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# Identification of transcriptional mechanisms downstream of nf1 gene defeciency in malignant peripheral nerve sheath tumors

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# IDENTIFICATION OF TRANSCRIPTIONAL MECHANISMS DOWNSTREAM OF NF1 GENE DEFECIENCY IN MALIGNANT PERIPHERAL NERVE SHEATH TUMORS

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# DEDICATION

**This work is dedicated to my parents and my wife Ze Zheng for their continuous support and understanding during the years of my education. I could not achieve my goal without them.**

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# LIST OF ABBREVIATIONS

4EBP1: eukaryotic translation initiation factors 4E binding protein 1

ALK: Activin-receptor-Like-Kinase

BMPs: bone morphogenetic proteins

CDK4: cyclin dependent kinase 4

CSRD: cysteine and serine rich domain

Dox: doxycycline

Edn1: Endothelin 1

EGFR: epidermal growth factor receptor

eIF4E: eukaryotic translation initiation factor 4E

ERK1/2: extracellular signal-regulated kinase1/2

ESC: embryonic stem cell

FDA: US Food and Drug Administration

FISH: fluorescence in situ hybridization

FTI: farnesyl protein transferase inhibitor

FTS: S-trans, trans-farnesylthiosalicylic acid

GAP: GTPase activating protein

GEF: guanine nucleotide exchange factor

GePS: Genomatix Pathway System

GRD: GAP-related domain

HSC: normal human Schwann cell

IPA: ingenuity pathway analysis

IRS1: insulin receptor substrate

MAPK: mitogen-activated protein kinase

MPNST: Malignant peripheral nerve sheath tumor

mTOR: mammalian target of rapamycin

mTORC1: RATOR (regulatory associated protein of mTOR) complex 1

mTORC2: RICTOR (rapamycin-insensitive companion of mTOR) complex 2

NLS: nuclear localization sequence

NSCLC: non-small cell lung cancer

NT5E: Ecto-5'-nucleotidase

PDGFR: platelet-derived growth factor receptor

PDK1: 3-phosphoinositide-dependent protein kinase 1

PH: PH-like domain

PI(3,4)P2: phosphatidylinositol 3,4-bisphosphate

PI(3,4,5)P3: phosphatidylinositol 3,4,5-trisphosphate

PI3K: phosphoinositide 3-kinase

PKA: protein kinase A

PKC: protein kinase C

qRT-PCR: quantitative polymerase chain reaction

RHEB: RAS homolog enriched in brain

S6K1: S6 kinase/ribosomal

SCLC: small cell lung carcinoma

SDS-PAGE: SDS polyacrylamide gel electrophoresis

SKPs: skin-derived precursors

STAT3: signal transducer and activator of transcription-3

SYN: Syndecan binding region

TGF-beta: transforming growth factor-beta

TSC: tuberous sclerosis complex

VEGFR: vascular endothelial growth factor receptor

# CHAPTER I: Neurofibromin, a RAS-GAP and more

## Introduction

Neurofibromatosis type I (NF1, OMIM 162200), formerly known as von Recklinghausen Disease, is an autosomal dominant genetic disorder with an incidence of 1:3000 live births. The clinical hallmark features of NF1 are cutaneous neurofibromas, café-au-lait spots, Lisch nodules, and freckling of axillary and inguinal regions (Huson, et al., 1988). Although most neurofibromas develop in adult patients, NF1 can also occur in much younger individuals with manifestations including cognitive deficits, bone deformations, plexiform neurofibromas, optic glioma and a variety of neurologic syndromes (Czyzyk, et al., 2003; Watson, 1967). This inherited disorder is due to the various mutations of the *Nf1* gene at 17q11.2 that encodes neurofibromin (Bader, 1986; Riccardi, 1992). Neurofibromin is known as a tumor suppressor because of its well characterized RAS GTPase activating protein related domain (GRD) which negatively regulates RAS activity by accelerating the hydrolysis of the active GTP-bound RAS (Xu, et al., 1990). Humans with a genetic mutation in one of the *Nf1* alleles show a predisposition for many different kinds of tumors. Patients with plexiform neurofibromas have increased lifetime risk for transformation to highly malignant peripheral nerve sheath tumors (MPNST) (Evans, et al., 2002b), and glioblastoma

multiforme can be another malignant manifestation in NF1 patients (Gutmann, et al., 2002). Surgery, the primary treatment, is limited by tumor infiltration and therefore patients often experience high relapse rates. Increased RAS and RAF/MEK/ERK pathways activities have been reported (Basu, et al., 1992) in the patients, however, RAS and/or MEK1/2 targeted therapeutic strategies have met with limited success (Kalamarides, et al., 2012).

The regulation of RAS pathway by RAS-GRD (330 amino acids) in neurofibromin is paramount in development and tumorigenesis; however, as a protein with 2818 amino acids, the functions of most other domains are not very clear. An *Nf1*$^{-/-}$ mouse model with complete loss-of-function of neurofibromin shows embryonic lethality resulting from cardiac abnormalities (Jacks, et al., 1994), but an inducible neurofibromin GRD alone could not rescue the lethality of *Nf1*$^{-/-}$ in mouse embryos (Ismat, et al., 2006). Another intriguing fact is that many different types of single nonsense mutations in the *Nf1* gene encoding region outside the GRD sequence can also lead to the *Nf1* manifestation in patients (L.M.Messiaen, 2008). These findings indicate that neurofibromin may participate in different mechanisms in addition to acting as a RAS GTPase activating protein in development and tumorigenesis. A new strategy is required to explore the function of neurofibromin in various cellular processes and mechanisms.

In this study, we hypothesize that the NF1-related aberrant gene regulations can be

identified by the systematic gene expression profile comparisons using MPNST cell lines with different *Nf1* status. By revealing and characterizing those gene expression changes, the signaling cascades associated with NF1 malignancy may be specified and served as druggable targets for the rational treatment of NF1-related tumors.

## *Nf1* gene structure and neurofibromin functions

The *Nf1* gene is located at 17q11.2 and spans 280 kb of genomic DNA. It has 57 constitutive exons and 4 alternative splices, encoding a 12 kb mRNA transcript, with a ~9 kb open reading frame (Upadhyaya M, 1998). The *Nf1* gene is conserved in many organisms. Bernards et al. reported more than 98% homology between human and mouse amino acid sequences (Bernards, et al., 1993) and approximately 60% homology between Drosophila and human (The, et al., 1997). A much conserved CpG-island-containing promoter has been found in the *Nf1* gene however hypermethylation of this region does not appear to be a common mechanism to silence *Nf1* expression in any NF1-related tumors (Horan, et al., 2000; Horan, et al., 2004). The *Nf1* gene has a myriad of pseudogene sequences on several other human chromosomes revealed by fluorescence *in situ* hybridization (FISH) using labeled *Nf1* cDNA, but none of these pseudogenes encodes a functional protein (Gasparini, et al., 1993). From the study of Luijten et al., these pseudogene sequences are the result of multiple independent

partial duplications of the *Nf1* gene at chromosome 17 followed by sequential inter-chromosomal transposition events (Luijten, et al., 2001).

Neurofibromin is ubiquitously expressed with highest expression level in neural tissues, bone, kidney and spleen (Theos and Korf, 2006). *Nf1* knockout in mice causes embryonic lethality because of abnormal heart development (Brannan, et al., 1994). The protein, neurofibromin, has ~280 kDa molecule weight with several domains such as RAS-GRD, cysteine and serine rich domain (CSRD), tubulin binding domain (TUB), Sec-14 domain, PH-like domain (PH), and Syndecan binding region (SYN) (Fig.1) (S. Welti, 2008). Using a yeast two hybrid system, several proteins have been reported to interact with neurofibromin, including Syndecan (Hsueh, et al., 2001), Caveolin (Boyanapalli, et al., 2006), tubulin (Bollag, et al., 1993), protein kinase A (PKA) (Izawa, et al., 1996) and C (PKC) (Mangoura, et al., 2006), kinesin-1 (Hakimi, et al., 2002), and the amyloid precursor protein (De Schepper, et al., 2006). However, the biological implications of those interactions are still not clear.

The most intensively studied domain in neurofibromin is RAS-GRD encoded by exon 21 to 27a and works as a GTPase activating protein (GAP) to accelerate the hydrolysis of RAS-GTP and inactivate RAS activity. Increased RAS activity has been demonstrated in the cells derived from both NF1 patients and transgenic mice. Phenotypic features of overactive RAS, such as increased proliferation and survival, have

been identified in *Nf1*$^{+/-}$ and *Nf1*$^{-/-}$ neural stem cells of mice (Dasgupta, et al., 2005). Hiatt et al. reported that the expression of the neurofibromin GRD domain, not p120GAP GRD can restore normal growth and cytokine signaling in primary murine embryonic (*Nf1*$^{-/-}$) fibroblasts and hematopoietic cell cultures (Hiatt, et al., 2001). Klose et al. demonstrated that a missense mutation in *Nf1* RAS GRD (R1276P) leading to an 8000-fold loss of catalytic activity compared to the wild type counterpart is sufficient to cause most NF1 phenotypes (Klose, et al., 1998).

However, some studies also indicated GRD independent tumor suppressor activities in neurofibromin. Johnson et al. reported the malignant transformation efficiency by v-HRAS in the neurofibromin overexpressed NIH3T3 cell line was much lower than the control cells (Johnson, et al., 1994). Another study by Ismat et al. showed that inducible ubiquitous expression of neurofibromin GRD rescued the mid-gestation lethality of *Nf1* null embryos, but the mouse died shortly after birth resulting from aberrant proliferation of neural crest-derived tissues (Ismat, et al., 2006). Shapira et al. showed that neurofibromin conferred sensitivity to apoptosis by both RAS-dependent and RAS-independent pathways (Shapira, et al., 2007). These studies suggest that RAS activity deregulation may not completely explain all the phenotypes in the patients and mice models, and neurofibromin GRD independent function may contribute to the biological development and tumor initiation.

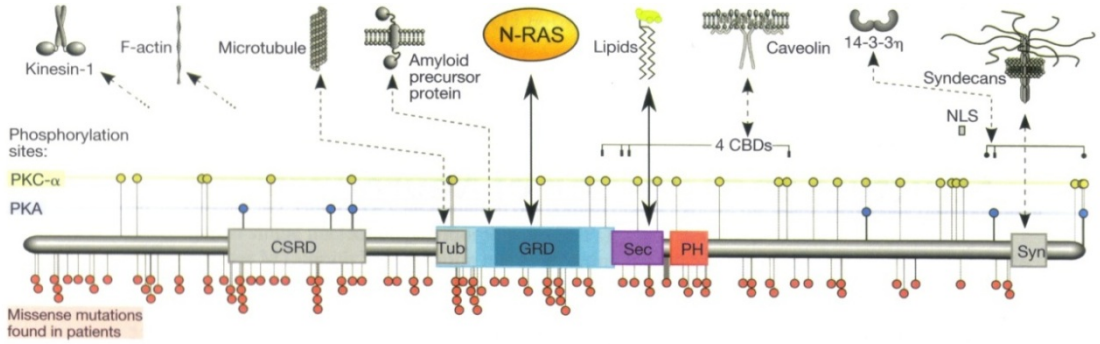



**Fig. 1 Domain scheme of neurofibromin with reported protein-ligand interactions.** Colored domains and interaction partners are confirmed by structural analysis, and grey domains are indicated by biochemical experiments. Red circles mark the positions of missense mutations found in patients (including amino acid deletions and tandem duplication). Additional features are potential phosphorylation sites for PKA (blue circles) and PKC-alpha (yellow circles, only serine phosphorylation) a bipartite nuclear localization sequence (NLS) and several caveolin binding motifs (CBDs). The GRD indicated in the dark blue is the minimal GAP domain, in midblue the crystallized fragment and in light blue whole fragment with sequence homology to the p120-GAP protein, overlapping with the Tub and Sec domain. CSRD: Cysteine and serine rich domain; Tub: tubulin binding region; Sec: Sec14-like domain; Ph: PH-like domain (D.Kaufmann, 2008). Figure is adapted from *Neurofibromatoses* (S. Welti, 2008) with modification.

For other domains in neurofibromin, Sec14 domain is a lipid-binding domain first identified in S. cerevisiae phosphatidylinositol transfer protein (Sec14p) and also reported in RhoGAPs. Sec14p-like proteins show a great amount of diversification in terms of physiological function and ligand specificity. In neurofibromin, Sec14 domain folds into a globular Sec14p-like lipid binding cage (D'Angelo, et al., 2006) closed by an amphipathic helical segment (Sha, et al., 1998). This structure enables Sec14 domain to hypothetically shuttle lipids between membrane compartments through the aqueous medium (D.Kaufmann, 2008). The PH domain of neurofibromin is identified by comparison with protein data bank, which is believed to interact closely with Sec14 domain in neurofibromin. Generally, PH-like domains show various functions in their host proteins which include structural scaffolds for ligand binding and coupling to signal transduction pathways (Di Paolo and De Camilli, 2006; Duncan, et al., 2005). However, it is hard to predict the precise function of the PH-like domain in neurofibromin considering limited similarity in sequence and structure with other members of the PH superfamily.

## Malignant peripheral nerve sheath tumor

Malignant peripheral nerve sheath tumor (MPNST) is a type of soft tissue sarcoma that develops from the peripheral nerves, preexisting benign neurofibromas, or Schwann

cells. Approximately 50% of MPNST occur in the setting of NF1 genetic disease (OMIM ID #162200) with the remainder occurring from NF2 patients or sporadically (Matsui, et al., 1993; Sorensen, et al., 1986). The lifetime risk for NF1 patients to develop an MPNST is 8~13% (Evans, et al., 2002b), and the five-year survival rate is 34-43% (Wanebo, et al., 1993). NF1 patients are most frequently diagnosed with MPNST in the third and fourth decades of life whereas the sporadic form of MPNST is most frequently diagnosed in the sixth and seventh decades of life (Evans, et al., 2002a).

MPNST is thought to arise from the accumulation of additional genetic events in precursor Schwann cells. Neurofibromas are benign tumors and may or may not be associated with the *Nf1* gene. Plexiform neurofibromas are almost exclusively *Nf1*-associated and easily progress to MPNST. Mouse model studies have indicated a heterozygous *Nf1* status was required for the Schwann cells derived plexiform neurofibroma formation and tumor microenvironment (Zhu, et al., 2002). Localized cutaneous neurofibromas and diffuse cutaneous neurofibromas are 90% sporadic and have lower malignant potential (Carroll and Ratner, 2008). However, whether the status of the *Nf1* gene is the only dominator to the malignancy is still questionable.

Currently, several MPNST cell lines are being used as *in vitro* study models, including ST88-14($Nf1^{-/-}$), T265($Nf1^{-/-}$), sNF96.2($Nf1^{-/-}$), sNF02.2($Nf1^{-/-}$) and STS26T($Nf1^{+/+}$). The first four cell lines are *Nf1*-deficient MPNST, whereas

STS26T(*Nf1*$^{+/+}$), with the wild type *Nf1* gene, is from a sporadic MPNST. A cytogenetic study of ST88-14(*Nf1*$^{-/-}$) showed that the *Nf1* locus has been deleted from one allele while the transcriptional activity on the other allele is greatly decreased (Reynolds, et al., 1992). In addition, a heterozygous nonsense mutation in *Nf1* (C910T) in codon 304 (R304X) of exon 7 was identified in this line (Barkan, et al., 2006). For the T265(*Nf1*$^{-/-}$) cell line, there is no *Nf1* mutation reported, however the neurofibromin was hardly detectable in it. The sNF96.2(*Nf1*$^{-/-}$) cell line was derived from an NF1 patient with a recurrent mass associated with nerve tissue diagnosed as MPNST. It has an abnormal karyotype and complete loss of heterozygosity with no detectable wild type *Nf1* allele (Fieber, et al., 2003). The sNF02.2(*Nf1*$^{-/-}$) was derived from a lung metastasis MPNST in an NF1 patient. The STS26T(*Nf1*$^{+/+}$) cell line, with the wild type *Nf1* gene, was established from a sporadic malignant Schwannoma, however, *Tp53* expression was completely absent (Dahlberg, et al., 1993; Miller, et al., 2006a).

## Targeting signaling pathways in the neurofibromatosis type I

### Neurofibromin-NRAS axis

Given the function of neurofibromin as a GAP, the increased RAS activity in neurofibromas and NF1-related MPNSTs is the strong rationale emphasizing the focus on neurofibromin-regulated RAS pathway as a potential treatment target in MPNST (Bottillo,

et al., 2009; Perry, et al., 2001). There are three types of related *Ras* genes, which encode highly homologous NRAS, HRAS and KRAS (isoforms 4A and 4B). Localization of RAS is critical for its activation. A post-translational modification called prenylation is required to facilitate attachment of RAS to inner cell membrane where the guanine nucleotide exchange factor (GEF) catalyzes the GTP to replace the GDP-bound RAS. During this process, a 15-carbon farnesyl group is transferred from a farnesyl pyrophosphate and linked to the cysteine from the C-terminus of the RAS, and thereafter, the last three residues of the C-terminus are cleaved and the prenylated cysteine is methylated, which enables the membrane localization. This modification that facilitates the inner membrane localization of RAS is a rate-limiting step for the activity of RAS (Basso, et al., 2006; Roy, et al., 2005). The GTP-bound RAS is activated and initiates a myriad of signalling cascades to control cell processes.

Two classes of drugs have been used to inhibit the activation of RAS. Lovastatin, from the statin family, can inhibit HMG-CoA reductase and has been clinically used for lowering cholesterol. As an intermediate of cholesterol biosynthesis, farnesyl pyrophosphate synthesis is impaired by HMG-CoA reductase inhibition (Morgan, et al., 2003), which subsequently impairs the prenylation of RAS. Phase I clinical trials to evaluate lovastatin on improvement of neurocognitive and learning deficits are currently ongoing (NCT00853580, NCT00352599). The second class of drugs belongs to the

farnesyl protein transferase inhibitor (FTI) family that can catalyze the transfer of a farnesyl group to RAS. Growth inhibition of ST88-14(*Nf1*$^{-/-}$) has been observed after the treatment with FTI BMS-186511, and the patients demonstrates good tolerance profiles (Widemann, et al., 2006; Yan, et al., 1995). Clinical trials using FTI such as tipifarnib to treat young NF1 patients and progressive plexiform neurofibromas (NCT00021541) passed a phase I trial but was suspended at the phase II trial. Some *in vitro* studies combining lovastatin with FTI suggested promising effects such as arresting cell cycle at the G1 phase and leading to apoptosis by increasing caspase activity in NF90-8(*Nf1*$^{-/-}$) and ST88-14(*Nf1*$^{-/-}$) with no toxic effects in normal rat Schwann cells (Wojtkowiak, et al., 2008). However, it was determined that FTI did not effectively block the NRAS and KRAS prenylation, membrane association and transforming activity, since another type of prenylation of NRAS and KRAS by geranylgeranyl transferase has been reported when farnesyl transferase is inhibited (Lerner, et al., 1997; Whyte, et al., 1997). It can be helpful to combine the inhibitors for the both geranylgeranyl and farnesyl transferases to suppress RAS activation *in vivo* (Sun, et al., 1998). Previous research from our group identified that HRAS is undetectable, KRAS is weakly detectable, and NRAS is the predominant form of RAS from the other two in MPNST cell lines (Mattingly, et al., 2006).

**The RAF-MEK1/2-ERK1/2 axis**

RAF is one immediate downstream mediator of RAS and is activated by RAS-GTP (Katz and McCormick, 1997). The significance of the RAF-MEK1/2-ERK1/2 axis in controlling the proliferation and survival of NF1-associated MPNSTs has been characterized in both animal models and human patient cell lines (Johannessen, et al., 2005; Mattingly, et al., 2006). This axis promotes cellular proliferation through upregulation of cyclin D1 expression, and increases the phosphorylation of cyclin dependent kinase 4 (CDK4) and retinoblastoma protein pRB (Chang, et al., 2003). Phosphorylated MEK1/2 has been reported to be present in 91% of 140 MPNST tissues (72 NF1 patients and 68 not), compared with 21% of benign neurofibromas (Zou, et al., 2009a).

Several studies have provided disappointing results for RAF-MEK1/2-ERK1/2 targeted strategies. Sorafenib is a tyrosine kinase inhibitor with multiple effects including inhibition of RAF-dependent phosphorylation of MEK1/2, vascular endothelial growth factor receptor (VEGFR) I, II and III, platelet derived growth factor receptor beta (PDGFRB) and c-Kit (Rini, 2007). However, the results from its clinical Phase II trial were disappointing because of its very limited effects on patients with advanced soft tissue sarcomas (von Mehren, et al., 2012). As the downstream effectors of RAS, MEK1/2-targeted strategies are promising (Diwakar, et al., 2008). The effects of

MEK1/2-blocking agents, such as U0126, CI-1040 and PD98059 were evaluated in the MPNST cell lines (Mattingly, et al., 2006). Although all three drugs showed concentration-dependent proliferation suppression in tested cell lines, PD98059 has primary cytostatic effects, and U0126 and PD184352 (CI-1040) were cytotoxic, which limited their clinical application (Mattingly, et al., 2006).

**The PI3K-AKT-mTOR axis**

Based on similar clinical features and molecular phenotypes with other disorders known as phakomatoses, Johannessen et al. found that neurofibromin regulated the PI3K-AKT-mTOR (mammalian target of rapamycin, mTOR) axis in NF1-associated MPNST (Johannessen, et al., 2005). Using a cell-based high-throughput chemical library screening approach, Banerjee et al. found that the growth of MPNST can be inhibited by cucurbitacin-I, an inhibitor of the signal transducer and activator of transcription-3 (STAT3), and demonstrated that neurofibromin can regulate cell growth through PI3K-mTOR-STAT3 signaling (Banerjee, et al., 2010).

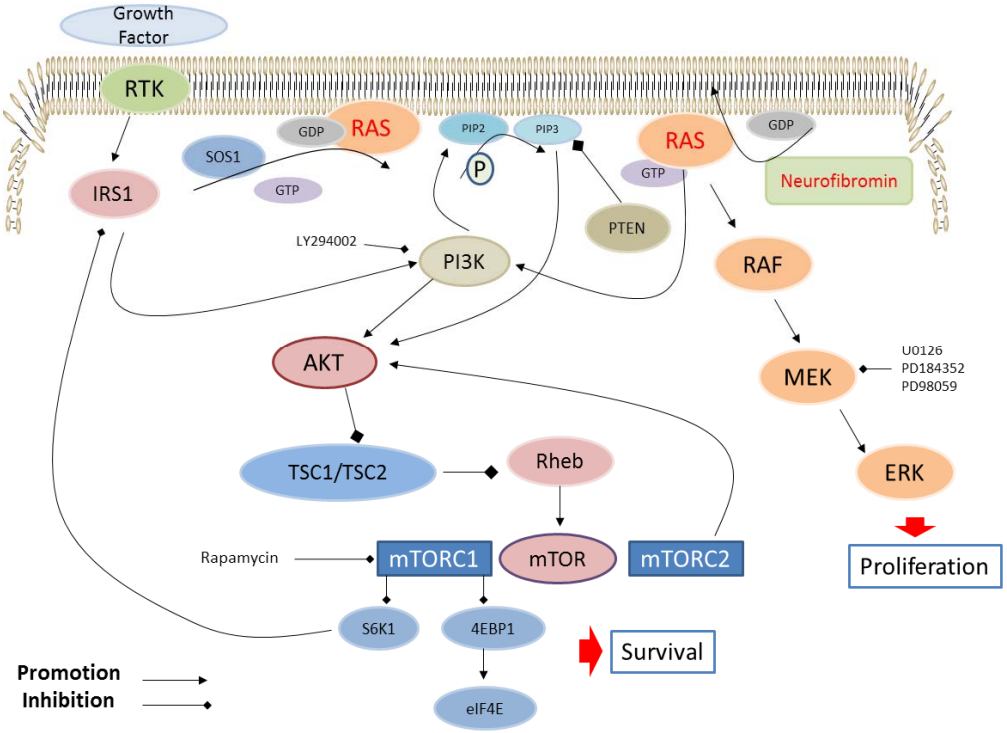



**Fig. 2 The signaling pathways downstream of RAS**

Loss of neurofibromin leads to the increased activity of RAS, and further elevates the RAF-MEK1/2-ERK1/2 axis and PI3K-AKT-mTOR axis, which promote cell proliferation and survival, respectively. Abbreviations: RAF, Raf proto-oncogene serine/threonine-protein kinase; ERK1/2, extracellular signal-regulated kinase; mTOR, mammalian target of rapamycin; PI3K, phosphoinositide 3-kinase; TSC: tuberous sclerosis complex; Rheb: RAS homolog enriched in brain; 4EBP1: eukaryotic translation initiation factors 4E binding protein 1; eIF4E: eukaryotic translation initiation factors 4E; S6K1, S6 kinase/ribosomal; IRS1, insulin receptor substrate 1; GF, growth factor.

The hyperactive RAS in the situation of *Nf1* deficiency can activate PI3K which catalyzes the two phospholipid second messengers, phosphatidylinositol 3,4,5-trisphosphate [PI(3,4,5)P3] and phosphatidylinositol 3,4-bisphosphate [PI(3,4)P2]. These two phospholipids promote the translocation of 3-phosphoinositide-dependent protein kinase 1 (PDK1), and PDK1 phosphorylates AKT at Ser473 and Thr308, which activates AKT and enables the phosphorylation of AKT downstream effectors including mTOR. The activated mTOR forms two complexes, mTORC1 and mTORC2 by binding to RAPTOR (regulatory associated protein of mTOR, complex 1) or RICTOR (rapamycin-insensitive companion of mTOR, complex 2), respectively. mTORC1 can activate the downstream S6 kinase (S6K1/ribosomal) and the eIF4E (eukaryotic translation initiation factor 4E) to regulate protein translation process (Guertin and Sabatini, 2005). mTORC2 can phosphorylate AKT leading to a positive feedback to further increase the activity of mTORC1. However, the S6K1, downstream of mTORC1, has a negative effect on AKT activity by phosphorylating insulin receptor substrate (IRS1) protein, the inactive form of IRS1 which cannot stimulate PI3K (LoPiccolo, et al., 2008). Both AKT and mTOR have been demonstrated to have increased activities in MPNST cell lines, sNF02.2($Nf1^{-/-}$), sNF96.2($Nf1^{-/-}$), T265($Nf1^{-/-}$), ST88-14($Nf1^{-/-}$) and the sporadic MPNST STS26T($Nf1^{+/+}$) and patient tissues (Zou, et al., 2009b). These studies focused interest on the mTOR pathway as a potential drug target.

Rapamycin and its several other analogues have been evaluated in the MPNST cell

lines. Rapamycin is an antifungal agent isolated from Easter Island. It has been approved by US Food and Drug Administration (FDA) for use after renal transplantation as an immunosuppressant. These compounds function as the inhibitor of mTORC1, which suppresses the downstream protein synthesis initiation (Wan and Helman, 2007). Rapamycin and its derivative RAD001 have been demonstrated to inhibit the proliferation of NF1-related and sporadic MPNST cell lines (Johannessen, et al., 2005) and the xenograft growth of STS26T($Nf1^{+/+}$) (Johansson, et al., 2008). However, the inhibitory effect of rapamycin and RAD001 on MPNST proliferation is reversible after stopping the drug treatment. Despite these limitations, several clinical trials (NCT00652990, NCT00634270, NCT01412892, NCT01365468, NCT01031901) are currently testing the rapamycin or RAD001 on plexiform neurofibromas, alleviation of tuberous sclerosis complex, and low-grade gliomas in children.

## Gene expression studies in NF1-related MPNSTs

Gene expression microarray studies have been widely used to identify the gene signatures of the MPNST. Lee et al. first applied the cDNA microarray to the comparison of T265($Nf1^{-/-}$) cell line and normal human Schwann cells, and they identified about 900 differentially expressed genes in T265($Nf1^{-/-}$) out of 4608 cDNA probes (Lee, et al., 2004). Watson et al. tested the primary human NF1-associated and sporadic MPNST samples by using oligonucleotide microarrays representing 8100

unique human genes, but they failed to define a reliable molecular signature to distinguish sporadic and NF1-associated MPNST tissue samples (Watson, et al., 2004). Miller et al. compared eight MPNST cell lines with normal human Schwann cells and identified a molecular signature consisting of 159 genes that could separate them (Miller, et al., 2006b). Research from this group compared the primary human samples from different subtypes of neurofibromas and MPNSTs, and the results indicated that the overexpressed gene *Sox9* may provide a biomarker of survival gene in NF1-related MPNSTs (Miller, et al., 2009).

The above studies have provided enormous data on gene expression changes in MPNSTs, however, a direct analysis of aberrantly expressed gene regulation by neurofibromin deficiency or their relationship to RAS-MEK signaling were not demonstrated.

## NF1 tumorigenesis and microenvironment

NF1 is an autosomal dominant disease, and haploinsufficiency of *Nf1* has been proven to induce some clinical traits in the NF1 patients. In particular, the study of Cichowski et al. suggested that loss of heterozygosity in the *Nf1* locus is required to form the neurofibromas (Cichowski, et al., 1999). To form the malignant neurofibromas, additional genetic defects in *Tp53*, *Pten*, and *Cdkn2a* have been reported (Castle, et al., 2003; Zhu, et al., 2002). Heterozygous mouse models with both *Nf1* and *Tp53*

developed MPNST with complete penetrance (Vogel, et al., 1999). In addition, overexpression of PDGFR (platelet-derived growth factor receptor) and EGFR (epidermal growth factor receptor) have been reported by gene expression profiling studies as well as by quantitative RT-PCR in MPNST tumor samples (Levy, et al., 2004).

The connection between *Nf1*-related malignancy and microenvironment has been well-established by the knockout mice studies. Although the combined *Nf1* and *Tp53* heterozygous mice showed 100% penetrance for MPNST occurrence, *Nf1* heterozygous mice failed to develop neurofibromas (Jacks, et al., 1994). However, when the *Nf1* was selectively knocked out in Schwann cells by Cre/LoxP methodology but with heterozygous *Nf1* status in other somatic tissues, the mice developed classic plexiform neurofibromas with mast cell infiltration, resembling human neurofibromas (Zhu, et al., 2002). This study confirmed the Schwann cell origin of plexiform neurofibromas and indicated that *Nf1* haploinsufficiency in the tumor surroundings and nullizygosity at *Nf1* locus in Schwann cell were both required for the neurofibroma formation. A recent study revealed that there are different susceptible windows for Schwann cells to develop plexiform neurofibromas (Le, et al., 2011). When *Nf1* was knocked out from Schwann cell precursors at E12.5 or immature stage in the neonates with the *Nf1* heterozygous background, all the mice exhibited plexiform neurofibromas along the spinal cord after 5 to 6 months, however, *Nf1* ablation in adult mice seldom leads to the tumor formation according to this study.

The microenvironment was demonstrated to contribute to *Nf1*-associated dermal neurofibromas. Le et al. identified *Nf1*-deficient skin-derived precursors (SKPs) that can give rise to plexiform or dermal neurofibromas with support from their local microenvironment after *ex vivo* ablation of *Nf1* in SKPs and subsequent implanting into the vicinity of the sciatic nerve in mice (Le, et al., 2009). This study highlighted that the surrounding neurons and adjacent cell types may form the specific microenvironment to facilitate the differentiation of SKPs to the Schwann cell lineage, which created an opportunity to form neurofibromas. A mouse embryonic stem cell (ESC) model has proved that neuregulin-1, normally secreted by neurons, could induce the ESC to differentiate into Schwann cells *in vitro* (Roth, et al., 2007). These facts emphasize the role of microenvironment in *Nf1*-related tumorigenesis.

In addition to the communication between Schwann cells and neurons during tumor formation, mast cells were identified as another effector in microenvironment to contribute to the process. When EGFP; $Nf1^{+/-}$ bone marrow was transferred to lethally irradiated mice (*Krox20;* $NF1^{flox/flox}$), multiple discrete tumors formed from the dorsal root ganglia of recipients and extensive EGFP labeled mast cells infiltration around the peripheral nerve were observed after 6 months (Yang, et al., 2008). Furthermore, Yang et al. demonstrated that bone marrow transplant with mutant c-kit receptor and $Nf1^{+/-}$ to the same recipients as above decreased the evidence of tumors, which indicated the inhibition of c-kit receptor could be an effective method to treat the neurofibromas (Yang,

et al., 2008). Currently, imatinib mesylate, an inhibitor of c-kit dependent tyrosine receptor kinase, is at the phase II clinical trial for neurofibroma treatment (Kalamarides, et al., 2012).

In summary, the knowledge of molecular mechanisms in NF1-related tumorigenesis has been greatly accumulated by recent studies, and many details indicate that the functions of neurofibromin are not limited to the GTPase activating protein to regulate RAS signaling. Since there are so few therapeutic strategies targeting NF1-related tumors in clinics, a systematic study to reveal the signaling cascades downstream of neurofibromin is required to identify the pathological mechanisms and pathways so as to suggest new therapeutic targets.

In the following chapters, we establish a high-throughput method to classify the aberrant gene expression changes according to the NRAS, MEK1/2 signaling in MPNST cell lines and reveal novel neurofibromin related but NRAS-MEK1/2 independent pathways.

# CHAPTER II: Identification of downstream gene expression regulation of neurofibromin

## Summary

The hypothesis in the dissertation is that the NF1-related aberrant gene regulations can be identified by systematic gene expression profile comparisons using MPNST cell lines with different *Nf1* status. We expected to use microarray analysis in MPNST cell lines to develop a detailed scheme of gene expression and identify novel regulation of downstream targets of neurofibromin thus leading to a better of understanding of molecular mechanisms of this disease and new concepts for drug discovery. Although the elevated NRAS and mitogen-activated protein kinase (MAPK) have been characterized in NF1 patients and animal models (Kraniak, et al., 2010; Martin, et al., 1990), the gene expression changes specific to these pathological pathways have not been elucidated. To answer these questions, we developed gene expression data by Agilent whole human genome microarray under designed scenarios where the NRAS and MEK1/2 activities were manipulated. ST88-14($Nf1^{-/-}$) was employed to identify neurofibromin related differentially expressed genes accumulated during the MPNST tumorigenesis and *Nf1* interference in STS26T($Nf1^{+/+}$) was used to identify acute *Nf1* deficiency responses. By integrating *Nf1*-dependent gene expression with that of altered

NRAS and MEK1/2 interference, we could discriminate neurofibromin-related from NRAS and MEK1/2 dependent gene expression changes, and these genes may reveal new mechanisms in neurofibromin-related tumorigenesis.

# Materials and Methods

## Cell culture and chemical treatment

Human MPNST ST88-14(*Nf1*$^{-/-}$) cells (a generous gift from T. Glover, University of Michigan, Ann Arbor, MI, USA) and STS26T(*Nf1*$^{+/+}$) cells (a generous gift from D. Scoles, Cedars-Sinai Medical Center, Los Angeles, CA, USA) were maintained in RPMI 1640 medium (Invitrogen) supplemented with 5% fetal bovine serum (Hyclone Laboratories). T265(*Nf1*$^{-/-}$) cell line (a generous gift from G. De Vries, Hines VA Hospital, Hines, Illinois, USA) was cultured in DMEM (Invitrogen) supplemented with 5% fetal bovine serum. sNF96.2(*Nf1*$^{-/-}$) and sNF02.2(*Nf1*$^{-/-}$) cell lines were purchased from American Type Culture Collection and cultured in DMEM supplemented with 10% fetal bovine serum. Normal human Schwann cell lines HSC291, HSC361, and HSC338 (generous gifts from Patrick M. Wood, University of Miami Miller School of Medicine, Miami, FL, USA) were cultured in DMEM supplemented with 10% FBS, 2 μM forskolin, and 10 nM heregulin. Cell lines were checked periodically for mycoplasma with Venor GeM Mycoplasma Detection Kit (Sigma-Aldrich). Cultures were propagated for no more than 3 months, 10 μM U0126 (CalBiochem) was applied to the ST88-14(*Nf1*$^{-/-}$) pre-seeded in 10 cm plate for 18h before harvest for mRNA.

## siRNA gene knockdown

Human *Nf1* siRNA, *NRas* siRNA, control siRNA and siRNA Transfection Reagent (Santa Cruz Biotechnology) were used according to the manufacturer's instructions. STS26T($Nf1^{+/+}$) cells were plated at $1.5X10^5$ cells per 10 cm plate 24 h prior to transfection. 4 µl of siRNA (~30nM) and 4 µl of siRNA transfection reagent, each diluted in 400 µl of OptiMem (Invitrogen), were combined and after a 30 minute incubation added to the 3.2 ml of OptiMem in each plate. The same amount of scrambled control siRNA was used as control. Following a 6 h incubation of cells with transfection solution, medium was replaced by growth medium. Cells were harvested 48 to 72 h later. For ST88-14($Nf1^{-/-}$), similar protocols were used for *NRas* knockdown and detection.

## Western blotting

Cells grown from 30% to 80% confluence were washed with ice cold PBS, scraped and then were lysed with RIPA buffer (150 mM NaCl; 1% Triton X-100; 0.5% deoxycholic acid, 0.1% SDS; 50 mM Tris-Cl; pH 8.0) supplemented with 2% protease inhibitor cocktail, 1% PMSF (from stock at 10 mg/ml in methanol), 1 mM $Na_3VO_4$, 1 mM $Na_4P_2O_7.10H_2O$, and 1 mM NaF. Secondary antibodies were conjugated to IRdye infrared dyes (Rockland). Signal was detected and the bands were quantified using the

Odyssey infrared imaging system and software (Licor Biosciences).

Antibodies used in these experiments were rabbit polyclonal anti-neurofibromin (#sc-67, Santa Cruze Biotechnology), goat polyclonal anti-NRAS (#ab77392, Abcam), mouse monoclonal anti-phospho-ERK1/2 (#9106, Cell Signaling), rabbit polyclonal anti-ERK1/2 (#9106, Cell Signaling), and mouse monoclonal anti-α-tubulin (#T5168, Sigma-Aldrich). Neurofibromin, phosphorylated ERK1/2 and NRAS in cell lysates were run on 8%, 10% and 15% SDS polyacrylamide gel electrophoresis (SDS-PAGE), respectively. Around 80 μg protein lysate was loaded in each well, and nitrocellulose transfer membrane (Protran, Whatmann GmbH) was used for protein transfer.

