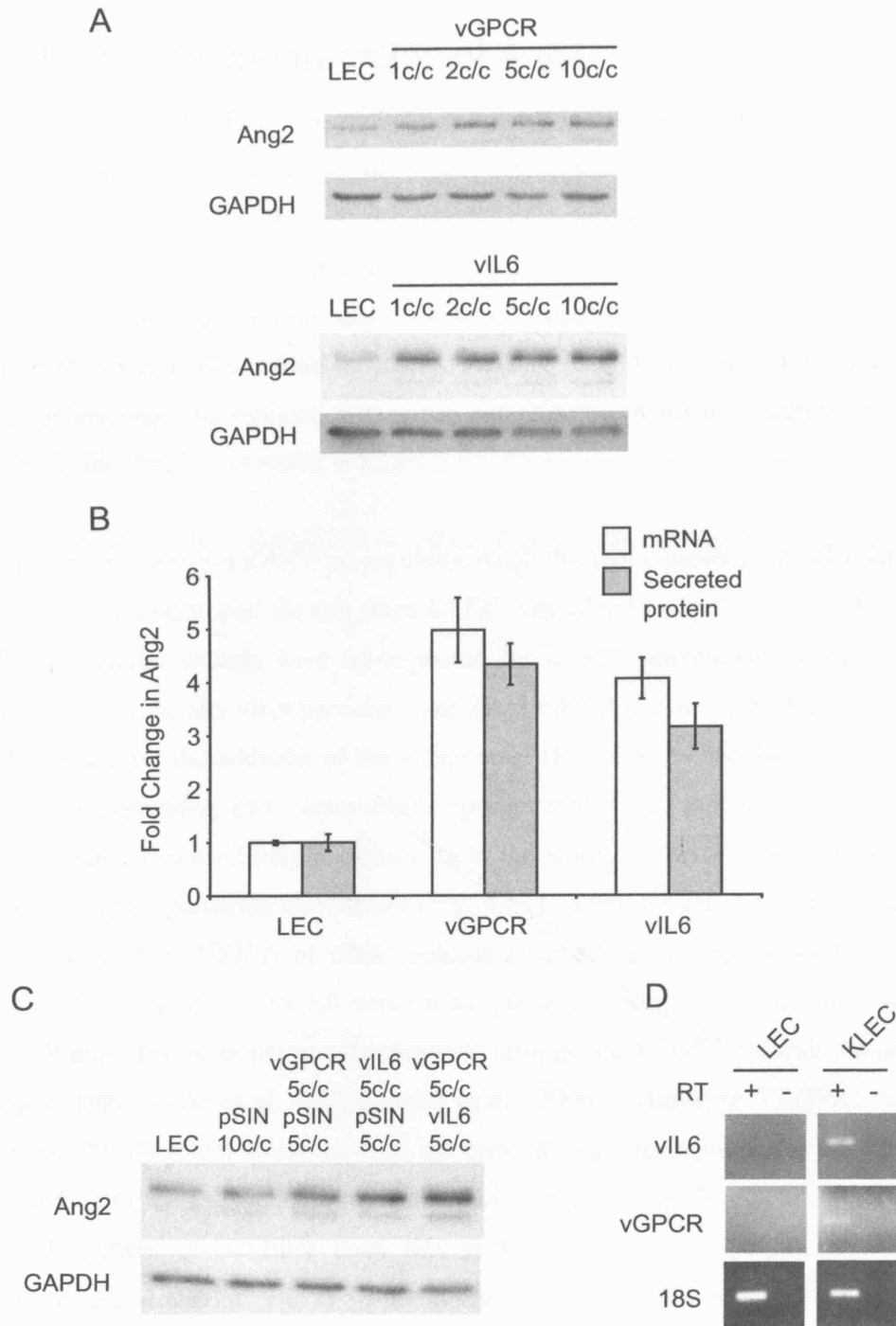
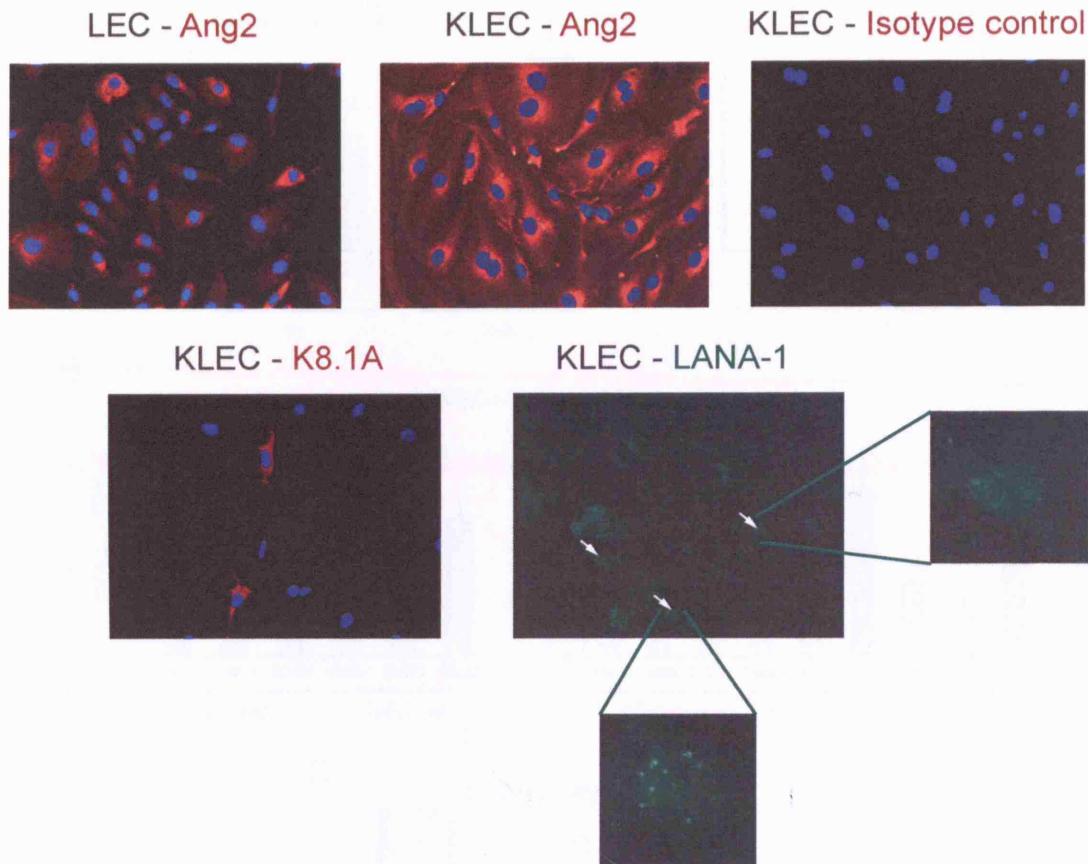


Figure 4.4. vGPCR and vIL6 up-regulate Ang2 expression. *A*, cell lysates of LEC infected (48–72 h p.i.) with increasing amounts of vIL6 or vGPCR lentiviral constructs were subjected to Western blot analysis for Ang2 and GAPDH. *B*, relative *Ang2* mRNA and secreted protein levels in the culture media of vIL6 and vGPCR expressing LEC. About nine copies per cell were present in infected cells. mRNA levels determined by qRT-PCR and secreted levels determined by ELISA were normalized to LEC. Experiment was done in duplicate. *C*, cell lysates of LEC infected with different combinations of pSIN, vIL6, and vGPCR encoding lentiviruses were subjected to Western blot analysis for Ang2 and GAPDH. *D*, expression of vIL6 and vGPCR in KLEC (72 h p.i.) shown by RT-PCR analysis. *18S* was used as a housekeeping control gene. *Columns*, mean; *bars*, SE.

4.4 Paracrine up-regulation of Ang2

To investigate further how lytic replication and vIL6 and vGPCR in particular are involved in the up-regulation of Ang2, immunofluorescence assays were performed (Fig. 4.5). Both LEC and KLEC expressed Ang2, with Ang2 immunoreactivity being higher in the latter. All cells in KLEC culture expressed similar levels of Ang2 despite only a small percentage of cells (~1%) undergoing lytic replication as determined by K8.1A staining (Fig. 4.5). This suggests that cells undergoing lytic replication may use paracrine mechanisms to contribute to the increased Ang2 expression in KLEC.

To investigate whether KSHV up-regulates Ang2 through a paracrine mechanism, supernatant (conditioned media) from KLEC was added to LEC. *Ang2* mRNA and intracellular protein were up-regulated by KLEC-supernatant (which was filtered to remove any virus particles), and *Ang2* mRNA was up-regulated as soon as 8 hours after the addition of the supernatant (Fig. 4.6A). Similarly, vGPCR and vIL6 expressing LEC supernatants up-regulated *Ang2*, indicating that both vGPCR and vIL6 are likely to contribute to the ability of KSHV to up-regulate *Ang2* through a paracrine mechanism (Fig. 4.6A). Interestingly, this mechanism does not involve VEGFA or other molecules signalling through VEGFR1 and VEGFR2 even though VEGFA was shown previously to up-regulate *Ang2*, and vGPCR and vIL6 were previously shown to up-regulate VEGFA (Mandriota and Pepper, 1998; Aoki et al., 1999; Sodhi et al., 2000). Blocking VEGFR1 and VEGFR2 by chemical inhibition does not prevent *Ang2* up-regulation by KSHV-infected or vIL6- and vGPCR-expressing LEC (Fig. 4.6B). The VEGFR1 and VEGFR2 chemical inhibitor used was previously shown to be an effective inhibitor in endothelial cells at 50 μ M (Zhao et al., 2004; Jin et al., 2005). The VEGFR1 and VEGFR2 inhibitor was not toxic to LEC because the number of live cells did not significantly change in the presence of the inhibitor compared to control samples (Fig. 4.6C).



Molecule stained	% KLEC positive
K8.1A	0.59 ± 0.24
LANA-1	13.2 ± 1.83

Figure 4.5. Ang2 staining in LEC and KLEC. Immunofluorescence assay for Ang2, K8.1A and LANA-1 in LEC and KLEC. The percentage of KLEC that are K8.1A or LANA-1 positive from the same infection is shown. LANA-1-positive cells had typical nuclear stippling. All KLEC expressed Ang2, and no LEC were stained positive for K8.1A or LANA-1. The isotype-matched control antibody was used to validate the specificity of the anti-Ang2 monoclonal antibody. DAPI was used for nuclear staining (*blue*). Magnification, $\times 200$. LANA-1 positive nuclei are indicated with arrows. Two LANA-1 positive nuclei are shown enlarged from the original image. Mean and standard deviation are used for the values in the table.

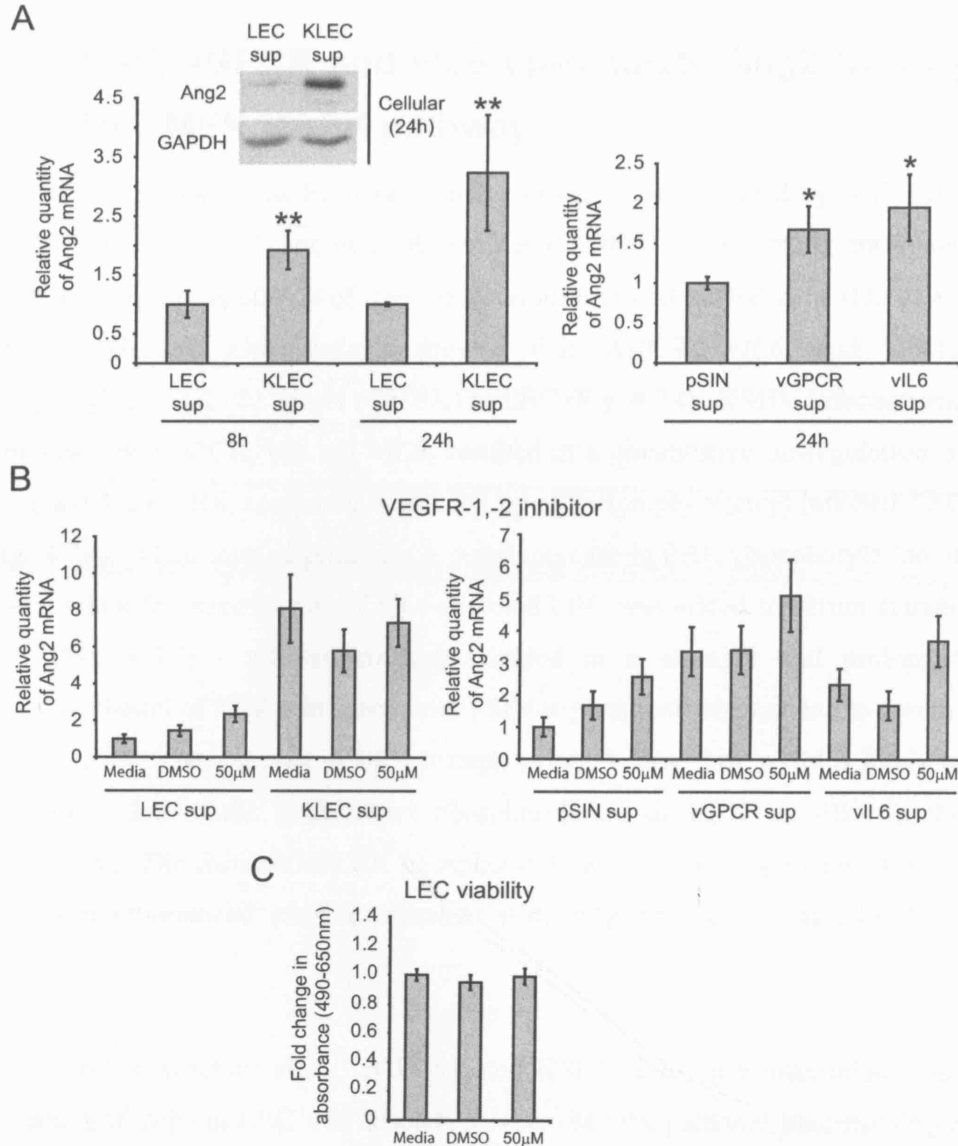


Figure 4.6. Ang2 is up-regulated through a paracrine mechanism. *A*, filtered supernatant (sup) (conditioned media) from LEC, KLEC, and LEC infected with pSIN, vGPCR, or vIL6 were added to uninfected LEC. Eight or 24 h later, RNA or cell lysates were collected and subjected to qRT-PCR or Western blot analysis for Ang2 and GAPDH. The Student's *t* test was used to assess the significance of differences between LEC incubated with the supernatant from vGPCR-expressing LEC, vIL6-expressing LEC or KLEC compared with LEC incubated with the supernatant from LEC or pSIN-infected LEC. *, $p < 0.05$; **, $p < 0.01$. *B*, effect of VEGFR-1 and VEGFR-2 inhibitor on the paracrine up-regulation of Ang2 transcription. Filtered supernatants from LEC and KSHV- or lentiviral-infected LEC were either added directly to LEC or were first mixed with DMSO or DMSO with 50 μ M VEGFR-1 and VEGFR-2 inhibitor. Cells were incubated for 18 h with the supernatant, after which their RNA was harvested, and two-step qRT-PCR analysis was performed. LEC were preincubated with either media, media containing inhibitor or DMSO for 5 h before the addition of the supernatant. *C*, LEC viability when LEC were exposed to the VEGFR-1 and VEGFR-2 inhibitor. LEC were incubated for 24 h with either media or media with DMSO or 50 μ M VEGFR-1 and VEGFR-2 inhibitor. The CellTiter 96® Aqueous One Solution Cell Proliferation Assay reagent was used to detect viable cells. The absorbance measured is directly proportional to the number of live cells in the well. Samples were normalised to LEC exposed to media. Expression of Ang2 mRNA was normalized to LEC exposed to either LEC or pSIN-supernatant from the same time point. Experiments were performed in triplicate. All lentiviral infected cells had 10 c/c. Columns, mean; bars, SE.

4.5 KSHV, vGPCR and vIL6 up-regulate Ang2 by way of the MEK MAPK pathway

The MAPK pathway has been previously shown to be activated by both vIL6 (Hideshima et al., 2000) and vGPCR (Smit et al., 2002; Cannon et al., 2003) and is involved in the regulation of *Ang2* transcription in endothelial cells (Oh et al., 1999). Western blot analysis showed that vGPCR, vIL6, and KSHV phosphorylate ERK (the target of MEK) in LEC (Fig. 4.7A). KSHV infection and expression of vGPCR, but not vIL6, resulted in a constitutive up-regulation of phosphorylated ERK compared with LEC or pSIN (empty vector) infected LEC (Fig. 4.7A). vIL6 instead promotes a pulse increase in ERK phosphorylation as shown when the supernatant of vIL6-infected LEC was added to serum-starved LEC (Fig. 4.7A). vIL6-supernatant resulted in a stronger and prolonged phosphorylation of ERK compared with pSIN-supernatant when added to serum-starved LEC. The increase in ERK phosphorylation caused by pSIN is likely to be mainly due to the background phosphorylation of ERK by FBS in the supernatant. The increase in ERK phosphorylation by vIL6 compared with pSIN was more pronounced when supernatant with only 0.5% FBS was used (Fig. 4.7B).

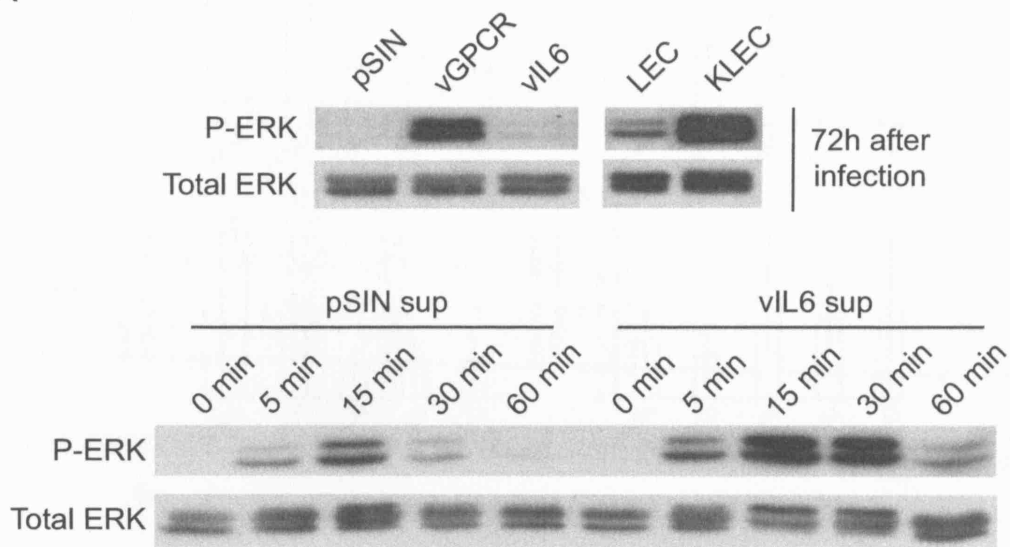
To investigate whether vIL6-, vGPCR-, and KSHV-induced transcriptional up-regulation of *Ang2* in LEC was dependent on the MAPK pathway, pharmacologic inhibition studies were performed. In initial studies, vGPCR- and vIL6-expressing LEC were incubated with different concentrations of the MEK-specific inhibitor PD98059 or the JNK-specific inhibitor SP600125, after which RNA was harvested and analyzed by qRT-PCR (Fig. 4.8B). *Ang2* mRNA in vGPCR-expressing LEC was significantly down-regulated by PD98059 to <25% of that present in the DMSO control. *Ang2* mRNA levels in vIL6-expressing LEC were also decreased by PD98059. In contrast, the JNK inhibitor SP600125 did not inhibit *Ang2* expression in either vGPCR- or vIL6-expressing LEC.

To investigate further whether vGPCR and vIL6 up-regulate *Ang2* through the MEK MAPK pathway, the pharmacologic inhibition studies were repeated using

a different and more potent MEK-specific inhibitor, U0126, and were extended to include pSIN–infected cells and LEC infected with both vGPCR- and vIL6-encoding lentiviruses (Fig. 4.8B). U0126 significantly inhibited the up-regulation of *Ang2* mRNA in vGPCR- and vIL6-expressing LEC and reduced the *Ang2* mRNA level to that observed in pSIN–infected cells. U0126 was able to inhibit *Ang2* transcription to a similar degree in LEC infected with both vGPCR and vIL6, which showed further that both genes up-regulate *Ang2* through the MEK MAPK pathway. Finally, U0126 was also able to significantly inhibit the up-regulation of *Ang2* in KLEC (Fig. 4.8B). This further supports the finding that KSHV up-regulates *Ang2*, at least in part, by the effect of vGPCR and vIL6 acting on the MEK MAPK pathway. In addition, U0126 inhibited *Ang2* expression in pSIN-infected cells suggesting that the MEK MAPK pathway regulates endogenous levels of *Ang2* in uninfected LEC.

The MEK inhibitors PD98059 and U0126 or the JNK inhibitor SP600125 used in the pharmacologic inhibition studies (Fig. 4.8) did not to affect LEC viability at the highest concentration used (Fig. 4.9A). PD98059 (Vinci et al., 2004; Trevisi et al., 2004; Kanda et al., 2005; Miho et al., 2005) and SP600125 (Miho et al., 2005; Wu et al., 2006) have been previously used to inhibit MEK or JNK respectively in endothelial cells. U0126 inhibited ERK phosphorylation in KLEC (Fig. 4.9B) and this is in accordance with previous studies using U0126 in endothelial cells to inhibit the MEK MAPK pathway (Vinci et al., 2004; Sharma-Walia et al., 2005).

A



B

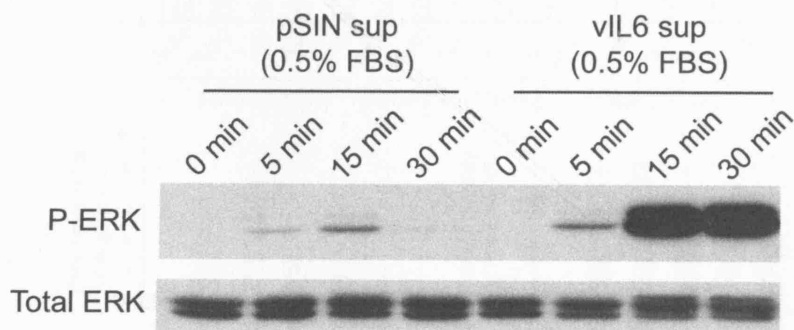


Figure 4.7. ERK activation in LEC by KSHV, vGPCR and vIL6. *A*, LEC were infected with lentiviruses or KSHV and were left for 72 h, or LEC were serum starved for 8 h, after which they were exposed to the supernatant (sup) from pSIN (10 c/c) or vIL6 (10 c/c)-infected LEC for different time periods. Cell lysates were then collected and subjected to Western blot analysis for phosphorylated ERK1/2 (P-ERK) and total ERK1/2. *B*, LEC were serum starved for 8h after which they were exposed for different time periods to supernatant with 0.5% FBS from pSIN (10 c/c) or vIL6 (10 c/c) expressing LEC. Cell lysates were collected and then processed as in (*A*).

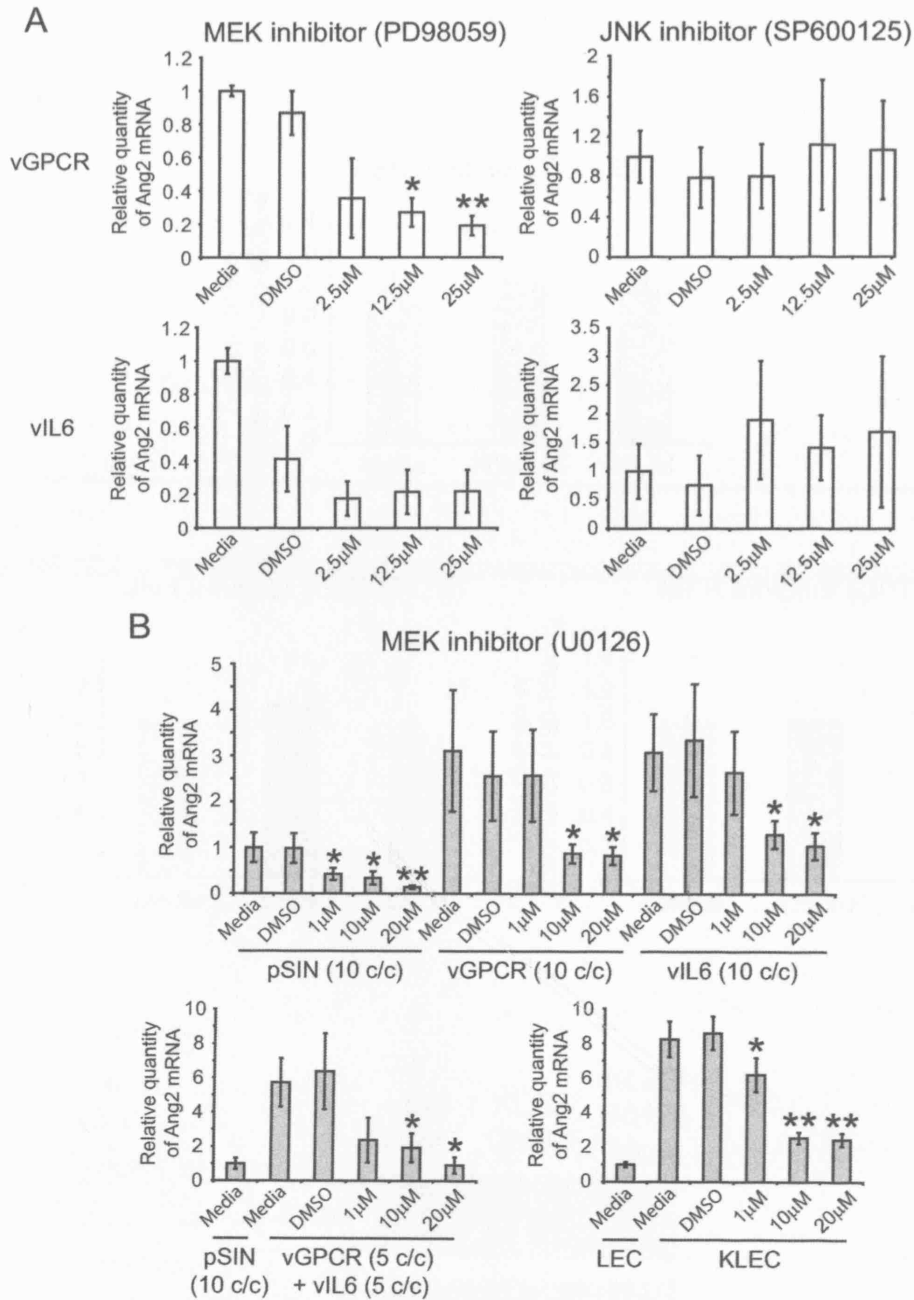


Figure 4.8. Effect of MAPK inhibitors on *Ang2* transcription in lentiviral infected LEC and KLEC. *A*, LEC were infected with either vIL6 or vGPCR-containing lentiviruses, and 72 h p.i., the media were changed for either fresh media, media containing DMSO, or media containing DMSO and different concentrations of an inhibitor. The MEK inhibitor, PD98059, and the JNK inhibitor, SP600125, were used, and infected cells had 9 c/c of either vGPCR or vIL6 lentiviruses. Cells were incubated at these conditions for 8.5 h, after which their RNA was harvested. Two-step qRT-PCR analysis was performed for *Ang2* on the extracted RNA. Expression of *Ang2* mRNA was normalized to vIL6 or vGPCR-expressing cells incubated with media only. *B*, inhibition studies were performed as in (*A*), except that LEC were infected with either pSIN, vGPCR, vIL6, vGPCR and vIL6 containing lentiviruses or KSHV. The MEK inhibitor U0126 was used, and lentivirus-infected cells had a total of 10 c/c. Expression of *Ang2* mRNA was normalized to pSIN media or LEC media for all samples. The Student's *t* test was used to assess the significance of differences between the DMSO controls and cells incubated with different concentrations of inhibitor. *, *p* < 0.05; **, *p* < 0.01. Experiments were performed in triplicate. Columns, mean; bars, SE.

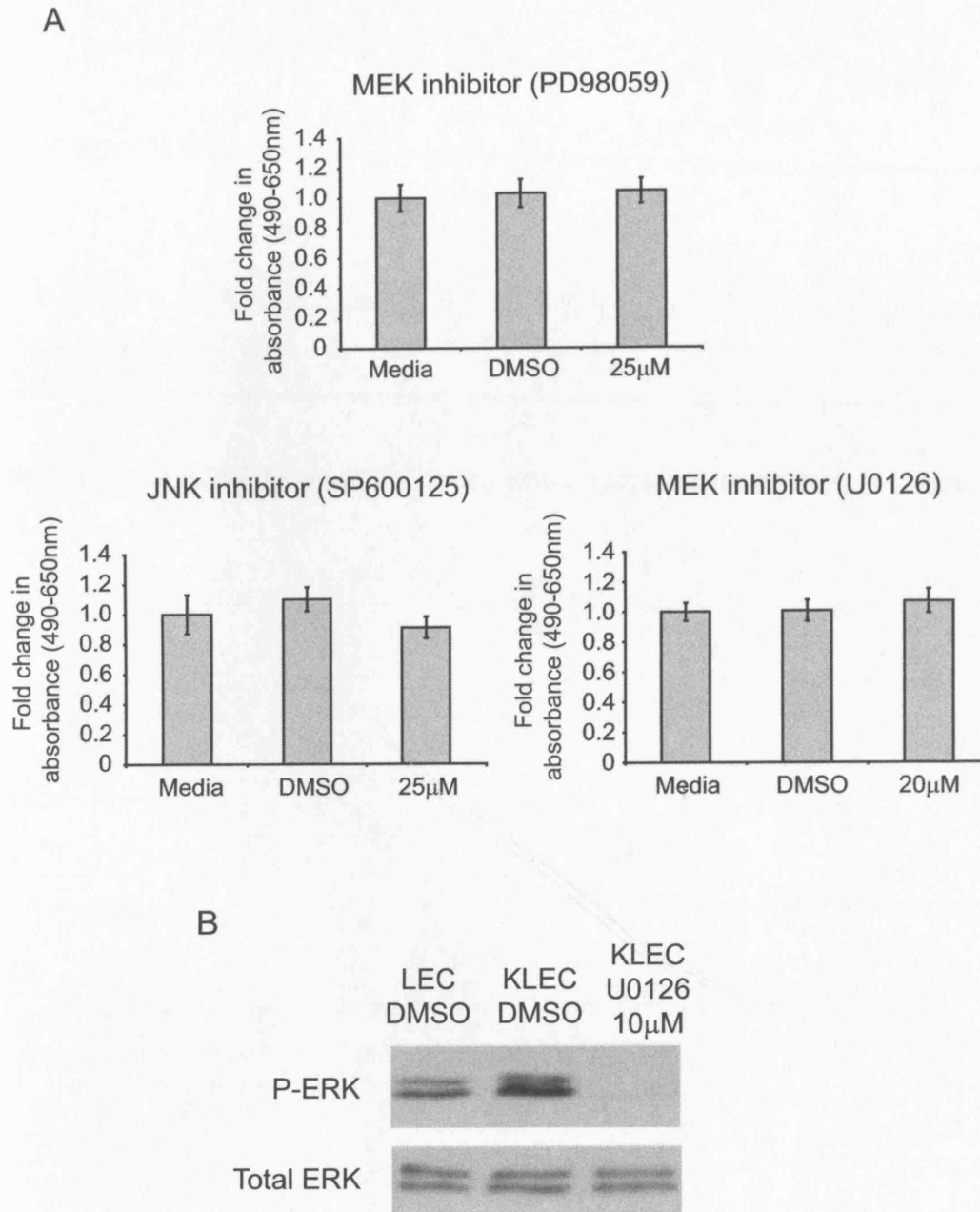


Figure 4.9. Effect of MAPK inhibitors on LEC. *A*, LEC viability when LEC were exposed to the MEK inhibitors PD98059 or U0126 or to the JNK inhibitor SP600125. LEC were incubated for 24 h with either media or media with DMSO or inhibitor. The CellTiter 96® AQueous One Solution Cell Proliferation Assay reagent was used to detect viable cells. The absorbance measured is directly proportional to the number of live cells in the well. Samples were normalised to LEC exposed to media. Experiments were performed in triplicate. *Columns*, mean; *bars*, SE. *B*, Western blot analysis for phosphorylated ERK1/2 (P-ERK) and total ERK1/2 for LEC and KLEC (72h p.i.) incubated for 6 h with media containing either DMSO or 10 µM U0126.

4.6 Ang2 and LEC tube formation *in vitro*

Ang2 expression in KS is likely to have an important functional role in this neoplasm. Since KS tumour cells display characteristics of LEC, and Ang2 has important effects on the lymphatic vasculature (Gale et al., 2002), the role of Ang2 in LEC tube formation was investigated using an *in vitro* Matrigel tube formation assay. The Matrigel tube formation assay is a widely used angiogenic assay in which the ability of cells to form three-dimensional tubes and structures in a matrix rich solidified gel is analysed (Auerbach et al., 2003). LEC have previously been shown to form tubes in Matrigel and Ang2 has previously been shown to increase HUVEC tube formation in a similar *in vitro* tube formation assay (Teichert-Kuliszewska et al., 2001; Nakamura et al., 2004).

Wells of 96 well plates were coated with Matrigel allowing LEC to form three dimensional structures. The number of cells seeded in each well was optimised so that tubes would readily form in each well by 24 hours (9000 cells per well) although tubes could be seen as soon as 12 hours after seeding cells (data not shown). If too few cells were seeded in wells, tubes would not form; when too many cells were seeded, the wells were too crowded and tubes were difficult to observe.

A similar number of tubes were formed when LEC were incubated with Matrigel in either 0.5% FBS media or full media and the number of tubes were unaffected with the addition of recombinant human Ang2 (rhAng2) (Fig. 4.10A). The rhAng2 used has been used in previous studies (Parikh et al., 2006; Harfouche and Hussain, 2006). The concentration of rhAng2 used is the same as previously described (Teichert-Kuliszewska et al., 2001). A significant increase ($p = 0.0047$) in the average number of tubes was seen when the angiopoietin (Ang1, Ang2 and Ang4) inhibitor Tie2-Fc (Teichert-Kuliszewska et al., 2001; Yamakawa et al., 2003) was added to full media compared to the IgG₁-Fc control [IgG₁ control 39.7 ± 3.2 tubes, Tie2-Fc 69.0 ± 4.0 tubes]. The increase in the number of tubes with Tie2-Fc results in a reduction in the size and occurrence of clusters of cell monolayers (Fig. 4.10A). The addition of Tie2-Fc to 0.5% FBS media has no affect on the degree of tube formation, indicating that supplements

present in full media are needed to promote further tube formation in the presence of Tie2-Fc.

The absence of significant change in the number of tubes when rhAng2 is added to either 0.5% FBS media or full media suggests that over-expression of Ang2 in this *in vitro* model has no significant effect on LEC tube formation. This was further supported when the tube formation assay was performed with the supernatants of uninfected LEC, lentivirus infected LEC and KLEC (Fig. 4.10B). No significant difference in tube formation was observed between LEC incubated with supernatant from un-infected or pSIN-infected LEC compared to LEC incubated with supernatant from vGPCR expressing LEC, vIL6 expressing LEC or KLEC. This is despite vGPCR expressing LEC, vIL6 expressing LEC and KLEC secreting higher levels of Ang2 in their conditioned media compared to un-infected or pSIN-infected LEC (Fig. 4.2B, Fig. 4.3 and Fig. 4.4B).

A similar effect to that observed in Figure 4.10A with the Tie2-Fc inhibitor was seen when the tube formation assay was performed with the supernatants of uninfected LEC, lentivirus infected LEC and KLEC (Fig. 4.10B). Tie2-Fc increased the number of tubes compared to the IgG₁-Fc control with LEC incubated with supernatant. However, no significant difference in the extent of the Tie2-Fc up-regulation of tube formation was observed in the presence of different supernatants (Fig. 4.10B).

This Matrigel tube formation model does not show a functional consequence on LEC of an up-regulation of Ang2. The observation that Tie2-Fc causes an increase in LEC tube formation suggests that LEC express a functional Tie2 receptor which binds to angiopoietins. It is likely therefore that under the correct conditions an up-regulation of Ang2 would affect LEC and KLEC biology.

The Matrigel work was not continued due to a timely publication demonstrating that KSHV induced up-regulation of Ang2 is functional and causes increased angiogenesis *in vivo* (Ye et al., 2007).

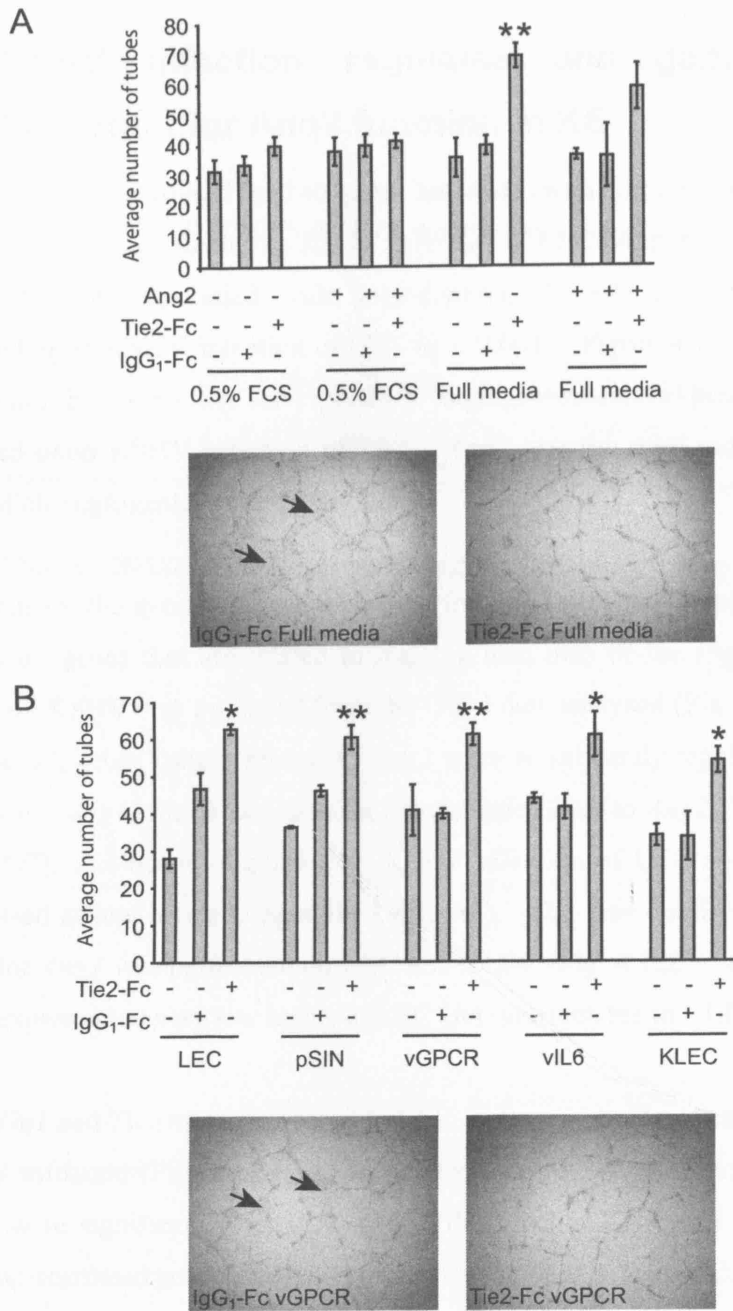


Figure 4.10. Ang2 and LEC tube formation in Matrigel. *A*, 9000 cells were resuspended in 100 μ l of appropriate media and seeded in Matrigel-coated 96 well plates. LEC were incubated for 24 h either with media containing only 0.5% FBS (0.5% FBS) or fully supplemented media (Full media). To study the effect of Ang2 on tube formation recombinant human Ang2 (rhAng2) (220 ng/ml), Tie2-Fc (20 μ g/ml) and control IgG₁-Fc (20 μ g/ml) were used and added to the appropriate media. Wells were photographed after 24h incubation and the number of tubes in each photograph was counted. Magnification, $\times 25$. *B*, Matrigel assay was performed with or without Tie2-Fc or IgG₁-Fc as in *A*, but with cells incubated in a mixture comprising of 50% of 0.5% FBS media and 50% supernatant from LEC, lentiviral-infected LEC or KLEC. Matrigel experiments were performed in triplicate for each condition. The Student's *t* test was used to assess the significance of differences between the IgG₁-Fc controls and cells incubated with Tie2-Fc. *, *p* value < 0.05; ** *p* value < 0.01. Photographs in *A* and *B* are examples of those used for quantitative tube formation analysis. Arrows, LEC monolayer clusters whose number and size were reduced in the presence of Tie2-Fc. Columns, mean; bars, SE.

4.7 KSHV infection regulates angiogenic factors important for Ang2 function in KS

GEM data were analysed for 240 genes associated with angiogenesis to determine angiogenic factors affected by KSHV infection of LEC (Appendix Table A1). Of the 240 genes associated with angiogenesis, 79 (~33%) were significantly affected upon KSHV infection of LEC ($q < 0.001$). Figure 4.11 displays a gene expression heat map that corresponds to angiogenesis-related genes significantly affected upon KSHV infection of LEC. *Ang2* was the third most up-regulated gene of all angiogenic factors assessed.

To focus on the genes that are important for *Ang2* pro(lymph)angiogenic effects and those genes that are related to *Ang2*, a heat map of the regulation of such genes by KSHV was produced from the GEM data analysed (Fig. 4.12A). Along with *Ang2*, other factors related to *Ang2* were significantly regulated by KSHV infection. *Ang1*, which can have an antagonistic effect to *Ang2* (Maisonpierre et al., 1997), was not up-regulated by KSHV infection of LEC and seemed to be expressed at low levels (Appendix Table A1). This was confirmed when qRT-PCR for *Ang1* was performed on LEC and KLEC (Fig. 4.12B). *Ang1* was found to be expressed at very low levels in LEC and undetectable in KLEC.

Both *Tie1* and *Tie2* were expressed in LEC, but were not significantly affected by KSHV infection (Fig. 4.12A and Appendix Table A1). Some angiopoietin-like genes were significantly affected by KSHV infection. *Angptl2* was one of the most up-regulated genes after infection (Fig. 4.12A and Appendix Table A1) and will be discussed in the next chapter. *Angptl4*, an anti-angiogenic factor (Ito et al., 2003), was the only angiopoietin to be significantly down regulated by KSHV-infection of LEC (Fig. 4.12A).

Importantly, VEGFRs and some of their ligands were significantly up-regulated by KSHV infection (Fig. 4.12A). However, *VEGFA*, a factor shown previously to be important for *Ang2* to promote angiogenesis, was not up-regulated by KSHV (Fig. 4.12A and C). Its receptors *VEGFR1* and *VEGFR2* were

significantly up-regulated, thus permitting endothelial cells, like LEC, to be more responsive to *VEGFA* and the related *VEGFB*. *VEGFC* and its receptor *VEGFR3* also appeared to be both up-regulated by KSHV infection (Fig. 4.12A). However qRT-PCR analysis suggests that *VEGFC* is not up-regulated by KSHV infection of LEC (Fig. 4.12C). The *VEGFC/VEGFR3* axis is essential for LEC, promoting lymphangiogenesis and is required, therefore, along with *Ang2*, to form a normal lymphatic system (Gale et al., 2002; Adams and Alitalo, 2007). Notably, vGPCR and vIL6 up-regulated *VEGFC* as well as *VEGFA* expression in LEC (Fig. 4.12C). Like LEC and KLEC, *Ang1* was expressed at very low levels in vGPCR and vIL6 expressing LEC (data not shown).

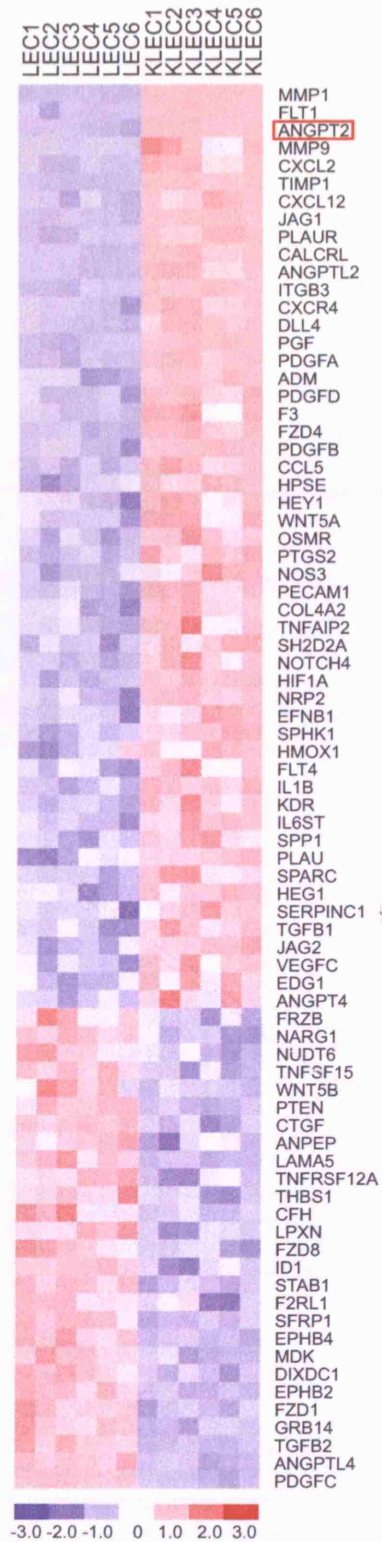
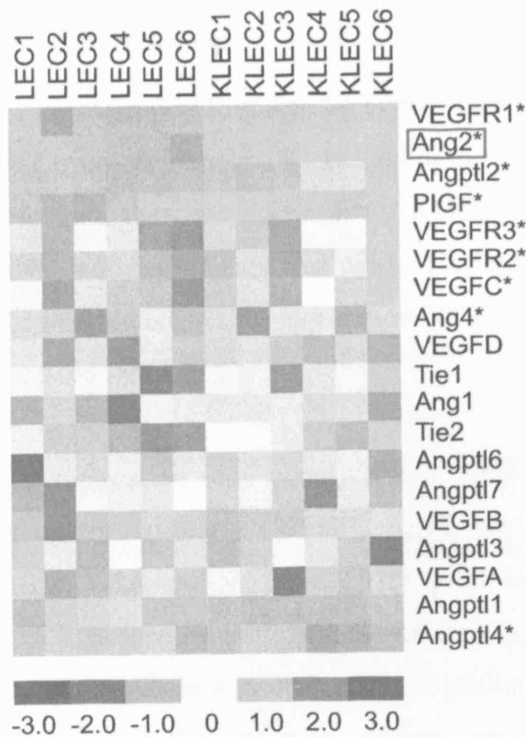


Figure 4.11. KSHV infection regulates an array of angiogenic factors. A heat map of 79 angiogenesis genes which significantly changed between LEC and KLEC samples ($q < 0.001$). Each gene is represented by a single probe-set (see Materials and Methods). Genes were ordered by amount of fold change between conditions with the uppermost gene displaying the highest positive differential expression and the lowermost gene displaying the highest negative differential expression. Gene symbols are used in the heat map. ANGPT2, angiopoietin-2 (Ang2). Ang2 is boxed.

A



B

Gene	LEC Ct	KLEC Ct
Ang1	37.2 ± 0.4	Undetectable (>40)
Ang2	27.3 ± 0.2	24.9 ± 0.1
GAPDH	21.9 ± 0.1	22.7 ± 0.1

C

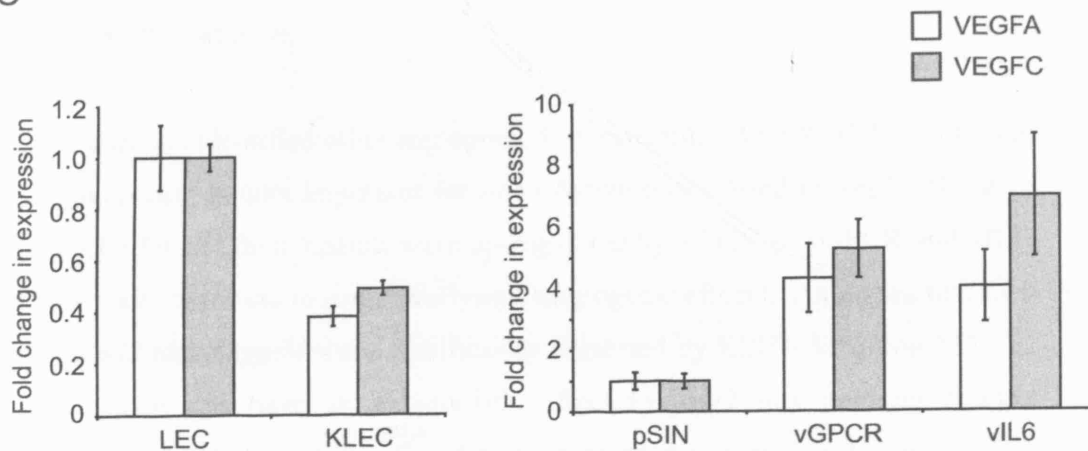


Figure 4.12. Angiogenic factors important for *Ang2* function are regulated by KSHV. *A*, a heat map of the relative changes in expression upon KSHV infection of LEC of genes important for *Ang2* function or related to *Ang2*. Genes were ordered by magnitude of fold change between conditions, with the uppermost gene displaying the highest positive differential expression. *, genes in which expression was significantly regulated by KSHV infection. A change in expression between LEC and KLEC is considered significant when $q < 0.001$. The expression of each gene is provided by a single microarray probe-set (see Materials and Methods). *Angptl5*, was not analysed because no *Angptl5* probe set was present on the Affymetrix hg-u133+2 GeneChips used. *Ang2* is boxed. *B*, qRT-PCR analysis of *Ang1*, *Ang2* and *GAPDH* in LEC and KLEC. Ct values are an indication of the level of gene expression in cells; the lower the Ct value the higher the amount of gene mRNA present in a particular sample. *Ang2* was up-regulated ~8.5 fold in KLEC compared to LEC. No *Ang1* signal could be detected in the KLEC samples. Experiments were performed in triplicate. Mean and standard error values are present in the table. *C*, relative mRNA levels of *VEGFA* and *VEGFC* in LEC, KLEC and lentiviral-infected LEC (10 c/c) determined by qRT-PCR. mRNA levels were normalized to uninfected LEC or pSIN levels, and the experiments were performed in triplicate. Columns, mean; bars, SE.

4.8 Summary

Ang2 protein was found to be expressed in KS lesions and it was confirmed that Ang2 is up-regulated in KLEC, an *in vitro* model of KS (Wang et al., 2004a). To investigate the mechanism(s) by which KSHV up-regulates Ang2 the selected KSHV lentiviral library was used. Two lytic genes vIL6 and vGPCR were found to up-regulate Ang2 expression in LEC and both vIL6 and vGPCR were expressed in KLEC.

Lytic replication only occurred in a small percentage of KLEC although Ang2 was up-regulated in all KLEC. Ang2 was up-regulated in a paracrine manner by KSHV, vIL6 and vGPCR. This provided a mechanism by which vIL6 and vGPCR expressed only in cells undergoing lytic replication could contribute to Ang2 up-regulation in all KLEC. Signalling through VEGFR1 and VEGFR2, by for example VEGFA, was not responsible for the paracrine up-regulation of *Ang2*. KSHV, vIL6 and vGPCR were found to up-regulate Ang2 through the MEK MAPK pathway.

GEM analysis identified other angiogenic factors regulated by KSHV infection of LEC including factors important for *Ang2* function or related to *Ang2*. Some of the VEGFRs and their ligands were up-regulated by KSHV or vGPCR and vIL6, which may contribute to *Ang2* pro(lymph)angiogenic effects. Angiopoietins such as *Angptl2* and *Angptl4* were significantly regulated by KSHV infection of LEC. *Ang1* which can have an antagonistic effect to *Ang2* was not significantly regulated by KSHV and was found to be expressed at very low levels in LEC. *Tie2* appeared to be expressed in LEC and KLEC and Matrigel studies suggested that *Tie2* was functional in LEC.

Chapter 5. Angiopoietin-like 2, a potential novel tumour angiogenic factor, is regulated by KSHV-encoded interferon regulatory factor 1

Angptl2 is a factor that is important for *in vivo* angiogenesis, however, its regulation and role in cancer has not been studied (Kubota et al., 2005). The primary aim of this chapter is to investigate the regulation of Angptl2 by KSHV and to start investigating the function of Angptl2 in cancer.

Like most other angiopoietin-like proteins, Angptl2 has no known receptor. *In vitro*, human Angptl2 prevents endothelial cell apoptosis and promotes endothelial cell sprouting (Kim et al., 1999; Kubota et al., 2005). Phylogenetic analysis showed that human and zebrafish Angptl2 proteins are closely related and are therefore likely to have similar functions (Appendix 1). Studies performed on zebrafish showed that Angptl2 is necessary for proper vascular network formation (Kubota et al., 2005). In addition, human Angptl2 has been shown to promote the growth of haematopoietic stem cells (Zhang et al., 2006).

GEM analysis revealed that Angptl2 was one of the most significant and highly up-regulated genes by KSHV infection of LEC and no other angiopoietin, besides Ang2, was as highly up-regulated as Angptl2 by KSHV (Fig. 4.11). Therefore, I decided to further investigate Angptl2.

5.1 GEM analysis of *Angptl2* in KS and other neoplasms

GEM analysis was performed to investigate whether *Angptl2* was expressed in KS and other neoplasms. Using GEM data from Wang et al., 2004, *Angptl2* was found to be expressed in KS and is up-regulated in KS compared to normal skin (Fig. 5.1A).

In collaboration with Stephen Henderson (CR-UK Viral Oncology Group), GEM data from our laboratory's cancer database were analysed to investigate *Angptl2* expression in other neoplasms besides KS (Appendix Table A2 and Fig. 5.1B). For this analysis the GEM data from a large carcinoma dataset (n = 168) containing tumours from 12 different organs were analysed (Fig. 5.1B). This dataset was chosen because: carcinomas are the most common types of cancer, the size of the dataset, the microarray data was obtained using the latest Affymetrix hg-u133+2 GeneChips and importantly *Angptl2* and *Ang2* expression varied significantly between the different tumours allowing a correlation analysis to be performed.

Angptl2 was found to be expressed in all tumours, as the microarray log expression values of its probe-sets are above 4 (Appendix Table A2). *Angptl2* was particularly highly expressed in tumours of the pancreas, colon and breast (Fig. 5.1B). However, the *Angptl2* expression profile did not correlate with the expression profile of expected angiogenic factors, such as members of the VEGF or angiopoietin family or their receptors (Fig. 5.1B). Instead, *Angptl2* clusters mainly with extracellular matrix associated factors such as collagens, fibrillin 1 (FBN1), lysyl oxidase (LOX) involved in cross linking collagens (Payne et al., 2007), as well as two matrix metalloproteinases which are involved in extracellular matrix degradation (Rundhaug, 2005). *Angptl2* also clusters with angiogenic inhibitors, thrombospondin-1, thrombospondin-2 and TIMP metalloproteinase inhibitor 2 and these factors are also associated with the extracellular matrix (Seo et al., 2003; Sottile, 2004).

When the same analysis, on the same set of tumours, was performed for *Ang2* the *Ang2* expression profile correlated with the expression profile of other genes involved in angiogenesis such *VEGFA*, placental growth factor, *VEGFR1*, *VEGFR2*, *VEGFR3*, *Tie1* and *Angptl4* (Appendix Table A3 and Fig. 5.2). In addition, unlike *Angptl2*, *Ang2* was most strongly expressed in conventional (clear cell) renal carcinoma which is a highly angiogenic neoplasm (Appendix Table A3 and Fig. 5.2). The result that the *Ang2* expression profile correlates with different genes compared to *Angptl2* would suggest that although *Angptl2* is expressed in a variety of neoplasms it is likely to be regulated differently than *Ang2*. The finding that *Angptl2* expression does not cluster with typical angiogenic factors, like *Ang2*, suggests that *Angptl2* could have a different role in tumour development and angiogenesis than other established angiogenic factors.

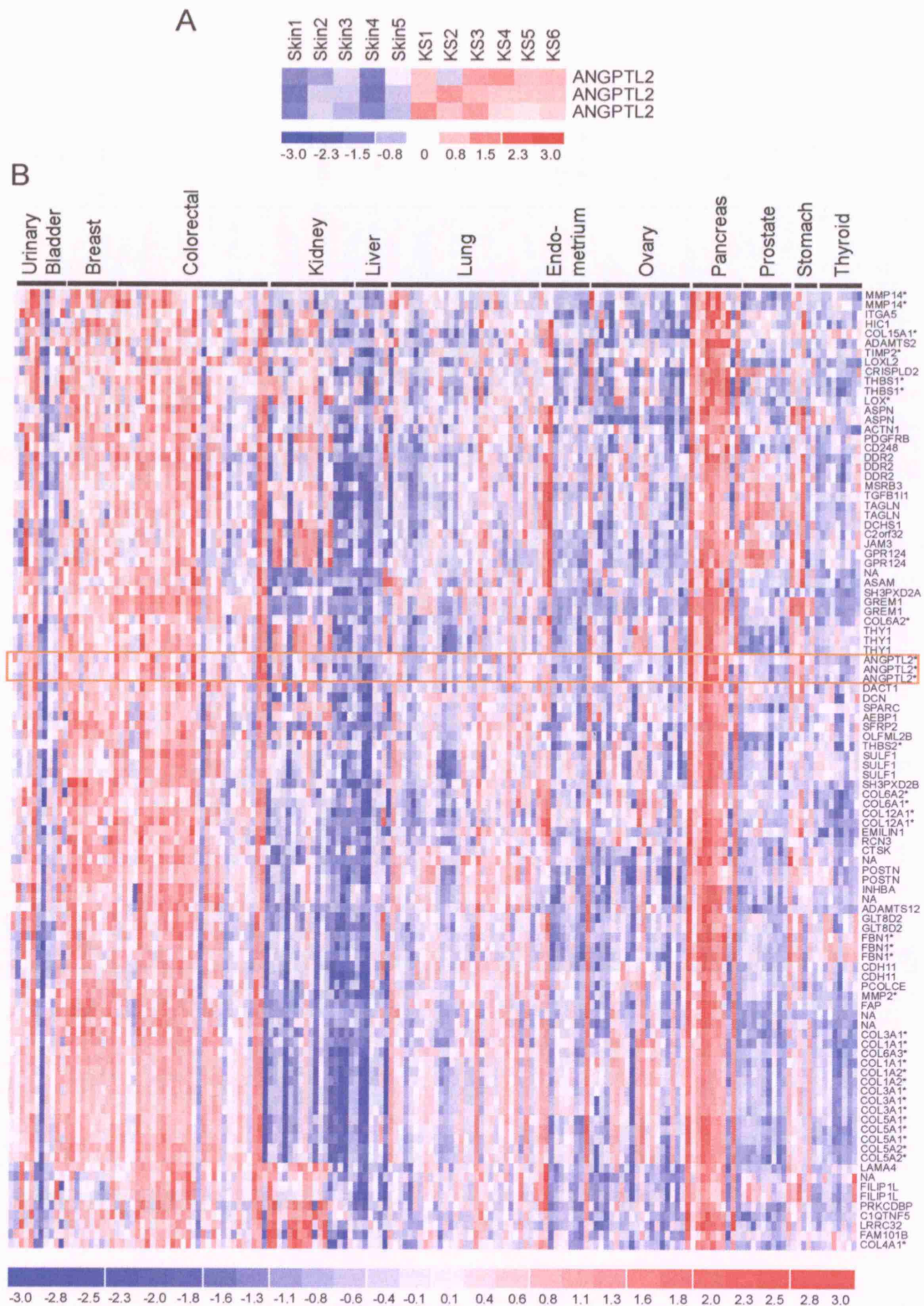


Figure 5.1. *Angptl2* expression in KS and other neoplasms. *A*, a heat map of *Angptl2* in skin versus KS. All *Angptl2* probe-sets present are shown. GEM data obtained from Wang et al., 2004. *B*, a heat map of *Angptl2* expression in a variety of carcinomas along with the expression of genes (as probe-sets) which show the highest correlation to the *Angptl2* expression profile in these neoplasms. For the correlation analysis, the *Angptl2* probe-set with the highest average expression across the carcinomas was used. The GEM data were obtained from the NCBI GEO database (GSE2109, n=168). NA, no gene name available. The *Angptl2* probe-sets are boxed. *, genes referred to in the text.

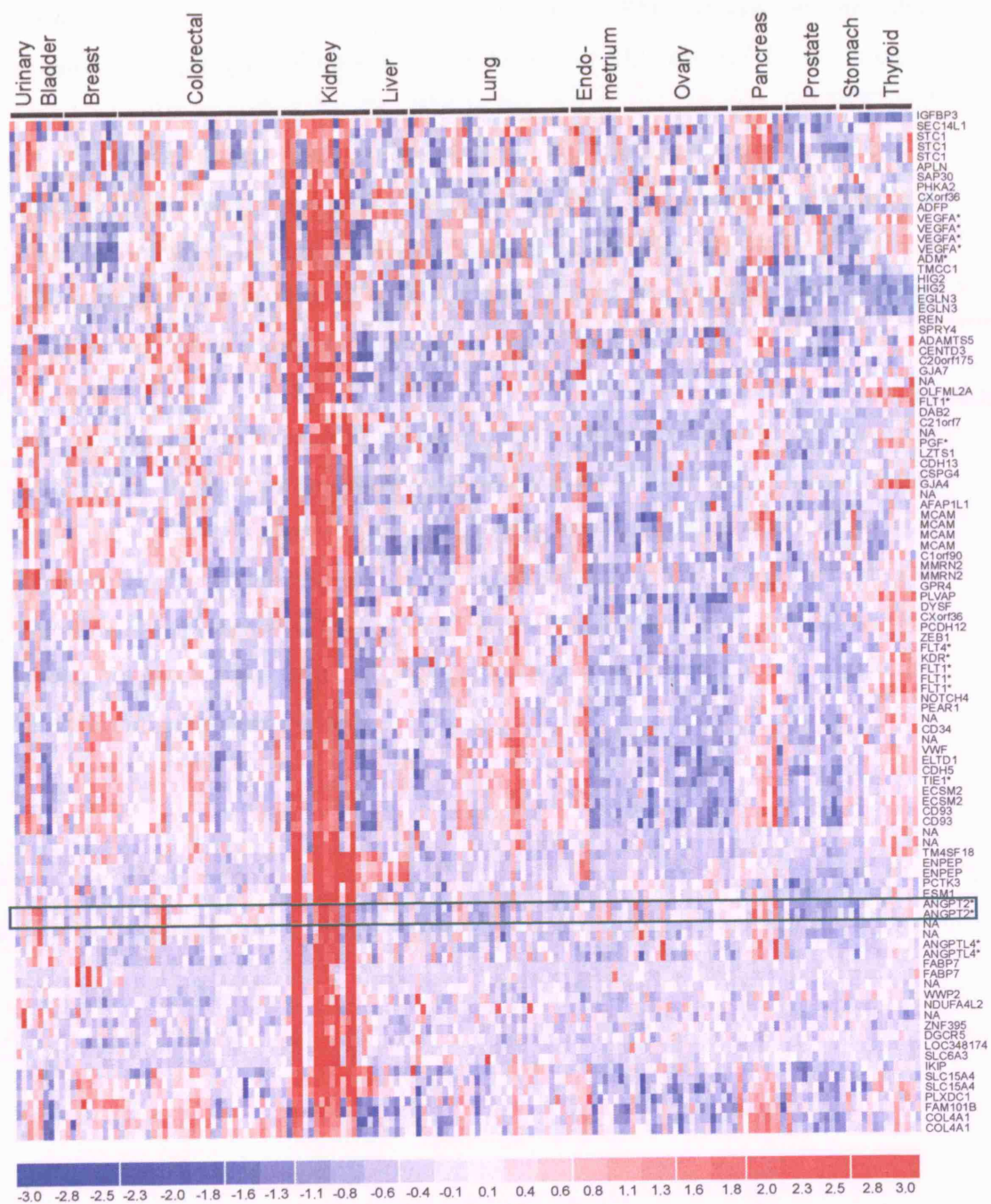


Figure 5.2. *Ang2* expression in neoplasms. A heat map of *Ang2* expression in the neoplasms analysed for *Angptl2* in (Fig. 5.1B) along with the expression of genes (as probe-sets) which show the highest correlation to the *Ang2* expression profile in these neoplasms. For the correlation analysis, the *Ang2* probe-set with the highest average expression across the neoplasms was used. The GEM data were obtained from the NCBI GEO database (GSE2109, n=168). NA, no gene name available. The *Ang2* probe-sets are boxed. *, genes referred to in the text.

5.2 *Angptl2* expression in KLEC

Using all three probe-sets specific for *Angptl2*, GEM analysis revealed that *Angptl2* was up-regulated upon KSHV infection of LEC and KSHV infection of blood vascular endothelial cells (BEC) (Fig. 5.3A). GEM data for BEC and KSHV-infected BEC (KBEC) were provided by Dimitrios Lagos (unpublished work, CR-UK Viral Oncology Group). qRT-PCR for *Angptl2* confirms that KLEC up-regulates *Angptl2* mRNA with *Angptl2* mRNA being up-regulated ~ 8 fold in KLEC compared to LEC (Fig. 5.3B). The increase in *Angptl2* mRNA in KLEC results in an increase in Angptl2 protein (Fig. 5.3C).

To investigate whether KSHV up-regulates *Angptl2* through a paracrine mechanism, supernatant (conditioned media) from LEC and KLEC was added to LEC and qRT-PCR analysis performed (Fig. 5.3D). *Angptl2* mRNA was not significantly up-regulated by KLEC supernatant, unlike *Ang2*, which was significantly up-regulated (Fig. 4.6A). *Angptl2* therefore is not up-regulated in a paracrine mechanism and *Angptl2* is likely to be regulated by a different mechanism, compared to *Ang2*.

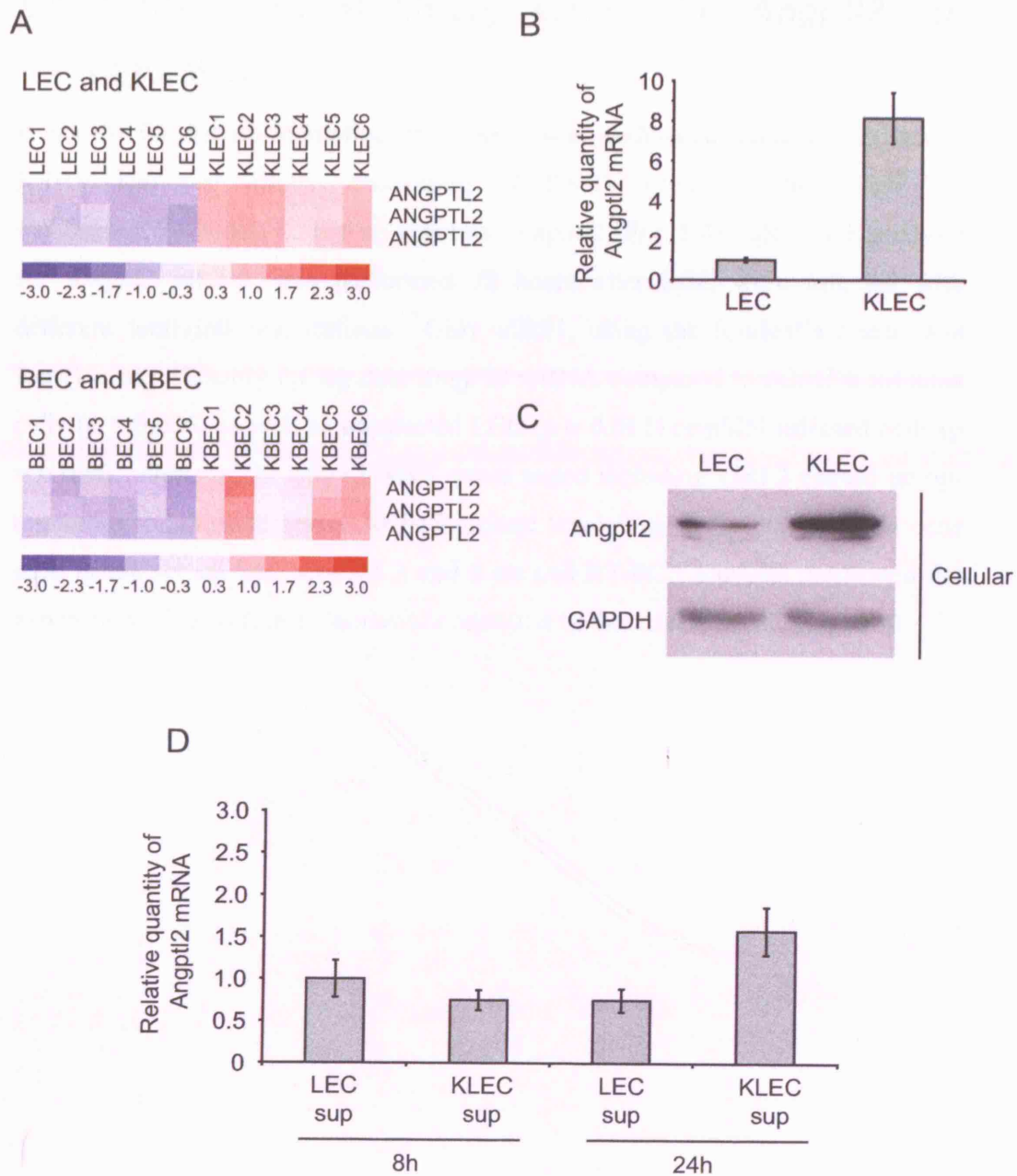


Figure 5.3. Angptl2 expression in KSHV-infected endothelial cells. *A*, heat maps of the relative changes of *Angptl2* expression in LEC versus KLEC and BEC versus KBEC. All probe-sets against *Angptl2* mRNA are shown. *B*, relative *Angptl2* mRNA levels for LEC versus KLEC (3 d p.i.) determined by qRT-PCR. mRNA levels were normalized to LEC, and the experiment was performed in triplicate. $p < 0.001$ between LEC versus KLEC using the Student's *t* test. *C*, Western blot analysis of Angptl2 total protein in cell lysates of LEC and KLEC (3 d p.i.). *D*, filtered supernatant (sup) from LEC and KLEC were added to uninfected LEC. Eight or 24 h later, RNA was collected and subjected to qRT-PCR analysis for *Angptl2*. mRNA levels were normalized to LEC sup 8 h and the experiment was performed in duplicate. $p > 0.1$ between LEC sup 8 h versus KLEC sup 24 h using the Student's *t* test. Columns, mean; bars, SE.

5.3 KSHV lentiviral library screen for *Angptl2* up-regulation

A screen for the up-regulation of *Angptl2* was performed using the expanded KSHV lentiviral library, containing 24 KSHV genes, to investigate the mechanism by which KSHV up-regulated *Angptl2* (Fig. 5.4). qRT-PCR analysis for *Angptl2* mRNA was performed 72 hours after LEC were infected with different lentiviral preparations. Only vIRF1, using the Student's *t* test, was found to significantly up-regulate *Angptl2* mRNA compared to pCSGW infected cells ($p = 0.026$) as well as uninfected LEC ($p = 0.011$) or pSIN-infected cells ($p = 0.004$). None of the other KSHV genes tested including vIRF2 caused an up-regulation of *Angptl2* above its background level (Fig. 5.4). All infected cells used in the screen had between 3 and 6 c/c and RT-PCR analysis confirmed the expression of the different lentiviral constructs in the infected LEC (Fig. 5.4).

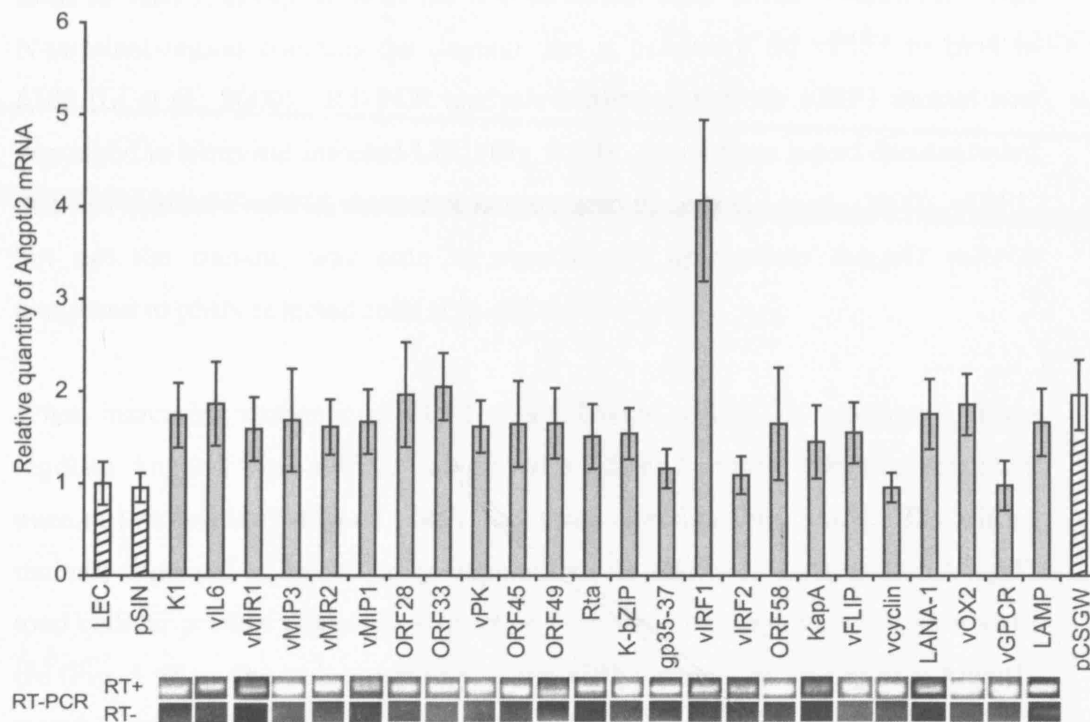


Figure 5.4. The KSHV lentiviral library screen for *Angptl2*. qRT-PCR analysis of *Angptl2* in lentiviral infected LEC. 0.8×10^5 LEC were infected with lentiviral preparations encoding particular KSHV genes and 72 h p.i. the cells were harvested and processed for qRT-PCR analysis. LEC, pSIN and pCSGW *Angptl2* levels are used as a guide for comparison and mRNA levels were normalized to LEC. The experiment was performed in duplicate. RT-PCR analysis confirming the expression of the individual KSHV ORFs in the lentiviral infected cells is shown. PCR was performed using samples processed with (RT+) or without (RT-) reverse transcriptase in the cDNA synthesis step. All lentiviral infected cells had 3-6 c/c. Columns, mean; bars, SE.

5.4 vIRF1 up-regulates Angptl2

qRT-PCR analysis for *Angptl2* on vIRF1 infected cells was repeated to confirm that vIRF1 up-regulated *Angptl2* (Fig. 5.5A). The vIRF1 mutant (vIRF1 Δ 1-82), cloned into the pSIN-MCS vector, was included in this analysis and was provided by Amy Hansen (CR-UK Viral Oncology Group). This vIRF1 mutant is the same as vIRF1, except it lacks the first 82 amino acids at the N-terminus. This N-terminal region contains the domain that is necessary for vIRF1 to bind to p300 (Li et al., 2000). RT-PCR analysis confirmed that the vIRF1 mutant was expressed in lentiviral infected LEC (Fig. 5.5A). A previous report demonstrated that this mutant's mRNA transcript is translated in cells (Li et al., 2000). vIRF1, but not the mutant, was able to significantly up-regulate *Angptl2* mRNA compared to pSIN-infected cells (Fig. 5.5A).

When increasing amounts of vIRF1 was delivered to LEC, it was found to up-regulate Angptl2 total cellular protein with Angptl2 protein being up-regulated even at low levels (1 c/c) of vIRF1 lentivirus infection (Fig. 5.5B). The vIRF1 mutant, appeared to be severely impaired in its ability to up-regulate Angptl2 total cellular protein with only a small up-regulation of Angptl2 being seen at 10 c/c (Fig. 5.5B). The reduced ability of the vIRF1 mutant to up-regulate Angptl2 may be due to the mutant not binding to p300, but may also be due to the mutant not binding to other factors or due to other parts of the vIRF1 protein being affected by this mutation. The mutant was used in experiments as a control. LEC infected with empty vector did not change Angptl2 total cellular protein compared to LEC, which indicates that lentiviral infection itself does not up-regulate Angptl2 protein (Fig. 5.5C). vIRF1 was expressed in KLEC (Fig. 5.5D) and therefore it is likely that vIRF1 contributes to the ability of KSHV to up-regulate Angptl2.

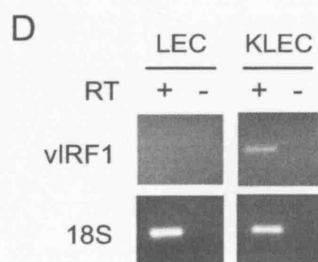
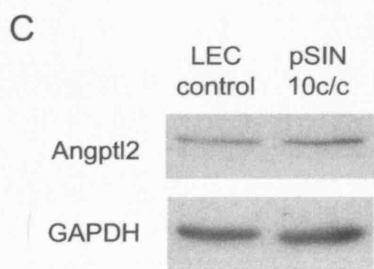
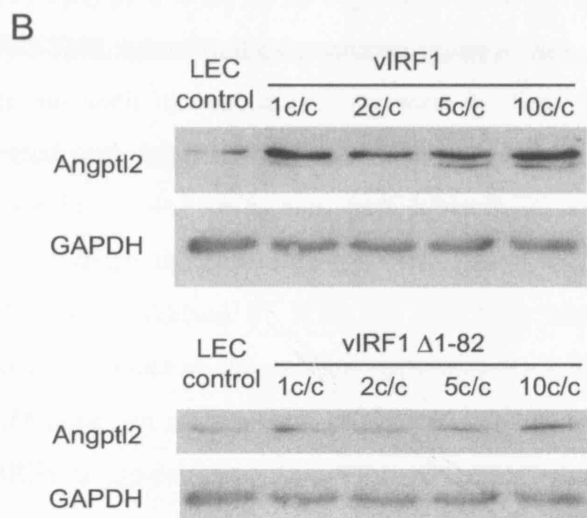
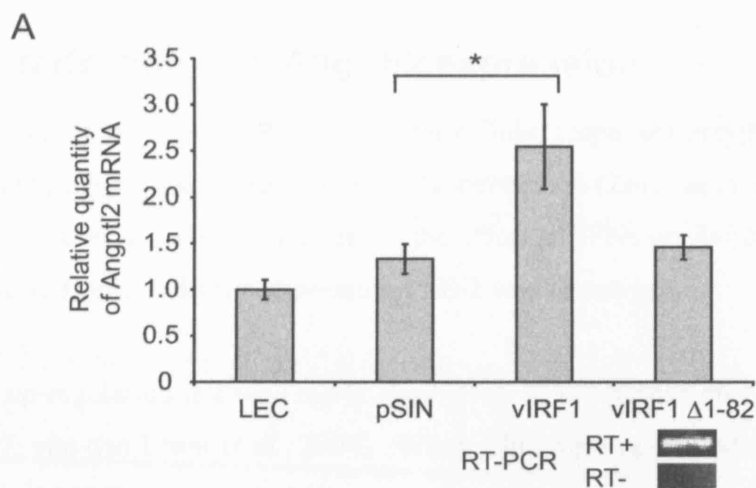


Figure 5.5. vIRF1 up-regulates Angptl2 expression. *A*, qRT-PCR analysis for *Angptl2* in uninfected LEC and LEC infected (72 h p.i.) with either empty vector (pSIN), vIRF1 or vIRF1 mutant (vIRF1 Δ1-82). mRNA levels were normalised to uninfected LEC and all lentiviral infected cells had 10 c/c. Experiment was performed in triplicate. The Student's t test was used to assess the significance of differences in *Angptl2* expression between pSIN-infected LEC and LEC infected with either vIRF1 or vIRF1 Δ1-82. *, $p < 0.05$. vIRF1 Δ1-82 lacks the first 82 amino acids of vIRF1 and is cloned into the pSIN-MCS vector. RT-PCR with samples processed with (RT+) or without (RT-) reverse transcriptase demonstrates the expression of vIRF1 Δ1-82 in lentiviral infected LEC. *B*, cell lysates of LEC infected (72 h p.i.) with increasing amounts of vIRF1 or vIRF1 Δ1-82 were subjected to Western blot analysis for Angptl2 and GAPDH. *C*, cell lysates of LEC or pSIN-infected LEC were processed as described in (*B*). *D*, expression of vIRF1 in KLEC (72 h p.i.) shown by RT-PCR analysis. 18S was used as a housekeeping control gene. Columns, mean; bars, SE.

5.5 Interferons and *Angptl2* expression

An important function of vIRF-1 is to alter cellular responses to type 1 and type 2 IFNs and to inhibit the expression of IFNs themselves (Zimring et al., 1998; Li et al., 1998; Lin et al., 2001). Therefore, the effect of IFNs on *Angptl2* expression in uninfected cells and cells expressing vIRF1 was investigated.

MHC-I up-regulation is a well established effect of interferons on cells (Hobart et al., 1997; van den Elsen et al., 2004). When LEC were incubated overnight with either type 1 IFN α or type 2 IFN γ an up-regulation of MHC-I surface expression on LEC of nearly 3 fold, quantified by geomean fluorescence, was observed (Fig. 5.6A). However, no such up-regulation was seen in *Angptl2* expression when LEC were incubated with these IFNs (Fig. 5.6B). A small significant increase in *Angptl2* expression (1.3 ± 0.1 fold) was seen when LEC were incubated with IFN γ , however, this small increase was not observed in empty vector infected cells (Fig. 5.6C). The addition of IFNs to vIRF1 expressing LEC did not significantly affect the extent of *Angptl2* up-regulation by vIRF1 (Fig. 5.6C). In summary, *Angptl2* does not appear to be an IFN α or IFN γ responsive gene and the ability of vIRF1 to up-regulate *Angptl2* is not significantly affected by the ability of vIRF1 to alter cellular responses to IFN α or IFN γ .