## RNA isolation and microarray analysis

Total RNA was extracted from the cells using RNeasy mini Kit (#74106, Qiagen) with genomic DNA removal by RNase-Free DNase Set (#79254, Qiagen). RNA integrity was determined by an Agilent Bioanalyzer 2100. Labeled targets were synthesized from the purified RNA using linear amplification and indirect labeling by incorporation of aminoallyl-labeled nucleotide with the TargetAmp 1-round aminoallyl-aRNA amplification kit 101 (Epicentre Technologies), which was subsequently modified by the covalent addition of Alexa dye (Epicentre Technologies).
Gene expression microarray experiments were performed using the 60-mer oligonucleotide arrays (Agilent Whole Human Genome Oligo Microarray chip 44K).

Two color hybridizations were performed by using a standardized common reference sample (Universal Human Reference RNA, Agilent) and the standard hybridization methods described by the manufacturer (Agilent).

Gene expression data was analyzed with the open source R Statistical Environment (www.r-project.org) using libraries from the Bioconductor Project (www.bioconductor.org). Microarray data was normalized within arrays using Lowess normalization followed by normalizing between arrays using quantile normalization as implemented in the Bioconductor library *limma* (Smyth, et al., 2005). Gene expression changes among samples were determined using a moderated t-test implemented in 'limma'.

## Gene ontology and pathway analysis

Ingenuity Pathway Analysis (IPA) software (Ingenuity System, http://www.ingenuity.com) and Genomatix software suite (http://www.genomatix.de/) were used in the gene function enrichment and pathway analysis. Generally, gene official names with fold change from different data sets were used as input, and the software generates the biologically significant terms or pathways based on the classic knowledge and latest literature reports. All the analyses were conducted following the manufacturer's instruction and default settings.

## Quantitative Real time PCR using SYBR green I

Three batches of independent total RNA from the same preparations for microarray were reverse transcribed by SuperScript® First-Strand Synthesis System (Invitrogene). The qRT-PCR SYBR green master mix was purchased from Invitrogene. ABI 7500 Sequence Detection System was used to determine the relative quantity of a specific gene from the cDNA template. Default running parameters were used. Primer sequences for validation are show in supplementary table 1.

# Results

## OncoCarta oncogene survey in the MPNST cell lines

Hyperactive RAS and MAPK activities are hallmarks of the abnormal signal transduction at the molecular level in NF1 patients. Whereas in most situations cells exhibit oncogene-induced senescence after activation of RAS, loss-of-function of *Nf1* in neurofibromas only results in a transitory growth arrest, and finally give rise to MPNSTs by escaping the growth limitation (Courtois-Cox, et al., 2006). A second hit could be one theory to explain this escape from oncogene-induced senescence; however, the mechanism is not completely clear.

Because MPNST cell lines are the malignant cell type developed from neurofibromas, these cell lines could hold the keys to the phenomenon. We assembled five MPNST cell lines, and sequenced 238 known mutations in 19 oncogenes, ABL-1,AKT-1, AKT-2, BRAF, CDK-4, EGFR, ERBB2, FGFR-1, FGFR-3, FLT-3, JAK-2, KIT, MET, PDGFRa, PIK3CA, H-RAS, K-RAS, N-RAS, and RET (Table 1) based on OncoCarta Panel V1.0 (Sequenom, San Diego, CA, USA) (Sun, et al., 2012). ST88-14($Nf1^{-/-}$), T265($Nf1^{-/-}$), sNF96.2($Nf1^{-/-}$) and sNF02.2($Nf1^{-/-}$) were derived from NF1 patients with either undetectable or extremely low neurofibromin protein expression as demonstrated by western blotting analysis (Fig. 3). STS26T($Nf1^{+/+}$) cells were derived from a sporadic MPNST and have functional neurofibromin (Kraniak, et al., 2010). We

first determined the neurofibromin level in all available MPNST cell lines and a normal human Schwann cell (HSC361), with the wild type of neurofibromin, was used as a positive control.

From the OncoCarta sequencing result, none of the candidate mutations was identified in the five different MPNST cell lines. This result suggested that oncogene mutation related effects were not necessary in the formation of MPNSTs, especially in the context of hyperactive NRAS due to neurofibromin loss. At the same time, this suggested that hyperactive NRAS, resulting from *Nf1* deficiency, in an *Nf1* haplo-insufficient microenvironment can initiate the neoplasia and the necessary changes in the surrounding tissues that promote the pro-survival signaling to the *Nf1* null Schwann cells leading to malignancy and bypassing the anti-cancer mechanisms.

## Pathway intervention and intersection analysis scheme in MPNST cell lines

To determine and classify neurofibromin-dependent gene expression, we applied pathway-specific interventions. Using chemical and genetic pathway interference in the ST88-14($Nf1^{-/-}$), we identified gene expression profiles specific to MEK1/2 and NRAS, the predominant RAS isoform in NF1-associated MPNST cell lines (Mattingly, et al., 2006). The comparison between ST88-14($Nf1^{-/-}$) and normal human Schwann cells (HSC) was used to capture the genes deregulated during tumorigenesis after loss of the

*Nf1* gene in ST88-14($Nf1^{-/-}$). Gene expression changes specific to an *Nf1* deficiency can be further revealed by siRNA interference to *Nf1* in STS26T($Nf1^{+/+}$), a sporadic MPNST cell line with wild type *Nf1* expression (Dahlberg, et al., 1993; Miller, et al., 2006b). Using Agilent whole human genome 4X44K two color microarrays, we investigated neurofibromin, NRAS and MEK1/2 related gene expression profiles.

The gene expression changes were defined as the following data sets (DS):

**DS-1**) siRNA targeted knockdown of human *Nf1* gene (versus a scrambled control siRNA) in STS26T($Nf1^{+/+}$), a sporadic MPNST, was performed to distinguish the gene changes specific to an *Nf1* knockdown.

**DS-2**) siRNA targeted knockdown of human *NRas* (versus a scrambled control siRNA) in ST88-14($Nf1^{-/-}$) was performed to identify *NRas* knockdown associated gene changes.

**DS-3**) Administration of the MEK1/2 inhibitor, U0126 (versus DMSO control) to ST88-14($Nf1^{-/-}$) to identify MEK1/2 pathway influenced genes.

**DS-4**) Comparison of gene expression of ST88-14($Nf1^{-/-}$), a *Nf1* associated MPNST cell line, versus gene expression of normal human Schwann cells (HSC) to identify gene expression changes associated with an *Nf1* deficiency.

In ST88-14($Nf1^{-/-}$), the *NRas* siRNA decreased the expression of NRAS on the protein level by 60% and decreased phosphorylated ERK1/2 by 50%, confirming that hyperactive NRAS in ST88-14($Nf1^{-/-}$) was a strong upstream signal activating the MEK-ERK pathway (Fig. 5a). U0126, an inhibitor of MEK1/2 in NF1 associated

MPNST cells (Kraniak, et al., 2010), reduced the level of phosphorylated ERK1/2 by 90% after 18 h treatment at 10 μM (Fig. 5b). In the sporadic MPNST cell line STS26T($Nf1^{+/+}$), *Nf1* siRNA (si*Nf1*) knockdown efficiency after 48 h of neurofibromin was evaluated by western blotting and neurofibromin was found to decrease by approximately 90% at the protein level compared to scrambled control siRNA treated (Fig. 5c). Phosphorylated ERK1/2 increased by about 1.6-fold in si*Nf1* treated STS26T($Nf1^{+/+}$) cells, indicating that the neurofibromin-NRAS-MEK1/2 axis was functional in the sporadic MPNST (Fig. 5c).

The differentially expressed gene lists from each comparison provided the basis for the intersection analysis of the gene expression profiles. The overlapped genes were then classified into cell signaling axes based on their trend of changes defined in Table 2. For example, given that MEK1/2 is downstream of RAS, if a gene is upregulated when NRAS is inhibited, and is also upregulated when MEK1/2 is inhibited, the regulation of this gene is hypothetically under control of RAS-MEK1/2 axis meaning that the suppressed RAS may upregulate that gene through the decreased activity of MEK1/2. With similar reasoning, we associated the overlapped genes to the specific signaling axis, and defined the genes that belong to neurofibromin related but NRAS and MEK1/2 independent.

Around 60 differentially expressed genes were randomly chosen to verify the microarray results by quantitative polymerase chain reaction (qRT-PCR) and ~97% of

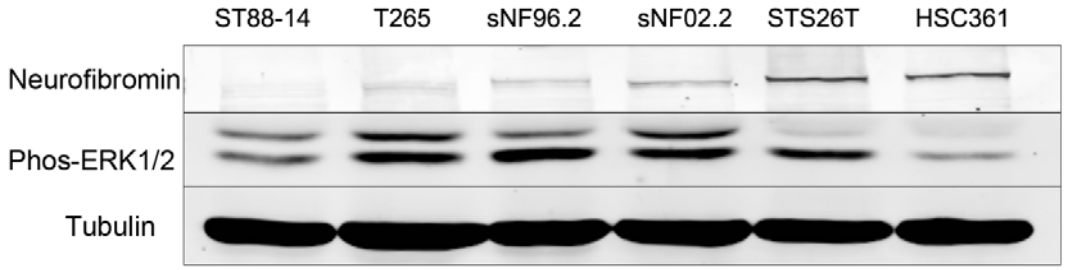



**Fig. 3 Neurofibromin and Phos-ERK1/2 in MPNST cell lines**

Neurofibromin is undetectable in ST88-14($Nf1^{-/-}$) and T265($Nf1^{-/-}$), and there is a very weak band in sNF96.2($Nf1^{-/-}$) and sNF02.2($Nf1^{-/-}$). Neurofibromin is wild type in STS26T($Nf1^{-/-}$) and HSC361. The phosphorylation of ERK1/2 increases in ST88-14($Nf1^{-/-}$), T265($Nf1^{-/-}$), sNF96.2($Nf1^{-/-}$) and sNF02.2($Nf1^{-/-}$) compared to the HSC361. The figure represents one of the three independent expmeriment replicates.

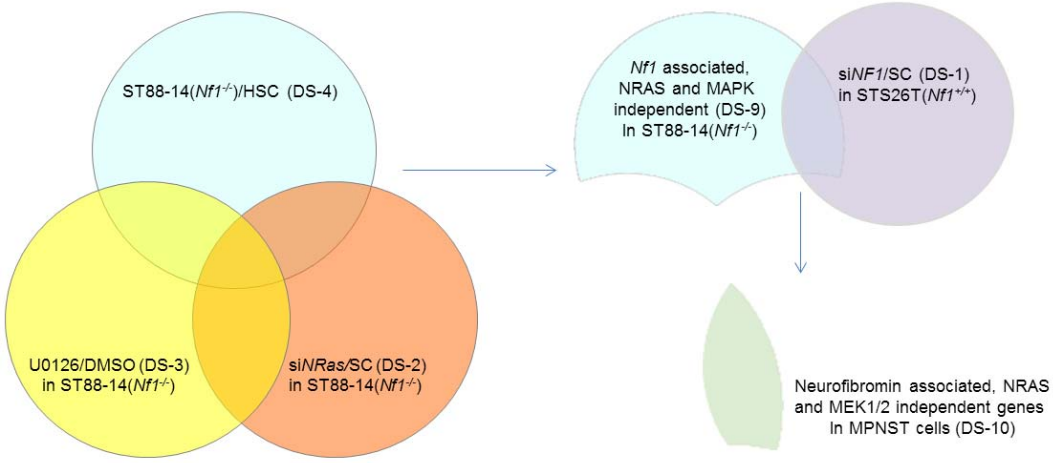



**Fig. 4 Scheme of intersection analysis of gene profiles**

The intersection analysis scheme of gene expression profiles is indicated by Venn diagram. The comparison scheme to identify expression changes associated to neurofibromin, but independent from NRAS and MEK1/2 pathways, is indicated.

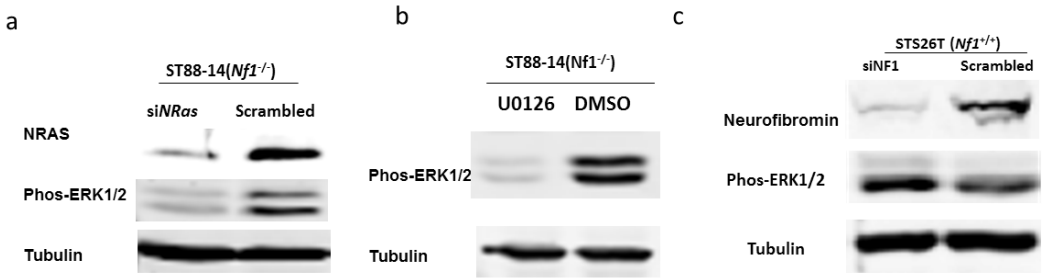



**Fig. 5 Verification of interference conditions in MPNST cell lines**

(a) Western blotting indicated the NRAS and phosphorylated ERK1/2 protein were greatly decreased comparing to scrambled control siRNA after 48h treatment of si*NRas* in ST88-14($Nf1^{-/-}$) cells. (b) Western blotting indicated the levels of phosphorylated ERK1/2 were significantly decreased after U0126 treatment of 18 h compared to DMSO control in ST88-14($Nf1^{-/-}$) cells. (c) Neurofibromin decreased after 48h treatment of si*Nf1* whereas phosphorylated ERK1/2 increased compared to scrambled control siRNA in STS26T($Nf1^{+/+}$) cell line.

the trends were confirmed. The verified list for genes and primers are provided in supplementary table 1.

## Intersection analysis revealed the pathway related gene expression changes in ST88-14(*Nf1*$^{-/-}$)

As we expected, in ST88-14(*Nf1*$^{-/-}$) cell line, when comparing the lists of genes from any two of the three experiments (ST88-14 vs. HSC, si*NRas* vs. control, and U0126 vs. DMSO), we found a substantial number of differentially expressed genes shared by the lists (Table 2). This demonstrated that our methods of inhibition, si*NRas* and U0126, were functionally consistent. The genes differentially expressed when comparing ST88-14(*Nf1*$^{-/-}$) and HSC included gene changes due to the tumorigenesis process in addition to the genes regulated by a wild type neurofibromin. We employed *Nf1* interference in STS26T(*Nf1*$^{+/+}$) to delineate the genes due to the neurofibromin deficiency from the genes associated with tumorigenesis.

The loss-of-function of neurofibromin and hyperactive NRAS have been characterized in ST88-14(*Nf1*$^{-/-}$) (Kraniak, et al., 2010). To identify specific targets of neurofibromin-NRAS axis (DS-5), we defined two patterns of gene expression changes in the comparisons of ST88-14(*Nf1*$^{-/-}$) versus HSC (DS-4) and si*NRas* versus scrambled control (DS-2): 1) gene expression upregulated in DS-4, but downregulated in DS-2, or 2) downregulated in DS-4 but upregulated in DS-2 (Table 2, DS-5 in supplementary table

2).

Gene set enrichment analysis (GSEA) by Genomatix Pathway System (GePS) revealed that the gene ontology (GO) term in biological process such as "positive regulation of heart contraction" (GO: 0045823), including genes *Adm* and *Tpm1*, and "cellular component morphogenesis" (GO: 0032989), including genes *Adm*, *Met*, *Ptprz1*, *Tpm1* and *Smad3* were significantly enriched. Another interesting gene consistent with these patterns was *Rgs16*, which can activate the GTPase of G protein alpha unit so as to inhibit the signal transduction from the outside of the cell. *Rgs16* expression in ST88-14($Nf1^{-/-}$) decreased by 5.6-fold and increased by about 2-fold in the si*NRas* treated compared to the scramble control siRNA. This pattern suggested *Rgs16* expression was regulated by neurofibromin-NRAS negatively associated with the increased RAS activity. Considering the complex signaling downstream G-protein subunits including ERK1/2, PI3K and adenylate cyclases, the downregulation of *Rgs16* by increased NRAS could serve another strong enhancer of the MPNST tumorigenesis. The loss of *Rgs16* has been reported in some breast cancers, associated with PI3K signaling (Liang, et al., 2009).

Gene expression that increased in ST88-14($Nf1^{-/-}$) compared to HSC in DS-4 and decreased in the U0126 treated cells in DS-3, or alternately decreased expression of genes in DS-4 but increased expression in DS-3, could be the regulatory targets of neurofibromin-MEK1/2 axis (Table 2, DS-6 in supplementary table 3). GSEA indicated

that ontology terms like “cell cycle” (GO:0007049, p-value=7.65e-8), “cell cycle arrest” (GO:0007050, p-value=3.49e-7) and “regulation of serine/threonine kinase activity” (GO:0071900, p-value=3.48e-4) were among the most significant terms. These biological process terms were consistent with the ERK1/2 suppression related cell cycle arrest (Meloche and Pouyssegur, 2007) and inhibition effects of U0126 to MEK1/2 (Mattingly, et al., 2006), suggesting deregulation of these processes after defects of neurofibromin-MEK1/2 axis in MPNSTs. *Sox9*, which is listed in DS-6, has been reported as a biomarker in MPNSTs because of its overexpression in NF1-related malignancies and its role in the tumor survival (Miller, et al., 2009). DS-6 confirmed that the *Sox9* expression was higher in ST88-14($Nf1^{-/-}$) compared to HSC and indicated that *Sox9* expression can be downregulated by U0126. Additionally, *Sox9* expression did not change in the si*NRas* treated sample, which indicated a new mechanism in which *Sox9* expression is regulated by neurofibromin-MEK1/2 but not by NRAS in ST88-14($Nf1^{-/-}$) cells.

Also in DS-6, we observed *Edn1* (Endothelin 1) to be strongly inhibited by U0126 (Fig. 6), indicating that the MEK1/2 cascade signaling was prominent in its mRNA expression regulation. Results from Integrated Pathway Analysis (IPA) identified that among the genes that have been reported to be regulated by EDN1, mRNA expression of 8 genes were positively associated with mRNA level of *Edn1* in DS-6, consistent with literature supported trend of change. These genes were *Apln*, *Cdc25a, Egfr, Errfi1, Fst,*

*Il8, Mmp9, and Ptger4* (Table 3) (Fig. 7). EDN1 is a secreted protein with multiple physiological effects on cellular development, differentiation, vasoconstriction and mitogenesis (Stow, et al., 2011). Actually, we have observed *Edn1* RNA to be highly expressed in several MPNST cell lines (Fig. 8). It may be an important effector under the regulation of neurofibromin-MEK1/2 axis during development and tumorigenesis.

Comparing DS-2 (si*NRas* vs. control) and DS-3 (U0126 vs. DMSO), genes both up-regulated or both down-regulated in the two different data sets, were identified as NRAS-MEK1/2 axis (Table 2, DS-7 in supplementary table 4). Ecto-5'-nucleotidase (NT5E) that converts AMP to adenosine was down-regulated in both data sets, and Sunaga et al. reported that NT5E was down-regulated in non-small cell lung cancer (NSCLC) lines with KRAS knockdown (Sunaga, et al., 2011). NT5E has also been associated with cell cycle and apoptosis in breast cancer, arterial calcifications and immunodeficiency diseases (Edwards, et al., 1978; St Hilaire, et al., 2011; Zhi, et al., 2010). Our study indicated its expression was positively controlled by NRAS-MEK1/2 axis in ST88-14($Nf1^{-/-}$) cells.

## Identification of neurofibromin-related gene expression changes independent from NRAS and MEK1/2 pathways in MPNST cells

For the three comparative scenarios involving ST88-14($Nf1^{-/-}$) cells (Fig. 4), removal from DS-4 of the genes that overlapped with DS-2 and with DS-3 enabled us to identify

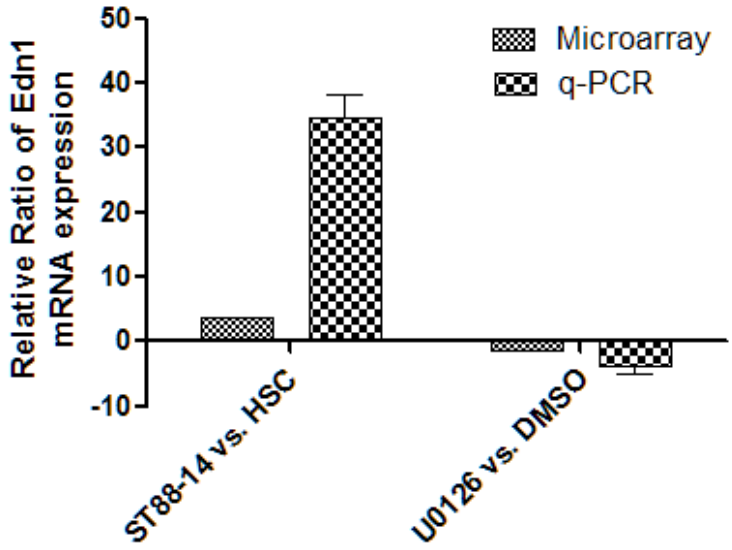



**Fig. 6 Quantitative RT-PCfR verification of *Edn1* expression in microarrays**

*Edn1* gene expression changes in microarrays is verified by qRT-PCR indicating the gene *Edn1* was overexpressed in the ST88-14($Nf1^{-/-}$) cells compared to the HSC. Data is presented as the means of three independent experiments ± SD.

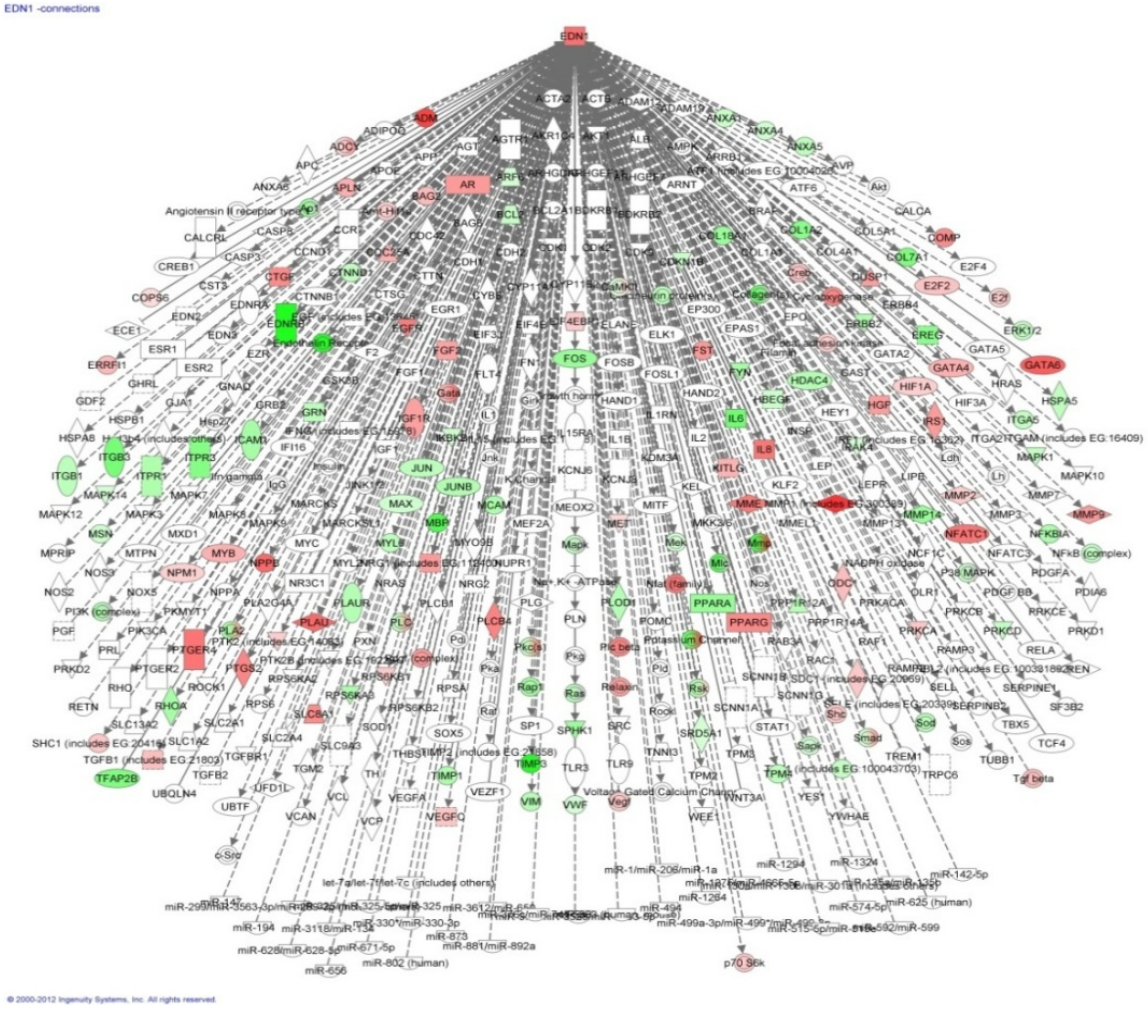



**Fig. 7 EDN1 related molecules network built by the IPA**

The network was built by the IPA pathway tool based on the literature. Each molecule was colored according to the ratios in the comparison between ST88-14(*Nf1*$^{-/-}$) and HSC, DS-4. Red indicates increased mRNA expression in ST88-14(*Nf1*$^{-/-}$) vs. HSC and green indicates decreased mRNA expression in ST88-14(*Nf1*$^{-/-}$) vs. HSC.

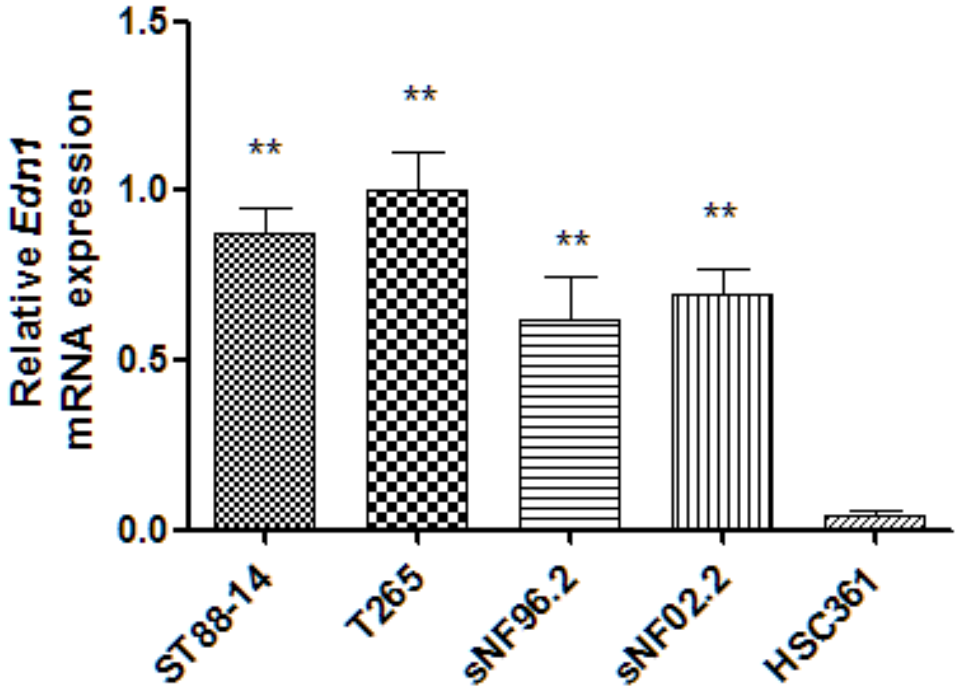



**Fig. 8 Quantitative RT-PCR analysis of *Edn1* mRNA expression in MPNST cell lines**

The relative *Edn1* mRNA expression of different MPNST cell lines and normal human Schwann cell (HSC361) are presented. *Edn1* mRNA expression was significantly higher in MPNST cell lines compared to the HSC. Paired t-test, n=3, **p<0.01. Data is presented as the means of three independent experiments ± SD.

those genes that were independent of the NRAS and MEK1/2 pathways, namely DS-9 (Fig. 4, Table 2, and DS-9 in supplementary table 6). The genes in this data set were NRAS and MEK1/2 independent but neurofibromin related in ST88-14($Nf1^{-/-}$) cells. There were 1474 down-regulated and 1223 up-regulated genes in DS-9. We performed pathway analysis using the GePS from the Genomatrix program, which can map the genes to the canonical and literature supported pathways (Werner, 2007). GePS provides the significance evaluation by fisher exact test to compare the expected number of genes in one pathway/term in the genome to the number of the genes mapped to the same pathway/term in the list. For the downregulated genes, the canonical pathway analysis and the literature pathway analysis are shown Table 4 and Table 5, $p < 0.01$. For the upregulated genes, the canonical pathways and literature supported pathways are shown as Table 6 and Table 7, $p < 0.01$.

We then created a dataset of *Nf1* directly regulated genes in Schwann cell derived MPNST cell lines, by knocking down *Nf1* with siRNA in STS26T($Nf1^{+/+}$) cells comparing to scrambled control siRNA (DS-1). By overlapping DS-9 with DS-1, we identified 142 unique genes that were downregulated and 73 unique genes that were upregulated in both DS-1 and DS-9, namely DS-10 (Table 2, Fig. 4 supplementary table 7). Genes in this overlap suggested that their expression was under the regulation of neurofibromin, but independent from the NRAS and MEK1/2 pathway. Among the downregulated changes, the canonical pathway analysis by GePS identified “NOTCH”

pathway genes, including *Adam10, Ncstn and Adam17*, and "Toll-like receptor signaling", including *Tollip* and *Mapk14* (Table 8). The literature supported pathways are shown in Table 9. For the upregulated changes, "signaling by *BMP2*" was reported by GePS to be significant (Table 10). The GO term SMAD signal transduction (GO:0060395, p-value=1.16e-3) including *Hipk2* and *Bmp2* was significant in the functional enrichment analysis by GePS. These results drew our attention to the aberrant expression of *Bmp2* in NF1-related MPNST cell. It was notable that GO term RAS GTPase binding (GO:0017016, p-value=4.70e-4) including *Dock4, Myo5b, Srgap1* and *Als2* was also significant in up-regulated changes indicating possible multiple regulatory mechanisms of activated NRAS activity after loss of function of neurofibromin.

## *Bmp2* overexpression was independent from the status of NRAS and MEK1/2 in MPNSTs but related to neurofibromin function

As members of transforming growth factor-beta (TGF-beta) superfamily, bone morphogenetic proteins (BMPs) play various roles in morphogenesis and homeostasis in many tissues. Recent studies have pinpointed the role of BMPs in molecular processes associated with different human cancers (Singh and Morris, 2010). Interestingly, we also found BMP2 as one of 2827 differentially expressed transcripts in Miller's microarray data on NF1 associated tissue samples, and based on that data, we found the there was a positive association between *Bmp2* expression and malignancy of

NF1-associated tumor (Miller, et al., 2009) (Fig. 9).

We verified differential *Bmp2* gene expression by quantitative RT-PCR under the experimental conditions analyzed by microarray (Fig. 10). Briefly, *Bmp2* mRNA was overexpressed in ST88-14($Nf1^{-/-}$) compared to the normal human Schwann cells. Consistent with the microarray data, there was no significant difference in ST88-14($Nf1^{-/-}$) treated with U0126 or si*NRas* compared to controls. In STS26T($Nf1^{+/+}$), three different si*Nf1* oligos were used to verify the association between neurofibromin and *Bmp2* expression. All three of the oligos significantly inhibited the neurofibromin and increased the *Bmp2* mRNA expression (Fig. 11). We next used an inducible oncogenic RAS expression system in STS26T($Nf1^{+/+}$) cells which mimic the loss of function of GTPase-activating domain of neurofibromin (Kraniak, et al., 2010) to study the *NRas* dependence of *Bmp2* expression in MPNST cells. After removal of doxycycline from the cultural media, the oncogenic RAS was induced and ERK1/2 phosphorylation was increased (Fig. 12). However, *Bmp2* expression did not change significantly with increased RAS activity in this cell model (Fig. 13), indicating that the increased expression of *Bmp2* mRNA was dependent on neurofibromin but independent of the NRAS activity.

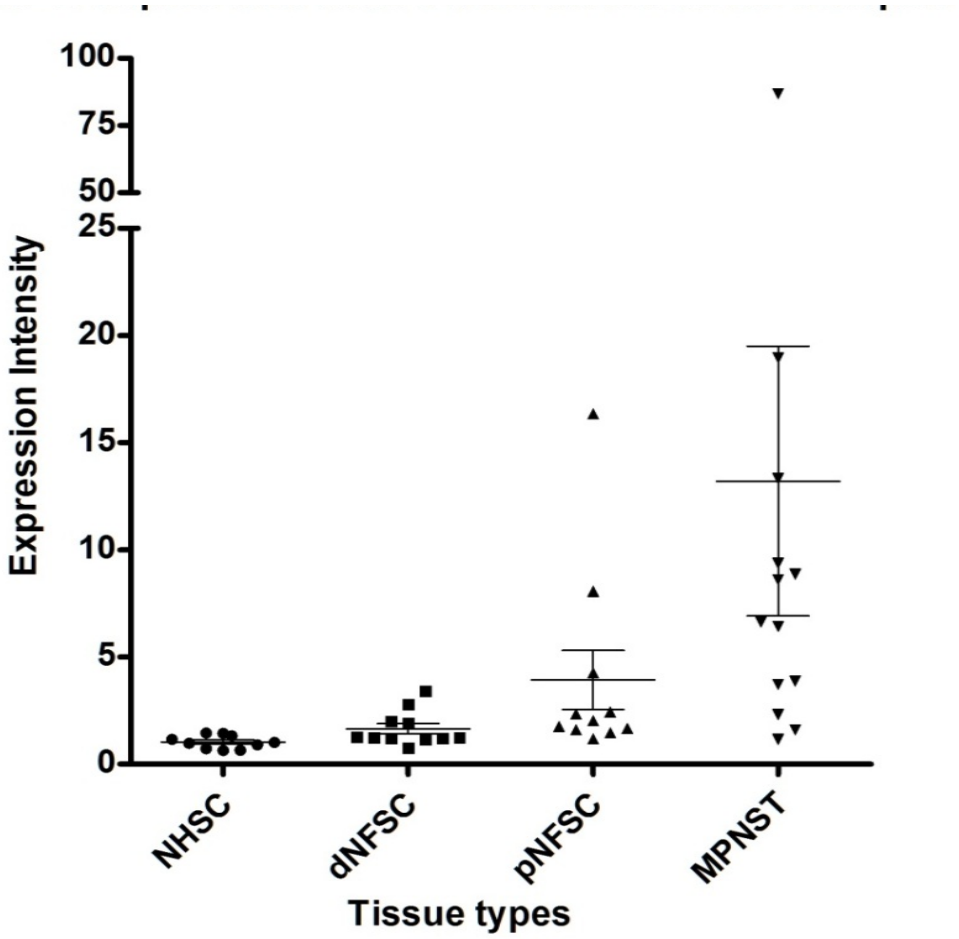



**Fig. 9 *Bmp2* mRNA expression in NF1-associated tissue samples**

The data plotted is from the gene expression study in NF1 patient tissues by Miller et al. 2009. The normalized probe intensities of *Bmp2* in normal human cells (NHSC) and different neurofibromas are shown. In normal human Schwann cells and cells from benign dermal neurofibromas, the expressions of *Bmp2* are relatively low. In high risk plexiform neurofibromas and malignant peripheral nerve sheath tumors, *Bmp2* expression is dramatically increased.

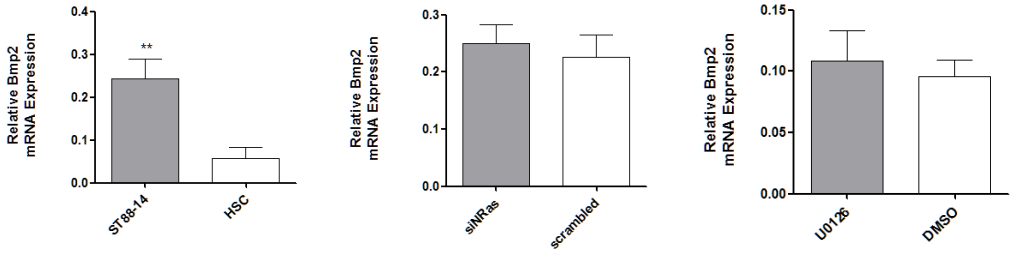



**Fig. 10 Quantitative RT-PCR verification of *Bmp2* mRNA change in different comparisons**

In ST88-14(*Nf1*$^{-/-}$), the expression of *Bmp2* was significantly higher than normal human Schwann cells (HSC). However, si*NRas* and U0126 failed to significantly affect *Bmp2* expression compared to the controls, respectively. Paired t-test, n=3, **p<0.01. Data is presented as the means of three independent experiments ± SD

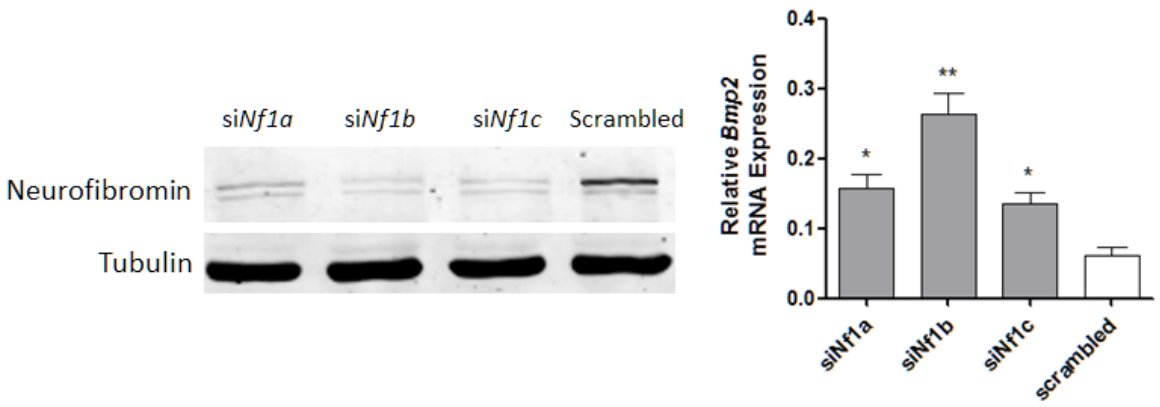



**Fig. 11 Neurofibromin status influences the Bmp2 mRNA expression in STS26T (*Nf1*$^{+/+}$)**

Three different si*Nf1* oligos inhibited neurofibromin expression in STS26T(*Nf1*$^{+/+}$) as shown in western blotting. *Bmp2* mRNA increased in STS26T(*Nf1*$^{+/+}$) after 48 h treatment with three different si*Nf1* oligos compared to the scrambled control, respectively. Paired t-test, *p<0.05, **p<0.01, n=3. Data is presented as the means of three independent experiments ± SD.