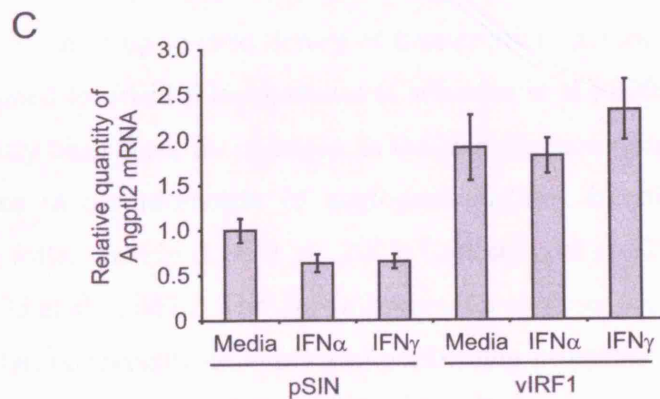
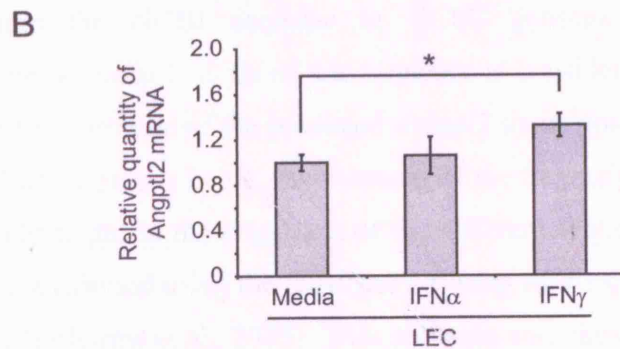
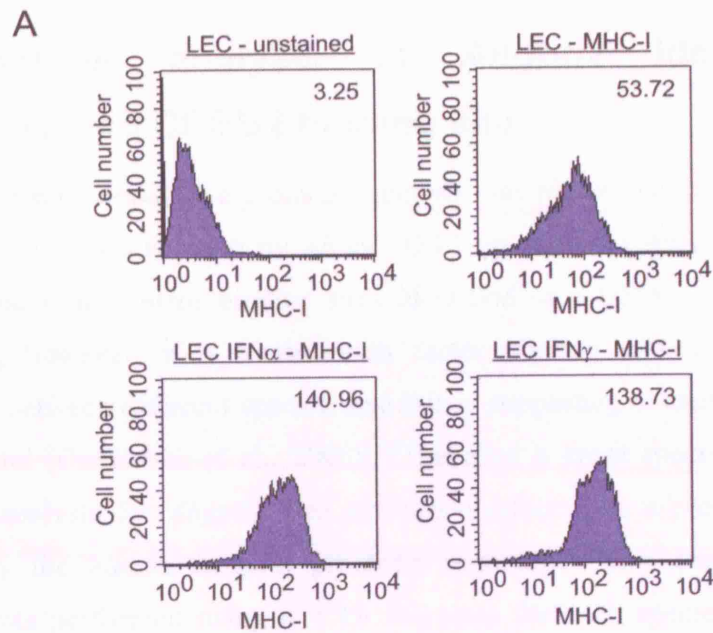


Figure 5.6. Regulation of *Angptl2* by IFNs. *A*, histograms, generated using flow cytometry, displaying the levels of MHC-I surface expression on LEC. The geomean fluorescence is shown in the top right corner of each histogram. LEC were incubated overnight with either media or media containing 150 U/ml IFN α or 1000 U/ml IFN γ before cells were collected and processed for flow cytometry. *B*, LEC incubated with IFNs like in (*A*) were subjected to qRT-PCR analysis for *Angptl2*. mRNA levels were normalised to uninfected LEC. *C*, Lentiviral infected LEC (60 h p.i.) incubated with IFNs like in (*A*) were collected and subjected to qRT-PCR analysis for *Angptl2*. All lentiviral infected LEC had 10 c/c and mRNA levels were normalised to pSIN-infected LEC incubated with media only. The Student's *t* test was used to assess the significance of increases in *Angptl2* expression between the media controls and the cells incubated with IFNs. *, $p < 0.05$ ($p = 0.023$). Experiments were performed in triplicate. Columns, mean; bars, SE.

5.6 Promoter analysis of *Angptl2* identifies a conserved CREB2 binding site

A cross species comparative promoter analysis was performed to gain an insight into the possible mechanisms by which vIRF1 up-regulates *Angptl2* (Fig. 5.7A). Many transcription factor binding sites identified in a DNA sequence are not functional; however, if a transcription factor binding site is evolutionarily conserved between different species then this is supporting evidence that the site is functional (Cartharius et al., 2005). Therefore a cross species comparative promoter analysis for *Angptl2* was performed rather than a promoter analysis using only the human *Angptl2* promoter sequence. The *Angptl2* promoter analysis was performed using a 7 kb sequence for each species, which were obtained from the NCBI database or UCSC genome bioinformatics site (<http://genome.ucsc.edu/>). 5 kb of this sequence is considered to be the *Angptl2* promoter and is upstream of the predicted *Angptl2* transcription start site with the rest of the 7 kb sequence being down-stream of the transcription start site and is present mainly to aid in the alignment of the different sequences. The promoter analysis was performed using the DiAlignTF (Using MatInspector) software from Genomatix (Cartharius et al., 2005). This software was chosen for the analysis as it contains the most up-to-date library of transcription factors publicly available and is designed to avoid false positives (Cartharius et al., 2005). This software has previously been used, for example, in the identification of transcription factor binding sites in the promoters of angiogenic factors, interferons and factors involved in inflammation (Lee et al., 2003; Cartharius et al., 2005; Schmelzer et al., 2007; Liu et al., 2007). The *Angptl2* promoter analysis obtained was verified by Sascha Ott (University of Warwick) performing promoter analysis using the BiFa promoter analysis software, using the RcMo database (University of Warwick).

From the promoter analysis it can be seen that *Angptl2*, unlike most other human genes, has a TATA-less promoter with no conserved TATA box being found in the 7 kb sequence analysed (Fig. 5.7A). However, other common promoter elements such as specificity protein 1 (Sp1) binding sites and a GC box which is

part of the same matrix family as Sp1 were present in the promoter close to the transcription start site as would be expected for these factors (Ogbourne and Antalis, 1998). These common promoter elements act by influencing the frequency of transcription initiation by RNA polymerase II and are key to obtaining any significant level of transcription (Ogbourne and Antalis, 1998; Lewis, 2000). Also Sp1 sites can be critically important for initiation of transcription in TATA-less promoters (Pugh and Tjian, 1991).

In addition to these common promoter elements, there are also other interesting regulatory elements in the *Angptl2* promoter (Fig. 5.7A). Firstly, the positive regulatory domain 1-binding factor 1 (PRDI1) site which binds to the transcriptional repressor PRDI1 is of interest as its sequence is very similar to sequences bound by IRFs and therefore vIRF1 could possibly bind to or affect binding and activity at this site (Kuo and Calame, 2004; Chen et al., 2007). However, the PRDI1 site may be too far from the transcription start site to be functional (Kakkis and Calame, 1987; Lin et al., 2002; Chen et al., 2007). Closer to the transcription start site there is a binding site for nuclear factor 1 (NF1), a common transcriptional activator (Bruggemeier et al., 1990; Zorbas et al., 1992) and a binding site for activator protein 4 (AP4) which can act as a transcriptional activator or repressor in both viral and cellular promoters (Mermoud et al., 1988; Badinga et al., 1998; Imai and Okamoto, 2006). An NF- κ B site is also present, however, this is unlikely to be functional as it is very close to the transcription start site and vFLIP, which activates NF- κ B, did not up-regulate *Angptl2* (Fig. 5.4).

A CREB2 binding site was also identified in the *Angptl2* promoter, to which CREB can also bind. CREB2 can act as a transcriptional repressor as well as a transcriptional activator and can bind to co-activators CBP/p300 (Karpinski et al., 1992; Liang and Hai, 1997; Fawcett et al., 1999; Schoch et al., 2001; Gachon et al., 2002). This is of interest as vIRF1 can bind to CBP/p300 and affect transcription factors which use these factors (Seo et al., 2000; Li et al., 2000; Lin et al., 2001). Therefore, a possible hypothesis is that CREB2 acts as a transcriptional repressor in the *Angptl2* promoter and, through vIRF1 interaction

with CBP/p300, or perhaps even vIRF1 interacting with CREB2 itself, vIRF1 prevents CREB2 from acting as a transcriptional repressor and therefore causes an up-regulation of *Angptl2* expression. This hypothesis is supported by the observation that when the p300 binding domain of vIRF1 is removed, vIRF1 no longer significantly up-regulates *Angptl2* mRNA (Fig. 5.5A).

Also important to note from the comparative promoter analysis of *Angptl2* are regulatory elements which were not found conserved in the promoter. These include interferon-stimulated response elements (ISREs), IRF binding sites and HIF-1 α binding sites. No vIRF1 binding sites in the human *Angptl2* promoter were found (manual analysis). The lack of any conserved hypoxia inducible factor sites in the *Angptl2* promoter suggests that *Angptl2* is not up-regulated by hypoxia in contrast to other angiogenic factors such as *VEGFA*, *adrenomedullin* (*ADM*), and *Ang2* (Forsythe et al., 1996; Ogita et al., 2001; Pichiule et al., 2004). This is supported by qRT-PCR analysis on HUVEC exposed to hypoxia. *VEGFA*, *ADM* and *Ang2* were significantly up-regulated in HUVEC exposed to hypoxia as expected, however, *Angptl2* was not up-regulated (Fig. 5.7B).

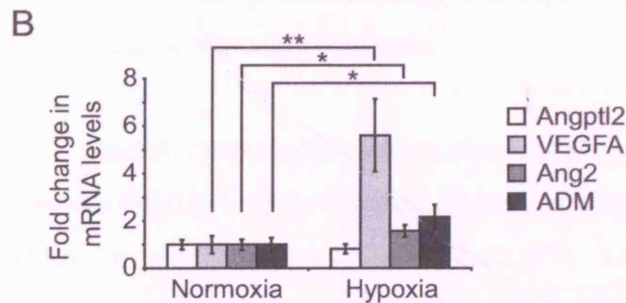
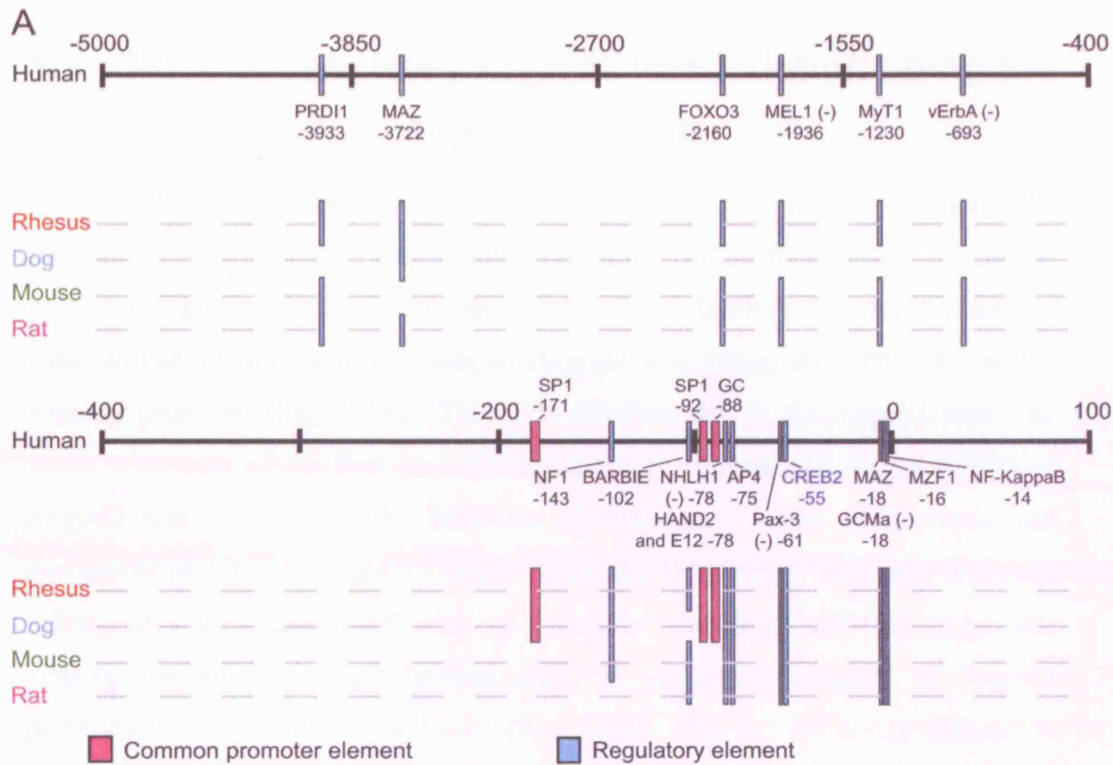


Figure 5.7. Promoter analysis of *Angptl2*. *A*, 7 kb sequences containing 5 kb of the predicted *Angptl2* promoter from human, rhesus monkey, dog, mouse and rat were aligned and analysed for transcription factor binding sites using the DiAlignTF software from Genomatix (Cartharius et al., 2005). The promoter analysis is shown as a schematic diagram with the horizontal lines representing the DNA sequence for each species and the vertical bars displaying the position of each conserved transcription factor binding site. The transcription factor binding sites are labelled according to their human forms. The common promoter elements are those elements present in most promoters that are important for the promoter to be active. The position of each transcription factor binding site is shown along with the DNA strand which is bound. Common promoter elements conserved between at least 3 species and regulatory elements conserved between at least 4 species are shown. Only conserved transcription factor binding sites before the transcription start site (+1) are shown. The CREB2 binding site is in blue. PRDI1, positive regulatory domain 1-binding factor 1; MAZ, myc associated zinc finger protein; FOXO3, forkhead box O3; MEL1, (MDS1/EVII-like gene 1) DNA binding domain 2; MyT1, Myelin transcription factor 1; vErbA, viral homolog of thyroid hormone receptor alpha1; SP1, specificity protein 1; NF1, nuclear factor 1; BARBIE, barbiturate-inducible element; NHLH1, nescient helix loop helix 1; HAND2 and E12, heterodimers of the bHLH transcription factors HAND2 (Thing2) and E12; AP4, activator protein 4; Pax-3, paired box 3; GCMA, Glial cells missing homolog 1; MZF1, myeloid zinc finger 1. *B*, qRT-PCR analysis of *Angptl2*, *VEGFA*, *Ang2* and *ADM* in HUVEC exposed to hypoxia (0.1% O₂) or normoxia (20% O₂) for 16 hours. β -actin was used as a house keeping control gene and mRNA levels were normalised to normoxia levels. Analysis was performed in triplicate. The Student's t test was used to assess the significance of increases in mRNA expression between normoxia and hypoxia. *, $p < 0.05$; **, $p < 0.01$. Columns, mean; bars, SE.

5.7 vIRF1 up-regulates *Angptl2* transcription using the first 1 kb of the *Angptl2* promoter

In vitro *Angptl2* promoter studies were performed to further investigate the mechanism by which vIRF1 up-regulates *Angptl2*. From the promoter analysis it was found that most conserved transcription factor binding sites were observed close to the transcription start site of *Angptl2* and within the first 1 kb of the *Angptl2* promoter (Fig. 5.7A). Therefore the first 1kb of the *Angptl2* promoter along with most of the first exon encoding the 5' untranslated region (UTR) of *Angptl2* was cloned into the luciferase reporter gene vector pGL3-basic and designated pGL3-1kb-Angptl2. In this vector the 1kb *Angptl2* promoter is cloned in front of a luciferase ORF with no promoter allowing luciferase enzymatic activity (measured through luminescence) to provide a measure of *Angptl2* promoter activity in transfected cells (Fig. 5.8A). Due to LEC being difficult to transfect, the *in vitro* *Angptl2* promoter studies were performed in 293T cells as these cells are easily transfected and readily available.

The cloned 1 kb *Angptl2* promoter was significantly active in 293T cells with the pGL3-1kb-Angptl2 construct giving ~10 fold higher normalised luminescence in transfected cells compared to pGL3-basic transfected cells (Fig. 5.8B). This is despite the *Angptl2* gene being expressed at very low levels in 293T cells (Fig. 5.8C). The 1 kb *Angptl2* promoter, however, was not as active as the simian virus 40 (SV40) promoter present in front of the luciferase ORF in the pGL3-control vector (Fig. 5.8B).

In order to determine whether vIRF1 could affect the *Angptl2* promoter activity the vIRF1 lentiviral construct and other lentiviral constructs were transfected into 293T cells along with the same amount of pGL3-1kb-Angptl2 or pGL3-basic. vIRF1 significantly up-regulated *Angptl2* promoter activity compared to 293T cells transfected with pSIN-MCS or vIRF1 mutant lentiviral construct (Fig. 5.8D). Both vIRF1 and vIRF1 mutant were expressed in transfected cells and over 95% of 293T cells transfected with pCSGW and pGL3-1kb-Angptl2 promoter were GFP positive indicating that efficient transfection was achieved

using the experimental protocol adopted (see Materials and Methods) (Fig. 5.8D). The effect of vIRF1 on *Angptl2* promoter activity in 293T cells is similar to the up-regulation of *Angptl2* transcription by vIRF1 in LEC. With the amount of vIRF1 induced up-regulation of the 1 kb *Angptl2* promoter activity compared to pSIN (1.7±0.1 fold) (Fig. 5.8D) being similar to the amount of *Angptl2* mRNA up-regulation in vIRF1 lentiviral infected LEC compared to pSIN-infected LEC (1.9±0.4 fold) (Fig. 5.6C). Therefore, it is likely that the ability of vIRF1 to up-regulate *Angptl2* is at least partly attributed to vIRF1 up-regulating *Angptl2* transcription rather than vIRF1 affecting *Angptl2* mRNA stabilisation.

The 1 kb *Angptl2* promoter was next mutated to further investigate how vIRF1 acts through the *Angptl2* promoter to up-regulate *Angptl2*. Promoter deletion constructs of the 1 kb *Angptl2* promoter were made with the pGL3-500bp-*Angptl2* and pGL3-319bp-*Angptl2* deletion constructs having 500 bp and 681 bp of the 1 kb *Angptl2* promoter removed respectively. Using these deletion constructs, vIRF1 induced up-regulation of *Angptl2* promoter activity compared to pSIN transfected cells was found to decrease in magnitude and significance as more of the 5' *Angptl2* promoter was deleted (Fig. 5.9A). This indicates that sites in the *Angptl2* promoter not immediately next to the predicted transcription start site but between -1000 to -319bp are important for efficient *Angptl2* up-regulation by vIRF1.

The CREB2 site near to the predicted transcription start site was mutated by site directed mutagenesis to determine whether this site was involved in the up-regulation of *Angptl2* by vIRF1. When the CREB2 site was mutated in the 1 kb *Angptl2* promoter it resulted in a decrease in promoter activity in both pSIN and vIRF1 transfected cells (Fig. 5.9B). However, the degree and significance of *Angptl2* up-regulation by vIRF1 compared to pSIN did not significantly change with the mutation of the CREB2 site (Fig. 5.9B) indicating that vIRF1 does not up-regulate *Angptl2* promoter activity using this site.

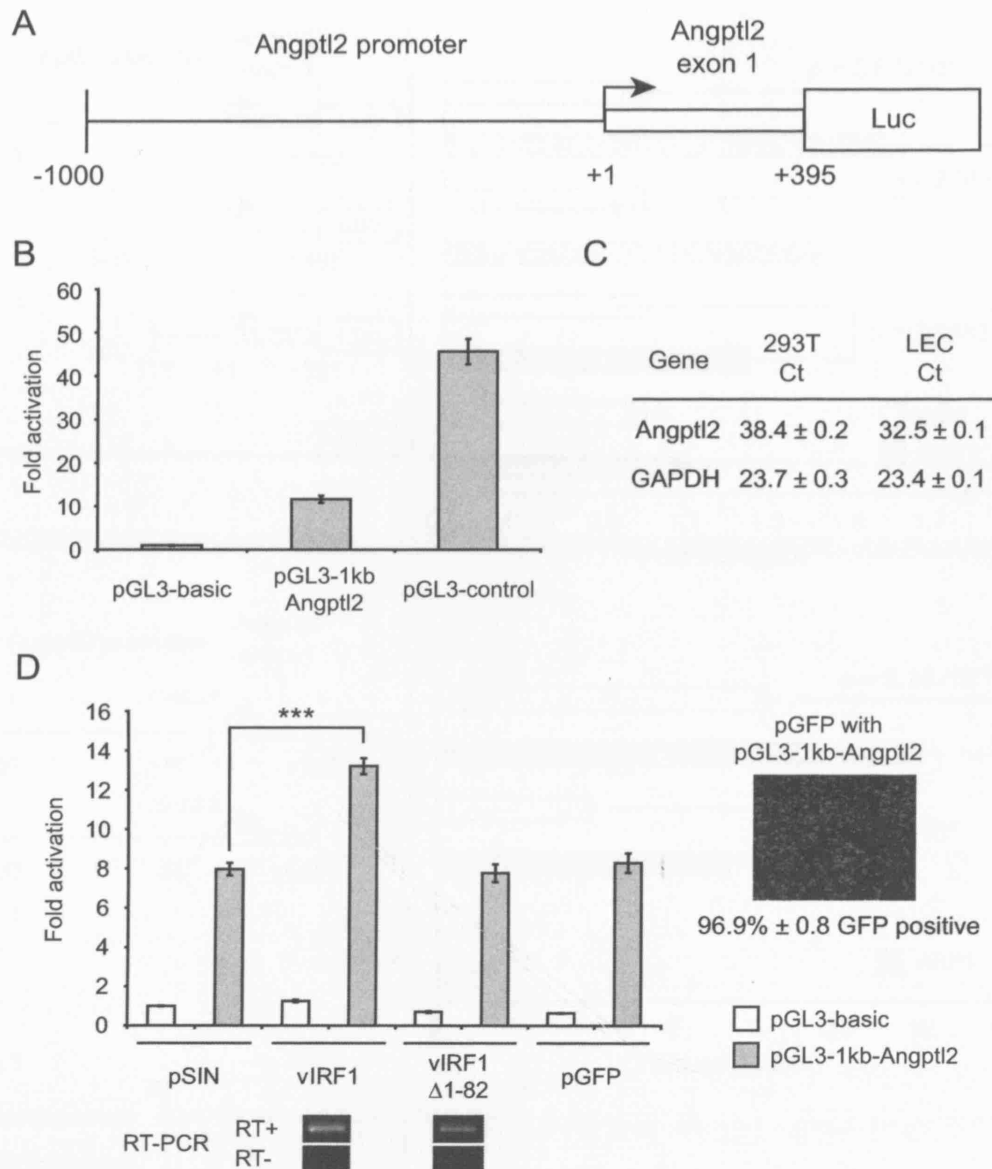


Figure 5.8. vIRF1 increases *Angptl2* promoter activity. *A*, a schematic diagram of the pGL3-1kb-Angptl2 reporter construct. The first 1 kb of the *Angptl2* promoter along with most of the first exon of *Angptl2* encoding the 5' UTR is cloned in front of the firefly luciferase (Luc) ORF in the pGL3-basic vector. *B*, 0.75×10^5 293T cells were transfected with 1 μ g of either pGL3-basic, pGL3-1kb-Angptl2 or pGL3-control (containing the SV40 promoter) and 48 h later the cells were harvested and the luminescence was measured as relative light units (RLU). The luminescence was normalised for total protein and then normalised to levels present in pGL3-basic transfected cells to give relative promoter activity. Experiment was performed in triplicate. *C*, qRT-PCR analysis of *Angptl2* and *GAPDH* in 293T cells and LEC. Experiments were performed in duplicate. Mean and standard error values are present in the table. *D*, same as (*B*) except 293T cells were transfected with 1 μ g of a lentiviral construct along with either 1 μ g of pGL3-basic or pGL3-1kb-Angptl2. Values were normalised to 293T cells transfected with pSIN plus pGL3-basic. Experiment was performed twice in triplicate. The Student's *t* test was used to assess the significance of increases in reporter activity between pSIN plus pGL3-1kb-Angptl2 transfected samples and other pGL3-1kb-Angptl2 transfected samples. ***, $p < 0.001$. RT-PCR analysis confirms the expression of vIRF1 and vIRF1 mutant (vIRF1 Δ 1-82) in transfected cells. Fluorescent microscope picture of 293T cells 48 h after transfection with 1 μ g pCSGW (pGFP) and 1 μ g pGL3-1kb-Angptl2 along with flow cytometry analysis to determine the percentage of GFP positive cells. Columns, mean; bars, SE.

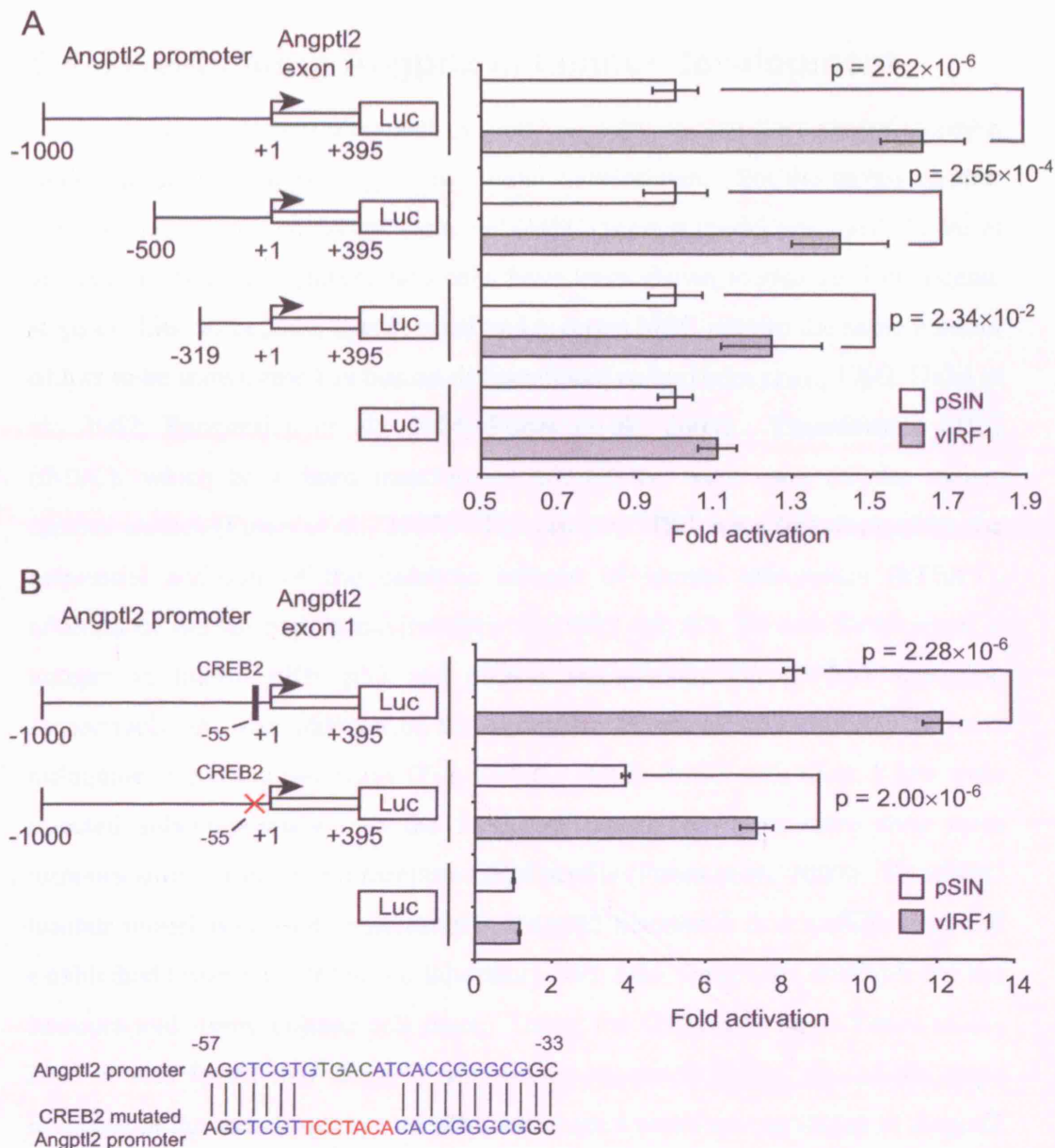


Figure 5.9. Mutation analysis of the *Angptl2* promoter. *A*, the effect of *Angptl2* promoter deletions on vIRF1 up-regulation of *Angptl2* promoter activity. 0.75×10^5 293T cells were transfected with either $1 \mu\text{g}$ of pGL3-basic or 1.5×10^{11} copies of either pGL3-1kb-*Angptl2*, pGL3-500bp-*Angptl2* or pGL3-319bp-*Angptl2* and made up to $1 \mu\text{g}$ using pGL3-basic. At the same time the 293T cells were transfected with $1 \mu\text{g}$ of either pSIN or vIRF1 lentiviral construct. 48 h later the cells were harvested and the luminescence was measured. The luminescence was normalised for total protein and then normalised to levels present in pSIN transfected cells for each of the different reporter constructs. *B*, the effect of mutating the CREB2 site on *Angptl2* promoter activity. The experiment was performed the same in (*A*) except 293T cells were transfected with $1 \mu\text{g}$ of either pGL3-1kb-*Angptl2*, pGL3-mutCREB2-*Angptl2* or pGL3-basic along with $1 \mu\text{g}$ of either pSIN or vIRF1 lentiviral construct. Values were normalised to 293T cells transfected with pSIN plus pGL3-basic. The mutated CREB2 site is shown in the schematic diagram as a red cross. The CREB2 site was mutated using site-directed mutagenesis and how the site was mutated in the 1 kb *Angptl2* promoter is shown. The CREB2 site is in blue with its core sequence shown in green and the bases replaced during site directed mutagenesis are shown in red. All experiments were performed twice in triplicate. The Student's t test was used to assess the significance of increases in reporter activity between pSIN and vIRF1 transfected cells for the different reporter constructs used. The p values are shown. Columns, mean; bars, SE.

5.8 Investigating Angptl2 in tumour development

In vivo mouse tumour studies with Angptl2 over-expression were started to begin to determine the role of Angptl2 in tumour development. For the mouse tumour studies a human mesenchymal stem cell (MSC) tumour model was used (Funes et al., 2007). Human differentiated cells have been shown to require 5 oncogenic steps or 'hits' to become transformed and primary MSC require the same number of hits to be transformed as human differentiated cells (Hahn et al., 1999; Hahn et al., 2002; Rangarajan et al., 2004; Funes et al., 2007). Transformed MSC (tMSC), which have been transformed genetically, were used for the mouse tumour studies (Funes et al., 2007). The primary MSC were transformed by the sequential addition of the catalytic subunit of human telomerase (hTERT), addition of human papillomavirus type 16 (HPV-16) E7, E6 and SV40 small T antigen to inhibit pRb, p53 and protein phosphatase 2A (PP2A) activities, respectively and the addition of the oncogenic H-*ras* to constitutively activate mitogenic signalling pathways (Fig. 5.10A). When tMSC with these 5 hits were injected subcutaneously into the flanks of immunodeficient mice they form tumours with a spindle-cell sarcoma GEM profile (Funes et al., 2007). The tMSC tumour model was used to investigate Angptl2 because it is a well-defined and established tumour model in our laboratory with microarray data available for the tumours and tissue culture cell lines. Using the GEM data from Funes et al., 2007 it was found that *Angptl2* was not up-regulated during any of the steps involved in the transformation of MSC although a small up-regulation of *Angptl2* was seen in the tMSC mouse tumours (Fig. 5.10B).

A tMSC cell line over-expressing Angptl2 was produced by cloning the *Angptl2* ORF into the retroviral vector pWZL-hygro containing hygromycin resistance. tMSC were infected with retroviral preparations and were selected to produce the Angptl2 tMSC cell line and the empty vector tMSC cell line (control tMSC cell line) containing the pWZL-hygro empty vector. qRT-PCR analysis confirmed *Angptl2* mRNA up-regulation in the Angptl2 tMSC compared to the empty vector tMSC (Fig. 5.10C). However, Angptl2 protein was not up-regulated in the cell lysates of Angptl2 tMSC compared to empty vector tMSC when the cell lines were grown in normal MSC media (Fig. 5.10D). Only when the cell lines were

grown overnight without serum was an up-regulation of Angptl2 protein in the cell lysates detected in the Angptl2 tMSC compared to the empty vector tMSC (Fig. 5.10E). This suggests that the increased Angptl2 protein is secreted in the Angptl2 tMSC compared to the empty vector tMSC when the cells are grown in normal MSC media and therefore not detected when the Western blot analysis was performed on the cell lysates.

Angptl2 or empty vector tMSC were injected into the flanks of immunodeficient mice and tumour volume was monitored until the tumours were harvested on day 29 after inoculation (Fig. 5.11). Angptl2 tMSC tumours initially grew slightly quicker than the empty vector tumours. After the initial growth in tumour volume both empty vector and Angptl2 tMSC tumours regressed in size. The empty vector tumours then quickly recovered and rapidly grew in size like other previously reported tMSC tumours. (Funes et al., 2007). However, the Angptl2 tMSC tumours failed to recover in size like the empty vector tMSC tumours. When the mice having the Angptl2 tMSC tumours were culled, small tumours were recovered although not visible from outside of the mice. Preliminary analysis suggests that the Angptl2 tumours have a high level of necrosis and lack vessels compared to empty vector tMSC tumours resulting in smaller Angptl2 tumours compared to the empty vector tMSC tumours (data not shown). Stainings are currently being performed to verify this and to determine in more detail the effect of Angptl2 over-expression on the tMSC tumours. However, the difference in growth and size of the Angptl2 and empty vector tMSC tumours indicates that Angptl2 does effect tumour development and therefore Angptl2 warrants further investigation to understand its expression and role in neoplasms.

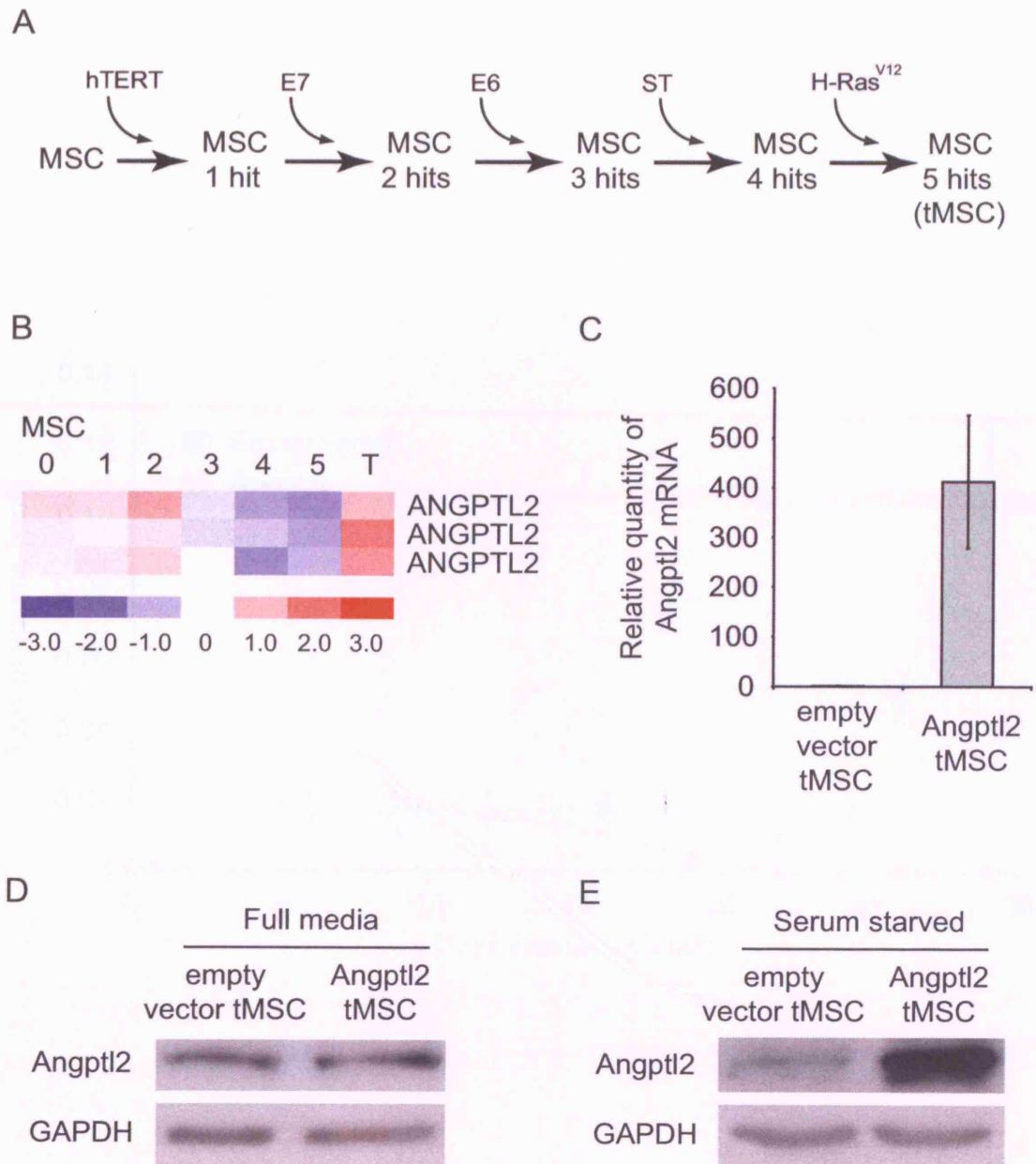


Figure 5.10. Angptl2 over-expression in transformed mesenchymal stem cells. *A*, schematic diagram of the stepwise transformation of parental MSC to transformed MSC (tMSC). The addition of each cellular or viral oncogene to the MSC is designated as a hit. Adapted from Funes et al., 2007. *B*, a heat map of the relative changes of *Angptl2* expression between the various in vitro MSC cell lines with different number of hits (0-5) and the tMSC tumours in nude mice (T). The GEM data were obtained from Funes et al., 2007 and is an average of 3 samples for each of the cell lines (0-5) and an average of 5 tumours for the tumour GEM data (T). All probe-sets against *Angptl2* mRNA are shown. *C*, tMSC were infected with an expression retroviral construct (pWZL-hygro) containing the *Angptl2* ORF or empty vector and were selected using hygromycin to produce Angptl2 tMSC and empty vector tMSC cell lines. The relative *Angptl2* mRNA levels for empty vector tMSC and Angptl2 tMSC grown in MSC media is shown and was determined by qRT-PCR. Experiment was performed in triplicate. *Columns*, mean; *bars*, SE. *D*, Western blot analysis of Angptl2 and GAPDH on the cell lysates of empty vector and Angptl2 tMSC cell lines grown in MSC media. *E*, same as (*D*) except cell lines were serum starved by being grown overnight in DMEM media containing no FBS.

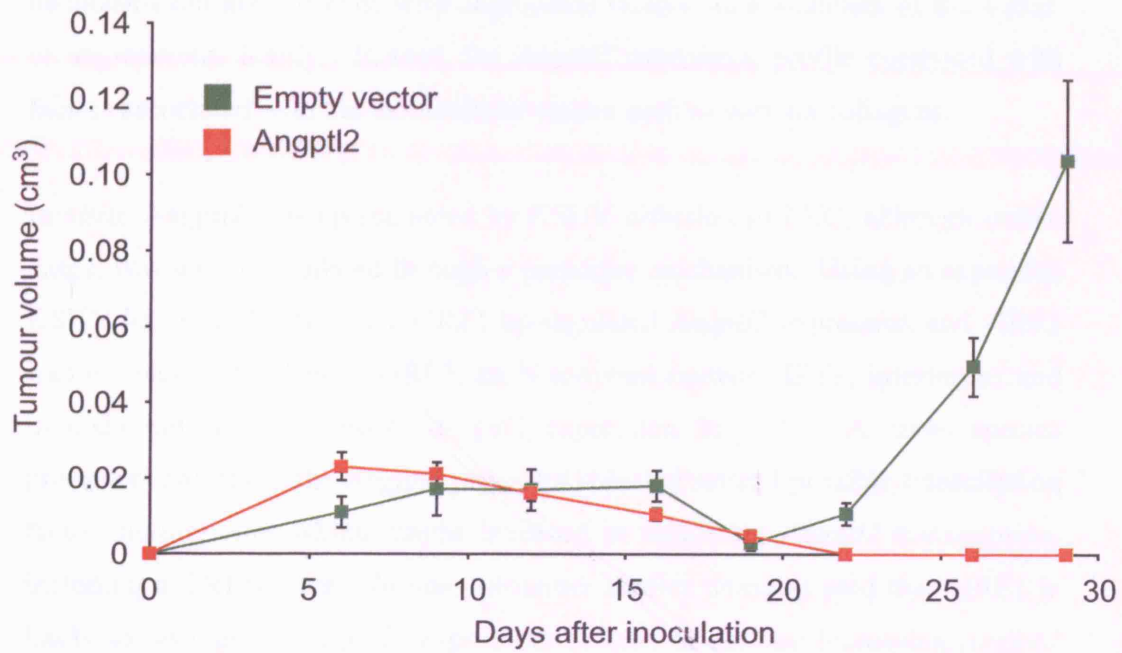


Figure 5.11. The effect of Angptl2 on tMSC tumour growth. 4×10^6 tMSC over-expressing Angptl2 or empty vector were injected subcutaneously into the flanks of immunodeficient mice. The tumour volumes were measured over time until day 29 when the tumours were harvested. The tumour volume was determined using the ellipsoidal method (See Materials and Methods). *Points*, mean tumour volume ($n = 6$); *bars*, S.E.

5.9 Summary

Angptl2 is a factor which affects endothelial cells and haematopoietic stem cells, however, its role and regulation in KS and other neoplasms has not been previously investigated (Kim et al., 1999; Zhang et al., 2006). GEM analysis revealed that *Angptl2* is up-regulated in KS compared to skin and is expressed in a variety of neoplasms. Unlike *Ang2*, the *Angptl2* expression profile in neoplasms did not correlate with angiogenic factors such members of the VEGF or angiopoietin family. Instead, the *Angptl2* expression profile correlated with factors associated with the extracellular matrix such as various collagens.

In vitro, *Angptl2* was up-regulated by KSHV infection of LEC, although unlike *Ang2*, was not up-regulated through a paracrine mechanism. Using an expanded KSHV lentiviral library only vIRF1 up-regulated *Angptl2* expression and vIRF1 was expressed in KLEC. vIRF2, an N terminal mutant vIRF1, interferons and hypoxia did not up-regulate *Angptl2* expression in LEC. A cross species promoter analysis of the *Angptl2* promoter revealed several possible transcription factor binding sites which maybe involved in regulating *Angptl2* transcription, including a CREB2 site. *In vitro* promoter studies demonstrated that vIRF1 is likely to up-regulate *Angptl2* expression at least in part by increasing *Angptl2* promoter activity. The conserved CREB2 site in the *Angptl2* promoter was found to be important for *Angptl2* promoter activity but not involved in the vIRF1 induced up-regulation of *Angptl2*.

Over-expression of *Angptl2* in a tumour model resulted in altered tumour growth with tumours of *Angptl2* over-expressing cells being smaller than the control tumours and therefore suggesting a role of *Angptl2* in tumour development.

Chapter 6. Discussion and future work

In this thesis a partial expression library of KSHV genes was constructed to investigate KSHV pathogenesis. Using the KSHV lentiviral library the regulation of Ang2 and Angptl2 was investigated and initial studies were undertaken to investigate the potential role of these molecules in KS development.

6.1 The KSHV lentiviral library

Using mainly a PCR cloning strategy various KSHV ORFs were cloned into the pSIN-MCS lentiviral vector to create a KSHV lentiviral library containing selected KSHV encoded genes (Table 3.1). The genes cloned into this expression library included most of the genes associated with KSHV latency: vIRF1, kapA, vFLIP, vcyclin, LANA-1, and LAMP, and several lytic genes. The genes cloned were mainly selected due to them being important for KSHV pathogenesis, such as LANA-1, which inhibits p53 and pRb function (Friborg, Jr. et al., 1999; Radkov et al., 2000), kapA, which is involved in cellular transformation (Muralidhar et al., 1998) and also many KSHV genes with cellular homologues which are thought to have been pirated from the host genome (Moore and Chang, 1998). These KSHV genes with cellular homologues, such as vIL6, vFLIP and vGPCR, have been shown to be involved in processes important for KS such as angiogenesis, transformation and cell survival (Jenner and Boshoff, 2002). The later expansion of the initial KSHV lentiviral library by other members of the laboratory continued to select genes particularly important for KSHV pathogenesis, rather than structural genes. Therefore, genes such as, KSHV's Rta, vMIPs, involved in angiogenesis (Boshoff et al., 1997; Stine et al., 2000) and vMIR2, which down-regulates MHC-I (Ishido et al., 2000), were cloned into the KSHV lentiviral library.

Lentiviruses were employed for this expression library, because they infect primary cells with a relatively high efficiency and are able to infect both dividing and non-dividing cells, unlike other types of retroviruses (Lewis and Emerman,

1994; Naldini et al., 1996). This is important as the KS spindle cells have a GEM profile most similar to that of LEC (Wang et al., 2004a) and therefore primary LEC were mainly used throughout the work to investigate KSHV and KS. Primary LEC, which are difficult to transfect, were found to be easily infected by lentiviruses with over 80% of LEC expressing GFP when 1 ml of GFP encoding pCSGW lentivirus preparation was added to 1×10^5 LEC (Fig. 3.6).

6.1.1 Titration of lentiviral preparations

To titre the lentiviral preparations, a qPCR based titration system was developed which quantitated the number of lentiviral DNA molecules present in infected cells to give average lentiviral copies per cell (Fig. 3.5). This system to titre lentiviral preparations based on quantitating lentiviral DNA in infected cells was chosen as it was previously found to be the most accurate method to titre lentiviral preparations (Sastry et al., 2002). The highly sensitive nature of the qPCR technique means this method was susceptible to contamination by external lentiviral plasmid or genomic DNA containing integrated lentiviral constructs. This problem was solved by ensuring that lentiviral cloning, genomic DNA preparation, qPCR plate preparation, addition of genomic DNA to the qPCR plate and running the qPCR were performed in separate rooms using separate equipment.

6.1.2 Lentiviral construct expression in LEC

qPCR quantification of the average lentiviral copies per cell of LEC infected with the GFP encoding pCSGW lentiviral preparation, revealed that when LEC had approximately 1 c/c only ~25% of LEC expressed GFP (Fig. 3.6). The low numbers of LEC expressing GFP was due to a large proportion of integrated lentiviral constructs not being transcribed. This is because a large proportion of integrated lentiviral constructs are present in parts of the genome not amenable to transcription (Sastry et al., 2002; Lizce et al., 2003). Therefore, even when 10 c/c of pCSGW were present in LEC, not all LEC expressed GFP.

All of the KSHV genes cloned into the pSIN-MCS construct for the selected KSHV lentiviral library were expressed in lentiviral infected LEC (Fig. 3.7). However, throughout the use of this lentiviral system it was often observed that the effects produced from KSHV genes expressed in lentiviral infected cells were often lower in magnitude compared to the effects seen in KSHV-infected LEC (KLEC). One possible reason for this is that lentiviral infected LEC express KSHV encoded genes at lower levels than in KLEC. vGPCR or vIRF1 infected LEC with 8 c/c have about 5-10 fold lower levels of KSHV gene mRNA expression compared to GFP sorted KLEC (Dimitrios Lagos, unpublished results, CR-UK Viral Oncology Group). The reason for low KSHV gene expression in lentiviral infected LEC compared to KLEC could be because there are hundreds of copies of KSHV genome per infected KLEC (Wang et al., 2004a) compared to only ~10 c/c of lentiviral construct in lentiviral infected LEC. Interestingly KS cells only have about 10 copies of KSHV genome per cell (Duprez et al., 2007) whereas PEL cells have about 100 copies of KSHV genomes per cell (Asahi-Ozaki et al., 2006).

6.1.3 Overview of the KSHV lentiviral library

The initial selected KSHV lentiviral library constructed contained 13 KSHV encoded genes. This expression library continues to grow and now consists of 31 KSHV genes and also includes each of the KSHV encoded miRNAs cloned individually into the lentiviral construct. The KSHV lentiviral library, in addition to being used to investigate Ang2 and Angptl2, has also been used to investigate the mechanism KSHV uses to regulate MHC-I (Lagos et al., 2007), Toll-like receptor 4 (Dimitrios Lagos, unpublished results, CR-UK Viral Oncology Group), calcitonin receptor-like receptor (CRLR) (Leonid Nikitenko, unpublished results, CR-UK Viral Oncology Group), the proteasome (Marie-Helene Malcles, unpublished results, CR-UK Viral Oncology Group) as well as other factors involved in KSHV's pathophysiological effects. The KSHV lentiviral library continues to be a useful tool to investigate KSHV pathogenesis and biology.

6.2 Studies into KSHV and Ang2

Ang2 is a crucial postnatal angiogenic factor, which also has an important role in lymphangiogenesis and inflammation (Maisonpierre et al., 1997; Gale et al., 2002; Fiedler et al., 2006). Increased Ang2 expression in tumours often results in increased angiogenesis and tumour growth, whereas Ang2 inhibition has the opposite effect. (Tanaka et al., 1999; Ahmad et al., 2001; Etoh et al., 2001; Oliner et al., 2004; Sarraf-Yazdi et al., 2007). Ang2 was previously shown to be up-regulated in the sera of individuals with KS, in the media of KLEC, and at the mRNA level in KS lesions (Brown et al., 2000; Wang et al., 2004a).

6.2.1 Ang2 in KS lesions

Here it was shown that Ang2 protein is highly expressed in early (patch stage) and late (nodular) KS lesions (Fig. 4.1). It has been previously shown that Ang2 is not expressed in normal adult tissues, except at sites of vessel remodelling (Maisonpierre et al., 1997) and often in human malignancies (Tait and Jones, 2004). In early (patch stage) KS lesions, areas of intense Ang2 staining were seen which could be sites of lytic KSHV replication (expression of vGPCR and vIL6). This correlates with observations that suggest the association of early KS with increased lytic viral replication (Staskus et al., 1997). As shown in a previous study, KSHV infection of LEC, an *in vitro* model of KS, caused an up-regulation of Ang2 and therefore making this a valid model to investigate the regulation of Ang2 by KSHV (Fig. 4.2) (Wang et al., 2004a).

6.2.2 Regulation of Ang2 by KSHV

Using the selected KSHV lentiviral library, vIL6 and vGPCR were found to up-regulate Ang2 secretion and are likely to contribute, at least in part, to the up-regulation of Ang2 by KSHV infection (Fig. 4.3). The up-regulation of Ang2 by KSHV, as well as vIL6 and vGPCR, was found to involve a paracrine mechanism (Fig. 4.6A). This reveals how the small percentage of cells undergoing lytic replication and expressing vGPCR and vIL6 (Jenner and Boshoff, 2002) can act on nearby cells to contribute to the overall increase in Ang2 expression seen in KLEC or KS (Wang et al., 2004a). Therefore, a relatively large population of

cells are up-regulating Ang2 despite the small percentage of lytic cells. The paracrine mechanism did not involve VEGFA or other factors signalling through VEGFR1 or VEGFR2 (Fig. 4.6B). Instead vGPCR and vIL6 result in the expression of other secreted factors, such as VEGFC and vIL6 itself, which may contribute to the paracrine up-regulation of Ang2.

Amongst other pathways, Ang2 expression is regulated by the MAPK pathway in endothelial cells (Oh et al., 1999; Hasegawa et al., 2004; Hegen et al., 2004). vIL6, vGPCR and KSHV activated the MEK MAPK pathway in LEC causing increased levels of phosphorylated ERK (the target of MEK) (Fig. 4.7). vGPCR caused a constitutive increase in phosphorylated ERK levels, whereas vIL6 caused a pulse up-regulation of phosphorylated ERK. This difference in the way the MAPK pathway is activated by vGPCR and vIL6 is probably due to vGPCR being a constitutively active receptor, unlike the gp130 receptor of vIL6 (Arvanitakis et al., 1997; Molden et al., 1997).

From pharmacologic studies it was shown that inhibiting the MEK MAPK pathway, inhibited the up-regulation of *Ang2* transcription by vIL6, vGPCR and KSHV (Fig. 4.8). This concurs with a study showing that KSHV up-regulates *Ang2* expression by activating activator protein 1 (AP1) and Ets1 transcription factors, which are activated by MAPK pathways and bind and activate the *Ang2* promoter (Ye et al., 2007). Both AP1 and Ets1 transcription factors were found to be activated in KSHV infected HUVEC by the MEK, JNK and p38 MAPK pathways (Xie et al., 2005; Ye et al., 2007). When the up-regulation of *Ang2* in KLEC was inhibited, using a MEK pharmacologic inhibitor, the up-regulation of *Ang2* in KLEC compared to LEC was not completely abolished. This indicates that other pathways apart from the MEK MAPK pathway, such as the JNK or p38 MAPK pathways, are likely to be involved in the up-regulation of *Ang2* by KSHV. However, from the pharmacologic inhibition studies, it is likely that MEK MAPK pathway is the main pathway for the up-regulation of *Ang2* by KLEC. This is because the MEK inhibitor suppressed *Ang2* mRNA levels to that of pSIN levels in vIL6 and vGPCR expressing LEC and the MEK inhibitor abolished most of the up-regulation of *Ang2* in KLEC. It is interesting to note that other genes in the KSHV genome, such as vFLIP and LAMP (K15), are

known to activate MAPK pathways such as the MEK or JNK MAPK pathway (Brinkmann et al., 2003; An et al., 2003), yet they did not up-regulate Ang2 in our study (Fig. 4.3). This could be because these viral genes activate different pathways in primary LEC, compared to the 293 or Cos7 cells used in previous studies. Whether vFLIP, LAMP or other KSHV encoded genes activate the MAPK pathways in LEC requires further investigation.

A summary of the proposed mechanism by which vGPCR and vIL6 up-regulate Ang2 expression is shown in Figure 6.1. In vGPCR-expressing cells, direct up-regulation of *Ang2* by vGPCR is likely to take place through its constitutive activation of the MEK MAPK pathway (Arvanitakis et al., 1997; Smit et al., 2002). vGPCR induces *Ang2*, in addition, indirectly by unknown secreted factor(s) (not VEGFA). vIL6-induced *Ang2* expression is likely to be via gp130 - the specific receptor for this viral cytokine (Molden et al., 1997). However, the contribution of other secreted factors in supernatants from vIL6-expressing cells on *Ang2* expression cannot be excluded.

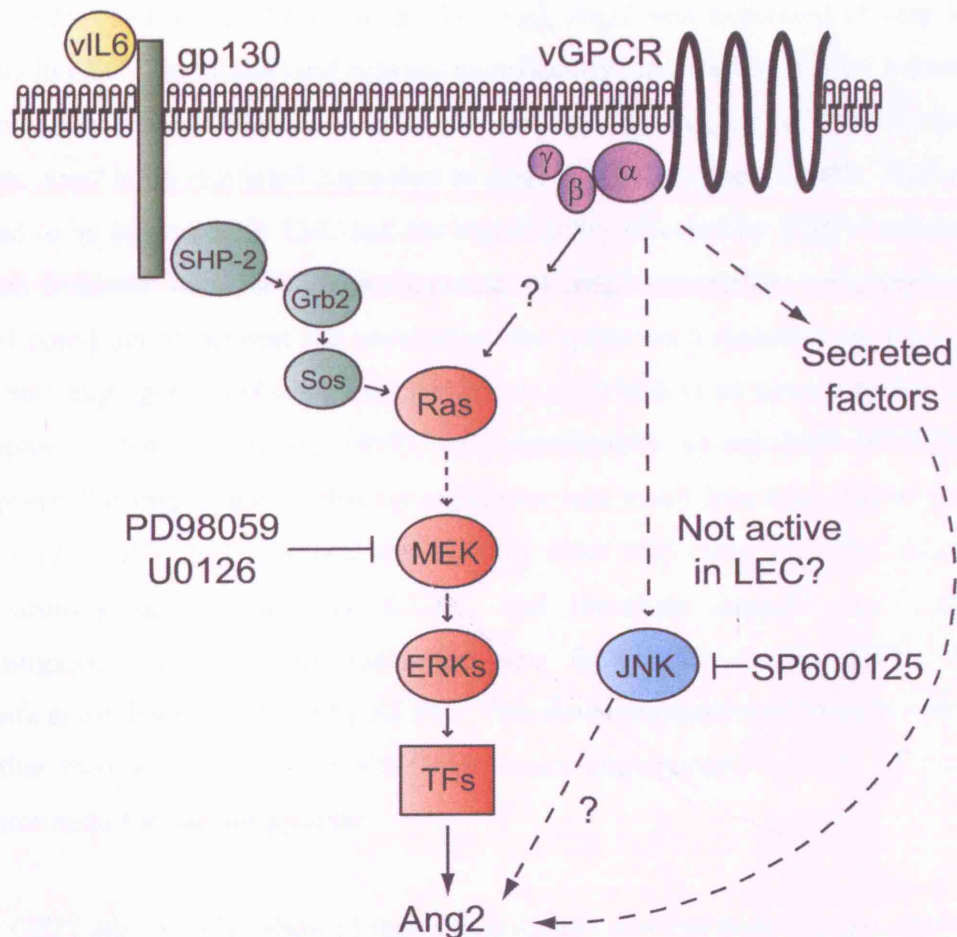


Figure 6.1. Schematic diagram of the proposed mechanism by which vIL6 and vGPCR contribute to the up-regulation of *Ang2* in KLEC. Although vGPCR has been shown previously to activate MEK, it has not been shown explicitly to be by way of Ras, although it is likely to be the case (Smit et al., 2002). The vIL6 signalling pathway is based on previous reports (Osborne et al., 1999). The points of action of pharmacologic inhibitors used are shown. *Solid arrows*, direct regulation; *dashed arrows*, indirect regulation of the target. *TFs*, transcription factors such as AP1 and Ets1 (Ye et al., 2007).

6.2.3 KSHV's regulation of angiogenic factors relevant or related to Ang2

GEM analysis of angiogenic factors was performed to investigate whether KSHV infection of LEC regulated factors related to *Ang2* or important for its function (Fig. 6.2). The observation that, unlike *Ang2*, *Ang1* was expressed at very low levels in LEC (Fig. 4.12B) and was not significantly regulated by KSHV infection is consistent with the expression profile observed in the majority of other tumours where *Ang2* is up-regulated compared to *Ang1* (Tait and Jones, 2004). *Tie2* was found to be expressed in LEC and not significantly affected by KSHV infection, which indicates how the relative increase of *Ang2* expression compared with *Ang1* could act to prevent the maturation and quiescence signalled by *Tie2* and promote angiogenesis (Gale et al., 2002). *Ang4*, which is an agonist to the *Tie2* receptor (Valenzuela et al., 1999), was significantly up-regulated by KLEC, however, the magnitude of this up-regulation was much less than that of *Ang2* (Appendix Table A1). *Angptl2* was the only other angiopoietin besides *Ang2* to be strongly up-regulated by KSHV, and therefore *Angptl2* was further investigated. *Angptl4*, an anti-angiogenic factor (Ito et al., 2003), was significantly down-regulated by KLEC. This down-regulation of *Angptl4* may be another mechanism by which KSHV promotes angiogenesis and the necessary environment for tumour growth.

The GEM analysis also showed that VEGFRs and some of their ligands were up-regulated by KSHV infection of LEC. This could be important for *Ang2* function because in the absence of active VEGFA, high levels of *Ang2* can induce capillary regression and endothelial cell death (Lobov et al., 2002). Two of the most highly up-regulated angiogenic genes by KSHV infection are members of the matrix metalloproteinase family (including matrix metalloproteinase 9), which degrade the extracellular matrix and release trapped growth factors such as VEGFA (Fig. 4.11) (Rundhaug, 2005). *Ang2* is involved in lymphangiogenesis, as is the essential VEGFC / VEGFR3 axis (Gale et al., 2002; Adams and Alitalo, 2007). KSHV up-regulates *VEGFR3* and perhaps also *VEGFC* under certain conditions such as during lytic replication when *vIL6* and *vGPCR* are expressed (Fig. 4.12C).

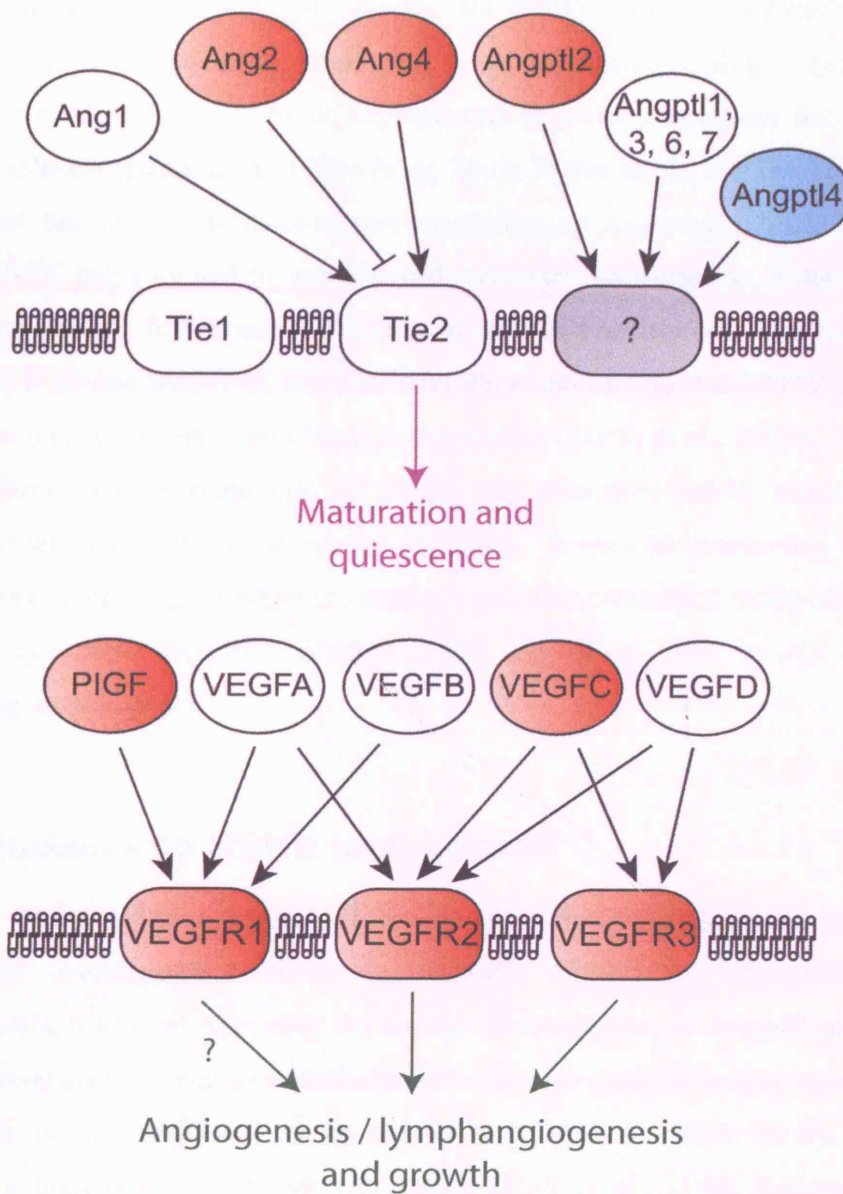


Figure 6.2. Regulation by KSHV of the angiopoietin family members and factors involved in Ang2 function. *Red*, gene expression that was significantly up-regulated by KSHV infection of LEC; *Blue*, gene expression that was significantly down-regulated; *white*, no significant change. The schematic diagram is based on the heat map from (Fig. 4.12A). A change in expression between LEC and KLEC was considered significant when $q < 0.001$.

6.2.4 Future work into Ang2 and KS

A recent publication demonstrated that the up-regulation of Ang2 secretion by KSHV infection of HUVEC was needed for KSHV to cause a paracrine up-regulation of angiogenesis *in vivo* using a mouse Matrigel plug angiogenesis assay (Ye et al., 2007). Tumour angiogenesis is a critical process for KS and other neoplasms (Hanahan and Weinberg, 2000; Mutlu et al., 2007). Therefore, Ang2 and the molecular mechanisms regulating its expression, including the MEK MAPK pathway and its associated downstream transcription factors, might present targets for future anti-KS therapeutics (Madhusudan and Harris, 2002). Recently, a mouse model of KS has been developed using the KSHV genome present in a bacterial artificial chromosome (BAC) (Mutlu et al., 2007). This KS model shows an up-regulation of Ang2 and therefore could serve as an experimental model to test anti-Ang2 therapies. It may be interesting also for future work to investigate whether Ang2 has important effects directly on the KS spindle cells, and therefore whether Ang2 has other roles in KS besides increasing angiogenesis.

6.3 Studies into KSHV and Angptl2

The role and regulation of Angptl2 in KS or other neoplasms has not been previously investigated. However, Angptl2 appears to be involved in angiogenesis, a process necessary for tumour development, as Angptl2 promotes the sprouting and survival of endothelial cells, is important for proper vasculature formation in zebrafish and is up-regulated in diabetic nephropathy, which displays a breakdown of proper vasculature (Kim et al., 1999; Kubota et al., 2005; Sun et al., 2007). In addition, Angptl2 is a haematopoietic stem cell growth factor and therefore may affect tumour inflammation (Zhang et al., 2006).

6.3.1 *Angptl2* expression in KS and other neoplasms

Using microarray data it was found that *Angptl2* was up-regulated in KS versus skin and was expressed in a variety of neoplasms especially in tumours of the pancreas, breast and colon (Fig. 5.1). However, the expression profile of *Angptl2*

in neoplasms did not correlate with expected angiogenic factors such as members of the VEGF or angiopoietin family and their receptors, as *Ang2* did in the same set of tumours (Fig. 5.2). Instead, the *Angptl2* expression profile correlated with the expression profile of extracellular matrix associated molecules such as collagens and matrix metalloproteinases. This GEM analysis is the first evidence that *Angptl2* is expressed in a variety of neoplasms, inferring it could have a role in tumour development. The observation that the *Angptl2* expression profile did not correlate with that of *Ang2* or other expected angiogenic factors suggests that *Angptl2* is regulated through a different mechanism in these neoplasms, compared to *Ang2*. Also, this suggests that *Angptl2* could have a different role in tumour angiogenesis, than these other well characterised angiogenic factors.

6.3.2 Regulation of *Angptl2* by KSHV

KSHV infection of LEC was found to up-regulate *Angptl2* mRNA and intracellular protein (Fig. 5.3). It is likely that KSHV infection also results in an increase in secreted *Angptl2* protein levels as is seen for *Ang2* (Fig. 4.2B). However, despite numerous attempts by Western blotting, *Angptl2* secreted protein could not be detected in either the supernatants of LEC, lentiviral infected LEC, KLEC or even transformed mesenchymal stem cells (tMSC) over expressing *Angptl2* (data not shown). This is likely to be due to technical difficulties associated with working with the secreted *Angptl2* protein in Western blot analysis. For future work, an *Angptl2* ELISA should be developed to confirm that changes in *Angptl2* intracellular protein result in changes in *Angptl2* secreted levels.

Unlike *Ang2*, *Angptl2* was not up-regulated when the supernatant of KLEC was added to uninfected LEC. This indicates that *Angptl2* was not up-regulated by KSHV in a paracrine mechanism using factors secreted from KLEC (Fig. 5.3D). Performing a screen with an expanded KSHV lentiviral library, only vIRF1 was found to up-regulate *Angptl2* and as vIRF1 is expressed in KLEC it is likely that vIRF1 at least contributes in part to the up-regulation of *Angptl2* by KSHV (Fig. 5.4). vIRF1 is latently expressed in KS and therefore it is likely that all KSHV infected cells in KS lesions up-regulate *Angptl2* (Dittmer, 2003).

Interestingly, vIRF2, unlike vIRF1, did not cause an up-regulation of *Angptl2* in LEC (Fig. 5.4). vIRF1 and vIRF2 are structurally dissimilar and while they share some functions such as inhibiting interferon and IRF responses they also have specific roles such as the inhibition of p53 by vIRF1 and the inhibition of NF- κ B signalling by vIRF2 (Zimring et al., 1998; Burysek et al., 1999a; Burysek et al., 1999b; Seo et al., 2001). The up-regulation of *Angptl2* specifically by vIRF1 and not by vIRF2 is therefore not unexpected. vIRF3 and vIRF4 were not tested, however unlike vIRF1, these genes are not expressed in KS latently infected cells (Dittmer, 2003).

The up-regulation of *Angptl2* by vIRF1 was not expected as vIRF1 or cellular IRFs have not been previously shown to up-regulate angiogenic factors such as members of the VEGF or angiopoietin family. Instead, IFN α and IFN γ whose signalling is mediated by IRFs, have previously been shown to inhibit tumour angiogenesis and the secretion of angiogenic factors (Rosewicz et al., 2004; Ribatti et al., 2006; Avnet et al., 2007; Paun and Pitha, 2007). However, IFNs were found not to effect *Angptl2* expression in LEC or lentiviral infected LEC, despite vIRF1 altering responses to IFNs (Fig. 5.6) (Li et al., 1998). *Angptl2* was also not up-regulated by hypoxia as are typical angiogenic factors such as VEGFA and Ang2 (Fig. 5.7B) (Forsythe et al., 1996; Pichiule et al., 2004). Therefore, these data suggest that *Angptl2* is not regulated like typical angiogenic factors in KS or in other neoplasms.

6.3.3 *Angptl2* promoter studies and vIRF1

Promoter analysis of *Angptl2* revealed several conserved transcription factor binding sites close to the predicted transcription start site of *Angptl2*, which are likely to have a role in regulating *Angptl2* expression (Fig. 5.7). vIRF1 was found to up-regulate *Angptl2* promoter activity indicating that it is likely that vIRF1 up-regulates *Angptl2* by increasing *Angptl2* transcription (Fig. 5.8). A CREB2 site near the transcription start site (-55bp) of *Angptl2* was found to be important for basal *Angptl2* promoter activity, although not involved in the up-regulation of *Angptl2* by vIRF1 (Fig. 5.9). Instead, the section of *Angptl2*

promoter between -1000 to -319bp was found to be particularly important for the up-regulation of *Angptl2* by vIRF1, although some vIRF1 induced up-regulation of *Angptl2* was still achieved when this part of the promoter was removed (Fig. 5.9).

vIRF1 is unlikely to bind directly to the *Angptl2* promoter as its DNA binding site is not present. Promoter mutagenesis studies suggest that vIRF1 up-regulates or activates one or more transcription factors which bind at several positions in the first 1 kb of the *Angptl2* promoter to cause an up-regulation of *Angptl2* promoter activity. Transcription factor binding sites further than 1 kb upstream from the transcription start site of the *Angptl2* promoter were not investigated *in vitro*. However, these upstream transcription factor binding sites are unlikely to be important, because the magnitude of the up-regulation of *Angptl2* promoter activity achieved by vIRF1 with the first 1 kb of the *Angptl2* promoter is similar in magnitude to the up-regulation of *Angptl2* transcription seen in vIRF1 infected LEC.

6.3.4 Function of *Angptl2* in cancer and future work

To begin to investigate the function of *Angptl2* in KS and other neoplasms *Angptl2* was over-expressed in a model of tMSC which form tumours in immunodeficient mice that are similar to spindle cell sarcomas (Funes et al., 2007). *Angptl2* over-expressing tMSC tumours grew differently and were smaller in size compared to the control tMSC tumours (Fig. 5.11). Preliminary analysis suggests that the *Angptl2* over-expressing tMSC formed tumours which were more necrotic with fewer vessels compared to the control tumours. As *Angptl2* had a significant effect on tumour growth in this tumour model, it suggests that *Angptl2* expression has an effect on human tumour development and therefore warrants further investigation. Increased expression of pro-angiogenic factors, like Ang2, in tumours normally results in increased tumour growth and angiogenesis (Ahmad et al., 2001; Bergers and Benjamin, 2003; Nikitenko et al., 2006). Perhaps *Angptl2* caused reduced growth and angiogenesis in the context of the tMSC tumour model because this model does not provide the correct environment for *Angptl2* to act as pro-angiogenic factor.

A possible hypothesis is that *Angptl2* cooperates with other angiogenic factors present in KS and other neoplasms to alter tumour vasculature and the tumour environment to ultimately promote tumour growth and development. Functional studies are required to investigate this. Therefore, future work will involve up-regulating *Angptl2* and knocking-down *Angptl2* expression using RNA interference (RNAi) in other tumour models and studying the effect of altered *Angptl2* expression on tumour development and biology. Proposed tumour models planned for these studies would be the Lewis lung carcinoma tumour model, to investigate *Angptl2* in the context of tumorigenesis in immunocompetent mice (Bertram and Janik, 1980), and the KSHV BAC mouse tumour model, (Mutlu et al., 2007) which would allow the effect of *Angptl2* on KS to be investigated. Other future work to further characterise the regulation of *Angptl2* would include performing immunohistochemistry in KS and other neoplasms to determine whether *Angptl2* protein is expressed in cancer and to further investigate how *vIRF1* up-regulates *Angptl2*. Chromatin immunoprecipitation (ChIP) studies could be performed to determine whether *vIRF1* binds to the *Angptl2* promoter (O'Neill et al., 2006).



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Appendix 1: Phylogenetic tree of angiopoietin family members

A phylogenetic tree of angiopoietin family members was produced in collaboration with Stephen Henderson (CR-UK Viral Oncology Group) (Fig. A1). Protein sequences of the human, mouse and zebrafish angiopoietin family members were obtained from the UniProtKB/Swiss-Prot database and then processed using BioEdit software (<http://www.mbio.ncsu.edu/BioEdit/bioedit.html>). After an initial CLUSTAL W (Thompson et al., 1994) alignment, large insert regions were removed to leave domains conserved between all family members for a second alignment. A neighbourhood joining tree was created using the second alignment and plotted using Treeview software (Page, 1996).

From this analysis, Ang2 and Angptl2 are not closely related and are more evolutionarily conserved with other angiopoietin family members than with each other (Fig. A1). Zebrafish and human Angptl2 are closely related and therefore observations made with zebrafish Angptl2 are likely to be relevant to human Angptl2 (Fig. A1).

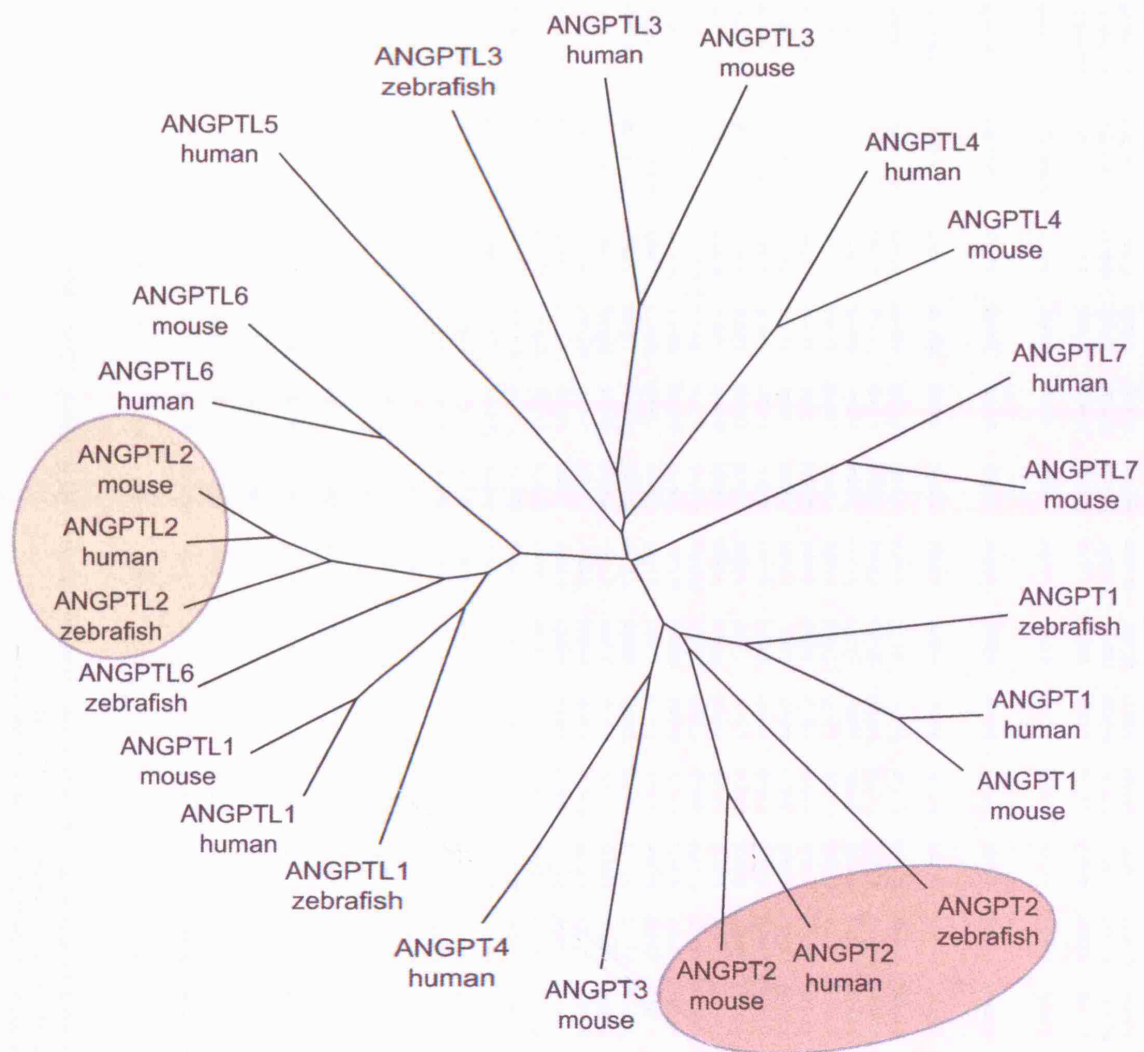


Figure A1. Phylogenetic tree of human, mouse and zebrafish angiopoietin family members. The analysis was performed using the amino acid sequences of the angiopoietin family members. The relative evolutionary distance between angiopoietin family members is shown by the branch lengths.

Appendix Table A1. GEM data of genes related to angiogenesis for LEC and KLEC.
Affymetrix hg-u133+2 GeneChip probe-sets that correspond to a list of 240 genes related to angiogenesis are shown. Microarray data was processed and assessed for differential regulation as described in Materials and Methods. Microarray data for all of the genes on the Affymetrix hg-u133+2 GeneChip are available from the ArrayExpress database (<http://www.ebi.ac.uk/arrayexpress>; accession number E-MEXP-561)

Affy ID	Gene symbol	Name	LEC1	LEC2	LEC3	LEC4	LEC5	LEC6	LEC1	LEC2	LEC3	LEC4	LEC5	LEC6	KLEC1	KLEC2	KLEC3	KLEC4	KLEC5	KLEC6	LEC-KLEC P-value	LEC-KLEC Φ -value	LEC-KLEC Φ -value	LEC-KLEC log2 Fold-Change	Average Expression (all conditions)	
202912_at	ADM	adenomedullin	9.43025	9.42325	9.40554	8.72301	8.96333	8.96389	10.56894	10.16239	10.63339	10.53470	10.79791	10.87514	4.08E-10	1.09E-08	1.52E+165362	0.286715744	0.13333809	0.074316363	0.000640842	0.001469848	0.001146948	1.52E+165362	9.89446	
216334_s_at	AGGF1	angiogenic factor with G patch and FHA domains 1	7.71680	7.39544	7.63911	7.67236	7.62445	7.44424	7.82540	7.79881	8.01169	7.77638	7.81964	7.98188	0.000640842	0.001469848	0.286715744	0.13333809	0.074316363	0.000640842	0.001469848	0.001146948	0.001146948	0.001146948	0.001146948	7.72561
222861_at	AGGF1	angiogenic factor with G patch and FHA domains 1	7.76980	7.62589	7.74220	7.59024	7.60516	7.61054	7.92308	7.84585	7.84075	7.77526	7.53836	7.82075	0.058420388	0.040301089	0.13333809	0.074316363	0.000640842	0.001146948	0.001146948	0.001146948	0.001146948	0.001146948	0.001146948	7.72397
208042_at	AGGF1	angiogenic factor with G patch and FHA domains 1	6.02297	5.77046	6.09151	6.14535	6.14809	6.16713	6.09094	6.17438	6.21144	6.07179	6.14826	6.07460	0.287249892	0.138135793	0.074316363	0.000640842	0.001146948	0.001146948	0.001146948	0.001146948	0.001146948	0.001146948	0.001146948	6.09141
210710_at	AGGF1	angiogenic factor with G patch and FHA domains 1	4.92561	5.28106	5.06679	5.31988	5.14865	5.25322	4.94870	4.89103	5.24844	5.16792	5.24558	5.18740	0.540377801	0.220573912	-0.050823143	0.000640842	0.001146948	0.001146948	0.001146948	0.001146948	0.001146948	0.001146948	0.001146948	5.14026
205141_at	ANG	angiogenin, ribonuclease, RNase A family, 5	7.17348	7.08118	7.13766	6.99719	6.99479	6.83490	6.96920	6.91845	7.00997	6.74105	6.9252	6.53644	0.090774466	0.058671642	-0.125595284	0.000640842	0.001146948	0.001146948	0.001146948	0.001146948	0.001146948	0.001146948	0.001146948	6.95707
205608_s_at	ANGPT1	angiotensinogen	5.00032	5.34810	5.01583	4.84977	5.20333	5.16711	5.27873	5.28391	5.16447	5.32395	5.30567	5.07592	0.021598624	0.018598727	0.205357846	0.074076351	0.028116111	0.046194816	0.028116111	0.046194816	0.028116111	0.046194816	0.028116111	5.20792
241119_at	ANGPT1	angiotensinogen	3.47090	3.71051	3.62076	3.64355	3.64427	3.68334	3.47090	3.79874	3.57726	3.71173	3.72248	3.92487	0.279663466	0.135407251	0.074076351	0.028116111	0.046194816	0.028116111	0.046194816	0.028116111	0.046194816	0.028116111	0.046194816	3.64701
205609_at	ANGPT1	angiotensinogen	3.43309	3.60943	3.57536	3.58282	3.53316	3.74327	3.69111	3.49634	3.45438	3.67300	3.73522	3.95376	0.671420397	0.257573225	0.028116111	0.046194816	0.028116111	0.046194816	0.028116111	0.046194816	0.028116111	0.046194816	0.028116111	3.59358
1552939_s_at	ANGPT2	angiotensinogen	3.37020	3.42253	3.21901	3.24870	3.26018	3.21156	3.15713	3.15078	3.24487	3.15743	3.14727	3.24372	0.089540202	0.046194816	-0.104830427	0.000640842	0.001146948	0.001146948	0.001146948	0.001146948	0.001146948	0.001146948	0.001146948	3.23595
205572_at	ANGPT2	angiotensinogen	9.86048	9.10226	9.82335	9.62965	9.59784	9.25595	13.44130	13.43918	13.47774	13.24276	13.24126	13.56640	9.75E-18	4.14E-15	3.866853373	11.52301	11.52301	11.52301	11.52301	11.52301	11.52301	11.52301	11.52301	11.52301
211148_s_at	ANGPT2	angiotensinogen	9.30880	9.34493	9.35073	9.17647	9.18595	8.90027	12.87742	12.91114	13.02760	12.82033	12.82642	13.02642	0.09540202	0.046194816	-0.104830427	0.000640842	0.001146948	0.001146948	0.001146948	0.001146948	0.001146948	0.001146948	0.001146948	11.52301
238034_at	ANGPT2	angiotensinogen	8.74207	8.93510	8.95387	8.57785	8.63221	7.93520	12.57923	12.70962	12.70962	12.59433	12.89588	12.89588	1.90E-16	4.96E-14	4.023727419	10.62125	10.62125	10.62125	10.62125	10.62125	10.62125	10.62125	10.62125	10.62125
205662_at	ANGPT2	angiotensinogen	6.86366	6.89005	6.84442	6.71032	6.85044	6.97938	6.85777	6.87002	6.78810	6.89680	6.81832	6.81423	0.691744748	0.262972675	-0.021540933	0.000640842	0.001146948	0.001146948	0.001146948	0.001146948	0.001146948	0.001146948	0.001146948	6.85044
221134_at	ANGPT4	angiotensinogen	5.62758	5.84125	5.81189	5.81189	5.91203	5.79684	6.07020	6.28445	6.04596	5.90543	6.21056	6.07298	0.000503461	0.000990051	0.276426277	5.90005	5.90005	5.90005	5.90005	5.90005	5.90005	5.90005	5.90005	5.90005
224339_s_at	ANGPT1	angiotensinogen-like 1	5.06539	5.62663	5.39703	5.11520	5.44255	5.25504	5.27343	5.08188	5.27343	5.08188	5.27343	5.08188	0.236603677	0.119173662	-0.105166484	0.000640842	0.001146948	0.001146948	0.001146948	0.001146948	0.001146948	0.001146948	0.001146948	5.28077
3162312_at	ANGPT1	angiotensinogen-like 1	3.62312	3.55190	3.49412	3.62596	3.60972	3.86838	3.68408	3.67698	3.57611	3.73511	3.74141	3.64617	0.457917425	0.195170688	0.047793133	3.65280	3.65280	3.65280	3.65280	3.65280	3.65280	3.65280	3.65280	3.65280
231773_at	ANGPT1	angiotensinogen-like 1	3.16674	3.16160	3.06927	3.02509	2.96928	3.03410	3.02492	3.04919	3.01676	3.09445	3.04685	3.29699	0.180656835	0.295327057	0.014347705	3.08152	3.08152	3.08152	3.08152	3.08152	3.08152	3.08152	3.08152	3.08152
213004_at	ANGPT2	angiotensinogen-like 2	8.29372	8.35993	8.27943	8.14549	8.19784	8.20382	10.33965	10.46587	10.44163	9.86608	9.82976	10.18496	1.16E-12	7.43E-11	1.941851064	9.21717	9.21717	9.21717	9.21717	9.21717	9.21717	9.21717	9.21717	9.21717
213001_at	ANGPT2	angiotensinogen-like 2	8.37097	8.18317	8.53425	8.11270	8.07700	8.79736	10.39837	10.59824	10.47031	9.87872	9.82340	10.30555	5.89E-11	1.91E-09	2.037682025	9.21009	9.21009	9.21009	9.21009	9.21009	9.21009	9.21009	9.21009	9.21009
219514_at	ANGPT2	angiotensinogen-like 2	6.71619	6.90443	6.96997	6.63760	6.64807	6.48705	7.49854	8.96932	8.92062	8.5062	8.45305	8.78979	1.85E-11	7.19E-10	1.945436545	7.69927	7.69927	7.69927	7.69927	7.69927	7.69927	7.69927	7.69927	7.69927
239039_at	ANGPT2	angiotensinogen-like 2	5.75014	5.84652	5.61676	5.64052	5.72360	5.66757	6.17767	6.26239	6.35516	5.93209	5.88602	6.16837	4.97E-05	0.000151781	0.421097362	5.91807	5.91807	5.91807	5.91807	5.91807	5.91807	5.91807	5.91807	5.91807
231684_at	ANGPT3	angiotensinogen-like 3	4.61416	4.54411	4.68833	4.49532	4.62398	4.58366	4.37850	4.40973	4.49517	4.54111	4.40973	4.43432	0.010011915	0.010128212	-0.171733455	4.50076	4.50076	4.50076	4.50076	4.50076	4.50076	4.50076	4.50076	4.50076
219001_at	ANGPT3	angiotensinogen-like 3	3.42671	3.54928	3.60222	3.54007	3.49211	3.60031	3.49811	3.41439	3.45925	3.99660	3.50732	3.49312	0.470614443	0.199198552	-0.038820708	3.51404	3.51404	3.51404	3.51404	3.51404	3.51404	3.51404	3.51404	3.51404
245799_s_at	ANGPT3	angiotensinogen-like 3	3.64557	3.92520	3.61431	3.53008	3.36204	3.52127	3.46813	3.41990	3.37278	3.50791	3.45814	3.30560	0.115062224	0.068527015	-0.090166929	3.47133	3.47133	3.47133	3.47133	3.47133	3.47133	3.47133	3.47133	3.47133
221009_s_at	ANGPT4	angiotensinogen-like 4	9.48523	9.19758	9.36822	9.26526	9.11312	9.05172	7.64246	7.63337	7.75080	7.30329	7.41759	7.8428	3.45E-12	1.80E-10	-1.751892326	8.6758	8.6758	8.6758	8.6758	8.6758	8.6758	8.6758	8.6758	8.6758
223333_s_at	ANGPT4	angiotensinogen-like 4	8.71936	8.65655	8.54720	8.73760	8.74488	9.29801	7.35921	7.30711	7.28049	7.03104	6.96558	7.30270	6.19E-11	1.98E-09	-1.581227664	7.99300	7.99300	7.99300	7.99300	7.99300	7.99300	7.99300	7.99300	7.99300
223967_at	ANGPT6	angiotensinogen-like 6	5.94318	6.35610	6.20928	6.33504	6.45122	6.48687	6.19589	6.37663	6.39674	6.5448	6.27037	6.52505	0.338655371	0.156081195	0.079280427	6.29689	6.29689	6.29689	6.29689	6.29689	6.29689	6.29689	6.29689	6.29689
208423_at	ANGPT7	angiotensinogen-like 7	4.71671	5.41942	4.99617	5.01564	5.04643	4.96763	4.82639	4.98818	4.81053	4.63032	4.90432	5.21947	0.221672654	0.113522064	-0.135015918	4.95849	4.95849	4.95849	4.95849	4.95849	4.95849	4.95849	4.95849	4.95849
202888_s_at	ANPEP	alanyl (membrane) aminopeptidase (aminopeptidase N, aminopeptidase M, microsomal aminopeptidase, CD13, p150)	9.12482	9.96483	9.14059	9.17824	9.22034	9.33802	8.55417	8.34302	8.77310	8.92222	8.87196	8.62183	6.40E-05	0.000194633	-0.480093927	8.92110	8.92110	8.92110	8.92110	8.92110	8.92110	8.92110	8.92110	8.92110
234576_at	ANPEP	alanyl (membrane) aminopeptidase (aminopeptidase N, aminopeptidase M, microsomal aminopeptidase, CD13, p150)	5.47923	5.75991	5.80999	5.62881	5.77425	5.47258	5.96992	5.63708	5.86997	5.74372	5.90565	6.06478	0.004200998	0.005099923	0.244872045	5.77607	5.77607	5.77607	5.77607	5.77607	5.77607	5.77607	5.77607	5.77607
234458_at	ANPEP	alanyl (membrane) aminopeptidase (aminopeptidase N, aminopeptidase M, microsomal aminopeptidase, CD13, p150)	4.78453	4.96472	4.91762	4.74748	4.86672	4.82159	4.72729	4.72816	4.47354	4.50212	4.84957	4.54779	0.008635146	0.009171749	-0.20903078	4.74259	4.74259	4.74259	4.74259	4.74259	4.74259	4.74259	4.74259	4.74259
206083_at	BA11	brain-specific angiogenesis inhibitor 1	6.71468	7.13546	6.74598	6.65508	6.66184	6.72656	6.70010	6.83714	6.61647	6.80607	6.71844	6.66596	0.035032305	0.027109002	-0.182737985	6.68206	6.68206	6.68206	6.68206	6.68206	6.68206	6.68206	6.68206	6.68206
200920_s_at	BTG1	B-cell translocation gene 1, anti-proliferative	10.82793	10.71981	10.71981	10.63972	10.52288	10.51158	10.57390	10.69774	10.89528	10.39891	10.64002	10.59369	0.997977764	0.337508773	-0.000184541	10.65668	10.65668	10.65668						

1559975_at	BTG1	B-cell translocation gene 1, anti-proliferative	3.87782	3.98756	3.71689	3.84101	3.78442	3.76510	3.90810	3.93735	4.05893	3.92735	4.00878	3.90181	3.83681	0.051887782	0.03676408	0.11942486	3.88175
206331_at	CALRL	calcium receptor-like	9.67482	9.74304	9.54776	9.54734	9.60078	11.76198	11.75849	11.58686	11.58469	11.58473	11.58473	11.58473	11.58473	1.47E-13	2.072943932	2.072943932	10.60187
210815_s_at	CALRL	calcium receptor-like	9.61905	9.43447	9.63777	9.06260	9.16121	11.71596	11.74446	11.64446	11.64446	11.64446	11.64446	11.64446	1.14E-10	2.196278892	2.196278892	10.48079	
234996_at	CALRL	calcium receptor-like	7.44759	7.12727	7.33889	7.18537	7.02004	7.24065	9.70723	9.61118	9.99772	9.77479	9.78699	9.45719	2.86E-13	2.499216892	2.499216892	8.47624	
212953_x_at	CALR	calreticulin	11.20435	11.04714	11.25843	10.98797	11.09173	10.86533	11.30118	11.33342	11.39464	11.03363	11.37146	11.25823	0.031844891	0.025169096	0.217101829	11.16454	
214315_x_at	CALR	calreticulin	10.20707	10.37949	10.46122	10.35450	10.47674	9.73966	10.91274	10.83468	10.83591	10.59838	10.83296	10.73717	0.000158801	0.000296798	0.52247071	10.53080	
212952_at	CALR	calreticulin	8.87314	9.30284	9.20110	9.64774	9.82733	10.80988	9.40477	9.42500	9.15290	9.55143	9.68796	9.36972	0.547382024	0.222500742	-0.137611231	9.50077	
216598_s_at	CALR	calreticulin	8.50227	8.30227	8.57178	8.61909	8.68008	8.56653	8.96135	8.65871	8.65871	8.65871	8.65871	8.65871	0.005338962	0.007058258	0.238720383	8.69103	
1555759_s_at	CCL1	chemokine (C-C motif) ligand 1	8.90421	9.18856	9.10023	8.72801	8.86685	9.20809	8.92523	8.92523	8.92523	8.92523	8.92523	8.92523	7.79E-06	7.79E-06	-0.878715117	8.55990	
210133_at	CCL2	chemokine (C-C motif) ligand 2	5.57036	5.62755	5.67571	5.55738	5.62755	5.67571	5.55738	5.62755	5.67571	5.55738	5.62755	5.67571	0.00148036	0.357837422	0.357837422	5.97981	
216598_s_at	CCL2	chemokine (C-C motif) ligand 2	9.91445	9.98879	10.00336	9.95533	10.00336	9.95533	10.00336	9.95533	10.00336	9.95533	10.00336	9.95533	0.00088441	0.00088441	-0.408060352	9.33617	
216598_s_at	CCL5	chemokine (C-C motif) ligand 5	7.55941	7.71963	7.49288	7.75150	7.51537	7.70926	7.81994	8.89920	8.79498	8.46735	8.46735	8.46735	1.15E-08	1.088626879	1.088626879	8.17066	
204895_at	CCL5	chemokine (C-C motif) ligand 5	6.60089	6.53390	6.89238	6.85088	6.88647	6.56276	7.37155	7.19669	7.07592	7.19669	7.07592	7.19669	6.57E-06	0.728300395	0.728300395	7.02253	
1405_L_at	CCL5	chemokine (C-C motif) ligand 5	4.61715	4.51685	4.19824	4.49320	4.40211	4.34736	5.92035	6.23300	5.91561	5.70222	5.70847	6.07590	5.1E-10	1.496733512	1.496733512	5.17754	
206991_s_at	CCR5	chemokine (C-C motif) receptor 5	7.86395	7.98412	7.88971	7.86385	7.86385	7.91674	7.95018	7.97672	8.06870	7.96525	7.91206	8.01177	0.067882193	0.045308374	0.0980324517	7.93702	
236923_x_at	CD36	CD36 antigen (collagen type I receptor, thrombospondin receptor)	7.29555	7.35333	7.38485	7.32580	7.35119	7.33444	7.25510	7.21260	7.43769	7.40208	7.32499	7.39188	0.323239542	0.004431075	0.004431075	7.34309	
209554_at	CD36	CD36 antigen (collagen type I receptor, thrombospondin receptor)	6.36068	6.61359	6.55244	6.31235	6.37092	6.42288	6.06734	6.14959	5.87862	6.08813	5.91829	5.95307	3.37E-05	-0.429636612	-0.429636612	6.22399	
206488_s_at	CD36	CD36 antigen (collagen type I receptor, thrombospondin receptor)	6.54172	6.44570	6.51032	6.81788	6.31422	6.19103	4.84546	4.82547	4.83342	4.83342	4.81980	4.72382	2.10E-06	-1.348603762	-1.348603762	5.46251	
209555_s_at	CD36	CD36 antigen (collagen type I receptor, thrombospondin receptor)	5.24484	5.60320	5.25471	5.34154	4.89521	5.08866	4.56262	4.39469	4.37465	4.56033	4.61052	4.79531	6.06E-06	-0.688359911	-0.688359911	4.90386	
228786_at	CD36	CD36 antigen (collagen type I receptor, thrombospondin receptor)	6.46653	5.92595	6.21822	5.19453	5.17149	5.03007	3.86529	3.85746	3.86526	3.75099	3.76831	3.86535	4.81E-08	5.39E-07	-1.987354265	4.71745	
241929_at	CD36	CD36 antigen (collagen type I receptor, thrombospondin receptor)	4.04278	4.34164	3.97796	4.14793	3.99716	4.30862	4.39638	4.52438	4.43500	4.38421	4.35579	4.31888	0.002302847	0.002302847	0.268647444	4.26923	
242197_x_at	CD36	CD36 antigen (collagen type I receptor, thrombospondin receptor)	3.74482	3.80385	3.76438	3.96594	4.15244	3.89037	3.75362	3.55049	3.86183	3.75520	3.82439	3.82439	0.002339893	-0.445496933	-0.445496933	3.81132	
204677_at	CDH5	cadherin 5, type 2, VE-cadherin (vascular epithelium)	11.87591	11.87777	11.91589	11.85160	11.81069	11.87062	11.60025	11.61922	11.83542	11.60941	11.60417	11.60417	0.001333422	0.001333422	-0.207518008	11.76332	
209498_at	CEACAM1	carcinoembryonic antigen-related cell adhesion molecule 1 (biliary glycoprotein)	8.65982	8.50133	8.72917	8.20297	8.21196	8.02729	8.12095	8.12095	8.15880	8.15880	8.15880	8.15880	0.00157165	0.002339893	-0.207518008	8.18933	
211883_x_at	CEACAM1	carcinoembryonic antigen-related cell adhesion molecule 1 (biliary glycoprotein)	7.62973	7.67141	7.58458	7.41662	7.36938	7.56218	7.45466	7.44115	7.51846	6.93955	7.41888	7.47054	0.083584717	0.053378253	-0.165277708	7.46535	
206576_s_at	CEACAM1	carcinoembryonic antigen-related cell adhesion molecule 1 (biliary glycoprotein)	7.27248	7.69573	7.46133	7.16147	7.18076	7.30843	7.24655	7.45523	7.25247	7.07132	6.82054	7.08996	0.063108789	0.042812006	-0.219022872	7.20386	
210610_at	CEACAM1	carcinoembryonic antigen-related cell adhesion molecule 1 (biliary glycoprotein)	7.02118	7.21909	6.76172	7.00288	7.01406	7.13067	6.74222	6.94884	6.93978	6.79265	6.82930	6.83144	0.034550259	0.028832843	-0.165255993	6.84227	
211889_x_at	CEACAM1	carcinoembryonic antigen-related cell adhesion molecule 1 (biliary glycoprotein)	6.77974	6.95450	6.80946	6.77191	6.65538	6.68582	6.68330	6.74038	6.73374	6.40155	6.39563	6.65029	0.031904854	0.025218176	-0.175517139	6.68688	
213800_at	CFH	complement factor H	6.57301	6.37377	6.69376	5.71223	5.71186	5.04486	5.54438	5.40119	5.47360	5.91381	5.47360	5.89140	0.003686991	0.000739269	-0.6493146038	5.86328	
243160_at	CFH	complement factor H	5.69438	5.71616	5.77449	5.96300	5.86094	5.80467	5.90596	5.90596	5.90596	5.52152	5.71422	5.74736	0.223992627	0.114018175	-0.0801666512	5.66532	
1554459_s_at	CFH	complement factor H	5.20914	5.32383	5.35416	5.22717	5.21137	5.19359	5.25504	5.21845	5.19444	5.07074	5.03966	5.28884	0.309567901	0.146022125	-0.060164681	5.20796	
204697_s_at	CHGA	chromogranin A (parathyroid secretory protein 1)	5.74334	6.22162	5.79193	5.79597	5.86094	5.78298	5.73783	5.73966	5.67793	5.79565	5.69537	5.87855	0.223458665	0.114196189	-0.096931884	5.80826	
203477_at	COL1A1	collagen, type XV, alpha 1	3.29714	3.23397	2.96800	3.23272	3.34713	3.34326	3.51771	3.32554	3.46828	3.51984	3.29647	3.79145	0.016803376	0.015254861	0.229546726	3.35148	
209081_s_at	COL1A1	collagen, type XVII, alpha 1	10.52893	10.48019	10.56290	10.35899	10.27199	10.06883	10.59634	10.83174	10.95832	10.51743	10.49798	10.71088	0.00446101	0.005045875	0.310707558	10.53026	
209082_s_at	COL1A1	collagen, type XVII, alpha 1	9.90545	9.65783	9.83744	9.62600	9.51903	9.05468	9.81303	9.94126	10.15782	9.56754	9.54486	9.82740	0.167014012	0.091368086	0.191914471	9.71270	
1555653_at	COL1A1	collagen, type XVII, alpha 1	6.16576	6.31341	6.33157	6.30842	6.14893	6.03913	5.90412	5.70703	5.99120	5.86088	6.05883	5.80115	0.00395182	0.004787418	-0.263833281	6.01912	
1588732_at	COL1A1	collagen, type XVII, alpha 1	3.82143	3.93136	3.80001	3.63971	3.81627	3.87441	3.87688	3.82390	3.84088	3.64952	3.64952	3.64952	0.644476989	0.280154429	-0.031290131	3.74019	
211964_at	COL4A2	collagen, type IV, alpha 2	12.54064	12.53586	12.68791	12.16433	12.23406	12.00655	13.17844	13.23520	13.37362	13.07386	12.97347	13.12937	6.23E-06	6.23E-06	7.75E-07	12.75817	
211966_at	COL4A2	collagen, type IV, alpha 2	11.10398	11.05546	11.25407	10.88861	10.96793	11.76913	11.64209	12.22714	11.82661	11.66738	11.96269	11.82661	7.49E-08	0.897949253	0.897949253	11.63887	
237624_at	COL4A2	collagen, type IV, alpha 2	5.53737	5.88828	5.79871	5.48880	5.81941	5.88498	6.03879	5.71184	5.91440	5.90061	6.14733	6.01167	0.021079292	0.018238348	0.218165294	5.84592	
214641_at	COL4A3	collagen, type IV, alpha 3 (Goodpasture antigen)	6.07722	6.25624	6.03940	6.15667	6.14621	6.25716	6.19251	6.17987	6.31912	6.10941	6.31912	6.17987	0.065702889	0.029564304	0.1262152	6.24869	
216898_s_at	COL4A3	collagen, type IV, alpha 3 (Goodpasture antigen)	5.70275	5.93048	5.48819	5.64753	5.88865	5.80781	5.92274	5.89008	5.82643	5.97926	5.92166	5.69421	0.039192556	0.029564304	0.151797104	5.80017	
216368_s_at	COL4A3	collagen, type IV, alpha 3 (Goodpasture antigen)	5.03433	5.29104	5.27539	5.30833	5.23781	5.17351	5.19328	5.04085	5.21406	5.37267	5.25381	5.37267	0.7033166	0.26583216	-0.02644589	5.21110	
216367_at	COL4A3	collagen, type IV, alpha 3 (Goodpasture antigen)	4.40419	4.51693	4.52442	4.48837	4.83725	4.66479	4.40999	4.36548	4.36443	4.47364	4.54750	4.36238	0.042384886	0.031414309	-0.154387735	4.49536	

216893_s_at	COL4A3	collagen, type IV, alpha 3 (Goodpasture antigen)	3.94437	3.96150	3.76438	4.06463	3.89435	3.78906	4.12652	3.97809	3.84638	4.10639	3.96592	4.32300	0.030646683	0.183164177	3.96447
216896_at	COL4A3	collagen, type IV, alpha 3 (Goodpasture antigen)	3.60343	3.67327	3.66816	3.84014	3.89410	3.82178	3.67941	3.92625	3.82984	3.90595	3.62795	3.95422	0.091147441	0.102190338	3.74208
222073_at	COL4A3	collagen, type IV, alpha 3 (Goodpasture antigen)	3.27650	3.17796	3.25694	3.26040	3.26526	3.23252	3.33537	3.16991	3.26589	3.23399	0.745557626	0.277097705	0.166586846	3.26687	
207442_at	CSF3	colony stimulating factor 3 (granulocyte)	7.56385	7.86041	7.37481	7.48974	7.48855	7.53197	7.38800	7.34276	7.19074	7.52900	7.46220	0.238605965	-0.077782934	7.43096	
209101_at	CTGF	connective tissue growth factor	13.21199	13.14593	13.21981	13.24998	13.20450	12.86554	12.84424	12.73224	12.90521	12.82168	12.69022	12.84101	-0.44344338	12.99410	
204470_at	CXCL1	chemokine (C-X-C motif) ligand 1 (melanoma growth stimulating activity, alpha)	9.10107	9.08196	9.23761	9.23193	9.25357	9.15757	9.37000	8.93318	9.23968	7.81693	7.66391	8.77556	0.016581434	-0.600903176	8.87663
204533_at	CXCL1	chemokine (C-X-C motif) ligand 1	8.86988	8.82047	8.82037	8.68954	8.84475	8.69420	8.54586	8.68734	8.12361	8.62625	6.05334	6.49322	0.001489929	0.465218296	6.12248
211122_s_at	CXCL11	chemokine (C-X-C motif) ligand 11	3.56548	3.70984	3.54376	3.49924	3.44454	3.29581	4.12851	3.78356	3.61590	3.67886	4.09012	0.001856216	0.407736051	3.72793	
210163_at	CXCL11	chemokine (C-X-C motif) ligand 11	3.42296	3.60965	3.45688	3.40047	3.39210	3.37944	3.91827	4.20154	3.55921	3.23113	3.44014	3.50024	0.072478215	0.200371916	3.54157
203666_at	CXCL12	chemokine (C-X-C motif) ligand 12 (stromal cell-derived factor 1)	7.66823	7.63216	7.14330	7.87814	7.47731	7.28109	9.75548	9.27239	9.58925	10.27558	9.85833	10.00079	2.33E-11	2.278266174	8.65250
206897_at	CXCL12	chemokine (C-X-C motif) ligand 12 (stromal cell-derived factor 1)	6.50400	6.56021	5.94848	7.13825	7.07152	6.51170	8.92900	8.23866	8.21801	9.29311	9.32493	8.85391	5.90E-07	2.361107027	7.65141
209774_s_at	CXCL2	chemokine (C-X-C motif) ligand 2	6.87404	6.46643	6.46822	6.96714	6.72654	6.72292	9.92584	9.64711	9.79378	8.64322	8.64572	9.50770	2.690317668	0.80450	
230101_at	CXCL2	chemokine (C-X-C motif) ligand 2	5.61815	5.78654	6.07206	5.74010	5.69093	5.92742	5.74858	5.74969	5.52727	6.52432	6.21740	5.76179	0.152439782	5.67533	
1569203_at	CXCL2	chemokine (C-X-C motif) ligand 2	5.05856	5.17976	5.05083	4.84040	4.96347	4.97281	5.35973	5.22103	5.60021	5.08124	5.13228	5.45203	0.003810899	0.296615723	5.19328
207860_at	CXCL3	chemokine (C-X-C motif) ligand 3	5.53840	5.38891	5.63315	5.28083	5.25764	5.66534	6.76919	6.38162	7.19900	5.45539	5.63678	5.58233	0.003223054	0.616831266	5.86596
214974_s_at	CXCL5	chemokine (C-X-C motif) ligand 5	5.65779	5.39471	5.43209	5.88498	5.97972	4.93150	6.25878	5.29960	6.16184	5.73592	5.68122	5.54845	0.270799944	0.185485477	5.61263
215101_s_at	CXCL5	chemokine (C-X-C motif) ligand 5	4.60754	4.17768	4.66450	4.44476	4.32354	4.39736	4.34987	4.16520	4.31204	4.19998	4.41389	4.58559	0.27465797	0.133533407	4.36863
207852_at	CXCL5	chemokine (C-X-C motif) ligand 5	3.33947	2.97685	3.10987	3.15496	3.28245	3.03191	3.05300	3.15912	3.03751	3.21861	3.12937	3.55367	0.629485903	0.245943442	3.17055
206336_at	CXCL6	chemokine (C-X-C motif) ligand 6 (granulocyte chemotactic protein 2)	3.56167	3.75597	3.55483	3.54153	3.40199	3.45705	3.57437	3.59788	3.56220	3.55367	3.57232	3.47428	0.010262329	0.256596205	3.56065
203915_at	CXCL9	chemokine (C-X-C motif) ligand 9	6.41344	6.59633	5.97419	6.08604	6.02893	6.17141	6.34812	6.37844	6.34493	6.28072	6.47002	6.47002	0.038180391	0.207981923	6.31571
1560791_at	CXCL9	chemokine (C-X-C motif) ligand 9	3.64433	3.72721	3.94014	4.36688	3.6821	3.77183	3.69760	3.64278	3.57877	3.76945	3.53423	3.92386	0.04467966	0.038180391	3.69591
217028_at	CXCR4	chemokine (C-X-C motif) receptor 4	11.02410	10.89907	10.97229	10.83598	10.87993	10.36799	12.54210	12.35626	12.79993	12.30029	12.35626	12.26261	7.11E-10	1.751557523	11.68242
211919_s_at	CXCR4	chemokine (C-X-C motif) receptor 4	10.41912	10.50384	10.38153	10.18176	10.17548	10.17188	12.21461	12.49548	12.29280	11.79563	11.79563	12.5333	4.23E-11	1.815470472	11.99627
209201_s_at	CXCR4	chemokine (C-X-C motif) receptor 4	10.21203	10.29117	10.19892	9.97230	10.1018	9.90859	12.00980	13.35226	12.48845	11.48895	11.59750	11.99285	5.20E-11	1.832901911	11.04532
202289_at	CYBB	systeme-rich, angioinogenic inducer, 61	12.39319	12.36108	12.56194	12.47916	12.48734	12.60006	12.50375	12.67819	12.74880	12.78740	12.72133	12.72133	0.003509885	0.004424821	12.58900
210764_s_at	CYBB	systeme-rich, angioinogenic inducer, 61	12.37897	12.17744	12.22771	12.13173	12.28952	12.30392	12.40374	12.43716	12.40374	12.32616	12.31030	12.34746	0.148432122	0.056901903	12.29030
214724_at	DIKDC1	DIK domain containing 1	9.21256	9.09496	9.25681	9.05776	8.89193	8.71249	8.24037	8.03955	8.35194	8.16359	7.90096	8.20876	0.8662436	-0.8662436	8.99479
1558340_at	DIKDC1	DIK domain containing 1	7.26577	7.24720	7.06317	7.19200	7.13243	6.97307	6.89755	6.85444	7.02365	6.90856	6.79879	6.86106	0.000876164	0.001192551	7.01731
1588342_x_at	DIKDC1	DIK domain containing 1	7.33468	7.37861	7.25386	7.08162	6.99973	7.23985	6.81799	6.68072	6.70856	6.38811	6.54235	6.52520	1.02E-05	-0.593018316	6.91155
209560_s_at	DLL1	delta-like 1 homologue (Drosophila)	5.21260	5.33558	5.30197	5.34755	5.35126	5.26956	5.89923	5.68072	5.34710	5.56634	0.1820765	0.0696071	0.0696071	0.117317469	5.33798
227938_s_at	DLL1	delta-like 1 (Drosophila)	6.18559	6.21617	6.07943	6.13214	6.22249	6.39476	6.07434	6.08300	6.08300	6.17845	6.17845	6.17845	0.128841154	0.074783416	6.15330
224215_s_at	DLL1	delta-like 1 (Drosophila)	5.06606	4.87588	4.94054	4.89763	4.38775	4.28193	4.72739	5.09487	4.89033	4.70649	4.90902	4.86513	0.118039863	0.146279615	4.75974
230568_x_at	DLL3	delta-like 3 (Drosophila)	6.80469	6.84852	6.96588	6.96161	7.05820	7.16921	7.27449	7.02424	7.04966	7.09933	7.05607	0.090240139	0.056756553	0.122200889	7.02912
229755_x_at	DLL3	delta-like 3 (Drosophila)	6.81696	6.93915	6.99000	6.94022	6.93891	7.09654	6.90303	6.98090	6.76297	6.99161	6.84539	6.94079	0.181885387	-0.049531882	6.92886
219537_x_at	DLL3	delta-like 3 (Drosophila)	6.20885	6.23408	6.13653	6.40029	6.21378	6.34294	6.51907	6.40776	6.51171	6.49769	6.53130	6.55813	0.000363054	0.264532569	6.38835
222996_s_at	DLL3	delta-like 3 (Drosophila)	6.24832	6.57951	6.55201	6.27223	6.45463	6.0906	6.14539	6.37378	6.09252	5.90028	6.11883	5.52544	0.00189215	-0.0377868973	6.23116
223525_at	DLL4	delta-like 4 (Drosophila)	8.12000	7.97190	7.92956	7.90155	7.88774	7.82124	8.41037	8.06521	8.96793	9.57144	9.64590	9.54590	6.45E-12	1.724811703	8.80107
203230_at	DVL1	disevelled, dsh homolog 1 (Drosophila)	8.56888	8.59799	8.50147	8.28549	8.38898	8.40293	8.20967	8.07583	8.09293	8.29557	8.27194	8.16179	0.000563506	0.001038096	8.31489
57532_at	DVL2	disevelled, dsh homolog 2 (Drosophila)	7.75166	7.67511	7.86548	7.80531	7.75352	7.62108	7.49097	7.60968	7.12472	0.098810658	0.009210624	-0.159046477	-0.159046477	7.69492	
218759_at	DVL2	disevelled, dsh homolog 2 (Drosophila)	7.15727	7.19636	7.15306	7.22576	7.18852	7.38335	7.12847	7.02885	6.86708	7.00416	7.06725	7.16780	0.019406063	-0.170448986	7.12883
201906_at	DVL3	disevelled, dsh homolog 3 (Drosophila)	8.73919	8.59890	8.66938	8.50535	8.40950	8.07867	7.84828	8.07867	8.25286	8.58504	8.11933	8.40188	0.250124804	-0.148866787	8.37250
201907_x_at	DVL3	disevelled, dsh homolog 3 (Drosophila)	6.52727	6.56990	6.77493	6.64138	6.60313	6.69270	6.53512	6.39698	6.54012	6.43266	6.49877	6.41686	0.036182606	0.027810007	6.53582
204858_s_at	ECGF1	endothelial cell growth factor 1 (platelet-derived)	7.35791	7.57091	7.46992	7.33669	7.39541	7.31903	7.31146	7.28463	7.34920	7.26749	7.42277	0.100547574	0.061744826	-0.101612229	7.35735
217497_at	ECGF1	endothelial cell growth factor 1 (platelet-derived)	5.20652	5.47350	5.7843	5.09462	5.32823	5.34494	4.97469	4.81387	4.68595	4.74340	5.00036	4.28495	0.000103727	-0.521190517	5.01078
204642_at	EDG1	endothelial differentiation, sphingolipid G-protein-coupled receptor, 1	10.59184	10.40988	10.32946	10.39607	10.39472	10.55528	10.80426	10.85700	10.64985	10.70683	10.83544	10.70683	0.000183623	0.000427194	10.59463
202023_at	EFNA1	ephrin-A1	9.95760	9.95587	10.00012	9.38265	9.41061	9.15159	10.11107	10.41441	10.24000	9.65779	9.97359	9.65779	0.06904117	0.041634305	9.81002
208256_at	EFNA2	ephrin-A2	4.93870	5.04511	5.05228	5.02469	4.93220	4.90719	4.96659	5.20880	5.08396	4.99754	4.77056	4.99754	0.582597199	0.032787795	4.99394
1553573_s_at	EFNA2	ephrin-A2	4.67182	4.74689	4.95761	4.79489	4.80605	4.78911	4.78370	4.79499	4.68222	4.81517	4.90075	4.92907	0.775321082	0.284485068	4.80295

EFNA3	210132_at	ephrin-A3	6.99007	7.13777	6.93877	6.50810	6.78409	6.69259	7.11346	6.87010	7.07261	6.99609	0.176385292	0.095243361	0.125219788	6.91832
EFNA5	207301_at	ephrin-A5	5.44189	5.81187	5.49131	5.48314	5.56166	5.50621	5.52885	5.52885	5.49952	5.49952	0.457538788	0.195154605	-0.049594989	5.52451
EFNB1	1559360_at	ephrin-A5	4.47575	4.37681	4.63159	4.50035	4.41416	4.40399	4.42586	4.42586	4.39736	4.42586	0.247870763	-0.041288453	4.51313	
EFNB1	202711_at	ephrin-B1	7.89589	7.84368	7.96285	7.93273	7.86938	7.80212	8.34709	8.23082	8.06332	8.58467	1.17E-05	0.616507886	8.14271	
EFNB2	902688_at	ephrin-B2	9.90289	9.88434	9.84155	9.29314	9.23094	9.23094	9.23094	9.23094	9.23094	9.23094	0.10640736	0.066550635	9.86011	
EFNB2	202689_s_at	ephrin-B2	7.93661	7.95532	8.04265	7.78344	7.55586	7.83449	8.40767	8.32138	7.70795	7.70795	0.03159461	0.0270179195	7.91770	
EGF	206254_at	epidermal growth factor (beta-urogastone)	3.86254	3.87791	4.10079	3.86501	3.95608	4.04484	3.83537	3.80613	3.90776	3.90616	0.149143237	0.083288966	3.91488	
EGFL7	218825_at	EGF-like domain, multiple 7	10.69336	10.92988	10.69469	10.58396	10.49795	10.48365	10.57489	10.54932	10.65873	10.66948	0.06510679	0.13330844	10.61800	
ENG	12.12446	engodlin (Olaie-Rendu-Weber syndrome 1)	10.23206	10.31716	10.13611	10.28599	10.20960	10.66161	10.72698	10.63490	10.62380	10.70634	0.000298919	0.321958758	10.62790	
ENG	229586_at	engodlin (Olaie-Rendu-Weber syndrome 1)	5.82344	5.92177	6.22674	5.80386	6.16445	6.00875	5.98983	5.98983	5.98936	6.17940	0.294242654	0.140616642	5.97415	
EPAS1	12.76470	endothelial PAS domain protein 1	12.68165	12.62334	12.61833	12.59895	12.68688	12.86471	12.96046	12.96871	12.43344	12.65905	0.629669339	0.245154013	12.67527	
EPAS1	200879_s_at	endothelial PAS domain protein 1	8.89711	8.96878	8.82963	8.48258	8.47553	8.78719	8.91409	8.91409	8.74379	8.74379	0.052774357	0.036928259	8.86981	
EPAS1	229904_at	endothelial PAS domain protein 1	6.34172	6.78850	6.75577	6.49414	6.65214	6.36884	6.36554	6.05343	6.34420	6.24881	0.005036092	0.006088169	6.40555	
EPAS1	237843_at	endothelial PAS domain protein 1	6.40516	6.41462	6.47330	6.37666	6.39006	6.47431	6.38257	6.28329	6.16406	6.21591	0.004216449	-0.184496333	6.32644	
EPAS1	235960_at	endothelial PAS domain protein 1	5.13172	5.38561	4.82528	5.06356	5.10560	5.19872	5.20867	5.01037	5.27946	5.20258	0.000107626	0.005113691	5.39097	
EPAS1	242888_at	endothelial PAS domain protein 1	5.23037	5.23366	4.73987	5.18374	5.23924	5.16334	5.48407	5.29919	5.29919	5.29919	0.089340668	0.187979789	5.75556	
EPAS1	230711_at	endothelial PAS domain protein 1	5.22396	5.21534	5.19827	5.24411	5.23961	5.53666	4.98905	5.01237	5.05852	4.90619	0.000292069	-0.33782401	5.12141	
EPAS1	205977_s_at	EPH receptor A1	6.19859	6.94527	6.10134	6.28334	6.19536	6.26484	6.29409	6.20185	6.32264	6.29974	0.207608282	0.107901336	6.27718	
EPHA1	211504_at	EPH receptor A1	6.11807	6.41122	6.11546	6.12622	6.11845	5.99304	6.02524	6.07725	6.18109	5.71730	0.283203613	0.140261566	6.10170	
EPHA1	241482_at	EPH receptor A1	3.79865	4.05531	3.99831	3.92477	4.05583	3.34509	3.20867	5.01037	5.09394	5.20258	0.573436882	0.230151746	4.03487	
EPHA10	236073_at	EPH receptor A10	6.41746	6.82795	6.07708	6.40265	6.47282	6.68515	6.49730	6.34207	6.24829	6.50425	0.253577465	-0.082515487	6.48926	
EPHA10	243717_at	EPH receptor A10	5.22022	5.75582	5.27233	5.37663	5.63857	5.41191	5.34110	5.30978	5.13897	5.13897	0.062597702	0.042541818	5.29924	
EPHA10	1553371_at	EPH receptor A10	5.20037	5.23266	4.73987	5.18374	5.23924	5.16334	5.48407	5.29919	5.29919	5.29919	0.089340668	0.187979789	5.29603	
EPHA2	203499_at	EPH receptor A2	5.95901	9.66892	9.81590	9.61537	9.10707	9.48445	9.43443	9.52175	9.46691	9.50537	0.005466077	0.006278119	9.58645	
EPHA2	206071_s_at	EPH receptor A2	5.68598	5.82705	5.92045	5.92322	5.72016	5.64378	5.56667	5.94684	5.40285	5.28860	0.178646682	0.096226978	5.72606	
EPHA3	211164_at	EPH receptor A3	3.60628	3.20676	3.58357	3.37497	3.31752	3.34282	3.31752	3.30219	3.43338	3.38373	0.752031355	0.278774867	3.36165	
EPHA3	206070_s_at	EPH receptor A3	6.271486	6.10809	6.16412	5.90771	6.06757	6.33148	6.02630	6.21406	6.12636	6.37108	0.171607243	0.097381244	3.24057	
EPHA4	228948_at	EPH receptor A4	4.98937	5.17273	5.24689	5.29232	5.34158	5.06083	5.35766	5.38772	5.53280	5.51942	0.288501752	-0.017477424	6.12356	
EPHA4	229374_at	EPH receptor A4	4.32102	4.35353	4.12846	4.39054	4.41674	4.62841	4.56983	4.50028	4.49735	4.84292	0.03364123	0.026267295	4.46672	
EPHA4	227449_at	EPH receptor A4	3.33391	3.16413	3.17969	2.96701	3.26200	3.52523	3.43422	3.56874	3.56173	3.54457	6.62E-05	0.000189584	3.38336	
EPHA5	12.76470	EPH receptor A5	5.93442	5.94380	6.05020	5.85455	5.73905	5.82366	5.63073	5.79849	5.79554	6.03510	0.943902336	-0.006202037	5.89794	
EPHA5	1557897_at	EPH receptor A5	5.51488	5.70001	5.51506	5.47072	5.63090	5.63098	5.57798	5.58252	5.61558	5.80075	0.156858311	0.087134983	5.62209	
EPHA5	241404_at	EPH receptor A5	5.75910	5.82480	6.13380	5.93166	5.65169	6.20095	5.04792	5.12431	4.92033	5.29308	0.06902686	0.041634304	5.48028	
EPHA5	215664_at	EPH receptor A5	4.92124	4.55010	4.65888	4.89141	4.98445	4.99040	4.25841	4.38641	4.00040	4.83665	3.86790	4.53360	4.49807	
EPHA5	237939_at	EPH receptor A5	4.26594	4.02349	3.99865	4.63242	4.54959	4.38343	3.69788	3.81884	3.60877	3.65144	2.25E-05	8.11E-05	4.89807	
EPHA5	231239_at	EPH receptor A5	3.46474	3.62852	3.66895	3.54353	3.75681	3.93590	3.33609	3.50079	3.45133	3.70075	0.06902686	0.041634304	3.98518	
EPHA6	231184_at	EPH receptor A6	4.00888	4.19026	3.94371	3.99889	4.11550	4.07979	4.33700	4.31526	4.22781	4.12172	0.00439236	0.00527814	4.15314	
EPHA6	1561306_at	EPH receptor A6	3.21500	3.86526	3.25352	3.33221	3.38535	3.27847	3.23113	3.42877	3.21442	3.42836	0.705165504	0.266641047	3.31840	
EPHA6	232789_at	EPH receptor A6	3.19298	3.13221	3.18594	3.15504	3.26251	3.19538	3.11435	3.14453	3.34883	3.20857	0.129944077	0.0648329185	3.18043	
EPHA7	229288_at	EPH receptor A7	4.00271	4.15308	4.28131	4.30111	4.40720	4.14120	4.19185	4.30361	4.47695	4.07871	0.031027182	0.024687064	4.16014	
EPHA7	208652_at	EPH receptor A7	3.46193	3.39407	3.33677	3.51260	3.52033	3.33964	3.35544	3.30219	3.31336	3.42580	0.035607246	0.027457254	3.38659	
EPHA7	1554029_at	EPH receptor A7	3.34326	3.26520	3.41473	3.39675	3.45058	3.50321	3.48953	3.40273	3.41757	3.28334	0.482288842	0.202849906	3.37183	
EPHA7	238533_at	EPH receptor A7	3.34475	3.16741	3.09046	3.13056	3.12357	3.13730	2.98601	3.01659	3.10631	3.07590	0.98090752	0.055678194	3.13444	
EPHA8	231796_at	EPH receptor A8	6.35078	6.82851	6.40241	6.54363	6.54590	6.61459	6.51037	6.73533	6.58011	6.56644	0.309289759	0.145931724	6.64899	
EPHA8	1554089_at	EPH receptor A8	6.03166	6.05946	5.93003	5.86828	5.96884	5.74486	5.82305	6.01106	5.80688	5.85399	0.197439008	0.10374392	5.88758	
EPHB1	217324_at	EPH receptor B1	7.04331	7.35227	7.09538	6.95276	7.09538	7.23753	7.38328	7.22571	7.11199	7.20386	0.066551363	0.00724196	7.21441	
EPHB1	210753_s_at	EPH receptor B1	5.97573	5.63475	5.93096	5.86667	6.26226	6.83243	5.81186	5.79038	6.01527	6.13140	0.744566209	0.278635907	5.98811	
EPHB1	211808_s_at	EPH receptor B1	5.05657	5.24295	5.19738	4.80948	5.08305	5.03625	5.13088	5.49470	5.13864	5.05507	0.123639039	0.072392191	5.14271	
EPHB1	230425_at	EPH receptor B1	4.34701	3.72572	3.52881	3.69168	3.77485	3.77485	3.82716	3.80038	3.71018	4.05477	0.009299789	0.009555326	3.77479	
EPHB2	210651_s_at	EPH receptor B2	8.80346	8.66821	8.70664	8.48076	8.74815	8.47413	7.73192	7.62296	7.62014	7.62296	1.71E-10	4.68E-09	8.75553	
EPHB2	209569_s_at	EPH receptor B2	8.83726	8.94421	8.82333	8.67033	8.60962	8.66346	7.35632	7.36841	7.44464	7.24911	2.71E-10	2.28E-11	8.04318	

21165_x.at	EPH2	EPH receptor B2	7.53688	7.26314	7.30740	7.53585	7.30481	7.30740	7.53585	2.75E-09	4.85E-08	-1.123756748	7.52985
209588_at	EPH2	EPH receptor B2	8.31082	8.53742	7.62727	7.56973	7.62727	7.56973	7.53585	2.75E-09	4.85E-08	-1.123756748	7.52985
234159_at	EPH2	EPH receptor B2	8.03888	8.07762	7.53378	7.54615	7.62727	7.47297	7.75303	2.81E-07	2.21E-06	-0.575875148	7.85382
233899_at	EPH2	EPH receptor B2	6.63356	6.64556	6.58929	6.61261	6.54553	6.45370	6.906239009	6.45370	0.262666262	0.033788454	6.57116
204600_at	EPH3	EPH receptor B3	6.44770	6.21008	6.17067	6.10550	6.93509	6.15673	6.18846	0.003043668	0.000635246	-0.329509146	6.27892
1438_at	EPH3	EPH receptor B3	7.39845	7.57215	7.24840	7.33614	7.34712	7.18311	7.17845	7.30481	0.006920455	-0.21442707	7.25022
202894_at	EPH4	EPH receptor B4	6.61882	6.62983	6.51731	6.51427	6.95477	6.83653	7.09860	0.008206924	0.00845232	0.007547888	6.71592
216880_s.at	EPH4	EPH receptor B4	10.01308	9.85515	10.12709	9.77885	9.68334	9.12487	9.19351	9.04254	0.008206924	0.007547888	6.71592
204718_at	EPH6	EPH receptor B6	8.50386	8.55224	8.76884	8.58332	8.49086	8.54772	8.13896	8.01444	5.15E-08	-0.811305366	9.48114
209798_s.at	ERAP1	endoplasmic reticulum aminopeptidase 1	8.30312	8.35331	8.40674	8.28789	8.21962	8.34409	8.34446	5.52373	5.20543	0.05977212	8.33517
210395_s.at	ERAP1	endoplasmic reticulum aminopeptidase 1	6.93379	6.74627	6.84244	6.67886	6.65134	6.90116	7.22721	8.18772	8.16529	0.904027417	8.27828
1564010_at	ERAP1	endoplasmic reticulum aminopeptidase 1	5.81242	5.65591	5.35094	5.39445	5.82334	5.98855	5.70782	5.73426	0.13902876	0.200141743	8.89600
214034_at	ERAP1	endoplasmic reticulum aminopeptidase 1	4.21447	4.04834	4.11539	4.15528	4.17649	4.01137	4.22586	4.21738	0.732231004	0.020338506	4.15849
214012_at	ERAP1	endoplasmic reticulum aminopeptidase 1	3.26667	3.17623	3.11263	3.20206	3.10337	3.13189	3.29656	3.17817	0.362779705	0.164338822	3.19551
218836_s.at	ERB2	v-erb-b2 erythroblastic leukemia viral oncogene homolog 2, neurofiblastoma derived oncogene	6.52037	6.87970	6.85127	6.70386	6.72037	6.87548	6.46692	6.83551	7.15609	0.148302991	6.75791
210930_s.at	ERB2	v-erb-b2 erythroblastic leukemia viral oncogene homolog 2, neurofiblastoma derived oncogene	5.18906	5.35595	5.06587	5.36739	5.39603	4.83892	4.97620	4.74675	4.65626	0.002339471	5.03495
234354_x.at	ERB2	v-erb-b2 erythroblastic leukemia viral oncogene homolog 2, neurofiblastoma derived oncogene	3.76756	3.87954	3.86579	3.78328	3.76659	3.86607	3.88194	3.76884	3.64075	0.067155787	3.74034
1569583_at	EREG	epiregulin	4.98142	4.95942	5.07302	4.85165	5.12208	4.82446	4.81814	4.93887	4.99199	0.187703552	4.92351
205767_at	EREG	epiregulin	3.07588	3.37585	3.25031	3.31883	3.15284	3.41572	3.11080	3.22836	3.19518	0.298859825	3.25725
202794_at	F2	coagulation factor II (thrombin)	6.48677	6.82192	6.75474	6.39744	6.43081	6.64256	6.49479	6.67651	6.48397	0.196504734	6.56126
203969_x.at	F2R	coagulation factor II (thrombin) receptor	10.66402	10.39116	10.45636	10.52455	10.52253	10.09845	10.75063	10.49210	10.71315	0.02219353	10.6308
1569642_at	F2R	coagulation factor II (thrombin) receptor	7.65224	8.00838	7.98172	7.98561	7.82401	7.95898	8.28796	8.17170	8.26228	0.01863176	7.97571
213506_at	F2RL1	coagulation factor II (thrombin) receptor-like 1	10.87383	10.83210	10.83533	10.47938	10.52046	10.46674	9.94942	10.19888	10.51966	0.000950334	10.211479
204429_at	F2RL1	coagulation factor II (thrombin) receptor-like 1	9.50124	9.45267	9.39152	9.19862	9.04293	9.48252	8.89164	9.05968	9.11832	0.00212387	10.27962
207221_at	F2RL3	coagulation factor II (thrombin) receptor-like 3	5.07105	5.10451	5.12585	5.00821	5.16123	4.77662	5.06659	5.07478	5.02925	0.001105276	8.97396
204362_at	F3	coagulation factor III (thromboplastin, tissue factor)	5.91885	5.87988	5.65363	5.71973	5.87183	5.64248	5.75733	5.79872	5.40286	0.784855314	6.05049
237414_at	F7	coagulation factor VII (serum prothrombin conversion accelerator)	6.93986	7.02135	6.97271	7.01021	7.01286	7.23203	7.06918	7.13057	6.93458	0.139136175	6.51058
207200_s.at	F7	coagulation factor VII (serum prothrombin conversion accelerator)	6.63248	6.83865	6.78972	6.50433	6.60325	6.51747	6.29444	6.34469	6.87589	0.28992743	6.98567
205117_at	FGF1	fibroblast growth factor 1 (acidic)	6.27846	6.18280	6.03390	6.21752	6.22663	6.25204	6.27299	6.28877	6.41878	0.002613238	6.51932
209240_s.at	FGF1	fibroblast growth factor 1 (acidic)	5.68135	5.76243	5.59684	5.64518	5.49785	5.65972	5.95206	5.85941	6.42284	0.286097393	6.30967
1552721_s.at	FGF1	fibroblast growth factor 1 (acidic)	3.48098	3.57498	3.62893	3.62311	3.65518	3.65131	3.65520	3.71932	3.71932	0.006661834	5.79610
230325_s.at	FGF2	fibroblast growth factor 2 (basic)	7.57768	7.19176	7.37829	7.35497	7.18892	7.02912	7.13092	7.26933	7.39163	0.498405699	3.62383
204421_s.at	FGF2	fibroblast growth factor 2 (basic)	7.78868	7.66651	7.73998	7.77560	7.43814	7.71489	6.43395	7.09493	7.16889	0.580673742	6.23822
204424_s.at	FGF2	fibroblast growth factor 2 (basic)	7.12098	6.46805	6.65500	6.84060	7.05119	5.00115	6.43726	6.20130	6.01388	2.01E-09	7.02465
204243_at	FGF6	fibroblast growth factor 6	4.61844	4.69051	4.75154	4.61674	4.63238	4.87210	4.86275	4.86404	4.86404	1.68E-12	5.80244
208417_at	FGFR1	fibroblast growth factor receptor 1 (fms-related tyrosine kinase 2, Pfeiffer syndrome)	7.12470	6.95999	7.15173	6.93752	7.00656	7.04832	6.95207	7.08333	6.96082	0.496285741	4.62381
211535_s.at	FGFR1	fibroblast growth factor receptor 1 (fms-related tyrosine kinase 2, Pfeiffer syndrome)	9.74422	9.57977	9.71733	9.67481	9.29042	9.46754	9.36051	9.48810	9.40302	0.035662584	7.26282
226705_at	FGFR1	fibroblast growth factor receptor 1 (fms-related tyrosine kinase 2, Pfeiffer syndrome)	9.24222	9.18765	9.22423	9.13525	9.14311	9.00938	9.03905	9.07928	9.03354	0.020689439	9.52972
210973_s.at	FGFR1	fibroblast growth factor receptor 1 (fms-related tyrosine kinase 2, Pfeiffer syndrome)	8.95614	8.81441	8.72800	8.78993	8.79635	8.84169	8.76236	8.65881	8.74075	0.160290371	9.08981
207937_x.at	FGFR1	fibroblast growth factor receptor 1 (fms-related tyrosine kinase 2, Pfeiffer syndrome)	8.10848	8.16118	8.07414	8.08403	8.11212	8.23493	8.22598	8.24880	8.34269	0.012696307	8.77988
215404_x.at	FGFR1	fibroblast growth factor receptor 1 (fms-related tyrosine kinase 2, Pfeiffer syndrome)	6.96428	6.86512	7.01950	7.00386	6.97089	6.98173	6.88882	6.93331	6.95992	0.165626501	8.21196
241724_x.at	FGFR1	fibroblast growth factor receptor 1 (fms-related tyrosine kinase 2, Pfeiffer syndrome)	6.39639	6.50423	6.50113	6.44879	6.49938	6.54448	6.48452	6.47420	6.68704	0.079585698	6.91715
													6.51942
													0.125577236
													0.067373286

207822_at	FGFR1	fibroblast growth factor receptor 1 (fms-related tyrosine kinase 2, Plieffler syndrome)	6.17067	5.86033	5.89715	5.66877	5.84569	5.51607	5.77149	5.98701	5.59927	5.65879	5.66652	5.80115	0.421162613	0.18358988	-0.077406833	5.78607
222164_at	FGFR1	fibroblast growth factor receptor 1 (fms-related tyrosine kinase 2, Plieffler syndrome)	5.73547	5.95175	5.86631	5.80567	5.73138	5.72210	5.45812	5.10413	5.45875	5.54218	5.70591	5.24267	0.000922446	0.001530029	-0.350152173	5.59370
208234_s_at	FGFR2	fibroblast growth factor receptor 2 (bacteria-expressed kinase, keratinocyte growth factor receptor, craniofacial dysostosis 1, Crozon syndrome, Plieffler syndrome, Jackson-Weiss syndrome)	6.78110	6.89922	6.80377	6.83451	6.70710	6.88051	6.85377	7.07210	6.89644	7.00292	7.09696	6.95845	0.011873642	0.011873642	0.162404446	6.89890
208042_at	FGFR2	fibroblast growth factor receptor 2 (bacteria-expressed kinase, keratinocyte growth factor receptor, craniofacial dysostosis 1, Crozon syndrome, Plieffler syndrome, Jackson-Weiss syndrome)	6.58088	6.90414	6.87232	6.43954	6.69571	6.59654	6.48172	6.48234	6.22867	6.32322	6.31761	6.32955	0.001220312	0.001914143	-0.286333565	6.50502
211389_at	FGFR2	fibroblast growth factor receptor 2 (bacteria-expressed kinase, keratinocyte growth factor receptor, craniofacial dysostosis 1, Crozon syndrome, Plieffler syndrome, Jackson-Weiss syndrome)	6.29887	6.83265	6.49357	6.25024	6.01059	6.55451	5.97036	5.83331	5.51170	5.91744	5.85188	5.38522	7.45E-05	0.000208078	-0.652753386	6.07136
208228_at	FGFR2	fibroblast growth factor receptor 2 (bacteria-expressed kinase, keratinocyte growth factor receptor, craniofacial dysostosis 1, Crozon syndrome, Plieffler syndrome, Jackson-Weiss syndrome)	5.54381	6.12681	6.21554	6.08585	6.26849	5.52900	6.18559	6.10397	5.86326	6.24689	5.99009	6.15977	0.30902531	0.145838916	0.12971156	6.02674
203608_s_at	FGFR2	fibroblast growth factor receptor 2 (bacteria-expressed kinase, keratinocyte growth factor receptor, craniofacial dysostosis 1, Crozon syndrome, Plieffler syndrome, Jackson-Weiss syndrome)	5.57614	5.36572	5.24592	5.67760	5.43565	5.88611	6.14726	6.03984	6.11778	6.18176	5.92102	6.13581	5.90E-06	2.81E-05	0.576605355	5.80255
211400_at	FGFR2	fibroblast growth factor receptor 2 (bacteria-expressed kinase, keratinocyte growth factor receptor, craniofacial dysostosis 1, Crozon syndrome, Plieffler syndrome, Jackson-Weiss syndrome)	5.85638	5.79038	5.61633	5.85621	5.87959	6.03485	5.68681	5.72611	5.81136	5.77597	5.86571	5.85145	0.218951041	0.112587863	-0.083216188	5.79784
211401_s_at	FGFR2	fibroblast growth factor receptor 2 (bacteria-expressed kinase, keratinocyte growth factor receptor, craniofacial dysostosis 1, Crozon syndrome, Plieffler syndrome, Jackson-Weiss syndrome)	5.89042	6.14371	5.59707	5.80133	5.36904	6.02408	5.50792	5.73841	5.53301	5.46262	5.72515	5.68356	0.253339789	0.12561413	-0.129165441	5.67303
208228_s_at	FGFR2	fibroblast growth factor receptor 2 (bacteria-expressed kinase, keratinocyte growth factor receptor, craniofacial dysostosis 1, Crozon syndrome, Plieffler syndrome, Jackson-Weiss syndrome)	6.14547	5.93759	5.88186	5.67970	5.86094	5.66699	5.58182	5.55369	5.16184	5.44189	5.57759	5.43860	0.000268819	0.000576016	-0.40280549	5.66066
203639_s_at	FGFR2	fibroblast growth factor receptor 2 (bacteria-expressed kinase, keratinocyte growth factor receptor, craniofacial dysostosis 1, Crozon syndrome, Plieffler syndrome, Jackson-Weiss syndrome)	5.71360	5.43169	5.66017	5.82745	5.68979	5.78138	5.63382	5.65050	5.71354	5.70668	5.22745	5.42080	0.293636896	0.140414314	-0.091715752	5.60466
208225_at	FGFR2	fibroblast growth factor receptor 2 (bacteria-expressed kinase, keratinocyte growth factor receptor, craniofacial dysostosis 1, Crozon syndrome, Plieffler syndrome, Jackson-Weiss syndrome)	5.51988	5.70959	5.49077	5.52219	5.67583	5.79525	5.88125	5.61592	5.51027	5.50365	5.53349	5.54845	0.409487988	0.179828527	-0.053414087	5.59221
240913_at	FGFR2	fibroblast growth factor receptor 2 (bacteria-expressed kinase, keratinocyte growth factor receptor, craniofacial dysostosis 1, Crozon syndrome, Plieffler syndrome, Jackson-Weiss syndrome)	4.95981	5.12976	4.84539	4.63117	4.82285	4.65125	4.84601	5.04799	4.72581	4.80939	4.81713	4.91122	0.357756247	0.162845316	0.080203346	4.81949
211388_at	FGFR2	fibroblast growth factor receptor 2 (bacteria-expressed kinase, keratinocyte growth factor receptor, craniofacial dysostosis 1, Crozon syndrome, Plieffler syndrome, Jackson-Weiss syndrome)	4.73555	4.92764	4.72584	4.61689	4.86228	5.00373	4.64041	4.43867	4.64041	4.65658	4.45120	4.48207	0.000863224	0.002398642	-0.260767065	4.68161

1560859_at	FGFR2	fibroblast growth factor receptor 2 (bacteria-expressed kinase, keratinocyte growth factor receptor, craniofacial dysostosis 1, Crozon syndrome, Pfeiffer syndrome, Jackson-Weiss syndrome)	3.47086	3.85798	3.48849	3.63847	3.58436	3.47302	3.59431	3.65688	3.48829	3.89203	3.67131	3.54459	0.423139866	0.184204152	0.045868753	3.56630
204379_s_at	FGFR3	fibroblast growth factor receptor 3 (achondroplasia, thanatophoric dwarfism)	5.74578	5.59116	5.81356	5.53253	5.64039	5.79532	5.69900	5.67062	5.68903	5.68960	5.57214	5.91928	0.771287631	0.283481294	0.02000134	5.69661
204380_s_at	FGFR3	fibroblast growth factor receptor 3 (achondroplasia, thanatophoric dwarfism)	5.05232	5.06025	4.99381	4.75289	4.93711	4.97381	4.74948	4.70456	4.69655	4.76066	4.74915	0.00864045	0.001453657	-0.348819258	4.78762	
1554961_at	FGFR4	fibroblast growth factor receptor 4	6.71129	6.92749	6.68372	6.53772	6.71020	6.63050	6.52676	6.58174	6.44702	6.54104	6.62864	0.025437323	0.021131086	-0.139484785	6.61374	
1554962_s_at	FGFR4	fibroblast growth factor receptor 4	6.38786	6.38861	6.34526	6.28926	6.29088	6.29161	6.29161	6.29161	6.16556	6.24870	6.07477	0.237079175	0.11936436	-0.072147983	6.28506	
211237_s_at	FGFR4	fibroblast growth factor receptor 4	6.24664	5.77077	6.47955	6.10524	6.13156	6.33097	6.22788	6.03043	5.88891	5.97796	6.14711	0.410889966	0.181986446	-0.083586698	6.13566	
204579_s_at	FGFR4	fibroblast growth factor receptor 4	6.28570	6.13500	6.15372	6.12877	6.32581	6.09276	5.89653	6.02158	5.84466	5.85491	6.06700	0.033044126	0.004817379	-0.215876233	6.07644	
206742_at	FIGF	c-fos induced growth factor (vascular endothelial growth factor D)	5.53858	5.41244	5.53110	5.38111	5.58610	5.48459	5.69382	5.53272	5.73807	5.69390	5.80534	0.001369579	0.002097	0.223688674	5.59592	
226497_s_at	FLT1	fms-related tyrosine kinase 1 (vascular endothelial growth factor/vascular permeability factor receptor)	7.0871	6.92546	7.47829	7.32438	7.34207	7.43255	7.23099	7.27329	7.24470	7.26731	7.25822	7.36549	2.77E-17	1.03E-14	5.02414626	9.81388
222033_s_at	FLT1	fms-related tyrosine kinase 1 (vascular endothelial growth factor/vascular permeability factor receptor)	7.53584	7.32129	7.67720	7.53887	7.68614	7.09053	7.11808	7.18403	7.11903	7.16590	7.18653	4.09E-19	3.98E-16	4.330215379	9.64010	
226488_at	FLT1	fms-related tyrosine kinase 1 (vascular endothelial growth factor/vascular permeability factor receptor)	6.47010	6.54707	6.61286	6.42985	6.86944	5.61982	6.16410	6.20706	6.23030	6.19332	6.11836	1.34E-18	8.75E-16	5.649706354	9.28304	
210287_s_at	FLT1	fms-related tyrosine kinase 1 (vascular endothelial growth factor/vascular permeability factor receptor)	5.22111	5.64289	5.29045	5.21423	4.99119	4.62310	4.78447	4.57203	4.70435	4.28042	10.25633	10.38177	3.25E-15	5.328729334	7.82720	
204406_at	FLT1	fms-related tyrosine kinase 1 (vascular endothelial growth factor/vascular permeability factor receptor)	4.92644	5.30189	4.97815	5.15112	5.00241	5.15974	5.06846	5.12387	5.30955	4.85170	5.14631	5.93506	0.520425773	0.214451235	0.055850412	5.11457
229902_at	FLT4	fms-related tyrosine kinase 4	8.49482	8.47471	8.73714	8.52456	8.15870	8.08406	8.94153	8.06389	9.31191	8.89461	8.69408	9.02773	0.00144283	0.000352024	0.577006062	8.66296
210316_at	FLT4	fms-related tyrosine kinase 4	8.29480	8.17511	8.34483	8.10925	8.11810	8.23857	8.46621	8.43378	8.43398	8.32887	8.41954	0.00679414	0.173321712	0.006879414	8.29944	
210317_at	FLT4	fms-related tyrosine kinase 4	7.02107	7.23436	7.23047	7.26175	7.09446	7.30072	7.22447	7.22447	6.96184	7.01776	6.80611	0.020567482	0.01790926	-0.183371189	7.09898	
221308_at	FRS2	fibroblast growth factor receptor substrate 2	5.67483	5.93876	5.71047	5.78032	5.76047	5.82032	5.92867	6.03093	5.89998	5.84691	5.72260	5.67527	0.316121125	0.148329508	0.069864701	5.81579
238486_at	FRS2	fibroblast growth factor receptor substrate 2	5.68837	5.76829	5.71652	5.91174	5.68664	5.89056	5.82024	6.01819	6.18892	5.79988	5.88616	5.72153	0.03695145	0.027780423	0.171694917	5.80933
226045_at	FRS2	fibroblast growth factor receptor substrate 2	5.38991	4.93813	5.09842	4.81886	4.73289	4.56814	4.77345	4.80020	4.70312	4.92595	4.50878	0.249269594	0.124053296	-0.136160473	4.85231	
1561887_at	FRS3	fibroblast growth factor receptor substrate 3	3.32033	3.15188	3.48310	3.28361	3.34729	3.45825	3.02046	3.18301	3.1874	3.18708	3.20772	3.16369	0.005929813	0.006751756	-0.195789558	3.24468
219907_at	FRS3	fibroblast growth factor receptor substrate 3	7.22870	7.04099	7.09795	6.96298	7.09619	7.02266	7.10866	7.09896	7.14328	6.91947	7.03425	7.08243	0.011730659	0.301008582	-0.011730659	7.07238
231273_s_at	FRZB	fizzled-related protein	5.19088	5.51423	5.40019	5.03189	5.13447	5.27915	5.03242	4.89771	4.93440	4.75032	5.02172	4.80279	0.000414549	0.000815327	-0.351877892	5.08250
203697_at	FRZB	fizzled-related protein	4.57137	4.71990	4.53746	4.38634	4.18706	4.35241	4.72729	4.67911	4.62902	4.70930	4.84453	0.005390308	0.006157851	0.248866785	4.58510	
203698_s_at	FRZB	fizzled-related protein	4.16309	4.38427	3.92903	3.93715	4.06773	4.29443	4.10099	4.07402	4.07402	4.13695	3.96184	4.14854	0.638378882	0.246458876	-0.035555846	4.10051
204451_at	FZD1	fizzled homolog 1 (Drosophila)	7.52817	7.39792	7.04523	7.10105	7.06538	7.14026	6.03655	6.29361	6.39234	6.24268	6.09303	6.18101	7.10E-09	1.08E-07	-0.951448864	6.71911
204452_s_at	FZD1	fizzled homolog 1 (Drosophila)	5.69207	5.46462	5.52916	5.28275	5.30614	5.32436	5.03083	4.85801	5.27628	5.37385	5.22036	0.07564399	0.008119892	-0.271563953	5.29739	
219754_at	FZD10	fizzled homolog 10 (Drosophila)	3.64886	3.93670	3.55488	3.60378	3.69860	3.73846	3.70333	3.41521	3.61797	3.70631	3.64366	0.177289952	0.09563796	-0.09849762	3.64726	
238129_s_at	FZD2	fizzled homolog 2 (Drosophila)	6.74210	7.30962	7.05766	6.78342	6.92740	7.04069	6.94324	6.92279	6.88887	6.95701	6.92621	7.13009	0.870789123	0.308053335	-0.013860776	6.97071
210220_at	FZD2	fizzled homolog 2 (Drosophila)	5.28941	5.04777	4.95842	4.80375	4.63005	4.85517	4.42131	4.75218	4.51458	4.44441	4.50035	4.71127	0.00108043	0.001735525	-0.408909061	6.97071
3.98696	FZD3	fizzled homolog 3 (Drosophila)	9.22975	9.27804	9.36227	9.08815	9.17779	9.10547	10.47436	10.40762	10.52760	10.27908	10.19564	10.43546	0.001867126	0.016586844	-0.187868813	9.87866
218665_at	FZD4	fizzled homolog 4 (Drosophila)	8.78650	8.58191	8.71974	8.52888	8.58612	8.38485	8.07970	8.00792	7.87647	7.80897	7.72094	7.97824	2.42E-08	3.01E-07	1.188048187	8.80094
229441_at	FZD4	fizzled homolog 4 (Drosophila)	6.77241	6.77582	6.63915	6.27419	6.72549	7.53586	7.63344	7.29731	7.25336	7.56689	7.02E-06	6.73E-06	0.772703409	-0.713313789	8.24501	7.08601
205196_at	FZD5	fizzled homolog 5 (Drosophila)	6.42347	6.36337	6.14417	6.31363	6.10974	6.51136	6.15045	6.18717	6.12450	6.18871	6.06173	6.16569	0.067698977	0.045316871	-0.147758009	6.23708
203987_at	FZD6	fizzled homolog 6 (Drosophila)	9.02341	8.71982	8.93964	8.57885	8.56522	8.21933	9.22332	9.39241	9.45613	8.78804	8.83897	9.31483	0.002193878	0.003054883	0.484605959	6.82165
203705_s_at	FZD7	fizzled homolog 7 (Drosophila)	3.50153	3.77949	3.48496	3.82883	3.64163	4.11700	3.96137	3.96137	4.17420	4.04542	3.87744	3.97901	0.00757278	0.008284585	0.280534542	3.86584
203706_s_at	FZD7	fizzled homolog 7 (Drosophila)	3.58445	3.95088	3.93963	3.97491	3.92196	3.72481	3.99500	3.54286	3.96365	4.03031	3.83351	0.227476651	0.115728965	-0.115129311	3.85737	
227405_s_at	FZD8	fizzled homolog 8 (Drosophila)	8.57769	8.48863	8.32866	8.27996	8.07071	7.99639	7.56877	7.4154	7.69349	7.71747	7.32066	7.24E-05	4.52E-05	-0.724194006	7.88177	
216587_s_at	FZD8	fizzled homolog 8 (Drosophila)	5.38920	5.56888	5.10057	5.43379	5.39613	5.33121	5.17179	4.83596	5.01660	4.82331	4.96448	7.54E-05	0.00021011	-0.384968695	5.78654	
224325_at	FZD8	fizzled homolog 8 (Drosophila)	5.20823	4.55430	4.99455	4.66426	4.59183	4.62248	4.44489	4.51353	4.42691	4.61512	4.57631	4.85902	0.081891683	0.052524007	-0.198293923	4.67179

207639_at	FZD9	fizzled homolog 9 (Drosophila)	6.34090	6.88746	6.54023	6.35066	6.38413	6.22711	6.35643	6.66097	6.72459	6.36349	6.11033	6.31202	0.863247463	0.30630012	0.016668916	6.41342
206204_at	GRB14	growth factor receptor-bound protein 14	6.04656	5.64841	5.51685	5.42810	5.74171	5.64383	4.38653	4.44591	4.25231	4.66220	4.67918	4.55655	2.27E-08	-1.177196573	5.08501	5.08501
223049_at	GRB2	growth factor receptor-bound protein 2	9.93724	9.98995	9.80221	10.02026	9.96787	9.80114	10.07147	10.04893	10.13085	10.13086	10.21027	10.18140	0.001515307	0.224640315	10.01660	8.97218
215075_at	GRB2	growth factor receptor-bound protein 2	8.92819	8.68162	8.69846	8.91484	8.96439	8.93708	9.06990	9.02319	9.25929	9.25929	9.11512	9.000102707	0.000269832	0.326753334	8.97218	8.97218
22872_at	GRB2	growth factor receptor-bound protein 2	7.28479	7.37026	7.23174	7.30727	7.29663	7.41191	7.37459	7.64476	7.55517	7.37091	7.47360	7.71637	0.007286119	0.201602346	7.41823	7.41823
210761_s_at	GRB7	growth factor receptor-bound protein 7	6.93838	6.92612	6.97683	6.84074	6.94348	6.92911	6.83790	6.96275	6.84171	6.83169	7.04098	7.15394	0.271990893	0.022393998	6.89897	6.89897
220480_at	HAND2	heart and neural crest derivatives expressed 2	5.88813	6.06172	5.98489	5.77555	5.93733	6.14340	6.04522	5.56546	5.52763	5.68901	5.63095	5.67800	0.011797171	-0.247023552	5.62639	5.62639
213069_at	HEG1	HEG homolog 1 (zebrafish)	9.76651	9.48665	9.43409	9.18383	9.24445	9.32533	9.79391	9.62475	9.74566	9.73811	9.81842	9.79500	5.04E-05	0.392514377	9.56537	9.56537
212822_at	HEG1	HEG homolog 1 (zebrafish)	8.92199	8.31133	8.49279	8.33287	8.27272	8.53991	8.51959	8.45508	8.58423	8.69425	8.51351	8.64351	0.017575608	0.168977663	8.48387	8.48387
1559037_s_at	HEG1	HEG homolog 1 (zebrafish)	4.36633	4.45843	4.60485	4.20790	4.22901	4.21233	4.09842	4.33868	4.18521	4.00689	3.95758	4.02627	0.0078767462	-0.245399521	4.22349	4.22349
44783_s_at	HEY1	hairy/enhancer-of-split related with YRPW motif 1	10.36097	10.31534	10.25594	9.98130	9.94391	9.49138	11.21430	11.41704	11.33602	10.82177	10.78747	11.19043	1.72E-05	1.036380856	10.57631	10.57631
218839_at	HEY1	hairy/enhancer-of-split related with YRPW motif 1	9.36775	9.28395	9.15322	9.08301	8.97912	8.58594	10.24804	10.41760	10.31484	9.60590	9.72380	9.94563	2.10E-05	0.983986216	9.55091	9.55091
222921_s_at	HEY2	hairy/enhancer-of-split related with YRPW motif 2	7.30802	7.48719	7.51839	7.42554	7.23310	6.73833	7.04112	7.07654	6.92915	7.11354	6.93236	7.15562	0.026860674	-0.243711669	7.16324	7.16324
219743_at	HEY2	hairy/enhancer-of-split related with YRPW motif 2	6.16329	6.01237	6.28713	6.11150	6.07475	5.71799	5.73887	5.61467	5.61622	5.50219	5.77149	7.80E-07	-0.464978759	5.89240	5.89240	
226828_s_at	HEYL	hairy/enhancer-of-split related with YRPW motif-like	6.97962	6.98970	6.87891	6.86457	6.87271	6.94535	6.83890	7.05520	6.77719	6.90890	6.82390	6.94582	0.816320708	0.294910012	-0.01334318	6.89830
220682_s_at	HEYL	hairy/enhancer-of-split related with YRPW motif-like	6.74885	7.14018	7.00446	7.02268	6.90566	6.93105	6.77071	6.77710	6.65995	6.80666	6.79515	6.56981	0.00264188	-0.233248637	6.84652	6.84652
209961_s_at	HGF	hepatocyte growth factor (hepatopoietin A, scatter factor)	6.74585	6.73780	6.65990	6.84318	6.70386	6.70736	6.68438	6.57888	6.60787	6.64780	6.78991	6.92920	0.753826434	-0.021653014	6.71373	6.71373
210986_s_at	HGF	hepatocyte growth factor (hepatopoietin A, scatter factor)	4.42408	4.95423	4.97258	4.71379	4.70070	4.76655	4.75245	4.68993	4.72746	4.73481	4.81069	4.72412	0.782668845	-0.021910101	4.74937	4.74937
210997_at	HGF	hepatocyte growth factor (hepatopoietin A, scatter factor)	4.35821	4.04163	3.94865	3.83315	3.97388	4.21701	4.34598	4.01303	4.01725	4.12733	3.97012	4.01915	0.822187305	0.296397814	4.07219	4.07219
209960_at	HGF	hepatocyte growth factor (hepatopoietin A, scatter factor)	3.87655	3.85286	3.92022	3.79104	3.71144	3.59152	3.64377	3.78811	3.67236	3.77954	3.79070	3.73854	0.382732713	-0.055420749	3.76288	3.76288
210755_at	HGF	hepatocyte growth factor (hepatopoietin A, scatter factor)	3.79994	3.29562	3.43314	3.48321	3.43881	3.58478	3.58645	3.49143	3.51017	3.50705	3.46368	3.63926	0.109248091	0.065881792	3.48413	3.48413
209989_at	HIF1A	hypoxia-inducible factor 1, alpha subunit (basic helix-loop-helix transcription factor)	11.35188	11.13055	11.29536	11.17706	11.26634	11.28692	11.89487	11.84867	11.98846	11.89667	11.91012	11.92701	9.97E-10	2.05E-08	11.57841	11.57841
238889_at	HIF1A	hypoxia-inducible factor 1, alpha subunit (basic helix-loop-helix transcription factor)	5.45323	5.72707	5.55069	5.64671	5.82173	5.88235	5.49611	5.30987	5.51850	5.43941	5.35936	5.36632	0.00396198	-0.232036999	5.53094	5.53094
203869_at	HMOX1	heme oxygenase (deacylating) 1	8.14163	8.70633	8.92001	9.15911	9.16656	9.65291	9.75173	9.41854	9.39126	9.89199	9.78612	9.74042	0.00040185	0.595094751	9.86913	9.86913
219403_s_at	HPSE	heparanase	8.41774	8.17722	8.37463	8.70505	8.75633	8.89807	9.65047	9.39884	9.48643	9.76311	9.67678	9.62098	3.03E-07	1.044597234	9.07714	9.07714
222881_at	HPSE	heparanase	8.02120	7.82732	8.07999	8.30643	8.16882	8.10711	8.21820	7.89000	8.03873	8.38974	8.38925	8.18718	0.537774804	0.060186234	8.15213	8.15213
206824_at	HSPB2	heat shock 27kDa protein 2	6.46428	6.79905	6.47735	6.40756	6.35520	6.53955	6.63870	6.60505	6.29188	6.30966	6.29488	6.08900	-0.167649479	-0.158603007	6.43936	6.43936
208937_s_at	ID1	inhibitor of DNA binding 1, dominant negative helix-loop-helix protein	11.88710	11.87820	11.92943	11.92486	11.99742	11.83854	11.28637	10.90111	10.81947	11.33775	11.48706	11.22203	7.90E-07	-0.705580225	11.54308	11.54308
207826_s_at	ID3	inhibitor of DNA binding 3, dominant negative helix-loop-helix protein	12.35539	12.26656	12.35375	12.20800	12.20107	12.00532	12.27327	12.26817	12.24679	12.08814	12.25259	12.20794	0.881638533	-0.009699336	12.28693	12.28693
208375_at	IFNA1	interferon, alpha 1	3.51166	3.65522	3.64325	3.47511	3.59047	3.24077	3.54151	3.43450	3.81572	3.71203	3.71984	3.59389	0.158161443	0.116835629	3.57783	3.57783
208173_at	IFNB1	interferon, beta 1, fibroblast	5.61020	5.87939	5.74844	5.52818	5.54195	5.74841	5.80791	6.01118	6.06331	5.98449	5.66785	5.60489	0.037220415	0.182143448	5.76717	5.76717
210354_at	IFNG	interferon, gamma	4.62094	4.67130	4.59994	4.78646	4.76251	4.79945	4.73482	4.43969	4.66656	4.70815	4.60688	4.60688	0.318203587	-0.064584207	4.67447	4.67447
211577_s_at	IGF1	insulin-like growth factor 1 (somatomedin C)	7.38147	7.25081	7.11311	7.04710	7.08949	7.04757	7.04016	7.11236	6.97792	6.96041	6.93739	6.90944	0.018028132	0.01613841	7.06227	7.06227
209542_x_at	IGF1	insulin-like growth factor 1 (somatomedin C)	6.52332	6.56539	6.52578	6.56796	6.60959	6.60938	6.42068	6.65373	6.44818	6.38730	6.31432	0.048959676	-0.125214852	6.50411	6.50411	
209540_at	IGF1	insulin-like growth factor 1 (somatomedin C)	4.83706	4.70473	4.52768	4.63981	4.63972	4.78249	4.70724	4.67535	4.81177	4.75374	4.81177	4.59513	0.238282333	0.032110953	4.70477	4.70477
209541_at	IGF1	insulin-like growth factor 1 (somatomedin C)	4.55288	4.62731	4.66539	4.52950	4.43411	4.57662	4.69985	4.71241	4.59513	4.58550	4.67117	0.042554317	0.031506878	4.62000	4.62000	
207433_at	IL10	interleukin 10	3.98423	4.06524	4.00881	3.96403	3.94865	4.03226	3.96759	3.96722	3.92959	4.13261	4.24892	4.02403	0.447706071	0.192061558	4.02510	4.02510
207180_at	IL12A	interleukin 12A (natural killer cell stimulatory factor 1, cytotoxic lymphocyte maturation factor 1, p35)	4.03279	4.33754	3.89819	4.10961	4.05017	4.24843	3.97664	4.12718	4.13347	4.03327	4.21738	4.21561	0.94671224	0.004802243	4.11486	4.11486
234408_at	IL17F	interleukin 17F	4.94380	5.29337	5.11937	4.69223	5.08526	5.04867	4.86338	5.10146	4.68489	4.78195	4.79443	4.84917	0.058552969	-0.175039391	4.93340	4.93340
206295_at	IL18	interleukin 18 (interferon-gamma-inducing factor)	3.60566	3.60566	3.56285	3.36181	3.62538	3.54737	3.57513	3.60164	3.57232	3.66186	0.784009505	0.286593062	0.015889512	3.58169	3.58169	
205067_at	IL1B	interleukin 1, beta	7.24484	7.21493	7.09740	7.17852	7.35999	7.13687	7.85689	7.78903	7.69517	7.77108	7.66020	7.84842	3.87E-07	0.564693401	7.48779	7.48779