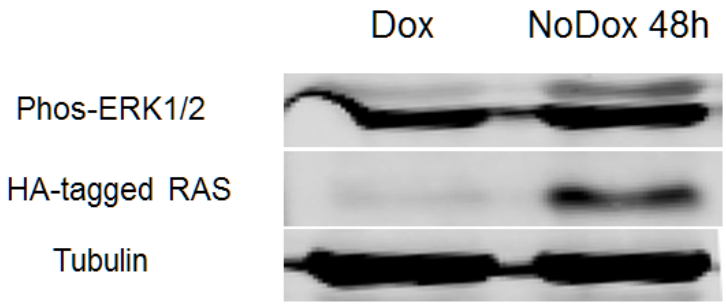



**Fig. 12 Inducible RAS expression system in STS26T(*Nf1*$^{+/+}$)**

HA-tagged oncogenic RAS was induced in STS26T(*Nf1*$^{+/+}$) with the removal of doxcycline (Dox) from the culture media. 48 h after Dox removal, the phosphorylated ERK1/2 and HA-tagged RAS increased.

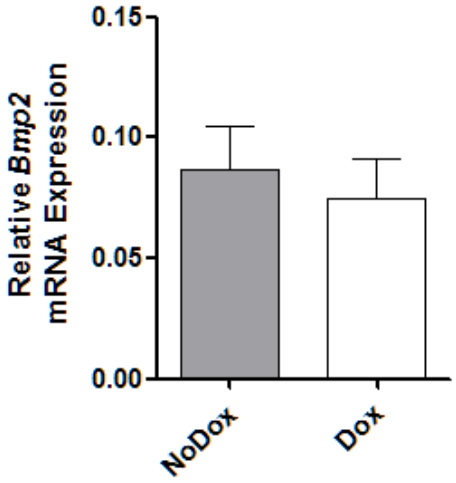



**Fig. 13 Inducible oncogenic RAS failed to change the expression of Bmp2 mRNA**

In STS26T(*Nf1*$^{+/+}$), oncogenic RAS was induced by removing doxycycline (Dox). The *Bmp2* mRNA accumulation did not change significantly compared with the non-induced cells (NoDox). The data shown is the means of three independent experiments ± SD. No significant difference identified by paired t-test, n=3, $p<0.05$.

# Discussion

The RAS-GAP domain of neurofibromin is the best described functional domain in this 250 kDa protein. However, the malignant phenotypes of neurofibromin deficient MPNST cells cannot be totally rescued by the GAP domain reconstitution alone (Ho, et al., 2007; Ismat, et al., 2006). Furthermore, RAS-targeted therapeutic approaches, such as S-trans, trans-farnesylthiosalicylic acid, provide limited efficacy in clinical studies of NF1 (Kalamarides, et al., 2012; Widemann, et al., 2006). The understanding of complex neurofibromin function in development and tumorigenesis requires insight into *Nf1* related biological processes not only associated RAS-MEK1/2-ERK1/2 axis but also independent of it.

To answer these questions, we used Schwann cell derived MPNST cell lines with different *Nf1* status and the gene expression profiles at multiple different means of interference to reveal the possible function of neurofibromin in MPNST. Because the *Nf1*-related neurofibromas seldom have oncogene induced senescence, we doubted whether there could be an oncogene mutation as an additional hit to *Nf1* heterozygous Schwann cells to promote tumorigenesis. We sequenced the known 238 mutations from 19 oncogenes in ST88-14($Nf1^{-/-}$), T265($Nf1^{-/-}$), sNF96.2($Nf1^{-/-}$), sNF02.2($Nf1^{-/-}$) and STS26T($Nf1^{+/+}$), however, none of these relatively common mutations in oncogenes were identified in the above five cell lines. Based on these results, we can say that oncogene

mutation related effects may not be necessary in the formation of MPNSTs, especially in the context of hyperactive RAS due to *Nf1* loss. The constitutively active RAS pathway provides strong pro-survival signals through its downstream RAF-MEK1/2-ERK1/2 and PI3K-AKT-mTOR signaling pathways. These activated pathways may abrogate the selective pressures against mutations in oncogenes such as *Akt1*, *Akt2*, *Braf*, and *Pi3kca* during tumorigenesis, and explain why the common oncogene mutations in cancer were not observed in this study. It is worth noting that among the five MPNST cell lines, only STS26T($Nf1^{-/-}$) has the null *Tp53*, and all of the others have the wild type *Tp53* (Li, et al., 2004; Lopez, et al., 2011; Miller, et al., 2006b).

In this study, we performed pathway-specific interventions to the MPNST cell lines using genetic and chemical methods. The intersection analysis of the gene expression changes across these treatments enabled us to classify those changes specific to the NRAS and MEK1/2 pathways, and further to discover novel changes in MPNST cell lines independent from those pathways. This is the first study that associates gene expression changes to specific pathways activated in MPNST cell lines so as to identify novel neurofibromin related gene expression changes independent of NRAS and MEK1/2 pathway. In ST88-14($Nf1^{-/-}$), the intersection analysis helps to classify DS-9, and DS-9 was further refined by neurofibromin association in STS26T($Nf1^{+/+}$) to create DS-10 which specified genes that were neurofibromin-related but NRAS and MEK1/2 independent changes in gene expression.

By using pathway analysis tools, such as Integrated Pathway Analysis (IPA), which has the ability to integrate literature mining with biological information, novel hypotheses can be generated. For example, EDN1 has been reported to play an important role in heart development (Chen, et al., 2010) and is associated with cardiac hypertrophy in patient cohort studies (Castro, et al., 2007). These facts may explain the embryonic lethality due to failure of heart development in the *Nf1* knockout mouse model and likewise increased risk for a variety of cardiovascular disorders in NF1 patients (Friedman, et al., 2002). We identified 8 potential downstream effectors of EDN1, those genes may contribute to the malignancy of MPNSTs cooperated with EDN1. Another example is the overexpressed gene *Adm* in DS-5. *Adm* encodes the protein adrenomedullin which functions as systemic vasodilator and natriuretic peptide, and high *Adm* mRNA level has been correlated to hypertension (Jiang, et al., 2004) and myocyte hypertrophy (Romppanen, et al., 1997; Tsuruda, et al., 2003). NF1 patients with hypertension have been reported (Demarchi, et al., 2011; Montani, et al., 2011), but the mechanism is still not clear. In the *Nf1* knockout mouse model, Xu et al. reported that cardiomyocyte-specific knockdown of *Nf1* contributed to cardiac hypertrophy (Xu, et al., 2009). These clues and the gene expression changes identified could serve as the mechanistic basis for an NF1-related cardiovascular disease study.

The expression pattern of *Bmp2* in the MPNST tissues and DS-10 drew our attention to the possible function of BMP2 in MPNSTs. *Bmp2* expression deregulation has been

associated to many types of cancers including ovarian (Kiyozuka, et al., 2001; Le Page, et al., 2006), glioma (Liu, et al., 2009), salivary adenocarcinoma (Hatakeyama, et al., 1993), pancreatic cancer (Kleeff, et al., 1999). The *in vitro* studies on the cell lines indicate that *Bmp2* transcripts increase about 17-fold in non-small cell lung carcinoma (NSCLC) (Langenfeld, et al., 2003) and about 25-fold in small cell lung carcinoma (SCLC) (Bieniasz, et al., 2009) compared to the normal tissue. The *Bmp2* copy number increase has been reported as well in early prostate cancer (Doak, et al., 2007). However, studies also show that exogenous BMP2 may lead to the cell cycle arrest in G1-phase in some gastric cancer (Wen, et al., 2004), and suppress estradiol-induced proliferation of MCF-7 mediated through upregulation of $p21^{CIP1/WAF1}$ protein and hypophosphorylation of pRB (Arnold, et al., 1999; Ghosh-Choudhury, et al., 2000). The growth stimulatory and inhibitory effects of BMP2 may vary according to the cell type, differentiation stage and the cancer microenvironment. The inhibitory effect of BMP2 is not observed in MPNST cell lines, as the levels of phosphorylated RB are generally higher in many MPNST cell lines than the normal human Schwann cell line (Miller, et al., 2006b) and $p21^{CIP1/WAF1}$ is even undetectable in T265($Nf1^{-/-}$) cell line (Lee, et al., 2004). These observations encouraged us to explore other possible mechanisms to explain the actions of BMP2 in MPNSTs.

| Gene name | Mutation sites checked |
|---|---|
| **ABL-1** | G250e, Q252h, Y253h, Y253F, e255K, e255V, D276G, F311L, T315I, F317L, M351T, e355G, F359V, h396r |
| **AKT-1** | V461L, p388T, L357T, e319G, V167A, Q43X, e17del |
| **AKT-2** | S302G, r371h |
| **BRAF** | G464r, G464V/e, G466r, F468C, G469S, G469e, G469A, G469V, G469r, G469r, D594V/G, F595L, G596r, L597S, L597r, L597Q, L597V, T599I, V600e, V600K, V600r, V600L, K601N, K601e |
| **CDK-4** | r24C, r24h |
| **EGFR** | r108K, T263p, A289V, G598V, e709K/h, e709A/G/V, G719S/C, G719A, M766_A767insAI, S768I, V769_D770insASV, V769_D770insCV, p753S, A750p, T751A, T751p, T751I, S752I/F, S752_I759del, L747_Q ins, e746_T751del, I ins (combined), e746_A750del, T751A (combined), L747_e749del, A750p (combined), L747_T750del, p ins (combined), L747_S752del, Q ins (combined) D770_N771.AGG/V769_D770insASV/V769_D770insASV, D770_N771insG, N771_p772.SVDNr, p772_h773insV, h773.NpY, h773_V774insNph/ph/h, V774_C775inshV, T790M, L858r, L861Q, e746_T751del, e746_A750del, e746_T751del, e746, T751del, S752D, L747_e749del, L747_T750del, L747_S752del, L747_T751del, L747_S752del, |
| **ERBB2** | L755p, G776S/LC, G776VC/VC, A775_G776insYVMA, p780_Y781insGSp, p780_Y781insGSp, S779_p780insVGS |
| **FGFR-1** | S125L, p252T |
| **FGFR-3** | G370C, Y373C, A391e, K650Q/e, K650T/M |
| **FLT-3** | I836del, D835h/Y |
| **JAK-2** | V617F |
| **KIT** | D52N, Y503_F504insAY, W557r/r/G, V559D/A/G, V559I, V560D/G, K550_K558del, K558_V560del, K558_e562del, V559del, V559_V560del, V560del, Y570_L576del, e561K, L576p, p585p, D579del, K642e, D816V, D816h/Y, V825A, e839K, M552L, Y568D, F584S, p551_V555del, Y553_Q556del |
| **MET** | r970C, T992I, Y1230C, Y1235D, M1250T |
| **PDGFRa** | V561D, T674I, F808L, D846Y, N870S, D1071N, D842_h845del, I843_D846del, S566_e571.K, I843_S847.T, D842V |
| **PIK3CA** | r88Q, N345K, C420r, p539r, e542K, e545K, Q546K, h701p, h1047r/L, h1047Y, r38h, C901F, M1043I |
| **H-RAS** | G12V/D, G13C/r/S, Q61h/h, Q61L/r/p, Q61K |
| **K-RAS** | G12C, G12r, G12S, G12V, G12D, G12A, G12F, G13V/D, A59T, Q61e/K, Q61L/r/p, Q61h/h |
| **N-RAS** | G12V/A/D, G12C/r/S, G13V/A/D, G13C/r/S, A18T, Q61L/r/p, Q61h, Q61e/K |
| **RET** | C634r, C634W, C634Y, e632_L633del, M918T, A664D |

**Table 1: Mutations assayed for each of the 19 oncogenes in the OncoCarta v1.0 Mutation Panel.**

A total of 238 mutations in 19 oncogenes were assayed in ST88-14($Nf1^{-/-}$), T265($Nf1^{-/-}$), sNF96.2($Nf1^{-/-}$) sNF02.2($Nf1^{-/-}$) and STS26T($Nf1^{+/+}$). There was no mutation mentioned in this table identified in all five cell lines.

| Data Set | Intersection Operation | Pattern Definition | Gene | Pathway Axis |
|---|---|---|---|---|
| DS-5 | DS-4 ∩ DS-2 | ( ↑ in ST88 ↓ in *siNRas*) OR ( ↓ in ST88 ↑ in *siNRas*) | 22 | **Neurofibromin-NRAS** in **ST88(*Nf1*$^{-/-}$)** |
| DS-6 | DS-4 ∩ DS-3 | ( ↑ in ST88 ↓ in U0126) OR ( ↓ in ST88 ↑ in U0126) | 208 | **Neurofibromin-MEK1/2** in **ST88(*Nf1*$^{-/-}$)** |
| DS-7 | DS-2 ∩ DS-3 | ( ↑ in *siNRas* ↑ in U0126) OR ( ↓ in *siNRas* ↓ in U0126) | 20 | **NRAS-MEK1/2** in **ST88(*Nf1*$^{-/-}$)** |
| DS-8 | DS-4 ∩ DS-2 ∩ DS-3 | ( ↑ in ST88 ↓ in *siNRas* ↓ in U0126) OR ( ↓ in ST88 ↑ in *siNRas* ↑ in U0126) | 5 | **Neurofibromin-NRAS-MEK1/2** in **ST88(*Nf1*$^{-/-}$)** |
| DS-9 | DS-4 \ (DS-2UDS-3) | ( ↑ OR ↓ in ST88) NOT IN (*siNRas* and U0126) | 2697 | **NRAS-MEK1/2 independent** in **ST88(*Nf1*$^{-/-}$)** |
| DS-10 | DS-1 ∩ DS-9 | ( ↑ in siNF1) AND [( ↑ in ST88) NOT IN (*siNRas* AND U0126)] OR ( ↓ in siNF1) AND [( ↓ in ST88) NOT IN (*siNRas* AND U0126)] | 73<br>142 | **Neurofibromin related NRAS-MEK1/2 independent** in **MPNSTs** |

**Table 2: Definition of data set and pathway association**

The patterns of gene change in data set comparison were defined to associate the genes to the specific signal axis. ↑: gene increase, ↓: gene decrease. ∩: Intersection operation, U: Union operation, \ : Relative Complement operation, **AND, OR, NOT IN**: Logic operation.

| Gene | Log Ratio ST88/HSC | Log Ratio U0126/DMSO | Location | Entrez Gene Name | Citation:PMID |
|---|---|---|---|---|---|
| APLN | 2.12 | -0.95 | Extracellular Space | apelin | 20843995 |
| CDC25A | 2.10 | -1.27 | Nucleus | cell division cycle 25 homolog A (S. pombe) | 14742443 |
| EGFR | 3.50 | -0.79 | Plasma Membrane | epidermal growth factor receptor | 17616694 |
| ERRFI1 | 1.86 | -1.16 | Cytoplasm | ERBB receptor feedback inhibitor 1 | 10749885 |
| FST | 2.72 | -1.25 | Extracellular Space | follistatin | 11790131 |
| IL8 | 3.68 | -4.89 | Extracellular Space | interleukin 8 | 10438717 |
| MMP9 | 2.76 | -0.76 | Extracellular Space | matrix metallopeptidase 9 (gelatinase B, 92kDa gelatinase, 92kDa type IV collagenase) | 21127388 |
| PTGER4 | 3.72 | -1.20 | Plasma Membrane | prostaglandin E receptor 4 (subtype EP4) | 15347673 |
| EDN1 | 3.83 | -1.525 | Extracellular Space | endothelin 1 | |

**Table 3: EDN1 related gene expression changes in DS-6 with literature supports.**

Based on the IPA analysis, the mRNA of 8 genes in DS-6, neurofibromin-MEK1/2 axis related data set, changed positively associated with the mRNA level of *Edn1* with literature supports. The Pubmed IDs of the specific support article are indicated.

| Canonical pathway | P-value | # Genes (observed) | # Genes (expected) | # Genes (total) | List of observed genes |
|---|---|---|---|---|---|
| Trk receptor signaling mediated by the MAPK pathway | 1.73E-04 | 11 | 3.207 | 34 | FOS, SRF, MAPK1, PRKCD, MLF2C, KRAS, MAPKAPK2, RIT1, RPS6KA1, MAPK14, RAP1A |
| CD28 signaling ( CD4 T cell receptor signaling (JNK cascade) ) | 2.64E-04 | 14 | 5.000 | 53 | HLA-DPA1, MAP2K2, ITPR3, FOS, HLA-DRB5, HLA-DRB1, JUN, ITPR1, HLA-DPB1, HLA-DRB3, PPP3CB, FOSL2, HLA-DRA, HLA-DRB4 |
| Ceramide signaling pathway | 2.66E-04 | 13 | 4.434 | 47 | RIPK1, MAP2K2, MAPK1, PRKCD, SMPD1, TRADD, PKRRA, ASAH1, RB1, CRADD, CTSD, BCL2, NFKBIA |
| IKK-NF-kappaB cascade ( CD4 T cell receptor signaling ) | 3.43E-04 | 20 | 8.867 | 94 | PIK3R1, HLA-DPA1, MAP2K2, ITPR3, FOS, HLA-DRB5, MAPK1, HLA-DRB1, JUN, ITPR1, HLA-DPB1, HLA-DRB3, PPP3CB, KRAS, IKBKB, FOSL2, FYN, HLA-DRA, NFKBIA, HLA-DRB4 |
| T cell receptor signaling (PLC gamma, PKC, Ras and ERK cascade) ( CD4 T cell receptor signaling (ERK cascade) ) | 4.19E-04 | 12 | 4.056 | 43 | HLA-DPA1, MAP2K2, ITPR3, HLA-DRB5, MAPK1, HLA-DRB1, ITPR1, HLA-DPB1, HLA-DRB3, KRAS, HLA-DRA, HLA-DRB4 |
| Osteopontin-mediated events | 9.60E-04 | 9 | 2.736 | 29 | PIK3R1, ITGB3, FOS, GSN, SPP1, MAPK1, JUN, ILK, NFKBIA |
| toll-like receptor pathway | 1.32E-03 | 10 | 3.396 | 36 | FOS, TOLLIP, TLR6, JUN, IKBKB, PPARA, MYD88, MAPK14, NFKBIA, CD14 |
| IL2-mediated signaling events | 1.37E-03 | 13 | 5.188 | 55 | PIK3R1, RHOA, MAP2K2, FOS, MAPK1, JUN, STAM, IRS2, KRAS, MAPKAPK2, FYN, MAPK14, BCL2 |
| signal transduction through il1r | 1.66E-03 | 10 | 3.490 | 37 | FOS, IL1RAP, TOLLIP, JUN, IKBKB, PLCB1, IL6, MYD88, MAPK14, NFKBIA |
| trefoil factors initiate mucosal healing | 1.66E-03 | 10 | 3.490 | 37 | PIK3R1, RHOA, MAP2K2, MAPK1, ERBB2, IKBKB, CASP9, RPS6KA1, NFKBIA, CASP6 |
| tsp-1 induced apoptosis in microvascular endothelial cell | 2.16E-03 | 7 | 0.660 | 7 | FOS, JUN, FYN, MAPK14 |
| PDGFR-beta signaling pathway | 3.13E-03 | 21 | 11.226 | 119 | ITGB3, RHOA, MAP2K2, FOS, SRF, MAPK1, PRKCD, LRP1, GAB1, JUN, RPS6KA3, ARPC1B, KRAS, C3orf10, DOK1, RABSA, FYN, PTEN, RAP1A, ARHGDIA, SPHK1 |
| p75(NTR)-mediated signaling | 3.17E-03 | 14 | 6.320 | 67 | APH1B, PIK3R1, NCSTN, RHOA, NGFRAP1, RHOB, IKBKB, CASP9, MYD88, NGFR, ARHGDIA, SORT1, CASP6, ADAM17 |
| antigen processing and presentation | 3.28E-03 | 5 | 1.132 | 12 | HLA-A, HLA-DRB1, B2M, TAP1, HLA-DRA |
| role of egf receptor transactivation by gpcrs in cardiac hypertrophy | 3.29E-03 | 9 | 3.207 | 34 | RHOA, MAP2K2, FOS, MAPK1, JUN, EDNRB, IKBKB, RPS6KA1, NFKBIA |
| ceramide signaling pathway | 3.29E-03 | 9 | 3.207 | 34 | RIPK1, MAP2K2, MAPK1, SMPD1, TRADD, CRADD, IKBKB, BCL2, NFKBIA |
| influence of ras and rho proteins on g1 to s transition | 4.19E-03 | 8 | 2.736 | 29 | PIK3R1, RHOA, MAP2K2, MAPK1, RB1, IKBKB, CDKN1B, NFKBIA |
| IKK activation signaling (through PKC theta and CARMA1:BCL10:MALT1) ( CD4 T cell receptor signaling (NF-kB cascade) ) | 4.27E-03 | 13 | 5.849 | 62 | PIK3R1, HLA-DPA1, ITPR3, HLA-DRB5, HLA-DRB1, ITPR1, HLA-DPB1, HLA-DRB3, IKBKB, FYN, HLA-DRA, NFKBIA, HLA-DRB4 |
| prion pathway | 4.68E-03 | 6 | 1.698 | 18 | HSPA5, LAMA2, LAMB2, LAMC1, LAMA4, BCL2 |
| Netrin-mediated signaling events | 5.26E-03 | 8 | 2.830 | 30 | TRIO, PIK3R1, DOCK1, RHOA, MAP2K2, MAPK1, FYN, PITPNA |
| er associated degradation (erad) pathway | 6.31E-03 | 6 | 1.792 | 19 | EDEM1, RBX1, MAN2A2, CANX, MAN1A2, MAN2B1 |
| Beta1 Integrin cell surface interactions | 7.44E-03 | 13 | 6.226 | 66 | CD81, LAMA2, COL11A2, COL7A1, SPP1, COL18A1, LAMB2, LAMC1, TNC, ITGB1, THBS2, LAMA4, CD14 |
| Il 6-mediated signaling events | 7.69E-03 | 10 | 4.245 | 45 | PIK3R1, TIMP1, IL1RN, FOS, A2M, PRKCD, GAB1, JUN, IL6, MAPK14 |
| Caspase cascade in apoptosis | 7.79E-03 | 11 | 4.905 | 52 | RIPK1, VIM, TTAP2A, GSN, SLK, TRADD, CRADD, CASP9, SATB1, BCL2, CASP6 |
| ErbB2/ErbB3 signaling events | 8.73E-03 | 9 | 3.679 | 39 | DOCK7, MAP2K2, ERBB3, FOS, MAPK1, JUN, PPP3CB, KRAS, ERBB2 |
| Signaling events regulated by Ret tyrosine kinase | 8.73E-03 | 9 | 3.679 | 39 | PIK3R1, RHOA, MAPK1, GAB1, JUN, GFRA1, IRS2, DOK1, RAP1A |
| ErbB4 signaling events | 9.72E-03 | 8 | 3.113 | 33 | ERBIG1, MAPK1, ERBG, ERBB2, HBEGF, FYN, WWOX, ADAM17 |
| pten dependent cell cycle arrest and apoptosis | 9.81E-03 | 5 | 1.415 | 15 | PIK3R1, ILK, ITGB1, CDKN1B, PTEN |
| ErbB receptor signaling network | 9.81E-03 | 5 | 1.415 | 15 | ERBB3, TGFA, ERBG, ERBB2, HBEGF |

**Table 4: Canonical pathways associated to the down-regulated genes in DS-9**

Downregulated genes in the DS-9 were uploaded to the GePS of Genomatix, and then mapped to the significant canonical pathways by GePS, $p < 0.01$.

| Pathway | P-value | # Genes (observed) | # Genes (expected) | # Genes (total) | List of observed genes |
|---|---|---|---|---|---|
| LYSOSOMAL | 6.13E-09 | 32 | 10.660 | 111 | TGOLN2, ARSA, PNPLA6, BACE1, CSH1, RAB6A, CTSB, GUSB, LAMP1, AGA, CLCN5, PMP22, NPC2, RNASE1, GBA, PLP1, SMPD1, RIOB, SCARB2, EIF2AK3, EEA1, RAB7B, RAB9A, CD63, LAMP2, CASP9, GNPTAB, TMEM9B, CTSD, RAB5A, NPC1, SORT1 |
| ENDOCYTIC | 3.81E-05 | 34 | 16.717 | 174 | TGOLN2, CD59, MMP14, ITSN2, BACE1, TLOT1, RAB6A, TSAP2A, LAMP1, CLCN5, NPC2, LYZ, A2M, IFI30, COL18A1, LRP1, ARF6, RHOB, SCARB2, EEA1, LRP8, B2M, PIK3C3, S100B, RHOJ, AKAP13, CD63, LAMP2, CTSD, RAB5A, NPC1, RABEP1, SH3KBP1, CD14 |
| RAB, MEMBER RAS ONCOGENE FAMILY | 9.65E-04 | 20 | 9.508 | 99 | ITSN2, RAB6A, RASD1, RAB18, LAMP1, SH3GLB1, RAB31, RAB14, RAB2A, ARF6, EEA1, PIK3C3, RAB6C, RAB7B, RAB9A, ITGB1, RAB5A, RABEP1, NGFR, UNC13B |
| RHOA RAS HOMOLOG | 2.87E-03 | 25 | 14.022 | 146 | MYL12B, LIMK2, RHOA, ARHGEF12, RTKN, MSN, PPP1R12A, DVL3, COL18A1, SRC, PLCE1, SLK, RHOB, ICAM1, CTNND1, EDNRB, ACTG2, TNC, ARHGAP5, AKAP13, RAP1GDS1, OPHN1, RDX, NGFR, ARHGDIA |
| SPHINGOMYELIN PHOSPHODIESTERASE 1, ACID LYSOSOMAL | 3.75E-03 | 6 | 1.632 | 17 | PRKCD, SMPD1, ASAH1, CTSD, SORT1, SPHK1 |
| MATRIX METALLOPROTEINASE | 4.54E-03 | 25 | 14.502 | 151 | MMP14, MMP28, TIMP1, MMP17, PEPD, CTSB, BSG, TSAP2A, MMP15, DDR1, CD9, TIMP3, SERPINE2, SPP1, MAPK1, LRP1, JUN, LGALS1, MMP19, GPNMB, ITGB1, MAPK14, MCAM, ADAM17, ADAMTS4 |
| FOCAL ADHESION KINASE 1 | 6.41E-03 | 24 | 14.118 | 147 | TRIO, MMP14, ARHGAP21, ITGB3, TIMP1, FMN2, PEPD, RHOA, ARHGEF12, NOV, SEMA3B, CD9, HLA-DRB5, SPP1, SLK, ILK, VWF, LGALS8, BST1, TNC, ITGB1, FYN, PTEN, MCAM |
| SECRETORY | 6.57E-03 | 42 | 28.620 | 298 | TGOLN2, CUTA, GIB1, BACE1, ANXA1, HSPA5, ATOX1, LGALS3, RAB6A, LMAN1, NCSTN, CTSB, GUSB, RAB18, LAMP1, ST6GAL1, FTH1, ITPR3, LYZ, RHOQ, CANX, PLP1, ABCA1, RAB2A, LRP1, RIOB, VWF, EIF2AK3, LLA1, ATP2A2, NUCB2, CALU, SCG5, SDF4, CPD, TAP1, TMED10, PPIB, CTSD, UNC13B, SORT1, ADAM17 |
| NUCLEAR FACTOR (ERYTHROID DERIVED 2), 45KDA | 7.59E-03 | 3 | 0.4802 | 5 | FOS, JUN, NFE2L2 |
| INTEGRIN LINKED KINASE | 9.14E-03 | 11 | 4.994 | 52 | MYL12B, PARVA, NOV, LEF1, SPP1, JUN, ILK, RHOB, MYL9, ITGB1, PTEN |

**Table 5: Literature based pathways associated to the downregulated genes in DS-9**

In GePS analysis, the downregulated genes in DS-9 were mapped to the significant pathways supported by literature, $p < 0.01$.

| Canonical pathway | P-value | # Genes (observed) | # Genes (expected) | # Genes (total) | List of observed genes |
|---|---|---|---|---|---|
| Validated targets of C-MYC transcriptional activation | 2.56E-04 | 17 | 6.712 | 87 | NPM1, BCAT1, PEG10, NME1, ENO1, ODC1, PIM1, TAF12, KAT2A, NME2, CDCA7, RCC1, DKC1, HSPD1, PMAIP1, TK1, NCL |
| alk in cardiac myocytes | 6.85E-04 | 8 | 2.083 | 27 | CHRD, BMP4, GATA4, BMP7, TGFB1, BMP2, NPPB, NKX2-5 |
| BARD1 signaling events | 7.92E-04 | 9 | 2.623 | 34 | NPM1, CCNE1, BACH1, FANCL, ATR, RAD50, CSTF1, FANCG, PCNA |
| hop pathway in cardiac development | 1.68E-03 | 3 | 0.309 | 4 | GATA4, HOPX, NKX2-5 |
| E2F transcription factor network | 5.90E-03 | 13 | 6.018 | 78 | CEBPA, CCNE1, RANBP1, TYMS, KAT2A, WASF1, E2F2, PRMT5, E2F6, MYBL2, TK1, PLAU, HIC1 |
| EphrinB-EPHB pathway | 7.60E-03 | 3 | 0.463 | 6 | EPHB4, EPHB2, EFNB2 |
| Syndecan-4-mediated signaling events | 9.45E-03 | 7 | 2.469 | 32 | FZD7, TFPI, FGF2, FGFR1, LAMA1, PTK2, MDK |
| cdk regulation of dna replication | 9.77E-03 | 5 | 1.389 | 18 | CCNE1, MCM2, ORC5, MCM6, KITLG |

**Table 6: Canonical pathways associated to the upregulated genes in DS-9**

The upregulated genes in DS-9 were mapped to the significant canonical pathway by GePS, $p < 0.01$.

| Pathway | P-value | # Genes (observed) | # Genes (expected) | # Genes (total) | List of observed genes |
|---|---|---|---|---|---|
| DIFFERENTIATION | 7.99E-07 | 69 | 38.713 | 524 | CEBPA, MYB, IL7, IFRD1, NME1, HOXA3, EZH2, BMP4, DLL1, PPARG, POU4F1, NFATC1, HOXA9, RLN2, GATA4, DKK1, TBX3, IGF2, GPRC5A, S100A2, BHLHE41, DKK2, MSX2, GOT2, CD24, MDFI, TAL1, BMP6, DMP7, WNT10B, TGFB2, GSC, NKX2-1, TNFRSF11B, HOXC13, TRIM15, MYBL2, MLST, NKX3-2, TGIF1, CLDN1, FGF9, TSHZ3, EXT1, OLIG1, MIR17HG, BMP2, CYP27B1, CD34, THY1, KITLG, CD70, NEFH, FOXL2, TCF3, ZFPM1, MDK, GATA6, NKX2-5, DIX1, IL17RD, MNAT1, PLAGL2, WNT5A, ZNF521, LIFR, WT1, HOXA5, STOM |
| HEDGEHOG | 1.45E-04 | 22 | 9.457 | 178 | CHRD, FOXG1, LHX2, BMP4, MTSS1, TBX3, GAS1, MSX2, WNT10B, NKX2-1, MEIS2, NKX3-2, FGF9, HMGB2, FOXA1, BMP2, ALDH1A2, TBX1, HOXA13, WNT5A, SMO, FOXF1 |
| WINGLESS TYPE | 1.06E-03 | 46 | 29.109 | 394 | TWIST2, EZH2, BMP4, NKD2, SULF2, SALL1, GPC4, BBS2, DKK1, TBX3, DKK2, DOCK4, FZD7, MSX2, FZD2, EPCAM, CD24, SIX1, MDFI, KIAA1199, SOX3, RAC1, WNT10B, RUNX3, DOCK3, TNFRSF11B, WNT3, MEST, HOXB9, FGF9, PITX2, HMGB2, EXT1, TCF15, LRP5, IRX3, BMP2, C7orf68, FOXL2, HIC1, NR0B1, NKX2-5, PLAGL2, WNT5A, LRP4, WT1 |
| LOW DENSITY LIPOPROTEIN RECEPTOR RELATED PROTEIN | 1.16E-03 | 17 | 7.536 | 102 | IGFBP3, LPL, DKK1, VSNL1, DKK2, CLU, RELN, MEST, SDC1, LRP5, CTGF, SORL1, PLAU, SHC1, MDK, WNT5A, LRP4 |
| DEVELOPMENTAL | 3.95E-03 | 17 | 8.422 | 114 | CEBPA, IL7, NME1, EZH2, BMP4, SIX1, RELN, RUNX3, NKX2-1, NEFH, FOXL2, TCF3, MDK, NKX2-5, WNT5A, SMO, WT1 |
| FIBROBLAST GROWTH FACTOR | 4.27E-03 | 27 | 15.884 | 215 | PTCH1, FOXG1, LHX2, BMP4, CDC1, SULF2, GPC4, TBX3, FGFR1, MSX2, SPRY1, SOX3, BMP7, FGF2, NKX2-1, WNT3, MEST, FGFR1, FGF9, EXT1, SDC1, HS6ST2, ALDH1A2, TBX1, DACH1, PLAU, IL17RD |
| CYCLIN D3 | 5.37E-03 | 6 | 1.699 | 23 | RPS6KB1, KIT, EIF4EBP1, AR, KITLG, TCF3 |
| AMP ACTIVATED PROTEIN KINASE | 5.37E-03 | 6 | 1.699 | 23 | NME1, KLC1, NME2, PRKCZ, TBC1D4, ATIC |
| NUCLEAR RECEPTOR SUBFAMILY 5, GROUP A, MEMBER 1 | 5.66E-03 | 8 | 2.807 | 38 | CDK7, DUSP1, GATA4, KAT2A, FOXL2, NR0B1, NR5A1, WT1 |
| E2F TRANSCRIPTION FACTOR 1 | 6.59E-03 | 9 | 3.472 | 47 | MYB, ATR, SKP2, TYMS, E2F2, MYBL2, PCNA, PHB, RNF2 |
| ERYTHROPOIETIN | 8.31E-03 | 11 | 4.876 | 66 | MYB, PIM1, LYN, HIF1A, KIT, TAL1, SOCS3, STAT5B, CD34, KITLG, SHC1 |
| FMS LIKE RECEPTOR TYROSINE KINASE 3 | 9.10E-03 | 8 | 3.029 | 41 | CEBPA, IL7, PIM1, LYN, KIT, TAL1, KITLG, DIX1 |
| PARATHYROID HORMONE | 9.31E-03 | 11 | 4.950 | 67 | ADCY1, PPARG, DUSP1, DKK1, MSX2, IRS2, BMP6, TNFRSF11B, EXT1, BMP2, CYP27B1 |

**Table 7: Literature based pathways associated to the upregulated genes in DS-9**

In GePS analysis, the upregulated genes in DS-9 were mapped to the significant pathways supported by literature, $p < 0.01$.

| Canonical pathway | P-value | # Genes (observed) | # Genes (expected) | # Genes (total) | List of observed genes |
|---|---|---|---|---|---|
| generation of amyloid b-peptide by ps1 | 5.01E-04 | 2 | 0.037 | 4 | ADAM10, BACE1 |
| Notch secretory pathway (C. elegans) | 6.63E-03 | 3 | 0.392 | 42 | ADAM10, NCSTN, ADAM17 |
| regulation of target gene expression by AP-1 | 1.89E-02 | 2 | 0.298 | 23 | MAPK14, TOLLIP |
| p75(NTR)-mediated signaling | 2.36E-02 | 3 | 0.626 | 67 | NGFRAP1, NCSTN, ADAM17 |
| p38 cascade (IL-1 signaling pathway) | 2.38E-02 | 2 | 0.243 | 26 | MAPK14, TOLLIP |
| regulation of target gene expression by AP-1 | 2.38E-02 | 2 | 0.243 | 23 | MAPK14, TOLLIP |
| NOTCH | 3.38E-02 | 3 | 0.719 | 77 | ADAM10, NCSTN, ADAM17 |
| ahr signal transduction pathway | 3.68E-02 | 1 | 0.037 | 4 | AIP |
| toll-like receptor pathway | 4.37E-02 | 2 | 0.336 | 36 | MAPK14, TOLLIP |
| signal transduction through il1r | 4.59E-02 | 2 | 0.346 | 37 | MAPK14, TOLLIP |

**Table 8: Canonical pathways associated to the downregulated genes in DS-10**

In GePS analysis, the downregulated genes in DS-10 were mapped to the significant canonical pathway, $p < 0.05$.

| Pathway | P-value | # Genes (observed) | # Genes (expected) | # Genes (total) | List of observed genes |
|---|---|---|---|---|---|
| MATRIX METALLOPROTEINASE | 4.47E-04 | 8 | 1.835 | 151 | CCL2, MAPK14, RUNX2, MCAM, CD151, DDR1, MMP17, ADAM17 |
| DISCOIDIN DOMAIN RECEPTOR | 5.69E-04 | 3 | 0.170 | 14 | MAPK14, RUNX2, DDR1 |
| JANUS KINASE | 3.82E-03 | 7 | 2.017 | 166 | CCL2, HEXIM1, KCNN4, IRF9, PMP22, SOCS2, IFI16 |
| AMYLOID BETA (A4) PRECURSOR PROTEIN | 6.58E-03 | 4 | 0.753 | 62 | ADAM10, MARCKS, NCSTN, BACE1 |

**Table 9: Literature based pathways associated to the downregulated genes in DS-10**

In GePS analysis, the downregulated genes in DS-10 were mapped to the literature supported significant pathways, $p < 0.05$.

| Canonical pathway | P-value | # Genes (observed) | # Genes (expected) | # Genes (total) | List of observed genes |
|---|---|---|---|---|---|
| Arf6 signaling events | 6.68E-03 | 2 | 0.122 | 35 | PXN, ADRB2 |
| Signaling by BMP | 1.43E-02 | 1 | 0.014 | 4 | BMP2 |
| Fc-epsilon receptor I signaling in mast cells | 2.01E-02 | 2 | 0.224 | 62 | LAT2, PXN |
| cell to cell adhension signaling | 4.26E-02 | 1 | 0.043 | 12 | PXN |
| phospholipase c-epsilon pathway | 4.60E-02 | 1 | 0.047 | 13 | ADRB2 |
| the prc2 complex sets long-term gene silencing through modif | 4.95E-02 | 1 | 0.0506 | 14 | RBBP4 |

**Table 10: Canonical pathways associated to the upregulated genes in DS-10**

The upregulated genes in DS-10 were mapped to the canonical pathway, $p < 0.05$.