39402_at	IL1B	interleukin 1, beta	6.05078	6.19833	6.09435	6.16173	6.27557	5.98519	6.59396	6.36261	6.43499	6.56690	6.47894	6.56532	9.93E-06	4.24E-05	0.360829144	6.30807
243977_at	IL6	interleukin 6 (interferon, beta 2)	6.20290	6.25150	6.25769	6.35379	6.45783	6.57073	6.39386	6.29488	6.50299	6.36986	6.35179	6.25933	0.685369524	0.261277779	0.027554486	6.35118
205207_at	IL6	interleukin 6 (interferon, beta 2)	5.68661	5.93654	5.68780	5.80974	5.73905	5.75497	6.73182	6.21592	6.13064	6.39845	6.65892	6.45561	1.70E-06	1.02E-05	0.660775882	6.10117
212195_at	IL6ST	interleukin 6 signal transducer (gp130, oncostatin M receptor)	11.97220	11.82666	11.91284	11.81618	11.8086	11.8086	11.65448	12.24374	12.21312	12.33177	12.33718	12.32233	6.32E-07	4.56E-06	0.486938099	12.06669
212196_at	IL6ST	interleukin 6 signal transducer (gp130, oncostatin M receptor)	10.56328	10.50579	10.64724	10.21250	10.23889	10.38617	11.16066	11.09644	11.35408	10.87598	10.83511	11.14201	2.78E-06	1.53E-05	0.651718822	10.75151
204863_s_at	IL6ST	interleukin 6 signal transducer (gp130, oncostatin M receptor)	8.73919	9.13126	8.81120	8.87979	8.82745	8.67030	9.74125	9.61852	9.84866	9.59048	9.36534	9.69666	0.000158751	0.000380196	0.631135486	9.32542
211000_s_at	IL6ST	interleukin 6 signal transducer (gp130, oncostatin M receptor)	8.77054	9.30362	8.77229	8.85994	8.84067	9.61837	9.65244	9.55201	9.62668	9.49187	9.26512	9.53826	0.001319165	0.0020038634	0.486652489	9.26938
204864_s_at	IL6ST	interleukin 6 signal transducer (gp130, oncostatin M receptor)	8.66679	8.95289	8.77113	8.86143	8.40595	9.13376	9.54153	9.41020	9.60485	9.90937	8.90012	9.33065	0.001088613	0.001745937	0.567494891	8.99904
234967_at	IL6ST	interleukin 6 signal transducer (gp130, oncostatin M receptor)	3.73838	3.97858	4.17884	3.79944	3.80076	3.90002	4.05885	4.01861	4.17884	4.20155	4.07576	4.56641	0.007897029	0.007897029	0.283500981	4.04109
234474_s_at	IL6ST	interleukin 6 signal transducer (gp130, oncostatin M receptor)	3.48211	3.56481	3.67600	3.50225	3.62503	3.70685	3.85716	3.78969	3.59155	3.61038	3.57054	3.77033	0.265947958	0.1300335439	0.06876807	3.62723
202859_s_at	IL6	interleukin 8	11.44327	11.23825	11.46277	12.01424	11.97509	11.59280	11.21790	10.47192	10.93892	10.58844	10.58844	10.58844	0.000594891	0.001062273	-1.348093817	10.94702
211506_s_at	IL6	interleukin 8 receptor, alpha	10.10514	10.04131	10.03544	10.44271	10.41380	10.15227	9.50373	8.60298	9.42898	9.70872	9.08670	8.61910	0.000198253	0.000281274	-1.775123307	9.31088
207094_at	IL6RA	interleukin 8 receptor, alpha	7.70103	7.68997	7.74207	7.75442	7.79612	7.70424	7.85475	7.77962	7.79889	7.76616	7.84115	7.95525	0.094147365	0.058647114	0.092820665	7.78622
207008_at	IL6RB	interleukin 8 receptor, beta	4.39233	4.45803	4.39097	4.16425	4.15245	4.25504	4.00322	4.07965	4.33200	4.02140	4.10301	3.89395	0.0071936	0.008314727	-0.230139822	4.18726
202351_at	ITGAV	integrin, alpha V (vitronectin receptor, alpha polypeptide, antigen CD51)	10.92770	10.89431	11.00384	10.96853	10.96927	10.52539	11.04570	10.96926	11.30284	11.06244	11.00240	11.12088	0.022863145	0.019437262	0.202913922	10.98246
241769_at	ITGAV	integrin, alpha V (vitronectin receptor, alpha polypeptide, antigen CD51)	4.92170	5.11307	4.89557	4.58191	4.60469	5.23516	4.91226	4.74234	5.15749	4.70416	4.86634	5.25156	0.513286875	0.212404235	0.080341885	4.88985
238251_at	ITGAV	integrin, alpha V (vitronectin receptor, alpha polypeptide, antigen CD51)	4.92747	4.70102	4.84276	4.41791	4.64077	4.91942	4.96556	4.82011	5.05868	4.94095	4.85398	5.3324	0.008548899	0.007240204	0.304028977	4.84357
232797_at	ITGAV	integrin, alpha V (vitronectin receptor, alpha polypeptide, antigen CD51)	4.35734	4.19026	3.98288	3.77272	3.90133	4.18025	4.24308	3.59986	4.55194	4.03551	3.99865	4.03543	0.917914715	0.319294655	0.013432264	4.07066
204622_s_at	ITGB3	integrin, beta 3 (platelet glycoprotein IIIa, antigen CD61)	7.72653	7.68831	7.60223	7.98776	7.85132	7.82909	9.73966	9.58714	9.63256	9.76684	9.69995	9.62306	1.29E-15	2.62E-13	1.894427765	8.72810
204626_s_at	ITGB3	integrin, beta 3 (platelet glycoprotein IIIa, antigen CD61)	7.56446	7.65152	7.64390	7.64869	7.52967	7.83963	8.65634	8.71479	8.49008	8.64374	8.71048	8.49345	3.97E-11	1.37E-09	0.972353919	8.13230
204628_s_at	ITGB3	integrin, beta 3 (platelet glycoprotein IIIa, antigen CD61)	7.61281	7.73176	7.41285	7.64904	7.48596	7.72275	8.54705	8.42616	8.41328	8.59118	8.69654	8.64283	2.20E-10	5.81E-09	0.950827424	8.07794
204625_s_at	ITGB3	integrin, beta 3 (platelet glycoprotein IIIa, antigen CD61)	8.86538	8.96766	8.68930	7.18235	6.80765	7.04522	8.09004	8.09986	8.28624	8.44851	8.40487	8.23479	7.61E-11	2.36E-09	1.351461154	7.58198
216261_at	ITGB3	integrin, beta 3 (platelet glycoprotein IIIa, antigen CD61)	6.49207	6.33104	6.35046	6.63864	6.22154	6.48544	6.87421	6.83664	6.56178	6.35315	6.43511	6.67326	0.043840039	0.032257773	0.202491892	6.52111
211572_at	ITGB3	integrin, beta 3 (platelet glycoprotein IIIa, antigen CD61)	5.44189	5.69349	5.63989	5.31681	5.41353	5.36114	5.35649	5.32053	5.24341	5.38986	5.05732	5.22081	0.019915507	0.017450088	-0.162621254	5.35268
215240_at	ITGB3	integrin, beta 3 (platelet glycoprotein IIIa, antigen CD61)	3.93240	4.19008	4.12517	3.95977	3.96610	3.96769	5.20448	5.06058	5.52411	5.00012	4.92260	4.92579	1.86E-09	3.46E-08	1.085129346	4.58443
209099_x_at	JAG1	jagged 1 (Alagille syndrome)	10.61357	10.59985	10.74033	10.65017	10.64589	10.44556	12.89119	12.62704	12.80038	12.81219	12.81594	12.72039	3.93E-17	1.42E-14	2.198661794	11.67519
216268_s_at	JAG1	jagged 1 (Alagille syndrome)	10.08768	9.96043	10.23977	10.2454	10.17632	9.90035	12.38584	12.28951	12.50049	12.44083	12.44083	12.44083	3.47E-16	8.68E-14	2.295742456	11.25772
209098_s_at	JAG1	jagged 1 (Alagille syndrome)	7.59760	7.02543	7.55424	7.7398	8.09157	10.32976	10.16217	10.52328	10.16217	10.52551	10.48335	10.29833	1.45E-13	1.39E-11	2.766970365	8.96691
231183_s_at	JAG1	jagged 1 (Alagille syndrome)	6.56553	6.83789	6.70504	6.70871	6.95283	6.94847	9.40522	9.27918	9.05033	9.34963	9.27947	9.26338	1.97E-11	7.57E-10	2.635566435	7.95326
232408_at	JAG1	jagged 1 (Alagille syndrome)	7.35321	7.21204	6.99914	7.04431	6.78421	7.41638	8.34807	8.28287	8.66466	8.60792	8.43770	8.46050	2.46E-10	6.34E-09	1.330036392	7.80023
209097_s_at	JAG1	jagged 1 (Alagille syndrome)	6.08986	6.45641	6.43985	6.39662	6.16509	6.24815	7.03590	6.77642	7.08356	7.32947	7.29277	7.30070	1.34E-06	0.850305574	6.72467	
236678_at	JAG1	jagged 1 (Alagille syndrome)	5.72143	5.62620	5.58403	5.68578	5.75319	6.30893	6.45397	6.29050	6.27089	6.89918	6.85581	6.95580	1.47E-05	5.78E-05	0.837785488	6.19881
229824_s_at	JAG1	jagged 1 (Alagille syndrome)	4.90489	5.34329	5.13480	5.21407	5.32944	5.22204	5.0834	5.28031	5.09939	5.25131	5.21451	0.915090921	0.318578281	0.008421875	5.19363	
32137_at	JAG2	jagged 2	9.16361	8.97079	9.05988	8.99560	8.99422	9.20835	9.39206	9.40166	9.41079	9.47083	9.45850	9.52967	5.91E-06	2.81E-05	0.361874819	9.26298
209784_s_at	JAG2	jagged 2	8.92550	8.99392	8.96643	8.90618	9.01656	9.07415	9.19705	9.23770	9.33388	9.27815	9.25737	9.32679	7.72E-05	9.41E-05	0.291696302	9.12631
203934_at	KDR	kinase insert domain receptor (a type III receptor tyrosine kinase)	9.99535	9.86635	9.99431	10.02266	9.90404	9.82186	10.55708	10.70525	10.41586	10.29153	10.46619	5.68E-07	4.16E-06	0.537000005	10.20260	
231629_x_at	KLK3	kallikrein 3 (prostate specific antigen)	8.77919	8.90410	8.74948	8.77559	8.72076	8.76196	8.79422	8.59589	8.78421	8.61860	8.65633	0.4638689	0.196985126	-0.043929674	8.77178	
204493_x_at	KLK3	kallikrein 3 (prostate specific antigen)	6.79456	7.14475	6.89202	6.74302	6.92728	7.00031	6.82854	6.82986	6.89270	6.89970	6.79653	6.69598	0.188927659	0.100428571	-0.09441877	6.87010
204582_s_at	KLK3	kallikrein 3 (prostate specific antigen)	6.43806	6.37576	6.59362	6.37077	6.24214	6.69847	6.18314	6.14387	6.14387	6.09816	6.11873	5.99208	0.000395226	0.000786248	-0.325221994	6.29019
205900_at	KRT1	keratin 1 (epidermolytic hyperkeratosis)	6.16551	5.96286	6.35458	6.42416	6.61045	6.53377	6.42631	6.47195	6.48213	6.46282	6.75559	0.118922623	0.066983322	0.158144765	6.42093	

LAMAS	210150_s_at	laminin, alpha 5	891381	9.00454	9.11746	8.81117	8.97687	8.95042	8.46453	8.49743	8.50852	8.41095	8.45292	8.45193	1.29E-07	1.22E-06	-0.490498165	8.70963
LAMAS	22670_t_at	laminin, alpha 5	6.66199	6.63068	6.72420	6.60877	6.77249	6.60893	7.06287	7.25574	7.01300	6.90991	6.94396	6.67640	7.47E-05	0.002208572	0.342437132	6.83906
LAMAS	206309_at	leucocyte cell derived chemotaxin 1	5.39765	5.64844	5.60304	5.11793	5.42350	5.34119	5.46405	5.58439	5.01255	5.21517	5.28807	5.77233	0.869681169	0.30770713	-0.018696506	5.39511
LAMAS	207092_at	lepin (obesity homolog, mouse)	4.66309	5.01389	4.90857	4.47127	4.84339	4.72433	4.67399	4.75903	4.65476	4.47739	4.55359	4.71808	0.170991317	0.09307981	-0.114616901	4.69678
LAMAS	216250_s_at	leupacin	8.26172	8.20881	8.23989	8.52399	8.42028	8.67287	7.77982	7.44179	7.47488	7.89969	7.83821	7.75353	1.74E-06	1.04E-05	-0.68603954	8.40272
LAMAS	244654_at	leupacin	4.32187	4.16143	4.39444	4.43114	4.18979	4.40221	4.61208	4.32423	4.44970	4.37290	4.85563	4.75353	0.049927661	0.035676212	0.181609257	4.40472
LAMAS	242778_at	leupacin	3.78603	3.85481	3.96736	3.97491	3.72043	3.95484	3.73047	3.60718	3.28422	3.47130	3.43986	3.93986	0.000981729	-0.335277782	0.000981729	3.70876
LAMAS	209035_at	midline (neurite growth-promoting factor 2)	6.76913	6.98450	6.86983	8.07068	6.87626	6.67940	8.10543	8.21552	7.78938	7.88625	7.93510	7.94149	1.21E-08	1.69E-07	-0.84433763	8.40158
LAMAS	242203_at	midline (neurite growth-promoting factor 2)	6.20516	6.50333	6.52201	6.28897	6.33693	6.07136	6.03915	6.05920	5.73816	5.75449	5.79211	5.99188	4.98E-05	0.000142356	-0.475130821	6.03840
LAMAS	204475_at	matrix metalloproteinase 1 (interstitial collagenase)	4.44568	4.57293	4.63706	4.64259	4.42777	4.44215	13.28401	13.06493	13.21537	13.14300	13.22299	13.05877	6.04E-27	1.12E-22	6.637979355	8.84595
LAMAS	227106_at	matrix metalloproteinase 19	8.38345	8.23078	8.39872	8.11332	8.17147	8.14722	8.11118	8.04404	8.09668	8.00061	7.92463	8.11883	0.007919806	0.00841303	-0.19014937	8.14440
LAMAS	204575_s_at	matrix metalloproteinase 19	6.11962	6.10079	6.25275	6.33523	6.29030	6.12354	5.95781	5.96705	6.07199	6.12692	6.05163	6.26410	0.051021906	0.041697856	-0.131502935	6.13795
LAMAS	201069_at	matrix metalloproteinase 2 (gelatinase A, 72kDa)	11.30162	11.43218	11.42258	11.19863	11.23380	11.05037	10.97693	11.12687	11.11868	10.80405	10.79868	11.05814	0.001849361	0.002667189	-0.280139874	11.12663
LAMAS	1566678_at	matrix metalloproteinase 2 (gelatinase A, 72kDa)	6.50249	6.68437	6.40035	6.41439	6.47562	6.65735	6.60135	6.80512	6.66879	6.69516	6.61562	6.72689	0.02171031	0.019874974	0.195611178	6.60731
LAMAS	1566877_at	matrix metalloproteinase 2 (gelatinase A, 72kDa)	4.06173	4.02593	3.96892	3.94333	4.07693	4.28893	3.86854	4.09471	4.05785	4.00655	3.94561	3.99153	0.310093593	0.146208194	-0.087163102	4.02738
LAMAS	203936_s_at	matrix metalloproteinase 9 (gelatinase B, 92kDa)	6.50426	6.56977	6.27974	6.55030	6.62255	6.42186	11.88212	11.23026	10.38135	7.49128	7.66409	10.99033	2.74E-05	9.50E-05	3.381925284	8.18233
LAMAS	219158_s_at	NMDA receptor regulated 1	8.63931	8.95450	8.89269	8.64116	8.54807	8.61425	8.41720	8.23209	8.30857	8.30354	8.16145	8.15715	7.78E-06	3.48E-05	-0.359831542	8.44175
LAMAS	226998_at	NMDA receptor regulated 1	7.61212	7.47169	7.49936	7.67219	7.57948	7.69843	7.38937	7.22333	7.38136	7.37425	7.30897	7.44135	0.001073004	0.001726578	-0.218965074	7.48259
LAMAS	222837_s_at	NMDA receptor regulated 1	6.76124	6.97444	6.67929	6.59744	6.72560	6.79835	6.72576	6.51591	6.63970	6.71039	6.70963	6.67191	0.343679047	0.157794399	-0.1218888	6.83216
LAMAS	1556382_s_at	NKDA receptor regulated 1	5.85887	5.97765	5.78130	6.01521	6.03295	5.64273	5.77887	5.81393	5.82555	5.77149	5.89061	5.90094	0.432280812	0.187142823	-0.054852271	5.86751
LAMAS	222036_at	NKDA receptor regulated 1	5.59726	6.20872	5.92324	5.79674	5.90424	5.76303	5.57284	5.27300	5.33315	5.52703	5.52703	4.96661	0.000551104	0.001020333	-0.494808831	5.61813
LAMAS	1556381_at	NKDA receptor regulated 1	4.18164	3.91241	4.15402	3.86274	4.20625	4.11929	4.20513	4.29739	4.21158	4.32028	4.25255	4.25255	0.01096443	0.01096443	0.225527117	4.19514
LAMAS	205681_s_at	nitric oxide synthase 3 (endothelial cell)	8.60357	8.26071	8.46977	8.48710	8.43248	8.78048	9.15419	9.01520	9.30396	9.37393	9.48018	9.43862	5.17E-07	3.86E-06	0.850161492	8.93077
LAMAS	229252_at	nitric oxide synthase 3 (endothelial cell)	4.53066	5.57785	5.54832	5.57048	5.58951	5.62008	6.69321	5.83589	5.80707	5.66626	5.68853	5.30030	0.18820204	0.100194729	-0.106658351	5.60855
LAMAS	229099_at	nitric oxide synthase 1, translocation-associated (Drosophila)	4.70120	5.23026	4.91122	4.98887	4.84959	4.45805	4.53956	4.69292	4.79547	4.55405	4.79547	4.45514	0.00524284	0.006542825	-0.27288478	4.72332
LAMAS	216902_at	Notch homolog 1, translocation-associated (Drosophila)	9.09384	9.13226	9.17782	9.89311	8.84733	8.99915	8.99603	8.80917	8.99113	8.96617	8.84600	9.00373	0.192728567	0.101965956	-0.083545144	8.99981
LAMAS	223509_at	Notch homolog 1, translocation-associated (Drosophila)	6.99307	7.06169	7.00382	6.90031	7.08452	6.85444	6.72300	6.84971	6.88973	6.77139	6.88603	6.80006	0.0003364604	0.004279676	-0.1964694	6.89473
LAMAS	202443_s_at	Notch homolog 2 (Drosophila)	8.60578	8.63661	8.98611	9.76089	9.68289	9.75177	9.58069	9.44752	9.53644	9.57808	9.45723	9.58636	0.004381151	0.005268468	-0.192953824	8.62753
LAMAS	212377_s_at	Notch homolog 2 (Drosophila)	8.91195	8.65128	8.95877	8.84934	8.82992	8.88083	8.68219	8.61426	8.67599	8.76899	8.67994	8.79551	0.003008703	0.003917035	-0.177202568	8.79142
LAMAS	210756_s_at	Notch homolog 2 (Drosophila)	8.32219	8.01184	8.21688	8.25971	8.04952	8.42926	8.17862	8.19800	8.51729	8.24851	8.35398	8.4376829	0.188895728	0.063364193	-0.189695292	8.24638
LAMAS	202445_s_at	Notch homolog 2 (Drosophila)	5.29181	5.30779	5.35264	5.32945	5.28449	5.37827	5.26467	5.20396	5.48470	5.9221	5.29569	5.89778	0.89215147	0.298117196	0.014977392	5.33066
LAMAS	202327_s_at	Notch homolog 3 (Drosophila)	7.11918	7.91655	7.55770	7.47067	7.68329	7.48144	7.39437	7.43409	7.19577	7.23235	7.23290	7.21668	0.021684571	0.019633441	-0.2519806	7.40862
LAMAS	203238_s_at	Notch homolog 3 (Drosophila)	5.96572	6.25660	5.91844	5.96944	6.04064	5.88996	5.86382	5.67744	5.63516	5.76218	5.89322	5.89322	0.005991161	0.006750412	-0.215833077	5.89290
LAMAS	243215_at	Notch homolog 3 (Drosophila)	4.86958	4.83430	4.59234	4.68817	4.55408	4.98304	4.62804	4.64550	4.47963	4.61013	4.51310	4.97298	0.224200945	0.114467893	-0.11218923	4.69749
LAMAS	205247_at	Notch homolog 4 (Drosophila)	8.33236	8.26339	8.17447	8.28903	8.12009	8.20467	8.18295	9.02271	9.21439	8.92688	8.67329	8.91850	2.20E-07	1.90E-06	0.665598463	8.57267
LAMAS	240786_at	Notch homolog 4 (Drosophila)	7.20718	7.53390	7.28724	7.35393	7.28718	7.39167	7.58170	7.58710	7.47705	7.31713	7.43453	7.43453	0.03707484	0.028340269	0.149441479	7.41339
LAMAS	206801_at	natriuretic peptide precursor B (atriuretic peptide receptor A)	5.74578	5.52484	5.87524	5.81751	5.90382	5.79849	6.66556	5.54269	5.67161	5.41268	5.58727	5.30197	0.005312282	0.006153585	-0.247279132	5.65394
LAMAS	204646_at	natriuretic peptide receptor Aguanlylate cyclase A (atriuretic peptide receptor A)	7.88231	7.78063	7.82028	7.76955	7.72564	7.84129	7.79553	7.62606	7.68876	7.54233	7.49194	7.57310	0.006595316	0.0072814	-0.182661561	7.71095
LAMAS	32825_at	natriuretic peptide receptor Aguanlylate cyclase A (atriuretic peptide receptor A)	7.12777	7.41557	7.01951	6.97911	7.09398	7.17183	7.39872	7.40499	7.32038	7.98282	7.12716	7.11463	0.208333223	0.108141238	0.005966384	7.18762
LAMAS	212298_at	neurophilin 1	9.93563	9.78854	9.91774	10.21476	9.94629	9.72184	9.78615	9.78977	10.23133	10.03286	9.96273	9.95951	0.665925097	0.253213404	0.039591312	9.94059
LAMAS	210510_s_at	neurophilin 1	8.76645	8.04701	8.06684	8.27586	8.12267	8.16083	8.77216	8.60383	8.63512	8.74621	8.74621	8.41285	1.98E-08	0.59851497	0.59851497	8.41285
LAMAS	233701_at	neurophilin 1	7.35229	7.54549	7.28452	7.39714	7.61658	7.63952	7.34707	7.42293	7.31500	7.33401	7.38845	7.59499	0.352571308	0.169300183	-0.069165292	7.43833
LAMAS	242677_at	neurophilin 1	6.10383	6.02687	6.04454	6.15945	6.06878	6.03357	6.18616	6.38556	6.28462	6.33153	6.38423	6.57392	0.882480661	0.053213753	0.171627375	6.30542
LAMAS	233626_at	neurophilin 1	6.40373	6.25984	6.09866	6.17805	6.18985	6.27909	6.02998	6.37767	6.38423	6.37767	6.37767	6.37767	0.882480661	0.053213753	-0.024670359	6.21540
LAMAS	210615_at	neurophilin 1	5.18617	5.12043	5.02089	4.90742	5.01614	4.98905	4.84070	5.12134	5.02222	5.09656	4.97246	4.96435	0.745759795	0.277159795	0.029752863	5.05473
LAMAS	239519_at	neurophilin 1	4.09489	3.85985	3.73222	3.98468	3.74331	4.25691	3.82473	3.88527	3.89550	3.72640	3.93137	3.84175	0.173758684	0.094200522	-0.124475021	3.87991

1561365_at	NRP1	neurotrophin 1	3.92142	3.65366	3.78622	3.96978	3.87017	3.61510	3.88960	3.81532	3.90320	3.83327	3.78965	3.65539	0.70128816	0.265530386	0.027846173	3.81665
240738_at	NRP1	neurotrophin 1	3.32748	3.26324	3.22097	3.15346	3.17097	3.42779	3.24316	3.11948	3.31246	3.19157	3.26502	3.43954	0.087207539	0.001053636	0.001053636	3.26118
225586_at	NRP2	neurotrophin 2	9.25688	9.14741	9.34945	9.08523	9.05901	8.64039	9.77924	9.81475	9.85799	9.70402	9.68607	9.79309	1.20E-06	0.64944887	0.64944887	9.44780
214632_at	NRP2	neurotrophin 2	8.33573	8.25105	8.23461	8.23375	8.11881	8.69537	9.24404	9.20604	9.34377	9.30281	9.23777	9.32177	2.19E-08	0.964472118	0.964472118	8.79379
229225_at	NRP2	neurotrophin 2	8.17150	8.18159	8.26421	8.20547	8.38070	8.67991	8.66368	8.93988	8.94095	8.73323	8.69457	8.73323	3.48E-05	0.539468439	0.539468439	8.58363
219387_s_at	NRP2	neurotrophin 2	8.0272	8.10842	8.04883	8.02865	8.27271	7.98764	8.24557	8.24752	8.41110	7.98526	7.96799	8.34735	0.076702121	0.049880094	0.170035442	8.08578
228252_at	NRP2	neurotrophin 2	2.82625	2.89415	2.83504	2.83521	2.90183	2.80716	2.80716	2.95441	2.83914	2.72389	2.76464	2.94222	0.389842122	0.173330566	-0.113728934	7.98004
210841_s_at	NRP2	neurotrophin 2	7.65214	7.58223	7.46820	7.58980	7.45198	7.90569	8.00046	8.05248	8.21173	7.97490	7.95460	8.04763	4.32E-05	0.483626493	0.483626493	7.83349
211844_s_at	NRP2	neurotrophin 2	7.26437	6.95679	6.95679	7.00380	7.07941	7.31116	7.92723	7.84493	8.10971	7.97411	7.83567	8.04763	2.23E-09	0.866140559	0.866140559	7.52846
223510_at	NRP2	neurotrophin 2	7.27397	7.25788	7.32057	7.15077	6.89121	7.19746	7.27105	7.32126	7.32107	7.13930	7.20006	7.30250	0.172192479	0.172192479	0.061701817	7.21346
6.47306_at	NRP2	neurotrophin 2	6.47306	6.53034	6.45956	6.34132	6.54387	6.71947	6.57742	6.70043	6.66483	6.53937	6.69718	6.85731	0.026002379	0.022754548	0.167318606	6.98983
5.45556_at	NRP2	neurotrophin 2	5.45556	5.86058	5.82593	5.84398	6.00012	5.89876	6.14796	6.03944	6.36989	6.02514	6.05581	6.21002	0.001973203	0.025387427	0.325387427	5.97652
230410_at	NRP2	neurotrophin 2	5.62818	6.23331	6.27749	5.75794	6.13940	5.96754	5.89627	5.91700	5.76891	5.66987	5.59755	5.65656	0.001513037	0.002272581	-0.373482211	5.84722
228102_at	NRP2	neurotrophin 2	5.80119	5.95336	5.83730	5.62397	5.74437	5.66679	5.70811	5.42097	5.76555	5.76278	5.67855	5.76278	0.164290027	-0.070383319	0.164290027	5.76085
223701_at	NRP2	neurotrophin 2	5.75341	5.64068	5.49035	5.62529	5.49035	5.79160	5.76429	5.85998	5.86295	5.75945	5.67932	5.67932	0.025501225	0.025501225	0.14888214	5.72931
210842_at	NRP2	neurotrophin 2	5.81343	5.22990	5.57795	5.39745	5.44880	5.25773	6.07142	5.79333	5.63722	5.77559	5.89375	6.29125	0.001629502	0.001629502	0.447851047	5.67717
228103_s_at	NRP2	neurotrophin 2	4.49181	4.94741	5.06594	5.03811	5.04163	4.71195	4.96959	5.18647	5.05792	5.08358	5.02884	4.84594	0.105231196	0.06173586	0.161666025	4.96302
220183_s_at	NUDT6	nucleoside diphosphate linked moiety X-type motif 6	6.98828	6.99186	6.79995	6.80451	6.97538	6.50239	6.52057	6.73982	6.61243	6.32483	6.23717	6.31313	0.000276215	0.000598247	-0.392703479	6.59421
214637_at	OSM	osteostatin M	6.87284	6.66416	6.50839	6.48914	6.83123	6.88107	6.63397	6.69882	6.40007	6.43571	6.43377	6.31763	0.011980073	0.011671341	-0.246142602	6.51903
230170_at	OSM	osteostatin M	6.44207	6.62903	6.64934	6.40450	6.37661	6.50485	6.29723	6.28524	6.24285	6.28760	6.10558	6.33613	0.001210657	0.001900552	-0.24366229	6.37924
205729_at	OSMR	osteostatin M receptor	6.62923	6.22046	6.65221	6.44596	6.16946	6.40710	7.32720	7.39041	7.72413	7.39842	7.10785	7.30088	2.39E-07	0.963642126	0.963642126	6.89149
1554005_at	OSMR	osteostatin M receptor	6.10088	6.27883	6.27677	6.21009	6.18078	6.33053	6.58746	6.78030	6.74886	6.61672	6.61672	6.61672	2.59E-06	0.460973352	0.460973352	6.46089
205463_s_at	PDGFA	platelet-derived growth factor alpha polypeptide	8.79734	8.82613	8.65851	9.00986	8.89566	8.89326	10.39970	10.52075	10.21477	10.35878	10.44924	10.44924	6.43E-12	1.563768795	1.563768795	9.62868
229830_at	PDGFA	platelet-derived growth factor alpha polypeptide	8.16583	8.24705	8.20328	8.59093	8.85791	9.01850	9.72618	9.86555	9.78876	10.04570	9.90120	9.90120	3.40E-08	1.399545198	1.399545198	9.16869
216867_s_at	PDGFA	platelet-derived growth factor alpha polypeptide	6.89217	7.02775	6.86202	6.63070	6.83277	6.87257	6.19523	6.23834	6.43212	6.26181	7.94655	8.36339	9.31E-11	1.352411196	1.352411196	7.56295
204200_s_at	PDGFB	platelet-derived growth factor beta polypeptide	9.02353	9.13582	9.12029	8.93849	8.92173	8.61193	10.02410	10.05908	10.11816	10.13844	10.12580	10.08474	5.30E-11	1.132955431	1.132955431	9.92541
216051_x_at	PDGFB	platelet-derived growth factor beta polypeptide	8.83466	8.96949	9.08723	8.82296	8.89295	8.49777	9.89440	9.91183	10.08674	9.96252	10.02280	10.04227	2.34E-09	1.169214929	1.169214929	9.39879
216055_at	PDGFB	platelet-derived growth factor beta polypeptide	6.30549	6.07852	6.28422	5.94110	6.19766	5.95890	6.20772	6.26524	6.36559	5.92613	6.10202	6.44096	0.425870303	0.185061537	0.075294964	6.16530
217112_at	PDGFB	platelet-derived growth factor beta polypeptide	5.04247	5.59888	5.01684	5.13001	5.03015	5.34893	5.39152	5.34899	5.39526	5.34893	5.44410	5.70893	0.021515903	0.018542877	0.244923729	5.31713
218718_at	PDGFC	platelet-derived growth factor C	9.97953	10.04440	10.08531	9.84059	9.77784	9.82255	6.89856	6.77438	6.71297	6.38441	6.85528	6.67030	2.15E-13	-3.340718394	-3.340718394	8.25468
222719_s_at	PDGFC	platelet-derived growth factor C	7.65927	7.79312	7.90339	7.80085	7.64980	5.39561	5.40617	5.58837	5.19013	5.33532	5.85298	1.00E-14	1.48E-12	-2.321990864	-2.321990864	6.19009
1563467_at	PDGFC	platelet-derived growth factor C	3.52388	3.57513	3.54099	3.61867	3.58481	3.82524	3.70124	4.00337	3.75202	3.48565	3.82112	3.72053	0.023434247	0.019152997	0.176317752	3.65916
218304_s_at	PDGFD	platelet-derived growth factor D	5.99593	5.61504	5.65994	5.73846	5.94355	5.33712	7.3062	7.24759	7.39678	6.98615	6.93808	7.44914	2.01E-10	5.39E-09	1.51040148	6.47119
222860_s_at	PDGFD	platelet-derived growth factor D	6.22062	6.30338	6.00017	5.92278	5.94738	6.05163	6.56550	6.67911	6.54285	6.29107	6.37854	6.51909	0.000180156	0.421335911	0.421335911	6.28333
223995_at	PDGFD	platelet-derived growth factor D	5.90081	6.03195	6.03195	5.97419	6.01911	6.03823	6.01898	6.07578	6.11181	6.22307	6.35949	6.06604	0.173142529	0.083544689	0.103119459	6.09430
239299_at	PDGFD	platelet-derived growth factor D	4.97030	4.47263	4.76284	4.33362	4.43662	4.62544	4.53938	4.48353	4.42380	4.49066	4.67368	4.67368	0.23453195	-0.051152668	-0.051152668	4.57467
215305_at	PDGFRA	platelet-derived growth factor receptor, alpha polypeptide	6.80612	6.94231	6.84488	6.89557	6.87959	7.08619	6.86726	6.86013	6.83929	6.77645	6.89220	6.94446	0.607746613	0.239695087	-0.030810243	6.89537
1554828_at	PDGFRA	platelet-derived growth factor receptor, alpha polypeptide	4.51188	4.72729	4.34463	4.59530	4.47770	4.69782	4.52574	4.67395	4.60054	4.45187	4.72407	4.92478	0.280958073	0.135877426	0.092054931	4.60413
211533_at	PDGFRA	platelet-derived growth factor receptor, alpha polypeptide	4.06890	3.88288	3.97124	3.77736	4.01926	4.05734	4.22157	3.98223	4.11634	4.05883	4.10903	4.24134	0.029724497	0.023688444	0.155392784	4.04353
203131_at	PDGFRA	platelet-derived growth factor receptor, alpha polypeptide	3.90843	4.00950	3.85291	3.66883	4.11122	3.78243	4.04991	4.17789	4.00385	4.04329	3.97541	4.39917	0.017946724	0.016084236	0.219397945	3.99855
202273_at	PDGFRB	platelet-derived growth factor receptor, beta polypeptide	6.09776	6.27678	6.27084	5.98991	5.99626	6.28416	5.97303	5.99182	5.8919	5.77877	5.81421	5.75439	0.000596685	0.001085154	-0.331385243	5.98239
208982_at	PECAM1	platelet/endothelial cell adhesion molecule (CD31 antigen)	12.56532	12.38108	12.61121	12.35617	12.29965	12.16368	13.31948	13.32759	13.39685	13.01760	13.14397	13.28017	2.19E-07	0.844926411	0.844926411	12.80031
208981_at	PECAM1	platelet/endothelial cell adhesion molecule (CD31 antigen)	11.73783	11.65648	11.84363	11.67488	11.65313	11.70450	12.61191	12.60830	12.82000	12.44631	12.42207	12.68380	1.00E-08	0.866992658	0.866992658	12.15524
208983_s_at	PECAM1	platelet/endothelial cell adhesion molecule (CD31 antigen)	11.31951	11.33271	11.32777	11.07892	11.02376	11.33078	12.24536	12.33921	12.36600	11.83597	11.88366	12.18148	5.24E-07	0.906371486	0.906371486	11.68876

155921_at	PECAM1	platelet/endothelial cell adhesion molecule (CD31 antigen)	7.51970	7.52561	7.67119	7.50435	7.66141	7.43623	7.68952	7.78943	7.73982	7.64561	7.83822	7.80908	0.003269306	0.004184382	0.196865301	7.65238	
206390_x_at	PF4	platelet factor 4 (chemokine (C-X-C motif) ligand 4)	7.26058	7.31218	7.19452	6.93756	7.09687	7.07560	7.11948	7.17438	7.12688	7.17235	7.14967	7.31291	0.642226067	0.249502056	0.031024783	7.16043	
209652_s_at	PGF	placental growth factor, vascular endothelial growth factor-related protein	8.24225	8.09911	8.06221	8.26058	8.35659	8.35748	8.19661	8.76693	8.93459	8.79287	8.97550	9.76991	0.87550	1.06E-14	1.51E-12	1.566528192	9.00987
215179_x_at	PGF	placental growth factor, vascular endothelial growth factor-related protein	8.06578	8.11721	8.05833	8.07568	8.06093	8.14616	8.09623	8.09766	8.24991	8.16050	8.15872	8.25127	0.123766597	0.072457023	0.081701607	8.12820	
210817_at	PHEX	phosphate-regulating endopeptidase homolog, X-linked (hypophosphatemia, vitamin D resistant rickets)	6.21047	6.48467	6.40717	6.25166	6.41230	6.16178	6.28131	6.20841	6.28630	6.33233	6.19559	6.41950	0.595311079	0.236476011	-0.035766685	6.30346	
155866_at	PHEX	phosphate-regulating endopeptidase homolog, X-linked (hypophosphatemia, vitamin D resistant rickets)	5.89475	5.74570	5.76077	5.89301	5.94578	5.91247	6.18960	5.88529	6.00796	6.21960	5.97902	6.04030	0.008670255	0.090303315	0.194684285	5.95619	
201860_s_at	PLAT	plasminogen activator, tissue	7.02246	7.57305	7.60313	7.12076	7.12628	7.52494	7.64385	7.52142	7.73897	8.27621	8.42588	7.90716	0.001678574	0.024266895	0.527147048	7.65534	
205479_s_at	PLXDC1	plasminogen activator, urokinase	3.31702	9.28314	9.38622	9.67239	9.80477	9.77851	8.99417	8.88530	8.98120	9.91387	9.95115	10.00866	0.80E-05	0.00022181	0.041636827	9.11578	
211668_s_at	PLAU	plasminogen activator, urokinase	8.45244	7.94303	8.15871	8.62599	8.59291	9.14387	8.87836	8.80812	9.07691	9.04334	9.05641	0.002929814	0.003833009	0.493314265	8.73115		
155753_s_at	PLAU	plasminogen activator, urokinase	3.93555	4.10905	4.04945	4.13507	3.56682	3.87666	4.06968	3.88447	3.91232	3.78997	3.71471	3.89566	0.313578956	0.147451177	-0.064089899	3.91835	
210845_s_at	PLAUR	plasminogen activator, urokinase receptor	9.16706	8.98177	9.07122	9.42609	9.28252	9.37393	11.33910	11.04562	11.08338	11.57928	11.63060	11.42292	4.48E-13	3.33E-11	2.125381363	10.28746	
211924_s_at	PLAUR	plasminogen activator, urokinase receptor	8.39963	8.19598	8.26886	8.70937	8.66807	8.46954	10.48452	9.99432	10.51437	10.86339	10.69337	11.61E-11	5.01E-10	2.115444209	9.50830		
214868_at	PLAUR	plasminogen activator, urokinase receptor	7.07871	7.03754	6.92193	7.61586	7.60909	7.81759	8.45742	8.05122	8.14831	8.85558	8.90560	8.52237	3.84E-06	1.99E-05	1.143280204	7.91844	
240033_at	PLG	plasminogen	6.05297	6.09971	6.18879	6.05297	6.06666	6.05913	5.98033	5.99032	5.93995	6.03345	6.19328	6.31639	0.7581817377	0.280314621	-0.020253788	6.07656	
209877_at	PLG	plasminogen	5.09165	6.19609	5.71147	5.93273	5.98368	5.82960	5.68745	6.01186	5.84123	5.66194	6.00007	5.47382	0.114069705	0.088077925	-0.154809286	5.65680	
209978_s_at	PLG	plasminogen	5.37582	5.51607	5.80131	5.65373	5.64621	5.88439	5.72560	5.64293	5.67655	5.67655	5.67404	0.848157419	0.203443502	0.047551697	5.63666		
230931_at	PLG	plasminogen	4.90589	5.20571	4.88619	4.87035	4.95983	5.24529	4.98490	5.07966	4.86494	4.88003	4.98227	4.97893	0.448588913	0.192302722	-0.056357007	4.99167	
1560136_at	PLXDC1	plexin domain containing 1	7.23018	7.46294	7.45148	7.40700	7.33005	7.38881	7.47923	7.63809	7.47270	7.50509	7.44172	7.55434	0.027427405	0.022403933	0.13645338	7.48684	
240963_x_at	PLXDC1	plexin domain containing 1	6.76490	7.05396	6.80948	6.69195	6.76747	6.81549	6.90945	6.77572	6.78241	6.77448	6.66304	6.84963	0.702332702	0.265823216	-0.025084931	6.60466	
214081_s_at	PLXDC1	plexin domain containing 1	5.03931	4.96201	4.44238	4.82482	4.73986	4.86081	5.00338	4.96408	5.35983	5.25601	5.17672	5.30181	0.001429393	0.362276042	0.002171683	4.99585	
219700_at	PLXDC1	plexin domain containing 1	4.93757	4.92448	4.92316	4.91940	5.11977	4.91341	4.79745	4.94875	4.92743	4.84441	4.91643	0.142031171	0.080703373	-0.103689206	4.82649		
205445_at	PRL	prolactin	5.90668	5.14539	5.06753	5.98333	3.92554	5.29388	5.31305	5.53131	5.28983	5.50659	5.98622	5.50191	0.004007141	0.225775719	5.31011		
226293_at	PROK2	prokinectin 2	3.44465	3.96814	3.42952	3.14448	3.40359	3.71549	3.41450	3.34328	3.40588	3.46738	3.40584	3.45260	0.642076151	0.249459548	-0.038883357	3.33287	
204304_s_at	PROM1	prominin 1	3.51411	3.57605	3.76178	3.59727	3.55097	3.52461	3.55177	3.63965	3.59248	3.58769	3.59665	3.65904	0.748019846	0.277748943	0.017614971	3.59627	
225363_at	PTEN	phosphatase and tensin homolog (mutated in multiple advanced cancers 1)	10.23721	10.43892	10.33660	10.33109	10.39483	10.39810	9.92134	9.89795	9.89133	9.86088	9.89337	9.95445	1.89E-07	1.68E-06	-0.438571786	10.36884	
204053_x_at	PTEN	phosphatase and tensin homolog (mutated in multiple advanced cancers 1)	9.37715	9.36524	9.29059	9.23454	9.12172	9.43689	8.82838	8.83195	8.87078	8.59189	8.64586	8.76088	3.20E-07	2.60E-06	-0.545380763	9.02966	
211711_s_at	PTEN	phosphatase and tensin homolog (mutated in multiple advanced cancers 1)	7.72164	7.51449	7.46245	7.70631	7.61465	7.56614	6.92298	7.12336	7.25967	7.26165	7.32122	7.19921	2.29E-05	8.24E-05	-0.445664034	7.38866	
228006_at	PTEN	phosphatase and tensin homolog (mutated in multiple advanced cancers 1)	7.38582	7.19691	7.25767	7.14471	7.17593	7.01006	7.22243	7.21381	7.43372	7.23646	7.28291	7.27058	0.223908114	0.114359461	0.081432977	7.25590	
227469_at	PTEN	phosphatase and tensin homolog (mutated in multiple advanced cancers 1)	7.22330	7.27438	7.32411	7.18992	7.18929	7.18975	7.17401	7.14631	6.92171	7.14427	7.21335	6.83051	0.031862054	0.035204466	-0.160531827	7.15196	
204054_at	PTEN	phosphatase and tensin homolog (mutated in multiple advanced cancers 1)	6.75753	5.86297	6.49739	6.74271	6.36534	6.83987	6.14414	6.18468	6.29653	6.42753	6.36432	6.65027	0.00801769	0.008491053	-0.281562796	6.85536	
222176_at	PTEN	phosphatase and tensin homolog (mutated in multiple advanced cancers 1)	4.59384	4.35354	4.44516	4.46546	4.50699	4.42551	4.39675	4.56164	4.41342	4.26510	4.32490	4.32884	0.186613907	0.099505701	-0.083309052	4.42343	
233254_x_at	PTEN	phosphatase and tensin homolog (mutated in multiple advanced cancers 1)	4.35454	4.37731	4.14157	4.41339	4.33713	4.31979	4.07193	4.13062	4.18736	4.21003	4.26799	4.19675	0.015068861	0.014000014	-0.179842195	4.26737	
240864_at	PTEN	phosphatase and tensin homolog (mutated in multiple advanced cancers 1)	3.92959	3.97610	4.06740	3.97983	3.85051	4.04829	3.82866	3.89289	3.76851	3.62201	3.67838	3.82637	0.002970638	0.033875942	-0.207481835	3.87155	
242622_x_at	PTEN	phosphatase and tensin homolog (mutated in multiple advanced cancers 1)	3.73626	4.10210	3.74783	3.69056	3.90497	3.86465	3.47616	3.53750	3.62076	3.44132	3.40165	3.58661	0.000231202	0.000511914	-0.330063447	3.67603	
233314_at	PTEN	phosphatase and tensin homolog (mutated in multiple advanced cancers 1)	3.44185	3.14647	3.36418	3.19390	3.36573	3.51283	3.69199	3.29650	3.37421	3.39704	3.51027	3.51283	0.120728115	0.071074493	0.124664038	3.39582	
205127_at	PTGS1	prostaglandin-endoperoxide synthase 1 (prostaglandin G/H synthase and cyclooxygenase)	6.53671	6.99051	6.68293	6.67571	6.73686	6.89779	7.03475	6.71804	6.74921	6.87707	6.93809	6.98322	0.119663898	0.070698597	0.125978869	6.81841	
205128_x_at	PTGS1	prostaglandin-endoperoxide synthase 1 (prostaglandin G/H synthase and cyclooxygenase)	6.18559	6.46354	6.47206	6.35887	6.12318	6.47216	6.85269	6.81063	6.45642	6.67332	6.86070	6.94541	0.000426076	0.000683265	-0.387298516	6.39355	

215813_s_at	PTGS1	prostaglandin-endoperoxide synthase 1 (prostaglandin G/H synthase and cyclooxygenase)	5.68689	5.25331	5.52405	5.65606	5.63725	5.51690	6.21578	6.03775	6.34013	6.57105	6.30553	6.53452	1.75E-07	1.57E-06	0.788381727	5.93993
238669_at	PTGS1	prostaglandin-endoperoxide synthase 1 (prostaglandin G/H synthase and cyclooxygenase)	5.64742	6.00443	5.73183	5.9873	5.84034	5.97419	5.56391	5.73219	6.56550	5.74874	5.56049	5.69718	0.075642662	0.049336975	-0.139987328	5.72950
240171_at	PTGS1	prostaglandin-endoperoxide synthase 1 (prostaglandin G/H synthase and cyclooxygenase)	5.69031	5.85909	5.76016	5.78805	5.86928	5.72377	5.53102	5.66138	5.64939	5.64518	5.64369	5.33277	0.002889942	0.003799006	-0.221203821	5.67117
204748_at	PTGS2	prostaglandin-endoperoxide synthase 2 (prostaglandin G/H synthase and cyclooxygenase)	5.08996	4.96688	5.13637	5.25227	4.99409	5.11614	6.23860	5.91523	5.70327	6.07932	5.93031	6.13465	3.81E-09	6.35E-08	0.902311286	5.54877
155497_s_at	PTGS2	prostaglandin-endoperoxide synthase 2 (prostaglandin G/H synthase and cyclooxygenase)	3.63165	3.78429	3.89932	3.81622	3.71846	3.87785	4.15475	4.06930	4.22382	4.19783	4.24374	4.46503	7.73E-06	3.47E-05	0.437810776	4.00684
209466_x_at	PTN	pleiotrophin (heparin binding growth factor 8, neurtie growth-promoting factor 1)	6.79683	6.89674	6.87375	6.75443	6.96358	6.80950	6.94334	6.93141	6.90679	6.92200	6.93992	6.99715	0.109863414	0.066256669	0.065798573	6.90387
208408_at	PTN	pleiotrophin (heparin binding growth factor 8, neurtie growth-promoting factor 1)	5.73592	5.70330	5.63538	5.25372	5.61443	5.75606	5.72207	5.92584	5.66315	5.63978	5.66106	5.63341	0.522897894	0.215207413	-0.050566332	5.64773
211737_x_at	PTN	pleiotrophin (heparin binding growth factor 8, neurtie growth-promoting factor 1)	5.45863	5.80284	5.57502	5.49861	5.68624	5.61969	5.66393	5.59058	5.57852	5.52738	5.55254	5.50931	0.567943302	0.228497742	-0.036127815	5.58844
1561889_at	PTN	pleiotrophin (heparin binding growth factor 8, neurtie growth-promoting factor 1)	4.96375	4.71916	4.82613	4.81257	4.91587	4.93778	5.03083	5.11827	5.05979	5.04302	5.01123	5.25245	0.0071491	0.001252443	0.240057093	4.96590
209485_x_at	PTN	pleiotrophin (heparin binding growth factor 8, neurtie growth-promoting factor 1)	3.36725	3.32751	3.45977	3.51177	3.51115	3.57831	3.51686	3.46213	3.44232	3.39118	3.34326	3.35367	0.468416564	0.198497246	-0.041055046	3.47210
204916_at	RAMP1	receptor (calcitonin) activity modifying protein 1	6.89318	7.45712	7.03738	6.71296	7.13177	6.95579	6.78959	6.78778	6.73209	6.44200	6.72841	6.46608	0.000641275	0.001147811	-0.450815748	6.82562
205779_at	RAMP2	receptor (calcitonin) activity modifying protein 2	7.98390	8.16755	8.19382	7.54306	7.60668	7.19959	7.89866	7.95457	7.87900	7.40957	7.48146	7.86658	0.844306054	0.301746189	-0.030560366	7.76895
205326_at	RAMP3	receptor (calcitonin) activity modifying protein 3	6.96530	6.91139	6.75288	6.61462	6.87160	6.81990	6.62893	6.98570	6.80542	6.73477	6.92490	7.96241	0.572563819	0.229885505	0.04424078	6.83490
212099_at	RHOB	ras homolog gene family, member B	11.81932	11.86410	11.97202	11.75689	11.72066	11.71361	11.83913	11.96219	11.97819	11.07728	11.59018	11.59018	0.042100455	0.03125764	-0.317616994	11.65301
1553982_s_at	RHOB	ras homolog gene family, member B	9.27848	9.25445	9.20508	9.19031	9.36974	9.19719	9.06566	9.30719	8.98465	9.58723	8.98465	9.01715173	-0.390245446	0.194898999	0.1715173	9.15757
228417_at	RHOB	ras homolog gene family, member B	6.10047	6.18362	5.82795	5.93393	6.11402	6.03163	5.87509	5.87989	6.69002	5.77409	5.81647	5.81647	0.02291834	0.002945172	-0.293149224	5.88869
1553985_x_at	RHOB	ras homolog gene family, member B	3.96112	3.8532	4.06119	3.91423	3.79997	3.71486	3.61686	3.64255	3.52999	3.80066	3.52999	3.52999	0.17694198	0.095448446	-0.104325542	3.81562
1553983_at	RHOB	ras homolog gene family, member B	3.14981	3.05970	3.16847	3.17418	2.94861	3.00560	3.15275	3.14197	2.96670	3.01323	3.08186	3.08186	0.83140983	0.298666104	-0.012525481	3.07763
226028_at	ROBO4	roundabout homolog 4, magic roundabout (Drosophila)	11.69683	11.51541	11.70986	11.67044	11.58978	11.81009	11.28698	11.81056	11.99446	11.89744	11.80660	11.94357	0.000897674	0.001229257	0.297390001	11.72676
220758_s_at	ROBO4	roundabout homolog 4, magic roundabout (Drosophila)	9.07361	8.71650	9.23940	9.35520	9.18261	8.75787	9.25443	9.43057	9.51413	9.52594	9.38449	9.51131	0.001388921	0.002122044	0.382446441	9.24542
204855_at	SERPINB5	serpin peptidase inhibitor, clade B (ovalbumin), member 5	4.95149	5.15403	4.95558	4.69616	4.70284	4.81732	4.90961	4.93204	5.00996	4.89448	5.12853	4.89964	0.297004062	0.14162409	0.082639281	4.92089
1555551_at	SERPINB5	serpin peptidase inhibitor, clade B (ovalbumin), member 5	3.46892	3.45437	3.46301	3.48923	3.45384	3.50283	3.38066	3.37215	3.34662	3.46539	3.41569	3.39255	0.216243808	0.11402551	-0.067981227	3.43277
1554491_s_at	SERPINC1	serpin peptidase inhibitor, clade C (antithrombin), member 1	5.01479	4.94467	4.96885	4.84768	4.95086	4.62483	5.10343	5.29216	5.34755	5.47409	5.31519	5.2090	0.000101119	0.0002866	0.3831610319	5.17708
210049_at	SERPINC1	serpin peptidase inhibitor, clade C (antithrombin), member 1	5.22653	5.02239	4.98864	5.21639	5.09718	4.74725	4.96659	5.46676	5.07883	5.11087	5.31105	5.4732	0.212656161	0.109891295	0.118837943	5.19315
202283_at	SERPINF1	serpin peptidase inhibitor, clade F (alpha 2 antiplasmin, pigment epithelium derived factor), member 1	5.54302	5.50392	5.27769	5.44104	5.42159	5.67343	5.73175	5.54935	5.65267	5.61603	5.7465	5.63893	0.031614552	0.025056979	0.1504503	5.65200
202037_s_at	SFRP1	secreted frizzled-related protein 1	8.99975	8.82592	8.95771	8.98046	8.91488	8.60943	7.98533	8.09010	8.05350	8.18937	8.05718	8.21547	3.49E-09	5.89E-08	-0.779899537	8.4818
202036_s_at	SFRP1	secreted frizzled-related protein 1	8.34953	8.32300	8.19262	8.06617	8.34977	8.99768	7.34126	7.54257	7.48778	7.66053	7.50520	7.48663	1.09E-07	1.08E-06	-0.92844038	7.96821
202035_s_at	SFRP1	secreted frizzled-related protein 1	6.49059	6.16794	6.41148	6.51488	6.50789	6.46026	5.77724	5.27202	5.70177	5.52356	5.63793	5.50636	3.03E-09	5.66E-08	-0.938193571	5.95559
228413_s_at	SFRP1	secreted frizzled-related protein 1	5.55150	5.81672	5.86894	5.85725	5.86574	5.86486	5.62197	5.50492	4.99847	5.21607	5.39995	5.34098	0.000122305	0.000309349	-0.456105342	5.57478
223121_s_at	SFRP2	secreted frizzled-related protein 2	5.93031	6.35784	5.85475	6.08896	6.05315	5.94929	6.09810	5.96678	6.07861	6.12692	6.01338	5.98901	0.932256883	0.322682029	0.006417343	6.44226
223122_s_at	SFRP2	secreted frizzled-related protein 2	4.88808	4.87699	4.68573	4.72213	4.87796	4.78240	5.11545	5.06158	4.96821	4.91395	4.96821	5.17292	0.00382581	0.004775521	0.214912178	4.91301
204051_s_at	SFRP4	secreted frizzled-related protein 4	5.36891	5.46533	5.33920	5.38599	5.44945	5.49156	5.44546	5.39784	5.53956	5.41796	5.43852	5.45125	0.213745286	0.033507629	0.03745286	5.43166
204052_s_at	SFRP4	secreted frizzled-related protein 4	3.95410	4.00084	4.03355	3.93544	3.99441	3.77202	4.00983	4.07847	3.98126	3.94542	4.00514	3.98573	0.31414253	0.147653309	0.060907997	3.97094
207468_s_at	SFRP5	secreted frizzled-related protein 5	6.36079	6.69949	6.31521	6.41096	6.37920	6.45344	6.29361	6.27603	6.59254	6.08003	6.27234	6.19398	0.003113233	0.004023841	-0.263406033	6.30479
207351_s_at	SH2D2A	SH2 domain protein 2A	6.08116	6.39995	6.20151	6.23727	5.92334	6.18891	6.73912	6.97346	6.64255	6.81753	6.98670	7.00661	2.31E-07	1.98E-06	0.688137274	6.51693

20665_s_at	SPARC	secreted protein, acidic, cysteine-rich (osteonectin)	13.03692	12.99851	13.01960	13.01245	12.88228	12.96595	13.40419	13.54185	13.54824	13.27013	13.25605	13.32648	6.79E-06	3.12E-05	0.40522208-9	13.18855
212687_at	SPARC	secreted protein, acidic, cysteine-rich (osteonectin)	11.36682	11.39003	11.47112	11.35499	11.30398	11.15169	11.73981	11.79954	11.83539	11.55870	11.85891	11.58095	4.93E-05	0.000150813	0.35614567-1	11.51781
219257_s_at	SPHK1	sphingosine kinase 1	9.79561	9.63486	9.72760	9.90914	9.74703	9.83391	10.29073	10.27458	10.38855	10.38140	10.51840	10.44725	1.89E-08	2.45E-07	0.608820834	10.70927
209875_s_at	SPP1	secreted phosphoprotein 1 (osteopontin, bone sialoprotein 1, early T-lymphocyte activation 1)	4.74261	4.88178	4.54576	4.48311	4.75837	4.64282	5.11796	5.04234	5.25076	5.29848	5.02655	4.96435	3.68E-06	1.93E-05	0.474329636	4.87957
1568574_x_at	SPP1	secreted phosphoprotein 1 (osteopontin, bone sialoprotein 1, early T-lymphocyte activation 1)	3.48360	3.67923	3.43094	3.62987	3.84605	3.87620	3.96231	3.92959	3.67067	3.81002	3.95863	4.06970	0.012005544	0.011081322	0.242705358	3.77890
38487_at	STAB1	stabilin 1	10.82269	10.62095	10.80943	10.73902	10.55420	10.75898	9.78279	9.93006	10.12482	9.96357	9.84745	10.02551	3.35E-09	5.29E-08	-0.77050796	15.33229
201150_at	STAB1	stabilin 1	10.20584	10.06035	10.26402	10.07892	10.10447	10.25738	9.30051	9.30463	9.46085	9.28027	9.15064	9.37773	4.97E-10	1.15E-08	-0.83342732	9.72972
1555319_at	STAB1	stabilin 1	7.00358	7.04680	7.28185	6.93643	7.12128	7.02207	7.07348	6.90679	7.01790	7.15908	7.16238	7.14894	3.892519629	0.31370761	0.209127208	7.07353
220114_s_at	STAB2	stabilin 2	6.57333	6.60812	6.44761	6.48914	6.61620	7.10003	6.95978	6.45283	6.43349	6.58553	6.66652	6.78195	0.594855726	0.236330682	-0.05219467	6.61213
237587_at	STAB2	stabilin 2	6.59883	6.61198	6.62586	6.4024	6.98670	6.97528	7.01950	6.97165	6.97052	6.87425	6.85411	6.89451	0.553454538	0.037638881	0.171025222	6.84196
243399_at	STAB2	stabilin 2	6.36995	6.38918	6.39566	6.28199	6.38316	6.50366	6.46688	6.56551	6.28558	6.33211	6.31307	6.33335	6.9854527	0.33017931	-0.062684289	6.38076
206702_at	TEK	TEK (tyrosine kinase, endothelial/venous malformations, multiple cutaneous and mucosal)	9.35296	9.22894	9.42496	9.19407	9.14341	9.15702	9.32230	9.31105	9.35218	9.43085	9.46551	9.41112	0.34305942	0.031800523	0.131942263	9.31620
217111_at	TEK	TEK (tyrosine kinase, endothelial/venous malformations, multiple cutaneous and mucosal)	8.02719	7.90699	7.65809	7.99972	7.95437	7.93457	8.04451	7.90164	8.03513	8.02909	8.01985	7.82825	0.40525246	0.178357566	0.056724187	7.94185
211258_s_at	TGFA	transforming growth factor, alpha	6.70185	6.75114	6.69057	6.74446	6.37700	6.92515	6.61930	6.52979	6.57158	6.70112	6.68351	6.72546	0.371963297	0.167030631	-0.068718995	6.68400
205015_s_at	TGFA	transforming growth factor, alpha	6.30495	6.55119	6.63352	6.17672	6.44746	6.68673	6.15482	6.07521	6.00740	5.99035	6.18319	6.68446	0.00211671	0.000478414	-0.44232419	6.27550
205016_at	TGFA	transforming growth factor, alpha	6.55962	6.08369	6.36115	6.41972	5.92848	6.37665	5.79884	5.96905	5.64888	5.67204	5.65200	5.43966	1.09E-05	4.58E-05	-0.735508405	5.99730
203085_s_at	TGFB1	transforming growth factor, beta 1 (Carnegie-Engelmann disease)	10.90310	10.87609	11.08874	10.87505	10.71202	10.72364	11.17980	11.37431	11.25523	11.12423	11.18647	11.26435	5.08E-05	0.000153965	0.367830528	11.04692
203084_at	TGFB1	transforming growth factor, beta 1 (Carnegie-Engelmann disease)	7.30411	7.18784	7.38262	7.17133	7.29913	6.92528	6.84716	6.80493	6.80885	6.96939	6.88939	6.63115	3.78E-05	0.000122292	-0.395793338	7.02872
228121_at	TGFB2	transforming growth factor, beta 2	7.47425	6.86378	7.06107	6.89700	6.88919	6.81991	5.43806	5.29313	5.64582	5.43960	5.28984	5.61031	5.11E-11	1.68E-09	-1.526409316	6.27850
220406_s_at	TGFB2	transforming growth factor, beta 2	6.45041	6.26726	6.54866	6.35121	6.27856	6.59420	6.07688	6.18871	6.80234	5.90991	6.25461	6.23727	0.001120594	0.001785706	-0.336830553	6.24640
220407_s_at	TGFB2	transforming growth factor, beta 2	6.40377	6.94535	6.56583	6.95288	6.34449	6.36592	5.18833	5.46324	5.53927	5.48324	5.53808	5.46529	9.29E-07	6.25E-06	-0.931699282	5.97274
209908_s_at	TGFB2	transforming growth factor, beta 2	4.57273	4.68178	4.48726	4.24892	4.39821	4.49863	4.05210	4.29476	3.98199	3.79339	3.73589	3.89234	4.74E-05	0.000146287	-0.507561047	4.21226
209909_s_at	TGFB2	transforming growth factor, beta 2	4.54796	4.39730	4.34426	4.83623	4.38640	4.48004	3.49311	3.73785	3.55055	3.53773	3.44783	3.89234	2.33E-07	1.104880895	-0.507561047	4.21226
209747_at	TGFB3	transforming growth factor, beta 3	6.76166	6.79643	6.74024	6.74024	6.77689	6.72214	7.10882	6.93684	6.92230	6.85751	7.01522	7.01522	0.014834232	0.0138314	-0.17673755	6.85090
1555540_at	TGFB3	transforming growth factor, beta 3	4.78373	5.31267	4.66896	4.89104	4.89781	5.15969	5.05977	5.14233	4.86283	5.14318	5.04673	5.10451	0.383787983	0.171424254	0.07624305	5.02177
224789_s_at	TGFB3	A receptor type II-like kinase, 530kDa	7.86323	7.48986	7.58668	7.57148	7.54557	7.26819	7.68653	7.58544	7.84619	7.65163	7.54463	7.69205	0.048945588	0.035638858	0.148077698	7.58937
206943_at	TGFB3	transforming growth factor, beta receptor (activin A receptor type II-like kinase, 530kDa)	4.87937	4.92384	4.78646	4.85261	4.88321	4.83510	5.29455	4.98535	4.90282	4.95479	5.00588	5.04688	0.015597988	0.014382214	0.171585728	4.94589
236581_at	TGFB3	transforming growth factor, beta receptor (activin A receptor type II-like kinase, 530kDa)	4.71713	4.81604	4.76355	4.63353	4.75049	4.86029	4.80405	4.79493	4.55445	4.70749	4.72390	0.21682372	0.01735373	0.041735373	4.72605	
239129_at	TGFB3	transforming growth factor, beta receptor (activin A receptor type II-like kinase, 530kDa)	3.39989	3.41468	3.47619	3.55592	3.39936	3.50443	3.32450	3.24819	3.34503	3.23290	3.16272	3.13730	0.001145891	0.001818216	-0.216488504	3.31802
239605_x_at	TGFB3	transforming growth factor, beta receptor (activin A receptor type II-like kinase, 530kDa)	3.20943	3.21679	3.12793	3.26012	3.21639	3.17419	3.24135	3.22352	3.22163	3.33447	3.24488	3.22371	0.337086298	0.155559777	0.047619283	3.22445
201108_s_at	THBS1	thrombospondin 1	12.83958	12.86881	13.02007	12.85093	12.85198	13.27476	12.48706	12.41129	12.51859	12.12764	12.08731	12.36525	3.73E-06	1.95E-05	-0.617832716	12.64177
201109_s_at	THBS1	thrombospondin 1	12.81451	12.74205	12.98186	12.83926	12.71018	12.99531	12.29978	12.44381	11.97378	11.91661	12.24295	12.42955	5.90E-07	4.30E-06	-0.671152044	12.51162
201110_s_at	THBS1	thrombospondin 1	11.93351	12.09821	12.2454	12.18276	12.1620	12.7805	11.90941	11.91742	12.18970	12.08296	12.01779	11.96426	0.132533528	0.076468443	-0.096620626	12.08690
201107_s_at	THBS1	thrombospondin 1	11.21424	11.25015	11.07919	10.98789	11.09324	11.91491	10.40746	10.32629	10.35411	10.04793	9.96078	10.25075	0.33533528	0.20E-07	-1.032047722	10.74038
239336_at	THBS1	thrombospondin 1	9.74806	9.31636	9.76249	9.10798	9.11731	8.51345	8.23706	9.90012	8.73077	8.15032	8.11707	8.62365	1.40E-06	9.75E-06	-1.169402659	8.70783
235096_at	THBS1	thrombospondin 1	8.74820	8.92561	9.17212	8.33519	8.40912	8.66732	8.99218	8.86986	8.90415	8.21860	8.22271	8.62365	0.647423504	0.25095112	-0.072051712	8.67357
215775_at	THBS1	thrombospondin 1	9.40654	9.11483	9.49955	9.02540	9.01332	8.48911	8.52167	8.40683	8.11890	7.87899	8.05250	8.54E-06	4.11E-05	-0.894557246	6.64418	
203093_at	THBS2	thrombospondin 2	5.63530	5.81014	5.68805	5.71635	5.68222	5.78975	5.77906	5.79480	5.72986	5.74009	5.63039	5.77149	0.334212749	0.154538572	0.049427126	5.74502
204468_s_at	TIE1	tyrosine kinase with immunoglobulin-like and EGF-like domains 1	11.26506	11.15119	11.24829	11.14421	10.91879	10.96054	11.24910	11.27163	11.54170	11.30902	11.25429	11.38410	0.006240766	0.036644586	0.215290736	11.27333
1560857_at	TIE1	tyrosine kinase with immunoglobulin-like and EGF-like domains 1	4.70400	4.53316	4.67609	4.53120	4.44349	4.42403	4.44703	4.40789	4.49545	4.15228	4.29347	4.47275	0.093751441	0.058457629	-0.143517336	4.44990
201686_at	TIMP1	TIMP metalloproteinase inhibitor 1	11.54346	11.41615	11.46548	11.39247	11.09955	13.99659	13.87857	14.06024	13.83113	13.98812	14.05988	14.07208	2.523990623	4.74E-16	2.523990623	12.72028
221914_at	TIMP1	TIMP metalloproteinase inhibitor 1	6.20416	5.85645	6.00315	5.96558	6.02547	6.09858	6.23497	6.26477	6.17520	6.36796	6.38682	6.38682	0.000676629	0.001196607	0.267174085	6.16840

231579_s_at	TIMP2	TIMP metalloproteinase inhibitor 2	12.3926	12.1434	12.21713	12.21266	12.17488	12.33924	12.34785	12.47398	12.29496	12.20939	12.38261	0.008774486	0.009120885	0.16444145	12.2927
224560_at	TIMP2	TIMP metalloproteinase inhibitor 2	11.66370	11.67826	11.60275	11.66288	11.61622	11.63817	11.67561	11.83786	11.74695	11.63535	11.81950	0.181410633	0.097328873	0.1740796	11.74092
203167_at	TIMP2	TIMP metalloproteinase inhibitor 2	9.64229	9.50284	9.78061	9.68641	9.62154	9.52917	9.87561	9.91018	9.91018	9.72720	9.87048	0.001506099	0.002263826	0.2428399	9.74853
1556837_s_at	TIMP2	TIMP metalloproteinase inhibitor 2	5.54046	5.51386	5.46156	5.61175	5.42680	5.21669	5.45767	5.46612	5.19786	5.37066	5.47980	0.284593856	0.137222772	-0.078126567	5.42262
1556839_at	TIMP2	TIMP metalloproteinase inhibitor 2	4.93976	5.13616	4.99175	4.81425	4.96858	5.32432	5.17400	5.27859	4.94455	4.88176	4.80285	0.859229689	3.305279055	-0.01704167	5.00395
201148_s_at	TIMP3	TIMP metalloproteinase inhibitor 3 (Sorby) fundus dystrophy, pseudoinflammatory	7.65338	7.82207	7.52822	7.40767	7.71714	7.57385	7.68641	7.61522	7.52864	7.59901	7.61465	0.563215914	0.22714473	0.046142419	7.64013
231888_at	TIMP3	TIMP metalloproteinase inhibitor 3 (Sorby) fundus dystrophy, pseudoinflammatory	7.11236	7.51520	7.27434	7.06331	7.04431	7.13852	7.29288	7.04522	7.11111	7.19047	7.22385	0.835598239	0.259203961	-0.016361316	7.18316
201149_s_at	TIMP3	TIMP metalloproteinase inhibitor 3 (Sorby) fundus dystrophy, pseudoinflammatory	6.12318	6.21645	6.10568	6.17107	6.43909	6.48303	6.50142	6.35234	6.36122	6.51984	6.50439	0.009662606	0.010089137	0.217750136	6.36529
240135_x_at	TIMP3	TIMP metalloproteinase inhibitor 3 (Sorby) fundus dystrophy, pseudoinflammatory	5.95142	6.28619	6.31333	6.02969	6.03166	6.18717	6.07120	6.25209	5.96234	5.87677	5.94364	0.280377647	0.135664275	-0.086559797	6.08496
201147_s_at	TIMP3	TIMP metalloproteinase inhibitor 3 (Sorby) fundus dystrophy, pseudoinflammatory	5.26557	5.64304	5.67289	5.23429	5.53352	5.40488	5.29818	5.45364	5.01133	5.01740	5.03211	0.003399027	0.304311987	-0.352103592	5.28298
201150_s_at	TIMP3	TIMP metalloproteinase inhibitor 3 (Sorby) fundus dystrophy, pseudoinflammatory	5.21934	5.06134	5.18402	5.01624	5.04221	4.87808	5.27628	5.37663	5.54062	4.96303	5.02943	0.041569903	0.030943747	0.226934584	5.17155
214955_at	TMPRSS6	transmembrane protease, serine 6	7.03056	7.37982	7.08472	7.15368	7.30945	7.25822	7.26570	7.26437	7.14409	7.21542	7.20647	0.45482735	0.194183377	0.05302432	7.22925
234367_x_at	TMPRSS6	transmembrane protease, serine 6	6.89656	7.32328	7.08763	7.12740	7.26866	7.03405	7.02913	7.01999	7.04987	7.03327	7.07766	0.228877026	0.116256198	-0.062957684	7.08197
232941_at	TMPRSS6	transmembrane protease, serine 6	5.41353	5.66113	5.55785	5.68353	5.43497	5.65004	5.33558	5.51348	5.34530	5.32461	5.12420	0.011670706	0.011438183	-0.208459397	5.46261
207113_s_at	TNF	tumor necrosis factor (TNF superfamily, member 2)	6.65893	6.85478	6.90658	6.42609	6.66684	6.71249	6.84216	7.04070	6.62859	6.74310	6.79068	0.221702757	0.113534034	0.103921089	6.75624
202510_s_at	TNFAIP2	tumor necrosis factor, alpha-induced protein 2	8.06490	8.07196	8.18958	7.86209	7.76397	7.73691	8.81138	8.73317	8.22237	8.20460	8.73063	0.68E-05	0.000256805	0.715755015	8.29778
202509_s_at	TNFAIP2	tumor necrosis factor, alpha-induced protein 2	6.92191	7.13359	6.87779	6.89071	6.96304	7.07584	7.25577	7.41975	7.38000	7.02184	7.04522	0.004714547	0.035831107	0.248293398	7.10629
218368_s_at	TNFRSF12A	member 12A	10.48565	10.54721	10.51024	10.76458	10.72933	10.81669	10.03243	9.80492	9.77867	10.26201	10.34888	1.02E-05	4.68E-05	-0.598810259	10.34238
205611_at	TNFSF12	tumor necrosis factor (ligand) superfamily, member 12	7.35425	7.14856	7.36325	7.37858	7.29445	7.09655	7.44015	7.46147	7.53321	7.29225	7.31770	0.051691096	0.036660531	0.13620386	7.34072
221085_at	TNFSF15	tumor necrosis factor (ligand) superfamily, member 15	4.20512	4.14048	4.23132	4.12627	4.24846	4.10445	3.82963	3.81855	3.65960	3.92945	3.69037	3.74563	1.57E-05	-0.397149022	3.97744
220065_at	TNND3	tenomodulin	4.16733	4.14407	4.30400	4.09303	4.20939	4.37656	4.20871	4.17340	4.42987	4.47110	4.38202	0.011019797	0.010398809	0.22225827	4.32886
205742_at	TNND3	tenomodulin	4.03187	4.24203	4.02860	3.99814	4.28091	4.24967	4.20824	4.29598	4.08224	4.20741	4.24623	0.077433924	0.013496873	0.112978173	4.32686
213201_s_at	TNNT1	tropomyosin T1, skeletal, slow	6.41989	6.0628	6.6332	6.59239	6.46410	6.57162	6.58050	6.60912	6.67133	6.69174	6.54663	0.163403347	0.089036999	0.08601598	6.60724
212171_x_at	VEGF	vascular endothelial growth factor	8.08134	8.16675	8.13361	8.33611	8.06071	8.03602	8.09780	7.99897	7.92949	7.74242	7.90237	0.009405685	0.00964215	-0.174692198	7.98202
210513_s_at	VEGF	vascular endothelial growth factor	7.33308	7.26156	6.93928	7.12096	7.21682	7.18066	7.03491	7.12919	7.15979	7.17186	7.23235	0.831772923	0.299754461	-0.14262283	7.16856
211527_x_at	VEGF	vascular endothelial growth factor	6.37311	6.9837	6.36146	6.37583	6.48914	6.68873	6.32685	6.07610	6.34070	6.19598	6.49030	0.72597	0.242063115	0.121282178	6.40421
210512_s_at	VEGF	vascular endothelial growth factor	6.42408	6.14442	6.32155	6.29567	6.27487	6.12222	6.37550	6.11148	6.28043	6.85449	6.77070	0.04200394	0.031198948	0.240256256	6.38393
203683_s_at	VEGFB	vascular endothelial growth factor B	7.30723	7.41980	7.28098	7.10319	7.09286	7.06336	7.08229	7.07883	7.10670	7.11062	7.12793	0.020152316	0.017620819	-0.154892065	7.17225
209946_at	VEGFC	vascular endothelial growth factor C	8.71463	8.40777	8.60053	8.51432	8.49591	8.36880	8.87364	8.79848	8.97724	8.67981	8.83121	0.000210094	0.000475664	0.317263198	8.67563
208570_at	WNT1	wingless-type MMTV integration site family, member 1	5.27960	5.31820	5.30874	5.27920	5.10697	5.26848	5.48668	5.61888	5.29559	5.47222	5.47379	0.00190638	0.002734696	0.233866596	5.37679
229154_at	WNT10A	wingless-type MMTV integration site family, member 10A	6.82548	6.93949	6.68858	6.61462	6.84852	6.75996	6.54506	6.65159	6.44570	6.37340	6.59605	0.004599912	0.00547521	-0.227657043	6.66495
223709_s_at	WNT10A	wingless-type MMTV integration site family, member 10A	6.02098	6.22711	6.08166	6.09621	6.06838	6.15079	6.32004	6.17450	6.05333	6.22440	6.23550	0.066794066	0.044716009	0.116541999	6.16579
206213_at	WNT10B	wingless-type MMTV integration site family, member 10B	7.06312	7.10847	7.09795	7.06456	6.97631	7.10952	7.11230	7.27952	7.14291	7.32261	7.17728	0.016995126	0.015388871	0.141664259	7.14082
205648_at	WNT2	wingless-type MMTV integration site family, member 2	5.76689	5.95822	5.76459	5.89380	5.82384	6.30444	5.91999	6.24481	6.09761	6.13403	5.99431	0.012596357	0.01245382	0.211345991	5.99530
206459_s_at	WNT2B	wingless-type MMTV integration site family, member 2B	6.54671	7.00983	6.48639	6.48002	6.44432	6.54400	6.24004	6.28617	6.38983	6.60353	6.46213	0.046282089	0.033654244	-0.196322568	6.48740
206466_s_at	WNT2B	wingless-type MMTV integration site family, member 2B	5.07546	5.37053	5.24852	4.77578	5.11787	5.15974	5.04872	5.30107	5.01443	5.10074	5.15091	0.689239111	0.305026734	0.016346314	5.13232
205990_s_at	WNT5A	wingless-type MMTV integration site family, member 5A	5.88985	5.57431	5.62466	5.67170	5.70365	5.82720	6.85926	6.91976	6.91468	6.01811	5.98219	2.06E-05	7.58E-05	0.969819533	6.10591
244388_at	WNT5A	wingless-type MMTV integration site family, member 5A	5.42367	5.66394	5.46709	5.59520	5.96340	5.38973	5.25259	5.26554	5.24618	5.36516	5.05753	0.001363637	0.020396874	-0.334592043	5.41655
213425_at	WNT5A	wingless-type MMTV integration site family, member 5A	5.15315	4.94601	4.98722	4.79189	5.06264	4.89571	5.12405	4.90817	4.90681	4.62347	4.66694	0.893804555	0.313848977	0.017400885	4.98149

231227_at	WNT5A	wingless-type MMTV integration site family, member 5A	3 81316	4 08007	3 96602	3 52879	3 71035	4 05160	3 86646	3 88985	3 92963	3 63306	3 76711	3 88498	0 963529777	0 3229620537	0 003851138	3 86026
223537_s_at	WNT5B	wingless-type MMTV integration site family, member 5B	5 39670	5 94277	5 84376	5 62421	5 76624	5 23755	5 12718	5 30978	5 22865	5 22195	5 19077	5 11536	0 000428199	0 0000836445	-0 436090799	5 41716
230299_s_at	WNT5B	wingless-type MMTV integration site family, member 5B	5 36971	5 71612	5 03479	5 16828	5 47962	5 46980	5 29947	5 07409	5 28480	5 40036	5 32921	5 28646	0 33736588	0 156659616	-0 0940271	5 32608
221029_s_at	WNT5B	wingless-type MMTV integration site family, member 5B	4 81429	5 18189	5 01096	5 07528	5 03012	4 83706	5 25049	5 08340	5 01024	5 20385	4 82422	5 12276	0 267946807	0 131045914	0 090909776	5 03706
210248_at	WNT7A	wingless-type MMTV integration site family, member 7A	6 28903	6 10889	6 07916	6 52835	6 34846	6 48958	6 19693	6 13272	6 19430	6 32580	6 46155	5 96472	0 316202814	0 148353664	-0 094409253	6 26021
238105_x_at	WNT7B	wingless-type MMTV integration site family, member 7B	7 55262	7 69589	7 73409	7 52324	7 51177	7 82056	7 50674	7 56233	7 45713	7 46513	7 53993	7 51722	0 046782054	0 033941867	-0 131612448	7 57389
217681_at	WNT7B	wingless-type MMTV integration site family, member 7B	5 63741	5 94259	5 72829	6 09372	5 66886	5 68992	5 81051	5 70704	5 71873	5 71266	5 79639	5 73466	0 539752907	0 220387695	-0 046460715	5 76990

Appendix Table A2. GEM data of *Angptl2* and correlated genes in a variety of neoplasms

GEM data was obtained from the NCBI GEO database (GSE2109) and was obtained using Affymetrix hg-u133+2 GeneChips
Microarray data was processed and assessed for differential regulation as described in Materials and Methods
Correlation analysis was performed using the *Angptl2* probe set 213001. at. NA, no gene name available.