# CHAPTER III: The role of BMP2 in MPNST cells

## Summary

The comparative analysis of gene expression profiles using data sets from mechanism-specific interventions enabled us to classify the signaling pathways that are regulated by neurofibromin. Among the neurofibromin-related genes whose expression was NRAS and MEK1/2 independent, we focused on the upregulation of *Bmp2*. BMP2 is a secreted protein which is overexpressed in many different tumor types and to be involved in various processes, reviewed by Singh et al. (Singh and Morris, 2010). The data from Miller et al. 2009 suggested the positive association of *Bmp2* expression with the malignancy of different stages of neurofibromas. To address this observation, we first confirmed the status of BMP2-SMAD1/5/8 signaling in MPNST cells. BMP2 stimulation promoted the phosphorylation of SMAD1/5/8 in MPNST cells after overnight serum starvation. Then, by targeted knockdown of BMP2 using shRNA and LDN-193189, a BMP2 signaling inhibitor, we blocked the BMP2-SMAD1/5/8 signaling in the MPNST cells. LDN-193189 effectively inhibited phosphorylated SMAD1/5/8 in a dose dependent manner. In MPNST cells treated with LDN-193189 and the stable BMP2 knockdown cell lines, there was no significant differences in growth rate. However, we found that cell migration and invasion of MPNST cell lines were impaired under the above conditions that blocked BMP2-SMAD1/5/8 signaling.

These findings suggest the overexpressed BMP2 in the MPNSTs contributes to the malignant phenotype of MPNST cells and can be used to manipulate the malignant phenotype of MPNSTs in patients.

# Materials and Methods

## Lentivirus shRNA mediated stable *NRas* knockdown and inducible oncogenic RAS expression system

Stable MPNST cell lines with targeted gene knockdown and scrambled sequence were constructed by lentivirus based shRNA technology. The lentivirus vector containing shRNAs targeting NRAS and scrambled sequence were packed using the Trans-Lentiviral™ Packaging System (TLP4615, Open Biosystem, Thermo) in 293T cells. The virus particles were harvested and titered according to the manufacturer's protocol. The ST88-14 cells were incubated with viral particles for 4 h and selected by 0.5 μg/ml puromycin for 5 days. Selected cells were confirmed by fluorescence microscopy for GFP expression.

Tet-off (BD Biosciences) cell line conditionally expressing the oncogenic form of RAS-G12V was established using the parent Schwann cell line STS26T($Nf1^{+/+}$). The procedure is described in a previous study from our lab (Kraniak, et al., 2010).

## Scratch recovery assay

Cells were seeded at $1x10^6$ cells/well in 6-well plates and pre-incubated with LDN-193189 at the same concentrations used in the scratch experiment overnight. The

scratch was made on 100% cell monolayer by a plastic tip. To better quantify the cell migration images, T265(*Nf1*$^{-/-}$) and ST88-14(*Nf1*$^{-/-}$) were infected by the GFP expressed lentivirus to create T265NonKD and ST88NonKD cell lines. T265NonKD cells were cultured at 0.1% or 5% FBS with 0 μM, 0.001 μM, 0.01 μM and 0.1 μM LDN-193189. Because ST88NonKD survived poorly with 0.1% FBS, 1% FBS were used in the experiment. ST88NonKD were cultured at 1% and 5% FBS with same LDN-193189 concentration series. Cell migration was monitored after 24 h of cell culture by Olympus IX71 fluorescent microscope, and the area of the scratched region in pixels was quantified by slidebook 4.2. This assay was repeated independently at least three times.

## Matrigel invasion assay

BD BioCoat™ Growth Factor Reduced MATRIGEL™ invasion Chamber was used to access the invasion ability of the ST88-14(*Nf1*$^{-/-}$) and T265(*Nf1*$^{-/-}$). Briefly, 2.5X10$^4$ cells were added to the upper chamber coated by Matrigel without serum but with the BMP2 and/or LDN-193189. Cells were stimulated by 200 ng/ml BMP2 for 24 h in the chamber before evaluation. Cells with LDN-193189 were pretreated with 0.1 μM/ml LDN-193189 overnight before seeding to the chambers, and the media was changed to fresh 0.1 μM/ml LDN-193189 with/without BMP2 200 ng/ml for 24 h for evaluation. 5% FBS was used as attractant in the lower chamber. After 24 h, the cells remaining in

the chamber were removed by the cotton swab and invaded cells present on the other side of the bottom of chamber were fixed and stained by Diff-Quick Stain (Biochemical Science, Inc., Swedesboro, NJ). The invaded cells were counted under the microscope and all experiments were repeated three times following the manufacturer's instructions.

## Statistical analysis

Experiments were subject to at least three independent replicates. For qRT-PCR and scratch assay results, paired t-test was used to determine the significant differences at 95% or 99% confident interval. For the western blotting results, one sample-test was used on the ratios between the treated and controls from different replicates, 95% or 99% confident intervals were indicated on the figures.

# Results

## BMP2 regulation of Smad1/5/8 activity is independent of NRAS in MPNST cells

In the canonical signaling, BMP2 exerts its function by binding to specific type I and II receptors to form a complex with a serine-threonine kinase activity resulting in the phosphorylation of SMAD1/5/8 proteins. Phosphorylated SMAD1/5/8 bind to SMAD4 and translocate to the nucleus to regulate gene expression (Massague, et al., 2005). However, the roles of BMP2 in tumorigenesis are diverse including the epithelial to mesenchymal transition, metastasis, and angiogenesis (Singh and Morris, 2010). We found that SMAD1/5/8 phosphorylation was increased in 3 MPNST cell lines, ST88-14(*Nf1*$^{-/-}$), T265(*Nf1*$^{-/-}$) and sNF96.2(*Nf1*$^{-/-}$), compared to normal human Schwann cells (Fig. 14a). The BMP2-SMAD1/5/8 pathway activity in ST88-14(*Nf1*$^{-/-}$) was further evaluated by BMP2 stimulation after overnight serum starvation. Treating with 100 ng/ml BMP2 stimulated the phosphorylation of SMAD1/5/8 in 15 min after overnight serum starvation, but with limited additional phosphorylation after BMP2 treatment at 200 ng/ml (Fig. 14b). Because BMP2 was overexpressed in MPNST cells, we suspected that the overexpressed BMP2 could promote SMAD1/5/8 activity. After si*Bmp2* treatment of ST88-14(*Nf1*$^{-/-}$) cells, *Bmp2* expression decreased by ~60%, as

determined by qRT-PCR (Fig. 15a) and the phosphorylation of SMAD1/5/8 was inhibited as demonstrated by western blotting (Fig. 15b).

A recent report indicated that suppression of RAS activity by salirasib, a S-trans, trans-farnesylthiosalicylic acid (FTS), inhibited the expression of *Bmp4*, and thereafter perturbed BMP4 related SMAD signaling in MPNST cell lines (Barkan, et al., 2011). To verify that NRAS suppression resulted in negative regulation of SMAD1/5/8 signaling, we transfected ST88-14($Nf1^{-/-}$) cells with si*NRas* and found that SMAD1/5/8 phosphorylation decreased by ~40% compared to control. However, when si*Bmp2* was transfected into ST88-14($Nf1^{-/-}$) cells, the phosphorylation of SMAD1/5/8 was inhibited by ~80%, greater than that from the NRAS knockdown alone (Fig. 15b). A combination of si*NRas* and si*Bmp2* failed to inhibit phosphorylation of SMAD1/5/8 beyond that of si*Bmp2* alone. We observed similar results in the comparison between *NRAS* stable knockdown cell line (ST88-*NRas*KD) and non-silencing control cell line (ST88-*Non*KD) (Fig. 16). Together, these data indicated that although both NRAS and BMPs can control downstream SMADs, BMP2 exerted a greater influence on the phosphorylation of SMAD1/5/8 than NRAS.

## LDN-193189 inhibits BMP2-SMAD1/5/8 in time and concentration dependent manner

To study the BMP2-SMAD1/5/8 pathway in the MPNST cell lines, we utilized

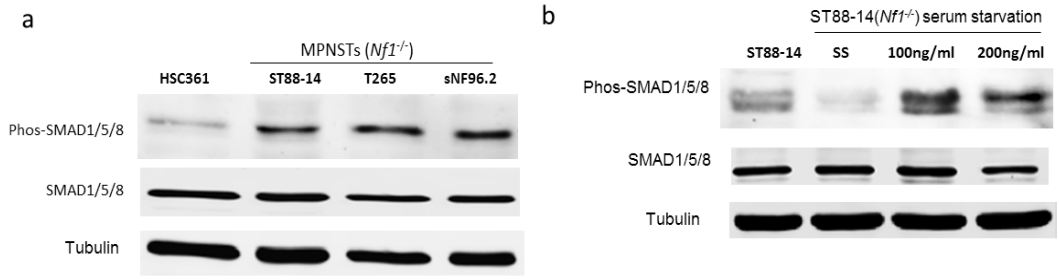



**Fig. 14 Status of phosphorylated SMAD1/5/8 in MPNST cell lines**

Western blotting indicated higher phosphorylation of SMAD1/5/8 in the MPNST cell lines compared to the normal human Schwann cells. BMP2 stimulation for 15 min was applied to ST88-14(*Nf1*$^{-/-}$) after overnight serum starvation. 100 ng/ml increased the phosphorylated SMAD1/5/8 about 2-fold. 200 ng/ml had limited effects to further increase the phosphorylation compared to 100 ng/ml suggesting the signaling pathway saturation in short time.

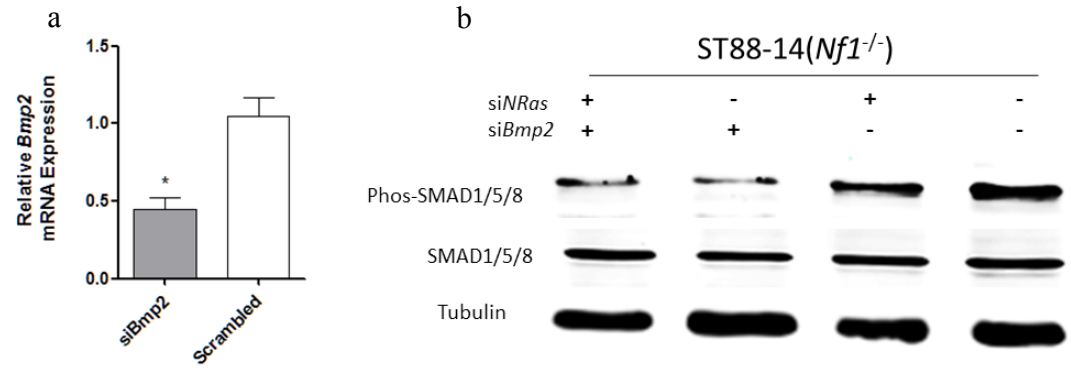



**Fig. 15 si*Bmp2* inhibited *Bmp2* mRNA accumulation and the phosphorylation of SMAD1/5/8**

(a) si*Bmp2* significantly decreased the *Bmp2* mRNA expression in ST88-14($Nf1^{-/-}$) cell line by quantitative RT-PCR. Paired t-test, n=3, *p<0.05. Data is presented as means of three independent experiments ± SD. (b) Western blotting indicated both si*NRas* and si*Bmp2* can decrease the phosphorylated SMAD1/5/8, however, si*Bmp2* has stronger inhibition effects on SMAD1/5/8 phosphorylation than si*NRas* alone.

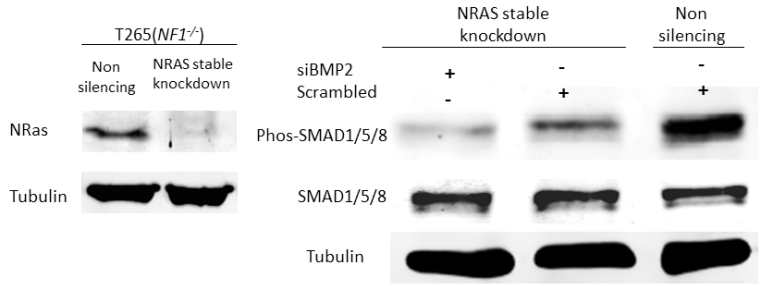



**Fig. 16 NRAS and BMP2 influence the activity of SMAD1/5/8 independently**

Western blotting indicated the decreased phosphorylation of SMAD1/5/8 in stable NRAS knockdown cell line ST88-*NRas*KD compared to the non-silencing control cell line ST88-*Non*KD. In ST88-*NRas*KD, 48 h after si*Bmp2* treatment, the phosphorylated SMAD1/5/8 decreased further compared to that in scrambled siRNA control sample.

LDN-193189 which has strong potency to bind BMP2 preferred type I receptors (known as Activin-receptor-Like-Kinase, ALK), ALK2, ALK3 and ALK6 (Cuny, et al., 2008) and subsequently suppress BMP2-SMAD1/5/8 signaling. We evaluated the inhibition efficacy of LDN-193189 at different concentrations and time interrvals in MPNST cells to optimize the drug application. We found that treatment of T265(*Nf1*$^{-/-}$) cells with 0.01 μM LDN-193189 for 15 min can inhibit phosphorylation of SMAD1/5/8 nearly completely (Fig. 17). We further evaluated the time dependency of the drug. T265(*Nf1*$^{-/-}$) were treated with 0.01 μM LDN-193189 and proteins were harvested at different time points. The inhibitory effects were rapid but decreased with time, and ~50% inhibition was retained at 24 h post treatment (Fig. 18).

## LDN-193189 inhibits the migration and invasion of MPNSTs *in vitro*

Late stage MPNSTs have been reported to frequently metastasize to the lungs, lymph nodes, and liver (Wong, et al., 1998). Because *Bmp2* expression increased in NF1-related malignant tumors (Miller, et al., 2009) (see Fig. 9), BMP2 may affect malignancy via enhancement of cell migration and invasion (Clement, et al., 2005; Gordon, et al., 2009). Therefore, we assessed BMP2 effects on these malignant properties of MPNST cell lines. We tested the MPNST cell line migration with various concentrations of LDN-193189, and quantified the ability of cells to migrate to the scratched gap. We quantified the cell migration images of two MPNST cell lines,

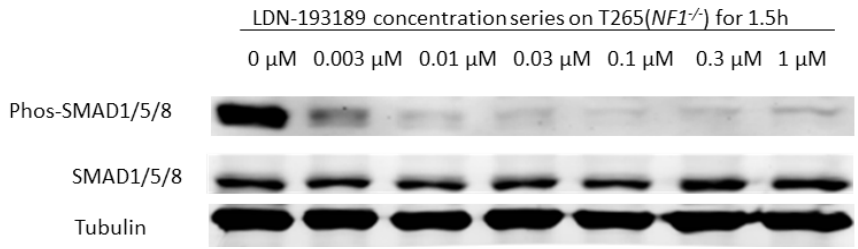



**Fig. 17 Efficacy of LDN-193189 concentration series to inhibit SMAD1/5/8 in T265(*Nf1*$^{-/-}$)**

LDN-193189 concentration series indicated the effective inhibition of the phosphorylation of SMAD1/5/8 after 1.5 h incubation in T265(*Nf1*$^{-/-}$) cell line with 5% FBS culture medium.

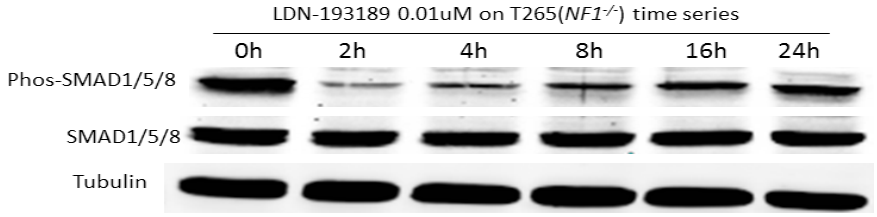



**Fig. 18 LDN-193189 time dependent inhibition of phosphorylation of SMAD1/5/8 in T265(*Nf*$^{-/-}$).**

0.01 μM LDN was applied to the T265(*Nf1*$^{-/-}$) and the proteins were harvested at the indicated time points. The phosphorylated SMAD1/5/8 decreased with time after the LDN-193189 treatment.

T265NonKD and ST88NonKD, which were previously infected by lentivirus with non-silencing shRNA expressing a green fluorescence protein (GFP). Using 0.1% and 5% fetal bovine serum (FBS) in T265NonKD, the area of the gap at different LDN-193189 concentrations was measured by determining the number of pixels in the gap (Fig. 19a). There were significant differences of the gap area starting from 0.01 μM with respect to the 0 μM at 24 h after the scratch. In order to determine whether the observed effects of LDN-193189 in the migration assay reflected effects on growth retardation, the growth rate of the cell line T265NonKD with 0.01 μM LDN-193189 at 0.01% FBS and with 0.1 μM LDN-193189 at 5% FBS were evaluated compared to the control, respective (Fig. 20). No significant effect on growth rate was observed at each condition, which suggested the cell growth did not influence the change in the area of the gap at 24 h in the scratch assay. Similar results were observed in ST88NonKD (Fig. 19b) with 1% and 5% FBS, respectively. To further confirm the specificity of BMP2 stimulated migration, we constructed the stable BMP2 knockdown line (ST88Bmp2KD) and non-silencing control (ST88NonKD) cell lines (Fig. 21a), and used them in the scratch assay (Fig. 21b). There were significant differences between the areas of gap from these two cell lines at 1% or 5% FBS concentrations at 24 h after the scratch (Fig. 21c), but no significant differences in the growth rate (Fig. 21d) of these two cell lines were observed. This indicated that the differences in scratch assay were resulting from cell migration and not proliferation rates within the scratch.

The effect of BMP2 on the invasion properties of MPNST cells was measured by low growth factor Matrigel invasion assay. Matrigel was placed on the bottom membrane in the upper chamber, and the cells that digested the Matrigel and invaded through the 8 μm pores were counted on the other side of membrane. Medium with 5% FBS in the well of each 24-well plate was used as the attractant and BMP2 and/or LDN-193189 were added into the serum free media in the upper chamber with same amount of cells. After 24 h, cells on the other side of membrane were stained by Quick-Diff and counted using microscopy. The ability of invasion of MPNST cells was significantly increased by 200 ng/ml BMP2 stimulation, and the addition of LDN-193189 completely blocked the effect induced by BMP2 on MPNST cell invasion (Fig. 22). *Bmp2* stable knockdown cells, ST88BMP2KD and T265BMP2KD, also had reduced invasive properties compared to ST88NonKD and T265NonKD, respectively (Fig. 23). Therefore, abrogation of BMP2 signaling in MPNST cells impaired the motility and invasive abilities of those cells and also suggested BMP2 signaling could promote the malignant phenotypes of MPNSTs. Collectively, these data indicate that the motility and invasiveness of MPNST, as malignant properties, could be reduced by using BMP2 as a therapeutic target.

# Discussion

In chapter II, the differentially expressed genes were classified according to the expression patterns. Based on the intersection analysis, neurofibromin-related but NRAS and MEK1/2 independent gene expression was identified in DS-10. From the DS-10, *Bmp2* was chosen for further study because of 1) the significance of BMP2 signaling in pathway analysis and 2) its expression profile in the data of Miller et al. 2009 that showed the positive association between *Bmp2* expressions with increasing malignancy of NF1-related tissues (Fig. 9). Interestingly, a case report suggested a connection between acute deterioration of plexiform neurofibroma and exogenous BMP2 treatment to facilitate bone fusion after surgery (Steib, et al., 2010).

*Bmp2* overexpression resulting from *Nf1* deficiency but independent of NRAS and MEK1/2 activities was verified in a variety of MPNST cell models. Although the convergence of NRAS and SMAD signaling was observed in this study, the regulation of SMAD 1/5/8 signaling by BMP2 was far stronger than that by NRAS alone, which indicated that BMP2-SMAD1/5/8 may contribute independently to MPNST formation or malignant phenotypes, via mechanisms to control cell motility, invasiveness and tumor growth, as it does in other tumor types (Singh and Morris, 2010). Although BMP2 and BMP4 have certain overlapping pathway and functional redundancy, these two factors are regulated by different mechanisms (Fritz, et al., 2004). Barkan et al. 2011 reported that

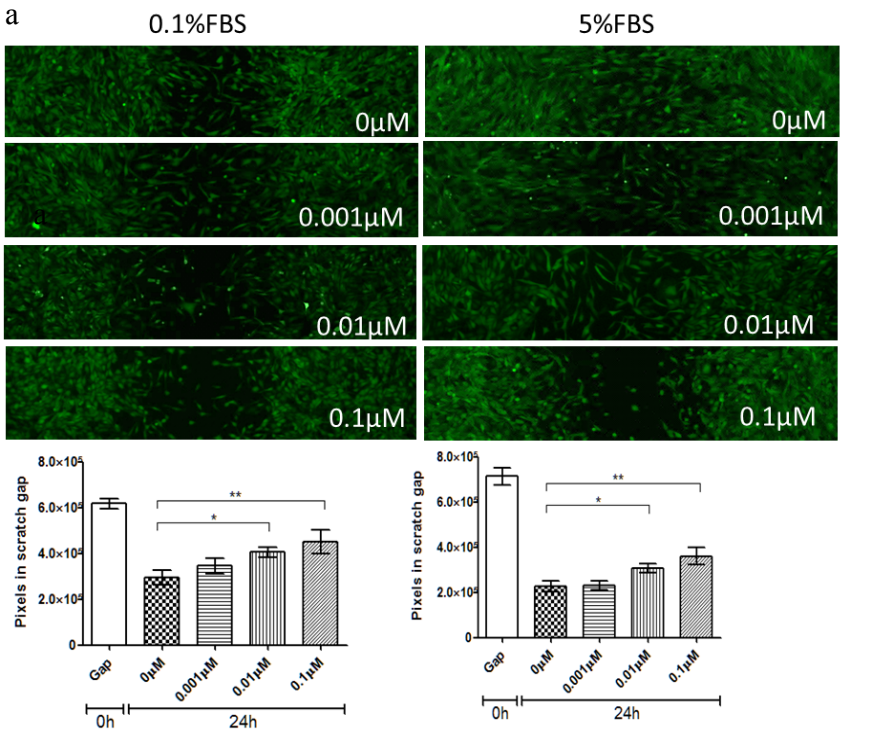
application of FTS in ST88-14 cell leads to significant alteration in transcriptome including decrease of expression of *Bmp4*. We did not find decreased *Bmp4* expression after inhibition of *NRas* by siRNA in our data set, but we identified the expression of *Gdf6*, also known as *Bmp13*, to be greatly increased in ST88-14($Nf1^{-/-}$) (DS-4) and decreased in si*NRas* treated sample (DS-2). GDF6 is believed to bind the same type I and II receptors as BMP2, which results in phosphorylation/activation of SMAD1/5/8 (Williams, et al., 2008). This mechanism may explain the phosphorylation/activation of SMAD1/5/8 that we observed in the regulation of SMAD1/5/8 by the NRAS pathway.

To evaluate BMP2-SMAD1/5/8 signaling in MPNST cell lines, LDN-193189, a selective inhibitor to BMP2-activated type I receptor kinase (ALK1, ALK2, ALK3, and ALK6), was employed in this study. LDN-193189 has been applied as the BMP-activated type I receptor inhibitor (Yu, et al., 2008), and a recent study indicated it can inhibit the ability of ALK2 and ALK3 to phosphorylate GST-SMAD1 *in vitro* at an $IC_{50}$ of 45 nM and 100 nM, respectively. However, its inhibition to ALK4 and ALK5 is with higher $IC_{50}$ at 0.3 μM and 0.5 μM, respectively, indicating a lesser effect on TGFβ signaling (Vogt, et al., 2011). From the specificity test in the same study, LDN-193189 inhibited 24 out of 121 protein kinases by >50% at 1 μM, which suggested us that a lower concentration was needed to minimize possible side effects. We studied the concentration dependency and time dependency of LDN-193189 in MPNST cell lines and chose 0.01 μM of LDN-193189 for the most of experiments in this study, which is

lower than the concentration that could have significant side effects based on study of Vogt et al 2011.

Inhibition of BMP2-SMAD1/5/8 signaling by LDN-193189 impaired the motility and invasiveness of MPNST cell lines *in vitro*, and these effects were confirmed by BMP2 shRNA interference by lentivirus infection. Gordon et al. reported BMP2 could increase MMP2 (type IV collagenase) expression in pancreatic cancer cell line through the SMAD1-dependent mechanism (Gordon, et al., 2009). This mechanism may have been present in the MPNST cells that we tested.

LDN-193189 can rapidly inhibit the BMP2-SMAD1/5/8 signaling at low concentrations, however, the inhibitory effect decreased with the time. There is no significant growth arrest effect on the MPNST cells, indicating the inhibitory effects of LDN-193189 on the malignant phenotypes could be reversible. This may limit its application for only BMP2 targeted treatment, but this strategy could still cooperate with other treatments to control the malignant phenotype of MPNSTs.


a
0.1%FBS
5%FBS
0μM
0.001μM
0.01μM
0.1μM
Pixels in scratch gap
Gap
0h
24h

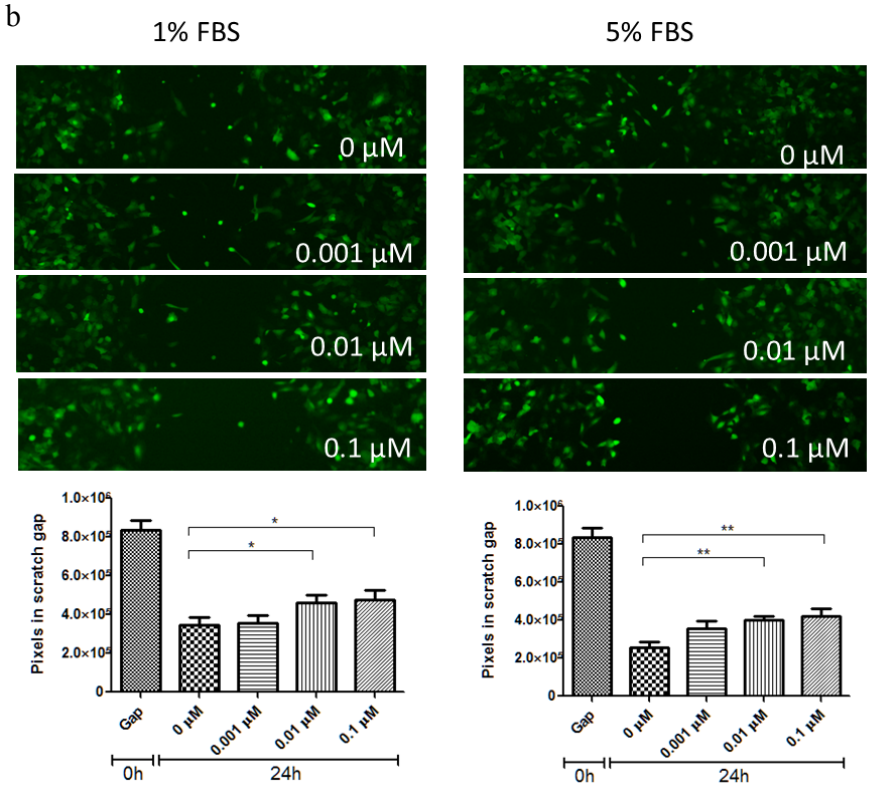

b
1% FBS
5% FBS
0 μM
0.001 μM
0.01 μM
0.1 μM
Pixels in scratch gap
Gap
0h
24h

**Fig. 19 Migration of MPNST cell lines with LDN-193189 at 24 h in scratch assay with different FBS concentration**

Scratch assay indicated the LDN-193189 treatment inhibition to migration under different FBS concentrations. Figures were captured under the fluorescent microscope at 24 h after scratches and then the pixels in the gap (the dark area) were quantified by Slidesbook software and shown as a bar graph. Paired t-test, * $p<0.05$, ** $p<0.01$. Data is expressed as means of three independent experiments ± SD. (a) T265Non(*Nf1*$^{-/-}$) migration at 0.1% FBS and 5% FBS (b) ST88Non(*Nf1*$^{-/-}$) migration at 1% and 5% FBS.

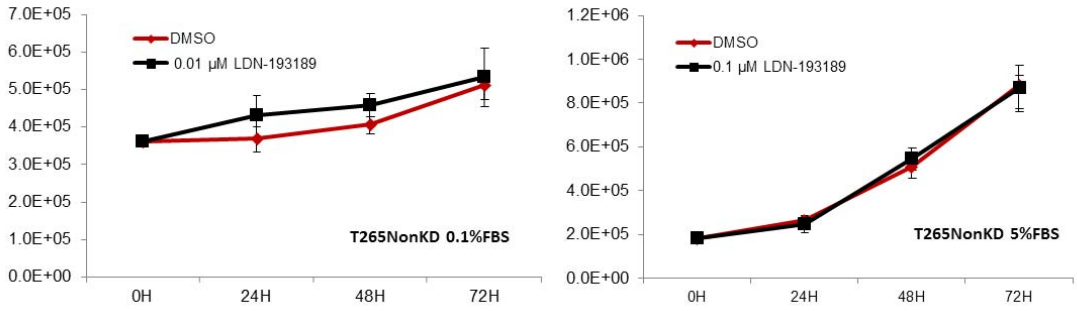



**Fig. 20 The growth curve of T265NonKD**

No significant differences were shown in the growth rate of T265NonKD cell lines at 0.1% FBS with 0.01 μM LDN-193189 or at 5% FBS with 0.1μM LDN-193189 compared with DMSO treated control at different time points, respectively. Data is expressed as mean ± SD, and this figure represents one of three independent experiments. Each time point was replicated 4 times within each experiment.

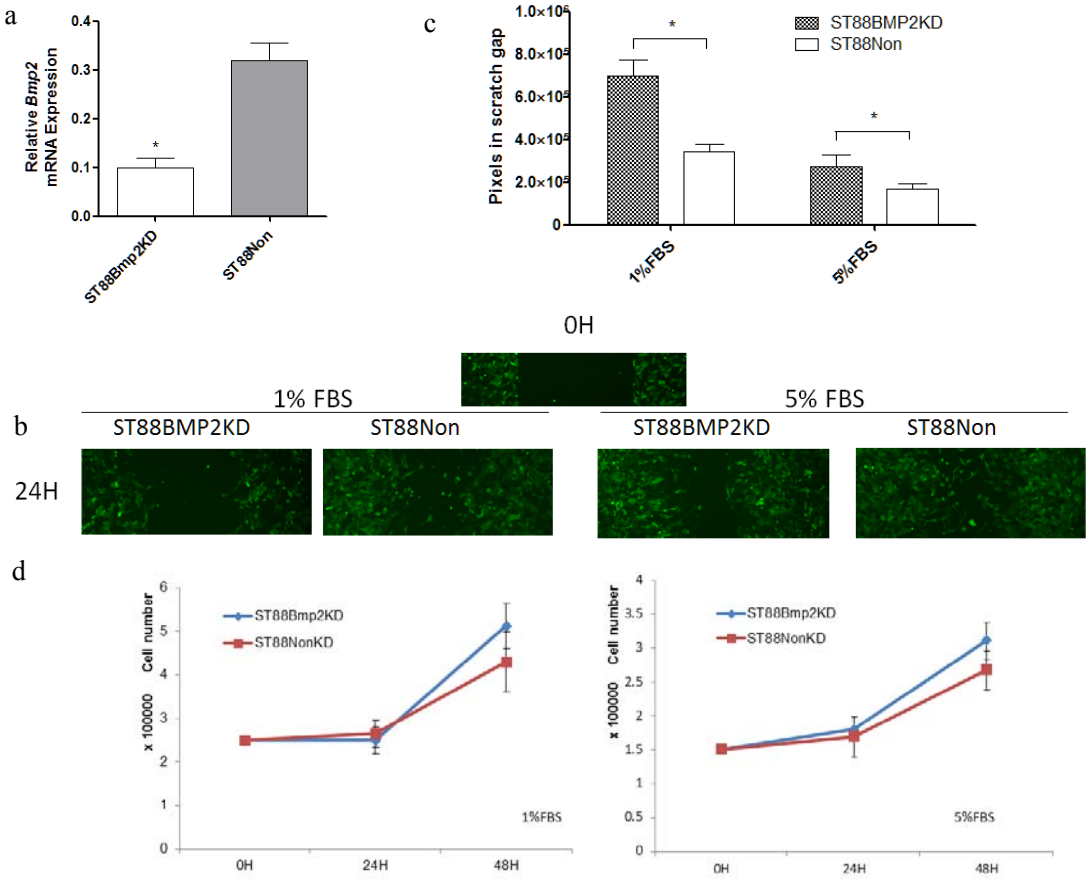



**Fig. 21 Bmp2 knockdown by lentivirus in ST88-14(*Nf1*$^{-/-}$) impaires cell migration**

(a) Quantitative RT-PCR indicated the endogenous *Bmp2* expression were significantly inhibited by the shRNA lentivirus in ST88-14(*Nf1*$^{-/-}$). Data is presented as mean of experiments ± SD, representing one of three independent replicates. (b) Scratch assay images compared the migration ability of ST88Bmp2KD and ST88NonKD at 24 h after scratch with 1% FBS and 5% FBS at 24 h. (c)The number of pixels in the gap (black area) from the images were quantified and shown as the bar graph. Data is represented as mean ± SD of three independent experiments, paired t-test, n=3, * $p<0.05$. (d) Cell growth curve of ST88Bmp2KD and ST88NonKD within 48 h. No significant growth

rate differences were observed between these two cell lines at 1% FBS and 5% FBS. This figure represents one of three independent experiments. Each time point was replicated 4 times within each experiment.

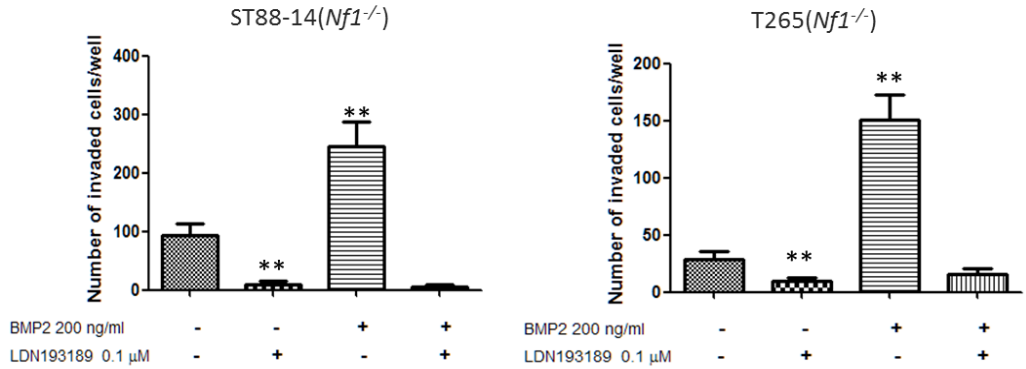



**Fig. 22 BMP2 and LDN-193189 influenced the invasion ability of ST88-14(*Nf1*$^{-/-}$) and T265(*Nf1*$^{-/-}$)**

The number of cells invaded to the matrigel and presented on the other side of the insert chamber under different conditions was quantified by microscopy after the Quick-Diff stain. With the 0.1 μM LDN-193189 in the upper chamber for 24 h, the invasion ability was significantly inhibited in both ST88-14(*Nf1*$^{-/-}$) and T265(*Nf1*$^{-/-}$) compared to the controls without treatments. 200 ng/ml BMP2 in the upper chambers for 24 h promoted the invasion of two cell lines significantly compared to the controls, and the BMP2-related invasion effects were blocked by LDN-193189. Data is expressed as means ± SD of three independent experiments, paired t-test, ** $p<0.01$, n=3.

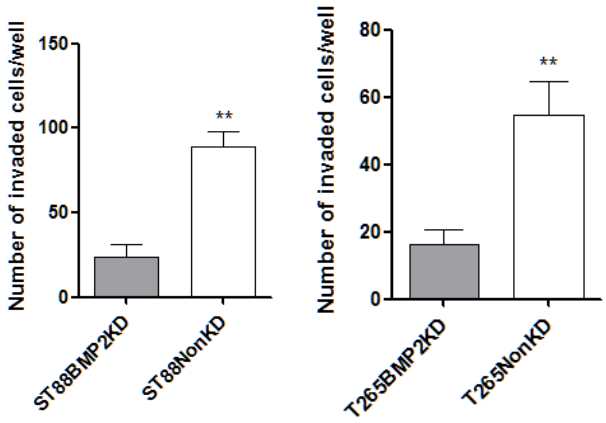



**Fig. 23 *Bmp2* stable knockdown lines indicated decreased invasion properties compared to the control lines.**

Cells were seeded at $2.5x10^4$ with no serum medium in the insert chambers and 5% FBS was used as attractant. The numbers of invaded BMP2 knockdown cell lines and control cell lines were counted. Data is presented as the mean ± SD of three independent experiments, paired t-test, ** $p<0.01$.

# CHAPTER IV: Conclusions and significance

In this dissertation work, I focused on a systematic screen of the downstream gene regulation resulting from neurofibromin deficiency in the MPNST cells. By associating the differentially expressed genes to biological pathways, I identified novel mechanisms to explain the malignancy of the MPNST cell lines and potential therapeutic targets for MPNST treatment.

Loss-of-function of *Nf1* predisposes the formation of multiple different tumors. Although many of these tumors are benign such as dermal, plexiform neurofibromas, and optical pathway gliomas (Lee and Stephenson, 2007), the patients can develop malignant tumors with high mortality such as MPNSTs and glioblastoma multiforme (Blatt, et al., 1986). NF1 patients with benign neurofibromas have 8~13% life risk to develop into MPNST (Evans, et al., 2002b) and up to 50% of MPNSTs are associated with *Nf1* deficiency (Matsui, et al., 1993; Sorensen, et al., 1986).

The clinical management of MPNST is quite challenging because of its inherently aggressive nature and limited diagnostic and therapeutic options. MPNST cells frequently undergo genetic alterations that cause them to be refractory to traditional treatments such as chemotherapy (Casanova, et al., 1999). Surgical resection as a treatment provides a limited outcome to both local recurrence and distant metastases. Many preclinical studies and clinical trials are currently testing strategies to target the

activated downstream pathways of neurofibromin in MPNSTs, including RAS, MEK1/2, and mTOR. A better understanding of the signaling transduction of neurofibromin in MPNST may provide novel therapeutic targets to control or reduce the malignancy of the tumor.

Gene expression profile screening is generally used to identify the disease signatures on the molecular level. Previous NF1-related large scale microarray studies mainly focused on differentiating the benign and malignant tumor types, or characterizing gene signatures of MPNSTs. Although the differentially expressed genes improved the understanding of NF1 disease, diverse information did not provide an integrated signaling network or reveal the aberrant gene regulation mechanisms in NF1-related tumors. Currently, the RAS and MEK1/2 targeted strategies are not very successful; however the interference to the alternative downstream target such as mTOR is promising. Novel targets for the tumor treatment can be offered by systematically screening to stratify the pathway related gene expression changes.

In this study, MPNST cell lines with different neurofibromin status provided good models to classify the signaling pathway related gene expression changes. The hyperactive NRAS and MEK1/2 have been characterized in ST88-14($Nf1^{-/-}$) (Mattingly, et al., 2006) and functions of wild type neurofibromin in STS26T($Nf1^{+/+}$) to regulate RAS and ERK1/2 activities have been confirmed as well (Kraniak, et al., 2010). By gene profile comparisons based on pathway interference in these two cell lines, I

associated the gene expression changes to the specific pathways in MPNSTs, which is the first time to provide the pathway-oriented gene regulations in MPNSTs. Furthermore, according to the biological causality among the interfered pathways, the set theory operation allowed us to identify the neurofibromin-associated but NRAS and MEK1/2 independent changes, enabling the possibility to study the neurofibromin deficiency related novel signaling associated or not with NRAS and MEK1/2.

In chapter II, I described the experiment design and set theory operations to associate the differentially expressed genes to the signaling axis. The results revealed the potential regulatory mechanisms for these genes, and a good example was *Sox9*. SOX9 was reported to function as a pro-survival biomarker in MPNSTs from Miller's large scale microarray analysis about NF1-related cells and tissues (Miller, et al., 2009). However, the mechanism of regulation of *Sox9* expression is unclear. According to our results, the increased expression of *Sox9* is probably dependent on the activated MEK1/2 in MPNSTs. Similar candidates, such like *Edn1*, *Nt5e* and *Rgs16*, that may influence the tumor formation and malignant phenotypes in each category are also discussed in chapter II.

Gene set enrichment analysis by GePS software identified significant gene ontology terms and pathway terms from the gene lists in each category, and the significant terms provide sources for hypothesis generation. From the canonical pathway analysis of the upregulated gene in DS-10, we found the term "signaling of BMP2". This term drew

our attention to the aberrant expression of BMP2 in the NF1-related cell lines and human samples. Actually, a positive association of *Bmp2* expression with the increasing malignancy of NF1 tumors has been indicated as one of 2827 differentially expressed transcripts in NF1-related tumors compared to the normal human Schwann cell in Miller's data. This suggested us a strong connection between the *Bmp2* overexpression and MPNST malignancy. I validated the *Bmp2* expression changes in microarray analysis by qRT-PCR. By using the inducible oncogenic RAS system in STS26T($Nf1^{+/+}$) cells, I concluded that the increased RAS and MAPK activity do not significantly influence the *Bmp2* expression in STS26T($Nf1^{+/+}$) cells.

Next, I evaluated the possible causality between BMP2 overexpression and malignant phenotypes in MPNST cell lines in chapter III. BMP2 overexpression has been reported in multiple tumors, such as prostatic adenocarcinoma, bladder cancer, breast cancer and prostate cancer (Hatakeyama, et al., 1993; Hung, et al., 2008; Miyazaki, et al., 2003), and involves many cancer processes, including metastasis, motility, and invasiveness (Langenfeld, et al., 2003; Park, et al., 2008). We found that the phosphorylation of SMAD1/5/8, the downstream effector of BMP2 signaling, is relatively higher in the MPNSTs than in the normal human Schwann cells. Then, by employing *Bmp2* shRNA or receptor inhibition by LDN-193189, we inhibited the BMP2-SMAD1/5/8 signaling in ST88-14($Nf1^{-/-}$) and T265($Nf1^{-/-}$) cells, and quantified their inhibitory effects on the cell migration and invasion. The results confirmed that

BMP2-SMAD1/5/8 inhibition impaired the migration and invasion properties of ST88-14(*Nf1*$^{-/-}$) and T265(*Nf1*$^{-/-}$) cells, indicating that the BMP2 controls these malignant properties of MPNST cells. Although NRAS regulation to the SMAD1/5/8 activity in our cell models was confirmed by NRAS specific siRNA and shRNA, we did not observed the *Bmp4* expression decrease as observed by Barkan et al. in their study of FTS treatment (Barkan, et al., 2011). Actually, our study suggests the expression decrease of *Gdf6* (*Bmp13*) could explain the inhibitory effects of NRAS knockdown on the SMAD1/5/8 activity, while the FTS related *Bmp4* decrease identified by Barkan et al. could be the FTS specific effects on the MPNST cells.

In summary, we systematically described the downstream gene expression changes in MPNSTs under the scenarios of *Nf1* knockdown, *NRas* knockdown and MEK1/2 inhibition. By comparing different data sets, the overlapped gene expression changes were associated to the pathways activated in the cell models. This is the first study to reveal the pathway-orientated gene expression changes in a MPNST cell line. I not only characterized the NRAS and MEK1/2 specific gene changes, but also identified ones that neurofibromin-related and independent of NRAS and MEK1/2, which provided novel molecular mechanisms to support the further drug target studies. We identified the overexpression of *Bmp2* and verified its roles in the malignant phenotypes in the MPNSTs. All these studies significantly expend our knowledge of gene regulations of MPNST, and offer novel insights in the future therapeutic strategy in NF1-related tumor

types.

# APPENDIX: SUPPLEMENTARY TABLES

## Suppl. Table 1: Primers for qRT-PCR

| Gene | Forward Primer | Reverse Primer |
|---|---|---|
| **ACTG2** | CTGGAGAAGAGCTATGAGCTG | ATCTCCTTCTGCATCCTGTC |
| **ANXA4** | CCGGTCTCGTGGGCAGAGGAA | ACTCAGGGCCAGACAGCGGG |
| **APC** | TGTCCCTCCGTTCTTATGGAA | TCTTGGAAATGAACCCATAGGAA |
| **ATF3** | GGCGGAGGTGGGGTTAGCTT | TGGGGCAAGGTGCTGAAAATCCT |
| **Bcl2** | GATGTCGCCCCTGGTGGACAAC | GGGCCGTACAGTTCCACAAAGGC |
| **BMP2** | GACACTGAGACGCTGTTCC | CCATGGTCGACCTTTAGG |
| **BMP4** | TCCATGCTGTACCTGGATGA | TGAGTGGATGGGAACGTGT |
| **CCND1** | TATTGCGCTGCTACCGTTGA | CCAATAGCAGCAAACAATGTGAAA |
| **CCND2** | TGGAGCTGCTGTGCCACG | GTGGCCACCATTCTGCGC |
| **CDH1** | CAGCCACAGACGCGGACGAT | CTCTCGGTCCAGCCCAGTGGT |
| **CDH2** | CCTGCGCGTGAAGGTTTGCC | CCAAGCCCCGCACCCACAAT |
| **CDKN2A** | CATAGATGCCGCGGAAGGT | CCCGAGGTTTCTCAGAGCCT |
| **CHEK1** | TCTCGGCTCCAGCACCACGA | GGCCGCTCTGGGCCTGAAAG |
| **CSNK1E** | TGAGGGGTCCTCTCTGTGCCC | CCGATCTTCCGTCCCAGGCG |
| **CTNNB1** | CCCACTGGCCTCTGATAAAGG | ACGCAAAGGTGCATGATTTG |
| **CTNND1** | TGCTGTGGTGGCTGGGATGC | AGGAGGGAGAGAGACCCCCTCA |
| **DKK1** | TTCCAAGAGATCCTTGCGTT | ACCCCATTGATTGTTATCTTGA |
| **DOCK4** | CAAGTTCTGCTCCATCGAGT | CTTTTTCAGGTGCAGAGAGATTTGG |
| **EDN1** | GAGAAACCCACTCCCAGTCC | GATGTCCAGGTGGCAGAAGT |
| **ETV4** | GAGGCCGAGCGAAGGAAATGCA | TTTTCGGGCGCAGCAGACAGTT |
| **FMN1** | TTTGCCTGCCTCGGTTGGGG | TGGGAGGGGGCATCCCAGAT |
| **FZD2** | TCTCCGGCTGCTCAGTCCGAC | AACTTTACTCGCGGCCGCAG |
| **GATA6** | CCTTCGGCGAGCGCTGTTTGTT | CTCTGCCGGAAAACTGCAGCCT |
| **GSK3Beta** | CTCCTCATGCTCGGATTCA | TGCAGAAGCAGCATTATTGG |
| **IGF2** | GTGCTGCATCGCTGCTTACG | GGAAGTACGGCCTGAGAGGT |
| **IGF2R** | GTTGTCTGCCCTCCAAAGAA | CCTTTGGAGTACGTGACAAG |
| **LEF1** | CGACGCCAAAGGAACACTGACATC | GCACGCAGATATGGGGGGAGAAA |
| **MAPK14** | GCCGAGCTGTTGACTGGAAG | GGAGGTCCCTGCTTTCAAAGG |
| **MMP1** | AAGACAAAGGCAAGTTGAAAAGCGG | TGGTTTCCCAGTCACTTTCAGCCC |
| **MMP2** | TGATCTTGACCAGAATACCATCGA | GGCTTGCGAGGGAAGAAGTT |
| **MMP9** | CCTGGAGACCTGAGAACCAATC | CCACCCGAGTGTAACCATAGC |
| **MSX2** | GGAGCGGCGTGGATGCAGGAA | AAGCACAGGTCTATGGAACGG |
| **MYC** | CGTCTCCACACATCAGCACAA | CACTGTCCAACTTGACCCTCTTG |

| Gene | Forward Primer | Reverse Primer |
|---|---|---|
| **MYLK** | GGCACCCCCGTGAGGAGACA | GGCCTTGGGCGTTGGAAGCA |
| **NPPB** | TGGGAAGCAAACCCGGACGC | GCCCGGGAAGGTGCTGTCTG |
| **NRP1** | CAGAGCGCTCCCGCCTGAAC | AAATGGCGCCCTGTGTCCCG |
| **PAX3** | GAGTGAGCGCGAGCCTCTGCAC | AGGTGGTTCTGCTCCTGCG |
| ***PIK3R3*** | GAGAGGGGAATGAAAAGGAGA | ATCATGAATCTCACCCAGACG |
| **PTEN** | CCGAAAGGTTTTGCTACCATTCT | AAAATTATTTCCTTTCTGAGCATTCC |
| **RUNX2** | CCAACCCACGAATGCACTATC | TAGTGAGTGGTGGCGGACATAC |
| **SMAD3** | TCCTGGCTACCTGAGTGAAGA | GTTGGGAGACTGGACGAAAA |
| **SNAI1** | CAGTGCCTCGACCACTATGCCG | CGGTGGGGTTGAGGATCTCCG |
| **SOX9** | AGACCTTTGGGCTGCCTTAT | TAGCCTCCCTCACTCCAAGA |
| **SPARC** | CTGCCTGCCACTGAGGGTTCC | TCCAGGCAGAACAACAAACCATCC |
| **SPIN4** | GCGAGCCCGCCATCTCTACG | CGTGAGCACTGGGACAGCGT |
| **TGFß1** | AAGGACCTCGGCTGGAAGTGC | CCGGGTTATGCTGGTTGTA |
| **Twist1** | CACTGAAAGGAAAGGCATCA | GGCCAGTTTGATCCCAGTAT |
| **VEGFA** | TTTACTGCTGTACCTCCACCA | ATCTCTCCTATGTGCTGGCTTT |
| **VEGFC** | GGGAAGAAGTTCCACCATCA | ATGTGGCCTTTTCCAATACG |
| **WNT10B** | GCACTGTATTGCTCCTCCCACTT | ATAGGGACTCCCCAGCCAAA |
| **WNT5A** | AGAAGAAACTGTGCCACTTGTATCAG | CCTTCGATGTCGGAATTGATACT |
| **Zeb1** | GGCAGAGAATGAGGGAGAAG | CTTCAGACACTTGCTCACTACTC |
| **Zeb2** | GTGACAAGACATTCCAGAAAAGCAG | GAGTGAAGCCTTGAGTGCTC |
| **ZNF185** | GCGGATCTGAGCAACTTGTC | TTCTGGGGTACTGGGATCTG |
| **PXN** | ATGGCTTCGCTGTCGGATTT | ATGAACCCTCCCTCGTCCTG |
| **KIT** | GCACAATGGCACGGTTGAAT | TGGGGATGGATTTGCTCTTTGT |
| **GATA4** | GGAGGAAGGAGCCAGCCTA | CCTATTGGGGGCAGAAGACG |
| **NKX2-5** | AGAGCCGAAAAGAAAGCCTG | CACCGACACGTCTCACTCAG |
| **LAT2** | AGTGGTGTTGGCATCAGCTT | GCCTCTTGTGATGCTGAGAGT |
| **FOXA1** | TGAAACCAGCGACTGGAACA | ATGTTGCCGCTCGTAGTCAT |

**Suppl. Table 2: DS-5**

DS-5, the intersection of DS-4 (ST88-14 vs. HSC) and DS-2 (siNRas vs. Scrambled control siRNA), is hypothetically under the control of Neurofibromin-NRAS axis in ST88-14($Nf1^{-/-}$) cells, and matching the pattern: 1) increase in ST88-14 vs. HSC but decrease in si*NRas* vs. scrambled control siRNA treated ST88-14, or 2) decrease in ST88-14 versus HSC but increase in si*NRas* versus scrambled control treated ST88-14.

| Gene In DS-5 | ST88 vs HSC .logFC | ST88 vs HSC .adjPVal | siNRas vs SC88 .logFC | siNRas vs SC88 .adjPVal | Discriptoins |
|---|---|---|---|---|---|
| **ADM** | 5.06 | 0.0000 | -0.68 | 0.0025 | adrenomedullin |
| **ANXA4** | -1.21 | 0.0000 | 0.60 | 0.0020 | annexin A4 |
| **ATCAY** | 2.89 | 0.0000 | -0.63 | 0.0035 | ataxia, cerebellar, Cayman type |
| **ATF3** | -1.42 | 0.0000 | 1.04 | 0.0002 | activating transcription factor 3 |
| **C9orf150** | -1.92 | 0.0000 | 0.69 | 0.0036 | chromosome 9 open reading frame 150 |
| **CLINT1** | 1.28 | 0.0000 | -1.18 | 0.0010 | clathrin interactor 1 |
| **EPB41L4B** | 2.81 | 0.0000 | -1.12 | 0.0003 | erythrocyte membrane protein band 4.1 like 4B |
| **FLI1** | 5.38 | 0.0000 | -0.67 | 0.0077 | Friend leukemia virus integration 1 |
| **GDF6** | 4.10 | 0.0000 | -0.76 | 0.0044 | growth differentiation factor 6 |
| **LMO7** | 2.14 | 0.0000 | -0.70 | 0.0020 | LIM domain 7 |
| **MET** | 1.00 | 0.0000 | -0.93 | 0.0000 | met proto-oncogene (hepatocyte growth factor receptor) |
| **PBLD** | -1.13 | 0.0000 | 0.66 | 0.0058 | phenazine biosynthesis-like protein domain containing |
| **PTPRZ1** | -4.50 | 0.0000 | 0.96 | 0.0017 | protein tyrosine phosphatase, receptor-type, Z polypeptide 1 |
| **RGS16** | -2.48 | 0.0000 | 1.02 | 0.0054 | regulator of G-protein signaling 16 |
| **SERBP1** | 0.79 | 0.0000 | -0.60 | 0.0024 | SERPINE1 mRNA binding protein 1 |
| **SH3D19** | -1.60 | 0.0000 | 0.65 | 0.0037 | SH3 domain containing 19 |
| **SMAD3** | 3.07 | 0.0000 | -0.76 | 0.0092 | SMAD family member 3 |
| **SNCAIP** | 3.15 | 0.0000 | -0.68 | 0.0086 | synuclein, alpha interacting protein |
| **SPIN4** | 1.43 | 0.0000 | -0.66 | 0.0041 | spindlin family, member 4 |
| **SRD5A1** | -1.03 | 0.0000 | 0.71 | 0.0035 | steroid-5-alpha-reductase, alpha polypeptide 1 (3-oxo-5 alpha-steroid delta 4-dehydrogenase alpha 1) |
| **THSD7A** | -3.26 | 0.0000 | 0.77 | 0.0094 | thrombospondin, type I, domain containing 7A |
| **TPM1** | 2.45 | 0.0000 | -0.79 | 0.0019 | tropomyosin 1 (alpha) |

**Suppl. Table 3: DS-6**

DS-6, intersection of DS-4 (ST88-14 vs. HSC) and DS-3 (U0126 vs. DMSO), is hyperthetically under the control the Neurofibromin-MEK1/2 axis in ST88-14(*Nf1*$^{-/-}$) cells with matching the pattern: 1) increase in ST88-14 versus HSC but decrease in U0126VsDMSO, or 2) decrease in ST88-14 versus HSC but increase in U0126 versus DMSO.

| Gene In DS-6 | ST88 vs HSC .logFC | ST88 vs HSC. adjPVal | U0126 vs DMSO .logFC | U0126 vs DMSO .adjPVal | Descriptions |
|---|---|---|---|---|---|
| **AFMID** | 1.48 | 0.0000 | -0.66 | 0.0025 | arylformamidase |
| **AHCYL2** | -0.92 | 0.0000 | 0.59 | 0.0010 | adenosylhomocysteinase-like 2 |
| **ANXA4** | -1.21 | 0.0000 | 1.24 | 0.0000 | annexin A4 |
| **APLN** | 2.12 | 0.0000 | -0.95 | 0.0064 | apelin |
| **ARG2** | -2.16 | 0.0000 | 1.19 | 0.0008 | arginase, type II |
| **ARHGAP11A** | 1.63 | 0.0000 | -1.05 | 0.0005 | Rho GTPase activating protein 11B; Rho GTPase activating protein 11A |
| **ARL2BP** | -0.87 | 0.0000 | 0.60 | 0.0005 | ADP-ribosylation factor-like 2 binding protein |
| **ARL6IP5** | -1.45 | 0.0000 | 0.85 | 0.0001 | ADP-ribosylation-like factor 6 interacting protein 5 |
| **ARMCX1** | -1.57 | 0.0000 | 0.80 | 0.0014 | armadillo repeat containing, X-linked 1 |
| **ARMCX3** | -2.60 | 0.0000 | 0.69 | 0.0019 | armadillo repeat containing, X-linked 3 |
| **ATF3** | -1.42 | 0.0000 | 1.01 | 0.0026 | activating transcription factor 3 |
| **ATP2B4** | -3.43 | 0.0000 | 1.04 | 0.0003 | ATPase, Ca++ transporting, plasma membrane 4 |
| **BRCA1** | 1.74 | 0.0000 | -0.85 | 0.0042 | breast cancer 1, early onset |
| **BTN3A1** | -1.83 | 0.0000 | 0.66 | 0.0008 | butyrophilin, subfamily 3, member A1 |
| **BTN3A2** | -2.37 | 0.0000 | 0.87 | 0.0072 | butyrophilin, subfamily 3, member A2 |
| **BTN3A3** | -1.90 | 0.0000 | 0.92 | 0.0038 | butyrophilin, subfamily 3, member A3 |
| **C11orf82** | 2.32 | 0.0000 | -0.85 | 0.0061 | chromosome 11 open reading frame 82 |
| **C12orf24** | 2.20 | 0.0000 | -0.71 | 0.0097 | chromosome 12 open reading frame 24 |
| **C15orf42** | 1.43 | 0.0000 | -0.96 | 0.0006 | chromosome 15 open reading frame 42 |
| **C15orf52** | -5.65 | 0.0000 | 0.78 | 0.0021 | chromosome 15 open reading frame 52 |
| **C1orf198** | -2.61 | 0.0000 | 1.09 | 0.0005 | chromosome 1 open reading frame 198 |
| **C3orf23** | -2.53 | 0.0000 | 0.99 | 0.0000 | chromosome 3 open reading frame 23 |
| **C3orf26** | 1.16 | 0.0000 | -0.81 | 0.0001 | chromosome 3 open reading frame 26 |
| **C4orf3** | -1.16 | 0.0000 | 0.71 | 0.0003 | chromosome 4 open reading frame 3 |
| **C5orf41** | -1.62 | 0.0000 | 1.11 | 0.0010 | chromosome 5 open reading frame 41 |

| Gene In DS-6 | ST88 vs HSC .logFC | ST88 vs HSC. adjPVal | U0126 vs DMSO .logFC | U0126 vs DMSO .adjPVal | Descriptions |
|---|---|---|---|---|---|
| **C6orf35** | -1.66 | 0.0000 | 0.76 | 0.0001 | chromosome 6 open reading frame 35; hCG1820764; tetratricopeptide repeat domain 28 |
| **C6orf89** | -1.50 | 0.0000 | 0.68 | 0.0005 | chromosome 6 open reading frame 89 |
| **C9orf140** | 1.45 | 0.0000 | -0.98 | 0.0005 | chromosome 9 open reading frame 140 |
| **C9orf150** | -1.92 | 0.0000 | 1.05 | 0.0001 | chromosome 9 open reading frame 150 |
| **CCNDBP1** | -1.49 | 0.0000 | 0.63 | 0.0043 | cyclin D-type binding-protein 1 |
| **CD55** | 4.89 | 0.0000 | -1.66 | 0.0000 | CD55 molecule, decay accelerating factor for complement (Cromer blood group) |
| **CD99L2** | -1.37 | 0.0000 | 0.68 | 0.0071 | CD99 molecule-like 2 |
| **CDC25A** | 2.10 | 0.0000 | -1.27 | 0.0001 | cell division cycle 25 homolog A (S. pombe) |
| **CDC6** | 1.26 | 0.0000 | -0.74 | 0.0024 | cell division cycle 6 homolog (S. cerevisiae) |
| **CDCA5** | 1.87 | 0.0000 | -0.85 | 0.0010 | cell division cycle associated 5 |
| **CEP72** | 2.42 | 0.0000 | -0.82 | 0.0007 | centrosomal protein 72kDa |
| **CHAF1B** | 1.73 | 0.0000 | -0.64 | 0.0062 | chromatin assembly factor 1, subunit B (p60) |
| **CHEK1** | 1.91 | 0.0000 | -0.66 | 0.0047 | CHK1 checkpoint homolog (S. pombe) |
| **CKS1B** | 0.99 | 0.0000 | -0.91 | 0.0001 | CDC28 protein kinase regulatory subunit 1B |
| **CLEC2B** | 1.88 | 0.0000 | -0.95 | 0.0058 | C-type lectin domain family 2, member B |
| **CNKSR3** | -2.05 | 0.0000 | 1.09 | 0.0005 | membrane associated guanylate kinase, WW and PDZ domain containing 1; CNKSR family member 3 |
| **COL13A1** | 3.41 | 0.0000 | -2.38 | 0.0003 | collagen, type XIII, alpha 1 |
| **COL16A1** | -2.83 | 0.0000 | 0.96 | 0.0016 | collagen, type XVI, alpha 1 |
| **COL1A2** | -2.98 | 0.0000 | 1.53 | 0.0078 | collagen, type I, alpha 2 |
| **CRISPLD2** | -2.15 | 0.0000 | 1.50 | 0.0008 | cysteine-rich secretory protein LCCL domain containing 2 |
| **CRYL1** | -3.61 | 0.0000 | 0.95 | 0.0003 | crystallin, lambda 1 |
| **CTPS** | 1.34 | 0.0000 | -0.72 | 0.0009 | CTP synthase |
| **DAAM1** | -1.31 | 0.0000 | 0.91 | 0.0066 | dishevelled associated activator of morphogenesis 1 |
| **DDIT4** | -1.69 | 0.0000 | 0.74 | 0.0062 | DNA-damage-inducible transcript 4 |
| **DECR1** | -1.53 | 0.0000 | 0.59 | 0.0077 | 2,4-dienoyl CoA reductase 1, mitochondrial |
| **DLC1** | -1.68 | 0.0000 | 1.00 | 0.0013 | deleted in liver cancer 1 |
| **DNAJC15** | -0.87 | 0.0000 | 0.59 | 0.0002 | DnaJ (Hsp40) homolog, subfamily C, member 15 |
| **DNMBP** | 1.84 | 0.0000 | -1.02 | 0.0000 | dynamin binding protein |
| **DSCC1** | 1.56 | 0.0000 | -1.10 | 0.0022 | defective in sister chromatid cohesion 1 homolog (S. cerevisiae) |
| **DTL** | 1.21 | 0.0000 | -0.72 | 0.0044 | denticleless homolog (Drosophila) |
| **DUSP16** | -2.27 | 0.0000 | 0.78 | 0.0015 | dual specificity phosphatase 16 |
| **E2F1** | 1.19 | 0.0000 | -0.76 | 0.0018 | E2F transcription factor 1 |

| Gene In DS-6 | ST88 vs HSC .logFC | ST88 vs HSC. adjPVal | U0126 vs DMSO .logFC | U0126 vs DMSO .adjPVal | Descriptions |
|---|---|---|---|---|---|
| **EDN1** | 3.83 | 0.0000 | -1.52 | 0.0000 | endothelin 1 |
| **EGFR** | 3.50 | 0.0000 | -0.79 | 0.0029 | epidermal growth factor receptor (erythroblastic leukemia viral (v-erb-b) oncogene homolog, avian) |
| **EIF2C2** | 1.31 | 0.0000 | -1.00 | 0.0000 | eukaryotic translation initiation factor 2C, 2 |
| **EPC1** | -1.88 | 0.0000 | 0.68 | 0.0079 | enhancer of polycomb homolog 1 (Drosophila) |
| **ERRFI1** | 1.86 | 0.0000 | -1.16 | 0.0013 | ERBB receptor feedback inhibitor 1 |
| **ESM1** | 4.30 | 0.0000 | -3.91 | 0.0000 | endothelial cell-specific molecule 1 |
| **ESX1** | 2.82 | 0.0000 | -1.53 | 0.0002 | ESX homeobox 1 |
| **ETV1** | 1.29 | 0.0000 | -0.79 | 0.0010 | ets variant 1 |
| **ETV4** | 2.52 | 0.0000 | -2.09 | 0.0000 | ets variant 4 |
| **EXO1** | 1.37 | 0.0000 | -0.65 | 0.0065 | exonuclease 1 |
| **FAM105A** | 3.18 | 0.0000 | -0.61 | 0.0012 | family with sequence similarity 105, member A |
| **FAM63A** | -2.85 | 0.0000 | 0.60 | 0.0099 | family with sequence similarity 63, member A |
| **FANCI** | 1.02 | 0.0000 | -0.72 | 0.0016 | Fanconi anemia, complementation group I |
| **FGFR3** | 2.10 | 0.0000 | -1.21 | 0.0024 | fibroblast growth factor receptor 3 |
| **FOXA2** | 4.61 | 0.0000 | -2.34 | 0.0000 | forkhead box A2 |
| **FOXD1** | 3.89 | 0.0000 | -0.92 | 0.0050 | forkhead box D1 |
| **FOXF2** | 1.83 | 0.0000 | -0.59 | 0.0031 | forkhead box F2 |
| **FST** | 2.72 | 0.0000 | -1.25 | 0.0021 | follistatin |
| **FTL** | -2.10 | 0.0000 | 0.93 | 0.0035 | similar to ferritin, light polypeptide; ferritin, light polypeptide |
| **GABPB1** | 1.13 | 0.0000 | -0.99 | 0.0000 | GA binding protein transcription factor, beta subunit 1 |
| **GBP1** | -3.53 | 0.0000 | 0.84 | 0.0016 | guanylate binding protein 1, interferon-inducible, 67kDa |
| **GLB1** | -1.99 | 0.0000 | 0.60 | 0.0022 | galactosidase, beta 1 |
| **GLS** | -2.38 | 0.0000 | 0.83 | 0.0049 | glutaminase |
| **GPR56** | -4.61 | 0.0000 | 1.04 | 0.0055 | G protein-coupled receptor 56 |
| **GRN** | -1.66 | 0.0000 | 0.76 | 0.0016 | granulin |
| **H6PD** | -1.65 | 0.0000 | 0.87 | 0.0013 | hexose-6-phosphate dehydrogenase (glucose 1-dehydrogenase) |
| **HAS2** | 5.15 | 0.0000 | -2.97 | 0.0000 | hyaluronan synthase 2 |
| **HBP1** | -1.47 | 0.0000 | 0.84 | 0.0056 | HMG-box transcription factor 1 |
| **HEATR5A** | -3.07 | 0.0000 | 0.80 | 0.0009 | HEAT repeat containing 5A |
| **HGF** | 2.61 | 0.0000 | -0.61 | 0.0063 | hepatocyte growth factor (hepapoietin A; scatter factor) |
| **HHIP** | 3.86 | 0.0000 | -1.69 | 0.0000 | hedgehog interacting protein |

| Gene In DS-6 | ST88 vs HSC .logFC | ST88 vs HSC. adjPVal | U0126 vs DMSO .logFC | U0126 vs DMSO .adjPVal | Descriptions |
|---|---|---|---|---|---|
| **HMGA2** | 7.96 | 0.0000 | -1.10 | 0.0030 | high mobility group AT-hook 2 |
| **HSPE1** | 1.11 | 0.0000 | -0.85 | 0.0002 | heat shock 10kDa protein 1 (chaperonin 10) |
| **IFIH1** | -1.99 | 0.0000 | 1.17 | 0.0002 | interferon induced with helicase C domain 1 |
| **IGBP1** | -1.49 | 0.0000 | 0.73 | 0.0001 | chromosome 14 open reading frame 19; immunoglobulin (CD79A) binding protein 1 |
| **IGF2BP3** | 4.64 | 0.0000 | -0.90 | 0.0093 | insulin-like growth factor 2 mRNA binding protein 3 |
| **IL8** | 3.68 | 0.0000 | -4.89 | 0.0000 | interleukin 8 |
| **INHBB** | 4.43 | 0.0000 | -1.70 | 0.0006 | inhibin, beta B |
| **ITGAV** | -2.13 | 0.0000 | 0.76 | 0.0085 | integrin, alpha V (vitronectin receptor, alpha polypeptide, antigen CD51) |
| **KCTD1** | -1.48 | 0.0000 | 0.69 | 0.0055 | potassium channel tetramerisation domain containing 1 |
| **KIAA0020** | 1.45 | 0.0000 | -0.62 | 0.0013 | KIAA0020 |
| **KLHL24** | -1.40 | 0.0000 | 0.81 | 0.0000 | kelch-like 24 (Drosophila) |
| **LHPP** | -3.11 | 0.0000 | 1.43 | 0.0000 | phospholysine phosphohistidine inorganic pyrophosphate phosphatase |
| **LIG1** | 1.39 | 0.0000 | -0.73 | 0.0022 | ligase I, DNA, ATP-dependent |
| **LIMD2** | 2.24 | 0.0000 | -0.60 | 0.0034 | LIM domain containing 2 |
| **LMO4** | -2.74 | 0.0000 | 0.72 | 0.0033 | LIM domain only 4 |
| **LRRC8C** | 1.51 | 0.0000 | -1.11 | 0.0000 | leucine rich repeat containing 8 family, member C |
| **LRRN1** | -4.21 | 0.0000 | 1.76 | 0.0001 | leucine rich repeat neuronal 1 |
| **LXN** | -5.62 | 0.0000 | 1.78 | 0.0031 | latexin |
| **LYAR** | 1.25 | 0.0000 | -0.89 | 0.0000 | Ly1 antibody reactive homolog (mouse) |
| **LYST** | -3.86 | 0.0000 | 1.03 | 0.0082 | lysosomal trafficking regulator |
| **MAGED1** | -0.87 | 0.0000 | 0.68 | 0.0001 | melanoma antigen family D, 1 |
| **MAP3K5** | 2.81 | 0.0000 | -0.86 | 0.0089 | mitogen-activated protein kinase kinase kinase 5 |
| **MATN2** | -2.69 | 0.0000 | 1.51 | 0.0041 | matrilin 2 |
| **MCM10** | 1.43 | 0.0000 | -0.96 | 0.0011 | minichromosome maintenance complex component 10 |
| **MMP9** | 2.76 | 0.0000 | -0.76 | 0.0012 | matrix metallopeptidase 9 (gelatinase B, 92kDa gelatinase, 92kDa type IV collagenase) |
| **MOXD1** | -5.46 | 0.0000 | 1.21 | 0.0018 | monooxygenase, DBH-like 1 |
| **MTAP** | 1.31 | 0.0000 | -0.70 | 0.0018 | methylthioadenosine phosphorylase |
| **MXD4** | -1.06 | 0.0000 | 0.73 | 0.0027 | MAX dimerization protein 4 |
| **MXRA8** | -4.41 | 0.0000 | 1.58 | 0.0091 | matrix-remodelling associated 8 |
| **MYO19** | 1.54 | 0.0000 | -0.64 | 0.0043 | myosin XIX |
| **NAV2** | -3.02 | 0.0000 | 1.33 | 0.0001 | neuron navigator 2 |

| Gene In DS-6 | ST88 vs HSC .logFC | ST88 vs HSC. adjPVal | U0126 vs DMSO .logFC | U0126 vs DMSO .adjPVal | Descriptions |
|---|---|---|---|---|---|
| **NETO2** | 3.29 | 0.0000 | -0.73 | 0.0028 | neuropilin (NRP) and tolloid (TLL)-like 2 |
| **NHS** | 1.30 | 0.0000 | -0.82 | 0.0008 | Nance-Horan syndrome (congenital cataracts and dental anomalies) |
| **NIPAL3** | -1.20 | 0.0000 | 0.76 | 0.0019 | NIPA-like domain containing 3 |
| **NOP16** | 1.16 | 0.0000 | -0.69 | 0.0036 | NOP16 nucleolar protein homolog (yeast) |
| **NOP56** | 1.74 | 0.0000 | -0.64 | 0.0020 | NOP56 ribonucleoprotein homolog (yeast) |
| **NOP58** | 1.27 | 0.0000 | -0.61 | 0.0010 | NOP58 ribonucleoprotein homolog (yeast) |
| **NOTCH2** | -1.00 | 0.0000 | 0.78 | 0.0002 | Notch homolog 2 (Drosophila) |
| **NQO1** | -1.75 | 0.0000 | 1.16 | 0.0017 | NAD(P)H dehydrogenase, quinone 1 |
| **NRP2** | -2.88 | 0.0000 | 0.91 | 0.0000 | neuropilin 2 |
| **NUDCD1** | 1.19 | 0.0000 | -0.75 | 0.0000 | NudC domain containing 1 |
| **NUP35** | 1.22 | 0.0000 | -0.75 | 0.0002 | nucleoporin 35kDa |
| **ODZ3** | -3.38 | 0.0000 | 0.76 | 0.0036 | odz, odd Oz/ten-m homolog 3 (Drosophila) |
| **OPTN** | -3.02 | 0.0000 | 0.82 | 0.0001 | optineurin |
| **ORC1L** | 1.38 | 0.0000 | -0.60 | 0.0034 | origin recognition complex, subunit 1-like (yeast) |
| **PAICS** | 1.52 | 0.0000 | -0.66 | 0.0001 | phosphoribosylaminoimidazole carboxylase, phosphoribosylaminoimidazole succinocarboxamide synthetase |
| **PBXIP1** | -1.10 | 0.0000 | 0.90 | 0.0000 | pre-B-cell leukemia homeobox interacting protein 1 |
| **PIR** | -1.62 | 0.0000 | 0.64 | 0.0099 | pirin (iron-binding nuclear protein) |
| **PNRC1** | -1.90 | 0.0000 | 1.40 | 0.0000 | proline-rich nuclear receptor coactivator 1 |
| **POLR3K** | 1.58 | 0.0000 | -0.78 | 0.0001 | polymerase (RNA) III (DNA directed) polypeptide K, 12.3 kDa |
| **PPAP2A** | -3.06 | 0.0000 | 1.35 | 0.0000 | phosphatidic acid phosphatase type 2A |
| **PPIL5** | 1.09 | 0.0000 | -0.78 | 0.0013 | peptidylprolyl isomerase (cyclophilin)-like 5 |
| **PQLC3** | -1.60 | 0.0000 | 0.68 | 0.0033 | PQ loop repeat containing 3 |
| **PRELID2** | 0.88 | 0.0000 | -0.66 | 0.0009 | PRELI domain containing 2 |
| **PSMB8** | -1.16 | 0.0000 | 0.60 | 0.0086 | proteasome (prosome, macropain) subunit, beta type, 8 (large multifunctional peptidase 7) |
| **PSMB9** | -1.11 | 0.0000 | 0.72 | 0.0035 | proteasome (prosome, macropain) subunit, beta type, 9 (large multifunctional peptidase 2) |
| **PSMC3IP** | 1.37 | 0.0000 | -0.75 | 0.0012 | PSMC3 interacting protein |
| **PTGER4** | 3.72 | 0.0000 | -1.20 | 0.0004 | prostaglandin E receptor 4 (subtype EP4) |
| **PTX3** | 2.98 | 0.0000 | -2.03 | 0.0000 | pentraxin-related gene, rapidly induced by IL-1 beta |
| **RAD18** | 1.14 | 0.0000 | -0.71 | 0.0022 | RAD18 homolog (S. cerevisiae) |
| **RAD54B** | 1.10 | 0.0000 | -0.74 | 0.0092 | RAD54 homolog B (S. cerevisiae) |
| **RASGRF2** | 2.28 | 0.0000 | -1.00 | 0.0010 | Ras protein-specific guanine nucleotide-releasing |