Affy ID	Gene Symbol	Name	Site ID	Urinary Bladder GSM102434	Urinary Bladder GSM102437	Urinary Bladder GSM117677
			Histology	Urothelial (transitional cell) carcinoma	Urothelial (transitional cell) carcinoma	Urothelial (transitional cell) carcinoma
213001_at	ANGPTL2	angiotensin-like 2		7 942501999	7 294879865	9 082673781
213004_at	ANGPTL2	angiotensin-like 2		5 720051954	5 420645493	7 305206898
201069_at	MMP2	matrix metalloproteinase 2 (gelatinase A, 72kDa gelatinase, 72kDa type IV collagenase)		9 863869189	8 163207603	11 39603171
219514_at	ANGPTL2	angiotensin-like 2		6 267568297	5 226260281	5 898895797
213869_x_at	THY1	Thy 1 cell surface antigen		7 934538076	7 273244874	8 907484531
226311_at	NA			7 691116458	7 385699452	8 0728929701
202766_s_at	FBN1	fibrillin 1		8 814746954	7 740501841	11 49666524
212488_at	COL5A1	collagen, type V, alpha 1		9 403481811	9 237618747	10 3780021
208851_s_at	THY1	Thy 1 cell surface antigen		8 312461886	7 630604996	9 280948299
203325_s_at	COL5A1	collagen, type V, alpha 1		8 203406928	8 123990581	8 791116394
201438_at	COL6A3	collagen, type VI, alpha 3		10 21816923	9 858807398	12 05231253
202765_s_at	FBN1	fibrillin 1		6 897419112	6 062630529	9 399221111
208850_s_at	THY1	Thy 1 cell surface antigen		7 571486582	6 875888168	8 451429182
212489_at	COL5A1	collagen, type V, alpha 1		7 437994742	7 303441352	8 03372854
204163_at	EMILIN1	elastin microfibril interfacer 1		6 52121397	6 235585216	7 976556358
221729_at	COL5A2	collagen, type V, alpha 2		9 418312041	9 035647147	9 336979014
201389_at	ITGA5	integrin, alpha 5 (fibronectin receptor, alpha polypeptide)		7 873927406	9 53031221	8 729355843
221730_at	COL5A2	collagen, type V, alpha 2		8 946507875	8 723103587	9 233713302
218468_s_at	GREM1	gremlin 1, cysteine knot superfamily, homolog (Xenopus laevis)		8 08027337	6 935393449	6 955376802
1555778_a_at	POSTN	perostin, osteoblast specific factor		9 42452762	9 351823985	8 504301088
202273_at	PDGFRB	platelet-derived growth factor receptor, beta polypeptide		7 315118224	7 38602054	9 709588431
218469_at	GREM1	gremlin 1, cysteine knot superfamily, homolog (Xenopus laevis)		8 855666479	7 237959298	8 100188692
201852_x_at	COL3A1	collagen, type III, alpha 1 (Ehlers-Danlos syndrome type IV, autosomal dominant)		12 46260394	11 93138454	13 04256895
202465_at	PCOLCE	procollagen C-endopeptidase enhancer		8 189522401	7 786429917	10 37250975
209955_s_at	FAP	fibroblast activation protein, alpha		7 776115592	6 772263747	7 955367609
213290_at	COL6A2	collagen, type VI, alpha 2		6 059742633	6 171342682	8 007506742
225442_at	DDR2	discoidin domain receptor family, member 2		7 429429524	6 276738325	9 491417373
210511_s_at	INHBA	inhibin, beta A (activin A, activin AB alpha polypeptide)		6 934446766	10 04570581	5 787998092
209651_at	TGFB11	transforming growth factor beta 1 induced transcript 1		7 592407098	7 620538508	8 853985661
226834_at	NA			5 471190929	5 802987444	8 30231172
201108_s_at	THBS1	thrombospondin 1		8 050308241	7 977855835	8 196613237
202998_s_at	LOXL2	Lysyl oxidase-like 2		7 61687385	8 172628346	7 194461256
219025_at	CD248	CD248 molecule, endostatin		7 480611719	7 336916127	9 667333889
235318_at	FBN1	fibrillin 1		4 501570515	4 265247426	7 43184694
219179_at	DACT1	dapper, antagonist of beta-catenin, homolog 1 (Xenopus laevis)		6 592220442	5 011060836	7 397673186
202403_s_at	COL1A2	collagen, type I, alpha 2		12 51915777	11 88445849	13 27480859
61734_at	RCN3	reticulocalbin 3, EF-hand calcium binding domain		6 667509692	6 733752358	7 782341026
232458_at	COL3A1	collagen, type III, alpha 1 (Ehlers-Danlos syndrome type IV, autosomal dominant)		7 577899587	7 56944754	7 748136112
207172_x_at	CDH11	cadherin 11, type 2, OB-cadherin (osteoblast)		8 260600969	5 544238185	7 537808472
213010_at	PRKCDBP	protein kinase C, delta binding protein		6 890419786	7 930818232	9 049763293
213125_at	OLFML2B	olfactomedin-like 2B		7 00815798	6 609345876	8 68378007
227140_at	NA			8 299780669	10 67360124	7 199266288
215446_s_at	LOX	lysyl oxidase		5 490668122	6 394295439	7 660841573
200665_s_at	SPARC	secreted protein, acidic, cysteine-rich (osteonectin) /// secreted protein, acidic, cysteine-rich (osteonectin)		11 4495457	11 08237098	12 35501097
210809_s_at	POSTN	perostin, osteoblast specific factor		11 13743579	11 28499347	10 72984165
226751_at	C2orf32	chromosome 2 open reading frame 32		5 955614459	6 192132528	9 269577525
209156_s_at	COL6A2	collagen, type VI, alpha 2		9 061418702	9 726094187	11 27318997
221447_s_at	GLT8D2	glycosyltransferase 8 domain containing 2		8 021648819	6 320215972	8 79290652
201792_at	AEBP1	AEB binding protein 1		8 962075811	8 994343668	10 67265955
215076_s_at	COL3A1	collagen, type III, alpha 1 (Ehlers-Danlos syndrome type IV, autosomal dominant)		12 92818246	12 43287163	13 3785952
229554_at	NA			5 369781122	5 101893968	7 382291817
222101_s_at	DCHS1	dachsous 1 (Drosophila)		6 363911303	4 989392056	7 863325839
212813_at	JAM3	junctional adhesion molecule 3		7 330011515	6 571828522	9 899998855
226997_at	ADAMTS12	ADAM metalloproteinase with thrombospondin type 1 motif, 12		6 398776691	6 617267703	6 328739471
212344_at	SULF1	sulfatase 1		7 562765653	6 973207714	7 962556999
227070_at	GLT8D2	glycosyltransferase 8 domain containing 2		8 133530232	5 600486178	8 699607658
202404_s_at	COL1A2	collagen, type I, alpha 2		12 1548594	11 52252257	12 29460934
202310_s_at	COL1A1	collagen, type I, alpha 1		12 09468428	11 71014464	12 83579941
221814_at	GPR124	G protein-coupled receptor 124		6 808599299	6 256923225	9 226647731
202450_s_at	CTSK	cathepsin K (pseudosyndostosis)		9 078811849	8 368557969	11 07131845
207173_x_at	CDH11	cadherin 11, type 2, OB-cadherin (osteoblast)		6 600005792	6 521496599	9 503446961
224396_s_at	ASPIN	asporin (LRR class 1)		5 202366322	4 963818498	4 344953214
1554966_a_at	FILIP1L	filamin A interacting protein 1-like		7 262847099	6 700577048	9 344564858
224817_at	SH3PXD2A	SH3 and PX domains 2A		8 201813547	8 9875971	9 618243766
226905_at	FAM101B	family with sequence similarity 101, member B		5 88078061	7 943570597	7 63820107
211161_s_at	COL3A1	collagen, type III, alpha 1 (Ehlers-Danlos syndrome type IV, autosomal dominant)		12 03608273	11 1400039	12 70939836
223499_at	C1QTNF5	C1q and tumor necrosis factor related protein 5		6 267155141	6 150708161	7 60557651
213428_s_at	COL6A1	collagen, type VI, alpha 1		9 552609018	10 38169434	11 61182709
219087_at	ASPIN	asporin (LRR class 1)		8 169253528	7 453436261	7 417660285
212353_at	SULF1	sulfatase 1		8 313627976	7 018345626	8 664535744
203477_at	COL15A1	collagen, type XV, alpha 1		7 512138819	8 051404488	9 977812403
204135_at	FILIP1L	filamin A interacting protein 1-like		8 044251475	7 526243347	9 873840191
212354_at	SULF1	sulfatase 1		8 899479909	8 378062891	9 484583122
226777_at	NA			6 808486061	5 928981546	6 859345954
225664_at	COL12A1	collagen, type XII, alpha 1		9 785274246	10 36407314	9 260889097
205547_s_at	TAGLN	Transgelin		11 10547836	9 349792259	12 57363893
211981_at	COL4A1	collagen, type IV, alpha 1		8 546576243	8 718626945	10 27236292
230218_at	HIC1	hypermethylated in cancer 1		5 403340531	5 056198537	6 860964508
202828_s_at	MMP14	matrix metalloproteinase 14 (membrane-inserted)		7 390513711	7 588298361	7 799470854

Urinary Bladder GSM137919	Urinary Bladder GSM46829	Urinary Bladder GSM53117	Urinary Bladder GSM53137	Urinary Bladder GSM88993	Urinary Bladder GSM89048
Urothelial (transitional cell) carcinoma	Urothelial (transitional cell) carcinoma	Urothelial (transitional cell) carcinoma	Urothelial (transitional cell) carcinoma	Urothelial (transitional cell) carcinoma	Urothelial (transitional cell) carcinoma
8 254797464	9 622340393	7 145993728	6 294592758	7 859684291	7 259212373
6 450946568	7 626712876	5 783298857	4 702979505	6 29481743	5 781011832
9 568088623	11 622945456	9 242218629	6 37380224	9 296338964	9 417273343
5 900851735	6 122596354	5 008788235	4 601650724	5 363196837	5 178884754
7 978035293	9 428376409	7 179901387	6 742445992	8 261288855	7 901846275
8 070256401	9 189157576	6 532782768	4 721143862	8 034947795	6 580501548
9 165788536	11 18103281	7 537850911	4 891743992	8 570048282	8 311706723
9 914134712	11 4212178	8 375119162	5 860718205	9 737233986	8 740907837
8 346268569	9 617642404	7 731923811	7 27139228	8 521541525	8 217268187
8 796784529	9 669728175	7 178489668	5 689052223	8 651618441	7 152287483
11 11535685	11 93222295	10 23969194	6 743954934	10 88909912	9 881293551
7 35354199	8 576295199	5 194523382	4 981314376	6 271516869	6 386969876
7 531779182	9 246571608	6 564189614	5 52978689	7 471223047	7 229759894
8 059964379	9 601797895	6 779656868	4 767282094	8 056548899	6 640026122
6 509572756	8 176387724	5 585397647	4 438383753	6 39739376	5 430628234
9 369544237	11 16891467	8 40951366	6 345306119	9 04892351	7 962457935
9 086274791	8 798154334	7 05788116	5 557221586	8 10069453	7 631419371
9 584733324	10 15745677	7 879643846	4 512265448	9 057333768	8 045149993
8 31076582	9 860148243	6 288441309	3 480709709	7 814087169	6 683410498
9 280923463	11 44632498	7 978932646	4 620314246	9 671861288	6 65090086
8 079027707	9 237087389	6 94727277	5 723227573	7 454100896	7 610671371
8 902349509	10 19782667	7 513726937	3 869204506	8 266732472	7 866267167
12 48957281	13 22423674	11 1748397	7 937485097	12 56983047	11 62288163
7 97694665	9 871391685	7 112059059	5 64088133	8 017088025	7 5708809
7 924288942	9 995392491	5 994776199	5 40367378	7 289752261	5 634330735
6 595146123	7 673968022	6 316478691	5 234613482	6 201894776	6 10028903
6 968775753	9 40067217	6 773832231	4 978103552	6 949370476	5 981643984
9 136652552	10 98004604	6 44538333	4 527605384	7 911040282	5 761635422
7 162414754	9 010720448	6 269737346	6 494262938	7 32636758	6 664820711
7 371243003	7 881430977	4 617010403	4 088312953	6 185024558	4 781031262
9 230985271	9 890652144	7 393264999	4 922566314	7 595372054	7 48251251
8 310667683	10 12065451	6 324546472	5 904696138	7 627728432	7 694561986
7 628624013	8 117440566	5 79271089	6 513181216	7 625713341	7 741922091
4 271392323	7 312616309	3 582498332	3 59374943	4 071561809	4 315255884
6 489649952	8 013552336	4 672025673	4 369916414	5 488180043	4 683707773
12 50376907	13 39919319	11 72692685	8 905772907	12 55077765	11 88608223
6 619981483	8 028945288	6 103700462	6 153529393	7 192858041	6 618641165
7 215288573	9 491155131	6 374390019	4 091800461	7 832309819	5 432457816
7 488572156	9 177655683	6 215068187	5 122751614	6 564481196	6 205351396
7 592418736	7 950125145	6 1815327	5 298118392	6 929291739	5 75246822
7 763829661	9 435936831	6 171128391	5 055020016	7 41369175	7 715370711
9 726719264	11 47648719	8 116953374	5 845303236	9 358618796	7 20852035
7 536609478	9 228106932	4 80540306	3 83780323	7 351669188	5 134824699
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6 377200579	7 938741818	5 998419027	5 814512308	6 472674939	6 629272794
9 379210154	11 24792606	8 377291008	5 272456673	9 861847121	8 5780876
7 931015957	8 542720062	6 064437061	5 908498031	6 686285716	6 549728264
9 077144097	11 45130805	8 458922538	5 93671603	8 902634429	7 77619302
12 92770872	13 24446126	12 1331954	8 636719716	13 06504535	12 23237948
7 254833624	8 881730133	5 636718905	4 766665438	5 871878529	5 693108746
5 970877191	7 345560075	6 001694712	4 696683195	6 189881441	5 999178782
7 780246169	9 106822485	7 396750586	6 483064036	6 714913329	7 194356869
6 436028547	8 766207678	5 866854571	4 54563163	6 91208412	6 024745085
7 207464975	9 967216146	6 124125129	4 944258103	8 304136076	5 313345299
7 217121498	8 52325715	5 229736996	4 09546545	5 059334656	4 377293276
12 09658043	12 88037929	11 21485806	8 356784233	12 19875588	11 32748593
12 14740259	13 42180671	11 08104183	7 911779349	12 22307658	11 40578828
7 00470349	7 681594873	6 516831646	6 195319274	6 686285716	6 198267188
9 862215579	10 9368058	8 48823072	6 816708015	9 29323838	8 160783945
9 014367806	10 42111008	7 825386424	4 845801842	7 823884039	6 998201842
5 089388625	5 994990985	3 964707718	3 572147958	3 922810099	4 258385295
7 703132441	8 601771449	7 114880689	5 096049174	6 973402346	7 676819978
8 457164409	9 673501558	8 169586847	7 315075001	8 046777698	7 496881756
7 251679104	8 349100144	6 299198398	4 910623533	6 556210291	6 00754857
11 68806125	11 96896694	11 41314815	8 181801804	11 84366886	11 396226274
6 392303009	8 433207397	6 139193815	5 688582865	5 988236403	6 358791699
10 52404591	10 73177895	9 045835153	6 825101955	10 34985107	9 567904837
8 063962826	9 08095635	7 280296374	4 021317852	6 299562987	5 827246862
7 605758947	10 36889347	7 157728745	4 113488365	8 824544097	5 620055476
9 935751328	9 37429756	7 642897971	5 108838588	9 275796118	8 182048361
8 40241891	9 331615334	8 083250299	5 627218759	7 836259589	8 489512998
8 588415451	10 90975986	8 15580675	5 503443967	10 1860982	6 678758442
5 916039036	8 677788878	4 810332819	3 882158042	6 446917951	4 944607976
10 07051736	12 30795429	7 263236058	8 503362214	10 73399289	8 624943021
9 862097605	12 42891171	9 879657702	6 11807758	10 21583844	9 155471149
9 523747024	10 25438694	7 202855959	7 302153226	8 810305412	8 991051979
5 624915432	6 526712402	5 197734054	4 718354916	5 101741144	4 850788495
9 016968974	8 596776947	7 15162392	6 326892733	7 975262389	7 390916842

Urinary Bladder GSM89073	Breast GSM46908	Breast GSM46933	Breast GSM46934	Breast GSM46947	Breast GSM46952	Breast GSM46953	Breast GSM46954	Breast GSM46955	Breast GSM46958	Breast GSM46962
Urothelial (transitional cell) carcinoma	Ductal Carcinoma	Ductal Carcinoma	Ductal Carcinoma	Ductal Carcinoma	Ductal Carcinoma	Ductal Carcinoma	Ductal Carcinoma	Ductal Carcinoma	Ductal Carcinoma	Ductal Carcinoma
9 291909881	7 788131525	8 183959812	8 517026931	7 211466728	9 022685276	8 084293892	7 557707512	8 36218819	8 188126402	7 830156772
7 522225161	7 071106474	6 588652299	6 510894188	5 381513056	6 632715903	5 925780965	5 826197964	6 550614913	6 265041014	5 872123368
11 59830143	10 03073165	10 46029505	11 6859388	9 80647591	10 76166214	11 18730039	10 43888067	10 69583328	10 31553501	11 20357823
6 782760889	5 227142685	5 881263979	5 868181779	4 902034014	5 953379506	5 713739813	5 048194698	5 609270987	5 092437067	5 364939282
9 164500982	8 713267108	9 518813581	9 04665644	7 941152734	8 85489609	8 781525419	8 274818589	8 12304057	8 654506557	7 916554826
7 965199023	7 890065073	8 716819069	8 765159563	7 142311426	9 104847038	8 001082168	7 743870506	8 413768516	7 286967423	7 73948115
9 848697501	8 180460995	10 57896879	11 57086804	10 00482511	10 93657616	10 4190361	9 23199984	10 20492985	9 35227442	9 962600224
10 88496014	10 33288427	10 74426013	10 7202262	9 381018057	10 54801818	10 20920103	9 77872425	9 880626091	9 613507545	9 51280794
9 517586005	8 965128177	10 04018031	9 727498051	8 595200096	9 58033393	9 804555095	9 064850662	8 862799842	8 942495015	8 461600316
9 73186324	8 476957528	9 291928853	9 802208735	7 884210345	9 361059965	8 995378999	8 225495847	8 607607507	8 428071346	8 283938506
11 61440118	10 84693319	10 77490986	12 38330754	10 66167735	11 92464062	11 71890175	11 71005913	11 40341409	11 50041779	11 79105938
7 817179582	5 082408665	7 789975018	9 642275851	7 706378232	8 948070485	8 196524063	7 586386868	7 745334396	6 484690859	7 571747766
9 032330498	6 368142857	8 614768374	9 082144785	7 686920281	8 807413609	8 447587507	7 934983249	8 170494145	7 762129883	7 852995486
9 058788516	8 980325009	8 840362555	9 293099279	7 387069295	8 916582221	8 545484137	8 02979641	7 937515557	6 877680776	7 867282887
8 772556544	5 537140686	7 247666607	7 495243529	7 001662547	7 792639602	7 820705278	7 73448598	8 857673721	6 407498911	8 06679756
10 3459684	10 55250168	10 68415048	11 52049966	9 595724789	10 7518221	10 11648564	10 52525844	10 1458189	9 639791178	10 35295856
9 417493454	6 865944491	8 417357897	7 679635476	7 177975312	7 851551396	7 892499234	7 417854434	7 717833996	7 730045136	7 438757028
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10 99499961	7 3505199	8 009011248	8 547547609	7 486147793	6 593610106	8 282572498	8 747939926	8 681566059	8 200699456	9 221788762
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13 58509432	12 47884906	12 93261203	13 75228722	12 44738846	13 27932867	13 01725371	12 81500542	12 83932232	13 19573603	12 9646771
7 576176456	6 03870224	8 500051977	8 365876372	6 954697743	6 189966437	7 864153841	7 416331612	7 578391117	6 203997661	8 831107976
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13 44018734	10 82856702	13 40879999	13 39531188	12 21707716	13 27002177	13 08624923	12 78952322	12 88087784	12 73254105	12 92079318
7 423222582	6 612986178	8 365656123	8 349958712	6 554929924	7 783564926	7 451081626	7 12441872	7 208726312	7 155812307	7 336544415
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10 3207316	9 613776444	9 587949307	11 13466618	8 946132218	10 07949018	9 883650927	9 15976201	8 679378989	9 865041677	9 96423251
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7 172643721	7 193899316	7 484207871	7 232204675	6 424856938	7 384351629	7 186629806	7 503821205	7 076273908	7 632948872	7 409051107
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Colorectal GSM38075	Colorectal GSM38077	Colorectal GSM38089	Colorectal GSM38105	Colorectal GSM38107	Colorectal GSM446819	Colorectal GSM46841	Colorectal GSM46845	Colorectal GSM46856	Colorectal GSM46857
Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma
9 13138504	8 459634185	8 331477197	7 916399001	8 065431238	9 352953749	8 953835076	9 462461928	8 1687129	9 048962014
7 442323044	6 483334216	6 519246206	6 055234094	6 422231279	6 988296856	6 802848099	7 275912591	5 842798933	6 940168863
11 48117815	10 51918681	10 55884035	9 531425017	10 00117265	11 81614227	10 21833578	10 07710675	10 16038286	10 97471492
6 699497334	5 869858776	6 013381332	5 277310062	5 790625247	5 582024574	5 737041414	6 860085421	5 057516066	5 96021066
9 154686358	8 381318686	8 45423177	7 864705478	7 759603461	10 08171607	6 682495853	8 924108123	8 411518303	9 347963494
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9 563849034	8 342419026	9 383213363	7 625175498	7 786174293	10 12035807	8 563498976	8 840750879	8 188834424	9 108207935
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Colorectal GSM48861	Colorectal GSM48865	Colorectal GSM48877	Colorectal GSM48879	Colorectal GSM48901	Colorectal GSM48969	Colorectal GSM48972	Colorectal GSM53087	Colorectal GSM53132	Colorectal GSM53168
Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma
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Colorectal GSM76546	Colorectal GSM76571	Colorectal GSM76575	Colorectal GSM88976	Colorectal GSM88982	Colorectal GSM89013	Colorectal GSM89074	Colorectal GSM89075	Colorectal GSM89094	Colorectal GSM89100
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9 501090461	7 155028388	6 652247343	7 402839562	7 306850031	8 380024969	7 395910745	7 238304782	9 918004411	9 079377936
7 054669358	4 413891338	4 392422036	5 502835708	6 047094084	6 236923969	5 213343296	5 476008399	9 357005971	7 27284391
8 552611429	7 890123486	6 603445475	7 382161342	7 857463765	7 659066532	8 016486263	7 626938842	8 972441438	8 906107247
9 602216317	7 015085939	7 363274177	8 467374469	8 853205251	8 907007967	8 971469487	8 18432222	9 446000385	8 13432222
8 174653554	7 361804707	7 023339058	7 6635798	8 079396315	8 657199362	7 814366671	7 481950732	9 088416548	8 529672594
6 401501306	6 247033241	3 835156717	4 090503172	4 576582053	8 087948272	4 480417436	4 054901058	6 495115302	6 495115302
7 597797332	6 643130615	5 26937106	5 576684674	5 988669008	6 946299528	5 083232469	4 756953148	7 483613787	7 252215209
13 14947252	12 87516275	10 84238796	12 12150495	12 21742213	12 86485844	12 35882617	11 44401989	13 81941236	13 76834854
7 78027527	6 960279638	6 89862184	6 495287034	6 812660201	7 274064416	6 501208523	5 919550583	8 32337248	8 643654216
9 278060339	6 929246359	4 789421734	6 686944296	6 651145107	7 494493494	7 130250724	6 064622455	8 767441495	8 135843314
8 580434934	8 508782766	6 114160232	7 095115199	7 139273303	8 236144237	7 1133092	6 001979354	8 61143226	8 726256783
8 122230974	6 587978581	6 241445731	6 96320803	6 557450627	7 725237825	6 488012327	6 480960634	8 387371399	8 179294974
8 292105097	8 820899976	6 256813962	6 888865131	7 396644218	9 424299671	6 808865862	6 386238584	8 961078193	8 612023582
11 19380906	10 15874902	7 188781279	8 418499781	9 161030112	8 849187349	8 178913941	8 040994453	9 057986428	10 37146302
7 58906203	7 084060847	5 010180069	5 975155287	6 026385116	5 996687466	5 956278361	5 583909893	8 666935474	9 372529388
12 33996129	11 96726905	10 17886167	11 35758693	11 4705151	12 1936841	11 31973118	10 36070229	12 74815693	12 9583429
12 34673943	11 6067700	9 482751242	10 79037047	11 11852497	11 17183118	10 57303905	9 333360399	12 35052982	13 06373183
7 47558252	6 754348738	5 536660491	6 584689243	5 920881813	7 05586599	6 473910054	6 013923632	8 761084282	8 168464683
9 900707921	7 733594175	7 37903786	9 095879662	9 594568797	10 3860024	8 812107064	8 475083565	11 19069376	11 016915
7 122902507	6 779586223	6 164056147	5 93318743	6 300771195	7 411844558	6 826212384	6 042720828	8 803676187	7 694100942
10 22958226	9 242001658	7 661603972	8 412819887	9 018956475	9 901703172	8 687067318	7 729339931	10 62232875	10 32362971
13 57796688	12 95516568	11 55514012	12 19702104	12 42744112	13 09437022	12 60989409	11 69443675	13 8007237	13 67673603
8 010072541	6 953909525	5 115100558	6 180297945	6 236869655	6 671399443	5 583684466	5 525517237	8 565032883	7 1888676
7 6868816	6 516565911	6 268874545	7 158442179	6 452248981	7 694619541	6 726072421	6 048495205	8 675800678	7 487893637
8 883143503	8 282942245	6 898975479	7 590504409	7 407225187	8 408499364	7 809258182	6 643144318	10 24443046	8 92021508
8 353682111	5 876819425	5 387081858	7 051313526	6 581834535	7 454391705	6 769806138	5 8824844	7 071286771	7 554381607
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7 921000941	6 923560033	4 787688266	5 787909091	5 785376469	7 349447416	5 664635252	4 83418035	9 290279002	7 319129482
12 83447002	12 69316637	10 46025105	11 69618274	11 65923679	12 34172124	12 04553467	10 67248773	13 37354321	12 8966277
12 46332605	12 07297169	9 434012438	11 33733251	11 70467605	12 4703597	11 94462739	10 68013667	13 55467845	13 47316533
7 078690197	6 160941964	5 640820704	6 860529051	6 440952259	7 563495076	6 993602003	6 929673841	8 333104442	7 322321845
9 7456488	8 99232946	7 626373944	8 863251541	9 46671646	10 30363323	9 349640607	8 656754188	10 9692961	9 381943626
10 85009032	10 40335569	7 860907704	8 583156362	8 794299366	10 12781123	8 437210754	7 654534559	10 39738395	10 19604773
7 462891973	4 814051261	3 978243474	4 499606566	5 40264789	5 642347882	4 748149319	3 986345691	7 6702473	8 537721395
8 505326825	7 974800986	7 108767578	7 417582077	8 336996079	8 583815709	7 763345228	7 800260596	9 76293295	8 669665996
9 388673019	8 708573159	8 159651029	7 942203151	8 108095195	8 541722459	8 455139259	8 162430722	9 439503869	9 978205485
8 568773232	6 965583992	6 13541802	7 077814477	5 806844192	7 189373699	6 516975242	6 789405109	7 93316912	7 84434609
12 92098457	12 35637073	11 20683768	11 27211225	11 34554096	12 17331685	11 3595065	10 60122461	13 39673028	12 82071786
7 097150653	6 825300704	6 107921153	6 82860067	6 752864144	7 627526637	6 736424561	6 362995162	7 816102125	8 511864771
10 53502106	9 385616223	8 531278573	9 900179696	9 999094957	10 86750847	9 810180018	9 258944255	11 59067747	11 26739189
10 74630657	8 017190934	6 693001781	7 837241988	8 068387528	8 931794428	6 940938678	4 969316103	10 44533427	11 02550963
10 84919407	9 221631452	6 742988519	8 329591618	8 519171022	9 770403166	7 970130962	6 485180892	9 768470426	10 28336004
10 77464873	8 333101784	7 764720029	9 060871287	9 098561009	9 77673765	8 839097024	8 194047095	10 76041021	9 96220536
9 326451426	8 733075575	8 031599163	8 336837105	8 86853545	9 146692949	8 413740155	8 43391261	10 16684094	9 25853318
11 32714148	9 866103546	7 866015082	9 32264338	9 629783	10 60080094	8 793646084	7 726141414	10 79190715	11 21166849
6 73349855	5 249435305	3 751608228	4 829672869	5 239551996	5 744135825	5 489180297	4 0169752	8 24332338	7 450546963
12 2800333									

Kidney GSM117706	Kidney GSM38073	Kidney GSM46825	Kidney GSM46826	Kidney GSM46847	Kidney GSM46858	Kidney GSM46875
Papillary renal cell carcinoma	Conventional (clear cell) renal carcinoma	Conventional (clear cell) renal carcinoma	Conventional (clear cell) renal carcinoma	Papillary renal cell carcinoma	Conventional (clear cell) renal carcinoma	Conventional (clear cell) renal carcinoma
5 5244146	8 084745184	8 937541576	7 359818073	5 483989567	7 728653943	7 647243009
4 227793825	6 704774258	6 846544131	5 283697172	4 616786727	5 97319995	6 039479565
7 110390823	7 649713017	8 127875879	8 173741719	6 885329224	8 090324538	7 008554175
4 792199543	5 80678103	6 021046359	5 141472242	4 550546603	5 392708408	5 267334697
6 183678132	9 139580279	8 926384327	8 208884393	6 492892469	9 450603097	9 073823519
4 427726064	6 405803014	6 838515047	6 527821384	4 647428129	5 603868898	7 347488879
5 71769979	8 760663794	8 654611854	9 079755271	6 723382762	8 863526909	8 300097436
5 766013262	6 818443935	7 818970136	7 966941068	5 702320498	7 666384647	7 516542928
6 735696189	9 850276921	9 458444742	8 334084978	6 976597974	10 03786562	9 537088722
4 713074081	5 910212151	7 131600604	6 800265876	4 488126974	6 468371094	5 957675386
4 80076423	8 582268198	8 877454797	8 908770219	5 942612259	9 370713428	8 40917735
4 708772977	7 236213611	6 540132956	6 766957399	5 087413386	6 888161729	5 857207992
5 277294046	9 811211642	8 980675858	7 687904695	5 804136034	9 810041173	8 903114058
3 258252612	5 323180601	6 200852303	6 271793177	4 02860475	6 125369221	5 664886978
4 317686925	5 35985864	6 040564988	6 081888869	5 068377331	6 67509754	5 823099423
4 270163307	8 466238936	8 422847449	7 529311076	4 901036572	7 238663402	8 411388124
6 075766493	8 265738124	8 31368932	6 950822073	6 676040625	7 948072648	8 325103032
4 206482543	5 17578458	7 496683053	6 111752909	4 187457784	6 825654239	7 337986026
3 459212275	3 442900743	3 502878522	4 615171796	3 454236631	3 236151465	3 229626942
4 199172839	7 882473393	7 780290787	6 336154551	4 932197026	9 060733233	8 731176205
5 943533254	8 90024744	9 383105503	7 697841406	5 830082931	9 367958341	9 223216733
3 892512391	3 278710334	3 604211151	5 054634652	3 568592735	3 68348232	3 861460601
6 889079908	10 60087285	7 17718333	10 59599854	8 151225955	10 47553839	9 757213959
6 23856754	7 531085882	7 448476286	8 399098304	6 15918237	7 684156057	6 296458999
5 287374592	5 382254063	5 747016522	6 115760619	5 074512132	5 864458566	4 920440205
5 732566059	6 549795144	6 558888867	6 705295446	5 786743574	6 463872669	6 311411659
4 914252382	7 1003421	7 25267406	8 07664376	4 338253431	7 62325195	6 856439001
4 522907218	5 135814	6 464175026	6 368864277	4 522186588	6 53986945	4 719886338
5 642550498	8 289851438	8 28157491	6 988950493	4 077399936	7 829756267	7 958379477
3 886588644	3 585868301	3 640177901	4 384693571	3 958093754	3 860596235	3 434369728
8 971873565	9 181134709	8 479161392	6 710927709	8 144453385	7 902527076	8 639770006
6 02966984	8 837374863	8 617645896	5 747977	6 789156572	7 146939547	8 760354941
6 797429814	7 741196075	8 116463782	7 519387359	6 164002301	7 761855832	8 154039854
4 021207331	4 886196472	4 844521647	5 240151651	3 563930205	4 966295713	4 966295713
3 632420144	4 956712858	5 973919537	8 092059408	4 501370367	7 612527445	4 314190241
7 962362446	10 66733077	10 99999502	11 5239258	9 28352146	10 90179465	10 16235383
5 674860246	6 688221621	6 508106513	6 493096236	5 904301588	6 845881858	6 423524487
3 626391413	5 632536445	4 14435916	4 541660893	4 919453842	5 922956523	3 878493709
4 943351224	7 075383758	7 251643795	6 66359762	5 088405257	7 678800703	7 214633929
6 595585901	8 583998281	9 550444693	7 61647332	7 655270961	8 416627326	8 866932633
5 642850701	8 280359644	8 363700596	7 677104	5 30780755	8 237683082	7 584833341
5 338309442	6 386221307	8 046843437	7 512917721	4 794742412	7 711066529	6 097576271
4 371385843	9 862637761	7 630395436	6 233445219	4 115867156	8 10636395	10 2362205
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6 003953691	9 276881345	9 465479038	8 500241115	6 758915965	10 55603886	10 40789129
6 157312544	7 855946907	8 481069442	5 653156339	5 846298599	8 030146071	8 102315635
6 733372313	9 247100961	9 369212991	8 815950732	8 315553653	9 020001383	9 149205075
5 689509835	5 558438055	5 943155206	6 207107251	4 520453303	6 959564125	5 879589819
6 656491419	9 944538084	9 802560971	9 349415232	9 279156925	9 872119492	8 251274734
7 794337274	11 18572859	11 19653421	11 23580424	8 775662628	11 19662628	10 41571599
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5 058766583	7 754762437	7 846169522	5 694776218	4 524653009	7 337683248	8 284135769
6 413859735	9 144996621	9 336095454	8 173952671	5 707217561	8 966345072	9 000762818
4 878302625	5 16831765	4 850324774	5 4369844	4 25875519	5 314554443	5 411113355
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4 755429161	4 2530422	4 880200676	5 443977363	3 577376782	6 643069942	5 102310974
5 686156217	9 405371187	9 99241188	10 45947552	7 766966648	9 298181194	9 493260475
6 851058115	8 646116511	9 713284672	10 70224821	7 399628826	8 977997335	9 159167643
5 332839735	8 103059788	8 544067022	7 029039144	5 546045472	8 079659908	7 778936922
8 707798407	6 391853862	6 193814823	7 381739895	8 157808888	8 501524238	5 893279901
4 849843192	8 148609949	8 157029715	7 364416294	4 417318068	8 972492409	8 651524763
3 771147679	4 199462338	5 201930265	5 029382691	3 574171487	4 951477628	3 338410329
7 154623846	10 06466119	8 258852137	7 746344437	7 701242408	7 452505448	7 668023436
6 72191937	8 558544341	8 745803222	7 003513565	7 76646147	8 13027059	8 427658504
4 585486293	9 589406204	9 232513372	6 500257561	5 181227112	8 471435234	9 829025281
5 445865782	9 843623963	10 10952902	10 31912088	7 478344738	9 950648348	9 427012817
5 29186281	7 921388244	8 336474543	7 131691663	7 076809654	7 8166612	7 716173453
7 925948866	9 329379329	9 346963132	9 346543887	9 013177793	8 955186444	9 584618434
4 053182402	6 13626329	8 044553855	7 9643693	3 657987636	7 477712499	5 422541933
8 954843611	8 624919369	8 282198649	7 826282317	4 630205558	7 432729771	7 86627708
5 51284903	8 85253916	9 336222518	8 375982355	6 327352807	10 05193584	9 942476264
7 860339219	10 4730052	8 983162907	8 113712493	8 023051758	8 160786667	8 23348273
9 83887841	9 28105202	8 678758123	8 54211976	5 413735538	8 033268133	8 327900255
3 977112472	3 900039469	3 987187763	3 922623702	3 801147259	4 317191926	3 872785616
5 236858491	7 6468851	8 150323708	8 798883109	5 810734756	8 5117851	7 810571114
6 442221799	10 50221843	10 54837136	10 94662323	6 441125645	10 89375238	9 250890064
7 513500052	11 26396486	10 89387954	8 872952011	8 216936558	10 56379827	11 27691157
4 714103098	5 321274511	6 081184746	5 82128115	4 953408668	6 042872583	5 690603131
6 848019463	7 137633675	7 144137372	7 203926557	7 217342776	7 575463809	7 288203788

Kidney GSM46881	Kidney GSM46882	Kidney GSM46892	Kidney GSM46929	Kidney GSM46939	Kidney GSM46944	Kidney GSM53060	Kidney GSM53092
Conventional (clear cell) renal carcinoma	Conventional (clear cell) renal carcinoma	Conventional (clear cell) renal carcinoma	Papillary renal cell carcinoma	Conventional (clear cell) renal carcinoma	Conventional (clear cell) renal carcinoma	Papillary renal cell carcinoma	Papillary renal cell carcinoma
9 299933171	8 206888034	8 397555922	5 660168027	8 764339031	8 070097744	5 624237487	6 714432787
7 042668857	6 086338836	6 00900628	4 899371281	6 653459594	5 980162033	5 848404438	5 151566684
7 685951075	9 324694391	8 2567642	6 177863711	8 705610284	8 201966277	8 467928976	6 200082403
6 079335867	5 132926537	4 942370375	4 983295129	5 173187007	5 174832521	4 880640042	5 101336761
9 417993849	8 791857507	8 590587306	6 889001278	8 622489663	9 61195084	7 20882967	9 012357201
7 222846471	8 15833226	6 894557652	5 079169131	7 218603103	5 782916235	5 187237229	5 971087203
9 399318605	10 0465067	8 951946855	6 95131757	9 514102644	8 465623026	7 422109631	6 290936883
8 658372101	10 03294042	7 824131609	8 296722879	8 778335485	7 324678138	6 157810478	6 881847621
9 753339616	9 25278785	9 347136716	7 434106031	9 506722079	10 07656878	7 598687322	7 088552546
7 360861281	8 374964439	6 879405736	6 123605494	7 41753074	6 25410331	4 980737633	5 446628717
9 308251545	10 45678445	9 538141783	7 457132443	9 353847401	8 567271199	6 190090875	7 375849036
6 924845681	7 531929863	6 736369269	4 776285009	6 983171643	5 838767396	5 341505064	5 276904555
8 948501827	8 591281144	8 467061739	5 595992847	8 22936181	8 695393765	5 145576893	5 368585908
6 884869144	8 223392867	5 724637145	5 776669457	6 720545069	5 320611305	4 925108943	5 038854124
6 521412044	7 854639383	6 713118915	5 5965621717	6 453876171	5 061752621	4 94577009	5 641374316
8 70280961	9 822017317	8 142644491	5 81516688	8 640395988	7 809552713	5 382766191	5 289719791
8 585154321	8 389645012	7 470217043	5 853998973	8 289428634	8 291419628	7 061440739	6 966343287
7 828668377	8 48163168	7 052348114	5 24872379	7 398925254	6 76488557	3 898218184	7 44667925
3 952732313	6 898789395	4 868292544	3 25404085	5 691504739	3 807824269	4 071173763	3 969588413
8 437550176	10 72992484	8 291155234	5 556529394	7 903159363	6 669254956	5 30896613	5 978661646
8 830519779	9 062132466	8 873639682	6 822927239	8 442452312	9 418459331	6 199991283	6 429569512
4 346821948	7 341875248	4 91628915	3 817985564	6 493196168	3 855515412	4 023482064	4 338127605
10 91122635	12 44284178	10 89681674	8 869345422	11 23453601	9 784175349	7 982553213	8 682849642
7 314078411	9 239027833	8 199234032	6 548653317	8 393582394	7 621926346	5 988842345	7 332772313
6 736443367	8 56223376	5 992862152	5 040129409	7 043803449	5 96311256	5 439637959	5 911096509
6 679263667	7 088098559	6 086660124	6 469770117	6 999588178	7 060552104	5 341622117	6 249650775
7 235062031	8 37144967	8 057435023	5 761118625	7 669088931	7 43804501	5 098834038	5 294570054
6 805687399	8 655607113	7 00131494	4 901791472	7 317411918	5 75867603	5 192268265	5 709085399
7 822797624	8 338499473	7 847272441	6 264391179	8 055938314	8 399743472	4 900970533	4 350599612
3 727151471	5 044654692	7 149212574	4 188898695	4 253653533	3 789530862	4 191033084	3 87391508
8 074100937	8 101938666	8 681608885	5 733078952	8 295204481	7 785547571	6 583034004	6 344575839
8 604204331	8 053589634	8 215809161	6 499288958	8 2968122	8 841226478	6 474735691	7 724476498
7 821763767	8 180296374	8 02046458	6 921650134	8 026227447	8 446048701	7 234656126	7 230058265
4 990388669	6 163168917	5 463200667	3 565225433	5 48425183	4 578044215	3 855918954	6 87479087
6 106842072	7 235217649	7 27084742	4 807889378	6 292426284	5 775233198	4 711882503	4 867977182
11 31423804	12 59836431	11 3161794	9 299232046	11 98694374	10 59862069	9 362948151	9 893737662
6 461069565	7 300439133	6 612867763	6 047494471	6 86609585	6 302443552	5 581787213	6 234986711
4 42001924	7 749260794	5 309100763	3 860067974	6 570099939	5 504361664	3 696721873	4 493401958
7 256488073	8 24373792	7 669057373	5 252644837	7 22852511	5 993825977	4 597312779	5 222844408
8 193362543	8 7589486	9 007100148	5 379406551	9 239789619	8 668086687	7 977855835	7 323290606
8 895068459	9 561983628	8 037473573	4 908991128	9 013677502	8 074481591	6 032382979	6 455361887
8 690165245	10 00639867	8 622492528	6 540169799	8 670401976	7 379304575	6 621621401	7 09073863
6 549283038	7 471626042	7 829149641	4 949399183	10 0902432	9 490299986	5 21547278	6 87479087
12 35331933	12 3259526	11 77606236	12 31011432	12 09942843	12 52576951	9 717236386	10 25624366
10 37210995	12 26209949	10 04684674	8 222462239	10 24978675	9 278826685	7 95947442	8 673559791
8 461368663	7 863305783	8 022827912	5 799777844	7 809151383	8 40538037	5 800330055	5 84576048
9 412393535	10 58301518	8 078902965	6 722353158	9 430155891	9 145010514	4 689043972	7 189704246
5 362588224	7 487939015	6 58617408	4 585762589	6 589684523	8 481262736	5 522684761	5 088287817
8 857547685	11 19782304	9 749623768	8 789760811	10 80643753	11 03854048	8 144697702	7 403030329
11 47506748	12 90105867	11 47084855	9 645915146	11 81941323	10 64221711	9 368176046	9 682321307
4 553881891	6 718886336	6 387922155	5 152516074	5 559833525	4 943671169	4 657247321	4 579334188
7 309714797	7 263667311	7 249972308	6 375644582	7 068889227	8 107133692	5 460504838	6 139677385
9 142041752	8 991935415	9 038288348	6 442095662	8 628122295	9 432533594	6 910442214	7 65614122
5 625301385	6 339975681	5 411428664	4 964982122	5 358084646	5 163958867	5 642467688	5 434596044
8 575649094	9 651200836	7 417863845	6 013825119	8 246873347	7 277500486	5 845125732	6 583651836
4 506252288	7 230689816	5 752870711	4 27493387	6 318519239	4 406703042	4 507463356	3 672891821
10 9860192	12 09332119	10 33973059	8 066273823	11 38954848	9 668237741	9 196620924	8 738964373
10 91055503	12 49975564	10 17327656	8 266261154	11 42846135	9 236652217	8 414066878	8 724738856
8 105248322	7 938485581	7 883016428	4 962430577	7 064426145	7 769665523	5 668937561	5 440998573
7 179422708	9 883474317	7 395959571	6 812214401	8 598440582	6 681830642	6 981484213	8 703513057
8 446110122	9 383963879	8 927342305	5 971508887	8 910957697	7 755619298	4 759312616	5 737275472
5 118110936	6 080181887	6 195763692	3 547037321	4 695091974	3 82987845	3 753223867	3 714872106
7 858573554	8 854049339	8 745794697	7 574000902	8 276861136	6 726074087	5 459404777	7 004553387
8 444293353	8 877330542	8 46731834	7 98935935	8 439840487	8 640697051	6 889586253	6 97832962
8 376218484	8 405661812	8 78580622	5 025041426	7 767751581	9 217524602	5 658805703	5 831238976
10 57372547	11 84407956	9 975735208	8 438157094	11 29586904	9 801979264	8 475376303	7 91675394
7 594148721	7 89084014	7 69549031	8 503732188	7 830495138	7 807532819	6 073175054	6 980864924
9 552767878	10 07908313	9 065658607	9 165119134	9 539340619	9 533762446	9 048327122	8 594416614
8 054160404	8 909062895	8 719446153	6 771258601	8 375301665	6 865448849	5 077000541	3 88665143
8 803524864	10 20132018	7 673880456	5 914775749	8 797381379	8 348677004	6 683787111	7 979176504
9 399960719	10 36200904	9 72077554	6 51381535	8 586992846	9 660815733	5 955286982	6 323546238
8 424150152	9 383584526	9 281695742	8 303468175	8 906414035	7 481459336	7 114131341	8 23303629
9 367866155	10 590590507	8 255951192	7 109375160	9 368259291	8 766740705	8 106951603	9 15853255
4 876598194	6 311170983	5 202730236	3 424304175	5 201061423	4 510209318	4 244890802	4 833136767
8 683494981	9 472806482	9 132244653	8 190086007	9 292959236	7 57698428	4 596881132	6 488054125
10 40446675	11 68491669	11 0970195	8 805439299	11 45266543	9 78404373	7 33118775	7 370743169
10 94846688	10 50364131	10 51249799	8 848548793	9 540732757	10 33506487	6 556186645	6 50454513
5 844197658	6 459993133	6 481664794	5 067682781	5 374010435	5 995681122	4 785985521	5 248164278
7 241283871	7 894346691	6 39196221	7 410820097	7 082142288	7 075968492	7 124795422	7 525747413

Kidney GSM53122	Kidney GSM89099	Liver GSM137909	Liver GSM137962	Liver GSM179952	Liver GSM203676	Liver GSM203750	Liver GSM231890	Liver GSM203751	Lung GSM102505	Lung GSM117610
Papillary renal cell carcinoma	Papillary renal cell carcinoma	Hepatocellular carcinoma	Hepatocellular carcinoma	Hepatocellular carcinoma	Hepatocellular carcinoma	Hepatocellular carcinoma	Hepatocellular carcinoma	Hepatocellular carcinoma	Bronchioloalveolar carcinoma	Squamous cell carcinoma
6 081543582	6 498023117	7 326685087	6 553924695	5 972654381	5 430990864	6 74913439	7 129562402	7 012012024	7 454348347	7 664172236
5 509353351	5 120508928	5 544194337	5 324347192	4 358685737	4 729290866	5 392467195	5 55010885	5 904404084	5 628230274	5 977069338
7 401047038	6 728217098	7 103864019	6 246988752	5 873755244	5 909941107	8 875725275	7 989327325	7 691647308	6 002545714	10 61971313
4 782315041	5 057575654	5 210178164	4 455984676	4 924168748	4 831781849	4 96716556	5 078777607	5 489267264	5 896534452	5 386349521
6 49401546	6 456886237	7 862357956	7 393103183	6 978336469	6 7671723265	7 72227774	7 477857242	8 871864698	6 875947009	8 68111733
5 772409457	5 626338948	6 896266321	6 449913773	5 279117994	4 615652943	7 65010947	7 185814856	7 700212469	5 207306022	8 439522125
7 803969526	6 869404479	8 876210227	7 92151003	6 38060437	5 689149105	9 454266034	8 950856713	10 08597436	6 912872072	10 17138208
6 131256608	5 865911167	8 157178472	8 351488876	6 016174455	5 649981166	9 124634641	8 19532537	9 629509596	7 196954278	10 71474108
7 410788894	7 164402706	8 367318085	7 785656391	7 262945143	7 38084574	8 456644157	7 889282146	9 233009895	6 903618256	9 143711212
5 461861247	4 540332781	6 70123543	6 335689587	4 856821347	5 424546279	7 549939037	7 030665872	9 256911408	5 70998594	9 220179424
4 672434334	6 017286789	8 257838594	8 802486348	7 301736785	7 049358954	10 0884558	9 438232844	8 599012783	6 439290354	11 30194272
5 864805651	5 216489343	7 242111239	6 214925089	5 150406258	4 413743675	7 579540496	6 847284946	8 347233981	6 327303194	8 477164664
5 938856497	5 385838824	7 24636856	7 36099472	6 60783825	6 038265067	8 089162412	7 225449363	8 737984479	6 346216395	8 192347057
4 221814522	4 302909596	5 959437056	6 090542248	4 397545148	3 837053142	7 519142872	6 326150059	8 580633246	5 495711043	8 55329075
5 175269804	5 197035452	6 113559392	5 053059655	4 306082968	4 106754617	6 567909967	6 120301088	4 973832928	4 50833723	6 991658648
8 948315314	4 747856752	7 539952925	7 435378016	6 33821184	6 117376041	8 781086691	8 039511443	8 717883985	5 86855533	10 58050587
6 806632347	6 359534506	8 511926487	7 979488878	8 57382239	7 153029513	7 53620599	8 220683105	8 007984758	7 002390811	8 381717606
5 580858044	4 523396088	7 188478678	7 164558421	5 303036581	5 061946244	4 130542327	7 395809598	7 688857858	4 344555596	10 15378148
3 656882157	3 838428818	3 945888157	4 366851446	3 184005778	3 415724754	6 66227378	5 514658034	4 009159014	3 70698768	7 493455184
4 616817719	4 303360256	5 794137062	6 008597239	3 868878523	3 768857383	9 253790312	8 098261433	7 953689133	5 095898331	11 41849890
5 763287158	5 89190314	8 002815964	7 577655169	6 595787162	6 632316502	7 828207194	9 539360414	9 735123946	7 083789205	8 150683025
3 825486796	3 746392472	4 158210722	5 599367528	3 280894265	3 086866313	7 101089246	6 545739366	4 852716725	4 592792924	7 982990751
8 936087075	8 084056641	10 5318457	10 46833518	8 089330782	7 081988152	11 35722793	11 14857914	11 18951522	5 595676332	13 21402081
5 91901261	6 791044973	7 690386599	7 753413997	6 142290582	5 523438514	9 198597205	8 129111245	6 778117979	6 43105495	5 157081142
5 211676925	5 255843075	6 133854546	5 532312396	5 293866734	4 825630177	7 250795276	6 310754834	6 67009516	5 645504343	9 11826079
5 948858658	6 413293256	6 288031993	5 782782357	5 354016071	5 798623511	6 306387582	6 190230324	7 482230257	6 191482219	6 695616498
4 569338626	5 068953239	6 1818898	5 997980354	5 729783625	5 558300141	8 825282356	6 88295538	8 599012783	5 778295303	7 829193268
4 565352326	4 933114121	7 579743339	6 963813862	5 378092323	4 476224208	7 020406809	6 981016261	6 27872054	5 919103731	8 554789602
4 68781103	4 623049113	5 978660132	5 505497494	5 186567235	4 546633081	6 489705271	6 186331489	8 064212717	5 041170429	7 846474137
4 502938828	4 123412818	3 881779841	3 887507548	3 1620606	3 510891932	4 32016767	4 187077394	8 314369902	6 23742316	8 165233989
7 526099987	6 232977615	8 187944325	8 684985299	5 189268532	5 768847135	9 129653789	7 10112844	7 867489861	5 919103731	8 226607389
8 007562575	5 219815576	6 783661454	6 766108259	6 7282354	6 17088122	6 936734656	6 315076596	9 125700247	6 550090392	8 800273573
6 482351165	7 106442354	7 463068006	7 152210313	6 432945794	6 500723698	7 243002191	7 331950858	9 892055385	7 145601174	5 439571997
3 971860204	3 66509804	4 478607815	4 142132624	3 78657915	3 715128858	5 270428665	4 868920554	6 673107481	4 525121813	7 525121813
4 624397773	5 328513148	5 015706276	4 246808483	4 228583772	3 619401188	6 360333596	5 257572342	4 724256033	4 985629522	6 967846728
4 678743517	9 597434412	10 48560913	10 65943351	8 353275394	7 378671545	11 37330971	10 822599229	12 66799278	8 31322183	13 46273365
5 567224697	5 537942709	6 040732651	5 931766146	6 146702557	5 615158327	7 65494899	6 46277229	6 366991529	7 295233964	7 70003308
3 572588723	4 447303964	3 970089445	4 971484288	4 287350309	4 25542118	6 975914124	5 489324984	5 680153106	5 959481114	8 569271851
5 17905307	5 308100972	5 574035081	6 782384562	4 622532283	4 597642434	7 760573008	6 29773154	9 512995528	5 283715512	8 585374156
7 683848295	7 057395112	6 303906396	5 375056913	5 569022082	4 908918959	6 695538748	6 53369817	7 536023057	5 406773556	7 646004801
6 090709952	4 939449266	6 849372484	7 11995966	5 870295789	4 765656908	6 923074461	5 759613157	8 433304011	6 930861199	7 881425974
4 265367793	6 23155434	8 579486917	7 872096458	6 8422785967	5 894404393	8 949932951	9 152956737	7 664390391	6 957812707	10 1951313
7 348477879	5 477661574	4 856587246	4 546880806	3 910401354	4 476991283	5 58819245	4 87485759	8 777689739	4 957828292	7 868451523
10 85657686	10 50471267	11 23570989	10 74474382	9 976876739	9 715376513	11 03551853	10 94381045	12 6131229	6 107074264	12 28373384
6 284048083	3 583147063	8 194717803	8 032878643	4 299908053	4 193406052	10 70096561	9 864631644	9 99262024	6 867032304	12 37390597
5 98181054	6 342620694	6 853982603	6 319927472	5 744434454	5 253392226	6 767455411	6 642829383	6 95384304	5 666724815	6 966936933
7 727667444	8 567633003	6 936359342	7 699078196	6 588446502	5 598949022	8 809684506	8 778004216	9 51129026	5 728602092	10 1502673
4 593600945	5 470255481	6 329688799	5 897731285	4 439854359	5 275132251	6 704239901	6 568071027	8 873458748	5 978588697	7 5985804324
6 217538172	9 332992295	8 520030252	7 422811164	6 093465379	6 071009272	8 944114462	8 491826917	7 759528192	7 086389447	10 85173499
7 294439386	9 163458094	11 17517891	11 12902454	8 55390924	7 714744614	11 90338164	11 75925485	11 72335318	7 94457451	13 4649809
6 151347972	4 674020912	4 696569645	4 553716499	4 431478159	4 49203424	6 789848924	5 883956241	4 931006461	5 336487909	7 749755086
5 654525379	4 798143089	6 498468481	5 724381679	5 721143259	5 200699749	6 133353446	6 189583846	5 443588603	5 604174937	6 462232311
7 39731528	6 225606934	7 789157141	6 49825845	6 319469165	6 261842253	7 831103757	7 127921458	6 727950038	5 973339712	7 770156564
4 924666358	4 874546206	5 591129098	5 680582248	5 200590771	5 170002614	6 059030988	5 584961067	5 541228819	6 195361071	7 305326839
6 414140154	5 45036033	5 976721133	6 787253394	4 560610799	4 60750664	7 946541604	6 18701445	8 678731661	5 832815473	9 879629424
3 46617276	4 22642203	4 270073929	4 373718606	3 948670569	3 879498336	6 152633421	5 723578593	8 465872615	4 727469696	7 383198032
6 438694462	7 321839645	9 85193297	10 26705081	8 120145336	6 238977427	10 41757396	10 23090381	12 14734076	6 722098023	12 95850239
7 954602697	6 954516027	9 492463497	10 3348766	7 976774239	6 199502762	10 80514068	10 50932354	10 58803787	6 830834041	12 95242891
5 587146399	5 280809344	6 967997876	6 387522698	5 85295931	4 970127406	6 741573961	6 583032859	5 416011594	6 027407565	7 119836007
6 456265182	9 788377112	8 714818084	6 971465354	6 099586762	5 268144352	8 291009292	9 344214954	7 040073142	6 090431252	10 45962906
3 736131664	5 843170207	6 075386411	7 124732228	3 374094616	3 865898687	9 139411236	7 846243229	10 90811148	4 542321686	9 971318069
3 571481644	3 839142444	6 337499794	4 751933977	4 101956802	4 195572094	7 06884291	6 340065267	4 225278664	5 045886582	6 242655675
7 361859979	6 882225864	7 690180963	6 0009981							

Lung GSM117829	Lung GSM117832	Lung GSM117871	Lung GSM117770	Lung GSM117772	Lung GSM137910	Lung GSM137912	Lung GSM137916	Lung GSM137931
Squamous cell carcinoma	Adenocarcinoma, NOS*	Bronchioalveolar carcinoma	Adenocarcinoma, NOS*	Bronchioalveolar carcinoma	Adenocarcinoma, NOS*	Adenocarcinoma, NOS*	Adenocarcinoma, NOS*	Adenocarcinoma, NOS*
8.634802373	7.995736829	6.843939329	6.740470049	7.306017368	8.104173884	8.345957475	8.640351825	7.486377657
7.068151979	5.923329498	5.00367088	5.169348261	5.809244712	6.231548015	6.281356382	6.719255043	5.756485726
9.943417122	9.59624339	8.225413964	8.382903124	9.537725298	9.430748541	9.384534036	9.52894223	9.466740149
6.084720776	5.059609191	4.886639695	4.84748042	4.890070658	5.045297224	5.410040489	5.790691417	4.718796629
8.039404024	7.516223362	6.841481482	7.025382649	7.89759177	7.889254419	8.700586579	8.172802118	7.690045922
7.251945648	6.790896751	5.699649144	5.378603135	6.293726239	6.357894218	7.271524731	6.863994414	6.438503504
8.097068173	8.75770458	7.770036482	7.775009288	9.223769317	9.336982559	9.849155157	9.560308186	9.635333467
9.90344734	9.714780432	7.997801458	8.861761015	9.353060708	9.489200497	10.08226461	9.475333287	9.236729455
8.309093783	7.767444427	7.054020894	7.429211367	8.169120023	7.86241229	8.606123021	8.352112237	8.020855516
8.379565789	7.808499011	6.418902748	7.316425748	7.836388962	7.661142021	8.102656326	8.034366559	7.551409432
10.85124288	10.95566885	9.692615691	9.146760552	10.61843533	10.9807578	11.25892846	10.89206131	10.95807686
6.780552779	7.318674442	6.417863356	5.077282634	6.36042979	7.114271448	7.57255143	7.895363763	7.518597839
7.484892998	7.30374944	5.750053776	6.306483458	7.092822758	7.081898645	7.759560569	7.549093347	6.847273869
7.817786642	7.078521048	5.283656555	6.167848795	7.091854049	6.912051082	7.722267007	7.533908959	6.834281509
6.504847886	6.513918057	5.191061994	5.155565625	6.761108158	5.432921248	6.72153317	6.265321181	6.893300904
9.122257118	8.511981583	7.040172181	7.958043235	8.782411999	8.828448319	9.589094892	8.862910092	8.027656722
7.715638224	7.80804466	7.330700833	6.548665728	7.207846414	7.307087047	8.158324043	7.795435941	7.851711016
8.980004141	8.488787317	6.440871797	7.513354273	8.377214191	8.452216943	9.172228958	8.9232823	7.900539866
8.199382199	7.266845129	5.357854867	4.450110769	7.380107782	7.72629222	8.426384694	7.523642005	4.265306564
10.57901621	8.09692431	8.200379983	6.967911344	8.826604191	10.04866246	11.13121699	11.10263408	8.935108107
7.11767393	7.693518301	6.862601661	6.496225834	7.34359538	7.737160047	8.575307917	8.527009537	8.071766185
8.847136521	7.729161677	4.04537028	5.606312503	8.418615637	8.914057932	9.14414013	8.113721887	4.682392872
12.45713006	12.18134372	10.27065122	11.12974575	11.59650474	11.99501968	12.50784222	12.43970566	11.75232603
8.056299938	8.012333801	7.222050862	7.18219583	7.908013276	7.775861952	8.905370147	8.492139797	7.833217043
7.820623893	7.464343859	6.365030856	6.509769248	7.146479896	7.666191898	8.662475886	7.814298473	6.19262372
6.050281383	6.163473562	5.947532658	5.220649076	5.776791284	5.969455556	6.564581998	6.321009133	6.195797774
6.89124755	6.813158541	6.517486843	6.074786405	6.999289944	7.349070434	7.853773186	7.37248694	7.631626419
7.239232371	7.103378308	5.843939641	6.239818958	7.456883103	7.24886964	7.853643681	7.34454398	6.179345178
7.549598075	6.814985328	5.663662811	5.917286338	6.167481129	6.103274127	7.164997212	6.547682721	6.408997385
5.847700417	5.920980219	4.617816997	4.095027814	5.715864897	6.313712311	6.071049527	5.691059119	6.604041737
7.478958579	6.826719623	6.628840255	6.102595393	6.966618485	6.536966778	8.887837113	7.796501186	8.906418289
7.608797501	7.648173318	7.478373811	6.0411141	6.818572095	7.806503453	7.855027335	7.785659627	6.27539482
6.905552693	7.041524723	7.131577057	6.531741142	6.587992866	7.264192612	7.613023515	7.817771408	7.296409557
4.658111065	4.518671682	4.414984411	3.818150364	4.88461545	4.888692989	5.276300099	4.950815195	5.543508558
5.646302357	5.655291817	4.373685294	6.085962566	5.684951876	5.626409082	6.049271362	5.502955564	5.583657173
12.04449679	12.03997519	10.41587661	11.3589613	11.34839471	12.0037931	12.51535549	12.29003744	11.68279952
6.883122351	7.224526807	5.900237086	6.445313464	6.403151333	6.305581986	6.995111983	6.439019204	6.13423198
6.439347745	6.873898745	4.952041835	5.338290208	6.636493828	6.580877028	7.329007486	6.131799319	4.937153822
7.35249392	7.511487823	6.956335896	6.476706975	8.599469756	7.625863833	8.472868498	7.712445395	8.622317039
7.272465089	6.437953451	7.007047811	5.498914615	7.831312582	6.542166382	7.192057488	7.166443657	5.993660997
6.216020111	6.806899951	5.591078263	7.342063132	7.165903307	6.858173579	8.374326579	7.710878479	6.879694554
9.047732929	8.206898272	6.888685131	8.468756289	9.434779343	9.222899277	9.47525565	8.385580239	5.753947795
6.455615886	6.118605046	4.519978164	5.314843811	5.727804757	6.242255567	7.089819723	6.85280366	6.773283073
11.40338368	11.3883491	10.14491299	10.48585492	11.01835764	11.45359499	12.06402152	11.80077982	11.29135362
12.43701888	10.70025633	10.17056533	9.530623077	11.0351945	11.91893123	12.48799245	12.41648088	10.85011992
6.427486175	6.9098741	5.93154672	5.496841923	6.711542109	6.356592518	7.106642994	7.314634858	7.72830566
8.718922598	8.120643029	7.448023943	7.096025617	8.378895588	7.898702351	9.195802488	8.642599152	8.163303722
6.259940993	6.904325103	6.272367161	6.187054116	6.604569045	6.892857923	7.2205824	6.906944495	7.019995663
8.710600808	9.356902361	8.275802334	8.162710022	9.246472396	9.072055059	9.968224669	8.97585674	9.050442585
12.90082997	12.62366209	11.01315484	11.82473884	12.26124016	12.54725351	12.8351824	12.90129124	12.32193731
7.44587946	7.159244854	5.439637538	5.724661808	6.763740455	7.211063369	7.247059209	6.603030167	8.09959011
6.158505035	6.559099421	5.488292861	5.580490831	5.927650334	5.577468905	6.960925324	6.745609463	6.600484899
7.936992493	7.64835148	6.947964949	7.506399748	7.701354673	7.681082637	8.403509945	8.246355631	8.257572556
7.419677637	6.264537197	5.992994993	5.90883712	6.403661676	6.522803603	7.329498688	6.689602812	5.885489139
9.081689652	7.338061337	6.424009809	6.791118093	7.244324234	7.758547983	8.705363529	7.900791937	5.895361138
5.790373172	5.353301121	3.971548269	5.392310175	6.141589894	6.084491606	6.840721703	6.524600197	6.115299971
11.93013184	11.52361044	9.399093202	11.0964967	11.03845898	11.5557555	11.99340984	11.80727393	10.83307735
11.513333991	11.93061773	9.23117599	11.05068291	11.05612695	11.36513343	11.79598783	11.65007935	10.38023645
6.768894501	6.499080876	6.661782664	6.055883281	6.699153442	6.859515978	7.32560366	7.030092025	6.756875145
8.984194705	8.713064545	8.445370675	7.180112644	9.266066992	9.25266119	10.43145106	9.321083342	9.575137954
8.916248039	9.064181921	8.055502677	7.905152873	10.47987408	9.382891401	10.16179729	9.305510936	10.28340149
5.897055656	5.178018202	5.170017373	4.113056598	5.267891509	4.456273065	6.079539343	5.807883405	4.105128387
7.72389185	7.261415221	6.489180859	5.163277836	8.468869533	8.80688439	8.373443454	9.056096688	8.425394151
9.29040922	8.598553106	8.736761646	8.770534597	8.889655243	8.782629606	8.814258553	8.451393076	8.294543916
8.370412115	6.456136899	6.223862266	5.519535746	6.207258722	7.439775259	7.118013086	7.846806967	7.487058395
11.71276629	11.89697723	9.569803329	10.64668237	11.3924841	11.64105576	11.99411172	11.89157259	11.4176034
6.273252012	6.463451367	6.868511347	5.804260527	6.214165981	6.257019503	6.793089603	6.487604699	6.251496364
9.258443721	9.000124904	8.78932927	7.67825096	8.967670355	9.472191517	10.12987918	9.872832935	9.580774723
8.730077888	8.117398767	7.501041195	5.301203358	8.629482113	7.989117205	9.324995233	8.551987943	6.989095182
9.883005964	8.381691151	6.51079629	7.514600797	8.744292879	8.663338912	9.994450683	9.066875209	5.619338238
8.301045397	7.334250717	5.56438304	6.378400212	7.444562782	7.971429646	9.960812417	9.519830458	6.809497914
8.37090518	8.08184476	6.940366341	6.423150786	9.100166997	7.729759897	8.993950834	8.51095942	9.165007455
10.35850587	9.10035829	7.595258154	8.275052028	8.883111976	9.130578648	10.29359885	9.621210155	7.458919127
7.737829385	5.817819837	4.437119237	7.460474709	4.743435256	5.433438221	6.17112924	4.607861023	5.279586254
9.430585157	8.095889757	7.021831215	6.234424171	7.708657176	8.344174965	9.448219184	8.962589171	6.447037352
9.696504549	9.509650674	8.040500707	8.191029949	9.611391871	9.040292768	9.926833832	9.636530885	8.45259383
9.80748999	8.846398779	7.442112436	7.564902087	7.670468429	8.673294677	10.0860044	9.558982002	8.824805299
5.617579281	5.80693417	5.342069988	4.943688132	5.157876486	4.89775263	5.894356531	5.542212901	5.67935577
7.984578885	8.09785724	6.867802281	7.075901556	7.229285815	7.503742672	7.577278421	7.719134345	7.435982888

Lung GSM137945 Adenocarcinoma, NOS ⁺	Lung GSM138001 Bronchioalveolar carcinoma	Lung GSM138002 Adenocarcinoma, NOS ⁻	Lung GSM46843 Bronchioalveolar carcinoma	Lung GSM46850 Squamous cell carcinoma	Lung GSM46860 Bronchioalveolar carcinoma	Lung GSM46868 Squamous cell carcinoma	Lung GSM46884 Squamous cell carcinoma	Lung GSM46904 Bronchioalveolar carcinoma	Lung GSM46936 Squamous cell carcinoma
7 013128528	7 908286835	6 901578833	7 730268012	8 396893636	7 015408891	7 77949746	8 954621242	7 688138343	7 581209833
5 346973005	5 992983547	5 297690523	5 767505983	6 395876129	5 224010665	5 520149172	7 014169016	5 205436218	5 465070807
8 725650711	8 907241359	7 91039247	10 1608033	10 15951713	9 242019218	9 166831641	11 04275561	9 629592063	9 984825668
4 726998189	5 359456759	4 756375213	5 224904427	5 858641236	4 91387766	5 04032611	5 508076367	4 754805791	4 775648533
6 100837243	6 724085748	6 774585263	7 353548324	8 054548991	6 723595386	7 446882963	9 192432825	7 510842717	7 770796999
5 742593532	5 883671832	5 96019608	7 125304888	8 121584431	5 763414541	6 914542364	9 115318723	6 709673724	7 662832665
8 250225405	8 863620568	8 317321067	8 946512656	9 308367534	8 637026501	8 057247181	10 81489013	9 153833733	10 00394817
8 197416182	8 065194071	8 537763046	9 599909825	10 01027787	8 628537544	8 825008263	11 05858563	8 438191509	9 543682471
6 952386628	7 191630707	7 202312074	8 008620344	8 718708474	7 434030352	8 207092911	9 409808739	8 00187819	8 170366111
6 578374753	6 731759535	6 955589051	8 504500293	8 685690699	7 474020228	7 424776899	10 02325651	7 31844866	8 041027445
9 839325959	9 76738822	10 3028788	10 38217471	11 59735653	10 39116977	10 43738188	12 14905667	10 2884432	11 02502878
6 47090245	7 192569697	6 53363837	6 507184138	7 161331739	6 665777837	5 453243746	8 058397176	5 822501314	7 25513112
5 941852752	5 82016833	5 96302816	6 995574342	7 907202544	6 875080418	6 597850514	8 70030312	5 970825511	7 162802396
5 907160267	5 784984139	5 889109917	7 550730953	8 730617333	7 170898616	6 502894562	9 444409227	6 040868086	6 402384508
5 988364053	5 916740459	5 809482503	7 207601968	7 537963462	6 266595861	6 988104754	8 492453984	7 311019064	7 766063452
6 844825853	7 053626283	7 177096053	8 335610462	10 39167826	6 594497564	8 491874491	11 22134726	7 509337836	9 368642197
7 182465474	7 282856873	6 514906103	6 815191124	7 893169188	6 925971108	7 888182953	8 835731758	8 230606438	7 893136972
7 474308007	7 195788644	7 004082445	7 201039107	9 419027935	7 642996229	7 683510907	10 20189234	6 19684329	9 730910187
3 861260707	3 959752961	5 118877845	3 872497504	8 955971359	5 775486355	5 440774557	8 288325339	3 705588615	7 683312382
5 407378338	5 622871362	4 998968503	7 624434295	10 82858642	8 396505475	8 752749382	10 98870195	7 431744412	10 07642542
7 551022403	8 022554784	7 438317105	8 534381621	8 325835476	7 518798711	8 053097366	8 976030654	8 907817984	8 372304801
3 960269459	4 040076592	5 918271355	4 694179773	9 086585985	5 960611541	6 450720246	8 676429085	3 936630279	8 162446759
10 37033125	10 07651558	10 78266393	11 15449722	12 73466184	10 90618717	11 00247554	13 50361763	10 3341016	12 38213292
7 704314334	7 548171027	7 263813104	8 333885881	8 496195155	7 836272927	8 323150371	9 71903962	8 510275873	8 42041293
6 106235445	6 122036343	6 150055021	6 8818578	8 904685135	7 402076128	7 02534641	8 903061966	5 921381494	7 830375119
6 100824676	5 983551005	6 16505337	7 216091756	6 536961277	6 087034191	6 329941857	6 939372462	7 319686866	8 827898983
6 875468354	7 51449365	6 15607737	7 735888606	7 864917064	7 053749264	7 450377513	8 759862981	8 654422316	7 912483288
5 130492562	5 345480288	5 964381227	6 323246484	8 378234136	7 394590279	7 479474954	8 974900557	8 151765648	8 350298436
6 095079831	6 888475943	6 09775266	7 867581264	7 385584772	7 043931876	6 996322137	7 998006612	7 947919514	7 294339323
5 75460509	5 241546658	4 976194768	5 558653702	7 017107774	5 125604888	5 783157949	8 269366168	5 589904184	6 401208172
6 624624415	6 752586916	6 589354154	6 683667138	8 08479972	7 990187145	6 086468849	9 041462817	6 245644388	7 310065107
5 84824392	6 061611541	7 108684683	6 295128894	8 795397449	8 361620318	7 299576139	8 707080266	6 442150412	6 823685004
7 037020219	7 304094135	7 134172437	7 059652582	7 454436243	6 56285482	7 347911894	8 639875462	7 604487532	7 525446192
4 95000313	4 814029093	4 352571704	4 78543265	4 894951625	4 741723584	4 062966565	7 022370831	4 981040182	5 542911162
4 060170998	6 187564868	4 605114537	5 875855524	6 30816759	5 533892324	5 161465439	6 587750311	5 497746394	6 183060544
10 48533091	10 7930194	10 95605213	11 47547189	12 61851148	11 28420583	11 22933404	13 42904806	11 64439509	12 2976577
5 686572789	5 638149968	5 756491037	6 542283687	7 097737756	6 313408862	5 748507664	7 83019109	6 771510907	6 82750191
5 424874315	5 119081316	5 067240203	7 154246856	6 91812747	6 087854884	6 252680582	9 471390605	6 216790491	7 442967796
6 976306452	7 402989669	6 282874273	7 708782003	8 880314769	8 395968255	7 524998745	9 089730949	8 21056522	8 367838667
6 855397057	7 551589647	6 490658854	7 180619593	7 505262581	7 742595887	6 99932538	8 029227876	8 263299592	7 715861243
6 457648278	6 351173226	6 399502771	7 10764277	7 593373407	7 343188733	7 391953905	8 855506264	7 672752385	8 436618241
6 48567307	6 837895458	7 245106603	7 850057647	9 906846287	8 712414978	8 582637116	10 44150917	6 813854214	9 715553538
5 318103258	6 091654139	5 197292556	6 473424069	8 161282901	7 072767126	5 205884247	9 226364462	5 975373066	6 879478793
10 44105987	10 78278073	10 82249959	11 13443357	11 91228573	10 9666201	10 79108778	12 83655616	11 48247503	11 50612945
7 284098827	7 978371781	7 630168392	9 645661805	12 06259989	9 694991782	11 11290477	12 36789239	10 05981841	11 7305764
6 746064675	7 412867377	5 767548012	7 42109345	7 164593928	6 970845818	7 266688859	7 82594954	8 40559629	7 374130018
7 322369559	8 139346715	8 409078913	9 674866406	9 743819608	7 883944731	9 08723894	10 62931761	5 919853883	9 588668324
5 929631674	6 511447162	5 866626033	6 938669887	7 234267856	6 433371937	6 496885284	7 870313194	7 060742817	6 996284895
8 226889667	8 679646369	8 69991722	9 899612808	9 528304768	9 675005277	8 422140257	9 981961246	10 38164872	9 475056959
11 15740287	10 93887366	11 52618659	11 61992187	13 01436475	11 56238051	11 55713753	13 66313939	11 1475596	12 84559012
5 77982792	6 090994233	5 921526332	6 107725551	8 765688879	8 256025373	6 592376062	8 9881936	7 217329324	7 170621734
5 545110692	6 555797243	5 771745948	6 621786875	6 285235289	6 323474841	6 647140049	7 30400553	7 261548673	6 301746781
7 438632528	8 081676521	7 293566995	8 90697486	7 778993815	7 694407366	7 919797657	9 033083024	9 261896654	8 32854262
5 364373853	6 064517079	6 234224984	6 178921108	7 570587519	5 884335301	6 866313911	8 571529632	5 776132888	7 051066678
4 534841115	5 493737819	5 327836118	7 446003185	9 679339028	8 202185244	7 227164217	10 07747512	5 82682883	8 115198063
4 761300394	5 500177506	4 164118576	6 29454898	6 656346587	6 170947657	5 318111122	8 6075806	6 549101874	6 968020379
9 051628042	9 691586128	10 37162635	10 55661198	11 96212570	10 465133	10 27330522	13 11737666	9 629956276	11 645898994
9 183541652	8 696439794	11 58263843	10 76600662	12 10925892	9 808566812	10 89158895	13 29610054	9 425370398	12 04648106
6 692179883	6 811310414	6 49124928	6 955293211	7 09000848	6 466912505	6 995801249	7 278781211	6 652171558	6 994185043
9 015756251	8 917954557	7 328565107	7 725829866	9 488803977	8 167899723	8 279663116	9 243383068	8 003720068	8 651737034
8 434264579	9 270306124	9 28804211	8 953411956	9 886281103	9 874123487	6 674468986	10 70570197	9 552365649	9 629688437
4 67982489	5 485576485	4 270402187	5 579918525	5 292565382	5 581736642	3 679792743	5 843774838	5 125072826	5 771141099
6 772073355	7 839972165	7 273728892	8 579802642	8 188360195	7 318671867	6 894400554	9 022347417	7 940784162	8 083131858
7 738277931	8 54612918	9 141047719	9 428921238	9 035048647	8 662718739	8 470078341	9 929730389	8 892987849	8 811717243
5 181322219	6 3821559	6 476203014	7 170335004	7 26483906	6 657013308	6 911723042	8 379387876	7 679197619	7 520491529
9 394969105	9 906181431	10 24417303	10 51119664	12 07666982	10 82210828	10 81873916	12 9936321	9 578258265	11 53708274
6 046621117	6 352096688	6 017895803	7 381526929	6 312721098	6 32081397	6 343194503	7 342306527	8 197016679	6 847375904
8 618031096	9 49854178	8 622694404	9 78679619	9 846198656	8 325428696	9 892122252	10 81612978	9 93496656	9 476328763
8 005783378	8 080385323	5 133511581	8 772564308	7 6965					

Lung GSM46973	Lung GSM46976	Lung GSM53167	Lung GSM76488	Lung GSM88949	Lung GSM88953	Lung GSM88981	Lung GSM89046	Lung GSM89060	Endometrius GSM46927
Squamous cell carcinoma	Squamous cell carcinoma	Squamous cell carcinoma	Bronchioloalveolar carcinoma	Squamous cell carcinoma	Bronchioloalveolar carcinoma	Bronchioloalveolar carcinoma	Adenocarcinoma, NOS*	Adenocarcinoma, NOS*	Endometriod carcinoma
8 055268481	6 988144647	7 384201985	9 257956035	6 971208024	8 358726084	8 00217668	7 83705994	8 061758157	7 415689923
6 260160202	5 29731663	5 839333643	6 789399508	5 919954425	6 700341545	6 171153364	6 029120965	6 37009658	5 473776313
10 36697347	8 982858737	9 295317904	10 67596023	8 787264024	10 87024198	9 934246094	10 04240843	9 048792876	11 25120499
6 281815265	4 764548974	5 256530669	6 25058284	5 250166825	6 23226569	5 434895014	5 565916349	5 399389594	5 097379909
8 257802021	7 929870898	7 932251041	8 992578907	7 708423375	8 496735472	7 577286448	8 275078754	7 080850278	7 829895705
7 850397635	7 387774332	7 375295403	8 916208482	6 523310059	8 758572949	5 544258272	7 929712052	5 671950327	7 239642619
9 166008932	8 878645506	9 045244147	10 63109349	8 739923642	10 20312339	9 775628479	10 26344479	8 333051709	8 791190596
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7 194351668	6 634590901	6 226964909	7 431853724	6 280843987	7 289879153	7 395067465	7 53316375	6 511966483	7 51442781
9 364973835	8 910365733	9 414098192	10 39306118	7 954618292	9 585137129	6 634816792	10 09750038	7 233777549	8 971958775
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9 367799665	7 712863692	8 624150846	9 823327211	8 088286065	9 362383962	7 042262989	10 03317585	10 03317585	7 861794637
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7 927200268	7 303248055	6 273871982	8 446792243	6 534721702	7 538066074	8 186379501	7 856130474	7 07431228	7 960251794
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9 754955345	9 087029146	9 726140171	10 89781886	8 578714408	10 93546727	9 876368104	9 994075467	9 450528408	9 403479506
12 67586079	12 070443	12 8542126	13 482833	12 39938163	13 49910085	11 40818394	13 33469016	11 73002447	12 67603189
7 31778598	7 934828527	6 61590363	7 958506297	6 304634749	6 096689453	6 096689453	8 317148105	6 992524303	5 93126460
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7 315733442	7 765270022	7 034684318	8 571549773	7 239906192	7 514034245	8 856446629	7 901580624	7 896901777	8 254001773
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9 454780673	8 294905704	8 114945232	9 081256825	7 805482073	7 391447443	6 646527803	8 933242306	6 638865368	9 25016461
5 566380646	6 292869525	6 227724495	7 960114963	4 722132579	6 642332308	6 190151071	6 773397031	4 476550018	6 705623458
11 22532441	10 81720846	11 84075876	12 85856444	11 29264237	12 97203879	10 12552999	12 78021868	10 5737797	11 36377569
11 95196709	10 80207297	11 73732185	12 93234945	11 35877183	11 2146242	9 783529704	13 00770833	10 07066994	11 60357785
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8 570875982	9 382112838	9 656258732	10 85336111	9 187077097	10 36063456	9 141600382	10 47273475	8 811659109	9 472784431
5 337612174	5 617171373	4 938492629	7 080159557	3 925712658	5 313671184	4 815355308	6 763292172	4 648205386	6 950960552
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5 98170785	6 637720184	6 634281319	7 709215953	6 855350197	6 94447755	7 786771912	6 764102726	6 657433301	7 139830125
11 30917521	10 88141087	12 02083751	12 48601808	11 06499791	12 75017521	9 946554843	12 45560644	10 19689418	11 73718271
6 074110294	6 872058842	6 590273946	6 837477715	6 207768743	7 06664616	6 402789945	7 523448916	6 66233153	6 90357464
10 01502243	9 046445354	10 25907595	10 71635719	9 448037832	11 62355402	10 27084326	10 28181325	8 798939565	10 75313063
7 269138886	8 714037629								

Endometrioid GSM46937	Endometrioid GSM46949	Endometrioid GSM53053	Endometrioid GSM53065	Endometrioid GSM53067	Endometrioid GSM53075	Endometrioid GSM53084	Endometrioid GSM53093	Endometrioid GSM53103	Ovary GSM117744	Ovary GSM137904	Ovary GSM46839
Endometrioid carcinoma	Endometrioid carcinoma	Endometrioid carcinoma	Endometrioid carcinoma	Endometrioid carcinoma	Endometrioid carcinoma	Endometrioid carcinoma	Endometrioid carcinoma	Endometrioid carcinoma	Serous Adenocarcinoma	Serous Adenocarcinoma	Papillary Serous Adenocarcinoma
8.393837886	8.423654162	5.992236746	7.080966099	6.860500816	6.660521128	7.670628426	6.267392463	6.733899988	8.552126777	7.700145341	7.950376552
6.615686192	6.812860476	5.253470566	5.728715527	5.734848401	5.539059123	5.531708066	5.287716252	5.158978557	6.873536555	6.062446034	6.192140085
9.851390364	10.36460766	7.18221367	9.053952574	8.7905507	9.161966276	9.139498699	7.954910995	8.354318859	11.69590408	7.440393294	8.866842535
5.181475682	5.534256047	4.960240281	5.020591062	4.865151615	4.96045374	5.090107279	4.94831106	4.820210435	5.948160167	5.364088947	4.543774289
8.473133204	9.200781715	6.894947277	6.88844119	7.309199287	7.651105144	8.275571836	8.866512228	6.980659053	9.76038633	8.763333616	7.990142293
8.832528655	8.599465133	5.250882647	7.754727634	6.581180042	7.142615764	7.42226882	5.550362217	5.601926813	9.008013446	5.415971821	4.759434938
10.08505803	10.20312339	6.429197821	7.837296391	7.370974857	8.471445174	9.872162424	7.722781484	6.756541657	10.91842908	8.139196923	6.786520526
10.3916195	10.64061057	6.624391042	8.852076138	7.911952175	8.593010976	9.370785855	6.892797111	6.791401789	12.01837756	8.323544085	8.762066013
9.254538986	9.726202273	7.546176792	7.908852902	7.97621064	8.064359546	8.647728885	7.255141884	7.361941078	10.02801041	8.924754079	8.27522058
9.541348961	9.596966582	5.468362977	7.448414527	6.719431428	8.100317773	8.513100946	6.180492044	5.978978643	10.98941499	7.3188347	6.742933379
11.80085643	11.58351819	7.981200707	10.23573831	9.584895055	9.436549863	10.60719141	7.831743938	8.249875257	11.89197818	9.876718663	9.263165134
8.215652595	8.212990426	4.636448708	5.928779079	5.549386985	6.659598181	6.581445476	5.433129695	4.445268955	9.215709542	6.063161143	5.975103878
8.660654916	9.009493853	5.609280628	6.470743053	6.55225361	7.22767071	7.33424435	5.296773894	5.849682391	9.286371461	7.10285005	6.42984065
9.20878472	9.07344088	5.36621793	5.737411354	6.442446456	7.236923544	7.334707063	8.868214111	5.612593383	10.29537237	6.205861148	6.873497791
8.066002922	9.136379007	5.820958908	5.410802664	5.338447161	5.969075974	5.996678371	5.322199572	5.930556284	8.186486576	5.82027896	6.859826709
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7.608003203	7.55114305	6.341626003	6.753259486	6.478507104	6.230112664	7.415824961	6.669785263	6.298723406	8.423464135	6.890676507	6.831475086
9.460472948	8.41375912	5.689046165	6.692878781	7.648560922	6.83746558	8.670525712	5.689046165	6.79241389	11.2291405	7.666980639	3.94329462
4.076401814	8.696235472	3.967972137	3.675196282	4.202906534	3.831310933	6.135537099	3.940778047	3.786428587	5.673788121	4.070886334	3.840034777
8.912259908	8.490202965	5.823303736	5.511942462	7.857936924	5.884117023	9.310089268	5.138532988	5.087635034	10.17747638	6.387742211	5.659808142
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4.110915841	9.229325742	4.680727418	4.091484653	4.729628028	4.287432361	7.716910186	3.863710572	4.934229703	6.502957065	4.728105494	4.722371559
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6.710844731	6.801089487	6.159783416	6.159783416	6.159783416	7.007036195	6.662620753	6.662620753	6.662620753	8.45226193	6.01342898	6.01342898
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4.452424											