| Gene In DS-6 | ST88 vs HSC .logFC | ST88 vs HSC. adjPVal | U0126 vs DMSO .logFC | U0126 vs DMSO .adjPVal | Descriptions |
|---|---|---|---|---|---|
| | | | | | factor 2 |
| **RFWD3** | 1.29 | 0.0000 | -0.97 | 0.0000 | ring finger and WD repeat domain 3 |
| **RGNEF** | 2.18 | 0.0000 | -1.28 | 0.0001 | Rho-guanine nucleotide exchange factor |
| **RGS17** | 2.54 | 0.0000 | -1.37 | 0.0024 | regulator of G-protein signaling 17 |
| **RGS5** | 3.62 | 0.0000 | -1.14 | 0.0026 | regulator of G-protein signaling 5 |
| **RIPK2** | 1.44 | 0.0000 | -0.90 | 0.0000 | receptor-interacting serine-threonine kinase 2 |
| **RNASEL** | -1.54 | 0.0000 | 0.73 | 0.0023 | ribonuclease L (2',5'-oligoisoadenylate synthetase-dependent) |
| **RNF144B** | -2.45 | 0.0000 | 0.91 | 0.0099 | ring finger protein 144B |
| **RPS6KA5** | -2.12 | 0.0000 | 0.84 | 0.0008 | ribosomal protein S6 kinase, 90kDa, polypeptide 5 |
| **RTP4** | -1.83 | 0.0000 | 1.28 | 0.0009 | receptor (chemosensory) transporter protein 4 |
| **S100A10** | -1.73 | 0.0000 | 0.74 | 0.0091 | S100 calcium binding protein A10 |
| **SAT2** | -1.34 | 0.0000 | 0.70 | 0.0019 | spermidine/spermine N1-acetyltransferase family member 2 |
| **SERF2** | -1.11 | 0.0000 | 0.61 | 0.0085 | chromosome 15 open reading frame 63; small EDRK-rich factor 2 |
| **SERPINB1** | -3.48 | 0.0000 | 0.78 | 0.0054 | serpin peptidase inhibitor, clade B (ovalbumin), member 1 |
| **SH3BP5** | -3.80 | 0.0000 | 0.84 | 0.0011 | SH3-domain binding protein 5 (BTK-associated) |
| **SHISA3** | 3.99 | 0.0000 | -1.62 | 0.0050 | shisa homolog 3 (Xenopus laevis) |
| **SIGLEC15** | 2.03 | 0.0000 | -1.17 | 0.0013 | sialic acid binding Ig-like lectin 15 |
| **SIN3B** | 1.20 | 0.0000 | -0.74 | 0.0030 | SIN3 homolog B, transcription regulator (yeast) |
| **SLC16A4** | -3.39 | 0.0000 | 1.11 | 0.0018 | solute carrier family 16, member 4 (monocarboxylic acid transporter 5) |
| **SLC17A5** | -3.39 | 0.0000 | 0.69 | 0.0078 | solute carrier family 17 (anion/sugar transporter), member 5 |
| **SLC19A1** | 1.46 | 0.0000 | -0.72 | 0.0038 | solute carrier family 19 (folate transporter), member 1 |
| **SLCO4A1** | 3.66 | 0.0000 | -1.34 | 0.0000 | solute carrier organic anion transporter family, member 4A1 |
| **SMURF2** | 2.51 | 0.0000 | -1.13 | 0.0013 | SMAD specific E3 ubiquitin protein ligase 2 |
| **SOLH** | 1.08 | 0.0000 | -1.04 | 0.0013 | small optic lobes homolog (Drosophila) |
| **SOX9** | 5.24 | 0.0000 | -1.40 | 0.0003 | SRY (sex determining region Y)-box 9 |
| **SPARC** | -2.68 | 0.0000 | 1.05 | 0.0063 | secreted protein, acidic, cysteine-rich (osteonectin) |
| **SPIN4** | 1.43 | 0.0000 | -0.78 | 0.0035 | spindlin family, member 4 |
| **SPTLC3** | -3.57 | 0.0000 | 1.48 | 0.0041 | serine palmitoyltransferase, long chain base subunit 3 |

| Gene In DS-6 | ST88 vs HSC .logFC | ST88 vs HSC. adjPVal | U0126 vs DMSO .logFC | U0126 vs DMSO .adjPVal | Descriptions |
|---|---|---|---|---|---|
| **STAMBPL1** | 2.33 | 0.0000 | -0.98 | 0.0002 | STAM binding protein-like 1 |
| **STAT6** | -5.88 | 0.0000 | 0.71 | 0.0009 | signal transducer and activator of transcription 6, interleukin-4 induced |
| **STEAP1** | 2.23 | 0.0000 | -0.94 | 0.0026 | six transmembrane epithelial antigen of the prostate 1 |
| **STX1A** | 2.12 | 0.0000 | -1.05 | 0.0035 | syntaxin 1A (brain) |
| **SVEP1** | 1.64 | 0.0000 | -0.78 | 0.0060 | sushi, von Willebrand factor type A, EGF and pentraxin domain containing 1 |
| **TBC1D8B** | -3.01 | 0.0000 | 0.99 | 0.0017 | TBC1 domain family, member 8B (with GRAM domain) |
| **TIPIN** | 1.36 | 0.0000 | -0.90 | 0.0004 | TIMELESS interacting protein |
| **TLR4** | 4.44 | 0.0000 | -1.44 | 0.0015 | toll-like receptor 4 |
| **TMEM48** | 1.07 | 0.0000 | -0.63 | 0.0017 | transmembrane protein 48 |
| **TMEM59** | -2.05 | 0.0000 | 0.68 | 0.0056 | transmembrane protein 59 |
| **TNFRSF10A** | 2.02 | 0.0000 | -0.87 | 0.0035 | tumor necrosis factor receptor superfamily, member 10a |
| **TNFRSF19** | -1.40 | 0.0000 | 1.59 | 0.0001 | tumor necrosis factor receptor superfamily, member 19 |
| **TP53INP2** | -1.95 | 0.0000 | 0.93 | 0.0041 | tumor protein p53 inducible nuclear protein 2 |
| **TRIM16L** | -1.29 | 0.0000 | 1.28 | 0.0000 | tripartite motif-containing 16-like |
| **TRMT6** | 2.03 | 0.0000 | -0.73 | 0.0021 | tRNA methyltransferase 6 homolog (S. cerevisiae) |
| **TRPA1** | 4.21 | 0.0000 | -2.05 | 0.0000 | transient receptor potential cation channel, subfamily A, member 1 |
| **TSPAN11** | -2.44 | 0.0000 | 1.35 | 0.0036 | tetraspanin 11 |
| **TSPAN31** | -1.39 | 0.0000 | 0.61 | 0.0046 | tetraspanin 31 |
| **UBE2C** | 1.60 | 0.0000 | -1.03 | 0.0000 | ubiquitin-conjugating enzyme E2C |
| **UCK2** | 1.20 | 0.0000 | -0.75 | 0.0002 | uridine-cytidine kinase 2 |
| **UHRF1** | 2.05 | 0.0000 | -0.81 | 0.0013 | ubiquitin-like with PHD and ring finger domains 1 |
| **UST** | -1.56 | 0.0000 | 0.65 | 0.0026 | uronyl-2-sulfotransferase |
| **VAV3** | -1.11 | 0.0000 | 1.15 | 0.0000 | vav 3 guanine nucleotide exchange factor |
| **VEGFC** | 1.52 | 0.0000 | -1.60 | 0.0000 | vascular endothelial growth factor C |
| **VKORC1L1** | 1.09 | 0.0000 | -0.61 | 0.0001 | vitamin K epoxide reductase complex, subunit 1-like 1 |
| **VRK1** | 0.91 | 0.0000 | -0.87 | 0.0000 | vaccinia related kinase 1 |
| **WDHD1** | 1.36 | 0.0000 | -0.67 | 0.0033 | WD repeat and HMG-box DNA binding protein 1 |
| **WDR5** | 1.02 | 0.0000 | -0.91 | 0.0000 | WD repeat domain 5 |
| **ZFYVE26** | -1.27 | 0.0000 | 0.74 | 0.0028 | zinc finger, FYVE domain containing 26 |

| Gene In DS-6 | ST88 vs HSC .logFC | ST88 vs HSC. adjPVal | U0126 vs DMSO .logFC | U0126 vs DMSO .adjPVal | Descriptions |
|---|---|---|---|---|---|
| **ZNF587** | 1.45 | 0.0000 | -1.12 | 0.0000 | zinc finger protein 587 |
| **ZNF695** | 1.46 | 0.0000 | -0.63 | 0.0014 | zinc finger protein 695 |

**Suppl. Table 4: DS-7**

DS-7, intersection of DS-2 (si*NRas* vs. SC) and DS-3(U0126 vs. DMSO), is hypothetically regulated by NRAS-MEK1/2 in ST88-14(*Nf1*$^{-/-}$) cells, with matching the pattern: 1) increase in siN*Ras* versus scrambled control siRNA treated ST88-14 and in U0126 versus DMSO, or 2) decrease in si*NRas* versus scrambled control treated ST88-14 and in U0126 versus DMSO.

| Gene In DS-7 | siNRas vs SC .logFC | siNRas vs SC88 .adjPVal | U0126 vs DMSO .logFC | U0126 vs DMSO .adjPVal | Descriptions |
|---|---|---|---|---|---|
| **ANXA4** | 0.60 | 0.0020 | 1.24 | 0.0000 | annexin A4 |
| **ARHGAP18** | 0.90 | 0.0014 | 0.67 | 0.0019 | Rho GTPase activating protein 18 |
| **ATF3** | 1.04 | 0.0002 | 1.01 | 0.0026 | activating transcription factor 3 |
| **BICD1** | -0.79 | 0.0052 | -0.94 | 0.0007 | bicaudal D homolog 1 (Drosophila) |
| **C21orf34** | 0.67 | 0.0090 | 1.34 | 0.0004 | chromosome 21 open reading frame 34 |
| **C2orf15** | 1.01 | 0.0031 | 1.12 | 0.0014 | chromosome 2 open reading frame 15 |
| **C9orf150** | 0.69 | 0.0036 | 1.05 | 0.0001 | chromosome 9 open reading frame 150 |
| **CHST11** | -1.15 | 0.0007 | -1.00 | 0.0003 | carbohydrate (chondroitin 4) sulfotransferase 11 |
| **KCTD9** | -0.60 | 0.0077 | -0.70 | 0.0004 | similar to Potassium channel tetramerisation domain containing 9; potassium channel tetramerisation domain containing 9; |
| **LOC100128822** | 0.74 | 0.0045 | 0.71 | 0.0018 | hypothetical LOC100128822 |
| **MGC3771** | 0.69 | 0.0059 | 0.85 | 0.0001 | hypothetical LOC81854 |
| **MORC4** | -0.79 | 0.0043 | -0.71 | 0.0025 | MORC family CW-type zinc finger 4 |
| **NT5E** | -1.55 | 0.0003 | -1.26 | 0.0000 | 5'-nucleotidase, ecto (CD73) |
| **PLAT** | -0.98 | 0.0018 | -0.73 | 0.0019 | plasminogen activator, tissue |
| **PTTG2** | -0.68 | 0.0093 | -0.66 | 0.0051 | pituitary tumor-transforming 1; pituitary tumor-transforming 2 |
| **PVRL3** | -0.76 | 0.0003 | -0.99 | 0.0001 | poliovirus receptor-related 3 |
| **SNHG8** | 0.96 | 0.0003 | 0.60 | 0.0019 | small nucleolar RNA host gene 8 (non-protein coding) |
| **SPIN4** | -0.66 | 0.0041 | -0.78 | 0.0035 | spindlin family, member 4 |
| **TFB1M** | -0.92 | 0.0004 | -0.92 | 0.0005 | transcription factor B1, mitochondrial |
| **TUFT1** | 0.85 | 0.0003 | 1.04 | 0.0000 | tuftelin 1 |

**Suppl. Table 5: DS-8**

DS-8, intersection of DS-4 (ST88 vs. HSC), DS-2 (si*NRas* vs. SC) and DS-3 (U0126 vs. DMSO), is hypothetically under the regulation of Neurofibromin-NRAS-MEK1/2 axis, with matching the pattern: 1) decrease in ST88-14 vs. HSC, increase in si*NRas* vs. scrambled control treated ST88-14, but decrease in U0126 vs. DMSO, or 2) increase in ST88-14 vs. HSC, decrease in si*NRas* vs. scrambled control treated ST88-14, but increase in U0126 vs. DMSO.

| Gene in DS-8 | ST88 vs HSC .logFC | ST88 vs HSC .adjPVal | siNRas vs SC .logFC | siNRas vs SC88 .adjPVal | U0126 vs DMSO .logFC | U0126 vs DMSO .adjPVal | Descriptions |
|---|---|---|---|---|---|---|---|
| **ANXA4** | -1.21 | 0.0000 | 0.60 | 0.0019 | 1.24 | 0.0000 | annexin A4 |
| **C21orf34** | -1.19 | 0.0001 | 0.67 | 0.0090 | 1.34 | 0.0004 | chromosome 21 open reading frame 34 |
| **ATF3** | -1.42 | 0.0000 | 1.04 | 0.0001 | 1.01 | 0.0026 | activating transcription factor 3 |
| **CHEK1** | 1.91 | 0.0000 | -0.58 | 0.0051 | -0.66 | 0.0047 | CHK1 checkpoint homolog (S. pombe) |
| **SPIN4** | 1.43 | 0.0000 | -0.66 | 0.0040 | -0.78 | 0.0035 | spindlin family, member 4 |

**Suppl. Table 6: DS-9**

DS-9 is obtained by removal of the overlapped gene with DS-2 (si*NRas* vs. SC) and with DS-3 (U0126 vs. DMSO). These genes are hypothetically Neurofibromin-related but NRAS and MEK1/2 independent.

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **A2M** | -6.22 | 0.0000 | alpha-2-macroglobulin |
| **AARSD1** | 1.21 | 0.0000 | alanyl-tRNA synthetase domain containing 1 |
| **AASDH** | -1.51 | 0.0000 | aminoadipate-semialdehyde dehydrogenase |
| **AASDHPPT** | 1.25 | 0.0000 | aminoadipate-semialdehyde dehydrogenase-phosphopantetheinyl transferase |
| **AASS** | -1.45 | 0.0000 | aminoadipate-semialdehyde synthase |
| **AATK** | -3.28 | 0.0000 | apoptosis-associated tyrosine kinase |
| **ABCA1** | -1.74 | 0.0000 | ATP-binding cassette, sub-family A (ABC1), member 1 |
| **ABCB7** | -0.78 | 0.0000 | ATP-binding cassette, sub-family B (MDR/TAP), member 7 |
| **ABHD12** | -1.58 | 0.0000 | abhydrolase domain containing 12 |
| **ABHD2** | -1.32 | 0.0000 | abhydrolase domain containing 2 |
| **ABHD6** | -3.20 | 0.0000 | abhydrolase domain containing 6 |
| **ABL2** | -1.14 | 0.0000 | v-abl Abelson murine leukemia viral oncogene homolog 2 (arg, Abelson-related gene) |
| **ABLIM3** | -3.31 | 0.0000 | actin binding LIM protein family, member 3 |
| **ABR** | -1.42 | 0.0000 | active BCR-related gene |
| **ACAA1** | -1.58 | 0.0000 | acetyl-Coenzyme A acyltransferase 1 |
| **ACADVL** | -1.26 | 0.0000 | acyl-Coenzyme A dehydrogenase, very long chain |
| **ACBD5** | -1.60 | 0.0000 | acyl-Coenzyme A binding domain containing 5 |
| **ACCN2** | 1.72 | 0.0000 | amiloride-sensitive cation channel 2, neuronal |
| **ACER3** | -2.13 | 0.0000 | alkaline ceramidase 3 |
| **ACOT9** | -1.17 | 0.0000 | acyl-CoA thioesterase 9 |
| **ACSL1** | -1.37 | 0.0000 | acyl-CoA synthetase long-chain family member 1 |
| **ACSS2** | 1.47 | 0.0000 | acyl-CoA synthetase short-chain family member 2 |
| **ACTC1** | -2.95 | 0.0000 | actin, alpha, cardiac muscle 1 |
| **ACTG2** | -3.96 | 0.0000 | actin, gamma 2, smooth muscle, enteric |
| **ACTR10** | -0.95 | 0.0000 | actin-related protein 10 homolog (S. cerevisiae) |
| **ACTR3B** | 1.23 | 0.0000 | ARP3 actin-related protein 3 homolog B (yeast) |
| **ACTR5** | 1.44 | 0.0000 | ARP5 actin-related protein 5 homolog (yeast) |
| **ACVR1B** | -1.36 | 0.0000 | activin A receptor, type IB |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **ACVR2A** | 1.02 | 0.0000 | activin A receptor, type IIA |
| **ACYP2** | -2.11 | 0.0000 | acylphosphatase 2, muscle type |
| **ADAM10** | -2.86 | 0.0000 | ADAM metallopeptidase domain 10 |
| **ADAM17** | -1.66 | 0.0000 | ADAM metallopeptidase domain 17 |
| **ADAM23** | -2.34 | 0.0000 | ADAM metallopeptidase domain 23 |
| **ADAMTS4** | -5.04 | 0.0000 | ADAM metallopeptidase with thrombospondin type 1 motif, 4 |
| **ADAMTS6** | 3.93 | 0.0000 | ADAM metallopeptidase with thrombospondin type 1 motif, 6 |
| **ADAMTS9** | -4.04 | 0.0000 | ADAM metallopeptidase with thrombospondin type 1 motif, 9 |
| **ADAMTSL1** | -3.03 | 0.0000 | ADAMTS-like 1 |
| **ADCY1** | 3.11 | 0.0000 | adenylate cyclase 1 (brain) |
| **ADD1** | -1.09 | 0.0000 | adducin 1 (alpha) |
| **ADD3** | -2.73 | 0.0000 | adducin 3 (gamma) |
| **ADI1** | -1.46 | 0.0000 | acireductone dioxygenase 1 |
| **ADRB2** | 2.01 | 0.0000 | adrenergic, beta-2-, receptor, surface |
| **AFAP1L2** | -5.13 | 0.0000 | actin filament associated protein 1-like 2 |
| **AGA** | -1.98 | 0.0000 | aspartylglucosaminidase |
| **AGFG1** | -0.82 | 0.0000 | ArfGAP with FG repeats 1 |
| **AGFG2** | 1.06 | 0.0000 | ArfGAP with FG repeats 2 |
| **AGPAT9** | -3.37 | 0.0000 | 1-acylglycerol-3-phosphate O-acyltransferase 9 |
| **AHCY** | 1.06 | 0.0000 | adenosylhomocysteinase |
| **AHI1** | -0.93 | 0.0000 | Abelson helper integration site 1 |
| **AHSA2** | 1.81 | 0.0000 | AHA1, activator of heat shock 90kDa protein ATPase homolog 2 (yeast) |
| **AIFM2** | -2.78 | 0.0000 | apoptosis-inducing factor, mitochondrion-associated, 2 |
| **AIG1** | -1.17 | 0.0000 | androgen-induced 1 |
| **AIMP2** | 0.65 | 0.0000 | aminoacyl tRNA synthetase complex-interacting multifunctional protein 2; stromal antigen 3-like 3 |
| **AK2** | 2.15 | 0.0000 | adenylate kinase 2 |
| **AK3L1** | 3.44 | 0.0000 | adenylate kinase 3-like 2; adenylate kinase 3-like 1 |
| **AKAP1** | 1.48 | 0.0000 | A kinase (PRKA) anchor protein 1 |
| **AKAP11** | -1.37 | 0.0000 | A kinase (PRKA) anchor protein 11 |
| **AKAP13** | -2.01 | 0.0000 | A kinase (PRKA) anchor protein 13 |
| **AKAP6** | -1.76 | 0.0000 | A kinase (PRKA) anchor protein 6 |
| **AKIRIN2** | -1.14 | 0.0000 | akirin 2 |
| **AKR1B1** | -1.85 | 0.0000 | aldo-keto reductase family 1, member B1 (aldose reductase) |
| **AKR1B10** | -2.78 | 0.0000 | aldo-keto reductase family 1, member B10 (aldose reductase); aldo-keto reductase family 1, member B10-like |
| **AKR1C1** | -2.22 | 0.0000 | aldo-keto reductase family 1, member C1 (dihydrodiol dehydrogenase 1; |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| | | | 20-alpha (3-alpha)-hydroxysteroid dehydrogenase) |
| **ALDH1A1** | -3.18 | 0.0000 | aldehyde dehydrogenase 1 family, member A1 |
| **ALDH1A2** | 2.46 | 0.0000 | aldehyde dehydrogenase 1 family, member A2 |
| **ALDH3A2** | -1.57 | 0.0000 | aldehyde dehydrogenase 3 family, member A2 |
| **ALDH3B1** | -1.11 | 0.0000 | aldehyde dehydrogenase 3 family, member B1 |
| **ALDH5A1** | 2.00 | 0.0000 | aldehyde dehydrogenase 5 family, member A1 |
| **ALDOA** | 1.17 | 0.0000 | aldolase A, fructose-bisphosphate |
| **ALG9** | -0.70 | 0.0000 | asparagine-linked glycosylation 9, alpha-1,2-mannosyltransferase homolog (S. cerevisiae) |
| **ALS2CR4** | 2.44 | 0.0000 | amyotrophic lateral sclerosis 2 (juvenile) chromosome region, candidate 4 |
| **AMIGO2** | 5.18 | 0.0000 | adhesion molecule with Ig-like domain 2 |
| **AMOTL1** | -1.44 | 0.0000 | angiomotin like 1 |
| **AMOTL2** | 2.42 | 0.0000 | angiomotin like 2 |
| **AMZ2** | 1.23 | 0.0000 | archaelysin family metallopeptidase 2 |
| **ANAPC1** | 0.80 | 0.0000 | anaphase promoting complex subunit 1; similar to anaphase promoting complex subunit 1 |
| **ANG** | -2.13 | 0.0000 | angiogenin, ribonuclease, RNase A family, 5 |
| **ANK2** | -2.71 | 0.0000 | ankyrin 2, neuronal |
| **ANK3** | -2.19 | 0.0000 | ankyrin 3, node of Ranvier (ankyrin G) |
| **ANKFY1** | -0.97 | 0.0000 | ankyrin repeat and FYVE domain containing 1 |
| **ANKH** | -1.23 | 0.0000 | ankylosis, progressive homolog (mouse) |
| **ANKRD10** | -1.48 | 0.0000 | ankyrin repeat domain 10 |
| **ANKRD12** | -1.74 | 0.0000 | ankyrin repeat domain 12 |
| **ANKRD17** | -1.28 | 0.0000 | ankyrin repeat domain 17 |
| **ANKRD18A** | 3.91 | 0.0000 | ankyrin repeat domain 18A |
| **ANKRD20A2** | 2.37 | 0.0000 | hCG2042718; chromosome 21 open reading frame 81; ankyrin repeat domain 20 family, member A1; ankyrin repeat domain 20 family, member A3; ankyrin repeat domain 20 family, member A2 |
| **ANKRD28** | -2.33 | 0.0000 | ankyrin repeat domain 28 |
| **ANKRD35** | -2.45 | 0.0000 | ankyrin repeat domain 35 |
| **ANKRD42** | -0.82 | 0.0000 | ankyrin repeat domain 42 |
| **ANKRD44** | -1.90 | 0.0000 | ankyrin repeat domain 44 |
| **ANKRD50** | -1.66 | 0.0000 | ankyrin repeat domain 50 |
| **ANKRD6** | -2.45 | 0.0000 | ankyrin repeat domain 6 |
| **ANKRD7** | 1.82 | 0.0000 | ankyrin repeat domain 7 |
| **ANKS1A** | -0.86 | 0.0000 | ankyrin repeat and sterile alpha motif domain containing 1A |
| **ANO6** | -2.22 | 0.0000 | anoctamin 6 |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **ANXA1** | -1.38 | 0.0000 | annexin A1 |
| **ANXA11** | -1.43 | 0.0000 | annexin A11 |
| **ANXA5** | -1.65 | 0.0000 | annexin A5 |
| **ANXA7** | -1.31 | 0.0000 | annexin A7 |
| **AP1G1** | -0.77 | 0.0000 | adaptor-related protein complex 1, gamma 1 subunit |
| **AP3D1** | -2.30 | 0.0000 | adaptor-related protein complex 3, delta 1 subunit |
| **AP4E1** | -1.18 | 0.0000 | adaptor-related protein complex 4, epsilon 1 subunit |
| **APBA2** | 1.90 | 0.0000 | amyloid beta (A4) precursor protein-binding, family A, member 2 |
| **APC2** | 2.04 | 0.0000 | adenomatosis polyposis coli 2 |
| **APH1B** | -1.51 | 0.0000 | anterior pharynx defective 1 homolog B (C. elegans) |
| **API5** | -0.95 | 0.0000 | API5-like 1; apoptosis inhibitor 5 |
| **AQP7** | -2.25 | 0.0000 | aquaporin 7 |
| **AQR** | 1.17 | 0.0000 | aquarius homolog (mouse) |
| **AR** | 2.70 | 0.0000 | androgen receptor |
| **ARF6** | -1.10 | 0.0000 | ADP-ribosylation factor 6 |
| **ARFIP1** | -1.56 | 0.0000 | ADP-ribosylation factor interacting protein 1 |
| **ARHGAP12** | -1.90 | 0.0000 | Rho GTPase activating protein 12 |
| **ARHGAP17** | 1.09 | 0.0000 | Rho GTPase activating protein 17 |
| **ARHGAP19** | -1.41 | 0.0000 | Rho GTPase activating protein 19 |
| **ARHGAP21** | -1.93 | 0.0000 | Rho GTPase activating protein 21 |
| **ARHGAP26** | -1.74 | 0.0000 | Rho GTPase activating protein 26 |
| **ARHGAP28** | 3.65 | 0.0000 | Rho GTPase activating protein 28 |
| **ARHGAP29** | 5.08 | 0.0000 | Rho GTPase activating protein 29 |
| **ARHGAP5** | -1.80 | 0.0000 | Rho GTPase activating protein 5 |
| **ARHGDIA** | -1.92 | 0.0000 | Rho GDP dissociation inhibitor (GDI) alpha |
| **ARHGDIB** | 2.43 | 0.0000 | Rho GDP dissociation inhibitor (GDI) beta |
| **ARHGEF12** | -1.26 | 0.0000 | Rho guanine nucleotide exchange factor (GEF) 12 |
| **ARHGEF19** | 1.26 | 0.0000 | Rho guanine nucleotide exchange factor (GEF) 19 |
| **ARID3B** | 1.92 | 0.0000 | AT rich interactive domain 3B (BRIGHT-like) |
| **ARID4A** | -1.07 | 0.0000 | AT rich interactive domain 4A (RBP1-like) |
| **ARIH2** | -1.09 | 0.0000 | ariadne homolog 2 (Drosophila) |
| **ARL16** | 1.39 | 0.0000 | ADP-ribosylation factor-like 16 |
| **ARL3** | -1.47 | 0.0000 | ADP-ribosylation factor-like 3 |
| **ARL4D** | -0.99 | 0.0000 | ADP-ribosylation factor-like 4D |
| **ARL5A** | -1.47 | 0.0000 | ADP-ribosylation factor-like 5A |
| **ARL8B** | -1.65 | 0.0000 | ADP-ribosylation factor-like 8B |
| **ARMC8** | 0.79 | 0.0000 | armadillo repeat containing 8 |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **ARMC9** | -2.52 | 0.0000 | armadillo repeat containing 9 |
| **ARNTL** | -1.94 | 0.0000 | aryl hydrocarbon receptor nuclear translocator-like |
| **ARNTL2** | 1.73 | 0.0000 | aryl hydrocarbon receptor nuclear translocator-like 2 |
| **ARPC1B** | -2.26 | 0.0000 | actin related protein 2/3 complex, subunit 1B, 41kDa; similar to Actin-related protein 2/3 complex subunit 1B (ARP2/3 complex 41 kDa subunit) (p41-ARC) |
| **ARSA** | -1.34 | 0.0000 | arylsulfatase A |
| **ARSE** | -1.55 | 0.0000 | arylsulfatase E (chondrodysplasia punctata 1) |
| **ARSJ** | 3.09 | 0.0000 | arylsulfatase family, member J |
| **ASAH1** | -3.01 | 0.0000 | N-acylsphingosine amidohydrolase (acid ceramidase) 1 |
| **ASAM** | 2.18 | 0.0000 | adipocyte-specific adhesion molecule |
| **ASAP3** | 2.79 | 0.0000 | ArfGAP with SH3 domain, ankyrin repeat and PH domain 3 |
| **ASB1** | 1.20 | 0.0000 | ankyrin repeat and SOCS box-containing 1 |
| **ASH2L** | -0.94 | 0.0000 | ash2 (absent, small, or homeotic)-like (Drosophila) |
| **ASL** | -1.53 | 0.0000 | argininosuccinate lyase |
| **ASRGL1** | 1.86 | 0.0000 | asparaginase like 1 |
| **ASTN1** | 2.71 | 0.0000 | astrotactin 1 |
| **ASTN2** | 1.52 | 0.0000 | astrotactin 2 |
| **ASXL1** | 0.83 | 0.0000 | additional sex combs like 1 (Drosophila) |
| **ATAD1** | -0.79 | 0.0000 | ATPase family, AAA domain containing 1 |
| **ATAD2** | 2.24 | 0.0000 | ATPase family, AAA domain containing 2 |
| **ATF6B** | -1.62 | 0.0000 | activating transcription factor 6 beta |
| **ATF7IP** | -1.71 | 0.0000 | activating transcription factor 7 interacting protein |
| **ATG16L2** | -1.94 | 0.0000 | ATG16 autophagy related 16-like 2 (S. cerevisiae) |
| **ATG3** | -0.62 | 0.0000 | ATG3 autophagy related 3 homolog (S. cerevisiae) |
| **ATG7** | -1.23 | 0.0000 | ATG7 autophagy related 7 homolog (S. cerevisiae) |
| **ATIC** | 1.53 | 0.0000 | 5-aminoimidazole-4-carboxamide ribonucleotide formyltransferase/IMP cyclohydrolase |
| **ATOX1** | -1.37 | 0.0000 | ATX1 antioxidant protein 1 homolog (yeast) |
| **ATP10A** | 2.43 | 0.0000 | ATPase, class V, type 10A |
| **ATP11C** | 1.56 | 0.0000 | ATPase, class VI, type 11C |
| **ATP1A1** | -1.94 | 0.0000 | ATPase, Na+/K+ transporting, alpha 1 polypeptide |
| **ATP1A3** | -1.81 | 0.0000 | ATPase, Na+/K+ transporting, alpha 3 polypeptide |
| **ATP1A4** | -1.11 | 0.0000 | ATPase, Na+/K+ transporting, alpha 4 polypeptide |
| **ATP2A2** | -1.32 | 0.0000 | ATPase, Ca++ transporting, cardiac muscle, slow twitch 2 |
| **ATP6AP2** | -1.83 | 0.0000 | ATPase, H+ transporting, lysosomal accessory protein 2 |
| **ATP6V0A4** | -1.98 | 0.0000 | ATPase, H+ transporting, lysosomal V0 subunit a4 |
| **ATP6V0B** | -1.58 | 0.0000 | ATPase, H+ transporting, lysosomal 21kDa, V0 subunit b |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **ATP6V0C** | -0.89 | 0.0000 | ATPase, H+ transporting, lysosomal 16kDa, V0 subunit c |
| **ATP6V0D1** | -1.61 | 0.0000 | ATPase, H+ transporting, lysosomal 38kDa, V0 subunit d1 |
| **ATP6V0E1** | -0.97 | 0.0000 | ATPase, H+ transporting, lysosomal 9kDa, V0 subunit e1 |
| **ATP6V1A** | -2.07 | 0.0000 | ATPase, H+ transporting, lysosomal 70kDa, V1 subunit A |
| **ATP6V1B2** | -1.97 | 0.0000 | ATPase, H+ transporting, lysosomal 56/58kDa, V1 subunit B2 |
| **ATP6V1C1** | -0.98 | 0.0000 | ATPase, H+ transporting, lysosomal 42kDa, V1 subunit C1 |
| **ATP6V1E1** | -1.64 | 0.0000 | ATPase, H+ transporting, lysosomal 31kDa, V1 subunit E1 |
| **ATP6V1H** | -1.65 | 0.0000 | ATPase, H+ transporting, lysosomal 50/57kDa, V1 subunit H |
| **ATP8A1** | -1.77 | 0.0000 | ATPase, aminophospholipid transporter (APLT), class I, type 8A, member 1 |
| **ATP8B3** | -2.96 | 0.0000 | ATPase, class I, type 8B, member 3 |
| **ATP9A** | 5.12 | 0.0000 | ATPase, class II, type 9A |
| **ATR** | 0.66 | 0.0000 | ataxia telangiectasia and Rad3 related; similar to ataxia telangiectasia and Rad3 related protein |
| **ATXN2L** | 1.30 | 0.0000 | ataxin 2-like |
| **AVPI1** | -3.00 | 0.0000 | arginine vasopressin-induced 1 |
| **AZGP1** | -3.74 | 0.0000 | alpha-2-glycoprotein 1, zinc-binding pseudogene 1; alpha-2-glycoprotein 1, zinc-binding |
| **AZI1** | 1.39 | 0.0000 | 5-azacytidine induced 1 |
| **B2M** | -3.51 | 0.0000 | beta-2-microglobulin |
| **B3GALT4** | -4.85 | 0.0000 | UDP-Gal:betaGlcNAc beta 1,3-galactosyltransferase, polypeptide 4 |
| **B4GALNT4** | 1.65 | 0.0000 | beta-1,4-N-acetyl-galactosaminyl transferase 4 |
| **BACE1** | -2.15 | 0.0000 | beta-site APP-cleaving enzyme 1 |
| **BACE2** | -3.41 | 0.0000 | beta-site APP-cleaving enzyme 2 |
| **BACH1** | 1.33 | 0.0000 | BTB and CNC homology 1, basic leucine zipper transcription factor 1 |
| **BAG2** | 1.82 | 0.0000 | BCL2-associated athanogene 2 |
| **BAI1** | 2.83 | 0.0000 | brain-specific angiogenesis inhibitor 1 |
| **BAIAP2L1** | 2.07 | 0.0000 | BAI1-associated protein 2-like 1 |
| **BAIAP2L2** | -1.96 | 0.0000 | BAI1-associated protein 2-like 2 |
| **BASP1** | 4.16 | 0.0000 | brain abundant, membrane attached signal protein 1 |
| **BATF3** | 1.91 | 0.0000 | basic leucine zipper transcription factor, ATF-like 3 |
| **BAZ1B** | 1.15 | 0.0000 | bromodomain adjacent to zinc finger domain, 1B |
| **BBS2** | 1.04 | 0.0000 | Bardet-Biedl syndrome 2 |
| **BBS7** | -1.13 | 0.0000 | Bardet-Biedl syndrome 7 |
| **BCAT1** | 4.11 | 0.0000 | branched chain aminotransferase 1, cytosolic |
| **BCL11B** | 2.20 | 0.0000 | B-cell CLL/lymphoma 11B (zinc finger protein) |
| **BCL2** | -1.42 | 0.0000 | B-cell CLL/lymphoma 2 |
| **BCL2L13** | -1.20 | 0.0000 | BCL2-like 13 (apoptosis facilitator) |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **BCL7C** | 1.11 | 0.0000 | B-cell CLL/lymphoma 7C |
| **BEND5** | 2.38 | 0.0000 | BEN domain containing 5 |
| **BEST1** | -2.55 | 0.0000 | bestrophin 1 |
| **BET1** | 1.05 | 0.0000 | hypothetical protein LOC100128542; blocked early in transport 1 homolog (S. cerevisiae) |
| **BFSP1** | 3.82 | 0.0000 | beaded filament structural protein 1, filensin |
| **BHLHB9** | -1.14 | 0.0000 | basic helix-loop-helix domain containing, class B, 9 |
| **BHLHE40** | -2.20 | 0.0000 | basic helix-loop-helix family, member e40 |
| **BHLHE41** | 2.00 | 0.0000 | basic helix-loop-helix family, member e41 |
| **BIN3** | -1.31 | 0.0000 | bridging integrator 3 |
| **BLMH** | -0.91 | 0.0000 | bleomycin hydrolase |
| **BMP2** | 1.77 | 0.0000 | bone morphogenetic protein 2 |
| **BMP2K** | -1.70 | 0.0000 | BMP2 inducible kinase |
| **BMP4** | 3.53 | 0.0000 | bone morphogenetic protein 4 |
| **BMP6** | 4.95 | 0.0000 | bone morphogenetic protein 6 |
| **BMP7** | 4.88 | 0.0000 | bone morphogenetic protein 7 |
| **BNC1** | 3.66 | 0.0000 | basonuclin 1 |
| **BNC2** | 1.98 | 0.0000 | basonuclin 2 |
| **BNIP3L** | -1.50 | 0.0000 | BCL2/adenovirus E1B 19kDa interacting protein 3-like |
| **BOD1** | 0.95 | 0.0000 | biorientation of chromosomes in cell division 1 |
| **BOLA2B** | 1.56 | 0.0000 | bolA homolog 2 (E. coli); bolA homolog 2B (E. coli) |
| **BOP1** | 2.31 | 0.0000 | block of proliferation 1 |
| **BPGM** | -1.45 | 0.0000 | 2,3-bisphosphoglycerate mutase |
| **BRI3** | -1.65 | 0.0000 | brain protein I3; brain protein I3 pseudogene 1 |
| **BRIP1** | 1.90 | 0.0000 | BRCA1 interacting protein C-terminal helicase 1 |
| **BSG** | -0.94 | 0.0000 | basigin (Ok blood group) |
| **BST1** | -3.39 | 0.0000 | bone marrow stromal cell antigen 1 |
| **BTBD1** | -0.81 | 0.0000 | BTB (POZ) domain containing 1 |
| **BTBD3** | -1.54 | 0.0000 | BTB (POZ) domain containing 3 |
| **BTD** | -3.25 | 0.0000 | biotinidase |
| **BTG1** | -2.10 | 0.0000 | B-cell translocation gene 1, anti-proliferative |
| **BTN2A2** | -1.76 | 0.0000 | butyrophilin, subfamily 2, member A2 |
| **BVES** | -2.29 | 0.0000 | blood vessel epicardial substance |
| **C10orf10** | -2.29 | 0.0000 | chromosome 10 open reading frame 10 |
| **C10orf11** | -2.61 | 0.0000 | chromosome 10 open reading frame 11 |
| **C10orf111** | 1.10 | 0.0000 | chromosome 10 open reading frame 111 |
| **C10orf114** | -2.44 | 0.0000 | chromosome 10 open reading frame 114 |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **C10orf116** | -2.33 | 0.0000 | chromosome 10 open reading frame 116 |
| **C10orf18** | -1.87 | 0.0000 | chromosome 10 open reading frame 18 |
| **C10orf2** | 0.88 | 0.0000 | chromosome 10 open reading frame 2 |
| **C10orf32** | -1.47 | 0.0000 | chromosome 10 open reading frame 32 |
| **C10orf35** | 2.36 | 0.0000 | chromosome 10 open reading frame 35 |
| **C11orf1** | 1.15 | 0.0000 | chromosome 11 open reading frame 1 |
| **C11orf61** | 1.86 | 0.0000 | chromosome 11 open reading frame 61 |
| **C11orf75** | 1.56 | 0.0000 | hypothetical LOC728675; chromosome 11 open reading frame 75 |
| **C11orf9** | 1.79 | 0.0000 | chromosome 11 open reading frame 9 |
| **C12orf26** | -1.66 | 0.0000 | chromosome 12 open reading frame 26 |
| **C12orf45** | 1.21 | 0.0000 | chromosome 12 open reading frame 45 |
| **C12orf47** | 1.85 | 0.0000 | chromosome 12 open reading frame 47 |
| **C12orf53** | 1.81 | 0.0000 | chromosome 12 open reading frame 53 |
| **C12orf66** | 1.01 | 0.0000 | chromosome 12 open reading frame 66 |
| **C13orf18** | -1.80 | 0.0000 | similar to protein phosphatase 1, regulatory subunit 2; protein phosphatase 1, regulatory (inhibitor) subunit 2 pseudogene 4; chromosome 13 open reading frame 18 |
| **C14orf128** | -1.64 | 0.0000 | chromosome 14 open reading frame 128 |
| **C14orf139** | -2.15 | 0.0000 | chromosome 14 open reading frame 139 |
| **C14orf147** | -2.09 | 0.0000 | chromosome 14 open reading frame 147 |
| **C14orf166** | -1.18 | 0.0000 | chromosome 14 open reading frame 166 |
| **C14orf4** | -1.31 | 0.0000 | chromosome 14 open reading frame 4 |
| **C14orf43** | -1.30 | 0.0000 | chromosome 14 open reading frame 43 |
| **C15orf41** | 2.07 | 0.0000 | chromosome 15 open reading frame 41 |
| **C15orf48** | -4.09 | 0.0000 | chromosome 15 open reading frame 48 |
| **C16orf5** | 2.41 | 0.0000 | chromosome 16 open reading frame 5 |
| **C16orf53** | 1.22 | 0.0000 | chromosome 16 open reading frame 53 |
| **C16orf59** | 1.49 | 0.0000 | chromosome 16 open reading frame 59 |
| **C16orf68** | 1.82 | 0.0000 | chromosome 16 open reading frame 68 |
| **C16orf74** | 3.12 | 0.0000 | chromosome 16 open reading frame 74 |
| **C16orf75** | 3.75 | 0.0000 | chromosome 16 open reading frame 75 |
| **C16orf86** | -1.88 | 0.0000 | chromosome 16 open reading frame 86 |
| **C17orf37** | -1.67 | 0.0000 | chromosome 17 open reading frame 37 |
| **C17orf39** | 1.37 | 0.0000 | chromosome 17 open reading frame 39 |
| **C17orf56** | 0.99 | 0.0000 | chromosome 17 open reading frame 56 |
| **C17orf58** | 1.91 | 0.0000 | chromosome 17 open reading frame 58 |
| **C17orf59** | -1.39 | 0.0000 | chromosome 17 open reading frame 59 |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **C17orf67** | 1.96 | 0.0000 | chromosome 17 open reading frame 67 |
| **C17orf72** | 2.47 | 0.0000 | chromosome 17 open reading frame 72 |
| **C17orf75** | 0.95 | 0.0000 | chromosome 17 open reading frame 75 |
| **C17orf79** | -0.70 | 0.0000 | chromosome 17 open reading frame 79 |
| **C17orf80** | 1.28 | 0.0000 | chromosome 17 open reading frame 80 |
| **C17orf86** | 1.92 | 0.0000 | chromosome 17 open reading frame 86 |
| **C17orf89** | 1.39 | 0.0000 | chromosome 17 open reading frame 89 |
| **C18orf32** | -1.34 | 0.0000 | chromosome 18 open reading frame 32 |
| **C18orf56** | 1.65 | 0.0000 | chromosome 18 open reading frame 56 |
| **C18orf8** | -0.84 | 0.0000 | chromosome 18 open reading frame 8 |
| **C19orf28** | -4.54 | 0.0000 | chromosome 19 open reading frame 28 |
| **C19orf56** | -1.07 | 0.0000 | chromosome 19 open reading frame 56 |
| **C19orf63** | -2.17 | 0.0000 | chromosome 19 open reading frame 63 |
| **C19orf66** | -2.24 | 0.0000 | chromosome 19 open reading frame 66 |
| **C1D** | 1.52 | 0.0000 | C1D nuclear receptor co-repressor; similar to nuclear DNA-binding protein; similar to hCG1791993 |
| **C1GALT1C1** | -1.43 | 0.0000 | C1GALT1-specific chaperone 1 |
| **C1orf103** | 1.97 | 0.0000 | chromosome 1 open reading frame 103 |
| **C1orf106** | 2.51 | 0.0000 | chromosome 1 open reading frame 106 |
| **C1orf174** | 0.72 | 0.0000 | chromosome 1 open reading frame 174 |
| **C1orf204** | 1.29 | 0.0000 | chromosome 1 open reading frame 204; V-set and immunoglobulin domain containing 8 |
| **C1orf213** | 2.00 | 0.0000 | chromosome 1 open reading frame 213 |
| **C1orf53** | 2.06 | 0.0000 | chromosome 1 open reading frame 53 |
| **C1orf59** | 3.28 | 0.0000 | chromosome 1 open reading frame 59 |
| **C1orf85** | -2.03 | 0.0000 | chromosome 1 open reading frame 85 |
| **C1orf88** | -1.49 | 0.0000 | chromosome 1 open reading frame 88 |
| **C1orf9** | 0.95 | 0.0000 | chromosome 1 open reading frame 9 |
| **C1QBP** | 0.78 | 0.0000 | complement component 1, q subcomponent binding protein |
| **C20orf108** | -1.09 | 0.0000 | chromosome 20 open reading frame 108 |
| **C20orf11** | 1.59 | 0.0000 | chromosome 20 open reading frame 11 |
| **C20orf111** | 1.13 | 0.0000 | chromosome 20 open reading frame 111 |
| **C20orf199** | 2.04 | 0.0000 | chromosome 20 open reading frame 199 |
| **C20orf20** | 1.57 | 0.0000 | chromosome 20 open reading frame 20 |
| **C20orf24** | 0.97 | 0.0000 | chromosome 20 open reading frame 24 |
| **C20orf27** | 1.24 | 0.0000 | chromosome 20 open reading frame 27 |
| **C20orf3** | -0.99 | 0.0000 | chromosome 20 open reading frame 3 |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **C21orf45** | 1.60 | 0.0000 | chromosome 21 open reading frame 45 |
| **C21orf91** | 1.03 | 0.0000 | chromosome 21 open reading frame 91 |
| **C22orf29** | 1.22 | 0.0000 | chromosome 22 open reading frame 29 |
| **C22orf32** | -1.32 | 0.0000 | chromosome 22 open reading frame 32 |
| **C22orf9** | -1.64 | 0.0000 | chromosome 22 open reading frame 9 |
| **C2orf27A** | -1.08 | 0.0000 | hypothetical LOC642669; chromosome 2 open reading frame 27A; hypothetical LOC644525 |
| **C2orf34** | -1.06 | 0.0000 | chromosome 2 open reading frame 34 |
| **C2orf44** | 1.19 | 0.0000 | chromosome 2 open reading frame 44 |
| **C2orf47** | 0.91 | 0.0000 | chromosome 2 open reading frame 47 |
| **C2orf79** | -0.92 | 0.0000 | chromosome 2 open reading frame 79 |
| **C3AR1** | -3.72 | 0.0000 | complement component 3a receptor 1 |
| **C3orf10** | -0.92 | 0.0000 | chromosome 3 open reading frame 10 |
| **C3orf52** | 1.65 | 0.0000 | chromosome 3 open reading frame 52 |
| **C3orf59** | 1.06 | 0.0000 | chromosome 3 open reading frame 59 |
| **C4orf19** | 1.72 | 0.0000 | chromosome 4 open reading frame 19 |
| **C4orf27** | -1.27 | 0.0000 | chromosome 4 open reading frame 27 |
| **C4orf32** | 1.63 | 0.0000 | chromosome 4 open reading frame 32 |
| **C4orf33** | -1.54 | 0.0000 | chromosome 4 open reading frame 33 |
| **C4orf49** | 2.66 | 0.0000 | chromosome 4 open reading frame 49 |
| **C5orf23** | 4.23 | 0.0000 | chromosome 5 open reading frame 23 |
| **C5orf30** | -1.31 | 0.0000 | chromosome 5 open reading frame 30 |
| **C5orf32** | -2.18 | 0.0000 | chromosome 5 open reading frame 32 |
| **C5orf34** | 1.26 | 0.0000 | chromosome 5 open reading frame 34 |
| **C6orf1** | -2.11 | 0.0000 | chromosome 6 open reading frame 1 |
| **C6orf106** | -0.96 | 0.0000 | chromosome 6 open reading frame 106 |
| **C6orf129** | -1.11 | 0.0000 | chromosome 6 open reading frame 129 |
| **C6orf134** | -1.26 | 0.0000 | chromosome 6 open reading frame 134 |
| **C6orf203** | -1.14 | 0.0000 | chromosome 6 open reading frame 203 |
| **C6orf204** | -1.12 | 0.0000 | chromosome 6 open reading frame 204 |
| **C6orf218** | -2.19 | 0.0000 | chromosome 6 open reading frame 218 |
| **C7orf13** | 1.23 | 0.0000 | chromosome 7 open reading frame 13 |
| **C7orf29** | -2.63 | 0.0000 | chromosome 7 open reading frame 29 |
| **C7orf30** | 1.07 | 0.0000 | chromosome 7 open reading frame 30 |
| **C7orf40** | 1.74 | 0.0000 | chromosome 7 open reading frame 40 |
| **C7orf58** | 2.75 | 0.0000 | chromosome 7 open reading frame 58 |
| **C7orf68** | 1.11 | 0.0000 | chromosome 7 open reading frame 68 |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **C8orf33** | 1.73 | 0.0000 | chromosome 8 open reading frame 33 |
| **C8orf4** | -3.77 | 0.0000 | chromosome 8 open reading frame 4 |
| **C8orf46** | -1.50 | 0.0000 | chromosome 8 open reading frame 46 |
| **C8orf58** | 1.08 | 0.0000 | chromosome 8 open reading frame 58 |
| **C8orf76** | 0.96 | 0.0000 | chromosome 8 open reading frame 76 |
| **C8ORFK29** | 1.53 | 0.0000 | hypothetical LOC340393 |
| **C9orf109** | 2.31 | 0.0000 | chromosome 9 open reading frame 109 |
| **C9orf116** | 1.37 | 0.0000 | chromosome 9 open reading frame 116 |
| **C9orf123** | 1.04 | 0.0000 | chromosome 9 open reading frame 123 |
| **C9orf80** | 1.03 | 0.0000 | chromosome 9 open reading frame 80 |
| **C9orf86** | 2.24 | 0.0000 | chromosome 9 open reading frame 86 |
| **C9orf91** | 1.36 | 0.0000 | chromosome 9 open reading frame 91 |
| **CA13** | -1.16 | 0.0000 | carbonic anhydrase XIII |
| **CAB39L** | -4.28 | 0.0000 | calcium binding protein 39-like |
| **CABLES1** | 2.58 | 0.0000 | Cdk5 and Abl enzyme substrate 1 |
| **CABLES2** | 2.31 | 0.0000 | Cdk5 and Abl enzyme substrate 2 |
| **CACNA1H** | 1.78 | 0.0000 | calcium channel, voltage-dependent, T type, alpha 1H subunit |
| **CACNA2D4** | -2.57 | 0.0000 | calcium channel, voltage-dependent, alpha 2/delta subunit 4 |
| **CACNG6** | 2.05 | 0.0000 | calcium channel, voltage-dependent, gamma subunit 6 |
| **CADPS2** | 2.24 | 0.0000 | Ca++-dependent secretion activator 2 |
| **CALB1** | 2.79 | 0.0000 | calbindin 1, 28kDa |
| **CALHM2** | -3.99 | 0.0000 | calcium homeostasis modulator 2 |
| **CALML4** | 1.66 | 0.0000 | calmodulin-like 4 |
| **CALU** | -1.88 | 0.0000 | calumenin |
| **CAMK1D** | 2.57 | 0.0000 | calcium/calmodulin-dependent protein kinase ID |
| **CAMK2D** | -0.92 | 0.0000 | calcium/calmodulin-dependent protein kinase II delta |
| **CAMK2G** | 1.40 | 0.0000 | calcium/calmodulin-dependent protein kinase II gamma |
| **CAMKV** | 1.31 | 0.0000 | CaM kinase-like vesicle-associated |
| **CAMTA1** | -1.01 | 0.0000 | calmodulin binding transcription activator 1 |
| **CANX** | -1.39 | 0.0000 | calnexin |
| **CAP1** | -2.47 | 0.0000 | CAP, adenylate cyclase-associated protein 1 (yeast) |
| **CAPN3** | -2.95 | 0.0000 | calpain 3, (p94) |
| **CAPN5** | -1.11 | 0.0000 | calpain 5 |
| **CAPRIN2** | -1.81 | 0.0000 | caprin family member 2 |
| **CAPS** | -2.29 | 0.0000 | calcyphosine |
| **CAPSL** | 0.97 | 0.0000 | calcyphosine-like |
| **CARD10** | -1.81 | 0.0000 | caspase recruitment domain family, member 10 |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **CARD6** | -1.92 | 0.0000 | caspase recruitment domain family, member 6 |
| **CARD8** | -1.08 | 0.0000 | caspase recruitment domain family, member 8 |
| **CARS2** | -1.68 | 0.0000 | cysteinyl-tRNA synthetase 2, mitochondrial (putative) |
| **CASKIN1** | 1.38 | 0.0000 | CASK interacting protein 1 |
| **CASP2** | 0.93 | 0.0000 | caspase 2, apoptosis-related cysteine peptidase |
| **CASP6** | -1.27 | 0.0000 | caspase 6, apoptosis-related cysteine peptidase |
| **CASP9** | -0.91 | 0.0000 | caspase 9, apoptosis-related cysteine peptidase |
| **CAT** | -1.19 | 0.0000 | catalase |
| **CAV1** | 1.56 | 0.0000 | caveolin 1, caveolae protein, 22kDa |
| **CBLB** | 2.00 | 0.0000 | Cas-Br-M (murine) ecotropic retroviral transforming sequence b |
| **CBR1** | -1.27 | 0.0000 | carbonyl reductase 1 |
| **CBR4** | -0.76 | 0.0000 | carbonyl reductase 4 |
| **CBWD5** | 2.08 | 0.0000 | COBW domain containing 5; similar to COBW domain containing 1; COBW domain containing 7; COBW domain containing 3 |
| **CCDC102A** | 2.12 | 0.0000 | coiled-coil domain containing 102A |
| **CCDC113** | 1.50 | 0.0000 | coiled-coil domain containing 113 |
| **CCDC137** | 1.65 | 0.0000 | coiled-coil domain containing 137 |
| **CCDC144NL** | 1.92 | 0.0000 | coiled-coil domain containing 144 family, N-terminal like |
| **CCDC22** | -0.87 | 0.0000 | coiled-coil domain containing 22 |
| **CCDC25** | -0.85 | 0.0000 | coiled-coil domain containing 25 |
| **CCDC3** | 3.72 | 0.0000 | coiled-coil domain containing 3 |
| **CCDC53** | -1.07 | 0.0000 | coiled-coil domain containing 53 |
| **CCDC55** | -1.19 | 0.0000 | coiled-coil domain containing 55 |
| **CCDC59** | -1.14 | 0.0000 | coiled-coil domain containing 59 |
| **CCDC71** | -2.64 | 0.0000 | coiled-coil domain containing 71 |
| **CCDC80** | -1.47 | 0.0000 | coiled-coil domain containing 80 |
| **CCDC85C** | 4.43 | 0.0000 | coiled-coil domain containing 85C |
| **CCDC86** | 1.42 | 0.0000 | coiled-coil domain containing 86 |
| **CCDC99** | 2.29 | 0.0000 | coiled-coil domain containing 99 |
| **CCK** | 3.93 | 0.0000 | cholecystokinin |
| **CCNE1** | 1.61 | 0.0000 | cyclin E1 |
| **CCNI** | -1.24 | 0.0000 | cyclin I |
| **CCNO** | 1.98 | 0.0000 | cyclin O |
| **CCPG1** | -2.04 | 0.0000 | cell cycle progression 1 |
| **CCR1** | -3.72 | 0.0000 | chemokine (C-C motif) receptor 1 |
| **CCT6A** | 0.69 | 0.0000 | chaperonin containing TCP1, subunit 6A (zeta 1) |
| **CCT6P1** | 0.90 | 0.0000 | chaperonin containing TCP1, subunit 6 (zeta) pseudogene 1 |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **CCT8** | 0.97 | 0.0000 | similar to chaperonin containing TCP1, subunit 8 (theta); chaperonin containing TCP1, subunit 8 (theta) |
| **CD109** | -1.32 | 0.0000 | CD109 molecule |
| **CD14** | -0.96 | 0.0000 | CD14 molecule |
| **CD164** | -1.12 | 0.0000 | CD164 molecule, sialomucin |
| **CD1D** | 4.11 | 0.0000 | CD1d molecule |
| **CD24** | 7.05 | 0.0000 | CD24 molecule; CD24 molecule-like 4 |
| **CD276** | -1.88 | 0.0000 | CD276 molecule |
| **CD2BP2** | 1.60 | 0.0000 | CD2 (cytoplasmic tail) binding protein 2 |
| **CD34** | 5.23 | 0.0000 | CD34 molecule |
| **CD3EAP** | 1.67 | 0.0000 | CD3e molecule, epsilon associated protein |
| **CD58** | -3.02 | 0.0000 | CD58 molecule |
| **CD59** | -1.82 | 0.0000 | CD59 molecule, complement regulatory protein |
| **CD63** | -2.47 | 0.0000 | CD63 molecule |
| **CD68** | -2.31 | 0.0000 | CD68 molecule |
| **CD70** | 3.40 | 0.0000 | CD70 molecule |
| **CD81** | -1.97 | 0.0000 | CD81 molecule |
| **CD9** | -3.05 | 0.0000 | CD9 molecule |
| **CD97** | -3.82 | 0.0000 | CD97 molecule |
| **CD99** | -1.94 | 0.0000 | CD99 molecule |
| **CDADC1** | -2.06 | 0.0000 | cytidine and dCMP deaminase domain containing 1 |
| **CDC14B** | -1.28 | 0.0000 | CDC14 cell division cycle 14 homolog B (S. cerevisiae) |
| **CDC14C** | -1.11 | 0.0000 | CDC14 cell division cycle 14 homolog C (S. cerevisiae) |
| **CDC42EP3** | 1.32 | 0.0000 | CDC42 effector protein (Rho GTPase binding) 3 |
| **CDC42SE1** | -1.28 | 0.0000 | CDC42 small effector 1 |
| **CDCA7** | 2.85 | 0.0000 | cell division cycle associated 7 |
| **CDCA7L** | 1.33 | 0.0000 | cell division cycle associated 7-like |
| **CDH13** | 3.83 | 0.0000 | cadherin 13, H-cadherin (heart) |
| **CDH15** | -2.72 | 0.0000 | cadherin 15, type 1, M-cadherin (myotubule) |
| **CDK2AP1** | -1.46 | 0.0000 | cyclin-dependent kinase 2 associated protein 1 |
| **CDK7** | 0.95 | 0.0000 | cyclin-dependent kinase 7 |
| **CDKL2** | -2.00 | 0.0000 | cyclin-dependent kinase-like 2 (CDC2-related kinase) |
| **CDKN1B** | -1.32 | 0.0000 | cyclin-dependent kinase inhibitor 1B (p27, Kip1) |
| **CDKN2A** | -3.86 | 0.0000 | cyclin-dependent kinase inhibitor 2A (melanoma, p16, inhibits CDK4) |
| **CDKN2AIPNL** | 1.06 | 0.0000 | CDKN2A interacting protein N-terminal like |
| **CDKN2C** | -2.84 | 0.0000 | cyclin-dependent kinase inhibitor 2C (p18, inhibits CDK4) |
| **CDS1** | 1.82 | 0.0000 | CDP-diacylglycerol synthase (phosphatidate cytidylyltransferase) 1 |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **CEACAM1** | -5.76 | 0.0000 | carcinoembryonic antigen-related cell adhesion molecule 1 (biliary glycoprotein) |
| **CEBPA** | 1.65 | 0.0000 | CCAAT/enhancer binding protein (C/EBP), alpha |
| **CEBPG** | 1.27 | 0.0000 | CCAAT/enhancer binding protein (C/EBP), gamma |
| **CELSR2** | -2.04 | 0.0000 | cadherin, EGF LAG seven-pass G-type receptor 2 (flamingo homolog, Drosophila) |
| **CENPH** | 1.42 | 0.0000 | centromere protein H |
| **CENPK** | 2.10 | 0.0000 | centromere protein K |
| **CENPV** | 3.80 | 0.0000 | centromere protein V |
| **CETN2** | 1.25 | 0.0000 | centrin, EF-hand protein, 2 |
| **CETN3** | 1.10 | 0.0000 | centrin, EF-hand protein, 3 (CDC31 homolog, yeast) |
| **CFDP1** | -0.89 | 0.0000 | craniofacial development protein 1 |
| **CGREF1** | 2.57 | 0.0000 | cell growth regulator with EF-hand domain 1 |
| **CHADL** | -1.76 | 0.0000 | chondroadherin-like |
| **CHCHD5** | -1.58 | 0.0000 | coiled-coil-helix-coiled-coil-helix domain containing 5 |
| **CHFR** | -1.49 | 0.0000 | checkpoint with forkhead and ring finger domains |
| **CHKB** | -1.54 | 0.0000 | choline kinase beta; carnitine palmitoyltransferase 1B (muscle) |
| **CHML** | 1.67 | 0.0000 | choroideremia-like (Rab escort protein 2) |
| **CHMP1B** | -1.36 | 0.0000 | chromatin modifying protein 1B |
| **CHMP2A** | -2.38 | 0.0000 | chromatin modifying protein 2A |
| **CHMP4A** | -0.97 | 0.0000 | chromatin modifying protein 4A |
| **CHRAC1** | 1.35 | 0.0000 | chromatin accessibility complex 1 |
| **CHRD** | 2.45 | 0.0000 | chordin |
| **CHRNA5** | 2.28 | 0.0000 | cholinergic receptor, nicotinic, alpha 5 |
| **CHST3** | -2.12 | 0.0000 | carbohydrate (chondroitin 6) sulfotransferase 3 |
| **CHURC1** | -2.19 | 0.0000 | churchill domain containing 1 |
| **CIB1** | -1.22 | 0.0000 | calcium and integrin binding 1 (calmyrin) |
| **CIITA** | -2.98 | 0.0000 | class II, major histocompatibility complex, transactivator |
| **CITED4** | 2.86 | 0.0000 | Cbp/p300-interacting transactivator, with Glu/Asp-rich carboxy-terminal domain, 4 |
| **CKAP4** | 2.92 | 0.0000 | cytoskeleton-associated protein 4 |
| **CLASP2** | -1.67 | 0.0000 | cytoplasmic linker associated protein 2 |
| **CLCF1** | -1.80 | 0.0000 | cardiotrophin-like cytokine factor 1 |
| **CLCN3** | -2.35 | 0.0000 | chloride channel 3 |
| **CLCN5** | -2.08 | 0.0000 | chloride channel 5 |
| **CLDN1** | 4.87 | 0.0000 | claudin 1 |
| **CLDN11** | 2.48 | 0.0000 | claudin 11 |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **CLDN23** | -1.64 | 0.0000 | claudin 23 |
| **CLDND1** | -1.04 | 0.0000 | claudin domain containing 1 |
| **CLIC4** | -1.82 | 0.0000 | chloride intracellular channel 4 |
| **CLIP1** | -1.01 | 0.0000 | CAP-GLY domain containing linker protein 1 |
| **CLIP4** | -2.00 | 0.0000 | CAP-GLY domain containing linker protein family, member 4 |
| **CLMN** | -3.09 | 0.0000 | calmin (calponin-like, transmembrane) |
| **CLN3** | 1.61 | 0.0000 | ceroid-lipofuscinosis, neuronal 3 |
| **CLN5** | -2.32 | 0.0000 | ceroid-lipofuscinosis, neuronal 5 |
| **CLOCK** | -1.30 | 0.0000 | clock homolog (mouse) |
| **CLP1** | 0.93 | 0.0000 | CLP1, cleavage and polyadenylation factor I subunit, homolog (S. cerevisiae) |
| **CLSTN1** | -1.41 | 0.0000 | calsyntenin 1 |
| **CLU** | 1.95 | 0.0000 | clusterin |
| **CMBL** | 2.72 | 0.0000 | carboxymethylenebutenolidase homolog (Pseudomonas) |
| **CMTM6** | -1.03 | 0.0000 | CKLF-like MARVEL transmembrane domain containing 6 |
| **CNN3** | -1.89 | 0.0000 | calponin 3, acidic |
| **CNOT1** | 1.44 | 0.0000 | CCR4-NOT transcription complex, subunit 1 |
| **CNP** | -2.68 | 0.0000 | 2',3'-cyclic nucleotide 3' phosphodiesterase |
| **CNPY2** | -2.17 | 0.0000 | canopy 2 homolog (zebrafish) |
| **CNPY3** | -1.12 | 0.0000 | canopy 3 homolog (zebrafish) |
| **CNRIP1** | 2.44 | 0.0000 | cannabinoid receptor interacting protein 1 |
| **CNTNAP1** | 1.90 | 0.0000 | contactin associated protein 1 |
| **CNTNAP3** | 6.08 | 0.0000 | contactin associated protein-like 3; contactin associated protein-like 3B |
| **COCH** | 4.21 | 0.0000 | coagulation factor C homolog, cochlin (Limulus polyphemus) |
| **COL11A2** | -4.08 | 0.0000 | collagen, type XI, alpha 2 |
| **COL12A1** | 1.52 | 0.0000 | collagen, type XII, alpha 1 |
| **COL14A1** | -4.56 | 0.0000 | collagen, type XIV, alpha 1 |
| **COL18A1** | -2.58 | 0.0000 | collagen, type XVIII, alpha 1 |
| **COL21A1** | 4.72 | 0.0000 | collagen, type XXI, alpha 1 |