Ovary GSM4688	Ovary GSM46910	Ovary GSM46918	Ovary GSM53036	Ovary GSM53054	Ovary GSM53069	Ovary GSM53100	Ovary GSM53124	Ovary GSM53129	Ovary GSM53144
Papillary Serous Adenocarcinoma	Papillary Serous Adenocarcinoma	Papillary Serous Adenocarcinoma	Serous Adenocarcinoma	Papillary Serous Adenocarcinoma	Serous Adenocarcinoma	Serous Adenocarcinoma	Papillary Serous Adenocarcinoma	Papillary Serous Adenocarcinoma	Papillary Serous Adenocarcinoma
6 42004137 5 244211104	5 544804446 4 718722708	7 459379517 6 065322479	8 185365595 6 915895972	8 185365595 5 19117062	6 690076611 5 490465325	7 131338893 5 812305569	7 454718616 6 044320923	7 646861468 6 123930387	6 05519599 5 856652953
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Ovary GSM53173	Ovary GSM53185	Ovary GSM76489	Ovary GSM76510	Ovary GSM88948	Ovary GSM88973	Ovary GSM89028	Pancreas GSM117645	Pancreas GSM117647	Pancreas GSM137958	Pancreas GSM152744
Papillary Serous	Papillary Serous	Serous	Serous	Serous	Serous	Serous	Ductal	Adenocarcinoma, NOS	Ductal	Ductal
Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Carcinoma	Carcinoma	Carcinoma	Carcinoma
6 324977062	7 367227861	6 856956844	5 730251194	7 743278927	6 555939849	7 434797254	10 20739575	8 50775024	8 103505091	10 84999453
9 684588447	9 148654325	7 629798274	7 111990257	9 746705749	6 883790501	9 202941974	12 03412103	10 15984016	10 42589377	12 14478186
5 285135851	5 259403523	4 785785192	4 70575843	5 433085406	4 650750353	5 125042778	8 04903768	5 882416867	5 174368211	8 752272493
8 313742663	7 998905288	6 75509006	8 903136714	8 925683513	7 24075358	7 238100129	10 88501485	8 848055945	8 619619496	10 16006495
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11 50970863	8 926113552	4 807427027	3 837200992	11 43455461	3 597170945	6 890447242	13 15709128	11 64857729	12 32974865	13 46130692
5 587755207	6 477183024	6 488954331	5 131520636	6 910250648	5 562143191	7 033833293	7 997265922	5 615689083	7 990795566	8 278271058
10 4751337	8 855104674	6 119848974	6 791694771	10 16827952	8 860272595	9 086532132	11 1532088	9 291683662	9 615111681	11 5820051
6 90086195	6 309734286	6 80415527	5 645473703	7 277773134	6 502809893	7 236195313	9 710520206	6 79878562	8 374947968	6 689316063
10 24415951	9 810309666	9 219294238	8 337835755	9 510761819	8 253187958	9 438432635	12 12752724	9 232135897	10 70955131	12 13365271
13 33863155	12 68500269	11 16198059	11 51694241	13 28444009	11 12824858	12 4580082	13 97742875	12 7452044	13 52908817	14 12688904
6 171742155	5 40865133	4 591001746	4 297835026	6 266317409	5 030449956	5 081264493	9 367963525	5 986248874	10 05116279	9 432968545
5 562879135	6 405008284	6 473817658	6 834154527	5 749570661	5 928453349	6 126192378	8 814544909	6 818281315	6 755098519	7 803980206
7 128286641	7 812494915	7 458886587	6 904787552	7 398911532	6 68450031	7 720427898	9 161381496	7 144490345	9 089250997	9 548653384
7 573440469	6 237887138	5 367765692	5 42083581	7 585618744	5 166236179	5 718119846	9 362038921	6 706332344	7 983519437	9 655210905
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9 425728148	8 683012055	6 827797911	5 935036762	9 879929245	6 999195735	8 056799071	11 93745993	9 789525573	10 81189313	11 89492173
9 520604852	8 470982282	9 496637402	5 751583364	9 30333495	6 537498486	9 461817809	11 66531629	8 767223203	10 72906848	11 35977458
4 201662384	3 918027724	3 485418906	3 558259353	4 363814652	3 533080445	3 893859406	9 952803815	6 262151285	8 675423968	9 535043368
7 081651754	6 405083077	6 638020723	4 717834513	7 854609208	5 614045822	7 326888105	9 80670533	8 720029895</		

Pancreas GSM179781	Pancreas GSM179869	Pancreas GSM203703	Pancreas GSM203761	Pancreas GSM53046	Pancreas GSM89045	Prostate GSM117726	Prostate GSM117727	Prostate GSM117741	Prostate GSM38079
Ductal Carcinoma	Ductal Carcinoma	Ductal Carcinoma	Ductal Carcinoma	non functional islet cell tumour	Ductal Carcinoma	Adenocarcinoma NOS ⁻	Adenocarcinoma NOS ⁻	Adenocarcinoma NOS ⁻	Adenocarcinoma NOS ⁻
8 9701719518	9 119554617	8 357504037	9 260584513	5 946136386	8 382788597	6 365814652	7 37518299	7 963671684	7 192902328
7 884083606	7 757767536	6 598239743	7 640387435	5 321153345	6 922048785	5 162641313	5 799814763	6 294378002	5 781641395
11 78171553	11 19970365	9 997294051	10 70342666	6 940553316	10 90488357	7 433887028	8 74063809	8 981614433	8 766264583
6 523269316	6 697131506	5 480481384	6 302130729	5 734504936	5 50025498	5 041161099	5 378263049	5 696759543	5 127247056
10 30854785	9 041628458	8 723569704	8 870302909	7 676920462	9 780143797	7 148268533	7 381993291	6 608818812	6 9455244
9 762411479	8 919397866	9 163631168	8 227276942	6 187178397	9 500587725	5 461192556	5 392576698	5 878611292	5 528208783
11 80680499	10 78177857	10 8386933	11 67642061	8 265451086	11 74385117	8 16636442	9 518811516	9 003308049	8 736177588
11 85801025	10 99094205	11 09623849	10 38467864	7 134312189	11 69032105	7 831621674	8 215160127	8 615847288	8 216096217
10 80710072	9 696800889	9 245500635	9 410472884	8 595920115	10 3346593	7 081148317	7 354665451	7 098239297	7 325455429
10 74291298	9 473576964	9 85923124	9 154722611	6 074310277	10 30652922	6 761387272	7 23452825	7 225744662	7 239211738
12 67252504	11 86275932	11 77954899	11 98945519	8 078161188	12 03477564	8 909109733	9 108179339	9 156591569	9 781788762
9 80236079	9 466923061	8 919185523	9 717953163	6 060582982	9 88608088	6 228621939	7 054854729	7 450881009	7 420979326
10 15620761	9 25299252	8 812246945	9 001321586	7 241880652	9 494280284	6 011741541	6 302238583	6 067932405	7 048309103
10 23110947	9 019257023	9 144641983	8 599181583	5 777317657	9 944930892	5 922523495	6 40622344	6 393137966	6 236747348
8 697561662	8 333548589	7 746322776	7 589526235	5 24882328	8 599122209	5 709586462	6 929026057	6 44670995	7 462319596
11 92347343	11 01013319	10 89539854	10 92455008	6 631378788	11 12518096	6 90592393	7 030735156	6 84197028	6 705235974
9 589054032	9 469124615	8 250009408	10 822325	6 395281613	9 384709386	7 145366514	7 983666044	7 909380132	8 256223598
11 5811318	10 69675799	10 08731306	9 7652695	5 676623495	11 12853054	6 23311849	6 224396033	5 943354866	6 466210308
11 33196346	10 50599691	8 795196362	11 45992381	3 847213565	10 5373438	3 906822845	4 358446276	6 845406442	5 856567381
11 38120914	11 22813906	9 556668074	8 394293742	9 410719355	11 75853987	5 548785851	6 683871633	6 105400665	7 443093902
8 715158753	8 995600252	8 640842413	8 999419144	7 871389879	9 24927615	6 67797971	6 900305948	7 311461073	7 267681377
11 56686482	11 01657139	9 483738303	11 69944247	4 915945407	11 13682235	4 573538533	5 812603353	8 193431592	5 883758167
13 67971216	13 55635023	13 00546927	12 97765661	10 33837059	13 71127144	10 64150086	11 33453731	10 34975421	11 03306099
9 951342996	9 142122555	9 016051332	10 0341396	7 252023076	9 78848909	7 265084868	7 735778021	8 077517615	8 024500232
10 46516991	9 763084082	9 982414562	7 072435263	5 222901164	9 920406175	5 411078361	6 095046336	5 842031872	5 549755243
7 696420417	7 46282792	6 943141334	7 924174721	6 410964019	7 80582796	5 923577817	6 283143796	6 320966614	6 318954078
9 341907848	9 057967002	8 41769111	8 748905584	5 657949557	9 180975926	6 975501088	8 335878307	8 62184726	8 495504355
10 43045131	10 33367443	9 561042056	8 730756735	5 01900611	9 592024456	4 437612888	5 09162084	6 009675417	5 574475578
9 662835132	8 401640587	8 513782917	6 64027517	4 785015528	9 04390186	6 925964676	8 851020807	7 980623471	9 121210388
8 492559594	6 881123647	5 427036452	6 882541994	4 483288132	7 491714984	4 769220088	5 860311642	6 410682824	5 659054046
10 82945364	10 08236126	9 637336601	11 32773721	5 508272462	9 651207879	5 71028701	6 368235874	8 371083549	7 270953871
9 832352668	9 756327502	8 856654226	7 909534572	4 726779345	9 00401927	6 214874062	6 685804158	5 82007143	5 86015865
8 122323124	7 788239847	8 224189332	9 705133307	7 502588353	9 990547099	6 696304346	6 582652828	7 276651968	5 759441886
9 790699907	6 692266898	6 928378011	8 220474721	4 67107198	9 934343455	4 131208387	4 762391788	4 998535124	4 842427409
8 322355782	7 124817652	7 704858573	5 779563913	4 598131694	8 336408855	5 26455448	6 302503593	6 647721967	5 924496923
13 75108359	13 51534151	13 12257906	12 72952431	10 53222327	13 66311062	10 6763129	11 2737541	10 58389576	11 79030042
8 780871775	8 146329442	8 049456657	8 253050162	6 579878027	8 28935529	5 941775464	6 020317993	6 500232631	6 528273054
9 195047673	8 827248682	9 119147006	8 250452999	5 166206634	9 476836239	4 523005609	6 045079782	5 145204356	5 244123339
9 933764307	9 077865842	9 243662681	7 837440461	5 127214595	8 952121935	6 096951143	6 207274339	6 97994759	7 217362882
8 667213089	8 446583558	7 764234943	7 230773193	5 954163361	8 101434132	5 864916167	6 707391416	6 452966669	7 398227909
9 606971101	9 056782934	8 887037541	8 15654209	5 535499181	9 03665597	5 55527204	5 974224694	5 92854789	5 880198907
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10 07476297	8 363283274	8 627901316	9 918266113	5 124180989	8 980119557	6 058404708	5 497642057	5 621221166	6 615094409
13 1997317	12 78835705	12 5361968	12 68811828	9 75362337	13 01257049	10 43587382	10 88211785	10 54994577	10 77963707
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8 171990455	7 854446802	7 469549257	8 639566951	6 950098775	8 39038778	6 088935978	7 464225491	7 637022311	7 821462318
10 99558034	10 56695115	9 827343025	10 61587189	8 370485339	10 60486361	8 727762813	8 992167024	8 702482975	9 962199651
8 621225355	8 143262886	8 008168605	8 005993247	6 74389303	8 199417688	5 932111712	6 342350931	7 464833499	7 242940548
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8 189537263	7 392685689	6 824287908	7 21185454	5 440195483	7 658846338	5 695583999	7 793917414	7 491770745	6 937041994
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9 255142624	7 910713749	8 281611598	6 22363742	5 272608249	8 709362359	5 116566847	5 29845082	5 227045273	4 060776899
11 34303845	10 83214875	10 05054178	7 191918163	5 895179332	10 18146517	5 967854093	6 882120519	7 12089853	8 548459576
9 396475266	7 54239137	7 427395942	8 156589388	5 546249666	8 443023027	5 354909699	5 631408042	6 282458267	6 028862862
13 42765079	13 023020736	12 93701438	12 31760865	8 550523959	13 37957769	10 34240051	10 62964175	9 85395625	10 40857329
13 73670228	12 97510906	12 81703321	12 22438599	9 050391279	13 57962083	9 555536183	9 863150231	9 029638506	10 21101179
7 901768367	8 215126622	7 707861029	7 773553544	6 382750345	7 785492	7 583663735	8 25244768	8 632478552	8 432609713
11 27463604	10 6507678	9 772974348	10 03244295	6 62274366	10 95400295	6 759183347	7 797525169	8 342267565	8 071705468
11 54972465	10 31190053	10 71561746	9 900403159	6 424097513	10 74348616	7 339527127	7 994195887	8 355134101	7 774953668
7 9848255	7 527635909	7 756976637	8 257434153	4 198971275	8 994875376	5 170052018	4 7704408	4 426799436	4 866916146
9 992547169	8 244698319	8 300514203	9 258567269	5 696571597	9 097837814	6 079509214	7 752411444	9 366156336	8 496919617
10 2763672	9 939243752	9 691150164	8 942097172	7 1185974	9 526503182	7 899429699	8 640244905	8 540613707	6 828852314
8 572466311	8 028514374	7 448065103	8 000322376	4 322446616	7 560464716	6 670788102	6 408685109	7 348263037	6 584676535
13 30266647	12 79847449	12 32530111	12 47726316	10 3466975	12 96699583	10 07761003	10 60321068	9 338065171	10 05658435
9 094745002	8 104121517	8 118664901	7 827682193	6 481397329	8 746501225	5 807320408	5 256903947	5 202713229	6 006214062
11 05206578	10 76501514	9 870245038	11 04284554	9 652231262	11 12357607	9 031248067	9 828218619	9 793210341	9 94834784
9 980134898									

Prostate GSM46866	Prostate GSM53061	Prostate GSM53114	Prostate GSM53152	Prostate GSM76516	Prostate GSM88977	Stomach GSM102495	Stomach GSM152595	Stomach GSM203666
Adenocarcinoma, NOS*	Adenocarcinoma, NOS*	Adenocarcinoma, NOS*	Adenocarcinoma, NOS*	Adenocarcinoma, NOS*	Adenocarcinoma, NOS*	Adenocarcinoma, Diffuse Type	Tubular Adenocarcinoma	Adenocarcinoma
7 348861298	7 236774147	6 15049165	6 892580476	6 944369094	6 571739606	9 275303128	8 339297836	8 735864663
5 676315837	5 753384725	4 886906169	5 593602543	5 420669016	5 394521714	7 215703407	6 519039652	7 210003646
9 079594813	8 273642325	7 588742806	9 033517799	7 563923013	7 68019309	10 75860669	9 697094805	10 04025768
5 038991569	5 124421035	4 907290399	5 373016288	5 313493907	5 143177563	5 768295072	5 754522999	6 622172494
6 749326616	7 702118211	6 693337342	7 511124317	6 754656271	7 076209339	9 15218897	8 557760878	8 6141438
6 467548912	5 728909026	5 072334303	7 692431437	4 910986025	6 124576485	7 876923298	6 607322124	7 309128461
8 342072251	8 673504277	7 916587455	8 4946511	7 809579369	8 017836458	11 41164114	9 654262173	10 583728
7 994068846	7 185697485	6 594898529	8 235433338	7 001219394	7 533290726	10 27193747	9 365998303	9 413078063
7 443129669	7 797695167	6 85873807	8 654724778	7 668876755	6 651643828	9 389440035	8 726192795	9 272760433
7 15289695	6 714434429	6 558301312	6 910295543	6 026404829	6 367579467	8 917260818	8 433667777	8 2337098
9 672801027	9 125699421	9 0884269	10 66097551	8 793342158	8 677431231	11 76774215	10 68957618	11 46856871
6 5554796	6 132180121	5 947433128	6 202237283	6 045785547	6 158463558	9 665819292	8 297451091	8 69183824
6 249104391	6 435844058	5 805817543	7 29537038	5 12506316	6 178683802	8 920859791	8 262176301	8 783001729
6 503430793	5 783902701	5 335424885	6 497032502	5 209560396	5 927290683	8 000593567	7 270619565	7 981763769
7 507698808	6 53600846	6 443322195	6 590289701	6 468329864	6 041818547	7 237761425	7 423438343	9 035095354
7 71665206	6 586861323	6 350796066	8 304886471	5 546159085	6 403639732	9 865707319	8 558563448	9 8798354
7 902080237	7 635832323	7 947810606	7 578539351	7 275173715	6 890347814	7 809929588	7 227366023	9 370687235
6 465782714	5 746184269	4 651830912	8 355329057	4 56854106	6 084730616	9 698033045	8 707862655	9 080833364
5 932678728	6 661582991	3 943285401	7 272813444	4 67104461	8 039728946	11 70977006	10 7575926	11 37344561
8 023456518	7 246228826	6 414115549	9 892839053	6 620803375	7 66531927	10 17403285	10 75117023	9 507737875
7 789522753	7 980255261	7 219181747	7 544093405	7 18833086	7 40523494	8 757429877	7 645521131	8 383090596
5 921142417	7 481852129	4 504197522	8 098324662	5 409471968	8 831277346	12 21717159	10 86614388	11 64660942
10 93929745	10 31130622	8 963111193	11 74571089	9 79398493	10 64858914	13 08319614	12 20163932	13 18947225
8 210810252	7 97694665	7 449339998	7 892870748	7 633680189	7 477678586	9 037768905	7 725428664	9 661994657
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6 44235379	6 31048616	6 422116694	6 423212866	5 684078999	6 028059214	7 210469675	6 373043045	7 735864052
7 903797501	7 399896068	7 41697187	6 491468934	7 59893129	7 119309488	8 995742294	7 346926689	9 45449848
6 453863905	5 699347577	4 651830912	6 556934419	4 717229198	6 445911898	8 587489442	5 908481746	7 082668216
7 947175101	8 35848592	8 215196298	5 833884023	8 482595462	7 454569583	8 167263239	6 979496745	9 613822797
5 721826454	4 742236998	5 218512391	5 586082867	5 217580762	4 843877573	7 90790544	6 667615006	8 901677981
7 872496004	6 693328375	6 30993552	6 696886396	6 375559433	6 681860118	8 784344067	7 378105648	8 941276141
6 506417256	6 270117901	5 908242657	7 292391709	5 75742801	6 117918693	7 559436819	7 975750423	7 282319421
6 682313437	7 492264939	6 887727267	7 137054219	7 016490272	6 417830234	8 091481398	7 497337678	7 697763083
4 517173649	4 957634544	4 560203412	4 339084111	4 536190115	4 170430871	7 161635613	4 672042169	6 550391713
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4 713841613	3 957684953	4 312265155	5 598871986	4 075451333	4 748883455	8 709203295	6 032048063	7 564368917
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10 61407578	10 32418583	9 151464183	10 89685679	9 20528278	10 27928145	12 32849562	11 02375959	11 77444019
9 555670066	9 796823188	8 828450457	11 57571004	8 92248068	9 671043049	11 85009089	11 74141444	11 58983251
7 185858965	6 968313073	6 646414738	6 193872003	6 032056434	6 284043344	8 43520973	6 755529747	8 20885971
9 389859795	8 85410846	8 345236418	8 922011894	8 123530076	8 223069718	8 452411354	8 657448544	10 99036235
7 262112762	6 638135295	5 989375184	6 050492532	5 975744611	6 556355009	8 461287331	7 065165388	8 388500883
9 304771384	8 991835404	8 34169536	9 479444412	8 532602399	8 725911378	10 50653285	8 895959766	10 22797793
11 47498537	11 39201599	10 1218327	12 28721259	10 74795449	11 31524801	13 48424004	12 35589001	13 45319406
6 009578586	4 883675147	4 793733558	5 805869285	4 830363537	5 243934364	10 68102028	6 89151857	7 726763064
6 508049408	7 1632585	7 035568026	5 544192251	7 156720501	5 671632882	7 601045852	6 318188365	7 766675778
8 241142588	8 474135871	8 29834065	6 470122478	8 485441688	7 998843366	9 963963433	8 252681853	9 68994962
4 810608049	5 249443698	5 264629841	5 542520098	4 876565914	5 07463204	6 886041828	5 919690045	6 134213429
8 059163007	6 825708916	5 894139865	8 134359904	5 955760756	7 707214369	8 306646526	7 661600408	8 959640764
6 881472999	5 646963632	5 899148453	4 655865593	4 908854322	5 899640125	8 145758478	6 400444526	7 867028711
10 53850858	10 15663929	8 973403357	11 20698464	9 443635774	9 765300975	12 49851529	10 97381615	11 94809384
10 57828137	9 615370159	8 156387454	11 54815221	8 911920666	9 559313896	11 30038981	11 09842913	11 97086917
8 391154244	7 707245855	7 900514467	6 206781296	7 409761299	7 218558759	8 256466191	6 92123777	8 650724177
8 559382167	7 295894015	6 739268911	9 991817747	6 305062831	7 614711006	11 0053692	9 494960887	9 537105088
8 600774894	8 663103503	7 682462011	8 524802031	7 209633813	8 657271342	10 74736642	8 567519314	10 46666679
6 161327522	4 423645995	3 864725814	3 689826377	3 922780934	5 299228208	9 142799912	7 291589267	9 361802745
8 752749307	7 311448487	8 374858443	6 486315607	7 221107884	7 482544312	9 282159362	8 64109235	10 07796003
7 774044301	8 057620971	7 742894607	7 233097238	8 380374969	7 236202118	8 580208727	7 604918251	8 515926657
7 140711279	6 562830555	6 526895806	6 084944641	6 079322712	6 352777889	7 78781204	6 544208282	7 209348732
10 4274184	10 58298751	9 322190616	10 99948486	9 539282611	10 05491639	12 66748571	11 18984883	12 31004321
6 037521631	6 291738548	5 392611439	6 239569695	5 812439965	6 081898424	7 633752861	6 838859399	7 395399331
9 193291137	9 220083364	9 221225738	9 798187379	9 151656542	8 345254304	9 946829345	10 04277222	11 03328316
8 413948904	7 475782049	4 942005487	5 037128227	5 453954188	8 565329507	11 55021063	9 691784991	11 2296061
7 840080175	7 594549562	5 493404687	8 882046157	5 223959288	7 857664045	9 61955452	7 228112282	9 476964015
8 907125533	9 296306237	8 443300014	8 388955821	7 728191834	9 987235077	9 633388247	8 997673135	9 992880827
9 198598265	8 365600784	9 02643665	7 597510168	7 893866599	8 095686421	9 82953352	9 338986274	10 40624122
8 638113835	8 703941409	6 978246679	9 919551469	7 647801295	9 024223984	9 756020128	8 016659205	10 01749793
4 121728074	3 683260607	3 693403211	5 360939591	3 673754201	3 819630713	4 843457506	3 984288135	4 230208808
10 05795417	5 759210755	8 340881496	7 962238915	7 69534214	8 102102173	10 84547005	9 829459191	10 45601729
12 43139282	12 07107939	12 15427537	9 564517104	12 17082206	11 58658206	11 64512317	10 86232033	13 40730023
8 152129626	7 767606438	7 38562109	5 151986497	7 393736851	7 689361845	8 500260003	9 322151339	9 114693728
5 802490987	5 849820396	5 366394355	5 133168644	5 064520006	5 102169664	5 984175523	5 764444646	7 107655577
6 810543245	6 68920752	6 403936755	7 036959413	6 734681125	6 758703299	7 617514819	6 218015301	7 376262827

GSM53039	GSM7652	Thyroid GSM102452	Thyroid GSM102560	Thyroid GSM117723	Thyroid GSM117735	Thyroid GSM138004	Thyroid GSM138023	Thyroid GSM138024	Thyroid GSM88998	Thyroid GSM89038
Adenocarcinoma	Adenocarcinoma	Papillary carcinoma	Papillary carcinoma	Papillary carcinoma	Papillary carcinoma	Papillary carcinoma	Papillary carcinoma	Papillary carcinoma	Papillary carcinoma	Papillary carcinoma
7 177674176	8 735706796	7 040812867	7 407012211	7 285650203	7 556463495	7 62374702	6 78410895	6 685407004	6 78845583	7 448858717
5 385476822	6 500290141	5 315595746	5 687746281	5 120936238	5 98696343	5 70266928	4 868554168	5 360489228	5 63776393	5 9259569104
8 169523423	10 07187084	7 847051254	8 292409036	8 380604156	8 303330459	7 8590532	7 191508955	8 204043722	7 486932573	8 848669276
5 433280957	5 728445546	4 67459215	5 031741989	4 942325734	5 04453328	4 919924109	4 7491957	4 618169628	5 172960492	5 141980262
7 547807748	8 873386368	7 4111763194	7 687293694	7 773427705	7 999035111	8 740001362	7 946607641	7 841153402	7 679098981	7 691801475
6 828952578	8 358436926	5 627578742	6 108471864	5 229558348	6 090942145	5 361722784	5 424395235	5 987439722	5 64218277	4 962560338
7 87404007	10 10557577	8 657404217	9 378726792	10 33257119	10 5495032	10 26962724	8 551033247	10 1824367	10 05658996	10 1661875
8 324298862	10 45396851	7 811420625	8 222732604	8 519917434	9 20045188	6 951547651	6 881847621	8 377405914	8 896561774	7 939586787
7 9883087	9 026737989	7 557249977	7 754710097	7 940283189	8 285375984	8 861311589	8 282615699	8 208364927	8 530830155	8 39426326
7 342256556	9 151330582	6 480158733	7 155903496	6 15286359	7 18102537	5 971073186	5 603253844	6 221415522	5 640417356	6 829133311
9 386171398	11 40692718	8 953057747	9 789030929	9 470018449	10 62827115	7 735962945	6 525707968	8 812169554	8 185855019	9 447254972
5 302739988	7 754778314	6 96926868	7 492290832	7 696095127	8 444790361	8 606683734	6 577668119	8 445017622	8 195902701	8 41805686
6 117105581	8 391741545	6 847795512	7 006314728	7 304998845	7 164252704	6 21479841	7 129267746	7 516932962	7 836372043	7 412543202
6 466159731	8 79677882	5 358659831	6 184451075	5 848404084	6 35048298	4 781356568	4 963361916	5 738073628	5 147051383	5 91126731
6 487243563	7 085525793	6 026777514	4 623522202	4 386625159	6 180021244	4 862520075	4 476683581	5 568218515	4 981013331	5 446381551
8 338822358	10 37332917	7 653896862	8 705463942	7 591683203	6 222173812	6 786026977	6 840602172	7 137517533	6 899231316	7 29656611
7 401485781	7 566679182	6 640912814	6 941340381	7 35188635	7 405947964	7 350681648	7 12944197	7 252312636	6 483427462	7 637804575
7 90530174	9 703532142	7 464152728	7 959815507	6 678197893	7 608763922	6 579500588	5 676478021	6 457030881	6 19053311	7 049738375
8 259726106	9 748272456	4 276200497	3 95906532	3 958403226	5 994924306	4 019462723	3 540520736	3 824665725	3 786447267	4 206208861
7 865192821	9 903747476	8 766869675	9 265178101	8 43599623	9 843001973	5 231442904	6 598510097	5 547614024	6 46414798	6 704774258
6 974459614	8 26178174	6 676926954	7 184471109	7 149648831	8 1746112	7 937849841	6 951144819	8 36069016	7 811557792	8 221815341
8 532635871	10 07501161	4 545776842	5 024780075	4 396858812	6 565692858	4 004657748	3 830080877	4 226852647	4 225485476	5 446962257
10 63659462	13 26692967	10 83105611	11 38293043	11 09229361	11 85030061	9 548898931	9 662699836	11 03724734	9 690652515	10 37853314
6 335416956	8 966592136	7 053405072	7 423312644	7 896753664	7 500835983	7 1788084	5 869873673	8 116990104	7 711780691	8 407472793
6 60538911	7 086334401	6 799722066	6 44401733	6 473589342	8 09858162	5 882127535	5 57533111	6 522991755	5 773633641	6 658229012
5 904120089	6 65142125	5 70062769	5 763278745	6 286741457	7 618610225	6 25210544	5 839059247	5 870248744	5 975097739	6 870315988
6 335088119	7 772977217	5 627533843	6 08867239	7 10735231	7 448094647	6 429532069	5 329720386	6 972657167	7 843690821	8 786478089
6 907349324	7 285752421	5 739898616	5 971251884	5 99449331	6 742126184	5 920073006	5 607497869	6 38839162	5 584836742	5 98103194
6 275951139	7 539408446	7 016117568	7 05586984	7 197597284	6 592999341	7 164203458	6 774593983	7 753619303	7 495691245	6 87751039
5 0598082	7 06409183	4 566285479	4 329241303	4 024937497	5 883970386	4 764375068	4 318727506	4 473118734	8 280322083	5 146681394
6 842552049	7 296857722	6 551320186	7 02866289	5 99449331	7 241036936	5 918006204	6 026786054	6 226529866	6 736998065	7 143705283
7 522059435	9 170051965	6 08466195	7 201077815	6 092672831	6 306887502	7 018065797	6 948551587	5 932796724	6 043577746	7 149736119
7 192242008	8 133821646	6 811748427	6 986120014	7 154441796	7 514337303	7 720705989	7 057890068	7 294443901	7 186979286	8 107444438
4 122959384	5 547611024	4 87537911	5 000265598	6 102398188	5 166526796	6 014237831	4 323737425	5 581828585	5 457179305	6 045218997
5 567195909	6 028293486	4 20836496	5 027117888	5 694684268	6 774109199	4 433364451	5 305751911	5 914304941	5 362725603	5 590510011
11 10689613	13 33654664	11 29615386	11 91228573	11 27559187	12 00570519	10 03015882	9 672946923	11 30764214	10 19591896	11 51651425
6 110686576	6 803558695	5 82552015	6 293343866	6 539001656	6 6399386475	5 957435676	5 855242434	6 15909175	5 75718748	6 740087272
5 083473916	8 049280863	4 826937307	6 369539834	5 364785013	6 250108782	3 739149072	4 722269842	5 681950214	4 353962485	5 041473482
5 85203856	7 47652034	6 48535434	7 405163673	6 153777041	8 210648884	6 932058688	5 485079187	7 04539084	8 095066364	6 331002296
6 662782594	7 132068578	6 247574776	6 197827251	6 203578266	6 624070828	5 914958256	6 734858356	6 341753887	6 369649541	7 369649541
6 560684448	7 218175296	6 07741043	7 062760294	7 3643106	8 197261497	6 645009455	6 036498597	7 294771773	6 67918086	8 024044911
8 521576802	8 874652482	7 163540927	7 592402922	7 237659116	7 237659116	6 874662652	6 6971564	7 633895393	7 161051846	7 627510043
5 45837308	7 093335147	6 643283029	6 623230867	5 552625735	6 322739537	4 850619102	6 486959749	6 065271143	5 497903489	6 73074338
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10 34872816	11 49657507	10 53878476	10 97911747	10 68511998	11 59295082	7 218665948	9 081271987	7 673694451	8 378132112	8 730556999
5 978024043	7 401506382	6 60084949	6 055766131	6 500472113	7 59320174	6 94867492	5 721344627	6 952548964	6 337948028	7 755761979
8 093815983	9 823117312	6 988751079	8 090096414	8 048442523	8 210200705	7 121458713	5 919092963	7 219614047	7 871480709	8 553982091
5 969605344	7 369292959	6 83349081	6 215523142	7 937524099	7 720233823	5 293970492	6 226984909	6 906067353	6 47890745	7 953727987
7 570453584	8 778941996	7 99261837	8 800887965	9 022670814	9 415122437	7 417159917	7 247869527	9 614365851	8 544540179	9 448918661
11 56177103	13 57919261	11 50768072	12 08689098	11 80124379	12 49587119	10 2248765	10 23664129	11 7197007	10 7235731	11 22634618
5 368226027	7 927544894	6 34356177	5 615837054	5 430068998	6 200144402	4 977917862	4 497501423	6 249584918	5 201077747	5 702966701
5 642975598	7 566040359	5 733519395	6 031170851	6 053777856	6 222775468	6 571843887	5 768649836	6 381392725	6 248477241	6 373745993
7 170646815	8 230971743	7 423934709	7 556076822	7 918883664	8 429063565	8 078452562	7 023461473	8 329504087	7 769908058	8 880466373
6 095333233	6 767962362	5 285581267	5 610493431	5 160755508	5 899002845	5 780687075	5 484163991	5 376590918	5 064731145	5 200859531
6 397279712	6 767250732	8 327436964	8 653096993	7 673485224	7 668487353	7 234903116	6 91393347	6 110161718	8 140415021	7 29162124
4 523632458	7 39888501	5 77262845	5 79618149	7 637526895	7 715770677	4 044805096	4 346350917	6 24235774	5 780062003	7 722162932
10 70694285	12 92408559	10 56840959	11 60373958	10 31082305	11 39393533	9 366408222	9 178763936	10 38749217	9 371195615	9 718788186
10 42951441	12 64418617	10 14589318	10 94167634	10 11193428	11 14786648	8 820292715	8 354283561	9 93022476	6 896844418	8 897848522
5 568875944	6 722899039	6 488561791	6 346013023	6 883838352	6 931080603	6 505514931	6 303117758	7 040172181	6 215365564	6 938217405
7 417386026	9 657602947	9 51097867	8 451582569	8 021287655	9 568954041	7 818089629	7 322414597	7 730472392	7 461487257	8 763955562
7 410516454	9 482640937	7 605408929	8 916542309	7 845301665	8 83427171	8 181678234	6 084565979	8 699580729	9 72115859	8 126005796
3 67938255	7 587414521	4 961428796	6 581732941	5 413049136	5 846185212	3 955892645	4 238691644	6 001934515	5 019152499	5 811258966
7 15690844	9 228423331	6 338114099	6 376627566	7 160207902	7 39787541	6 686890572	5 946424069	7 095087729	6 647988955	5 837707106
7 759992211	8 370186128	7 316222382	7 298250499	7 995709972	7 819798465	7 568774336	7 402816181	7 256018231	7 471183714	7 841161564
7 034131648	7 448815602	7 086162658	6 714301171	6 862575933	7 265223491	8 11814389	7 359781068	6 859342884	6 375865904	7 537220567
10 52419004	12 95165173	10 32540054	11 28101909	10 27487884	11 56712364	8 88574666	9 158903672	10 51126242	9 342320475	9 85906872
6 024494634	6 941557171	6 014856173	5 860661035	6 332817563						

Appendix Table A2. Continued.

Affy ID	Gene Symbol	Name	Site ID	Urinary Bladder	Urinary Bladder	Urinary Bladder	Urinary Bladder
				GSM102434	GSM102437	GSM117677	GSM137919
			Histology	Urothelial (transitional cell) carcinoma	Urothelial (transitional cell) carcinoma	Urothelial (transitional cell) carcinoma	Urothelial (transitional cell) carcinoma
1555724 s at	TAGLN	Transgelin		1132809644	962612984	128614147	1035724362
228396 at	NA			5574517098	5174008631	8047523107	5476328496
211160 x at	ACTN1	Actinin, alpha 1		8598486675	9971567203	9342964258	9421484207
231823 s at	SH3PXD2B	SH3 and PX domains 2B matrix metalloproteinase 14 (membrane- inserted)		7553848025	7684376139	788505113	7759572243
160020 at	MMP14			7735384576	7520677509	8085969257	8781742747
225782 at	MSRB3	methionine sulfoxide reductase B3		716284178	7035508825	1004434175	6902126926
202202 s at	LAMA4	laminin, alpha 4		7074781231	6548405057	9536869955	7579304551
65718 at	GPR124	G protein-coupled receptor 124		5620881051	5318434225	8009607431	6022248929
231879 at	COL12A1	collagen, type XII, alpha 1 discoidin domain receptor family member 2		5758298335	7011176468	5240180498	628459525
205168 at	DDR2			7013157749	5995128	8005231022	6208898601
202311 s at	COL1A1	collagen, type I, alpha 1		834525984	7530317125	8600740334	6924734501
203083 at	THBS2	thrombospondin 2		9189965664	8734224356	1007044083	9450473042
203835 at	LRRRC32	leucine rich repeat containing 32 ADAM metalloproteinase with thrombospondin type 1 motif, 2 cysteine rich secretory protein LCCL domain containing 2		875134751	6410482718	9263678375	6918447543
214454 at	ADAMTS2			5176180685	4737498809	604001569	5206053216
221541 at	CRISPLD2			8519221634	6548690073	94007741	9659683503
223121 s at	SFRP2	secreted frizzled-related protein 2 discoidin domain receptor family, member 2		9721642248	8088920565	120798299	8195654421
227561 at	DDR2			8536770466	7308985397	1028742783	801518234
224560 at	TIMP2	TIMP metalloproteinase inhibitor 2		8973218986	8511337678	1161824713	10264918
228082 at	ASAM	adipocyte-specific adhesion molecule		5060193617	5532477715	5868518539	5928836509
201109 s at	THBS1	thrombospondin 1		817417259	8416348992	8876493525	1005649563
211813 x at	DCN	decorin		1080017405	9675072832	1305771085	1141314815

Urinary Bladder GSM46829	Urinary Bladder GSM53117	Urinary Bladder GSM53137	Urinary Bladder GSM88993	Urinary Bladder GSM89048	Urinary Bladder GSM89073	Breast GSM46908	Breast GSM46933	Breast GSM46934
Urothelial (transitional cell) carcinoma	Urothelial (transitional cell) carcinoma	Urothelial (transitional cell) carcinoma	Urothelial (transitional cell) carcinoma	Urothelial (transitional cell) carcinoma	Urothelial (transitional cell) carcinoma	Ductal Carcinoma	Ductal Carcinoma	Ductal Carcinoma
12 00348502	10 20408003	7 59033398	10 32061217	9 505736492	12 48312285	6 683434085	10 97078544	11 42649989
7 450558117	5 113528384	4 943707838	5 801082084	5 647300807	6 485897708	6 730503803	6 345824047	7 509870396
9 797907867	8 097621001	7 330513675	8 875679389	7 715034623	9 449343987	7 118667954	8 794551626	9 980339524
9 283929384	7 010781083	7 150528496	7 563712337	6 841467824	8 705315968	6 94689666	9 768714597	9 836120383
8 678090192	7 403471814	7 016810202	7 913425677	7 764809803	7 935856227	7 054106663	8 381713666	8 382508566
9 407424612	6 188291292	3 768492033	5 953963028	5 602379944	8 951558321	7 838520034	7 853853916	8 848251867
8 54956114	5 887837616	4 955784056	6 859179191	6 868989213	8 596259212	8 575297978	8 704447513	8 3035957
6 688920577	5 703004477	5 26535409	5 617662085	5 768270437	6 256713549	7 044583141	6 414151378	7 050422278
9 485793866	4 197929747	5 556045284	6 816068305	5 079595356	7 185443052	4 310366896	7 130774643	8 526368092
8 951057561	6 614011273	5 771395206	6 215260375	5 891545128	7 084844668	5 938023468	7 276774934	8 404009869
10 344580669	7 263635334	4 475493097	7 613879897	6 492717871	9 23087526	5 079329316	9 974666318	10 68725693
11 71571852	8 959506977	8 898339904	9 334476694	7 415365054	11 27315272	11 0317318	10 60270868	11 14935543
7 782152981	6 391935287	6 083394514	6 548949197	6 870317737	7 511277909	5 898489457	6 768143531	8 225343659
5 988411505	4 91039194	4 664726333	5 651494625	5 271599252	5 427354391	5 772862804	5 405930281	5 591249153
10 70887899	8 722962511	6 750454016	8 297232435	7 881277894	9 499561427	8 497427874	8 935352427	9 950952708
12 26817159	7 124513537	5 433927955	8 511177668	8 838730009	6 687465816	7 853989048	11 26522479	12 0546872
9 982159787	8 376638056	5 844874523	7 808530587	7 138785696	9 470819531	8 38785444	9 240436235	9 60138235
11 40683898	8 259621832	7 641977862	9 860456187	8 738634162	11 388701	8 552449857	10 04519191	11 22309164
5 818980004	4 812873225	4 732130162	5 25746194	4 831618421	6 32079473	5 228905787	5 778540312	6 028904962
10 80935473	9 080824537	5 832034402	9 014815291	9 026922128	11 42907858	7 463801363	9 367755708	9 884837163
12 83910498	9 971482676	6 629395418	10 82092642	10 33881883	12 42592617	9 779200254	11 2427367	12 87738342

Breast GSM46947	Breast GSM46952	Breast GSM46953	Breast GSM46954	Breast GSM46955	Breast GSM46958	Breast GSM46962	Kolorektal GSM38075	Kolorektal GSM38077	Kolorektal GSM38089	Kolorektal GSM38105
Duktal Karcinoma	Duktal Karcinoma	Duktal Karcinoma	Duktal Karcinoma	Duktal Karcinoma	Duktal Karcinoma	Duktal Karcinoma	Adenokarcinoma	Adenokarcinoma	Adenokarcinoma	Adenokarcinoma
9 780222128	10 42551337	10 81924904	10 78263114	9 705662624	8 122488837	10 49250243	12 35243324	11 42246683	11 98649248	10 23540787
5 340470015	6 027871996	6 094990634	6 908438791	6 053350409	6 126192378	6 6874691	6 954344851	6 352307342	6 459889222	6 199411384
8 573784595	9 346711057	9 694734764	9 204310818	8 956566644	8 344262767	8 918684532	10 23232478	8 96718611	10 17317467	8 898998095
8 775432039	9 697928976	8 485198229	8 4099952	8 660181596	7 719114506	8 871136669	9 138509862	7 936811934	8 379916102	7 759470806
7 665163028	7 994387969	8 535689922	7 253890072	8 227780237	7 922964037	8 121330949	9 209924931	8 386402722	8 728425387	7 87516939
7 383863481	7 85770392	7 808858792	8 570270068	7 130706077	7 210874485	8 017702787	8 411084925	7 427793193	8 110623425	6 898662841
8 290464743	8 62694164	7 592461468	7 863651863	7 467520708	8 687167862	7 882279887	8 369011549	7 397074725	8 013480847	7 61772747
5 665975468	6 484221955	5 894614054	6 708979799	5 952282043	6 68547032	6 573958425	6 237284956	5 975220846	5 941025747	5 747284762
6 9132877	7 466536252	6 382022059	6 253857637	8 574286895	4 276812409	6 172052579	9 231169608	7 693001681	8 013163652	6 673225842
6 629087077	7 66612304	7 448408237	7 809155296	7 408364526	6 109844987	7 537736215	8 64847261	7 606278568	8 021625988	7 082360342
9 099776805	9 96892524	9 604085319	10 08069922	9 644966825	7 04827184	9 770309558	10 37849385	8 377979168	9 728910413	7 567044537
9 774307314	10 43704475	10 51900701	10 04226792	9 226644874	10 9289364	10 86026249	10 32183753	8 521873321	11 3938837	7 678767045
6 889661538	7 496829095	8 012012772	7 099721208	8 157152043	7 784238368	7 763487503	7 558473825	7 041084028	7 440580293	6 700547053
4 862758859	5 958375717	5 202708473	4 819120352	5 543544943	4 644955545	5 006767585	6 606380211	5 275138007	5 948512386	4 908074181
8 6059557	9 459692902	8 808371813	9 785064579	8 585776928	8 918324749	8 773485337	8 219095164	8 222735011	8 73844528	8 080533773
10 9673414	11 68438196	11 07248573	11 47377974	10 11895504	9 473484062	11 35098611	10 0856391	9 493394305	11 52784423	8 713195389
8 386514288	9 285815679	8 771279866	9 349434564	8 261039241	9 319022856	9 024180066	9 498702838	8 355267897	8 59449884	8 3728122
9 912995119	10 82472385	10 59359323	10 46872899	10 54152108	10 1961632	10 86148958	10 97450392	9 765958745	10 802491	8 945038918
5 342474893	5 283951724	4 964856118	5 109535134	4 942466363	5 26322581	5 400191223	6 031479976	5 677969944	5 526828169	5 741832369
8 950814453	8 879457991	8 185869806	8 7102286	9 210465864	6 98939649	8 975989213	9 438231495	7 810709639	9 439411236	8 847299886
10 73449096	12 31348259	11 9431467	12 17380343	11 30974594	10 74814251	12 2652409	11 86487671	11 34240087	11 48738835	11 12770655

Colorectal GSM38107	Colorectal GSM46819	Colorectal GSM46841	Colorectal GSM46845	Colorectal GSM46856	Colorectal GSM46857	Colorectal GSM46861	Colorectal GSM46865	Colorectal GSM46877	Colorectal GSM46879
Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma
12 3212206	10 95488279	11 78361133	12 06781941	9 883442636	11 57424943	11 95267035	10 82333351	12 05705442	9 97754976
6 95791828	7 495514517	7 316047487	7 389155453	6 676948626	6 925047439	7 422156879	6 709089345	8 158357003	7 480557453
8 807521266	9 554270554	9 438594294	9 77864551	8 901022071	9 667762775	9 665871144	8 774770568	9 290254961	9 027666287
7 519808797	9 448903357	8 001877864	8 238977612	8 280291174	8 767709475	8 835508853	8 397110683	8 714156995	8 513167547
7 382888491	8 406289585	7 829499652	8 570226033	8 078774279	8 74580672	8 324090761	7 9635737	7 920927265	7 438712645
8 948483471	8 853070889	9 083858327	8 576492488	7 10439261	8 251287614	8 798888692	8 127924695	9 762911856	8 89391613
8 261967137	8 873366977	9 031734017	8 804735494	8 06396521	8 345048467	8 759353781	8 8525878	9 465078656	8 52753964
6 057966674	6 77890922	6 216411443	6 346938526	6 130133722	6 246033203	6 408594027	6 307858255	6 97638271	6 640372537
5 984694272	8 122735422	8 268597676	8 751666543	7 293314591	9 051238268	8 595348364	6 229567536	8 175285163	7 35649265
8 259103199	7 710913442	7 88696481	8 162259592	6 786233637	8 26811735	8 348958143	6 985014234	8 666202941	7 67397428
6 458815274	10 75050173	9 421772351	9 62671533	9 33658235	9 914615229	10 29148911	8 546371476	9 91467543	9 772232328
8 080269067	12 17785919	10 13659196	9 969435905	9 344214954	10 91370263	11 44682335	10 56056872	10 69419295	10 93612755
6 974556928	8 269842175	7 382538676	8 008623355	7 102998858	7 800327385	7 727922346	7 533618565	7 953184353	8 395574282
4 842796429	5 716050293	4 867571375	6 056637298	4 968400337	6 167861895	5 404654812	5 104238869	5 45683697	5 298680342
8 555217775	9 821505678	8 431527628	8 693237703	7 807737796	8 761333795	8 996464747	8 249170027	8 926815639	9 404099659
10 89304012	11 82843223	9 239447798	8 899477604	7 848731792	9 365397864	10 34091848	9 061405052	10 22249833	11 90126242
9 833594991	9 657912033	9 506883891	9 209865002	8 505076141	9 141815444	9 529489402	9 204891288	10 10501229	8 912294452
10 02467154	11 01982173	10 56672456	10 04101884	9 784774762	10 64365709	10 50010196	10 32978951	11 05028152	10 20257582
6 141177233	5 771374298	5 76629235	5 997531627	5 070312925	5 950864966	5 923407713	5 147482451	5 883879256	4 881641809
9 471903144	10 66680766	8 819264523	10 62230687	8 742271925	9 778399766	9 842780535	8 266629091	10 23842543	9 992488347
11 97846556	12 22355778	11 62041814	11 19028034	10 56413759	11 76264049	12 02433581	10 77475737	12 00816685	12 21755128

Colorectal GSM46901	Colorectal GSM46969	Colorectal GSM46972	Colorectal GSM53087	Colorectal GSM53132	Colorectal GSM53168	Colorectal GSM76546	Colorectal GSM76571	Colorectal GSM76575
Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma
10 3918224	13 66681097	11 59272065	8 243049867	11 52628348	10 85176489	12 43962059	10 32800693	8 88236654
7 637629686	8 46277129	6 668044825	5 50386548	7 339051331	6 591693694	7 902884596	6 403397287	5 671849722
9 07778078	10 64906668	8 993143413	8 355461883	9 08699936	9 195058044	9 599977668	8 578426293	7 443471653
8 438051744	8 723505497	8 347029356	6 541364535	7 682091666	8 034395361	7 776454915	7 411287327	6 573661767
7 698884137	8 373528473	7 599851517	7 188711441	7 479193494	7 268854177	7 194647527	6 855629801	7 137459551
8 391707321	10 570133374	7 977189513	4 285145507	8 974068156	6 973110588	9 72079893	7 458344534	5 419248348
8 476701894	9 324730934	8 04514717	6 415231866	8 164091834	7 721784278	9 241499058	7 750774319	7 185309572
6 547211249	6 518243024	5 624238783	5 458848405	5 747965989	5 775402878	6 347371537	5 761881758	5 511116661
6 718569029	8 640108942	6 767570003	4 695081897	8 695811773	6 507141617	7 066761845	5 416314134	5 136765723
6 871266394	9 714479653	7 867437105	5 43489006	7 76857805	6 946706457	7 631791693	6 347136621	5 924889129
9 848679134	10 05220276	7 649601748	5 595597652	10 32090741	9 644176366	9 720670059	9 450819496	6 306690278
10 52877467	10 63368868	9 391658034	5 605545999	11 67837675	10 41406197	11 1845896	10 99067472	6 217302363
8 307327375	7 442869635	7 264789295	5 859830012	7 471661755	7 511429605	8 025879347	7 772110036	6 468037733
5 028370192	5 036300758	5 455764839	4 673633818	5 044897599	5 2845665	5 173423405	4 881225514	4 609565179
8 698772832	9 157952678	8 557936721	6 061499905	7 902990973	8 533355013	8 456227324	8 27562767	8 208829843
9 378699301	10 35130501	9 782604155	5 066423863	10 68944084	10 26454136	9 31227578	10 69855193	5 332526697
9 021370094	10 68968884	8 876725491	6 774250082	10 00133977	9 246113811	10 573202	8 597022929	7 799314261
10 18922209	10 91224885	9 523507862	7 042156332	10 0141173	9 817776311	10 30104893	9 051066603	8 319366646
5 346506249	7 228418678	6 334770565	4 537843334	6 000253067	5 307894809	6 035458838	4 671019249	4 876555226
8 938852423	10 39994275	9 489801217	6 242888269	9 879277029	8 459309121	9 038981795	8 95305562	7 914673066
10 93027101	12 34777572	11 39110259	8 005865693	11 27848662	10 18036677	11 15209396	11 44442759	9 173437796

Colorectal GSM88976	Colorectal GSM88982	Colorectal GSM89013	Colorectal GSM89074	Colorectal GSM89075	Colorectal GSM89094	Colorectal GSM89100	Kidney GSM117706	Kidney GSM38073
Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Papillary renal cell carcinoma	Conventional (clear cell) renal carcinoma
10 36291533	9 869601081	10 56123414	9 774906977	8 901667642	13 47564332	13 01858458	7 138124063	10 74724305
6 503081365	5 850038767	7 068044415	6 214672308	6 226047742	8 255319394	7 343023851	6 953135647	7 460685318
8 555994342	8 860890206	8 431455836	8 691457929	8 406737928	9 927488003	9 67293906	7 511157811	8 685565309
6 522789332	7 819752365	7 397587416	7 51215365	7 125908814	8 416698154	8 34594525	6 574993299	7 51005807
7 49576578	7 424826547	7 784770694	7 496426621	7 214497522	7 90308113	7 965229763	7 072640685	7 404884453
6 976464916	6 063465789	7 163099637	6 326112687	5 458061526	10 43484927	9 284365945	7 762679152	7 943105417
8 045469064	7 827203697	8 816793023	7 553450774	7 412544479	9 221867821	8 908813062	9 154099336	8 521851757
5 677083905	5 858244096	6 211126198	5 632669729	5 664191118	6 671073875	6 14600419	5 117514398	6 784883671
4 702202714	6 814610751	6 453810275	6 759079379	4 747231243	7 494455495	7 631816253	3 626391413	5 22811055
5 912401316	6 013474593	6 736583732	5 867772773	5 718218587	8 198936697	7 611361274	5 465137832	6 589971166
6 571516989	7 317489442	8 631410501	7 194701358	4 860625426	10 64433703	10 09723281	4 077412156	4 895441201
9 060962438	9 814953744	10 33528788	8 930238148	6 94369291	11 20304792	11 50969113	7 952160314	6 880355711
7 356064814	7 57205998	8 368065715	7 122161241	6 74842228	8 008246956	8 267389656	5 868729704	8 800555359
4 645985718	5 741493275	6 084612825	5 472641806	4 70745478	6 221167534	6 380046399	4 348029391	4 490822295
8 061581033	8 430452566	9 258949957	7 741075865	7 19008723	10 19798127	9 348882495	5 355455655	7 923235436
6 131963885	6 137604947	8 128353237	7 28902642	4 839937999	12 57017952	10 54130715	4 846525856	5 125307588
8 326960257	8 083106586	8 843100535	7 413877687	7 548035941	10 2035039	9 761444125	6 208461192	7 987166143
9 059412688	9 681525311	10 39270709	9 645751535	8 484514104	11 21985476	10 57131155	10 15500634	9 409171562
4 776292772	5 191730256	5 030407783	5 141954593	4 969316103	6 894454988	5 819405912	4 244344726	3 976779268
7 889801908	8 907143362	8 824725552	8 39307344	8 430102471	9 559444745	9 465291153	9 41952906	9 975446833
9 670302335	10 6652357	11 48932428	10 29903968	9 5741218	12 93322236	11 59934714	8 6027714	6 486384412

Kidney GSM46825	Kidney GSM46826	Kidney GSM46847	Kidney GSM46858	Kidney GSM46875	Kidney GSM46881	Kidney GSM46882	Kidney GSM46892
Conventional (clear cell) renal carcinoma	Conventional (clear cell) renal carcinoma	Papillary renal cell carcinoma	Conventional (clear cell) renal carcinoma	Conventional (clear cell) renal carcinoma	Conventional (clear cell) renal carcinoma	Conventional (clear cell) renal carcinoma	Conventional (clear cell) renal carcinoma
10 39628339	10 72741827	7 112659931	11 01710492	9 163165375	10 30868789	11 36679829	10 23991263
7 445933375	6 260157674	5 426505301	6 927309648	6 961850405	6 422630171	7 543145075	7 415220331
8 754962524	8 300346362	8 093249829	8 484067829	8 081725346	8 550124474	9 532536967	8 577070358
7 225452697	6 7111757019	6 34324001	6 615599688	7 181957226	6 843763952	8 236377043	7 274221038
7 289620848	6 547671553	7 21392787	7 846224782	7 416259879	7 042694454	8 114877947	6 282001568
8 498471275	7 710123313	7 05972539	8 379432374	7 62193872	8 703648441	8 853004921	8 601924008
9 300428008	7 497623964	7 354264753	8 653684488	8 743861169	9 348699515	9 09148981	7 7683539
6 933840932	5 801739242	4 984179961	6 529214833	6 452547282	6 703841181	6 825581116	6 260443547
4 775986726	5 377589185	3 891346044	5 562687236	4 543929101	5 191481893	6 003392479	6 258965116
7 063394049	7 300910212	5 11597353	7 445127259	6 263681097	6 356632548	7 414527842	7 410183391
6 775539689	7 247905363	4 286790377	5 188922011	5 879642497	7 723649289	9 202695265	6 459297578
8 180507763	9 247994041	8 002582404	9 821068618	6 470242154	9 125306097	10 88076331	9 019393721
9 089547874	7 453483425	6 237690963	8 999786738	8 978271581	8 350232752	9 289437871	9 111890274
4 546232997	4 742492912	4 356995615	4 572427869	4 486489808	4 689205724	5 059361489	4 693705463
7 840021835	7 552762947	6 360833187	8 792082981	8 397009985	8 084300151	8 669179833	9 036830123
6 766229814	9 290098203	4 734570743	5 426533113	4 40925656	5 001584368	10 86876717	5 416433031
8 206107364	8 911198455	5 691330436	8 478433782	8 060059726	8 407994696	9 140845302	8 220005992
9 917020951	9 757852838	10 130391	10 34763959	10 0802717	9 921389765	10 98537278	10 21132003
4 557286906	4 428954871	4 518436181	4 039189588	4 050851903	4 341748294	4 323426958	4 775804803
9 488066008	7 377485979	9 057810309	8 890557043	9 592683828	9 381936765	9 034167927	10 08594822
7 96919386	10 73076451	8 251019072	10 48818141	6 581586336	8 866987449	11 45218611	10 94758402

Kidney GSM46929	Kidney GSM46939	Kidney GSM46944	Kidney GSM53060	Kidney GSM53092	Kidney GSM53122	Kidney GSM89089	Liver GSM137909	Liver GSM137962
Papillary renal cell carcinoma	Conventional (clear cell) renal carcinoma	Conventional (clear cell) renal carcinoma	Papillary renal cell carcinoma	Papillary renal cell carcinoma	Papillary renal cell carcinoma	Papillary renal cell carcinoma	Hepatocellular Carcinoma	Hepatocellular Carcinoma
8 044872937	11 20726127	9 700386656	7 775512833	7 481275015	6 80837918	7 889242952	9 950647081	8 952725614
6 865102757	7 007791932	7 026781679	5 307531046	5 83794812	5 171723984	4 966137011	5 872630289	5 687717168
8 464280037	9 180008767	8 467035189	7 578374447	8 269360014	7 950737189	6 967211635	8 321589239	8 4743361
7 69497721	7 730756079	6 655259154	6 275393194	6 997281956	6 554934251	6 04347283	5 775828203	6 065072728
7 270762956	7 252249063	7 476174602	7 175019252	7 2453974	6 895849473	7 471524021	7 49873144	7 500042659
5 312439339	8 90873246	8 142512287	6 400513404	4 377455789	5 468697456	6 592183385	7 411613113	5 006773695
9 614802183	8 338964454	9 202459641	8 070853663	5 620043497	7 833647515	4 207231146	7 03524841	7 410387875
4 994805619	6 487162822	7 264804253	5 37045618	5 230668709	5 365345417	5 300384443	6 023913644	5 63251748
3 937866258	5 381423861	4 202055483	3 832445828	4 056479504	3 82792031	3 901838278	3 88566941	3 628387996
5 268505073	8 819370157	5 789244117	6 158545206	6 009617995	5 465220398	5 471023766	5 524898762	5 945165575
4 116412367	8 070174465	5 195594638	5 020161878	4 439683383	4 397077738	4 163392649	4 87870322	4 980639885
7 596984806	9 972949764	7 272190334	8 785129658	10 58477372	10 20434283	8 010463076	9 395072384	8 783124759
6 958811822	8 434657994	9 228864645	6 349564868	6 986120102	6 196845586	6 214449829	7 344091612	6 723126473
4 216004501	4 808290061	4 602184926	4 705033528	4 604575554	4 651605213	4 598600024	4 835724344	4 715156601
8 035556094	8 121027433	7 451745652	4 600199328	5 981208217	6 088093794	6 494897777	7 136699879	6 935055372
5 533578548	8 724990496	7 01882755	6 017843489	5 254583961	6 084585346	4 975492716	4 616460086	5 162077446
6 869770746	8 571333624	8 606992421	6 718010327	6 755222836	5 691694043	6 272433487	7 320283051	6 637684476
9 698887484	10 41323345	9 45404855	9 157812032	10 17387961	9 707525396	10 78792053	8 747178113	8 204285999
4 141577962	4 53645336	4 491945542	4 886134309	4 720527407	4 781150549	4 660177667	4 896517691	4 122018208
6 788472026	9 295485386	8 436693138	7 635175189	7 205760217	8 516040057	7 31505379	9 13014233	9 07904393
9 360592114	10 87954757	8 510268655	7 76152465	7 57717825	5 966746644	9 101253525	10 89403219	8 827486143

Liver GSM179952	Liver GSM203676	Liver GSM203750	Liver GSM231890	Liver GSM203751	Lung GSM102505	Lung GSM117610	Lung GSM117629	Lung GSM117632
Hepatocellular Carcinoma	Hepatocellular Carcinoma	Hepatocellular Carcinoma	Hepatocellular Carcinoma	Hepatocellular Carcinoma	Bronchioloalveolar carcinoma	Squamous cell carcinoma	Squamous cell carcinoma	Adenocarcinoma, NOS*
7 028467732	7 114612449	9 451131531	9 223209051	10 62076883	6 629242964	10 78846118	10 07710527	9 943468655
4 537514781	4 9097098	5 858165403	6 342210951	4 842047897	5 810638943	5 618539421	6 390346804	6 10563705
7 461482908	7 822676699	8 542679071	7 923340038	9 266983795	6 732250226	9 000455877	8 584773991	8 175327851
6 792808056	6 459271231	6 723031916	6 257885544	8 309706294	7 231874141	8 164612397	7 888040968	7 397818591
6 92194313	7 009344831	7 072168762	6 891904469	7 835212536	8 551663979	8 790150275	7 641645619	8 183077109
4 426259096	4 045408082	6 505657721	6 601875395	8 440509653	3 779855314	7 718202407	7 099153578	6 605622037
5 928577869	5 082504004	6 823834002	6 799518776	6 314027243	4 594290308	7 7889803	6 85908731	6 804368933
5 180734873	5 251492947	5 978556243	5 749607655	5 470459635	6 019404639	6 328434149	6 149856789	5 788323104
3 522673625	3 722189273	5 283099654	3 900508588	9 09954019	4 144876775	7 922591464	5 77786392	4 201707713
6 020247438	5 801185534	6 501688101	6 37187334	8 41984814	5 976389318	7 169748543	6 189874142	6 16130131
4 302310001	3 709589963	7 532773008	7 100827863	7 134642992	4 156425041	9 488124782	7 418086641	6 59108921
5 273528689	5 532318998	9 704806862	9 1385549	8 032296735	6 592997011	11 05284124	9 832889056	9 659355433
7 008732451	6 778513302	7 989153988	7 258212148	6 189270581	7 090312018	7 062421143	7 415746032	7 659245213
4 68132678	4 61551886	5 585639937	5 117985805	5 552981919	5 353715721	6 128572462	5 018358723	4 790863853
6 052242468	5 092126099	8 277309285	7 808856214	8 761999188	5 802297219	8 811996528	7 77708806	9 003305872
4 915456586	4 987355373	6 225469069	4 815159783	5 728754279	5 960840522	10 63139816	9 480662689	8 855510074
6 709110256	7 041613519	7 572311503	8 499936355	9 571377884	6 393340195	8 276352196	7 544656376	7 631571225
6 514002284	7 597681459	8 93833347	9 11005989	10 63861978	5 515598511	10 2454136	9 208270532	9 518579249
4 605816632	4 471313762	4 624388862	4 357136122	6 662340895	6 604967582	5 996029885	5 730818015	5 001419432
5 25263403	5 798354853	9 631803456	8 11271999	8 341160465	4 796529456	8 497453343	8 461291915	9 579796725
5 642690002	5 926984809	11 03819645	10 4970288	8 804583667	7 457501343	11 97327066	10 96695525	11 47916978

Lung GSM117671	Lung GSM117770	Lung GSM117772	Lung GSM137910	Lung GSM137912	Lung GSM137916	Lung GSM137931	Lung GSM137945	Lung GSM138001
Bronchioloalveolar carcinoma	Adenocarcinoma, NOS*	Bronchioloalveolar carcinoma	Adenocarcinoma, NOS*	Adenocarcinoma, NOS*	Adenocarcinoma, NOS*	Adenocarcinoma, NOS*	Adenocarcinoma, NOS*	Bronchioloalveolar carcinoma
8 662056453	8 664569034	9 724115048	9 389716829	10 24804633	9 909774389	9 550548672	8 700843687	10 1723158
6 746713836	5 39819137	6 234800187	5 909752344	7 031356174	5 992953741	6 553796969	6 059870776	6 816588454
7 786287431	9 066484399	7 665671477	8 184752767	9 010259381	8 319941477	8 559151463	7 120567994	8 393100827
6 922830813	6 89451647	7 378842779	7 355828255	8 12002448	7 568683658	7 336252673	7 042730788	6 283609663
7 423938609	7 472575855	7 37623239	7 833906486	7 643199977	7 518092264	7 779675096	7 351034349	7 635549816
5 12918323	5 328718209	6 75878062	6 007830331	7 26413357	6 994670707	7 163828506	6 447598623	7 472950687
5 99719139	5 615124882	7 518578891	7 448860892	8 525392543	8 026959827	7 955865045	6 240787209	8 071583583
5 693577948	5 531264318	6 03128877	5 857195508	6 364970128	5 951618252	5 741014447	5 440880737	5 880375553
4 178404133	3 710994316	3 890859024	4 231666932	5 337279745	4 693112044	3 928690855	3 887387873	4 601096331
5 975955755	5 856136338	6 040300013	5 975528437	6 624068383	6 149519441	6 2502218	5 684497479	6 171997484
4 862770775	6 860226888	5 947086154	5 924664204	7 550993514	6 576330001	4 741726446	4 629138766	4 595905184
7 554728866	8 187099909	9 450449971	9 407982914	10 61720729	9 340818002	9 041917739	7 096673406	7 773196514
6 599076143	6 34464858	6 398654824	6 306893493	7 210993571	7 431295292	7 26506979	6 477563521	7 766494199
4 828645252	4 58817373	4 600413532	4 34942408	4 548048489	5 027087159	5 026931553	4 618328221	4 413985964
7 126771526	7 349250765	7 863424884	7 639068267	8 533967721	8 260820636	9 206482446	8 027615394	7 933039758
5 887892934	7 3693956	7 641421704	8 905364278	9 307763351	9 77829405	7 191665063	6 117680587	7 035443586
6 872417926	7 287325559	7 990364015	8 39819468	8 725813813	8 09873149	8 556510917	7 731061398	8 187877896
9 121820056	7 19825334	9 577275023	8 865132644	10 41532624	10 36717277	10 44941569	9 74914387	9 761363723
4 457204892	4 934323314	4 902832512	5 646389757	5 214869593	5 181672344	6 069378437	4 665956734	4 386226304
6 47195406	7 019175646	7 750571849	6 875790096	8 623193791	8 669194676	10 22391809	6 733417254	7 911648952
10 47891738	9 311067523	10 62894699	11 39187794	11 61123314	11 70924748	11 99361859	11 3092446	11 44295078

Lung GSM138002	Lung GSM46843	Lung GSM46850	Lung GSM46860	Lung GSM46868	Lung GSM46884	Lung GSM46904	Lung GSM46936	Lung GSM46973
Adenocarcinoma, NOS	Bronchioloalveolar carcinoma	Squamous cell carcinoma	Bronchioloalveolar carcinoma	Squamous cell carcinoma	Squamous cell carcinoma	Bronchioloalveolar carcinoma	Squamous cell carcinoma	Squamous cell carcinoma
8 902274139	10 67254859	10 08451758	10 01865442	8 826007398	10 69334818	10 67985842	10 33208789	9 932971994
5 87387601	6 877693634	6 263349706	7 007712835	6 118254968	7 054697111	7 674874837	6 638355077	5 697769978
8 483215658	8 895611013	8 802595612	8 67452611	8 003275007	9 177512721	8 877619029	8 89540291	9 199865523
7 721275735	7 642652789	8 638888238	6 964645627	7 551873748	9 174737861	7 687539967	8 111759385	8 056065204
7 7100476	7 157959531	8 000961756	7 122303847	7 402667829	8 01235962	6 696508343	7 811128716	8 465938828
6 244742134	7 829990581	7 290303447	7 473820369	7 406743736	8 593289219	9 356643562	8 106509438	5 787551136
6 048056619	7 28257687	8 020110562	7 323637262	7 479474954	9 065528704	8 346934581	7 832293191	6 964431031
5 735505528	5 711088202	6 008144224	5 649059355	6 045887983	6 490060922	5 976819314	5 937207223	5 516104747
3 92693205	4 889582719	6 576834688	5 543831097	3 862253407	6 905349524	4 052336064	4 912735184	6 734043517
5 817147118	6 975307251	6 937570225	6 58960798	6 78079114	8 045295036	7 016306445	7 298837385	7 36616139
5 99876246	6 899909133	9 764679975	7 413275704	6 621562656	10 96538904	4 39357318	8 860274649	7 793489203
8 089858543	8 764891426	10 04650091	9 207497183	9 018491628	10 87052246	7 339011567	9 583133597	9 97386797
6 193381952	6 869221425	7 080799478	6 656902353	6 828393167	8 010798002	7 875977123	7 995808713	6 897621612
4 497517519	4 875942632	4 90879795	4 232690719	4 444571016	5 6083446	5 031172614	4 814411565	5 368992021
7 291497218	8 47665975	8 866021494	6 754921453	7 67262782	10 04706688	8 607283543	9 078263507	7 929900091
7 162735586	7 585841586	9 796280703	6 339333668	8 548320663	11 35771629	8 52964466	10 41223591	9 798219042
7 228527767	8 645294162	8 52406628	7 785982077	8 600069245	9 451268801	9 302520339	9 024784083	8 300999642
9 69660365	10 31161473	9 699977867	9 701010042	9 703611678	10 69771467	10 88713498	10 27257409	10 02467154
4 261376088	4 709097913	5 51554625	4 852269269	5 001066205	5 825284868	4 680673516	4 90455948	6 093926489
6 54457476	6 848089506	8 950837586	8 854389278	6 0275265	10 3647089	6 070647052	9 021091159	8 713838095
10 18865319	11 28611144	11 9682047	11 27539465	10 16589617	11 82544501	12 1119114	11 40074407	11 53187369

Lung GSM46976	Lung GSM53167	Lung GSM76488	Lung GSM88949	Lung GSM88953	Lung GSM88981	Lung GSM89046	Lung GSM89060	Endometrium GSM46927
Squamous cell carcinoma	Squamous cell carcinoma	Bronchioalveolar carcinoma	Squamous cell carcinoma	Bronchioalveolar carcinoma	Bronchioalveolar carcinoma	Adenocarcinoma, NOS"	Adenocarcinoma, NOS"	Endometrioid carcinoma
8 973144613	9 703321391	11 02210209	9 58026148	9 693789131	12 16543901	11 01459946	9 600816053	11 76186427
6 914781219	6 547132153	7 390481721	5 555528315	6 567839859	7 762901956	6 481895578	6 264492162	6 668909614
8 89538401	8 677384272	9 185878198	7 958610494	8 347404099	9 076332798	8 656379999	7 551342354	9 100180289
7 899580519	7 349834778	8 362790068	7 059852608	8 386353929	7 296297764	8 21644226	7 621337113	8 731752963
7 018374721	7 454046118	7 649913688	7 406889406	7 849901717	7 37160604	7 38561277	7 430211106	8 092285468
7 861339228	7 7064152	8 210916365	5 337745391	7 088195302	8 784687536	7 640831727	5 242968203	8 919458226
7 562225964	6 586066405	8 333377304	6 640891124	7 603807084	8 039334271	7 270406879	6 504339819	8 025348537
6 448698307	5 419183522	5 764387322	5 394355863	5 693710289	5 711191771	5 660580985	5 72626041	6 303526621
4 492759721	6 155303957	6 81680861	3 958250623	6 039136197	3 747207915	5 905664689	4 136574147	7 293049692
6 232554572	6 652337056	6 974782776	5 722693034	6 32347636	7 218820662	6 511047756	5 744142935	7 42519643
7 906598946	8 668974427	9 504189443	7 211384112	10 03581692	4 706722076	9 170106115	4 499173088	8 422309841
9 351185147	9 227864133	11 47232477	8 810050646	10 98027553	8 875483597	10 48980838	9 447641681	8 498793854
7 326990766	6 782320363	7 583186785	7 457737352	6 756230883	8 354958146	6 938383411	6 821860188	6 53580052
4 286290863	5 28841722	5 170159378	5 30274728	5 910241158	5 339019274	5 347952809	4 82447973	4 454409124
8 238173739	7 44523721	8 279501442	7 64704492	7 391327614	8 914838997	8 523882639	7 669101807	7 773170293
9 768320875	8 932169343	10 16874436	9 543559515	8 560899072	9 611400782	11 35379808	8 121773666	6 84308192
8 08016077	8 153041408	9 921072561	7 438418071	8 735613944	9 464084351	8 629760657	7 936770673	8 964014282
9 719325751	9 271326053	10 94859401	9 075475919	10 91663624	11 05572822	10 11333445	9 83802845	10 3742583
4 455156644	5 172766614	5 510018278	4 908622027	6 316448793	5 156981109	5 433798813	4 74259776	5 385934717
8 666126874	8 115124331	8 387551555	8 037172808	7 932251041	8 618690566	9 606703515	8 059755522	8 322407509
10 89378877	10 45912751	11 67145704	10 29181714	11 61601848	12 03316383	11 51831191	10 89578887	11 0904347

Endometrium GSM46937	Endometrium GSM46949	Endometrium GSM53053	Endometrium GSM53065	Endometrium GSM53067	Endometrium GSM53075	Endometrium GSM53084	Endometrium GSM53093	Endometrium GSM53103	Ovary GSM117744	Ovary GSM137904
Endometrioid carcinoma	Endometrioid carcinoma	Endometrioid carcinoma	Endometrioid carcinoma	Endometrioid carcinoma	Endometrioid carcinoma	Endometrioid carcinoma	Endometrioid carcinoma	Endometrioid carcinoma	Serous Adenocarcinoma	Serous Adenocarcinoma
13 70628668	13 75429702	9 406250481	10 56301758	9 315321789	9 631633059	10 7686227	8 685250506	10 24317733	12 30967688	10 12274512
7 291692245	9 712412271	5 499597382	5 125811035	5 508444667	6 023966017	5 732194165	5 322950989	5 592126444	7 296147207	5 072068969
10 20258095	10 10971481	7 410504426	8 396330093	8 026847013	8 236558582	9 017977359	7 837949382	7 937020951	9 302873976	8 572660462
8 485224977	8 392067179	7 390168981	7 819010843	6 647831805	7 488194876	7 171419738	7 285137312	7 377506403	8 586343188	6 195574814
7 341341639	7 599796538	7 202660025	7 254680137	7 395950189	7 239883298	7 253570616	8 866869992	6 801972159	8 666288244	7 509878304
10 4262314	10 97283481	5 67696385	6 554575997	5 3005968	6 724867174	6 7178788	5 533505837	5 895154175	9 208373178	6 945899835
8 389386957	10 25467294	6 192906491	5 81953444	6 49561696	7 451582927	7 134760763	6 278992124	6 650091363	8 447847009	7 005786511
6 853191042	7 795671674	5 419893619	5 69792432	5 975873975	5 505998068	5 624832964	5 154378359	5 123695772	6 499334984	5 972501139
9 041503534	9 731619183	6 300491111	5 292455333	6 208643107	6 593159236	4 97143933	4 543874031	5 815533803	7 538540291	4 436816143
8 588519153	8 272550082	6 045700759	7 071397233	6 431707836	7 147373267	6 871551474	5 796997403	6 595152779	7 870289398	6 629315319
9 585252953	9 679365713	5 127132975	7 598029658	7 599025656	7 663728689	7 770133925	5 334165343	5 445223221	10 49456079	5 758258953
7 961397103	9 02392917	5 59242571	6 693393743	7 416882637	7 780927362	9 840994176	6 496659184	5 920991969	11 79217314	9 194753953
6 3110765	7 831796679	5 892031918	6 25269016	6 535112689	6 68326277	6 802193384	6 523896045	5 828791063	7 7462115	7 511846736
5 953977747	6 33613944	4 383498283	5 004730842	4 751447582	4 732789698	5 335225688	4 66262017	4 278063561	6 145014381	4 479962822
10 01499812	9 847564799	5 554871159	7 104444868	6 581311353	7 131157797	8 514029009	6 090080816	5 865527899	10 93766719	7 006224365
5 236541188	4 861270708	5 179492115	5 200559965	9 327287622	8 126310742	8 937560104	5 141219916	4 803871367	9 983386017	5 140586252
9 749732434	10 56338783	8 205677304	8 993515779	8 479358791	9 301846822	9 001045838	8 155743254	8 000475189	9 666521589	8 987945957
10 65179793	11 59439202	7 946551846	9 479143493	8 686373829	8 508257267	9 495241311	7 97061643	8 791694508	11 51398337	9 277082455
6 316646494	7 23296892	4 85457994	5 30207766	5 011427315	4 790758098	5 046568534	4 71337395	4 56163318	6 486272751	4 724840581
8 783705847	8 679621889	6 54779186	6 705036785	7 71657509	8 563363627	7 747155471	6 355242044	7 052651339	10 41450472	7 444402199
11 83514999	12 30070451	9 470726288	10 2871266	10 1235113	10 52973182	10 05052489	8 907399846	9 666084378	12 48881601	10 49976311

Ovary GSM46839	Ovary GSM46898	Ovary GSM46910	Ovary GSM46918	Ovary GSM53036	Ovary GSM53054	Ovary GSM53069	Ovary GSM53100	Ovary GSM53124
Papillary Serous Adenocarcinoma	Papillary Serous Adenocarcinoma	Papillary Serous Adenocarcinoma	Papillary Serous Adenocarcinoma	Serous Adenocarcinoma	Papillary Serous Adenocarcinoma	Serous Adenocarcinoma	Serous Adenocarcinoma	Papillary Serous Adenocarcinoma
9 032084973	9 038103402	8 147293552	10 67969307	10 24402791	11 18356689	9 000954539	9 803445854	11 99953462
5 341015799	4 968221114	4 647162391	5 29531791	5 306255657	5 984146179	5 223464856	4 645619187	6 983130336
8 729279169	8 217815782	8 647049439	9 812647314	9 07307443	8 825337723	8 18221154	7 644548637	8 892209013
7 016335627	7 390013608	7 120819844	7 950060676	7 805325501	7 693879185	7 11454052	7 509457728	7 796625575
7 21033219	8 785889763	6 673873974	7 580417754	7 660627493	7 334096984	7 278800039	7 287572663	7 141597417
5 104475323	8 509679471	5 595098064	7 515961308	6 813681622	6 904786776	6 274718511	8 20032191	8 345319606
4 31429472	6 977084685	6 233829236	7 094745038	8 895853508	6 21881273	7 399636772	4 868946452	6 901918531
6 342725182	5 356886671	5 357222416	5 726681735	5 694224522	5 730390896	5 631441042	5 119198216	5 581097463
3 963848812	4 563126568	4 602184574	5 764994699	4 859637206	5 58258977	6 169230061	6 114291991	9 386765311
5 795448104	5 845448357	7 325290607	6 936311478	7 269440882	8 20367539	6 328323301	6 385232307	7 208788682
5 988881646	7 609475955	6 644222679	9 665924497	9 665572217	8 195593698	7 861864913	4 403197464	10 1819327
6 457535271	8 093299307	7 302131536	11 13061926	10 29411309	9 398564988	8 546624706	5 01335084	10 44368196
5 432113547	5 671373225	5 836760396	6 718463562	6 854135211	6 393708514	6 525014808	6 913606206	6 956114677
4 754286484	4 062077674	4 085885518	4 498816151	5 311616486	5 031886757	4 596230419	4 846498304	4 915052204
4 330808951	6 821117747	6 971642443	8 239970837	8 21211225	6 536834718	6 207701054	4 68834568	6 618077811
5 304515004	8 775491456	4 750958579	6 376574449	7 950109791	5 689621643	5 492958641	5 924161225	8 219737367
7 446119392	7 540004231	9 82835258	8 342879048	8 479720904	10 1386271	8 669243792	7 75485815	9 756193111
10 11211347	9 773781476	9 281813058	9 825257473	10 61011182	10 22735398	9 650509149	9 916079647	10 01289774
4 495166095	5 67702898	4 555140499	4 640629306	5 771958646	5 224754409	4 936866709	4 71996629	4 978331073
6 42498045	6 913869742	6 066157136	9 449369684	9 051780224	8 871541223	6 66858098	6 240079917	9 001827736
9 9801556	9 609912295	8 821108458	11 0946905	10 17662116	11 73016128	9 63642158	5 899658172	11 40947283

Ovary GSM53129	Ovary GSM53144	Ovary GSM53173	Ovary GSM53185	Ovary GSM76489	Ovary GSM76510	Ovary GSM88948	Ovary GSM88973	Ovary GSM89028
Papillary Serous Adenocarcinoma	Papillary Serous Adenocarcinoma	Papillary Serous Adenocarcinoma	Papillary Serous Adenocarcinoma	Serous Adenocarcinoma	Serous Adenocarcinoma	Serous Adenocarcinoma	Serous Adenocarcinoma	Serous Adenocarcinoma
11 64182205	9 744866054	10 11666349	9 319698425	8 937385296	7 362507438	9 914954868	8 250960517	9 728260647
6 628881028	5 100082389	5 6664757	5 816097379	5 361847903	5 274123885	5 189506281	5 114697219	5 417486754
8 968739834	8 502264171	8 6784417	8 544647609	7 340434119	7 580854661	8 348719662	7 550007546	8 19601926
8 64764579	7 577252924	7 705054245	6 911546443	6 83164872	7 079730397	7 475266535	7 280911869	7 112328198
7 718885394	7 029949888	7 57420755	7 101642611	6 777082761	7 003387193	7 606262529	7 42698831	7 236859059
8 584381483	5 580360513	5 949949382	7 053556172	6 788616838	4 799500074	6 043721607	5 006988583	6 619665465
7 885086252	6 756931631	6 431019494	6 864888114	5 978134924	5 489359111	7 200671355	5 419258442	6 166455314
5 737829074	5 197788324	5 390648118	5 706668175	5 748709858	5 377292822	5 613041572	5 592835662	5 593323877
6 382867519	6 232251599	7 213215334	3 897933843	4 466266618	3 899002251	7 730753657	4 830941167	5 623378142
7 861201837	6 71452918	6 269107841	6 732785367	5 875358722	5 708908903	6 532669028	6 863419977	6 899783556
10 71067008	9 049496516	10 39507336	8 137369251	7 46261229	4 732309598	9 273302249	5 336197554	8 153052134
11 24004886	8 522006848	10 31472476	10 52716091	6 956397466	5 364675182	10 01264811	5 151434107	9 188431151
7 163551484	6 303288253	5 700660818	7 798005886	5 721127085	5 977882383	7 593198579	6 886135553	6 770711572
5 490878819	4 626072161	5 41096885	4 667639291	4 557297208	4 644504265	5 30584425	4 770531108	4 928979825
9 896609803	6 31724953	8 118334625	6 793252175	6 260838216	5 794514308	6 327431766	4 625897287	7 384917304
9 006941635	4 779350426	8 070985366	7 747942677	5 13501653	4 385458951	7 095005452	4 858734578	6 727754836
10 02077216	7 920584792	8 357231519	8 800178509	8 948539062	7 695966405	8 124881672	9 076431862	8 047922502
10 46801593	9 133179828	10 19515891	9 689117501	9 584734429	8 926101267	9 819655167	9 01986141	10 00173697
5 924616309	4 525579459	5 439962651	4 995564835	4 713334024	4 578005169	5 332818347	4 86840705	5 014037086
9 513374524	7 426572874	8 644043937	7 026009856	6 876813785	6 50868944	7 774449723	5 480088116	8 380677957
11 47010801	10 02825804	11 00638757	10 3286208	10 46777829	6 901073519	11 46340927	9 214634158	11 20049709

Pancreas GSM117645	Pancreas GSM117647	Pancreas GSM137958	Pancreas GSM152744	Pancreas GSM179781	Pancreas GSM179869	Pancreas GSM203703	Pancreas GSM203761	Pancreas GSM53046	Pancreas GSM89045	Prostate GSM117726
Ductal Carcinoma	Adenocarcinoma, NOS	Ductal Carcinoma	Ductal Carcinoma	Ductal Carcinoma	Ductal Carcinoma	Ductal Carcinoma	Ductal Carcinoma	non functional islet- cell tumour	Ductal Carcinoma	Adenocarcinoma, NOS*
12 84818697	11 06616914	11 51357356	12 23504714	12 47355054	12 00537241	11 29539441	11 36379362	8 413205799	12 12522676	11 37232555
7 718545818	5 992251997	7 2493064	8 139229856	7 864134968	7 032747568	7 295197503	7 584920256	5 38605688	7 678213432	5 06601916
9 847382418	8 633223586	8 657367886	9 664794903	9 592065429	9 675013194	9 851050441	9 142907089	7 679147847	9 40019883	8 041433271
9 325635873	7 260998373	8 39516599	9 621608021	9 329108358	8 924756777	8 456373381	8 600631235	6 814085054	8 96236544	6 812326552
9 852594756	8 022617877	8 251510586	10 01234304	8 120108683	9 070959766	8 202297061	7 627412783	7 246286064	7 731287967	6 704182759
9 869462162	7 5348736	8 51943752	9 332264509	9 844925448	9 036755843	8 45589508	8 816821892	5 137180548	8 896500394	7 873627018
9 422210712	7 855263747	8 522559455	9 029592684	9 388123089	9 00225631	8 14201095	9 21660688	5 01900611	8 821962573	6 403237818
6 772363803	5 856495583	7 294774349	6 948991378	6 390716781	7 083840134	6 550033164	6 549676875	5 506997587	6 303036746	6 430019485
9 868833552	6 980097574	6 435160728	10 83590169	9 235332402	8 42611054	8 381140919	6 367457716	3 689154861	7 586630143	4 39617298
8 317822118	6 524906688	7 055273422	9 108332918	6 665872198	8 573772346	7 687789823	8 259869116	6 478504385	7 82331084	6 122993296
10 65074082	8 509024306	8 425339703	11 11485254	10 93431441	9 770265659	9 738615655	9 212415832	4 76108044	9 49318509	4 5491899
12 30646288	9 694419783	11 13619138	12 43683644	12 0735205	11 44417687	11 31775109	10 30486309	6 304583733	11 8758203	6 968112521
9 248604945	7 534991893	8 893360478	9 612085732	9 000034939	8 97378554	8 715849171	8 741245826	6 264056277	9 670467204	6 817038612
6 862603472	5 508530055	5 635494382	7 710272658	6 484216986	6 410305715	6 493388057	6 429164959	5 272608249	6 273382032	4 808178141
10 51746029	9 279811527	10 29974085	10 05648661	10 70799925	10 84875201	9 837431274	10 91615057	8 167445429	10 86273851	9 866027431
11 69368824	9 689541784	11 90160997	12 22880494	12 53275471	11 78297467	11 34611048	11 40968733	9 047997509	12 46594903	5 611912139
9 962708082	8 136651702	9 548764992	10 18030963	10 0002042	9 695604244	9 334021371	9 651823448	7 971819565	10 19328502	7 773894484
11 95422244	10 04580149	11 03434893	11 98119327	11 37340831	11 0281898	10 94505419	10 49251181	8 574250061	11 84999098	8 896478112
7 277832578	5 548275025	5 467581639	7 153443042	6 275762573	5 930476567	4 705022416	7 019692562	4 562409049	5 694024554	4 474587737
10 11284306	9 396406971	10 28726141	9 860810995	11 75021857	10 71552761	10 39142967	12 56578325	5 984122751	11 07385959	5 72819598
12 73980517	11 17220951	12 69494019	13 09223255	12 58505951	12 14153311	12 08365295	12 75139318	10 1654838	12 41447178	9 293174777

Prostate GSM117727	Prostate GSM117741	Prostate GSM38079	Prostate GSM46866	Prostate GSM53061	Prostate GSM53114	Prostate GSM53152	Prostate GSM76516	Prostate GSM88977
Adenocarcinoma, NOS ⁺	Adenocarcinoma, NOS ⁺	Adenocarcinoma, NOS ⁺	Adenocarcinoma, NOS ⁺	Adenocarcinoma, NOS ⁺	Adenocarcinoma, NOS ⁺	Adenocarcinoma, NOS ⁺	Adenocarcinoma, NOS ⁺	Adenocarcinoma, NOS ⁺
12 81782554	12 28602428	13 19910241	12 33991387	12 31854284	12 07038302	9 834780276	12 34449661	11 76966615
6 502918643	6 312061316	6 960109348	5 628082751	6 050264021	6 052188186	6 100300985	5 928007088	5 370615598
8 757327833	8 63816972	9 813713278	8 88073144	9 049838321	8 945765613	7 957424754	8 85509169	8 249654359
6 980390547	7 496311406	7 165169399	7 086414037	6 867180004	6 869696216	7 63923855	6 675873836	6 103587132
7 125704248	7 287729371	7 240929873	6 946418794	7 210675299	6 958979715	7 544236624	6 989130463	7 1007017
9 633921137	8 896266393	9 660234717	8 592972648	8 503615283	8 716214564	5 418600937	8 304135864	7 729293432
7 037544748	6 694839691	6 754408478	6 601596164	6 849336127	6 939499439	6 043034263	6 460572473	5 895967389
6 592143706	6 74628989	6 860113033	6 853526955	6 505243723	6 440082788	5 436131734	6 030607791	5 841078881
4 079346153	4 63228739	5 848819486	7 723112575	4 558056706	4 500525219	4 322985616	4 471219065	4 431929896
6 223971626	7 290857401	8 123771628	6 709673724	7 659152875	7 247577983	6 60082709	6 81087244	6 043729496
5 379012996	4 800185687	4 954774514	6 975463688	5 674937445	4 66591022	6 730961209	4 363060629	4 848241524
6 516744865	7 551828522	6 674621683	8 301677535	7 104125507	5 852095435	9 290381617	5 182063339	8 662738569
6 994192844	6 552761148	5 55394804	6 818755512	7 168930172	6 524212414	6 077020587	6 384736527	6 755814803
4 805234884	5 096776125	4 811585789	4 166273546	4 825717351	4 817138839	5 141991877	4 633444916	4 970800822
10 01318963	10 33200167	9 799268338	9 441449959	8 330948439	9 650484351	7 483994702	9 440788127	7 907062392
7 610046029	8 7351218	8 514298496	8 151919077	7 396525707	5 618260899	7 082742769	6 693903972	7 470220266
8 880858514	9 217262601	9 399016965	8 684504972	9 050053718	9 071652275	8 326118354	9 005943952	8 022988721
9 790567515	10 54366758	10 05611438	9 726343341	9 172050339	9 093315956	10 0108955	9 018730378	9 713555971
5 129506802	4 946040997	5 091338515	4 738436529	4 802555801	5 034725489	5 154759332	4 934705658	4 715891774
7 623771307	9 851241951	7 670876975	9 030338089	6 999812705	8 248166934	7 244316113	6 889290065	7 748524311
11 18749178	11 58461697	11 89794949	11 55127339	10 17892279	9 595301708	10 00212597	9 66873481	9 785713827

Stomach GSM102495	Stomach GSM152595	Stomach GSM203666	Stomach GSM53039	Stomach GSM76562	Thyroid GSM102452	Thyroid GSM102560	Thyroid GSM117723	Thyroid GSM117735	Thyroid GSM138004	Thyroid GSM138023
Adenocarcinoma Diffuse Type	Tubular Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Papillary carcinoma	Papillary carcinoma	Papillary carcinoma	Papillary carcinoma	Papillary carcinoma	Papillary carcinoma
12 03367668	11 02697244	13 47649507	9 040706759	10 2871474	8 973277011	9 364840179	9 584928182	9 623847846	6 662954612	8 783707467
8 873687306	6 368428531	7 816573765	5 79005478	7 015726256	6 610046347	5 676208024	7 278280978	6 114488857	5 733524946	5 468988293
8 674947111	8 406019143	10 0886144	8 193981212	8 709992972	7 913692808	8 249750352	7 601830529	8 407338494	8 200430394	8 041958525
7 487636683	7 228118394	7 239493142	7 016448867	7 457007407	6 819867445	7 375542753	7 123399494	6 497809067	6 905337189	7 364912658
8 150679776	7 447853403	7 73934606	7 293293829	7 333589109	7 541396541	7 105609336	7 376599953	7 742484839	7 853985904	7 620419003
9 345651378	7 349916663	10 02197935	5 727859765	7 792052897	5 542456603	5 950856678	7 491484207	6 740463385	6 081412297	5 268821083
8 890025949	8 171820832	7 974384102	7 032613977	8 921876131	6 516786586	6 453527618	6 821809618	6 922620968	7 921241659	6 904058658
7 103308573	6 073102925	6 599544003	4 964629826	5 880230859	5 656665259	5 270091458	6 015565063	6 202448146	5 961636149	5 706848471
6 846034224	6 210761414	7 97612883	4 780931084	6 97343828	4 460566155	5 17304365	4 212655153	4 115478942	3 49660343	3 936555306
7 099455117	7 09420279	8 741302127	6 083455619	6 762440407	5 739556883	5 854817398	5 601472741	6 070436176	6 162690111	5 548973741
6 088899462	6 037155982	8 390536175	6 906653699	9 927436382	5 83960469	7 233737973	5 064081188	5 765668457	4 093738813	4 891223258
10 57647888	9 082357134	9 027638046	9 991182242	9 824845249	8 157673705	8 928332153	8 501758083	9 669553142	5 647763128	5 835718823
8 473909202	6 530668537	7 780966696	6 460729939	7 257544806	6 895311728	6 020181214	6 917267653	7 416842773	6 858405372	6 329842906
4 752008158	4 6857708	5 700572495	4 553851288	5 155233866	4 509579673	4 797966815	5 297129066	5 196711247	4 40058036	4 150069665
9 195897579	8 775636348	8 58409007	7 518243707	9 392094877	6 734583998	6 881437372	8 36130262	8 139110028	7 217531639	7 309334803
10 53591882	8 687857191	10 89776552	5 80775415	7 602819677	8 24998459	8 155514998	9 268872349	9 963559848	5 120412474	5 412061442
10 04371606	8 797194819	9 960495336	8 285254639	9 571476496	7 263265242	7 676893107	8 042409951	8 564377691	7 236912533	6 268225935
11 01495745	9 692644195	10 9956027	8 459151192	9 681610427	9 351751132	8 968978447	9 875169301	9 925682061	9 271293251	9 577572414
6 185538344	5 641154723	7 009240872	4 923671525	5 564303691	4 873297568	4 839648219	5 087908135	5 140361562	3 99921176	4 508077815
9 582137559	7 818212669	9 21227072	6 896849535	8 515133713	6 792242067	7 84651498	6 886569932	7 738277931	5 724153349	5 945133359
13 07535421	12 20864855	12 65148906	9 425982706	11 2189602	10 13544556	9 867096719	11 2869239	11 79447145	7 041385872	6 957436985

Thyroid GSM138024	Thyroid GSM88998	Thyroid GSM89038
Papillary carcinoma	Papillary carcinoma	Papillary carcinoma
9 88724009	9 24633924	11 37173476
6 71956435	6 31341829	8 392267511
7 90025972	7 49226433	7 420946779
6 49912431	6 61588102	7 097927648
7 58951868	7 10187268	7 130093992
7 49005718	6 40671942	9 077473301
7 45256268	6 97080741	7 707506811
6 07675115	5 5012565	5 674135498
4 07556124	4 0598192	4 241855957
5 94724172	6 7242112	7 050135128
4 37528025	4 73046467	4 683979796
9 24482878	6 45282625	8 493996655
7 74510827	6 52902658	8 000549305
4 73476843	4 44338227	5 108038944
7 08147274	6 75579396	9 718928348
8 35234009	5 70163336	10 2296949
7 93429604	8 32984849	9 206260978
10 1423823	9 18204496	10 66619693
4 78766492	4 46148685	4 624654053
6 94085272	7 39664099	8 403218723
10 7234023	10 2076547	12 70222503

Appendix Table A3. GEM data of *Ang2* and correlated genes in a variety of neoplasms

GEM data was obtained from the NCBI GEO database (GSE2109) and was obtained using Affymetrix hg-u133+2 GeneChips

Microarray data was processed and assessed for differential regulation as described in Materials and Methods

Correlation analysis was performed using the *Ang2* probe set 205572_at. NA, no gene name available.

Affy ID	Gene symbol	Name	Site ID	Urinary Bladder	Urinary Bladder	Urinary Bladder
				GSM102434	GSM102437	GSM117677
			Histology	Urothelial (transitional cell) carcinoma	Urothelial (transitional cell) carcinoma	Urothelial (transitional cell) carcinoma
205572_at	ANGPT2	angiotensin 2		5 14721562	6 284568816	5 991576228
211148_s_at	ANGPT2	angiotensin 2		4 996703665	5 846217402	5 066351997
237261_at	NA			3 881683359	4 784416873	3 928890403
236034_at	NA			4 845337182	6 426512608	5 565236861
208394_x_at	ESM1	endothelial cell-specific molecule 1		4 72742829	5 497558183	4 507161761
226497_s_at	FLT1	fms-related tyrosine kinase 1 (vascular endothelial growth factor/vascular permeability factor receptor)		5 403193026	6 171109121	5 852928817
226498_at	FLT1	fms-related tyrosine kinase 1 (vascular endothelial growth factor/vascular permeability factor receptor)		3 717884792	4 070049526	4 223540484
212171_x_at	VEGFA	vascular endothelial growth factor A		8 593700276	9 747868886	7 2332447
222033_s_at	FLT1	fms-related tyrosine kinase 1 (vascular endothelial growth factor/vascular permeability factor receptor)		5 635183304	6 165189335	7 306834113
209652_s_at	PGF	placental growth factor: vascular endothelial growth factor-related protein		5 2937213	7 261738149	5 546426387
218484_at	NDUFA4L2	NADH dehydrogenase (ubiquinone) 1 alpha subcomplex 4 like 2		8 019687185	10 20529793	6 72410968
205247_at	NOTCH4	notch homolog 4 (Drosophila)		6 0663606	5 579904566	6 924697363
219134_at	ELTD1	EGF, latrophilin and seven transmembrane domain containing 1		5 530320269	5 380525809	8 730285176
206236_at	GPR4	G protein-coupled receptor 4		5 744969324	5 390832621	5 905709786
223333_s_at	ANGPTL4	angiotensin-like 4		6 086643243	5 330564316	5 889185593
226955_at	AFAP1L1	actin filament associated protein 1-like 1		4 427331945	6 070560107	5 366455029
204726_at	CDH13	cadherin 13, H-cadherin (heart)		4 175358643	4 466383717	4 078228164
47550_at	LZTS1	leucine zipper, putative tumor suppressor 1		4 22661118	3 983402461	4 726284677
211981_at	COL4A1	collagen, type IV, alpha 1		8 546576243	8 718626945	4 702236292
211527_x_at	VEGFA	vascular endothelial growth factor A		6 566324436	8 213827043	5 07818966
221009_s_at	ANGPTL4	angiotensin-like 4		5 803701547	5 902962005	6 841475561
210869_s_at	MCAM	melanoma cell adhesion molecule		5 403857819	6 376249148	8 250711946
230022_at	LOC348174	secretory protein LOC348174		5 58335309	4 283961664	3 889666913
204597_x_at	STC1	stanniocalcin 1		3 940177405	6 705644369	6 306901935
210287_s_at	FLT1	fms-related tyrosine kinase 1 (vascular endothelial growth factor/vascular permeability factor receptor)		3 432171651	3 338206359	3 434270583
228339_at	ECSM2	endothelial cell-specific molecule 2		4 569804935	4 614409129	6 853509919
218660_at	DYSF	dysferlin, limb girdle muscular dystrophy 2B (autosomal recessive)		7 352124733	6 700056852	7 742934332
211340_s_at	MCAM	melanoma cell adhesion molecule		7 449088313	7 788447665	10 08231942
206836_at	SLC6A3	solute carrier family 6 (neurotransmitter transporter, dopamine), member 3		5 709609055	5 946393273	5 497611814
223657_at	C1orf90	chromosome 1 open reading frame 90		5 160489487	5 340536815	5 061953576
204845_s_at	ENPEP	glutamyl aminopeptidase (aminopeptidase A)		3 548620974	3 537768908	4 641199851
244025_at	NA			4 301089982	4 613010564	4 927379951
218950_at	CENTD3	centaurin, delta 3		6 423392546	6 274201094	7 813716037
214297_at	CSPG4	chondroitin sulfate proteoglycan 4 (melanoma-associated)		4 219274974	5 541727062	4 698720322
228618_at	PEAR1	platelet endothelial aggregation receptor 1		5 849777895	5 977066478	7 502887714
239058_at	NA			5 08950702	4 950932403	6 542258815
218507_at	HIG2	hypoxia-inducible protein 2		7 001833084	8 287723615	7 618503352
221529_s_at	PLVAP	plasmalemma vesicle associated protein		7 522772325	7 118345543	8 655916892
210512_s_at	VEGFA	vascular endothelial growth factor A		9 943167172	11 12246238	9 279101421
219232_s_at	EGLN3	egl nine homolog 3 (C elegans)		6 285836004	7 551735214	4 860179542
209087_x_at	MCAM	melanoma cell adhesion molecule		7 218024539	7 291027751	9 720936197
210513_s_at	VEGFA	vascular endothelial growth factor A		7 159253031	9 274895583	6 584781142
213349_at	TMCC1	transmembrane and coiled-coil domain family 1		6 167338263	7 17925889	5 577656633
209543_s_at	CD34	CD34 molecule		6 37858891	5 462881901	7 984010317
222911_s_at	CXorf36	chromosome X open reading frame 36		4 924915823	4 332703587	6 237851338
205029_s_at	FABP7	fatty acid binding protein 7, brain		3 275326534	3 221788587	2 990592813
219091_s_at	MMRN2	multimerin 2		6 851429415	5 497558183	7 977411815
229902_at	FLT4	fms-related tyrosine kinase 4		3 722736362	3 890013535	4 726245155
1554452_s_at	HIG2	hypoxia-inducible protein 2		7 866163758	8 685044494	7 983208837
204595_s_at	STC1	stanniocalcin 1		5 534592859	7 762803281	6 830834125
204677_s_at	CDH5	cadherin 5, type 2, VE-cadherin (vascular epithelium)		5 647354706	4 889542484	8 628876231
240058_at	NA			3 73454736	3 596508109	3 895449041
202912_at	ADM	adrenomedullin		7 748712013	10 70658417	9 566329606
202112_at	VWF	von Willebrand factor		7 726050738	7 797701466	11 73352574
226905_at	FAM101B	family with sequence similarity 101, member B		5 88078061	7 943570597	7 63820107
209086_x_at	MCAM	melanoma cell adhesion molecule		6 75134751	6 474156714	8 443788722
225043_at	SLC15A4	solute carrier family 15, member 4		7 060936502	7 745528295	7 2025805
221489_s_at	SPRY4	sprouty homolog 4 (Drosophila)		6 954714532	7 452736131	7 059928245
219656_at	PCDH12	protocadherin 12		6 502574	6 075540951	7 530358834
229487_at	NA			4 196664048	3 879219618	6 962847105
238169_at	NA			3 478823565	3 30678878	3 47198658
241381_at	CXorf36	chromosome X open reading frame 36		5 274932979	4 577921453	6 191315662
202877_s_at	CD93	CD93 molecule		5 982183342	7 809579467	8 447883498
204844_at	ENPEP	glutamyl aminopeptidase (aminopeptidase A)		4 016596214	4 282385344	6 852048732
206367_at	REN	renin		4 537332298	4 171976952	4 990147351
239952_at	ZEB1	zinc finger E-box binding homeobox 1		4 085643575	3 974314397	4 482101815
205030_at	FABP7	fatty acid binding protein 7, brain		3 561894798	3 971031694	3 860644162
209122_at	ADFP	adipose differentiation-related protein		7 926708382	9 432894808	9 822934403
230746_s_at	STC1	stanniocalcin 1		5 150095912	8 647896667	7 555199839
211980_at	COL4A1	collagen, type IV, alpha 1		10 30778876	10 15141982	11 65820667
40687_at	GJA4	gap junction protein, alpha 4, 37kDa (connexin 37)		5 613259051	4 9922320561	7 657762085
213075_at	OLFML2A	olfactomedin-like 2A		6 301974325	7 695566849	7 185270121
240873_x_at	DAB2	disabled homolog 2, mitogen-responsive phosphoprotein (Drosophila)		4 651227034	5 232745353	5 885904308
204468_s_at	TIE1	tyrosine kinase with immunoglobulin-like and EGF-like domains 1		4 43002656	4 791607994	7 465869296
202083_s_at	SEC14L1	SEC14-like 1 (S cerevisiae)		4 334126135	5 589052781	5 502293546
236480_at	NA			4 558388328	5 95944265	4 352636205
222856_at	APLN	apelin, AGTRL1 ligand		5 847015328	6 414288214	6 12502035
217177_s_at	NA			3 572339121	3 869518225	4 226471905
222847_s_at	EGLN3	egl nine homolog 3 (C elegans)		7 142917534	8 997772121	5 638520886
202878_s_at	CD93	CD93 molecule		7 061434898	9 146151733	10 1376292
212143_s_at	IGFBP3	insulin-like growth factor binding protein 3		10 82706128	8 859604373	8 329843773
236249_at	IKIP	IKK interacting protein		4 153446797	4 695933545	4 277101493
228776_at	GJA7	gap junction protein, alpha 7, 45kDa (connexin 45)		5 263375947	8 581046314	7 257260239

Urinary Bladder GSM137819 Urothelial (transitional cell) carcinoma	Urinary Bladder GSM46829 Urothelial (transitional cell) carcinoma	Urinary Bladder GSM53117 Urothelial (transitional cell) carcinoma	Urinary Bladder GSM53137 Urothelial (transitional cell) carcinoma	Urinary Bladder GSM88993 Urothelial (transitional cell) carcinoma	Urinary Bladder GSM89048 Urothelial (transitional cell) carcinoma
7 130586502	7 484316733	4 611218642	5 425183165	5 203904699	5 870849226
6 213304765	6 585886877	4 687698061	5 4865925	5 095367303	5 301533532
4 91207421	5 865801162	3 820725652	4 305321113	3 734194569	4 884238803
6 288618099	7 51918648	5 306387625	5 834264869	5 619190687	6 209688372
5 061543343	6 592811111	4 654940035	5 582597904	5 149185287	5 578051
6 668211415	8 192924431	5 769707462	6 113851601	5 920586807	6 178986199
6 268521156	8 730116991	3 742862913	4 849438732	4 882010636	4 668696386
9 171722203	10 91954399	7 841697891	9 00205068	8 600071571	9 122793317
6 61941753	7 920426301	5 926692001	6 218670548	6 50746596	6 619927756
5 253350637	6 850067388	4 960235015	4 533795722	5 096772554	5 047495668
6 298572616	9 102423668	6 892548955	8 570407293	6 124631636	7 07952859
6 123443252	6 625984237	6 114365413	5 8736597	6 030165548	6 592913495
7 065255116	7 666408782	5 334647454	4 673015303	6 208198897	5 913398185
5 975509204	5 890878543	5 278838077	5 269013286	5 602367887	5 532805785
7 481670745	6 483943683	6 111841977	6 867637093	5 834673507	5 6790334
4 933060063	5 481255163	3 811303358	4 081629755	4 510815604	4 127658724
3 92513145	5 682940074	3 953832128	3 478688487	3 857201662	4 05544256
4 240667534	5 543903204	4 417622959	4 772508586	4 344278501	4 438213305
9 523747024	10 25439684	7 202855959	7 302153226	8 810305412	8 991051979
7 333815214	8 000106892	4 975750571	7 565626787	6 786894589	7 578569799
7 519999516	6 382938985	6 23608634	7 781259448	6 687015301	5 815610755
6 485308916	7 401204987	5 496107621	5 848321698	6 713590967	6 843683841
4 047080699	4 313781932	4 061386063	4 479136047	3 843190395	4 114335383
8 7091856	8 078987172	5 670400074	6 133035821	6 113086538	5 39258957
3 571527843	3 743495836	3 539981847	3 382702441	3 465451075	3 457899634
5 266759813	5 497660617	4 615123657	4 252848031	4 725857045	5 068207468
7 238667505	7 858889196	6 472661905	6 555947283	7 44559925	7 285575308
8 168393393	9 228298124	6 92162684	7 572722689	8 485542028	8 289878285
5 262975716	6 26205279	5 394856669	4 992498945	5 358470793	6 198213584
5 252701972	5 511845696	4 949110374	4 561539345	5 115066399	4 957640542
3 849212703	5 845322356	3 786201305	3 736961224	3 998220225	3 776005564
4 685211905	5 656945948	4 938034897	4 567986734	4 548076389	4 151217679
7 701914494	7 774101234	7 01637831	6 947358338	7 29903875	7 107294892
4 150719428	4 580501696	3 781493503	3 667168677	3 986483455	4 049571394
6 043689568	6 287801262	5 590531733	5 777552443	6 223236808	6 103450595
6 443787628	5 994530618	4 76171539	4 324732353	5 356261885	5 197171396
7 039420785	9 497720345	6 311924159	9 255491633	6 413826481	6 832680761
8 258535006	8 435146117	6 877380968	6 750173096	7 794035046	8 407819353
11 04950721	11 21963874	9 755099285	11 02412361	10 64212042	11 09119052
7 117631195	8 586802276	5 111192645	7 629017433	6 463344207	5 206448926
7 803357582	8 733628714	7 245605804	7 230126551	7 968862966	7 805020157
8 102386787	8 42482144	6 589628591	7 976422961	7 559294421	7 797604203
6 466158638	7 551493164	6 167329152	7 223477536	6 630493428	6 423183014
6 229643424	6 785244904	6 280092147	6 240712269	6 22957937	6 551749271
5 045169322	4 828098507	4 376770819	4 506104744	4 622744536	5 046174797
3 099194035	2 902586365	2 990835597	2 885434681	3 128883381	3 162919134
7 69268555	9 520120962	5 670787676	5 928591519	6 548457259	7 502606961
3 509154902	4 392117912	3 464883287	3 374553874	3 704200499	3 860518524
7 392679431	9 334876582	6 964871744	6 359179103	6 921052667	7 53368849
9 850762384	8 011830528	7 041293079	6 931431589	6 842732481	6 421237167
6 754041813	7 129563895	5 631862036	4 971065884	6 118834886	6 277262635
3 444790986	3 797712315	4 112732563	3 681374285	3 720781526	3 710373219
10 51334102	10 70638155	8 497315049	9 49354701	10 44740469	9 396551045
9 208953482	8 972414179	7 103023019	7 518103921	8 468061459	9 125805581
7 251679104	8 349100144	6 299198398	4 910623533	6 556210291	6 00754857
6 643578515	7 194753261	6 321959891	6 674123817	7 004035525	7 241332634
7 853266848	7 996943948	7 404441362	6 828517821	7 709025282	7 296190164
7 045848296	6 615893858	5 814696807	5 746627498	6 54062058	6 534671475
6 29776738	6 946835798	6 249100588	6 035753856	6 674061182	6 636244557
4 213992368	5 756933286	4 127561589	3 962551598	3 633285324	3 927408062
3 429798188	4 031764343	3 537589684	3 339024754	3 40845975	4 238821953
4 902567885	4 495935923	4 568095485	4 350755289	4 789617489	4 798557092
7 738038594	7 399847359	6 793747656	5 776362725	7 238298849	6 754855183
4 44149913	7 087755764	3 731877474	4 475987141	4 428559662	4 774107238
6 219132997	4 638609895	4 703690533	4 643609942	4 786014671	5 21644202
3 796200801	4 676800091	4 08327346	4 054116604	4 150572158	3 802066166
3 949222915	3 725887695	4 65464807	3 792428977	3 977139784	3 979915475
10 43857661	10 36731709	7 976698214	10 27779209	9 001431132	10 29594376
10 69880261	9 602303664	7 996721888	7 921965006	7 62904491	6 325046297
11 05789943	11 32014284	9 165072316	8 878283444	10 59305656	10 89199464
5 36981467	6 287868366	5 35800088	5 084201432	5 385908035	5 754209953
7 850100559	8 548909628	6 638600393	7 02160107	8 189028139	7 682130115
5 10522169	5 393347056	4 531623205	4 730839159	5 250513303	5 45630163
4 464879331	6 706466721	4 020999597	3 717656107	4 318209777	4 896021046
6 949037314	7 13615836	4 448082741	4 728860097	5 758911023	5 106209008
4 785218305	5 103143365	4 27052899	4 665550919	4 307504675	4 158214379
6 234968501	6 365369904	5 879498363	5 483462588	5 781097159	5 429587029
3 629313113	3 819139919	3 643732687	3 71587108	4 035883415	4 004123148
7 321602504	8 308196159	6 753576417	7 571905535	6 916410827	6 548283795
9 443275263	9 901528026	7 340604049	5 734337263	8 025072789	7 904901855
10 79882134	11 14775576	5 454193201	10 93108317	7 717791153	11 27146321
5 006348827	5 954616276	4 159558888	4 205087966	5 03756953	4 289895351
6 631005899	8 094710445	4 496548418	5 456206128	5 872133861	6 98812268

Urinary Bladder GSM89073 Urothelial (transitional cell) carcinoma	Breast GSM46908 Ductal Carcinoma	Breast GSM46933 Ductal Carcinoma	Breast GSM46934 Ductal Carcinoma	Breast GSM46947 Ductal Carcinoma	Breast GSM46952 Ductal Carcinoma	Breast GSM46953 Ductal Carcinoma	Breast GSM46954 Ductal Carcinoma	Breast GSM46955 Ductal Carcinoma	Breast GSM46958 Ductal Carcinoma	Breast GSM46962 Ductal Carcinoma
4 901995471	5 267672818	6 540201702	5 22988846	4 730879408	5 408106141	4 945834618	4 97254628	5 914298158	5 154808384	4 918677363
4 411207468	5 036566949	5 653273277	5 095974242	4 588363254	5 203239222	5 141643873	4 648120129	5 507934651	4 68249283	4 769868765
3 8117762	4 307998516	5 164734966	3 921565412	3 869690455	4 42581296	4 18081856	4 202148884	4 766751971	4 368650909	3 776333378
5 061419654	5 819017998	5 147239879	5 246877659	4 605387182	5 713959397	5 376425616	5 203145469	5 908840417	5 957136492	4 818804933
4 586852871	5 819096531	5 959861985	4 747031868	4 464397496	4 252610101	5 006914462	4 567648304	4 766751971	5 272455549	4 508854632
5 88021116	6 808815691	6 933250808	5 909606858	5 353363187	5 735354512	5 966528678	6 054202121	6 052502012	6 582379792	5 658665306
4 652167071	5 189966358	7 515511633	5 799118902	5 070050372	5 551196789	6 352975531	6 268579215	6 314664167	5 034523732	5 432908381
8 313255785	7 305202769	9 131347026	7 846693236	8 572114891	8 074358936	8 945496392	8 042017751	7 938812041	7 428373872	7 946279978
6 226389128	6 940832674	7 446126906	6 456681668	5 770456424	6 545252008	6 68261341	6 543062762	6 169136385	7 523311145	6 468039261
4 477595846	4 969996661	7 796884136	5 756597951	5 075092129	5 802131585	5 731836867	5 613853398	5 039620994	6 151815307	5 249043555
6 377169345	5 630161209	9 127957301	6 500774997	6 177611746	6 820514183	7 172574243	6 367482712	6 411706246	6 900115319	6 483821894
6 439304994	5 75126256	6 531247548	6 430962649	5 579302015	6 151953035	6 321324914	6 556023118	6 376640325	6 900142125	6 2390658
6 489097436	7 338481278	6 906344074	8 230364825	6 205472726	7 925774169	7 269038931	8 013258574	7 224460612	8 214300036	6 822856107
5 263837706	6 073294111	6 032898904	5 471132928	5 223610079	5 569629707	6 176870452	5 388199334	5 279145063	6 341650565	5 448394487
6 377273404	5 790565156	7 246471201	5 066327828	6 003348163	5 636596008	5 232895686	4 868186158	5 379478036	5 111079739	5 387030548
4 089755402	3 895150073	5 014076289	4 630193043	4 377201883	4 959003198	4 384877562	4 466939634	4 435304225	4 674082831	4 014054897
3 815610878	3 722380207	4 427823747	3 888171631	3 169521125	3 854900168	3 695862049	3 791848687	3 601889442	3 701139249	3 124775367
4 497797139	5 40839098	5 417286637	4 954075431	4 115843626	4 860719542	4 878676679	5 458827492	4 704974157	4 771371152	5 099551034
9 906842436	6 27598894	9 61120708	8 30407016	9 221939823	9 765057031	9 63805412	8 205426794	9 260204074	8 010174699	8 645824004
6 478012082	4 248276482	5 815181344	5 763759229	5 805968911	5 285556648	6 194911216	4 584040963	4 846725823	3 984970907	4 632777161
6 403194504	6 522371775	7 496666408	5 50354574	6 408246344	5 85583278	5 511905014	5 109600268	5 826235992	5 814548154	5 828340621
7 107033662	4 947982098	7 293429946	6 552986062	6 444600662	6 766097761	6 902529816	6 637672115	6 736661507	6 986879435	6 479905178
3 941520123	3 998344237	4 455577726	3 787969337	3 820658204	3 958854019	3 775598828	3 944029648	3 927435175	4 13077249	4 931801238
5 907626593	6 854475719	7 197549001	5 861441668	5 114934005	5 49364227	5 619895713	5 424769401	9 530053721	6 057421212	8 706509284
3 194633427	3 558577911	3 903697286	3 272895236	3 443030762	3 227379605	3 474599609	3 014654705	3 244601368	3 529871572	3 327757818
5 085600992	5 365849784	5 573451859	5 873045857	4 875368162	6 359493864	5 497660617	6 65807058	5 902880321	6 3496978	5 71568497
7 713167145	7 320836425	7 844727506	6 968559193	6 893239243	7 571719861	7 547769359	6 929257337	7 020074772	7 388791176	6 728735291
8 281100465	9 074882672	9 074410114	8 375970592	8 083259178	8 814828919	8 798722617	8 601644291	8 696267938	7 587147738	8 023993232
5 143095914	5 462302453	6 473451581	5 361005723	5 342838313	5 524508065	5 491885108	5 005869926	5 174099994	5 38493843	5 144275989
5 354624016	5 641278911	5 986082555	5 170590079	5 012028151	5 381325197	5 460359621	5 185665083	4 85394522	5 146126615	5 377761498
3 715397806	4 392237643	5 529630995	4 182783582	3 386064491	4 675958525	4 339659346	4 39505549	4 085364955	4 053097785	3 915569749
4 719693629	4 95203175	4 664279959	4 390487328	4 372026557	4 085557053	4 834628419	3 911229993	4 054613004	4 277106893	4 223258601
6 705320443	6 45444964	7 054393753	7 093338843	5 889261907	7 498170454	6 766843223	7 039855985	6 704556402	6 936388052	6 874644519
4 360617163	3 868767247	4 658188288	4 060282768	3 664878921	4 039518536	4 32761777	4 015716872	4 134171569	3 967840963	4 171594506
5 61470503	6 671485081	6 405637482	6 663506021	6 061260122	7 208285259	6 676683748	7 241214624	6 405975514	7 14677245	7 759914861
4 757898311	4 914152108	5 499119937	5 891856512	5 596495617	7 598450491	5 189519789	5 148349088	5 177501446	5 175548689	4 80130796
6 249007035	6 726634289	8 974973515	6 866895488	9 127903735	7 257424139	8 105901752	6 593228116	6 977112169	6 955567201	7 73102449
7 803654007	7 27322	7 68452945	8 296281128	7 42396385	8 296368312	8 59045817	7 990242658	7 856799042	8 020991943	7 963802761
10 36299816	9 792402071	9 702426731	9 288556621	9 698771208	9 009060474	9 689127176	9 387129736	8 728679366	9 270278879	9 073220863
6 105986475	5 181527504	6 908089135	5 147654247	5 109822303	4 775879126	5 456198499	5 62150674	4 953232891	5 142614354	5 237098382
8 198751083	8 915155784	8 925367834	7 82963615	7 245311806	8 038003678	8 330334095	7 931647506	8 097700816	9 199435610	7 550022716
7 152002667	5 672724342	6 496906885	6 631559754	6 51234006	6 216138641	6 507835264	5 451327987	5 589348573	5 720337174	5 061189814
6 962615237	5 213095966	6 929496253	6 29311117	5 898991226	5 758478154	5 438181964	6 458075525	6 348447579	5 108898537	6 166313337
6 430392511	6 289291936	6 567981635	6 994517845	5 873580325	7 268914803	7 235520906	7 373128889	7 355612047	7 097790337	7 041792331
4 745991729	4 516334986	4 600826915	3 845906537	4 431706199	4 793381786	4 950794771	4 682895131	5 20099537	5 20099537	4 342424087
3 094771685	3 476854638	7 966126289	3 127702277	7 885645921	3 289002678	5 875395952	3 249537983	3 04789998	3 792071009	3 78561887
7 084069893	6 692580728	6 179192219	6 794474465	6 128897782	7 025147601	7 036428598	6 392678993	6 546165552	6 941749893	6 39817095
3 077159564	3 347301242	4 475504431	3 871404714	3 728231638	4 481083107	4 535244819	4 382551422	4 143249592	3 93728791	3 979729896
7 0899409	6 38802763	8 462779487	8 147671502	7 321061517	8 136316214	6 518387483	6 98711089	6 714311827	6 153890914	5 816319337
7 171376226	7 008529758	6 966891243	6 412345887	5 349409283	5 029518893	6 014436423	5 838857989	11 78558771	5 76292633	6 821850406
6 815333493	6 803109482	7 757856882	7 255556672	6 188051439	7 745325321	7 050036085	7 265616531	6 432232295	7 826453915	7 286453915
3 803948795	3 758181265	3 828259433	3 429803354	3 32206236	3 339731538	3 481143138	3 273177078	3 288260145	3 374490951	3 298028846
8 975454442	8 790338243	9 021940304	7 079796104	7 6027684864	7 760224457	8 356281664	6 658709388	9 985182618	7 538480987	7 453531453
9 015394909	8 123315409	9 129687445	9 048977871	8 569562265	9 754187966	9 588132031	9 273162057	8 798524832	10 00875998	9 272448394
7 172643721	7 193899316	7 484207871	7 232204675	6 424656938	7 384251629	7 186629606	7 503821205	7 409673908	7 076273908	7 076273908
6 918319981	6 069007856	7 136992106	6 494573708	6 499272622	6 876841277	7 001861204	6 358024176	6 747187165	6 377146518	6 20659989
7 691697933	7 053044795	8 547130448	8 166735927	8 305263077	7 866949716	7 735306713	7 670108056	7 90537149	7 55567603	7 803635719
7 019728133	6 559880868	7 549990807	6 973120415	6 375027035	6 82889927	9 210840342	7 306044825	6 812771584	7 106767153	6 734771114
6 221180856	6 693179523	7 153660145	6 39110979	5 581475474	6 811428264	6 613716939	6 397496296	6 249140866	7 242407664	6 172523963
4 356459669	5 747203304	5 353692301	6 196313743	5 421618541	6 160410137	5 289495824	6 233139629	5 124633934	4 310869764	6 126420245
3 680102639	3 724633524	4 00852968	9 341424445	3 17079184	3 801365634	4 071799014	4 434089979	3 43474254	4 334633604	3 53139423
4 647568831	4 551419716	5 41226279	5 166075412	4 60181567	5 651126054	5 727039714	5 142451734	4 973817599	5 147698272	4 93098756
8 069203474	6 38037958	6 978725622	7 765643908	6 959790871	7 455675033	7 538217901	7 218027928	6 923596432	7 52046896	6 511335781
5 077632186	4 381577525	6 425288531	4 728994347	3 669971329	5 122938839	4 949303248	5 675001003	5 432545551	4 952417171	4 963072635
4 35776513	4 893968775	4 29684108	4 208628924	4 194077748	4 430203459	5 116171062	4 185603076	4 30545848	4 443177294	3 660450942
4 211890832	4 406846486	4 445641631	4 242155259	3 848747338	4 177456663	4 558889432	4 198424012	4 237604486	4 961130235	4 009624868
3 612841813	4 85435664	9 46774508	3 954309592	9 652397719	4 944079593	7 436668045	4 559320444	3 813658248		

Colorectal GSM38075	Colorectal GSM38077	Colorectal GSM38089	Colorectal GSM38105	Colorectal GSM38107	Colorectal GSM46819	Colorectal GSM46841	Colorectal GSM46845	Colorectal GSM46856	Colorectal GSM46857
Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma
5.396325536	4.91581872	5.543785263	5.292465392	4.635093494	6.273161339	6.392355323	7.714928915	5.047581	6.298445665
5.063792386	4.694344431	4.553865634	5.12140988	4.797530365	5.523186132	5.792516218	7.600431918	5.045419273	5.210254491
3.798889694	3.6234777	3.797934529	3.963747876	3.992778946	4.992636438	4.737096005	5.728507444	4.167519201	4.386528413
5.467652131	5.13538306	5.403262134	5.523192332	5.06892755	6.105283427	5.612871142	7.419713698	5.49679817	5.287485139
4.84724298	4.645161864	4.772671647	4.967241976	4.522721432	5.959038302	5.228226275	6.738826789	4.88258024	5.547195709
5.255032581	5.412481394	6.081432118	5.764574096	5.22801638	7.335698781	6.188342848	7.523188767	6.210992606	5.914546582
4.986934912	4.650615656	6.70482184	5.9492947	4.873602474	7.643105355	6.589523076	7.853046691	6.503175363	5.961515369
8.769050412	8.754185194	9.213620926	8.935690991	8.641037186	9.953393563	8.259726106	10.89072831	9.485612259	8.828683030
5.870204901	5.569696616	6.350472789	6.530183964	6.08028208	7.030290099	6.537343731	7.750945279	6.502732606	6.286428334
4.990019546	5.177313137	4.984382126	5.102070851	4.735194195	5.699735588	5.266051075	6.638920525	5.404326436	5.575699458
6.327108269	6.788696183	5.917241954	6.202920591	6.074207555	6.273131291	6.642640642	7.09450402	6.046097495	6.945739356
6.116899908	5.578117871	5.726617854	5.440720058	5.481463978	6.255296153	6.153163779	6.42902215	5.861127314	5.945280772
6.138647528	5.327859886	6.287420744	6.389261467	5.859906925	7.278505282	6.453280064	7.915977405	5.933958436	6.749863373
5.096271796	5.147005579	5.109350731	5.377850055	5.224441141	5.814400694	5.349109659	6.15664251	5.12127979	5.422081089
5.402429276	5.056013762	5.1205961	5.606968967	5.525627725	6.782046153	5.13442512	5.316606943	5.362913172	5.472259147
4.526301415	3.692897149	5.027629914	4.036677513	3.979154196	4.0438010761	4.043809972	5.30555028	4.150616508	5.47562913
3.715512402	3.541026052	3.673552469	3.394259408	3.617037431	5.9228582	3.905211676	5.85045098	3.727521475	3.706043465
4.283640486	3.941784538	4.523629693	3.906720799	3.842962734	5.742508335	4.843526792	4.643044756	3.711294866	4.50483372
10.11452785	9.574910246	9.843953794	9.338745933	8.688016105	9.726487549	9.700046073	11.11282568	9.725046791	9.970118777
6.80799981	6.501213893	7.505225978	6.769627766	6.478782808	6.931634243	5.978185458	9.677089066	9.220315464	6.822878121
5.018533203	5.43866019	5.437262479	5.559026077	5.392375189	7.194951849	5.432539691	5.719722917	5.456026688	5.368176282
6.436028547	6.346800861	6.013506441	6.151024316	6.437353106	6.46889441	6.896656448	6.091858096	6.04594696	6.370466602
4.252833693	3.796794834	3.949017986	4.088476263	3.908484193	3.868899297	4.095483928	4.265846638	4.122610278	3.606656407
5.037358645	4.64408799	5.521467479	5.590774435	4.56784594	7.72645588	5.381048427	7.292454282	5.285951562	6.80797582
3.366541949	3.321380002	3.532348169	3.454228471	3.225817849	3.548896674	3.457198059	4.249952648	3.161657207	3.292934178
5.556195514	4.986155545	5.315172978	5.168939975	5.175475167	5.933982806	5.355991426	6.200571088	5.045155393	5.561401508
7.082344481	6.956150586	7.016658568	6.606766286	7.131597062	7.614498955	7.042186769	7.724085422	6.604869737	6.957636415
8.278699509	8.149023823	7.800627846	8.207145598	8.352943166	9.023693383	8.707621392	9.344705878	8.161768982	8.313133816
5.444998393	5.528185052	5.552534343	5.084088376	5.008703963	5.465518473	5.074849735	5.377147455	5.229452708	5.173362097
5.194006316	5.294664422	5.20804708	5.126392147	5.104681499	5.608822719	5.512045493	5.839871665	5.431706429	5.504610201
3.862419416	3.348750884	3.926303037	3.71367236	3.967360307	3.56588276	4.829131536	4.464701911	3.866216373	3.530186353
4.223912294	3.928780542	4.33306628	4.216527117	4.617758731	6.079293323	4.300081699	4.765300745	4.213531609	5.174303987
6.913271848	6.904113257	6.853542521	6.43189206	6.553260397	7.135210163	8.180304804	7.934548692	7.051910408	6.938957301
4.016159639	3.424789997	4.501103208	3.581022902	3.837817585	4.145569351	4.142599675	4.217136263	3.747149778	3.929579535
6.021483267	6.108846038	6.567674906	6.045918592	6.09488545	6.064439177	6.317020714	6.54294198	6.04594696	6.542942029
5.153409896	4.431121563	4.760285425	4.374648994	4.460791994	5.967140618	5.431626601	4.996540549	4.600443845	4.42167819
7.604231968	7.515438106	6.821590095	6.90434468	5.807243421	9.365728561	6.23317707	7.988580744	7.195881615	6.939237596
7.931005481	8.163384426	7.629225731	8.200201461	7.886715157	7.498856473	7.570312714	9.133795286	7.58848736	7.890428673
9.378637054	9.245594675	10.07303813	10.12203028	9.644777953	11.02153442	9.477972744	11.38785326	10.4216802	8.702567518
5.389542513	5.19929602	5.177159382	6.47647072	6.617536609	7.118714421	6.23479769	4.945888241	5.47024475	5.25293065
8.023829121	7.248921317	7.347240536	7.389939475	7.886771575	8.448059349	8.504905957	8.777633081	7.541352472	8.732783326
7.733769934	7.473709761	8.366639805	7.947551519	7.233696957	7.547191567	6.738961383	10.37032596	7.289617157	7.479957996
6.622312484	5.671836366	6.065077186	6.384891241	5.882570154	7.219766421	6.231620578	6.401748732	6.225464291	6.10210228
6.754871665	6.385435345	6.479739568	6.227098195	6.921461321	6.56910839	6.17867268	7.281274606	5.930171347	6.62294422
4.842175838	4.346082163	4.886352549	4.482666405	4.629953226	5.105269868	4.979836026	5.834947638	5.93566372	6.602022503
3.013879587	2.971268631	2.851170406	2.911640955	2.934552431	3.108682564	3.164547353	2.857112535	2.956695315	2.855366412
5.846386425	5.766498521	6.055081398	5.796709371	6.036902804	5.947670809	6.213062039	6.199507659	5.760641858	5.51637041
4.140446393	3.81885999	4.038648851	3.624008875	3.548308294	4.121697578	3.749339061	4.031239999	3.86872293	3.945257034
7.267247616	7.409464291	6.708746118	6.875406873	5.624712085	8.504698542	6.359195357	8.460638735	5.7661163145	6.719876328
5.674309356	5.405305339	5.917252438	6.362023368	4.483254695	7.479287645	5.928778599	8.046642743	5.715033229	6.407703591
6.759787447	6.227466768	6.278935092	6.443507826	6.432994878	7.608802183	6.873527515	7.597811146	6.32540252	6.892870689
3.403682	3.468614301	3.422801405	3.463558085	3.455344568	3.450606374	3.434918068	3.619075932	3.448042056	3.474505045
8.964446177	8.342745028	8.90425974	9.495558772	8.626978531	10.85899136	9.633833988	8.892530473	9.089078461	9.100520252
8.855743689	8.365458548	8.597406111	8.468225093	8.880949987	8.452617591	8.842856239	9.659041143	8.353227097	9.75252086
7.686411066	6.730177337	6.839716204	6.967394037	7.510197171	8.184451006	7.141565967	8.409697886	7.351275827	7.771029049
7.000455653	6.59561035	6.768162139	6.430057968	6.92339003	6.134736609	6.821555816	7.614696186	6.015159422	6.356932643
7.992210024	7.580901648	7.925054539	7.556638313	6.955571232	8.011816211	8.1051167	7.55064301	7.360857782	7.901471849
7.892578381	7.470824895	8.061222268	7.407886355	7.345565856	9.040250187	8.514165994	8.069454847	7.365044124	7.802331689
6.385558634	6.318389037	6.365286015	6.221494359	6.284691108	7.560628767	6.082843331	6.589352507	5.917529706	6.257284937
4.868207121	4.458799932	4.790534619	4.757128439	4.889740915	4.784647011	4.581741052	5.208912253	4.148474187	4.602015023
3.435201003	3.674433201	3.391324149	3.59020259	3.472084341	3.972540399	3.473893092	3.891869646	3.667149562	3.665513319
4.838834042	4.659959498	4.85607914	4.613288676	4.745790227	5.105448094	4.527158968	5.124373012	4.53916427	4.713278525
7.325557424	6.87933423	7.013929445	7.063886113	7.06442336	7.220142594	7.009468994	8.41197593	6.499168489	7.215685791
4.289049347	3.708532633	4.384406103	4.130815464	3.964915345	4.941002132	5.156117947	4.963395091	4.797704434	4.278886492
4.876275429	4.083126566	4.741832123	4.426821377	4.165096284	4.597286597	3.975556551	7.441196447	4.045104714	4.448125144
4.277208132	3.729351056	4.178175744	3.63545318	3.812406461	4.138520913	4.075234484	4.542818977	4.251818505	3.94945406
3.827781149	3.967480326	3.639367404	3.697979794	3.935992899	4.060394763	3.823315705	3.693576394	4.05035885	3.97839263
10.19996949	8.787016123	9.664145999	8.778323574	8.697085276	10.42161139	9.091398595	10.90854666	8.802028075	9.246279333
6.011414449	5.572404445	6.849033256	6.371544455	3.903705354	8.671256954	7.311191541	9.189291006	6.699226006	7.304638329
10.83259765	10.39654891	10.6365896	10.44061426	9.857668576	11.31645092	10.7245045	11.67395994	10.45214383	10.8304003
5.586084683	5.322094446	5.649212326	5.25487064	5.434098802	5.557857579	5.642529557	5.753829116	5.356830097	5.588798909
7.441153581	6.504387549	7.487522612	6.523620407	7.500505046	5.630624984	7.537058213	7.358748326	6.503797983	6.948585407
5.166018072	4.928588933	5.101130686	5.36680093	5.485524044	5.846215911	4.987789915	5.58237962	5.127809685	5.085589683
5.688448392	4.831292086	5.720805958	5.046571795						

Colorectal GSM46861	Colorectal GSM46865	Colorectal GSM46877	Colorectal GSM46879	Colorectal GSM46901	Colorectal GSM46969	Colorectal GSM46972	Colorectal GSM53087	Colorectal GSM53132	Colorectal GSM53168
Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma
6 158408624	5 313519461	5 573963299	5 695573884	4 960504983	5 631418091	5 15769076	4 920705179	5 124190788	5 052567287
5 410226529	5 294490849	5 203032465	5 514505254	4 672984046	5 169165918	4 761692199	5 417552962	5 3579315	5 349343711
4 370037259	4 131362941	4 434794868	4 450885585	4 175272419	4 15275665	3 799173193	4 13465521	4 185231141	4 126189176
5 741788513	5 221316952	5 904044836	6 473108933	5 353059143	5 504555456	5 223630049	5 323113193	5 406170729	5 82620042
5 966061583	5 398734454	5 514179593	6 374257772	5 167412603	4 896608113	4 762285598	5 010142525	5 313354463	4 928579108
6 272867592	5 944872551	6 589959818	6 567850316	6 44583059	5 730520434	5 516304548	5 456393357	6 510293304	6 495999975
6 808439172	5 913600463	6 42098876	6 700184561	6 753139496	5 65151873	5 741297122	3 950720599	4 559801675	4 428557542
9 052147921	9 356258112	8 442498627	8 856900162	9 306264857	8 647473592	8 791828157	7 960822242	9 200115968	8 459585067
6 831813064	6 640111193	6 797992435	6 967327915	6 901902841	6 493562723	6 160028787	5 783674927	6 674265194	6 542649428
5 30173331	6 068811188	6 03477253	5 532854399	6 215887728	5 15436652	4 978543745	5 071111075	4 920349433	4 621834724
6 423349374	6 35025016	6 075996322	6 395118838	5 637043519	6 2341787845	6 239728631	6 519178584	6 649869907	6 189215366
5 958735693	6 288978266	6 659763416	6 484511374	6 091847748	6 033645687	5 324490783	5 179010882	6 074633942	5 745183292
7 186105477	6 219555467	8 036226279	7 472218423	6 978929868	7 326271756	5 713291912	4 397592874	5 541415663	6 577024763
5 275018396	5 445431206	5 113008727	5 225248669	5 556146697	5 405277577	4 816752778	5 417637555	5 180763907	5 508995887
5 304867663	5 438449906	4 892550645	4 757247611	5 150005105	5 879642497	5 435020463	6 028105532	5 575753736	5 617357232
4 703842695	3 575301462	5 105889881	4 735477816	4 705018473	5 088429719	4 112852752	4 040573746	4 529627166	4 30687407
4 393527293	3 793963245	5 485858408	4 691636006	5 886506656	8 444947436	3 723918788	3 79071744	4 702242239	4 453522355
5 286160909	4 337287129	4 917904777	5 740844255	4 699047213	4 105650026	3 944287771	4 254630083	4 982045908	4 743021135
10 06491839	9 11303507	10 94267444	10 37465174	10 8586876	10 967217962	10 5868876	8 97516638	9 712109099	8 167417697
7 098794851	5 986614253	5 515131026	5 637973588	6 118328854	8 881589007	6 905846587	6 045482957	7 434767933	6 46924729
5 450847733	6 021042517	4 928603272	5 325234651	5 251329933	5 94744129	5 517062019	5 037933577	5 517047014	7 37428573
6 45655826	6 259069072	7 531397738	6 78754752	6 256717624	8 743115378	5 695496058	6 143563549	6 27377812	6 154554621
3 780930088	4 164577683	3 619767462	4 393687256	3 610438701	3 784997515	3 948888889	4 424092285	3 978482713	3 890891959
6 649278545	5 114296501	7 314748371	6 731518937	6 289196423	6 459953006	6 70369454	4 434482073	6 1758186041	7 154605592
3 490373994	3 341567996	3 063217446	3 162593549	3 178223235	3 332875749	3 469710705	3 464956328	3 618917725	3 577891324
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Colorrectal GSM76546	Colorrectal GSM76571	Colorrectal GSM76575	Colorrectal GSM88976	Colorrectal GSM88982	Colorrectal GSM89013	Colorrectal GSM89074	Colorrectal GSM89075	Colorrectal GSM89094	Colorrectal GSM89100
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6 265371507	5 955434122	5 229129309	5 917128611	5 653627785	5 562105081	5 624586024	5 617475018	5 665765802	5 227484762
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Kidney GSM117706	Kidney GSM38073	Kidney GSM46625	Kidney GSM46826	Kidney GSM46847	Kidney GSM46858	Kidney GSM46875	Kidney GSM46881
Papillary renal cell carcinoma	Conventional (clear cell) renal carcinoma	Conventional (clear cell) renal carcinoma	Conventional (clear cell) renal carcinoma	Papillary renal cell carcinoma	Conventional (clear cell) renal carcinoma	Conventional (clear cell) renal carcinoma	Conventional (clear cell) renal carcinoma
4 60863349	9 413214723	10 0052265	6 315546742	4 508695241	6 934418049	8 089560174	9 15512628
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3 577802689	7 285805143	8 399141104	4 482309647	3 343716778	4 536101144	6 331422764	7 217575883
5 301125531	9 399644718	9 702085346	6 424128084	4 327880948	6 557841935	7 594750015	9 231572774
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Kidney GSM46882	Kidney GSM46892	Kidney GSM46892	Kidney GSM46839	Kidney GSM46944	Kidney GSM53060	Kidney GSM53092	Kidney GSM53122	Kidney GSM89099
Conventional (clear cell) renal carcinoma	Conventional (clear cell) renal carcinoma	Papillary renal cell carcinoma	Conventional (clear cell) renal carcinoma	Conventional (clear cell) renal carcinoma	Papillary renal cell carcinoma	Papillary renal cell carcinoma	Papillary renal cell carcinoma	Papillary renal cell carcinoma
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5 849958785	6 627998382	6 736444901	6 80654					

Liver GSM137909 Hepatocellular Carcinoma	Liver GSM137962 Hepatocellular Carcinoma	Liver GSM179952 Hepatocellular Carcinoma	Liver GSM203676 Hepatocellular Carcinoma	Liver GSM203750 Hepatocellular Carcinoma	Liver GSM231890 Hepatocellular Carcinoma	Liver GSM203751 Hepatocellular Carcinoma	Lung GSM102505 Bronchioloalveolar carcinoma	Lung GSM117610 Squamous cell carcinoma	Lung GSM117629 Squamous cell carcinoma
5 308715663	5 923746127	5 385099213	6 004124273	4 526438773	4 798154885	6 129483666	5 279237587	4 722914723	4 725951182
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4 193627996	4 378327258	4 101656249	4 054067761	3 369143704	3 649503941	4 051646958	4 214002119	3 71951558	3 964367181
6 078461269	5 684499947	5 528265632	5 703092225	5 05706114	4 845447258	6 190579683	6 11735264	5 431116046	5 347667174
6 243342321	5 863737389	5 52141749	6 503209791	4 194958795	5 17406112	5 699347577	4 677520993	4 619857491	5 270150325
6 753387428	6 709031016	5 867633322	6 184624401	6 360553574	6 305845514	6 544941928	5 202973184	6 750870246	6 545266365
5 69972506	6 136731121	5 490725671	6 011360233	6 147779363	4 39285179	6 151006751	3 762872159	6 136446512	6 024915698
8 918224997	9 061107012	8 674812269	9 278305615	8 678897326	8 357610736	9 579298377	7 622410011	8 729571171	8 208355514
7 567141596	6 967396696	6 660952137	7 09056418	7 147049474	7 457689893	6 852919063	6 510144946	6 152227459	6 715328903
5 372287149	4 731015074	4 415109687	4 486947235	4 717482228	4 790489837	4 723291313	5 352211973	6 838408407	4 956604431
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6 649019603	6 204668227	5 962730774	6 147093515	6 428212338	6 210421675	6 415066717	6 196840003	5 870629579	6 753521255
6 829056451	6 211929384	6 022927359	6 020559344	6 83928297	7 144423085	6 817287167	4 713858481	5 570227853	5 370162202
5 79523016	5 117061086	5 098735399	4 782728476	4 910107653	5 485618174	5 221535388	5 805547341	4 890404527	4 681458271
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4 188229293	3 775400286	4 478659501	3 719696232	3 70057467	4 104751407	4 115194932	3 784528374	3 656185346	3 401120708
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8 406776263	9 589431089	8 309519449	8 324663288	7 358215718	7 578700338	10 1674838	6 854025505	11 42478957	10 9631753
9 299561767	8 052853073	7 828142249	7 624557782	8 264129975	7 624059796	8 85583974	6 191990231	7 979758098	9 007305433
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6 450860241	6 257598854	6 168510707	5 963398749	6 145539986	6 566831289	6 777220178	6 759249149	6 853484553	6 110043115
7 150380642	7 944316091	7 944316091	7 319204164	7 583666225	7 610012023	7 714713577	7 234884204	7 293085793	6 885874931
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4 154130698	3 816604331	6 909388611	6 241130984	6 807250906	6 64460464	6 875783096	7 25227262	6 648557071	6 157222881
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7 929991839	5 980953748	6 609786046	6 598620428	8 753882265	6 97760976	6 66920394	6 747878231	7 452212769	6 7291287
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4 91354926	4 079767196	4 084383678	4 019576789	4 498072187	4 375940806	4 903688328	5 173842772	4 854297461	4 541095796
3 951333629	3 997348297	3 838475861	4 185948539	3 58625459	4 114049582	4 271265227	4 728962697	4 065652354	4 245333961
11 66622746	11 01824027	11 76533874	10 74630518	11 2866755	3 875745886	3 842351553	5 399022643	3 984668637	3 765264001
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10 90673855	10 29711337	9 85586879	9 367297375	10 22082728	10 48324105	10 588			

Lung GSM117632 Adenocarcinoma, NOS [*]	Lung GSM117671 Bronchioalveolar carcinoma NOS [*]	Lung GSM117770 Adenocarcinoma, NOS [*]	Lung GSM117772 Bronchioalveolar carcinoma NOS [*]	Lung GSM117910 Adenocarcinoma, NOS [*]	Lung GSM137912 Adenocarcinoma, NOS [*]	Lung GSM137916 Adenocarcinoma, NOS [*]	Lung GSM137931 Adenocarcinoma, NOS [*]	Lung GSM137945 Adenocarcinoma, NOS [*]
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4 905174045	4 061028356	4 561842108	4 532399611	5 396310905	5 940637077	5 837203071	4 4855606	4 613830407
3 736473103	3 668858483	3 863691622	3 766113488	4 189247531	4 330102617	4 597808485	4 088541984	3 69276591
5 552111397	5 088541233	5 768061378	5 30219002	6 317096215	6 369374964	5 688271248	5 613626327	5 104803742
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3 96808162	4 12260503	3 978883564	3 938610589	4 180098362	3 773426763	3 883347277	4 943569562	3 82036205
10 04025878	8 923501369	8 655221247	8 61410629	8 59893796	10 36643863	9 687105964	10 40157474	8 526037203
7 723271346	4 124436716	4 940345567	6 536916287	7 733819728	8 421039203	9 51921314	7 517827775	4 772024649
10 46073016	9 154364194	9 729115526	9 897039433	10 67844997	11 67958973	11 10302811	10 51280548	9 566270156
5 591035006	5 548422598	5 43139866	5 486386788	5 384901047	6 14301179	6 17741134	6 532462521	5 034866283
6 177508335	5 844569834	6 087253538	6 055783545	6 34921932	7 271152801	6 504894223	5 96965516	6 624828889
5 252283282	5 889612103	5 034279913	4 902107282	4 55954636	5 11391392	4 965716732	6 198508322	4 947984932
4 946343372	4 768831666	4 765377347	5 23233381	4 608180354	6 475638888	5 436728644	5 641112211	5 078727428
4 964852698	5 458748061	5 457852311	5 252588849	7 137603448	6 195668311	7 060842855	7 78094462	4 630235154
4 285842803	4 327456724	4 482101164	4 285926157	4 600951806	4 220296715	4 141858284	4 119974059	4 942011403
6 152112609	5 98972317	5 688887836	5 465084454	6 393210404	6 136493735	6 327937728	6 141335674	6 687802671
3 859579604	3 649371082	3 663598253	3 752982347	3 826804199	3 946995049	3 994150937	4 422635484	3 829380716
6 356299864	5 604843334	6 79711709	6 791461182	5 810829787	5 912369151	7 844464428	5 039581825	5 139893051
9 101985344	8 174545073	7 250471767	8 11993209	8 104864006	9 931958964	9 622838187	9 574662064	7 344770426
9 192609022	5 962149601	8 328442043	8 894891903	8 23434249	8 429991225	4 936341644	6 523326775	6 042916346
4 262849817	3 807893969	4 250501937						

Lung GSM138001 Bronchioalveolar carcinoma	Lung GSM138002 Adenocarcinoma, NOS	Lung GSM46843 Bronchioalveolar carcinoma	Lung GSM46850 Squamous cell carcinoma	Lung GSM46860 Bronchioalveolar carcinoma	Lung GSM46868 Squamous cell carcinoma	Lung GSM46884 Squamous cell carcinoma	Lung GSM46904 Bronchioalveolar carcinoma	Lung GSM46936 Squamous cell carcinoma
4 644062395	4 662170023	5 050232897	6 463849612	4 077799739	4 572835179	6 49713849	4 48999732	4 96282286
4 236995575	4 398959575	4 779733722	6 055706719	4 18571535	4 430705508	5 606282628	4 545468707	5 069261038
3 860264999	3 871740906	3 710617879	4 885261113	3 500524229	3 655346211	4 661471336	4 217475537	4 232779889
5 289961277	5 190434037	4 728154626	6 170028036	4 053623852	4 951884069	5 88879117	5 182819574	5 149950061
4 756818946	4 959326513	4 724448922	6 223692521	4 75760115	4 655181569	6 584870976	5 014087382	5 022799021
5 955186382	5 583001093	6 093135741	7 060287237	5 473149293	6 773807202	8 108676166	6 442274354	6 411254934
5 530687236	4 420449418	6 19742536	7 323582777	5 364940122	6 807127335	8 039775864	6 8480873	6 386878678
8 272901176	9 754701869	8 904512353	9 699202726	7 936468501	8 758100693	9 503638756	9 186179145	8 72695654
6 959483899	6 678418852	6 889245136	7 46425432	6 336701764	7 181740933	7 722180722	7 423840468	6 865822533
4 866248121	5 128926364	5 007481973	5 632093501	4 578970556	5 315918226	5 234840481	5 098044836	4 818353683
6 713335124	7 004198232	6 634278488	9 999226568	6 849451084	7 47400284	6 719004141	6 807018712	6 4737134
6 718420124	5 955191529	6 350501439	6 136929535	6 14555195	6 631253051	6 721667266	7 440637539	6 449841189
6 40399631	4 956999502	6 417780099	6 498727836	6 312673698	5 60819775	8 409570423	7 15715085	6 828461853
5 528198084	5 297563765	5 022127576	5 190946952	4 900630832	5 440109943	6 114625649	6 058642477	5 107411154
5 74825121	6 181047883	4 746998573	6 16168368	6 014889086	5 128991629	6 991580924	5 761986842	5 179554517
4 173063927	4 341375496	4 615226887	5 151944775	4 618733191	4 700629471	5 337193081	6 253501103	5 18962347
3 950022764	3 334083758	3 696100793	3 95550616	3 948125681	3 822499113	4 433979217	4 787583483	3 782547266
4 028018081	4 009280375	4 266744939	4 948335511	4 253197915	4 8019445	5 660968276	4 388888635	5 052266344
8 911832316	8 784103473	9 081492679	9 725275156	8 313472375	8 420724151	10 29342922	9 118877784	9 10104828
6 627336685	8 05911174	6 260978359	7 942364368	6 116196162	4 858732143	6 650566172	5 049076043	5 344673699
5 961958948	6 977817803	4 8752167	6 082553474	6 109809282	5 3912296	6 753104167	5 661902676	5 777169633
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5 057819296	5 710098569	5 257542374	6 25061372	6 424433909	5 338602235	7 489499185	4 828000042	5 836566828
3 624918555	3 222682966	3 23287266	3 69030079	3 32981119	3 467583329	3 396093545	3 56595604	3 31254562
5 711798889	4 848364486	6 002426406	5 822505988	5 643492528	6 050791591	7 067584196	7 575228148	5 994674971
6 98284519	6 887633374	6 912040933	7 512019437	7 586063373	7 341664218	8 315057974	7 481785654	7 552013575
7 609191982	7 849726463	8 636580738	8 011947724	7 733995048	7 885129271	9 140519307	9 757343649	8 57685988
5 457619777	9 660780213	5 772906412	5 329751844	5 139050738	5 278452226	7 19577524	5 719931304	5 198543298
5 29547508	5 059262198	5 412884779	5 244100447	4 901044115	5 517481058	5 98641282	6 419512409	5 574157359
4 281529788	3 540722577	4 313376796	4 033707246	3 530969973	3 789949891	5 655897339	3 85502067	4 557658019
4 179081627	4 368285617	4 13398814	4 944608408	3 777713833	4 472168291	6 34822689	4 495769827	4 867072557
7 03337899	6 388298361	7 051920863	7 169838195	7 061529144	7 656350997	7 55075018	8 489479206	7 78736341
3 862228666	3 917690794	4 012451938	3 745820877	3 837702385	4 516504208	4 179820085	4 884238628	3 873286841
6 031559977	6 273041211	6 910840784	6 24849113	5 946845017	6 505373714	6 742528202	7 777251466	6 918943625
5 640695755	4 752504905	4 944213101	4 7127548	4 585167298	4 558130312	4 641618286	5 342828112	5 298258384
6 228060815	7 178088218	7 333935589	7 677884216	6 151142303	7 336277922	7 216881669	5 725459412	6 614961468
6 919713369	7 06668207	7 686139319	7 487095055	6 152173316	7 091532659	8 351347	7 471614854	7 153174947
10 42285368	11 65278164	9 766912072	10 75165659	9 373442685	9 799555885	10 82801826	10 17913924	9 892332088
5 721644001	4 9023039	4 546177224	7 733181714	5 482562954	5 244907819	6 550467112	4 839047596	5 322310888
6 896274832	7 265769874	8 098466917	7 478596004	7 078792991	7 569333498	8 497448421	9 576004726	7 679420702
7 245901155	8 477924807	6 591424582	8 394616179	6 932171377	5 651432505	7 026626347	5 568988538	6 089443505
5 843077217	6 144704797	6 707660943	6 529270529	7 496185733	6 141952587	6 45639106	5 664361985	6 523803859
7 033777876	6 070487174	7 204581954	6 436341015	6 076534342	6 278033548	7 497598003	7 547403929	6 803030303
4 494592795	4 580047961	4 181238342	4 557930919	4 280833199	4 128187385	4 842631087	4 630295191	4 472951032
2 920783581	3 219010244	3 133720575	2 947362225	2 944734427	2 963978635	3 570372358	3 302708821	2 737353599
8 900166214	5 911854733	5 95985777	5 588105594	5 679000575	6 337183363	6 91687955	7 492146274	5 14100794
4 394369665	3 945844922	5 524112642	4 438019326	3 820047889	4 547602904	4 447761544	5 496501708	4 443273728
6 499948537	7 252458923	6 923719981	8 192466186	6 202954035	6 647139591	7 296277627	5 716201286	6 075418622
5 264472735	6 321568827	5 225341625	6 188500841	6 68612296	5 035524547	7 820942754	4 616528821	5 922942146
7 774887186	7 107268664	7 171017134	7 592322903	7 542167627	7 478669163	8 489475223	9 181658721	7 880280425
3 588423158	3 64706846	3 128823343	3 158000097	3 138831005	3 43990674	3 141537461	3 537997942	3 329349614
8 870188552	8 38533393	6 959873597	8 9568844	6 951443378	9 88713557	10 19356574	7 48040936	9 38029339
9 602912418	8 661855721	9 882892513	9 116848861	8 84955638	9 337935168	10 14079322	10 90429724	10 02057099
6 3821559	6 476203014	7 170335004	7 26483906	6 657013308	6 811723042	8 379387876	7 679197619	7 520491529
6 641562372	6 294175295	6 277547084	5 961350741	5 716243584	5 891733488	6 653177259	6 502120752	6 518039772
7 205267854	7 157523911	7 442436404	7 593935211	7 631810556	7 447794114	7 859163269	7 367270745	7 820283526
7 492502252	6 900094337	7 835253978	7 371518928	8 825155846	6 830682098	8 221929405	8 327851008	7 995910488
6 829169007	6 413859735	6 734344934	6 46310196	6 273128689	6 586080671	7 237786772	8 162933239	6 742290241
3 574937422	4 002399736	4 375569225	4 634344544	4 488412853	4 780256137	5 056144975	5 287209317	5 41004931
3 518440885	3 679496864	3 596178698	3 82559227	4 18487367	3 381999868	4 019104519	4 15525023	3 626384745
4 973434439	4 460621337	4 528876659	4 592835244	4 575248457	4 779767319	5 091298284	5 592642056	4 645227605
7 534496665	6 596318772	6 857411718	7 315856804	7 434026063	6 816452168	8 008036625	7 95150818	7 5240319
5 626516619	4 748077735	5 479561375	4 467751894	4 357228684	4 585184417	7 500515585	3 956709552	5 34801558
4 449493718	4 523013786	4 303689045	4 304668743	4 4355412	4 470940029	4 56760745	4 689315474	4 347114248
4 987682336	3 947439605	4 151312791	3 973822812	3 969964012	4 523781216	4 507750754	5 792270869	4 390949161
3 98724813	4 530482786	3 882455378	3 695997347	3 894667899	4 916694221	5 568968831	4 106967337	3 639753103
8 35859043	11 16591915	7 812273086	9 493564759	8 543808789	8 895099139	10 18702806	9 934762246	9 427498992
5 639186299	6 738631577	5 462463611	8 14784646	8 121857522	6 819449969	9 784289791	5 345829632	6 62813639
10 63517786	10 65628867	10 43735014	10 65359949	5 532312533	10 28605146	11 51624355	10 86406406	10 34899996
6 138889709	5 452415255	5 601576333	5 773215052	5 327583142	5 510184072	6 285157511	6 220841056	5 880443093
6 031548453	6 570606891	7 36324114	8 211176435	6 18888052	7 112697808	6 838241036	7 440949483	7 416496645
5 167435806	5 209352043	4 165100613	5 005599248	5 796985407	4 81619608	5 08715693	5 223452874	5 129705352
5 801463478	5 29303398	6 728856643	5 942862847	6 203818071	6 597850514	7 434826323	8 29048701	6 970019194
6 14522579	5 441551877	5 935102446	6 475423678	6 393987202	6 356938322	8 221739354	6 156674696	6 926511353
4 159862119	4 578137893	4 461833181	4 054200703	3 897354134	4 442679106	3 89413667	4 140990295	3 804161254
5 891550866	6 267185619	6 225357112	6 125089135	5 196025224	6 107604888	5 857942617	6 99534934	6 097569527
3 619885377	3 793916001	3 833332981	3 70890613	4 048181815	4 043466018	4 299616933	4 932733237	4 554468881
6 128952454	5 668387009	5 225177187	8 157257473	5 544220239	5 624850081	6 507555627	5 245532062	5 184561042
9 227927961	8 128666865	8 816129476	8 935056824	9 022270111	8 969677521	10 11150238	10 529004403	9 676763382
7 039496069	8 535290549	8 667576204	8 174762221	7 887929138	8 23950428	9 599862755	6 372388292	8 506913525
4 333672145	3 970772273	4 607227511	5 024548975	4 550083928	5 331485949	5 53450128		

Lung GSM46973 Squamous cell carcinoma	Lung GSM46976 Squamous cell carcinoma	Lung GSM53167 Squamous cell carcinoma	Lung GSM76488 Bronchioloalveolar carcinoma	Lung GSM86949 Squamous cell carcinoma	Lung GSM86953 Bronchioloalveolar carcinoma	Lung GSM88981 Bronchioloalveolar carcinoma	Lung GSM89046 Adenocarcinoma NOS	Lung GSM89060 Adenocarcinoma NOS
5 950231932	5 238083277	4 864583427	5 238147602	4 957391401	4 718076665	5 133335369	4 855332098	5 045612401
5 951919488	4 708757342	4 609467128	5 0775203	4 882321446	5 081597553	4 918839955	5 200351631	4 792410721
4 616240533	4 40803706	3 924232582	4 257337824	3 963276636	3 877415439	3 808377501	3 657095284	4 136574147
5 814786687	5 426041277	5 046633776	5 222143505	5 192882428	5 40681671	4 875356628	4 923188531	5 373579722
4 994452698	5 155567207	5 104594963	5 368197255	4 818063489	4 675244529	4 653152449	4 800101677	5 173262078
6 72126095	6 818315305	6 561622096	6 174032029	5 852096847	5 704820536	5 441801696	5 695351574	6 095718439
6 759060638	7 045829735	4 838674025	5 201408401	5 33506942	4 599669366	4 689431643	4 316137973	5 114465196
9 902461171	8 788558367	8 566549185	8 818448472	8 295754132	8 538114582	7 410503257	8 380060736	8 580417337
6 82842636	6 766728068	6 631768387	7 011698407	6 277814096	6 197895445	6 676449083	6 195533477	6 228101491
5 834656259	5 391495248	5 067855695	5 425118586	4 949454174	4 3833387	4 970136589	5 091015312	4 925826793
10 41092882	6 865133699	6 825180467	6 062881455	7 486994432	6 320361414	6 488170567	6 302390107	5 672287418
5 742985148	6 24685038	5 632777226	6 019005732	6 382723221	6 266919277	6 66995386	6 753398215	6 179615681
5 793800025	6 456169272	5 649502772	6 258710543	5 740036258	5 782026732	6 115146549	6 091864037	5 851221819
5 354593886	5 667999988	5 19387689	5 189845947	5 474378492	5 608225732	5 692633964	5 239013434	5 218038462
6 38042627	5 249792176	5 926329003	6 044773681	5 482222743	5 39914963	5 483376796	6 091780425	5 3610345794
3 979078616	4 211296563	4 033294578	4 441628238	4 077075826	3 980031606	4 572230373	4 657108313	4 664812811
3 800754	3 732542806	3 757086746	3 77197406	4 769015308	3 503995837	4 954981277	3 397649088	3 62311834
4 338788486	5 066895378	4 624484731	4 743344488	4 334281447	4 259245812	4 333508298	4 476450821	4 344497866
8 9896861	8 805624502	8 729287691	9 191131033	6 83612867	8 550472276	8 242840725	9 813468413	8 531349174
8 043096207	5 285393939	6 577764169	6 065855535	6 546250974	5 455327162	5 17318287	6 439550104	6 80281197
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3 977306823	3 9591126	3 900038553	3 735625734	3 793526857	5 395874669	4 238518039	3 736926515	4 012922743
5 916717648	6 288401922	6 418741307	6 133743753	6 076376509	3 459797907	3 490928359	6 863647228	6 536939286
3 827247314	3 306652326	3 574038281	3 607962774	3 671027239	5 042599657	5 981830266	3 793513656	3 219893147
4 800899573	5 355065145	5 082030754	5 538902497	5 280260562	7 108854345	7 150737891	5 168510172	4 865265909
6 995116691	7 081202866	7 479872403	7 449319969	7 382127477	7 062114991	7 208482401	7 338731934	7 338731934
6 736858994	8 645025261	7 627414705	8 305507465	7 544505614	6 391569951	9 4329569	7 769297913	7 62727133
5 342201179	5 226955015	5 808303097	5 809258699	5 66104465	4 806565657	5 66007541	5 664424507	5 56273317
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5 911377232	7 107123058	6 498718586	6 817537771	6 73064305	6 34195673	7 368377743	6 587102439	6 354547329
3 429658124	3 83313221	4 027095364	4 022866067	4 115578624	3 844799252	4 875356628	3 844000289	3 801390096
8 03160764	5 987306884	5 638427967	6 596304061	5 929892495	5 801152702	6 292967477	5 947965113	6 212161346
4 661127155	5 256339854	4 786580794	5 253460283	5 009303434	4 601972294	6 514057991	5 058844902	4 620436496
7 56838024	8 312475167	6 358625213	6 546341395	6 930581619	7 091829685	5 815257092	6 952590227	7 572117142
7 917720392	7 420589923	7 692200243	7 73752023	7 71244509	7 271895896	7 57240677	8 155185708	7 586123579
9 964357161	9 855892805	10 54953161	10 58194396	9 86604659	10 66761666	9 6047872	9 772094673	10 3767956
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Endometrioid carcinoma	Endometrioid carcinoma	Endometrioid carcinoma	Endometrioid carcinoma	Endometrioid carcinoma	Endometrioid carcinoma	Endometrioid carcinoma	Endometrioid carcinoma	Endometrioid carcinoma	Endometrioid carcinoma	Endometrioid carcinoma
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6 255165513	6 545135489	6 64396618	3 550064483	4 215701822	4 043367683	4 195348723	3 789221019	4 286341661	3 581900657	3 581900657
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7 139830125	7 617805177	7 458476272	5 118179541	7 390053561	7 163477111	7 030664472	5 901734879	5 587066245	5 291617869	5 291617869
6 685819221	6 672318123	7 737959816	6 59467343	6 98533556	6 57020715	6 877651478	6 814397408	5 72022194	5 95154007	5 95154007
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8 451689715	6 822517361	7 19400608	6 113559477	7 996083729	6 288896763	7 401288514	6 822111568	5 971983166	6 179284523	6 179284523
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3 719672713	3 522624337	3 632452788	4 018800251	3 893347408	4 152457507	3 884797985	7 449379603	4 09487767		

Ovary GSM117744	Ovary GSM137904	Ovary GSM46839	Ovary GSM46898	Ovary GSM46910	Ovary GSM46918	Ovary GSM53036	Ovary GSM53054	Ovary GSM53069
Serous Adenocarcinoma	Serous Adenocarcinoma	Papillary Serous Adenocarcinoma	Papillary Serous Adenocarcinoma	Papillary Serous Adenocarcinoma	Papillary Serous Adenocarcinoma	Serous Adenocarcinoma	Papillary Serous Adenocarcinoma	Serous Adenocarcinoma
5 06299388	7 218136616	4 550044835	6 382896413	4 996507588	5 02772127	6 375819027	4 559704162	4 784986486
4 834404835	6 152866601	4 189137403	5 984629257	4 673537947	4 912368909	6 092169668	4 71615242	5 364939282
4 006134245	4 910477831	4 308283542	4 547672241	4 024875184	4 326979986	4 621450069	3 855607582	3 898887186
5 358597358	6 242233278	8 041225009	6 135588933	4 94854251	5 460117675	6 236493721	5 06288288	5 324254814
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6 114164105	6 172135239	6 247654359	6 617865632	5 547208214	5 562742359	6 629294019	5 81565588	6 005530504
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5 64843195	5 374408089	5 452449589	5 419503349	5 230359567	5 151713378	5 66599311	5 788320771	5 594665232
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4 744395469	4 633418655	4 382414373	4 219689462	4 486966472	4 411698103	4 618457081	4 094000056	4 276204795
6 501211808	8 531539168	4 77148504	6 620520474	6 383323196	6 749549654	6 829205086	5 890062671	6 523805544
4 111082898	3 836292199	4 191812134	4 039976828	3 868872716	3 838335503	4 098764464	3 801350263	4 019273251
5 871249852	6 447647504	6 274110781	6 116181313	5 945685084	5 891085879	6 548501575	6 489406529	6 104029789
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7 433950796	7 771449668	4 054510654	7 004999306	7 782424724	8 349036606	7 463143248	7 402756983	8 192310352
7 268584612	5 692146521	7 036428654	7 415212382	5 784901573	6 285435292	8 225284472	6 844019852	6 844019852
10 32622825	11 5699232	8 285221797	10 49263999	10 28446149	10 97334129	10 89432597	9 932866527	9 636116807
4 786565735	7 703055751	5 383521425	6 249589265	6 003530394	7 582418886	7 155580894	5 982694443	5 158122873
6 862560471	7 076572879	5 684247169	7 777164766	7 279969222	6 853771803	8 468285436	7 080082342	7 332197716
7 458467535	8 848289097	5 297472391	6 212023234	5 831374266	7 625499114	7 863968177	7 113631551	6 300215276
6 29978113	7 355834274	6 33896491	6 380634136	6 590025274	6 658539327	6 403613242	6 366500855	5 989589624
6 245978806	6 262180999	6 488859098	5 902913759	8 011152001	6 187991833	6 303837299	6 301003894	6 014631788
4 93428234	4 893311687	5 235845249	4 692572892	4 196977936	3 807302976	5 567566214	5 307123881	4 524400733
3 165226115	3 138551744	3 497432996	3 163156017	2 923407554	3 084745218	2 99119834	3 033921287	3 108266335
5 193471851	6 955584786	5 56356265	5 65967106	6 633759246	6 613084089	6 399012426	5 250994589	5 533389447
4 003980038	3 639607284	3 823761986	3 884249203	3 327371462	3 386910515	4 517218844	3 553688451	3 825968289
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8 576350414	8 843289956	5 489297887	7 306696536	9 237078055	9 749790592	9 843240337	8 541130607	8 14848627
8 688133874	9 045908157	7 012085261	8 519208207	8 081522307	8 168028967	9 192545042	8 062352843	7 958750836
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6 255776962	6 482409676	5 872281926	5 065280399	5 695503973	5 498422648	7 685279404	6 34270005	6 492703263
7 462420275	7 319828227	5 304515004	7 124217577	7 131438147	7 546499688	7 645598207	7 384323756	6 786167794
7 755761321	7 875569577	6 704790837	8 174330853	5 473149293	7 155267504	6 578966359	6 860056248	6 507675211
6 846922975	6 340018028	6 443406372	5 869328659	5 742503773	5 865143721	7 075116961	6 642605554	6 302416201
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4 650267015	4 487487218	4 748380056	4 780116454	4 325676009	4 407999461	5 197092127	4 594495015	4 586067556
6 501298515	6 562304193	6 057294447	6 060759863	5 568779492	6 292737137	7 454240434	6 537637321	6 409110763
5 754329046	6 06857917	4 039976828	4 547307871	5 371147921	4 013528165	5 25670253	3 879438878	3 846202391
4 591509915	4 81303427	5 208428237	4 271159107	4 339713791	4 339713791	4 315980259	5 244909231	4 613279157
4 087773912	4 01899026	4 039976828	3 674282975	3 675707255	3 687852918	3 774702941	4 351025577	3 895217537
4 11268847	4 498697244	4 623501632	3 975836105	3 74850214	3 766631882	4 276205749	4 227535095	4 010986142
9 846286356	9 00755184	6 454709396	8 218624026	10 31373354	10 08007387	11 46967923	8 422987257	7 821350683
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6 904178189	6 336202191	5 393359345	6 581097451	7 021430838	6 315422477	7 938399979	6 590293625	6 737016751
4 971658015	4 852482887	4 555785535	4 558717526	4 464015903	4 314232201	5 223794478	4 974299615	4 533886667
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6 119151025	6 62262483	3 665286154	6 44924932	4 872788166	6 390400313	7 380336266	5 680233246	7 761524088
4 236696196	4 193583888	4 075195777	4 469785906	4 180499				

Ovary GSM53100	Ovary GSM53124	Ovary GSM53129	Ovary GSM53144	Ovary GSM53173	Ovary GSM53185	Ovary GSM76489	Ovary GSM76510	Ovary GSM88948
Serous Adenocarcinoma	Papillary Adenocarcinoma	Papillary Adenocarcinoma	Papillary Adenocarcinoma	Papillary Adenocarcinoma	Papillary Adenocarcinoma	Serous Adenocarcinoma	Serous Adenocarcinoma	Serous Adenocarcinoma
5 249962393	5 228427181	5 030956608	5 180617261	4 733341477	4 886681063	4 897430817	5 561086844	5 724638785
5 359220543	5 123374819	5 529804301	5 527575905	5 038590978	4 692134204	4 466195957	5 175237144	5 67884151
3 797880351	3 861477645	3 719578777	4 011786634	3 991823055	4 058823351	3 853008405	4 290575157	4 390315666
4 683986195	5 81033998	5 184983963	5 494719482	5 108866338	5 45212655	5 339353356	5 899446917	5 659446267
5 265190214	4 952654596	4 96765452	5 139139603	4 97242292	5 737645636	4 988982395	6 130462812	5 408265705
5 337887586	6 437279312	6 177275551	5 033501374	5 358560332	6 336195694	5 077921528	5 283950029	5 82726954
3 597631307	4 37264576	4 663417844	3 542402758	3 640836073	4 179129373	3 91063046	4 304313445	4 681386867
7 964094007	8 429485062	8 804237622	8 117430854	8 405154168	9 144788788	7 958184634	7 906105023	9 403758839
5 674830562	6 519111944	6 156171778	5 964691957	5 872285397	6 430183768	5 869798065	5 232844883	6 406962539
4 683639617	4 735139883	4 852748104	5 025260101	4 930679918	5 044781916	4 442267222	6 118726375	4 526403306
5 79244655	8 159478055	7 12007684	6 152053985	6 40566884	6 4621053	5 798057223	6 868559165	6 067264091
5 867426052	5 553250277	5 780380106	5 99475817	6 045846817	5 554522675	5 721615532	6 152382909	6 229750109
4 471840575	5 42544927	5 090341094	5 620415155	4 201076173	5 245005686	5 226951636	4 778041548	5 066235232
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4 431665215	4 501037922	5 047241343	4 385481253	4 168477997	4 633514634	4 269111278	4 139711584	4 236207368
6 701370857	8 072441522	8 760295016	8 207031518	8 0788740401	8 177580333	6 691892282	7 9352431	8 829477358
5 945442472	6 523904972	7 260896474	5 824821667	6 778673475	7 141116198	5 242755405	6 035975747	7 986295808
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3 585568791	3 479401742	3 81414844	3 814849257	3 511268657	3 294257182	3 245474798	3 181454366	3 329108303
4 674601328	4 709861959	4 577131433	4 816572173	4 650292703	4 810643037	4 399727911	4 455198426	4 748136476
5 511618795	6 833129858	6 636789491	7 069122413	6 501664678	6 55036648	6 256049692	6 473392809	6 514574544
7 959430904	7 408638515	7 690080362	7 439698093	7 980602944	8 497638603	7 462724836	8 445867735	6 894639332
5 487641312	5 400991847	5 367944645	4 97644568	5 648442365	5 769031141	5 442132258	5 334899083	5 855104377
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7 378723923	7 010163152	7 183479271	6 556840626	6 759492482	6 815902358	5 916823642	6 082632329	7 559676095
6 204928645	3 620530842	3 915351737	3 735272434	3 794796492	4 166645577	3 702924191	4 410955216	4 097095214
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6 234933225	7 004878995	7 36123539	5 75308153	6 862079277	6 832399674	5 847660298	5 864859849	6 042540176
9 63833177	10 87311672	10 74100987	9 662230014	10 48978496	11 46694237	10 25920492	9 987999642	10 78409235
4 076532791	7 231298583	5 139685013	6 999613765	6 103147922	6 865787552	4 985246012	5 006637573	6 679467267
7 376997413	7 178033917	7 578387039	7 151002024	7 289982382	8 118377374	7 196447013	8 05423901	6 895733436
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3 297511435	2 939866043	3 112467775	3 388089251	3 388089251	3 07803007	2 972381758	3 207592066	2 993554456
7 106108108	5 31095356	5 377649557	5 594897326	5 900539877	5 726319038	6 167160783	5 402139105	6 361419692
3 718830822	3 415895334	3 858245016	3 813143925	3 161297204	4 010840491	3 630769807	3 826583491	3 859344648
7 65269364	7 233279683	8 183412506	7 830242251	8 810889814	6 948439457	7 442886789	8 110058218	9 184262879
5 185618746	7 011820834	6 875023707	5 350239869	6 052992274	6 15457375	5 808094124	6 13441948	6 601304775
3 311523259	6 50756249	5 572616928	5 439535318	4 901707785	5 361144227	5 478336323	5 481768258	5 962434933
3 460643519	5 330286209	3 754635849	3 430102676	3 366725365	3 729477652	3 682747701	3 566263859	3 58729909
3 378769455	10 32898349	9 994971421	8 590428688	9 358398169	8 991150933	8 068946801	7 781690013	10 21564575
6 479677446	7 146559531	7 289677268	8 515270536	7 844863768	7 612438236	8 228512421	8 600520114	8 174624495
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6 615914929	6 12616307	6 319408787	6 178972732	6 575834375	6 428301434	6 212171814	6 780639697	6 439372759
7 270462878	7 354030579	7 328745137	7 189322634	6 872310609	7 319841784	7 220869692	6 874499667	7 096626976
5 867173699	6 902982001	6 611155761	7 223646683	6 064261547	7 725450325	5 415094091	5 763709241	9 464777719
5 858631456	6 459463086	6 617195249	6 504312035	5 680350299	6 268928674	6 051110581	6 345636344	6 348199752
3 802522044	3 935434075	4 076637218	4 365660192	4 128184505	4 239939623	4 169141833	3 80643663	3 982256494
3 477342774	3 681552088	3 431650346	3 676398814	3 512332463	3 581961249	3 534496295	3 609128374	3 389276835
4 089190218	4 651631694	4 331145895	5 043304263	4 628468449	4 502541797	4 298116241	4 454038432	4 415315124
5 547623295	6 023348702	6 5032344	6 8609235	6 033762868	6 152757691	5 823039862	5 947712192	6 607878881
4 195807422	3 940358596	4 284372866	4 301074852	4 036991059	5 070371276	6 087671076	6 491504025	4 930413591
4 355381594	4 783935803	4 395330786	5 012116681	4 687893998	4 823002104	4 685260081	4 430772237	5 059442967
3 823246683	4 099007123	4 083048487	3 762184325	3 713643233	4 013728544	3 899132743	3 946566816	3 836695453
3 933372284	3 869409684	4 092261243	4 465423386	4 301278519	4 122142822	3 975380574	3 995799263	3 972573019
6 116589731	8 029814301	10 08338713	8 787688242	8 548611979	9 268212479	7 76075515	9 359958772	8 972210532
4 354166786	8 701680498	8 668107431	7 125329615	8 844863768	7 199671008	6 803522724	7 109340478	7 686231512
8 703451912	10 04128144	10 42905961	9 988623733	10 05903219	10 8861961	9 158607292	10 05149407	10 3851026
5 633143252	5 389166954	5 932059849	5 500786878	5 628003507	5 891060802	5 779777059	5 615243061	5 457257511
6 874952076	8 986883894	7 203807711	5 672123562	7 606670483	7 733680737	5 59713293	7 067205647	5 988277831
4 647826018	5 066714495	4 815256483	4 981317307	4 936999475	4 586366165	4 365415011	4 920489856	4 774103388
3 62296231	4 108016369	4 195807422	3 711512591	4 304482343	4 322789657	4 756025908	5 048617905	4 336000225
4 920821345	4 413269771	5 573592566	8 406479483	4 512433768	5 606258205	4 869946239	5 353854436	6 032503909
3 960297285	4 314962468	4 281786064	3 727667605	4 32425287	4 715244322	4 264696877	4 328294229	3 842823275
6 416474731	6 113291926	6 036063565	5 185880805	4 654799975	6 059366468	5 786899547	6 337824993	4 830099621
5 347808281	3 891459759	3 522470071	3 700960583	6 312010981	3 737356001	3 6347424	3 693147568	3 454968191
5 155729314	7 424640995	6 277830532	8 186507346	6 756707282	7 198651824	6 185925902	5 654420608	5 707888148
6 050218216	7 301564853	7 843271719	7 900348445	8 835889426	7 055284112	6 491128732	7 377582108	7 840215956
8 757640469	7 834397042	8 694384025	8 048905534	8 227346193	6 756699155	7 188566008	8 164069794	7 99541995
5 467242694	4 53							

Ovary GSM88973	Ovary GSM89028	Pancreas GSM117645	Pancreas GSM117647	Pancreas GSM137958	Pancreas GSM152744	Pancreas GSM179781	Pancreas GSM179869	Pancreas GSM203703	Pancreas GSM203761	Pancreas GSM53046
Serous	Serous	Ductal	Adenocarcinoma, NOS	Ductal	Ductal	Ductal	Ductal	Ductal	Ductal	non functional islet- cell tumour
5 655987237	5 886530963	5 9181136	5 438210005	5 259642653	6 944759867	5 978771028	6 698279824	5 92017468	7 298644809	4 39605252
5 429880253	5 286337291	5 329237432	5 236938789	4 850089597	7 186946114	5 636844462	6 535925867	4 982993615	6 558497393	4 410317041
4 064091712	4 519767869	4 158360435	4 114547574	3 858783371	4 651251547	4 288135821	4 494082455	4 085177895	4 621441473	3 587056928
6 295341075	5 427016566	5 718865848	5 447843096	5 350200762	6 701812812	5 982018668	6 501184265	5 917798807	6 370335626	4 832881551
5 466112803	5 358302212	5 293367454	4 441424127	4 931506178	6 554032164	5 14103765	4 993994167	6 039378199	4 125573884	4 805272043
5 515370301	6 074902662	6 196747215	5 379449013	6 100812758	6 771949214	7 657047181	7 84590045	7 055686283	8 39429935	6 399754566
3 868056277	5 3945745	5 632064273	4 85666031	4 765177336	6 656114697	6 549371331	7 988889694	6 533374493	7 685082808	3 759539503
9 464254136	8 953148961	8 632635157	8 103505091	8 103505091	9 639923712	9 294099852	9 171275563	9 196100046	9 261013026	7 659202601
5 451170041	5 992488991	6 418673936	6 408021518	6 941944987	6 648054698	6 551078557	7 353783722	6 87401154	8 066918211	7 143737004
4 604243398	3 9295199	5 466243702	5 614124322	5 440808099	5 416433031	5 446507804	6 394936054	5 036256255	5 557396258	5 142177332
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6 07940753	5 849545117	5 924768576	5 966778398	6 429595259	6 050372824	5 962730774	6 942635819	6 253871301	6 886293606	5 493909614
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Pancreas GSM89045	Prostate GSM117726	Prostate GSM117727	Prostate GSM117741	Prostate GSM38079	Prostate GSM46866	Prostate GSM53061	Prostate GSM53114	Prostate GSM53152	Prostate GSM76516
Ductal Carcinoma	Adenocarcinoma, NOS*	Adenocarcinoma, NOS*	Adenocarcinoma, NOS*	Adenocarcinoma, NOS*	Adenocarcinoma, NOS*	Adenocarcinoma, NOS*	Adenocarcinoma, NOS*	Adenocarcinoma, NOS*	Adenocarcinoma, NOS*
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Prostate GSM88977	Stomach GSM102495	Stomach GSM152595	Stomach GSM203866	Stomach GSM53039	Stomach GSM78562	Thyroid GSM102452	Thyroid GSM102580	Thyroid GSM117723	Thyroid GSM117735	Thyroid GSM138004
Adenocarcinoma, NOS*	Adenocarcinoma, Diffuse Type	Tubular Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Papillary carcinoma	Papillary carcinoma	Papillary carcinoma	Papillary carcinoma	Papillary carcinoma
4.708413908	4.491309208	4.425855142	4.12659659	4.897914003	5.807280599	5.512440949	5.334444581	4.77582523	5.883970386	5.977868052
5.112816875	4.46137981	5.171293218	3.823608412	4.899524815	5.263784346	5.126818539	4.772512777	5.140826929	5.577850178	4.800336183
3.845237414	3.861821201	3.73128451	3.531088896	3.630521521	3.633021738	3.944131808	3.714597485	3.764066969	4.207867419	4.103314252
5.035036394	5.567764639	5.263689257	4.918510886	5.328686286	5.391812265	5.190145651	5.486485004	5.865860172	5.523712988	5.933514859
4.859170116	5.151076085	4.459556224	4.788596884	4.821156892	4.774512361	4.501644946	4.393678028	5.252766102	5.021867236	6.811397145
5.467097408	6.084670916	5.118079438	5.172543973	6.105628063	6.196521924	6.255282669	6.357782056	7.220472245	6.324513582	7.7712557059
4.026044531	4.509922524	3.959758481	4.351399639	4.057181814	4.477276478	5.762935251	5.356120869	6.233716715	5.087051652	7.015441479
8.083433592	7.373745571	7.281130331	8.068469426	7.541130931	8.182472824	8.080039034	8.527413724	9.154119489	8.456835232	9.800637381
5.856381994	7.239513136	6.138630011	5.926692001	6.850398070	6.952565857	7.755965395	7.071966559	8.475091578	7.303038383	8.85183053
4.271752809	4.818680113	5.360896349	4.726431615	4.954753575	4.998827248	5.347059854	4.717202136	6.573875213	6.115318029	6.727092915
6.291816489	5.448756839	6.553746997	6.105990462	6.097974758	5.86326242	6.077393122	6.228178543	6.69891901	6.51345481	6.892915621
6.255914419	6.363831507	5.84030878	6.013594768	5.859558114	6.310454545	6.204475938	5.942095961	7.072178198	5.962730074	6.874662652
5.080474424	6.896953696	5.885667099	6.239155643	5.287299009	7.336889527	6.536711716	6.25806735	6.988852342	6.699165837	8.035978289
5.141503709	5.574617856	5.912490639	5.845561117	5.391621614	5.74002913	5.60341975	5.748890994	5.867413439	5.255400532	5.646576716
5.187746885	5.024989587	5.334121205	5.145000759	5.831358988	5.359179646	5.348600787	5.47503214	5.648527279	5.845555874	5.863324319
3.78750338	4.164230381	4.917191193	4.147870387	3.541637549	4.33986159	4.338717034	4.390867552	4.210957775	3.868125517	5.295415642
3.772830455	3.560155649	3.90314323	3.458159194	3.501486701	4.599752462	4.098982949	4.091072782	3.456300976	3.328833666	4.821854221
4.01986238	4.878112921	3.924689796	4.885843021	4.319315457	4.382443003	4.303502319	4.279379966	4.163145991	4.430902514	4.673512155
7.689361845	8.500206003	9.322151339	9.114693728	7.752070296	9.596395851	7.978521285	8.127080819	8.388190394	8.852276922	10.25875198
5.841843017	5.234713855	5.686735658	5.604595709	5.454943847	5.539625418	6.354000166	6.818128196	7.391993209	6.64495154	8.143316629
5.530191408	5.768403691	5.959155495	4.58445559	6.05851995	5.571873876	5.688524696	5.418102043	5.64773695	6.314481298	6.847795512
5.135823663	6.464045208	6.494385851	6.017712778	5.409127219	6.757674597	5.80989452	4.8542193	5.732922261	6.068778547	6.895455564
4.154856502	4.162134523	4.182485258	4.138993438	3.870493845	4.088716286	3.573815432	3.703802446	4.209295506	3.747710562	6.3670979096
4.411529162	4.207958425	3.965330065	4.937293122	5.973340444	6.50735742	5.711138502	6.794565163	6.958227429	5.084147993	5.010478037
3.471018882	3.732004115	3.654026253	3.302717633	3.408443127	3.704788828	3.367237749	3.843665058	3.753970703	4.19048172	3.878913303
4.482912269	5.151076085	5.051417716	6.642728262	4.783023983	5.441208957	5.101867884	5.005799567	5.602128668	5.482714744	5.72482808
6.727728904	6.62415639	6.64101235	7.291003007	6.48104047	7.008889801	7.22129037	7.385135184	7.455533944	7.453838634	7.936581672
6.778165961	7.952689978	7.477926753	9.653690849	7.457060242	8.30534356	7.391641343	7.279281797	7.358686976	7.297677828	8.400953559
5.529541992	5.55915871	5.844757003	5.494438229	5.484185844	5.351936304	5.558154932	5.18066856	5.789984499	5.479935895	5.551811511
5.305421679	4.792826696	5.812797842	5.000670981	5.24569589	5.491966994	4.614841151	4.711113973	5.089738093	5.347296521	5.815034034
3.68290865	3.836371759	3.93557579	3.621307926	3.371002261	4.080402383	3.524581467	3.8358155	3.722811161	3.605169994	4.394952236
4.704868914	4.438871003	4.164632744	4.281327308	4.537011269	4.92621995	4.530642453	4.53388558	5.045743111	4.358912136	5.649730281
5.67128977	6.836615079	6.594113844	6.621947616	5.829275077	6.785978007	6.824274082	6.912045895	6.984555304	6.753129739	7.447803552
4.072865831	4.262280999	3.747290213	4.158628711	3.93105087	4.101317014	3.818380074	3.9942985	4.379271466	3.89585377	4.136271428
5.856142128	6.501068085	6.331707269	5.964590905	5.838768243	5.977258405	5.697430725	5.925240329	6.831320108	6.596276541	6.292371469
5.076374573	5.339303635	4.442053946	5.126203969	4.757370447	4.858567883	5.587926199	5.276435607	5.862454567	5.097832495	5.012406204
6.517755447	6.484824175	5.698613725	5.882009433	6.502345559	5.240840989	5.702264282	6.158428971	5.855675738	5.346847977	5.917140385
6.864204028	8.320852313	7.596853879	8.449338036	7.516205697	8.148484016	8.321792884	8.130689046	9.879699444	8.487706219	9.39433355
9.903725081	9.885312756	9.029816715	8.725625993	10.02774934	10.20188021	10.592766887	10.49160925	11.47604222	10.586424228	12.005601892
4.491114188	5.236870355	4.831412422	5.618835712	6.036710641	5.5275574059	4.767076057	4.718959067	4.281645191	4.987890008	4.311021744
6.757087216	7.528538624	7.50361938	8.85416141	7.214078861	7.86553502	6.448634101	6.77478859	6.314537959	6.840981587	8.073724206
6.802285876	6.228010912	7.004340099	8.941031281	5.997897817	6.7274743117	7.264721388	7.53376919	7.864961461	7.214680271	8.561786359
7.618671658	5.210680703	5.148917479	5.096402843	5.558896645	5.530585401	5.614559786	6.737530918	6.256941749	5.646470925	6.014563856
6.138401784	6.69058989	5.96694959	6.748025782	6.852842568	6.325382945	6.143610735	6.028788015	7.044133079	6.595247457	6.877970744
4.61582841	4.92019599	4.339534301	4.920814852	4.723242869	5.087403238	4.918979174	5.075888027	4.617994338	4.887444774	5.586724523
2.884426356	2.941890525	3.3273145	3.02467644	3.093061546	2.996219893	3.179553255	2.975225149	3.045560501	3.452944708	3.191370668
5.238012195	6.32078705	6.153838619	6.9959201	4.852111636	6.360559513	5.702832128	5.830158384	6.602924576	6.277117081	6.777699722
3.514637046	3.214794969	3.618784361	4.020078377	3.979078616	3.659704702	3.449136538	3.502549631	4.542474975	4.387486272	4.5126897497
7.111519652	6.647919851	5.608108671	6.586545758	6.748800183	6.251394852	6.336033324	6.329962447	6.128303073	6.385972663	5.790201733
5.757957297	5.996891497	6.22004637	5.838211341	6.384598134	7.10895297	6.316616928	7.811797114	7.426282832	6.61160564	6.904132446
5.133390962	6.400052742	6.431331183	6.409493195	5.730797938	7.446988197	6.472829279	6.313297573	7.340664037	6.570846458	8.309404512
3.598032693	3.769121774	3.396049334	3.524476188	3.524476188	3.678640345	3.502669945	3.544794768	3.641368022	3.772114707	4.39491970352
8.151520482	7.957338557	8.28856793	8.817414197	5.940898731	8.427258346	8.739498779	10.3014111	7.903405109	7.91438935	8.175841061
6.382159847	9.493571668	8.71861711	8.194622517	8.000415268	8.950877038	8.843326029	8.342978583	9.643790687	9.734829001	6.417618899
6.352777889	7.87819204	6.544208282	7.203418264	7.034131646	7.448815602	7.096162658	6.714301171	6.862575933	7.265223491	8.11814389
5.981541456	6.29909701	6.795194915	6.191967895	6.282720593	6.420352674	6.403580668	6.175774692	6.55050415	6.069302683	7.093545499
7.143372014	6.744900664	7.012199268	7.245890589	6.952369169	7.556112798	7.682508147	8.175877673	7.388868089	7.353485839	7.535377537
5.076374992	6.32720306	6.550480566	6.236610937	7.442354583	7.801000326	6.682252328	6.691909806	7.271152794	6.440223438	7.52123266
6.124389098	6.272803942	6.403843	6.250980842	6.082375892	6.912329157	6.769860425	6.886871104	7.251324537	6.573965499	7.306808898
3.98054248	4.417465676	4.252989492	4.486559745	4.030926526	4.694965249	4.103863854	4.204117283	4.528681432	4.282145584	4.422844147
3.587571395	3.797367724	3.811629974	3.431535049	3.447405255	3.796669977	3.851385449	4.087756408	4.455711998	3.737912677	4.04457815
4.485138027	5.105118258	4.392756079	5.398341403	4.589071732	5.097957457	4.596363807	4.611356259	4.650438344	5.061888291	5.725222162
6.0										

Thyroid GSM138023 Papillary carcinoma	Thyroid GSM138024 Papillary carcinoma	Thyroid GSM88998 Papillary carcinoma	Thyroid GSM89038 Papillary carcinoma
5.28426525	5.83404538	6.04237449	5.30300496
5.06158461	5.893343863	5.9001947	5.231172591
3.78867094	3.998803131	4.22006091	3.939495758
5.50844943	5.548456554	5.68632321	5.624763928
5.58704895	5.569497706	5.8191796	4.502034332
6.61706575	8.007249721	7.76255741	7.535384189
5.84647404	6.974989944	7.35678071	7.085704038
8.5294284	9.564170134	9.66203399	8.830185609
7.11696844	9.235254906	7.91840969	8.47166782
6.05404676	6.447521008	5.80245422	6.145777136
6.35489779	7.090509012	6.73135967	6.173823095
6.2829378	6.965502187	6.68224228	6.887514514
6.69323304	7.548678952	6.97082886	7.43199438
5.85055416	5.991507173	5.3851505	5.435194715
5.88262403	5.955176233	6.07916126	5.406996215
4.22129977	4.098898586	3.93909623	4.744667925
3.94059697	4.526340201	3.86345213	5.00459336
4.34888681	4.484122795	4.42507782	4.202089824
9.09754983	9.591010351	8.9380418	8.09259181
6.31076731	7.836148181	8.36204082	7.491671386
6.45721923	5.871957841	6.17878061	5.763028588
5.89673589	6.508033435	6.08306864	6.515602729
4.04917283	3.963368031	3.70642121	3.86067238
5.12572669	4.286440688	6.16142812	8.382132228
3.46888895	4.116454846	4.00991215	4.551798031
5.12305761	5.640459555	5.41534742	5.866394251
6.86665183	7.566489028	7.44781472	7.43870395
8.05271648	8.30058862	7.95933092	8.040448474
5.44104292	5.392151833	5.20030461	5.347516991
5.24089692	5.823708464	5.3793983	4.748804375
3.91956141	4.772906262	4.88849078	4.42462242
4.49810694	4.515986738	4.19476213	5.823318947
6.40390864	7.386554465	6.80592073	7.295137103
3.8950797	4.51525884	3.92385901	4.048387591
6.40045075	6.718360562	6.17131934	6.152619229
5.47269221	5.691992915	4.73801883	5.528130921
6.04390742	6.098503072	5.46706361	5.891074745
8.2028526	9.214816216	8.94322063	9.682522048
10.3808825	11.9175624	11.7974425	11.21691871
4.70350055	4.768534917	4.57853274	4.737106895
7.05540889	7.70748302	7.79514059	7.800136998
6.97626298	8.192038912	8.51700713	7.602088653
6.20850254	6.118470344	6.42163789	6.384081568
6.30181995	6.548923574	6.6675921	7.89806293
4.97079224	5.149486935	4.96814546	4.710867048
3.12116107	3.177799582	3.11632108	3.96011462
6.31743691	6.486702289	5.97112408	7.244703555
3.53408536	4.353642208	3.88891331	4.707038026
5.98291788	6.74326751	5.84500843	6.011433981
6.33258856	5.859080441	7.1003136	9.194974591
6.97705711	7.725719004	7.225403	7.746767511
3.6086166	3.322226775	3.67461803	3.546632801
9.50850439	8.98291551	8.75583192	9.131808057
9.38124192	9.08769443	9.02785284	9.783406498
7.35978107	6.859342884	6.3758659	7.537220567
6.74787093	6.715904976	6.48874571	6.964385258
7.39560271	7.432964906	7.31924791	7.048017368
6.82256672	7.230976565	7.21694854	7.042703151
6.74731998	6.961580822	6.77252919	6.966429421
4.21210815	4.460356743	4.53974054	5.476212391
4.01574665	4.974954782	4.26581537	3.758543452
5.16348687	5.28392374	4.78565844	5.634532717
6.82950633	7.569462805	6.62301482	7.728173494
4.75518733	5.812872166	5.38548688	5.451072148
4.87084078	4.708169462	5.03956837	4.453085342
4.12007	4.97870969	4.13350066	4.415385807
4.22222916	4.137530394	3.80034188	6.267777067
8.52425095	8.606210098	8.24716894	8.64136777
6.99313678	5.390134057	7.86553512	9.693643243
10.7991243	11.2274504	10.388899	10.0578012
7.01411728	9.054665946	8.42006329	6.862939178
9.34490444	9.875259747	9.02747702	8.751312081
4.92743581	4.999551921	4.77638777	4.79838455
5.10319721	5.586532196	5.14502681	5.028592202
5.92124873	5.994478972	5.73369402	6.165921663
3.98256724	3.639201243	3.78638389	4.078350964
8.28812304	5.903703134	5.63386038	5.70461448
3.87168899	3.850189311	3.80512601	4.633475125
4.54381451	5.447629171	5.57853375	5.041360342
8.37323535	9.323560517	8.13827165	9.623670309
5.85864367	5.808933435	7.07431563	6.858781014
4.96411367	5.059311253	4.75111113	4.812910766
5.39639125	7.281148511	7.00538104	5.678652432

Appendix Table A3. Continued.

Affy ID	Gene symbol	Name	Site	Urinary Bladder	Urinary Bladder	Urinary Bladder
			ID	GSM102434	GSM102437	GSM117677
			Histology	Urothelial (transitional cell) carcinoma	Urothelial (transitional cell) carcinoma	Urothelial (transitional cell) carcinoma
230061_at	TM4SF18	transmembrane 4 L six family member 18		3.93928491	4.188419095	5.474558724
214797_s_at	PCTK3	PCTAIRE protein kinase 3		6.530348326	7.16973587	6.078197049
227654_at	C20orf175	chromosome 20 open reading frame 175		4.289414928	6.236869635	7.009709766
225057_at	SLC15A4	solute carrier family 15, member 4		7.170682874	7.679374794	7.628324727
221211_s_at	C21orf7	chromosome 21 open reading frame 7		3.75403213	4.070049526	3.947288539
204900_x_at	SAP30	sin3A-associated protein, 30kDa		5.911122306	6.033298768	6.654890604
206439_s_at	PHKA2	phosphorylase kinase, alpha 2 (liver)		8.538617594	6.839679132	6.3700024
236262_at	MMRN2	multimerin 2		5.943734976	3.435332415	6.479241233
240384_at	WWP2	WW domain containing E3 ubiquitin protein ligase 2		5.105378616	4.901987058	5.088843131
215244_at	DGCR5	DiGeorge syndrome critical region gene 5 (non-coding) kinase insert domain receptor (a type III receptor tyrosine kinase)		5.36589713	5.033895572	5.028672832
203934_at	KDR	tyrosine kinase		4.528964063	5.077634064	6.447160285
219700_at	PLXDC1	plexin domain containing 1		5.073117232	5.825744002	6.953781226
229357_at	ADAMTSS	ADAM metalloproteinase with thrombospondin type 1 motif, 5 (aggrecanase-2)		4.424214995	4.36014467	7.687611851
1558397_at	NA			4.911240204	5.168283488	6.448553596
227780_s_at	ECSM2	endothelial cell-specific molecule 2		6.217345247	5.523122788	8.421348821
1556314_a_at	NA			4.185847754	3.428404686	5.632497578
232694_at	ZNF395	zinc finger protein 395		4.137601736	3.893151109	3.751066135

Urinary Bladder GSM137919	Urinary Bladder GSM46829	Urinary Bladder GSM53117	Urinary Bladder GSM53137	Urinary Bladder GSM88693	Urinary Bladder GSM89048	Urinary Bladder GSM89073	Breast GSM46908
Urothelial (transitional cell) carcinoma	Urothelial (transitional cell) carcinoma	Urothelial (transitional cell) carcinoma	Urothelial (transitional cell) carcinoma	Urothelial (transitional cell) carcinoma	Urothelial (transitional cell) carcinoma	Urothelial (transitional cell) carcinoma	Ductal Carcinoma
4.047080699	6.150060377	3.750482823	3.826639648	4.430052003	4.146598533	4.129413041	4.485512729
6.836866084	6.500805296	6.703341636	6.234568348	6.800038221	6.246996848	6.540105289	6.823481386
5.657852079	6.062490679	4.809377527	6.177415762	7.050343851	5.447944316	6.296002937	5.652203906
6.130956873	7.976738646	6.833810198	7.344522866	7.502425202	7.31187666	7.765679669	7.286863331
4.107289745	4.407602168	3.572142112	3.751619085	3.866178249	3.564728798	4.078181188	4.280748859
6.688084612	7.560866485	5.777934997	6.8660994	5.962745866	5.41122028	6.859113307	6.502797532
6.063866205	9.065236051	5.655377825	8.048871782	5.79657522	7.33784604	6.067944636	6.274058141
6.236835985	9.382499943	4.477740622	4.069269622	5.73638825	6.814330935	6.164944541	5.602703626
4.516445985	4.662917195	4.475690958	4.834840702	5.095367303	4.716386095	4.610365922	4.933268756
5.188758354	4.709785088	5.582040328	5.008151972	5.002344897	5.258166079	4.918145132	5.592516181
5.146533403	7.350245497	5.012791876	4.922061799	5.17199908	5.624660366	5.389751614	5.92881786
6.306296195	7.555139019	4.954633023	4.285187557	5.484197024	5.880460135	6.141585171	7.15331112
4.757797124	6.71990728	4.500297449	4.323638128	5.079991713	4.318599475	4.787500139	6.975564427
5.073767559	6.788866047	4.732661401	4.693223824	5.203239728	5.458587661	6.006969135	5.306250095
6.132531586	6.70912427	5.527285701	4.893349655	5.927688878	6.164678029	6.356716018	7.153099684
4.292640623	4.455436541	4.071345807	3.685925715	4.642182102	3.966019998	4.012871886	5.252607059
3.665589238	4.319874693	3.817698577	4.647581511	4.066654277	3.648675485	3.753191317	4.228438852

Breast GSM46933	Breast GSM46934	Breast GSM46947	Breast GSM46952	Breast GSM46953	Breast GSM46954	Breast GSM46955	Breast GSM46958	Breast GSM46962	Colorectal GSM38075
Ductal Carcinoma	Ductal Carcinoma	Ductal Carcinoma	Ductal Carcinoma	Ductal Carcinoma	Ductal Carcinoma	Ductal Carcinoma	Ductal Carcinoma	Ductal Carcinoma	Adenocarcinoma
4.771576586	5.392077294	5.037905438	5.969087636	4.505297019	6.421058935	5.798417689	5.733341585	5.061256326	4.033876315
8.282672783	5.696786791	7.787478944	6.301734908	6.582507898	5.890711232	6.723269267	6.385162273	6.163909733	6.516017748
4.583109179	5.425868461	4.643030382	5.033726842	5.982656941	5.205074595	5.302028799	6.169646837	6.048623208	5.7676714
8.104784602	8.094362514	8.392117702	8.265220019	7.743163538	7.973992542	8.081717888	7.803534504	7.830589904	7.783723483
4.681934341	4.021197989	4.44756774	4.425920349	5.055768652	4.296359724	4.327514977	4.244837187	4.342424087	4.162575294
7.890957791	6.436472257	7.37923854	7.004659851	6.442806257	7.910795419	5.786889908	6.049045589	6.292087458	5.822899408
7.596145426	6.718921085	7.793300268	6.696726612	6.843212348	7.227953184	6.951824274	6.22250134	7.667704718	7.111088175
4.430945773	5.331360283	4.205312489	5.361989623	4.776564169	6.038916808	4.727219395	5.374678815	5.166179953	3.953528237
4.45273948	4.657237948	4.314319907	4.408104354	4.59375864	4.12089916	4.492665994	4.439629171	4.479919014	4.564883888
4.904174446	4.636120094	4.227712616	4.61974854	5.005356381	4.270972292	4.572493504	4.87267753	4.570074735	4.710405034
6.378751744	6.718957438	5.960460372	6.638868191	7.000813578	7.018437455	6.121242458	6.413181008	6.755240739	5.918971086
6.987534382	8.853533298	6.258122001	7.537117897	7.175825385	7.784657553	7.844227444	7.945208252	7.575758814	6.596534981
6.894078284	5.805302758	8.283733	6.35478692	5.035282382	6.923821833	4.718936489	5.187828638	5.575559096	4.99045929
6.284865161	5.184982853	6.753022241	7.282296347	6.209048404	5.865414138	6.06491468	5.951579647	5.93542815	5.519615988
6.82228845	7.274372055	6.043898024	7.741143085	7.331426059	7.581351556	7.057969021	7.594287537	6.963804847	6.089186875
5.005514775	6.037661864	5.536332519	5.927662071	5.39589795	6.003783276	5.791052382	5.522305764	5.087230093	4.477545616
4.174264496	4.106438625	4.081316825	3.801276885	4.344206422	4.457472086	3.728840013	4.331789657	4.089711799	4.002887602

Colorectal GSM38077	Colorectal GSM38089	Colorectal GSM38105	Colorectal GSM38107	Colorectal GSM46819	Colorectal GSM46841	Colorectal GSM46845	Colorectal GSM46856	Colorectal GSM46857	Colorectal GSM46861
Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma
4.100609304	4.550367216	4.351311119	4.27280021	4.750805827	4.226115628	5.499413505	3.990544361	4.476671225	4.529564109
7.228961964	7.468656994	6.738846354	6.781877861	7.828903439	6.325786812	6.78604574	6.96433599	6.830823511	6.494066826
5.36627313	4.342968801	5.741825847	5.784628779	5.345482387	5.154886821	5.999875449	5.665591505	6.166338241	5.077794719
7.149607493	7.809290436	7.324809477	7.193610426	7.861671075	8.10099797	7.924679139	7.295248955	7.543814301	7.746632018
3.876745776	3.40907462	4.046335076	3.724797353	3.979813354	4.138727087	4.102191413	4.067646873	4.529423126	3.947863061
6.540409476	6.314108022	6.226415229	5.988809785	7.720256239	7.590114611	6.885863301	7.377394228	6.62218375	6.984021696
7.368679568	6.445638377	7.524133408	6.494645352	7.423222045	7.012237335	6.71781051	7.311952533	6.936568333	7.295910712
3.790568376	3.883583351	3.840533859	4.123828712	4.452918989	4.395972447	5.198798692	3.989509516	4.024185713	4.490356392
4.538389825	4.738491646	4.704225805	4.633003199	4.4093613	4.629609849	4.52338341	4.378911745	4.500918492	4.522952162
4.935264142	4.682109217	4.986280991	5.054170206	5.216796423	4.70949508	4.688278769	4.54356573	4.841662607	4.467166513
5.637275487	5.555425437	6.074075372	5.508409689	5.767535339	5.706138355	7.064175641	5.7926626	5.854041596	6.247185436
6.029803536	6.016308718	5.816573526	5.957725061	6.505876008	6.042115418	6.92631946	6.105169761	6.688780557	6.820289892
4.753048114	5.331290598	6.005175311	5.782515004	7.206816474	5.615853935	7.452233497	5.417178193	5.392949288	6.513861406
5.307957066	4.887814343	5.640415339	5.521798783	5.523369374	5.285212643	7.113338495	4.979290014	6.052243492	6.120502668
6.456810689	6.190349777	6.355219585	6.454025104	6.751959264	6.491729189	7.318615954	5.976577006	6.466914382	6.684582815
4.372294335	4.259839152	5.152261243	4.976834351	4.098110872	4.345544372	5.380280946	4.117683346	4.51377808	4.184003888
4.354363782	3.887157175	3.878578519	3.863178555	4.04138583	3.983558848	3.582920658	4.285127532	3.999026586	3.814317105

Colorectal GSM46865	Colorectal GSM46877	Colorectal GSM46879	Colorectal GSM46901	Colorectal GSM46969	Colorectal GSM46972	Colorectal GSM53087	Colorectal GSM53132	Colorectal GSM53168	Colorectal GSM76546
Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma
4.634798846	6.350407036	5.149939217	4.614967681	5.797542972	4.123054186	3.7681519	4.382720021	3.591115178	4.557026439
7.521151386	6.783425911	7.035496251	6.869890509	6.517132226	6.570119031	6.273397615	6.270182098	6.753733552	6.610119708
5.79196856	7.249547072	4.359678757	4.947072582	6.674435339	5.352521254	4.675575116	4.529339592	4.912399456	5.06225079
7.572374285	8.075565323	8.215770076	7.828220333	7.775565237	7.258659425	7.2393983	7.478455167	7.453890229	7.719290767
4.395466433	4.834326558	5.448055746	4.068896364	4.492826878	3.784911607	3.325431272	3.829531237	3.580525194	4.142842239
6.210065872	7.754875748	7.477726522	7.1880244	7.094426559	6.63648294	6.514363702	6.502800819	6.345128744	6.519573172
6.861812061	7.437104627	7.186202597	7.21706447	6.803851046	6.93063475	6.796328819	6.202502581	6.450276128	6.50240104
3.841152428	5.362678025	4.776637703	4.879024247	5.11163675	3.720673375	3.563405987	3.873428042	3.973479697	4.639978853
4.399314686	4.422913216	4.640625419	4.317171939	4.248289946	4.484280446	4.642294243	4.851181787	4.717822452	4.40859743
4.801297912	4.473341907	4.492984458	4.855895094	4.656309863	4.888732445	5.477729818	5.066290985	4.943878925	5.136661367
6.136612372	7.390953154	6.703195661	6.136236603	6.113639873	5.421702934	4.99234462	5.426987395	5.433109823	5.843648088
6.399375991	7.662193086	7.746785552	6.709562701	6.789391626	5.473386473	4.579028826	5.392463831	5.681409387	6.097708132
5.352385581	7.009047777	6.368774028	6.122803583	6.855038089	5.197237796	4.358164968	5.831478337	5.007660331	6.897207617
5.71315324	6.985481567	5.680792668	5.823178248	6.712419312	5.455983964	5.147885938	4.903145799	4.920935378	5.281808068
6.380590161	7.461428846	6.715457474	6.744744692	7.368096453	6.189404477	5.560047726	5.709569484	6.356716018	5.984320434
4.675023759	6.338329841	5.68306718	4.713007885	5.731424893	4.658206298	3.864247321	3.764594936	4.410801108	4.464947481
4.344868202	3.560296144	3.873221972	3.981745099	3.474692827	4.122362887	3.974352803	3.866827991	4.03280906	4.200500896

Colorectal GSM78571	Colorectal GSM78575	Colorectal GSM88976	Colorectal GSM88982	Colorectal GSM89013	Colorectal GSM89074	Colorectal GSM89075	Colorectal GSM89094	Colorectal GSM89100	Kidney GSM117706
Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Papillary renal cell carcinoma
4.893738117	4.196691581	4.802666884	4.147778044	4.427656577	4.238976415	3.998946209	4.539320449	4.015439507	5.138277943
6.029767779	7.613981876	6.7142837	6.642957336	6.977717837	7.174941418	6.610476877	6.079871805	6.884389175	6.771960086
5.209668893	4.554719987	5.649123535	5.659216924	5.871705908	5.625073876	6.170261511	6.628682738	4.830959832	5.439448614
7.537587527	5.915391583	7.230896796	7.627261438	6.613218305	6.828876597	7.24169118	7.34516533	7.060678579	8.284102794
3.617246016	3.653966109	3.640163831	3.297835752	3.614496199	3.708354277	3.785204138	4.289011648	3.756961668	3.820274933
5.94764519	6.828391786	6.062184031	6.722482411	6.45765494	6.840976338	6.197500429	6.351973143	6.484953266	6.227192873
6.49151676	6.154410977	7.24253204	6.209711273	6.839059567	6.866233872	6.52033362	6.054477934	6.025980857	7.009653032
3.443364331	3.794316554	4.176729384	4.022084872	4.331544177	4.060862346	3.947178798	5.43500278	4.252701279	3.463010942
4.537057539	4.425578718	4.802662079	4.837925277	5.104596681	4.546080261	4.837925277	4.587625224	4.96071301	4.333196649
5.005116154	5.213553339	5.568408833	5.211638513	4.905974075	5.011677689	5.105037492	5.439791106	5.459426739	4.64437614
5.414071218	5.017204809	5.188318352	5.211155725	6.205292477	5.709586793	5.100852419	6.01250155	5.52917153	4.860808317
5.584201661	4.955399344	6.47423797	6.096635056	7.286155686	6.07811398	5.526863703	6.783093304	5.8759249	5.055408146
4.938190241	4.807568599	4.985009108	4.978647589	5.475948635	5.277001989	4.857055493	6.357227495	5.92323579	4.737508084
5.082484117	5.473455045	5.845274519	5.31169538	5.575228511	4.852580228	4.874510175	7.226614511	5.797789915	4.619986671
5.816589276	5.775862947	6.0229292	6.169217914	6.968792659	5.914145999	5.706321648	7.102964292	6.73181089	5.837056799
3.79454684	3.93356953	4.213642064	4.028525926	4.53866253	4.106898726	4.034384221	4.686210312	3.952134856	4.086294468
3.786378187	4.002545168	4.171966608	4.175666356	3.514829187	3.895609633	4.155205772	3.881384911	4.233484049	4.170216715

Kidney GSM38073	Kidney GSM46825	Kidney GSM46826	Kidney GSM46847	Kidney GSM46858	Kidney GSM46875	Kidney GSM46881	Kidney GSM46882	Kidney GSM46892
Conventional (clear cell) renal carcinoma	Conventional (clear cell) renal carcinoma	Conventional (clear cell) renal carcinoma	Papillary renal cell carcinoma	Conventional (clear cell) renal carcinoma	Conventional (clear cell) renal carcinoma	Conventional (clear cell) renal carcinoma	Conventional (clear cell) renal carcinoma	Conventional (clear cell) renal carcinoma
9.402025447	8.665767534	4.826304179	7.062050358	8.39012072	9.698591061	7.481481171	8.088586906	8.672079124
9.920086221	9.977026603	6.95402038	6.765257043	9.1782179	10.61817863	8.820683223	8.771764563	10.44784731
7.465005983	7.353420726	7.658593104	4.69410892	7.716928859	7.973031459	8.664987744	8.335355024	9.238584075
9.22489504	9.404696606	7.75750423	8.642170994	9.371940595	9.217089546	9.288271269	9.055435595	9.185923625
6.03871824	5.69035808	6.193498154	3.233882345	4.853947482	4.770954202	6.000822964	6.878542898	5.718582527
8.842162632	7.961461204	4.830400696	6.474897793	7.854006578	8.400917614	7.176656962	7.921119559	7.787438845
9.697578292	9.81936906	7.028427212	6.929544203	8.607425714	9.870190035	8.736158738	7.791141815	9.515806067
7.208247646	7.312744842	4.453565957	3.340790854	7.273755236	7.068767349	5.975154106	6.063192877	7.191321011
6.31944133	6.383519393	4.840930988	4.699408852	6.091124422	6.710602537	5.512826064	4.999608593	6.506459196
8.164035336	7.806831331	5.254366299	5.083696731	9.109031075	8.345820086	8.314507983	6.064576448	7.524689171
9.982947878	9.733527052	6.687743954	4.564945342	9.637721603	10.32260752	8.482745032	8.72306067	9.206488107
8.154284048	8.366174089	5.989116146	4.852073105	8.414707142	7.191080159	9.035262323	7.696700752	8.214811648
8.493422809	7.565280796	5.83643871	3.924218665	6.696369508	7.904647791	6.88852166	7.363800944	7.448344843
8.217386148	7.597834775	5.573027864	4.629735561	8.223226152	7.739688559	6.460492155	7.202195022	7.546325992
8.169448965	8.691162651	6.959131217	5.296743495	7.850210612	8.494175795	8.120459608	7.831617527	8.099681017
7.593896978	8.347896782	4.361746748	3.723102426	7.303677684	7.991381565	7.1138028	6.505596479	7.527173016
7.95245745	6.486674681	4.13148121	3.90318032	6.707970515	7.311860602	5.112434345	4.568740614	6.746851934

Kidney GSM46929	Kidney GSM46939	Kidney GSM46944	Kidney GSM53060	Kidney GSM53092	Kidney GSM53122	Kidney GSM69099	Liver GSM137909	Liver GSM137962	Liver GSM179952
Papillary renal cell carcinoma	Conventional (clear cell) renal carcinoma	Conventional (clear cell) renal carcinoma	Papillary renal cell carcinoma	Papillary renal cell carcinoma	Papillary renal cell carcinoma	Papillary renal cell carcinoma	Hepatocellular carcinoma	Hepatocellular carcinoma	Hepatocellular carcinoma
8.532867362	8.127762118	8.891816019	7.075617839	5.910970616	6.535131496	7.306103223	5.885387843	3.713449565	4.987362178
6.867865385	8.760715831	9.667756165	7.319072671	7.713600055	7.269728324	6.85173688	6.13535924	6.025565687	5.451748976
6.300293878	6.558882878	8.81676244	6.029123243	5.32732616	4.830726415	5.290838858	4.650089956	4.31482238	4.374221112
8.358112717	10.01727348	9.74959618	8.099288216	8.337273119	8.905711547	8.353162463	7.884387335	7.950155723	7.929865158
3.653845552	8.118764288	6.8018031	3.779872106	3.802372592	6.153050295	3.749752511	4.010488095	4.095282705	4.205610738
6.737902771	8.170813279	8.941964375	6.833073111	5.14089033	5.903750872	6.165118227	6.334961388	7.531418708	6.58205216
8.955097528	9.194319678	9.245792898	6.045563113	6.523441862	6.296818698	6.38938312	8.152253538	6.758988023	8.205189406
4.034638379	5.852850382	7.587287346	3.989759198	3.876288981	3.588951089	3.409228894	4.596145017	3.558824007	4.282060816
4.520252091	6.033484628	6.943158322	4.912053826	4.774519224	5.020702707	5.040104088	4.792079575	4.884513278	5.205748204
4.882568013	7.407090381	6.88371721	4.823218729	6.079730208	5.331309457	5.220776508	5.079198557	4.83231397	4.663858772
4.781040131	7.242138315	9.252540132	4.863645078	4.624372788	4.591965105	4.608401126	7.376823718	5.701281898	6.81921113
4.801897218	7.904941447	9.129155064	4.502882325	4.819827433	4.742084185	5.275051227	5.884682224	5.57846646	4.938235602
6.81305753	6.402689707	7.872654293	6.054473061	4.002997126	3.694400943	4.237638073	5.46517296	5.594568948	5.185499844
4.837321551	7.945691142	7.993184908	5.088550538	4.831898792	5.261299824	4.988390216	5.353053927	4.558718892	5.012429708
5.075495475	7.2515907	8.674666902	5.088513756	5.37038996	5.932528212	5.436403846	6.753102138	5.731744977	5.997554661
3.877736642	8.174919637	7.321314051	3.903783063	3.743823401	3.818287968	3.912047158	5.463788419	4.386013847	4.422757885
4.893089426	8.876191211	6.359047177	3.851194264	4.812765044	4.914380816	4.028853263	3.995168304	3.649283076	3.866040896

Liver	Liver	Liver	Liver	Lung	Lung	Lung	Lung	Lung	Lung
GSM203676	GSM203750	GSM231890	GSM203751	GSM102505	GSM117610	GSM117629	GSM117632	GSM117671	GSM117770
Hepatocellular Carcinoma	Hepatocellular Carcinoma	Hepatocellular Carcinoma	Hepatocellular Carcinoma	Bronchioloalveolar carcinoma	Squamous cell carcinoma	Squamous cell carcinoma	Adenocarcinoma, NOS*	Bronchioloalveolar carcinoma	Adenocarcinoma, NOS*
4.82271792	5.914393912	6.013540157	4.143836544	4.810469578	3.799365759	3.353883838	3.631965235	4.251500068	3.47239526
6.610590997	7.16603084	5.982370536	6.11828559	6.539678778	6.007696281	5.952523077	6.884239507	7.081060433	5.230133056
3.933785359	4.622052145	4.848021295	4.459374353	5.071365322	4.554999671	4.386362839	4.586158188	4.485815843	4.798509138
7.680432506	7.758023346	7.660064226	8.034790783	5.065152896	7.119285288	7.509553379	7.88581511	7.482961133	7.129588517
3.856103953	4.730227043	4.177163809	3.784016813	3.48002555	3.565800901	3.519397221	4.03764464	3.70310567	3.066608596
5.992437893	6.861291139	6.882907459	7.208056408	6.162556286	6.412285416	6.011868958	6.150677988	6.60826356	5.755380252
8.284827642	7.637180509	7.877287562	6.649092908	5.722240953	6.762487524	6.85375467	5.795244787	6.806573049	6.178267146
3.994115906	5.201901026	5.036763298	3.72098016	3.959005114	3.925853951	4.436614772	3.593708613	4.233220241	4.076842446
4.443647814	4.820108693	4.282611162	4.529819444	6.378142163	4.774002223	4.72371808	4.974463553	4.507877805	4.386749439
5.022033186	4.852600231	5.142928887	5.038649814	6.287379589	4.90666781	4.94926229	5.222690707	5.508000306	5.444711852
5.7821941	7.283391143	7.550700527	5.828179214	4.953296515	4.935431935	4.954037546	9.35075549	5.425647365	5.995597085
4.720497124	6.257927945	4.824496419	5.784201014	4.867730246	6.163722578	5.389815083	5.591054846	7.114693274	4.760346344
3.97908653	4.823935637	4.908860333	4.978182463	4.815315256	5.932950088	4.543781359	4.498807078	3.803368992	4.438050342
5.342163183	5.662378244	5.782404715	5.589681736	5.497774686	5.049899029	5.431851546	5.70583061	5.284268911	5.02200093
5.661582852	6.607458251	6.398310663	6.150559686	6.091878108	5.971579296	6.044698634	6.609066937	6.381050194	5.450942439
4.73799939	5.715261753	5.443034472	4.593176794	4.246364687	3.865749302	4.0575416	4.51539914	4.194988808	3.76926758
3.663807388	3.6091356	3.529808837	3.970112996	4.101563606	3.701987987	3.32442625	4.018201157	3.784557192	3.840848309

Lung GSM117772 Bronchioloalveolar carcinoma	Lung GSM137910 Adenocarcinoma, NOS*	Lung GSM137912 Adenocarcinoma, NOS*	Lung GSM137916 Adenocarcinoma, NOS*	Lung GSM137931 Adenocarcinoma, NOS*	Lung GSM137945 Adenocarcinoma, NOS*	Lung GSM138001 Bronchioloalveolar carcinoma	Lung GSM138002 Adenocarcinoma, NOS*	Lung GSM46843 Bronchioloalveolar carcinoma
3.859574629	4.097850733	5.688237238	4.378224235	5.050542541	3.99459428	4.957176654	3.986247274	4.887158067
7.129175946	7.043938881	6.793103816	6.98112323	6.722209981	6.931996346	6.58769499	6.975806153	7.801678085
4.403812705	5.107397641	4.374287382	5.148488049	4.95674412	4.425493824	4.333040005	4.477279668	4.140036799
7.685332371	7.233820001	8.255109246	7.909318254	7.905611339	6.855007365	7.312631477	6.953041198	7.57073297
4.311772283	3.585201937	4.208953324	3.613429362	3.781468321	3.471554579	4.468935151	4.192717829	4.180410298
5.695672752	5.808832905	6.443797491	6.106275062	6.765227954	5.261159812	5.996515127	5.955191529	5.730645787
6.611220144	6.822341958	6.148238271	6.145137363	6.218729874	6.477113444	6.696094448	6.15917584	6.585424951
4.138507851	3.990367874	4.657712471	4.847620874	4.381422553	4.145393523	4.333967673	3.843652536	4.377403872
4.371135793	5.07648126	4.711300828	4.603513603	4.639071551	4.614046347	5.022285178	5.10249854	4.545440438
5.432003533	5.684726304	5.241581897	5.467063611	5.27010247	5.121134079	5.308649109	4.934036227	5.011677689
7.208227698	5.805697707	7.374119311	6.999276372	5.837522121	5.694211426	7.025557156	7.772670765	7.041489676
7.44705616	5.585995425	7.572174307	6.375526095	5.322904115	4.332597764	5.427171927	6.182038658	5.47881561
4.423432254	5.430386535	5.373601905	7.355427172	4.416812181	3.718808146	4.99524946	3.790008553	5.61736997
4.946407039	5.836351356	6.919784791	6.397796824	5.477157443	4.830654696	5.836363234	5.027527429	6.700912503
6.206262715	6.217774707	7.374459684	7.117597136	6.881497644	5.874250793	6.685752238	5.954920903	6.993332786
4.001963387	4.314446745	6.060613474	4.77933098	4.766975151	4.461894886	4.937367348	4.26818814	4.463432835
3.643405344	4.133702183	3.865550843	3.928971832	3.90592024	4.018453585	3.711640803	3.750308039	3.896454144

Lung GSM46850	Lung GSM46860	Lung GSM46868	Lung GSM46884	Lung GSM46904	Lung GSM46936	Lung GSM46973	Lung GSM46978	Lung GSM53167	Lung GSM76488	Lung GSM68949
Squamous cell carcinoma	Bronchioloalveolar carcinoma	Squamous cell carcinoma	Squamous cell carcinoma	Bronchioloalveolar carcinoma	Squamous cell carcinoma	Squamous cell carcinoma	Squamous cell carcinoma	Squamous cell carcinoma	Bronchioloalveolar carcinoma	Squamous cell carcinoma
4.73582204	4.392414667	3.791252409	5.870887234	4.673896831	4.956431943	3.780616192	4.349308401	3.813929909	4.533257113	3.900804056
6.164319546	6.670484501	6.891070637	6.287819106	7.0133521	7.533480981	6.254651411	6.533345819	7.536789139	6.911508126	6.172427725
5.07622088	3.990544669	5.028101023	5.400157802	4.904788821	5.189101841	5.454203925	4.258152403	4.742188126	4.923880734	4.694955489
7.797797605	7.370441446	7.817794247	8.243847245	7.448116678	8.205726269	7.527954918	7.476276288	7.549793041	7.653374733	7.045792207
4.837135385	4.285783261	3.832754489	5.139365987	4.837301464	4.673529	3.674321988	4.698975306	3.674513248	4.185767737	3.761413066
6.477583646	6.178420124	6.846122499	7.911982746	6.051608061	6.195057228	7.294157975	7.079702563	6.01851888	6.255801427	6.864087105
6.775893892	6.720378585	7.840957128	6.790327505	6.575485169	6.862868189	7.177781531	6.73204399	7.084157555	6.011602406	6.561529616
3.888171631	4.370530797	4.312945089	6.067807045	6.345326324	5.839681973	3.914377614	5.161447779	3.956601718	4.84741962	4.424829844
4.65563573	4.294018486	4.69175616	4.575021321	4.429731932	4.05681092	4.877974792	4.505874148	4.793569161	4.78982289	4.722874874
4.806406592	4.399519049	4.781214851	4.823878923	5.550826136	4.58849693	4.97665848	4.860261984	5.309254053	5.252536778	5.076669765
6.353133614	7.022588212	6.218560899	7.229022388	7.385600789	7.078540936	5.913358664	6.262501401	5.827128253	6.019197736	5.514152314
5.773304344	6.252364322	5.89933886	7.488246787	6.301072995	6.049045589	5.611278448	6.101012729	6.203808547	5.979226208	5.333668914
5.558169914	4.336789639	5.583341531	6.850976689	4.824415213	4.721675482	4.374013259	4.8094911	5.214904487	6.029809061	4.39405019
5.89646	6.321234479	6.939403532	7.52451308	8.215419397	6.853633992	6.144693409	6.375413354	5.525147353	6.438526218	5.307310496
6.782822758	6.41775936	6.971486723	7.731598576	6.587674287	7.182963499	6.173312442	6.845263146	5.688975703	5.908933793	6.24707206
5.126623145	5.073931679	5.484442458	5.359152146	6.770657888	5.847826323	4.362889701	5.453963311	3.836292199	4.447238016	3.962035587
4.180290937	3.724712948	3.876850714	3.856618375	4.137647568	3.806891199	4.218126505	3.858008632	3.979541257	4.213595007	4.202640953

Lung GSM88953 Bronchioloalveolar carcinoma	Lung GSM88981 Bronchioloalveolar carcinoma	Lung GSM89046 Adenocarcinoma, NOS*	Lung GSM89060 Adenocarcinoma, NOS*	Endometrium GSM46927 Endometrioid carcinoma	Endometrium GSM46937 Endometrioid carcinoma	Endometrium GSM46949 Endometrioid carcinoma	Endometrium GSM53053 Endometrioid carcinoma	Endometrium GSM53085 Endometrioid carcinoma
4.004132087	5.621810813	3.871854743	4.019232829	5.07545492	5.803923848	6.603674889	3.828535258	3.725917599
6.705725832	6.665554364	6.744335469	6.932626588	6.523495889	5.941513676	6.023920358	7.019240781	6.328198446
5.901234916	4.4071953	4.831743515	4.582024365	5.007959527	4.967593624	9.084735033	4.530303203	4.844968522
7.314766761	7.345993901	7.741253894	7.839963718	8.012790531	8.044162999	8.32284659	6.902408243	7.590638029
3.716340928	4.414899581	3.817875784	3.62776101	3.889492168	3.818604403	5.448845021	3.518286852	3.044828082
6.515819594	5.756610785	6.224442287	6.089686513	6.71151754	6.730272546	7.031116115	6.413156259	7.505978122
6.51647012	6.373663258	6.230043375	6.591713718	7.321687969	8.837019423	7.148280063	6.144697967	6.378493849
4.219689462	5.384925405	4.178934857	4.300895232	4.503097047	4.868564476	6.407317346	3.851426481	3.682779378
4.859541067	4.768754383	4.589754182	4.701468175	4.711188988	4.12102415	4.364893194	4.666460821	4.626523731
5.34317557	4.949542624	4.829759599	5.078239785	4.703373559	4.665810781	4.671927937	5.018215446	4.967146928
8.348458567	5.742356821	6.068976784	6.026271504	7.050440313	7.086394867	7.84702036	5.055514429	5.098873461
7.791358335	5.46080648	5.783323119	5.689824265	6.715959926	6.709186941	8.488879985	5.210045386	4.863018843
5.094123079	4.738920838	4.834935205	5.054770858	6.409429665	6.840574318	8.770805561	4.750874396	4.517700799
5.298987243	6.592469714	5.517241317	5.017374797	5.864359897	5.269408649	6.52049062	4.883886956	4.789901149
6.079532274	7.324015558	6.433472778	6.098574645	7.552713296	6.723043836	8.016655504	5.900199044	5.241577284
4.055209518	4.837378997	4.382599316	4.570720146	5.47588088	6.046551869	6.221970171	3.789707896	4.009694229
3.64684342	3.821560385	3.965198659	3.869575126	4.160703048	3.877493724	3.715163841	4.267140682	3.922270509

Endometrium GSM53067	Endometrium GSM53075	Endometrium GSM53084	Endometrium GSM53093	Endometrium GSM53103	Ovary GSM117744	Ovary GSM137904	Ovary GSM46839	Ovary GSM46898	Ovary GSM46910
Endometrioid carcinoma	Endometrioid carcinoma	Endometrioid carcinoma	Endometrioid carcinoma	Endometrioid carcinoma	Serous Adenocarcinoma	Serous Adenocarcinoma	Papillary Serous Adenocarcinoma	Papillary Serous Adenocarcinoma	Papillary Serous Adenocarcinoma
3 976620898	4 031519268	4 212360318	3 947228755	4 216227589	4 302104959	4 245018174	4 072288605	4 582416434	4 166563731
6 532895121	6 58848645	6 272169973	6 825757219	7 056974109	6 792620133	7 495470945	7 054227049	7 060417704	7 291335921
5 081254667	4 902807076	5 259413848	4 57032325	4 845649859	5 347252196	4 503155517	5 574263386	4 517722909	6 230750636
6 921829121	7 225691748	7 201905255	7 231409921	6 999083184	7 670457563	7 339760075	5 304515004	7 083223765	7 397216185
3 536387144	3 519601038	3 631271129	3 196491158	3 532261329	3 760092014	3 674996073	3 687450194	3 855593953	3 643004926
6 504294642	6 740131495	6 184415079	6 133853129	7 221793061	7 316806664	6 197405126	5 250529259	8 13632632	7 132827065
6 737326824	6 536390686	6 286932544	6 500780426	6 764207701	6 535497095	7 643199001	4 507711708	7 330833627	6 673141375
3 976877438	3 606767187	4 130925201	3 799707124	3 609313362	3 806307947	4 74778826	4 11521044	3 927389879	4 438543001
4 514513904	4 429523747	4 461494002	4 356540236	4 40569685	4 959076333	4 760598403	4 449183512	5 193849421	4 347783788
5 237482466	5 029199012	5 212711045	5 294796088	4 990015311	4 68524426	5 213985453	5 777344181	5 170429538	4 479979413
6 009714829	6 040715134	5 701279809	5 42935985	5 33227353	5 545767057	5 289833465	4 816202899	5 713307199	5 178643951
6 254214349	5 638984477	6 188265495	5 330807397	5 409218083	7 035266393	5 542250366	4 822261066	5 816666546	4 300020674
7 413446568	5 149289801	4 577425777	4 790664518	4 955476478	5 509323384	4 568671967	6 123982838	4 879557141	4 052442647
4 957973271	4 729763827	4 98511849	5 125799016	4 53214857	5 425467578	4 727033527	4 923019284	5 031211573	4 624031816
6 004804681	5 791523712	5 808375143	5 733774704	6 003669534	5 569953202	5 96694719	6 003171066	6 047984876	5 210320887
4 130697475	4 132718081	4 651889214	3 915369973	3 782527437	3 970957555	4 276901403	4 201183741	4 489113156	3 911706208
3 959626997	3 963132812	3 517190128	3 73169254	4 608112712	3 794819005	3 59388975	3 481385827	4 038261187	4 126704885

Ovary GSM46918	Ovary GSM53036	Ovary GSM53054	Ovary GSM53069	Ovary GSM53100	Ovary GSM53124	Ovary GSM53129	Ovary GSM53144	Ovary GSM53173
Papillary Serous Adenocarcinoma	Serous Adenocarcinoma	Papillary Serous Adenocarcinoma	Serous Adenocarcinoma	Serous Adenocarcinoma	Papillary Serous Adenocarcinoma	Papillary Serous Adenocarcinoma	Papillary Serous Adenocarcinoma	Papillary Serous Adenocarcinoma
3 964414318	4 476726319	3 847644866	4 35126815	4 000275901	3 880779396	4 348890644	4 194309169	4 006564035
6 892810072	7 345004887	6 534464457	6 423764077	6 893815446	6 705542012	6 468501549	6 807536449	6 893362514
5 29808241	5 371984147	4 411315071	4 342047973	4 230854961	4 860143497	4 930875876	4 822659051	5 120982678
7 71814431	7 292804056	6 707175279	6 369760475	6 809820598	7 353097625	6 973225382	5 807268215	6 351860791
3 744570844	5 510831277	3 486669668	3 622048183	3 449592868	3 59544336	3 614496199	3 019933911	3 392458365
6 370101544	7 032028358	5 906084469	5 433988129	7 841456934	6 241789852	6 084697313	6 330731568	5 893833715
8 232563013	7 052682066	6 979346597	6 399045423	6 674036543	6 932904398	6 284395528	7 383300826	6 992233556
5 022503643	4 875209985	4 095043713	3 951009968	5 653828278	3 732999717	3 892400066	3 552306285	4 28269112
4 431522162	4 652571944	4 584694458	4 570122622	4 570273204	4 51616946	4 545440438	4 564037106	4 96981135
4 763208334	5 345982869	5 363085184	5 633147436	4 972485137	5 035814105	5 123688232	5 071286608	5 325908994
5 235874064	6 314572863	4 742113859	5 380047215	4 95413285	5 537874642	5 732571219	4 864217553	4 922831258
4 95843774	5 577313088	5 759831771	4 827764192	4 445743148	5 987575669	5 502558104	5 280967457	5 622804516
4 97340933	5 207115633	4 5491762	4 48157636	4 968759524	4 969067405	6 150586862	4 484093931	5 065031859
4 499035277	5 402748937	4 639198641	5 189081469	4 861462273	4 877452752	4 940613292	4 943710523	4 723243477
5 588133574	6 258230836	5 510098522	5 867098374	5 561538625	5 878482617	5 580566992	5 792082614	5 795745625
3 798576379	4 103647688	4 303962329	4 092305078	3 691431536	3 912166436	3 855920397	4 721365435	3 638302717
4 033233026	3 959005114	3 985082589	4 039211456	4 28517677	4 460935983	4 133828795	4 365660192	3 888838639

Ovary GSM53185	Ovary GSM76489	Ovary GSM76510	Ovary GSM88948	Ovary GSM88973	Ovary GSM89028	Pancreas GSM117645	Pancreas GSM117647
Papillary Serous Adenocarcinoma	Serous Adenocarcinoma	Serous Adenocarcinoma	Serous Adenocarcinoma	Serous Adenocarcinoma	Serous Adenocarcinoma	Ductal Carcinoma	Adenocarcinoma, NOS
4 230255482	4 271776349	4 095466574	3 677822489	4 461091828	3 610042471	4 263038104	4 036934868
7 607068957	7 753049168	6 602885124	7 159300174	6 124043094	7 027802262	6 68442028	7 470867344
4 773145571	4 334147447	5 858018586	5 40155805	4 989407378	5 490895333	4 841858735	5 038377187
7 151231691	7 846932709	7 078621443	6 699339285	7 395334254	7 104621906	8 374175811	6 90032918
3 343006923	3 711098533	3 608339211	3 680638772	3 32072952	3 498221199	4 025044277	3 650665835
5 590410183	5 599969047	6 982832086	7 274358376	5 866822797	5 929967375	6 897200603	5 971826842
6 724958961	6 891395666	6 887716736	7 078196532	8 313246572	6 661782664	6 65385457	6 503307229
4 230764383	4 474229594	3 935679157	4 67943737	3 335212075	3 959597484	4 160320921	4 312459635
4 814068885	4 753366243	4 784180643	4 851169796	4 770531108	4 314726885	4 447218809	4 831252558
5 318467288	5 058415761	4 796260324	5 137183393	5 567814938	4 794167695	5 13718136	5 366877712
5 121012136	4 938043658	4 935934271	5 300691713	5 033807048	5 302464107	5 457190269	5 284810762
5 565760052	5 138547383	5 322926409	5 873730172	4 65290844	5 291501596	7 7259529	5 614367819
7 385198049	4 797647861	4 558034016	4 946612066	6 590005306	4 360260372	6 149830371	5 079099595
4 754478411	4 881357151	4 682621969	4 584486925	5 446879518	4 655957135	5 191490548	5 774649038
5 52805795	5 365107333	5 128126892	5 640091254	5 80393738	5 18601418	5 914809117	6 306543892
3 895521438	3 713282166	4 221305267	3 596944346	3 931968428	3 965919054	4 143271273	4 492647677
4 10183797	3 805834979	4 108454591	4 199094781	3 799117671	3 931156147	3 970223449	4 085597232

Pancreas GSM137958	Pancreas GSM152744	Pancreas GSM179781	Pancreas GSM179669	Pancreas GSM203703	Pancreas GSM203761	Pancreas GSM53046	Pancreas GSM89045	Prostate GSM117726	Prostate GSM117727
Ductal Carcinoma	Ductal Carcinoma	Ductal Carcinoma	Ductal Carcinoma	Ductal Carcinoma	Ductal Carcinoma	non functional islet- cell tumour	Ductal Carcinoma	Adenocarcinoma, NOS ⁻	Adenocarcinoma, NOS ⁻
4.25142281	5.714980842	4.676012005	3.977215665	4.232740979	4.380927631	4.238060782	4.616864752	4.722376611	4.440235691
6.403418074	6.223372018	5.890718987	7.391369081	7.245843639	5.516643784	6.747182097	6.19122911	5.002571944	5.554892612
4.817079264	5.435029314	4.754005582	4.968157534	4.340064401	4.313021724	4.14708736	5.050672025	4.448766175	4.171424398
7.879217111	8.11331059	8.253649533	7.959427721	8.517998508	7.752371052	6.918256334	8.142922582	7.02803052	7.705749079
3.708037019	3.993026499	4.861695964	3.899033498	4.10959034	3.80935278	3.652653097	4.154016582	3.67294884	3.978295339
7.006867514	7.215328101	7.761961164	6.667678795	7.149472316	8.066990108	5.356573922	6.998158516	6.732796065	6.86775477
6.37408514	6.612828507	6.106755962	6.023345202	6.466326995	6.040433122	7.286216878	6.024396051	7.133208541	6.930981564
4.213227917	3.805994195	5.207203644	4.99622283	4.150680762	6.478425482	4.028469123	5.288717661	4.244720384	4.50796667
4.513253308	5.153555683	5.012116681	4.770854004	4.307795961	5.347284067	4.573384809	5.016974205	4.736150854	4.550967744
5.211811418	4.837777239	4.590226546	5.358137801	4.970661085	5.274050249	5.449830545	5.092196414	5.080440389	4.949316883
5.599271051	5.362588227	6.04422914	5.775544283	5.783169307	6.030585613	6.066327906	6.140734954	5.742633851	5.392422201
7.0029927	7.367434035	7.047782435	6.311535224	7.137922698	5.637774647	4.637788439	7.591445537	5.442875145	5.760459295
5.590615064	5.838970717	6.300278507	8.012059114	5.526436284	7.005923205	4.29804778	5.371308448	4.276701013	4.912407979
5.890957737	5.277304807	6.15658404	6.457247576	5.048466603	6.858424446	5.363506106	6.283362293	4.860582415	5.004391837
6.738572221	5.851966009	6.916407341	7.154647268	6.515351429	8.26917647	5.545173808	7.068856834	5.653579992	5.795742322
5.358062963	4.123965702	3.877792848	4.605564199	4.772950109	3.945081928	4.294295507	5.557383754	4.37065445	3.852380354
3.947058432	4.078696591	3.736475182	3.66987326	4.071776749	3.288977036	4.336328629	3.65737679	3.882790058	4.270706157

Prostate GSM117741	Prostate GSM38079	Prostate GSM46866	Prostate GSM53061	Prostate GSM53114	Prostate GSM53152	Prostate GSM76516	Prostate GSM88977	Stomach GSM102495
Adenocarcinoma, NOS	Adenocarcinoma, NOS	Adenocarcinoma, NOS	Adenocarcinoma, NOS	Adenocarcinoma, NOS	Adenocarcinoma, NOS	Adenocarcinoma, NOS	Adenocarcinoma, NOS	Adenocarcinoma Diffuse Type
4.312599241	4.192371416	3.935814191	4.486861508	4.273625049	3.470866593	3.73261431	3.801635198	4.088299433
6.287633839	5.931348201	6.122656548	6.524643502	6.065942863	6.640508686	6.315844556	6.230878853	5.804994569
4.597387206	4.323528627	4.470012221	4.6850186	4.333285601	5.131760897	4.410246345	4.2912857	5.84241597
7.4628323	7.3174094	7.635957093	6.471137654	6.978494958	6.775746168	6.642028314	7.391224351	7.758506568
3.517275077	3.764286531	4.041159194	3.57681382	3.63609135	3.460556829	3.433542152	4.076850451	3.626693086
7.018033866	5.982548171	7.078183619	6.411384151	6.676117378	6.489495889	6.431175718	6.632494587	6.924495521
6.771202065	7.407686871	7.476898241	6.645685139	7.017287416	6.441215278	7.114689558	7.535062534	5.857437332
4.679504831	3.367715919	3.986601461	5.103638332	4.045693691	3.970125606	3.822584568	3.951276015	5.020704329
5.193265091	4.927394935	4.409431739	4.739176355	4.813820734	4.624204652	4.500198507	4.575575182	5.122719537
5.243090563	4.969555664	4.666014251	5.480174811	5.139882102	5.109478198	5.259918838	5.038197305	5.391387365
5.753371577	5.341262789	5.824558204	6.373566437	6.147865477	4.958845896	5.251518697	5.042034874	5.881559443
5.337250241	5.147887042	5.960876948	5.141675584	5.062641434	5.134363103	4.726495372	5.81489068	7.438561009
5.483457367	5.509800294	4.698484634	5.117442452	4.746553011	4.356044272	4.465712589	4.279544586	6.065782097
4.763874691	4.731827358	4.659075088	5.564862358	4.753732209	5.09698152	4.786443128	4.58268796	5.68538509
5.833990859	5.643345041	5.886194891	6.316552134	5.73364523	5.918579511	4.924164217	5.703954052	6.854941906
4.675412795	4.089242137	3.705229907	4.776059531	3.711798839	3.866838084	3.848507803	3.58396326	5.553451904
3.574835393	4.0849392	4.226112069	3.754770456	3.78779204	4.424360538	4.619985305	4.034341035	3.484236

Stomach GSM152595	Stomach GSM203666	Stomach GSM53039	Stomach GSM76562	Thyroid GSM102452	Thyroid GSM102560	Thyroid GSM117723	Thyroid GSM117735	Thyroid GSM138004	Thyroid GSM138023	Thyroid GSM138024
Tubular Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Adenocarcinoma	Papillary carcinoma	Papillary carcinoma	Papillary carcinoma	Papillary carcinoma	Papillary carcinoma	Papillary carcinoma	Papillary carcinoma
4 355786161	4 511342253	4 029060329	5 419465118	4 569511909	4 575144406	4 445459461	5 297573656	7 030962556	5 283811197	6 679026829
6 175648367	6 372301016	6 66796886	5 898273936	6 506342858	6 456530101	6 359890746	6 754902417	6 774388351	6 53389224	6 159008637
5 152043394	4 648142838	5 623338173	5 49763909	4 489286847	3 744830094	5 052986544	5 169848119	4 227036062	4 43169205	4 736881748
6 454359814	7 598528305	6 320646099	6 949451558	8 335733077	8 518847147	7 594608893	7 336268478	7 939631139	8 482759349	8 26310664
3 556011159	3 593103056	3 64424401	3 657360531	3 691800201	3 721600599	3 67584275	3 599040275	3 780780348	3 976463086	4 337658404
5 985966359	6 936800307	7 973794916	6 614449708	6 966332955	6 773461789	6 771797882	6 356420985	6 082481483	5 958245534	6 31780257
5 978505361	6 318768361	6 103183835	5 765189887	6 774863913	6 986120014	6 822186567	6 210496947	6 920029361	6 666265852	7 060424948
3 945050286	4 707830707	3 457912656	4 492396171	4 220691846	4 346211869	4 859908078	4 334961221	5 180243639	4 415629854	5 256194904
4 510557733	4 854009236	4 892891643	4 614220099	5 138937665	4 776258982	4 775284506	4 987958465	4 900223426	4 938833465	4 518047023
5 044842911	5 115349411	5 449891207	4 899977755	4 784413202	5 137042917	5 329761794	5 385155679	5 178343938	5 67036049	5 377825723
5 331861851	5 194167785	5 181866433	6 115180769	6 402115185	6 352399551	6 847441798	6 228133203	7 99897817	6 223850084	8 131144883
5 65094839	6 231957754	4 981727408	6 567642307	6 104924814	5 622753601	5 578941041	6 181006618	6 859618575	5 481367413	7 382734588
5 595241656	4 631596899	5 200647362	6 36941799	4 609219279	5 196186828	5 903003708	6 015004661	4 367015476	4 113293165	5 671976439
5 489390993	5 408790121	5 526949878	7 123176501	4 773394412	4 953386608	5 458805682	6 114768777	4 790739738	5 630026361	5 512314792
7 084091963	6 731951914	5 598799615	6 647504194	6 41278207	6 094150685	7 03230648	6 521109921	7 324623925	6 555692814	7 035022491
4 364071654	4 870686507	4 033961658	4 154145905	4 798806756	4 992784084	5 255111144	5 888592657	6 474140885	4 856158177	5 668150729
4 482783359	4 028111282	4 400135769	3 914092405	3 33365246	3 77693413	3 832468247	3 97862578	3 826084185	4 049172828	3 921684125

Thyroid GSM88998	Thyroid GSM89038
Papillary carcinoma	Papillary carcinoma
6.025329115	5.423875227
7.116847067	6.117875288
5.199465648	5.46636181
8.086746357	7.456804276
3.77550105	4.714418113
6.449731815	6.423065916
7.080700082	6.805014266
4.792109652	5.792370064
4.390945783	4.907599902
5.054410232	5.055939803
7.748582493	7.049862633
6.678424912	5.409330064
5.804498516	7.564117346
5.155989432	6.335823725
6.126789461	7.010884754
5.064496318	5.164512627
4.298620738	4.008161234



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