| **COL4A3BP** | -3.42 | 0.0000 | collagen, type IV, alpha 3 (Goodpasture antigen) binding protein |
| **COL4A5** | 1.38 | 0.0000 | collagen, type IV, alpha 5 |
| **COL4A6** | 1.51 | 0.0000 | collagen, type IV, alpha 6 |
| **COL7A1** | -3.26 | 0.0000 | collagen, type VII, alpha 1 |
| **COL9A2** | -3.59 | 0.0000 | collagen, type IX, alpha 2 |
| **COL9A3** | -2.95 | 0.0000 | collagen, type IX, alpha 3 |
| **COMP** | 3.07 | 0.0000 | cartilage oligomeric matrix protein |
| **COPS6** | 0.93 | 0.0000 | COP9 constitutive photomorphogenic homolog subunit 6 (Arabidopsis) |
| **COQ9** | 0.99 | 0.0000 | coenzyme Q9 homolog (S. cerevisiae) |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **COX17** | -1.02 | 0.0000 | COX17 cytochrome c oxidase assembly homolog (S. cerevisiae) |
| **COX4I1** | -1.28 | 0.0000 | cytochrome c oxidase subunit IV isoform 1 |
| **COX7A2** | -0.84 | 0.0000 | cytochrome c oxidase subunit VIIa polypeptide 2 (liver) |
| **CPA4** | 5.06 | 0.0000 | carboxypeptidase A4 |
| **CPD** | -1.54 | 0.0000 | carboxypeptidase D |
| **CPEB1** | -2.35 | 0.0000 | cytoplasmic polyadenylation element binding protein 1 |
| **CPM** | 1.45 | 0.0000 | carboxypeptidase M |
| **CPNE3** | -1.37 | 0.0000 | copine III |
| **CPNE5** | -1.41 | 0.0000 | copine V |
| **CPT1C** | -3.69 | 0.0000 | carnitine palmitoyltransferase 1C |
| **CPT2** | -1.07 | 0.0000 | carnitine palmitoyltransferase 2 |
| **CPVL** | 4.57 | 0.0000 | carboxypeptidase, vitellogenic-like |
| **CRABP2** | 2.62 | 0.0000 | cellular retinoic acid binding protein 2 |
| **CRADD** | -1.62 | 0.0000 | CASP2 and RIPK1 domain containing adaptor with death domain |
| **CRBN** | -1.77 | 0.0000 | cereblon |
| **CREB3L2** | -1.29 | 0.0000 | cAMP responsive element binding protein 3-like 2 |
| **CREB3L4** | 1.60 | 0.0000 | cAMP responsive element binding protein 3-like 4 |
| **CREBL2** | -2.23 | 0.0000 | cAMP responsive element binding protein-like 2 |
| **CREBZF** | 2.16 | 0.0000 | CREB/ATF bZIP transcription factor |
| **CRELD1** | -1.49 | 0.0000 | cysteine-rich with EGF-like domains 1 |
| **CREM** | -1.29 | 0.0000 | cAMP responsive element modulator |
| **CRHBP** | -1.78 | 0.0000 | corticotropin releasing hormone binding protein |
| **CRIM1** | 2.33 | 0.0000 | cysteine rich transmembrane BMP regulator 1 (chordin-like) |
| **CRIP1** | -1.75 | 0.0000 | cysteine-rich protein 1 (intestinal) |
| **CRLF1** | -4.05 | 0.0000 | cytokine receptor-like factor 1 |
| **CRLS1** | 1.19 | 0.0000 | cardiolipin synthase 1 |
| **CRMP1** | 3.09 | 0.0000 | collapsin response mediator protein 1 |
| **CRNDE** | 3.53 | 0.0000 | hCG1815491 |
| **CRNKL1** | 1.07 | 0.0000 | crooked neck pre-mRNA splicing factor-like 1 (Drosophila) |
| **CRY1** | 1.42 | 0.0000 | cryptochrome 1 (photolyase-like) |
| **CRYAB** | -5.56 | 0.0000 | crystallin, alpha B |
| **CRYGS** | -3.56 | 0.0000 | crystallin, gamma S |
| **CSDA** | 1.60 | 0.0000 | cold shock domain protein A; cold shock domain protein A pseudogene 1 |
| **CSDE1** | -1.00 | 0.0000 | cold shock domain containing E1, RNA-binding |
| **CSGALNACT2** | -1.75 | 0.0000 | chondroitin sulfate N-acetylgalactosaminyltransferase 2; novel protein similar to chondroitin sulfate GalNAcT-2 (GALNACT-2) |
| **CSH1** | -0.89 | 0.0000 | chorionic somatomammotropin hormone 1 (placental lactogen) |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **CSNK1E** | -1.53 | 0.0000 | casein kinase 1, epsilon |
| **CSNK2A2** | 1.08 | 0.0000 | casein kinase 2, alpha prime polypeptide |
| **CSRNP1** | -0.80 | 0.0000 | cysteine-serine-rich nuclear protein 1 |
| **CSRP1** | -2.39 | 0.0000 | cysteine and glycine-rich protein 1 |
| **CSRP2** | -3.11 | 0.0000 | cysteine and glycine-rich protein 2 |
| **CSTB** | -1.16 | 0.0000 | cystatin B (stefin B) |
| **CSTF1** | 0.99 | 0.0000 | cleavage stimulation factor, 3' pre-RNA, subunit 1, 50kDa |
| **CSTF2T** | -2.12 | 0.0000 | cleavage stimulation factor, 3' pre-RNA, subunit 2, 64kDa, tau variant |
| **CTDSPL2** | 1.33 | 0.0000 | CTD (carboxy-terminal domain, RNA polymerase II, polypeptide A) small phosphatase like 2 |
| **CTGF** | 3.10 | 0.0000 | connective tissue growth factor |
| **CTNNA1** | -1.94 | 0.0000 | catenin (cadherin-associated protein), alpha 1, 102kDa |
| **CTNNAL1** | -1.38 | 0.0000 | catenin (cadherin-associated protein), alpha-like 1 |
| **CTNND1** | -1.56 | 0.0000 | catenin (cadherin-associated protein), delta 1 |
| **CTNND2** | 3.16 | 0.0000 | catenin (cadherin-associated protein), delta 2 (neural plakophilin-related arm-repeat protein) |
| **CTNS** | -1.62 | 0.0000 | cystinosis, nephropathic |
| **CTPS2** | -0.99 | 0.0000 | CTP synthase II |
| **CTSA** | -1.19 | 0.0000 | cathepsin A |
| **CTSB** | -1.83 | 0.0000 | cathepsin B |
| **CTSC** | -2.40 | 0.0000 | cathepsin C |
| **CTSD** | -2.70 | 0.0000 | cathepsin D |
| **CTSH** | 1.68 | 0.0000 | cathepsin H |
| **CTSL2** | 2.03 | 0.0000 | cathepsin L2 |
| **CTSO** | -2.54 | 0.0000 | cathepsin O |
| **CTSZ** | -3.74 | 0.0000 | cathepsin Z |
| **CTTNBP2NL** | -0.90 | 0.0000 | CTTNBP2 N-terminal like |
| **CUTA** | -1.25 | 0.0000 | cutA divalent cation tolerance homolog (E. coli) |
| **CXorf23** | -1.83 | 0.0000 | chromosome X open reading frame 23 |
| **CXorf26** | -1.60 | 0.0000 | chromosome X open reading frame 26 |
| **CXorf38** | -1.13 | 0.0000 | chromosome X open reading frame 38 |
| **CYB561D2** | -1.49 | 0.0000 | cytochrome b-561 domain containing 2 |
| **CYB5R3** | -1.34 | 0.0000 | cytochrome b5 reductase 3 |
| **CYBRD1** | -1.17 | 0.0000 | cytochrome b reductase 1 |
| **CYLD** | -1.83 | 0.0000 | cylindromatosis (turban tumor syndrome) |
| **CYP24A1** | 3.22 | 0.0000 | cytochrome P450, family 24, subfamily A, polypeptide 1 |
| **CYP27B1** | 2.39 | 0.0000 | cytochrome P450, family 27, subfamily B, polypeptide 1 |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **CYP4V2** | -3.21 | 0.0000 | cytochrome P450, family 4, subfamily V, polypeptide 2 |
| **CYTSB** | -2.14 | 0.0000 | cytospin B |
| **D4S234E** | 2.37 | 0.0000 | DNA segment on chromosome 4 (unique) 234 expressed sequence |
| **DAAM2** | -2.13 | 0.0000 | dishevelled associated activator of morphogenesis 2 |
| **DACH1** | 3.93 | 0.0000 | dachshund homolog 1 (Drosophila) |
| **DAD1** | -0.96 | 0.0000 | defender against cell death 1 |
| **DAG1** | -2.92 | 0.0000 | dystroglycan 1 (dystrophin-associated glycoprotein 1) |
| **DAPK1** | 3.12 | 0.0000 | death-associated protein kinase 1 |
| **DBI** | -1.52 | 0.0000 | diazepam binding inhibitor (GABA receptor modulator, acyl-Coenzyme A binding protein) |
| **DBNDD1** | -2.15 | 0.0000 | dysbindin (dystrobrevin binding protein 1) domain containing 1 |
| **DBT** | -1.24 | 0.0000 | dihydrolipoamide branched chain transacylase E2 |
| **DCAF13** | 1.34 | 0.0000 | WD repeats and SOF1 domain containing |
| **DCPS** | -1.22 | 0.0000 | decapping enzyme, scavenger |
| **DCTN6** | -1.96 | 0.0000 | dynactin 6 |
| **DCTPP1** | 2.12 | 0.0000 | dCTP pyrophosphatase 1 |
| **DCUN1D1** | 0.67 | 0.0000 | DCN1, defective in cullin neddylation 1, domain containing 1 (S. cerevisiae) |
| **DDAH1** | 2.17 | 0.0000 | dimethylarginine dimethylaminohydrolase 1 |
| **DDB2** | 1.40 | 0.0000 | damage-specific DNA binding protein 2, 48kDa |
| **DDR1** | -2.96 | 0.0000 | discoidin domain receptor tyrosine kinase 1 |
| **DDX10** | 1.07 | 0.0000 | DEAD (Asp-Glu-Ala-Asp) box polypeptide 10 |
| **DDX17** | -1.11 | 0.0000 | DEAD (Asp-Glu-Ala-Asp) box polypeptide 17 |
| **DDX23** | 0.93 | 0.0000 | DEAD (Asp-Glu-Ala-Asp) box polypeptide 23 |
| **DDX27** | 1.30 | 0.0000 | DEAD (Asp-Glu-Ala-Asp) box polypeptide 27 |
| **DDX46** | 1.24 | 0.0000 | DEAD (Asp-Glu-Ala-Asp) box polypeptide 46 |
| **DEFB109P1** | -3.42 | 0.0000 | defensin, beta 109, pseudogene 1; defensin, beta 109, pseudogene 1B |
| **DEGS1** | -1.65 | 0.0000 | degenerative spermatocyte homolog 1, lipid desaturase (Drosophila) |
| **DENND1A** | 1.01 | 0.0000 | DENN/MADD domain containing 1A |
| **DENND2A** | 3.05 | 0.0000 | DENN/MADD domain containing 2A |
| **DENND2D** | 2.22 | 0.0000 | DENN/MADD domain containing 2D |
| **DENND3** | 2.29 | 0.0000 | DENN/MADD domain containing 3 |
| **DENND5A** | -1.72 | 0.0000 | DENN/MADD domain containing 5A |
| **DEPDC4** | 1.33 | 0.0000 | DEP domain containing 4 |
| **DERA** | -1.49 | 0.0000 | 2-deoxyribose-5-phosphate aldolase homolog (C. elegans) |
| **DEXI** | 1.32 | 0.0000 | dexamethasone-induced transcript |
| **DFFA** | 0.96 | 0.0000 | DNA fragmentation factor, 45kDa, alpha polypeptide |
| **DGAT2** | 2.09 | 0.0000 | diacylglycerol O-acyltransferase homolog 2 (mouse) |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **DGCR2** | -1.20 | 0.0000 | DiGeorge syndrome critical region gene 2 |
| **DGKD** | 1.51 | 0.0000 | diacylglycerol kinase, delta 130kDa |
| **DGUOK** | -0.78 | 0.0000 | deoxyguanosine kinase |
| **DHODH** | 1.35 | 0.0000 | dihydroorotate dehydrogenase |
| **DHRS1** | -1.74 | 0.0000 | dehydrogenase/reductase (SDR family) member 1 |
| **DHRS7** | -1.27 | 0.0000 | dehydrogenase/reductase (SDR family) member 7 |
| **DHRS7B** | -0.95 | 0.0000 | dehydrogenase/reductase (SDR family) member 7B |
| **DHX35** | 1.33 | 0.0000 | DEAH (Asp-Glu-Ala-His) box polypeptide 35 |
| **DHX58** | -2.79 | 0.0000 | DEXH (Asp-Glu-X-His) box polypeptide 58 |
| **DIABLO** | 0.80 | 0.0000 | diablo homolog (Drosophila) |
| **DIDO1** | 1.97 | 0.0000 | death inducer-obliterator 1 |
| **DIP2B** | -1.91 | 0.0000 | DIP2 disco-interacting protein 2 homolog B (Drosophila) |
| **DIP2C** | -2.75 | 0.0000 | DIP2 disco-interacting protein 2 homolog C (Drosophila) |
| **DIS3** | -1.18 | 0.0000 | DIS3 mitotic control homolog (S. cerevisiae) |
| **DKC1** | 1.84 | 0.0000 | dyskeratosis congenita 1, dyskerin |
| **DKK1** | 5.15 | 0.0000 | dickkopf homolog 1 (Xenopus laevis) |
| **DKK2** | 2.93 | 0.0000 | dickkopf homolog 2 (Xenopus laevis) |
| **DKK3** | -3.36 | 0.0000 | dickkopf homolog 3 (Xenopus laevis) |
| **DLGAP4** | -1.54 | 0.0000 | discs, large (Drosophila) homolog-associated protein 4 |
| **DLL1** | 2.95 | 0.0000 | delta-like 1 (Drosophila) |
| **DLL3** | 2.93 | 0.0000 | delta-like 3 (Drosophila) |
| **DLX1** | 1.47 | 0.0000 | distal-less homeobox 1 |
| **DLX4** | 3.16 | 0.0000 | distal-less homeobox 4 |
| **DMKN** | 2.71 | 0.0000 | dermokine |
| **DMXL1** | -1.86 | 0.0000 | Dmx-like 1 |
| **DNAH14** | 0.87 | 0.0000 | dynein, axonemal, heavy chain 14 |
| **DNAJA3** | 1.62 | 0.0000 | DnaJ (Hsp40) homolog, subfamily A, member 3 |
| **DNAJB11** | -0.67 | 0.0000 | DnaJ (Hsp40) homolog, subfamily B, member 11 |
| **DNAJB12** | -1.23 | 0.0000 | DnaJ (Hsp40) homolog, subfamily B, member 12 |
| **DNAJC1** | -1.80 | 0.0000 | DnaJ (Hsp40) homolog, subfamily C, member 1 |
| **DNAJC2** | 1.43 | 0.0000 | DnaJ (Hsp40) homolog, subfamily C, member 2 |
| **DNAJC21** | 0.92 | 0.0000 | DnaJ (Hsp40) homolog, subfamily C, member 21 |
| **DNAJC22** | 1.98 | 0.0000 | DnaJ (Hsp40) homolog, subfamily C, member 22 |
| **DNAJC3** | -1.64 | 0.0000 | DnaJ (Hsp40) homolog, subfamily C, member 3 |
| **DNAJC6** | -1.92 | 0.0000 | DnaJ (Hsp40) homolog, subfamily C, member 6 |
| **DNALI1** | -4.36 | 0.0000 | dynein, axonemal, light intermediate chain 1 |
| **DOCK1** | -1.36 | 0.0000 | dedicator of cytokinesis 1 |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **DOCK10** | 1.53 | 0.0000 | dedicator of cytokinesis 10 |
| **DOCK3** | 1.56 | 0.0000 | dedicator of cytokinesis 3 |
| **DOCK4** | 1.55 | 0.0000 | dedicator of cytokinesis 4 |
| **DOCK7** | -1.07 | 0.0000 | dedicator of cytokinesis 7 |
| **DOCK8** | 2.07 | 0.0000 | dedicator of cytokinesis 8 |
| **DOK1** | -1.15 | 0.0000 | docking protein 1-like protein; docking protein 1, 62kDa (downstream of tyrosine kinase 1) |
| **DPF2** | 0.88 | 0.0000 | D4, zinc and double PHD fingers family 2 |
| **DPF3** | 2.15 | 0.0000 | D4, zinc and double PHD fingers, family 3 |
| **DPP8** | -1.15 | 0.0000 | dipeptidyl-peptidase 8 |
| **DPYSL2** | 1.42 | 0.0000 | dihydropyrimidinase-like 2 |
| **DPYSL4** | 3.01 | 0.0000 | dihydropyrimidinase-like 4 |
| **DRAM2** | -1.32 | 0.0000 | DNA-damage regulated autophagy modulator 2 |
| **DSN1** | 1.64 | 0.0000 | DSN1, MIND kinetochore complex component, homolog (S. cerevisiae) |
| **DST** | -1.61 | 0.0000 | dystonin |
| **DSTN** | 1.11 | 0.0000 | destrin (actin depolymerizing factor) |
| **DTWD2** | -1.53 | 0.0000 | similar to DTW domain containing 2; DTW domain containing 2 |
| **DUS4L** | 1.84 | 0.0000 | dihydrouridine synthase 4-like (S. cerevisiae) |
| **DUSP1** | 2.55 | 0.0000 | dual specificity phosphatase 1 |
| **DUSP10** | -2.05 | 0.0000 | dual specificity phosphatase 10 |
| **DUSP12** | -1.21 | 0.0000 | dual specificity phosphatase 12 |
| **DUSP5P** | 0.96 | 0.0000 | dual specificity phosphatase 5 pseudogene |
| **DUSP8** | -1.74 | 0.0000 | dual specificity phosphatase 8 |
| **DUXAP10** | 3.18 | 0.0000 | double homeobox A pseudogene 10 |
| **DYNC1I1** | -1.80 | 0.0000 | dynein, cytoplasmic 1, intermediate chain 1 |
| **DYNC1I2** | -0.85 | 0.0000 | similar to dynein cytoplasmic 1 intermediate chain 2; dynein, cytoplasmic 1, intermediate chain 2 |
| **DYNC1LI2** | -2.13 | 0.0000 | dynein, cytoplasmic 1, light intermediate chain 2 |
| **E2F2** | 1.59 | 0.0000 | E2F transcription factor 2 |
| **E2F6** | 1.15 | 0.0000 | E2F transcription factor 6 |
| **E2F8** | 2.34 | 0.0000 | E2F transcription factor 8 |
| **EBF4** | 1.50 | 0.0000 | early B-cell factor 4 |
| **ECHDC1** | -1.83 | 0.0000 | enoyl Coenzyme A hydratase domain containing 1 |
| **ECHDC2** | -4.02 | 0.0000 | enoyl Coenzyme A hydratase domain containing 2 |
| **ECM1** | -2.22 | 0.0000 | extracellular matrix protein 1 |
| **EDEM1** | -0.92 | 0.0000 | ER degradation enhancer, mannosidase alpha-like 1 |
| **EDNRB** | -7.37 | 0.0000 | endothelin receptor type B |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **EEA1** | -1.24 | 0.0000 | early endosome antigen 1 |
| **EEF1A2** | 3.47 | 0.0000 | eukaryotic translation elongation factor 1 alpha 2 |
| **EFEMP1** | 6.53 | 0.0000 | EGF-containing fibulin-like extracellular matrix protein 1 |
| **EFHA1** | -3.82 | 0.0000 | EF-hand domain family, member A1 |
| **EFHD1** | 2.64 | 0.0000 | EF-hand domain family, member D1 |
| **EFNA4** | 1.49 | 0.0000 | ephrin-A4 |
| **EFNB2** | 2.03 | 0.0000 | ephrin-B2 |
| **EGFL8** | -3.50 | 0.0000 | EGF-like-domain, multiple 8 |
| **EGLN3** | 3.28 | 0.0000 | egl nine homolog 3 (C. elegans) |
| **EGR3** | -2.74 | 0.0000 | early growth response 3 |
| **EHBP1** | -3.61 | 0.0000 | EH domain binding protein 1 |
| **EID2** | 1.22 | 0.0000 | EP300 interacting inhibitor of differentiation 2 |
| **EID2B** | 1.09 | 0.0000 | EP300 interacting inhibitor of differentiation 2B |
| **EIF1** | -1.27 | 0.0000 | similar to eukaryotic translation initiation factor 1; eukaryotic translation initiation factor 1 |
| **EIF1AD** | 0.96 | 0.0000 | eukaryotic translation initiation factor 1A domain containing |
| **EIF2AK3** | -1.67 | 0.0000 | eukaryotic translation initiation factor 2-alpha kinase 3 |
| **EIF3C** | 1.24 | 0.0000 | eukaryotic translation initiation factor 3, subunit C |
| **EIF3F** | -1.25 | 0.0000 | eukaryotic translation initiation factor 3, subunit F; similar to hCG2040283 |
| **EIF4B** | 0.66 | 0.0000 | similar to eukaryotic translation initiation factor 4H; eukaryotic translation initiation factor 4B |
| **EIF4EBP1** | 1.33 | 0.0000 | eukaryotic translation initiation factor 4E binding protein 1 |
| **ELF1** | -2.09 | 0.0000 | E74-like factor 1 (ets domain transcription factor) |
| **ELFN2** | 3.40 | 0.0000 | extracellular leucine-rich repeat and fibronectin type III domain containing 2 |
| **ELK3** | 1.40 | 0.0000 | ELK3, ETS-domain protein (SRF accessory protein 2) |
| **ELL2** | 2.06 | 0.0000 | elongation factor, RNA polymerase II, 2 |
| **ELMO2** | 0.78 | 0.0000 | engulfment and cell motility 2 |
| **ELMOD1** | 2.62 | 0.0000 | ELMO/CED-12 domain containing 1 |
| **ELMOD2** | -1.27 | 0.0000 | ELMO/CED-12 domain containing 2 |
| **ELOVL7** | 2.85 | 0.0000 | ELOVL family member 7, elongation of long chain fatty acids (yeast) |
| **EME1** | 1.85 | 0.0000 | essential meiotic endonuclease 1 homolog 1 (S. pombe) |
| **EMG1** | 1.18 | 0.0000 | EMG1 nucleolar protein homolog (S. cerevisiae) |
| **EMILIN3** | 1.10 | 0.0000 | elastin microfibril interfacer 3 |
| **EMP2** | -2.50 | 0.0000 | epithelial membrane protein 2 |
| **ENG** | -0.85 | 0.0000 | endoglin |
| **ENO1** | 1.57 | 0.0000 | enolase 1, (alpha) |
| **ENOSF1** | -3.42 | 0.0000 | enolase superfamily member 1 |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **ENOX2** | -1.18 | 0.0000 | ecto-NOX disulfide-thiol exchanger 2 |
| **EPB41L1** | 1.89 | 0.0000 | erythrocyte membrane protein band 4.1-like 1 |
| **EPB41L2** | -1.28 | 0.0000 | erythrocyte membrane protein band 4.1-like 2 |
| **EPB41L3** | -2.11 | 0.0000 | erythrocyte membrane protein band 4.1-like 3 |
| **EPCAM** | 2.17 | 0.0000 | epithelial cell adhesion molecule |
| **EPHB2** | 3.26 | 0.0000 | EPH receptor B2 |
| **EPHB4** | 1.27 | 0.0000 | EPH receptor B4 |
| **EPHX4** | 1.95 | 0.0000 | epoxide hydrolase 4 |
| **EPRS** | -0.87 | 0.0000 | glutamyl-prolyl-tRNA synthetase |
| **ERBB2** | -1.99 | 0.0000 | v-erb-b2 erythroblastic leukemia viral oncogene homolog 2, neuro/glioblastoma derived oncogene homolog (avian) |
| **ERBB3** | -5.22 | 0.0000 | v-erb-b2 erythroblastic leukemia viral oncogene homolog 3 (avian) |
| **ERC1** | -3.07 | 0.0000 | ELKS/RAB6-interacting/CAST family member 1 |
| **ERCC5** | -0.99 | 0.0000 | excision repair cross-complementing rodent repair deficiency, complementation group 5 |
| **EREG** | -2.92 | 0.0000 | epiregulin |
| **ERLIN1** | -0.83 | 0.0000 | ER lipid raft associated 1 |
| **ESD** | -1.28 | 0.0000 | esterase D/formylglutathione hydrolase |
| **ESPNL** | 1.39 | 0.0000 | espin-like |
| **ESYT2** | -1.40 | 0.0000 | family with sequence similarity 62 (C2 domain containing), member B |
| **ETS2** | 1.79 | 0.0000 | v-ets erythroblastosis virus E26 oncogene homolog 2 (avian) |
| **EVC** | -1.90 | 0.0000 | Ellis van Creveld syndrome |
| **EVI2A** | -2.04 | 0.0000 | ecotropic viral integration site 2A |
| **EVL** | 2.31 | 0.0000 | Enah/Vasp-like |
| **EXOC1** | -0.74 | 0.0000 | exocyst complex component 1 |
| **EXOSC10** | -1.61 | 0.0000 | exosome component 10 |
| **EXOSC5** | 1.16 | 0.0000 | exosome component 5 |
| **EXT1** | 2.26 | 0.0000 | exostoses (multiple) 1 |
| **EXT2** | -1.38 | 0.0000 | exostoses (multiple) 2 |
| **EYA2** | 1.51 | 0.0000 | eyes absent homolog 2 (Drosophila) |
| **EZH2** | 1.83 | 0.0000 | enhancer of zeste homolog 2 (Drosophila) |
| **F2R** | 3.02 | 0.0000 | coagulation factor II (thrombin) receptor |
| **F2RL1** | 3.17 | 0.0000 | coagulation factor II (thrombin) receptor-like 1 |
| **F2RL2** | 4.61 | 0.0000 | coagulation factor II (thrombin) receptor-like 2 |
| **FABP7** | -5.06 | 0.0000 | fatty acid binding protein 7, brain |
| **FADS2** | -2.65 | 0.0000 | fatty acid desaturase 2 |
| **FAF2** | 0.70 | 0.0000 | Fas associated factor family member 2 |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **FAM102A** | -3.67 | 0.0000 | family with sequence similarity 102, member A |
| **FAM105B** | 0.84 | 0.0000 | family with sequence similarity 105, member B |
| **FAM108A1** | -1.43 | 0.0000 | family with sequence similarity 108, member A4; family with sequence similarity 108, member A5; family with sequence similarity 108, member A1 |
| **FAM109B** | -0.86 | 0.0000 | family with sequence similarity 109, member B |
| **FAM116A** | -1.35 | 0.0000 | family with sequence similarity 116, member A |
| **FAM117B** | 1.40 | 0.0000 | family with sequence similarity 117, member B |
| **FAM119B** | 0.76 | 0.0000 | family with sequence similarity 119, member B |
| **FAM127B** | -1.35 | 0.0000 | family with sequence similarity 127, member B |
| **FAM134A** | -1.58 | 0.0000 | family with sequence similarity 134, member A |
| **FAM155A** | 3.80 | 0.0000 | family with sequence similarity 155, member A |
| **FAM161A** | 1.77 | 0.0000 | family with sequence similarity 161, member A |
| **FAM169A** | 5.15 | 0.0000 | family with sequence similarity 169, member A |
| **FAM175A** | -1.15 | 0.0000 | family with sequence similarity 175, member A |
| **FAM176A** | 2.79 | 0.0000 | family with sequence similarity 176, member A |
| **FAM177A1** | -1.35 | 0.0000 | family with sequence similarity 177, member A1 |
| **FAM181B** | 1.40 | 0.0000 | family with sequence similarity 181, member B |
| **FAM184A** | 2.03 | 0.0000 | family with sequence similarity 184, member A |
| **FAM188A** | -1.58 | 0.0000 | chromosome 10 open reading frame 97 |
| **FAM189A2** | -2.12 | 0.0000 | chromosome 9 open reading frame 61 |
| **FAM190B** | -1.46 | 0.0000 | KIAA1128 |
| **FAM19A5** | -4.40 | 0.0000 | family with sequence similarity 19 (chemokine (C-C motif)-like), member A5 |
| **FAM20C** | -2.47 | 0.0000 | family with sequence similarity 20, member C |
| **FAM21A** | -1.41 | 0.0000 | family with sequence similarity 21, member B; family with sequence similarity 21, member A |
| **FAM21C** | -1.68 | 0.0000 | family with sequence similarity 21, member D; family with sequence similarity 21, member C |
| **FAM24B** | 1.92 | 0.0000 | family with sequence similarity 24, member B |
| **FAM27E1** | 1.46 | 0.0000 | hypothetical LOC100287333 |
| **FAM3C** | -1.67 | 0.0000 | family with sequence similarity 3, member C |
| **FAM41C** | -1.15 | 0.0000 | family with sequence similarity 41, member C |
| **FAM46A** | -2.84 | 0.0000 | family with sequence similarity 46, member A |
| **FAM47E** | -1.92 | 0.0000 | family with sequence similarity 47, member E |
| **FAM50B** | -3.20 | 0.0000 | family with sequence similarity 50, member B |
| **FAM59A** | -3.20 | 0.0000 | hypothetical protein LOC100130616; family with sequence similarity 59, member A |
| **FAM60A** | 1.78 | 0.0000 | similar to hCG2020539; family with sequence similarity 60, member A; similar |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| | | | to family with sequence similarity 60, member A |
| **FAM63B** | -1.69 | 0.0000 | family with sequence similarity 63, member B |
| **FAM69B** | 2.96 | 0.0000 | family with sequence similarity 69, member B |
| **FAM82B** | -1.42 | 0.0000 | family with sequence similarity 82, member B |
| **FAM83D** | 2.29 | 0.0000 | family with sequence similarity 83, member D |
| **FAM84A** | 2.37 | 0.0000 | hypothetical LOC653602; family with sequence similarity 84, member A |
| **FAM86A** | 1.52 | 0.0000 | family with sequence similarity 86, member B2; family with sequence similarity 86, member A; family with sequence similarity 86, member B1 |
| **FAM8A1** | -0.72 | 0.0000 | family with sequence similarity 8, member A1 |
| **FAM96B** | -1.27 | 0.0000 | family with sequence similarity 96, member B |
| **FANCG** | 1.91 | 0.0000 | Fanconi anemia, complementation group G |
| **FANCL** | 1.40 | 0.0000 | Fanconi anemia, complementation group L |
| **FAR2** | 4.76 | 0.0000 | fatty acyl CoA reductase 2 |
| **FARSB** | -1.66 | 0.0000 | phenylalanyl-tRNA synthetase, beta subunit |
| **FAS** | 1.87 | 0.0000 | Fas (TNF receptor superfamily, member 6) |
| **FASTKD2** | 0.92 | 0.0000 | FAST kinase domains 2 |
| **FASTKD3** | 1.80 | 0.0000 | FAST kinase domains 3 |
| **FASTKD5** | 0.62 | 0.0000 | FAST kinase domains 5 |
| **FBL** | 1.71 | 0.0000 | fibrillarin |
| **FBLN2** | -2.41 | 0.0000 | fibulin 2 |
| **FBN2** | 5.48 | 0.0000 | fibrillin 2 |
| **FBXL15** | -1.40 | 0.0000 | F-box and leucine-rich repeat protein 15 |
| **FBXL16** | 5.56 | 0.0000 | F-box and leucine-rich repeat protein 16 |
| **FBXL17** | -1.63 | 0.0000 | F-box and leucine-rich repeat protein 17 |
| **FBXL2** | -1.22 | 0.0000 | F-box and leucine-rich repeat protein 2 |
| **FBXL20** | -1.05 | 0.0000 | F-box and leucine-rich repeat protein 20 |
| **FBXL21** | 4.72 | 0.0000 | F-box and leucine-rich repeat protein 21 |
| **FBXL3** | -1.36 | 0.0000 | F-box and leucine-rich repeat protein 3 |
| **FBXL4** | -1.07 | 0.0000 | F-box and leucine-rich repeat protein 4 |
| **FBXO25** | -3.10 | 0.0000 | F-box protein 25 |
| **FBXO30** | -1.45 | 0.0000 | F-box protein 30 |
| **FBXO32** | -2.85 | 0.0000 | F-box protein 32 |
| **FBXO33** | -0.86 | 0.0000 | F-box protein 33 |
| **FBXO38** | -3.51 | 0.0000 | F-box protein 38 |
| **FBXO7** | -2.21 | 0.0000 | F-box protein 7 |
| **FBXO8** | -1.51 | 0.0000 | F-box protein 8 |
| **FCGR2A** | -3.74 | 0.0000 | Fc fragment of IgG, low affinity IIa, receptor (CD32) |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **FCGRT** | 3.54 | 0.0000 | Fc fragment of IgG, receptor, transporter, alpha |
| **FCHSD2** | 2.40 | 0.0000 | FCH and double SH3 domains 2 |
| **FCRLA** | -5.77 | 0.0000 | Fc receptor-like A |
| **FDXR** | 1.56 | 0.0000 | ferredoxin reductase |
| **FERMT1** | 3.58 | 0.0000 | fermitin family homolog 1 (Drosophila) |
| **FERMT2** | -2.64 | 0.0000 | fermitin family homolog 2 (Drosophila) |
| **FGD6** | 2.07 | 0.0000 | FYVE, RhoGEF and PH domain containing 6 |
| **FGF13** | 5.86 | 0.0000 | fibroblast growth factor 13 |
| **FGF2** | 2.46 | 0.0000 | fibroblast growth factor 2 (basic) |
| **FGF5** | -3.63 | 0.0000 | fibroblast growth factor 5 |
| **FGF9** | 1.18 | 0.0000 | fibroblast growth factor 9 (glia-activating factor) |
| **FGFR1** | 2.46 | 0.0000 | fibroblast growth factor receptor 1 |
| **FGFRL1** | 2.06 | 0.0000 | fibroblast growth factor receptor-like 1 |
| **FHDC1** | -4.79 | 0.0000 | FH2 domain containing 1 |
| **FICD** | -0.97 | 0.0000 | FIC domain containing |
| **FIG4** | -1.09 | 0.0000 | FIG4 homolog (S. cerevisiae) |
| **FIGNL1** | 1.65 | 0.0000 | fidgetin-like 1 |
| **FJX1** | 2.26 | 0.0000 | four jointed box 1 (Drosophila) |
| **FKBP1A** | -2.04 | 0.0000 | FK506 binding protein 1A, 12kDa |
| **FKBP2** | -1.61 | 0.0000 | FK506 binding protein 2, 13kDa |
| **FKBP4** | 0.86 | 0.0000 | FK506 binding protein 4, 59kDa |
| **FLAD1** | 1.02 | 0.0000 | FAD1 flavin adenine dinucleotide synthetase homolog (S. cerevisiae) |
| **FLJ22536** | -2.91 | 0.0000 | hypothetical locus LOC401237 |
| **FLJ30064** | -2.42 | 0.0000 | hypothetical protein LOC644975 |
| **FLJ32255** | -1.70 | 0.0000 | hypothetical protein LOC643977 |
| **FLJ35934** | 3.11 | 0.0000 | FLJ35934 protein |
| **FLJ39632** | 3.54 | 0.0000 | hypothetical LOC642477; hypothetical LOC400879 |
| **FLJ40504** | 5.79 | 0.0000 | hypothetical protein FLJ40504 |
| **FLOT1** | -1.44 | 0.0000 | flotillin 1 |
| **FMN1** | -3.62 | 0.0000 | formin 1 |
| **FMR1** | 1.07 | 0.0000 | fragile X mental retardation 1 |
| **FN3KRP** | 0.97 | 0.0000 | fructosamine 3 kinase related protein |
| **FNBP1** | 1.16 | 0.0000 | formin binding protein 1 |
| **FNIP2** | -1.34 | 0.0000 | folliculin interacting protein 2 |
| **FNTA** | -1.11 | 0.0000 | farnesyltransferase, CAAX box, alpha |
| **FNTB** | -2.63 | 0.0000 | farnesyltransferase, CAAX box, beta |
| **FOS** | -2.59 | 0.0000 | v-fos FBJ murine osteosarcoma viral oncogene homolog |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **FOSL2** | -1.45 | 0.0000 | FOS-like antigen 2 |
| **FOXA1** | 4.68 | 0.0000 | forkhead box A1 |
| **FOXD3** | -0.74 | 0.0000 | forkhead box D3 |
| **FOXD4** | 1.53 | 0.0000 | forkhead box D4 |
| **FOXF1** | 4.67 | 0.0000 | forkhead box F1 |
| **FOXG1** | 6.09 | 0.0000 | forkhead box G1 |
| **FOXK2** | 1.61 | 0.0000 | forkhead box K2 |
| **FOXL2** | 4.52 | 0.0000 | forkhead box L2 |
| **FOXN2** | -1.58 | 0.0000 | forkhead box N2 |
| **FOXP1** | 2.41 | 0.0000 | forkhead box P1 |
| **FRG1** | -0.82 | 0.0000 | FSHD region gene 1 |
| **FRMD5** | -2.25 | 0.0000 | FERM domain containing 5 |
| **FRMD6** | -1.49 | 0.0000 | FERM domain containing 6 |
| **FSTL1** | 3.40 | 0.0000 | follistatin-like 1 |
| **FTH1** | -1.97 | 0.0000 | ferritin, heavy polypeptide 1; ferritin, heavy polypeptide-like 16; similar to ferritin, heavy polypeptide 1; ferritin, heavy polypeptide-like 3 pseudogene |
| **FTHL17** | -1.40 | 0.0000 | ferritin, heavy polypeptide-like 17 |
| **FTSJ3** | 0.91 | 0.0000 | FtsJ homolog 3 (E. coli) |
| **FUCA2** | -1.55 | 0.0000 | fucosidase, alpha-L- 2, plasma |
| **FUK** | -1.50 | 0.0000 | fucokinase |
| **FUNDC1** | -1.10 | 0.0000 | FUN14 domain containing 1 |
| **FUT11** | -1.40 | 0.0000 | fucosyltransferase 11 (alpha (1,3) fucosyltransferase) |
| **FXN** | 1.39 | 0.0000 | frataxin |
| **FXYD3** | -3.74 | 0.0000 | FXYD domain containing ion transport regulator 3 |
| **FXYD6** | 2.63 | 0.0000 | FXYD domain containing ion transport regulator 6 |
| **FYCO1** | -1.35 | 0.0000 | FYVE and coiled-coil domain containing 1 |
| **FYN** | -2.26 | 0.0000 | FYN oncogene related to SRC, FGR, YES |
| **FZD2** | 2.18 | 0.0000 | frizzled homolog 2 (Drosophila) |
| **FZD4** | -1.88 | 0.0000 | frizzled homolog 4 (Drosophila) |
| **FZD7** | 1.66 | 0.0000 | frizzled homolog 7 (Drosophila) |
| **GAB1** | -1.75 | 0.0000 | GRB2-associated binding protein 1 |
| **GABARAP** | -1.70 | 0.0000 | GABA(A) receptor-associated protein |
| **GABARAPL2** | -1.52 | 0.0000 | GABA(A) receptor-associated protein-like 2 |
| **GABPB2** | -2.43 | 0.0000 | GA binding protein transcription factor, beta subunit 2 |
| **GABRA2** | -3.22 | 0.0000 | gamma-aminobutyric acid (GABA) A receptor, alpha 2 |
| **GADD45A** | 2.50 | 0.0000 | growth arrest and DNA-damage-inducible, alpha |
| **GAL3ST1** | -3.89 | 0.0000 | galactose-3-O-sulfotransferase 1 |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **GALE** | 1.40 | 0.0000 | UDP-galactose-4-epimerase |
| **GALK2** | -1.64 | 0.0000 | galactokinase 2 |
| **GALNT10** | 1.32 | 0.0000 | UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 10 (GalNAc-T10) |
| **GALNT14** | 5.02 | 0.0000 | UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 14 (GalNAc-T14) |
| **GALNTL1** | 3.31 | 0.0000 | UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase-like 1 |
| **GAPVD1** | -1.05 | 0.0000 | GTPase activating protein and VPS9 domains 1 |
| **GART** | 1.68 | 0.0000 | phosphoribosylglycinamide formyltransferase, phosphoribosylglycinamide synthetase, phosphoribosylaminoimidazole synthetase |
| **GAS1** | 3.72 | 0.0000 | growth arrest-specific 1 |
| **GAS2L1** | -1.21 | 0.0000 | growth arrest-specific 2 like 1 |
| **GAS2L3** | -3.02 | 0.0000 | growth arrest-specific 2 like 3 |
| **GAS5** | 1.64 | 0.0000 | growth arrest-specific 5 (non-protein coding) |
| **GAS8** | -1.45 | 0.0000 | growth arrest-specific 8 |
| **GATA4** | 2.15 | 0.0000 | GATA binding protein 4 |
| **GATA6** | 4.28 | 0.0000 | GATA binding protein 6 |
| **GATM** | -3.56 | 0.0000 | glycine amidinotransferase (L-arginine:glycine amidinotransferase) |
| **GBA** | -1.98 | 0.0000 | glucosidase, beta; acid (includes glucosylceramidase) |
| **GBE1** | -1.74 | 0.0000 | glucan (1,4-alpha-), branching enzyme 1 |
| **GBP2** | -2.05 | 0.0000 | guanylate binding protein 2, interferon-inducible |
| **GCNT1** | -2.34 | 0.0000 | glucosaminyl (N-acetyl) transferase 1, core 2 (beta-1,6-N-acetylglucosaminyltransferase) |
| **GDE1** | -1.85 | 0.0000 | glycerophosphodiester phosphodiesterase 1 |
| **GFPT2** | 3.00 | 0.0000 | glutamine-fructose-6-phosphate transaminase 2 |
| **GFRA1** | -3.74 | 0.0000 | GDNF family receptor alpha 1 |
| **GFRA3** | -2.68 | 0.0000 | GDNF family receptor alpha 3 |
| **GFRA4** | -1.45 | 0.0000 | GDNF family receptor alpha 4 |
| **GGH** | -1.53 | 0.0000 | gamma-glutamyl hydrolase (conjugase, folylpolygammaglutamyl hydrolase) |
| **GGNBP2** | -0.87 | 0.0000 | gametogenetin binding protein 2 |
| **GIYD1** | 1.26 | 0.0000 | GIY-YIG domain containing 2; GIY-YIG domain containing 1 |
| **GJA3** | -2.29 | 0.0000 | gap junction protein, alpha 3, 46kDa |
| **GJB1** | -2.49 | 0.0000 | gap junction protein, beta 1, 32kDa |
| **GJC3** | -2.18 | 0.0000 | gap junction protein, gamma 3, 30.2kDa |
| **GK** | -1.83 | 0.0000 | glycerol kinase 3 pseudogene; glycerol kinase |
| **GKAP1** | 3.18 | 0.0000 | G kinase anchoring protein 1 |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **GLG1** | -1.35 | 0.0000 | golgi apparatus protein 1 |
| **GLIPR1** | -1.94 | 0.0000 | GLI pathogenesis-related 1 |
| **GLIS1** | 4.07 | 0.0000 | GLIS family zinc finger 1 |
| **GLRX** | 1.38 | 0.0000 | glutaredoxin (thioltransferase) |
| **GLT8D1** | -1.22 | 0.0000 | glycosyltransferase 8 domain containing 1 |
| **GLTP** | -2.24 | 0.0000 | glycolipid transfer protein; glycolipid transfer protein pseudogene 1 |
| **GLYATL1** | 1.78 | 0.0000 | glycine-N-acyltransferase-like 1 |
| **GM2A** | -1.34 | 0.0000 | GM2 ganglioside activator |
| **GMFB** | -1.94 | 0.0000 | glia maturation factor, beta |
| **GMPPB** | -1.26 | 0.0000 | GDP-mannose pyrophosphorylase B |
| **GMPS** | 1.07 | 0.0000 | guanine monphosphate synthetase |
| **GNAL** | 2.73 | 0.0000 | guanine nucleotide binding protein (G protein), alpha activating activity polypeptide, olfactory type |
| **GNAS** | 1.11 | 0.0000 | GNAS complex locus |
| **GNG2** | -2.90 | 0.0000 | guanine nucleotide binding protein (G protein), gamma 2 |
| **GNG7** | -2.52 | 0.0000 | guanine nucleotide binding protein (G protein), gamma 7 |
| **GNPTAB** | -1.70 | 0.0000 | N-acetylglucosamine-1-phosphate transferase, alpha and beta subunits |
| **GNPTG** | -2.07 | 0.0000 | N-acetylglucosamine-1-phosphate transferase, gamma subunit |
| **GOLGA7** | -1.11 | 0.0000 | golgi autoantigen, golgin subfamily a, 7 |
| **GOLGA8A** | 3.05 | 0.0000 | golgi autoantigen, golgin subfamily a, 8B; golgi autoantigen, golgin subfamily a, 8A |
| **GOLGA8E** | 2.63 | 0.0000 | golgi autoantigen, golgin subfamily a, 8E |
| **GOLGA8F** | 2.31 | 0.0000 | golgi autoantigen, golgin subfamily a, 8D; golgi autoantigen, golgin subfamily a, 8C; similar to Golgin subfamily A member 8-like protein 1; golgi autoantigen, golgin subfamily a, 8F; golgi autoantigen, golgin subfamily a, 8G |
| **GOSR2** | 1.06 | 0.0000 | golgi SNAP receptor complex member 2 |
| **GOT2** | 1.39 | 0.0000 | glutamic-oxaloacetic transaminase 2, mitochondrial (aspartate aminotransferase 2) |
| **GP9** | -1.22 | 0.0000 | glycoprotein IX (platelet) |
| **GPAT2** | 3.61 | 0.0000 | hypothetical protein LOC150763; similar to hCG1732629; similar to glycerol-3-phosphate acyltransferase, mitochondrial |
| **GPC1** | -2.72 | 0.0000 | glypican 1 |
| **GPC4** | 4.52 | 0.0000 | glypican 4 |
| **GPER** | -4.15 | 0.0000 | G protein-coupled estrogen receptor 1 |
| **GPM6B** | -4.93 | 0.0000 | glycoprotein M6B |
| **GPN3** | 1.39 | 0.0000 | GPN-loop GTPase 3 |
| **GPNMB** | -6.49 | 0.0000 | glycoprotein (transmembrane) nmb |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **GPR126** | -2.30 | 0.0000 | G protein-coupled receptor 126 |
| **GPR137B** | -3.58 | 0.0000 | G protein-coupled receptor 137B |
| **GPR155** | -2.91 | 0.0000 | G protein-coupled receptor 155 |
| **GPR158** | -3.56 | 0.0000 | G protein-coupled receptor 158 |
| **GPR19** | 1.59 | 0.0000 | G protein-coupled receptor 19 |
| **GPRC5A** | 2.42 | 0.0000 | G protein-coupled receptor, family C, group 5, member A |
| **GPRC5B** | 1.58 | 0.0000 | G protein-coupled receptor, family C, group 5, member B |
| **GPRC5C** | 2.18 | 0.0000 | G protein-coupled receptor, family C, group 5, member C |
| **GPSM2** | -1.57 | 0.0000 | G-protein signaling modulator 2 (AGS3-like, C. elegans) |
| **GPX1** | -0.98 | 0.0000 | glutathione peroxidase 1 |
| **GRAMD3** | -1.62 | 0.0000 | GRAM domain containing 3 |
| **GRASP** | -2.40 | 0.0000 | GRP1 (general receptor for phosphoinositides 1)-associated scaffold protein |
| **GSC** | 2.78 | 0.0000 | goosecoid homeobox |
| **GSN** | -2.85 | 0.0000 | gelsolin (amyloidosis, Finnish type) |
| **GSTM4** | -1.02 | 0.0000 | glutathione S-transferase mu 4 |
| **GSTO1** | -1.02 | 0.0000 | glutathione S-transferase omega 1 |
| **GSTT2** | -5.59 | 0.0000 | glutathione S-transferase theta 2B (gene/pseudogene); glutathione S-transferase theta 2 |
| **GTDC1** | -1.78 | 0.0000 | glycosyltransferase-like domain containing 1 |
| **GTF2B** | -0.76 | 0.0000 | general transcription factor IIB |
| **GTF2F2** | -0.99 | 0.0000 | general transcription factor IIF, polypeptide 2, 30kDa |
| **GTPBP10** | 1.23 | 0.0000 | GTP-binding protein 10 (putative) |
| **GTPBP2** | -0.83 | 0.0000 | GTP binding protein 2 |
| **GTPBP3** | 1.25 | 0.0000 | GTP binding protein 3 (mitochondrial) |
| **GTPBP4** | 0.97 | 0.0000 | GTP binding protein 4 |
| **GTPBP6** | -1.03 | 0.0000 | GTP binding protein 6 (putative) |
| **GUSB** | -1.19 | 0.0000 | glucuronidase, beta |
| **GYLTL1B** | 1.67 | 0.0000 | glycosyltransferase-like 1B |
| **H2AFJ** | -1.69 | 0.0000 | H2A histone family, member J |
| **H2AFY** | 1.63 | 0.0000 | H2A histone family, member Y |
| **H2AFY2** | 3.73 | 0.0000 | H2A histone family, member Y2 |
| **H3F3A** | -1.14 | 0.0000 | H3 histone, family 3B (H3.3B); H3 histone, family 3A pseudogene; H3 histone, family 3A; similar to H3 histone, family 3B; similar to histone H3.3B |
| **HACL1** | -1.78 | 0.0000 | 2-hydroxyacyl-CoA lyase 1 |
| **HADHB** | -0.97 | 0.0000 | hydroxyacyl-Coenzyme A dehydrogenase/3-ketoacyl-Coenzyme A thiolase/enoyl-Coenzyme A hydratase (trifunctional protein), beta subunit |
| **HARBI1** | -0.59 | 0.0000 | harbinger transposase derived 1 |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **HAUS5** | 1.58 | 0.0000 | HAUS augmin-like complex, subunit 5 |
| **HAUS6** | 1.49 | 0.0000 | HAUS augmin-like complex, subunit 6 |
| **HAUS7** | 2.36 | 0.0000 | three prime repair exonuclease 2; HAUS augmin-like complex, subunit 7 |
| **HBEGF** | -1.29 | 0.0000 | heparin-binding EGF-like growth factor |
| **HBS1L** | -1.30 | 0.0000 | HBS1-like (S. cerevisiae) |
| **HBXIP** | -1.31 | 0.0000 | hepatitis B virus x interacting protein |
| **HCP5** | -2.42 | 0.0000 | HLA complex P5 |
| **HDGFRP3** | 1.46 | 0.0000 | hepatoma-derived growth factor, related protein 3 |
| **HDHD2** | -1.29 | 0.0000 | haloacid dehalogenase-like hydrolase domain containing 2 |
| **HECTD1** | -0.99 | 0.0000 | HECT domain containing 1 |
| **HELQ** | -1.23 | 0.0000 | helicase, POLQ-like |
| **HEPH** | -3.35 | 0.0000 | hephaestin |
| **HERC5** | 3.25 | 0.0000 | hect domain and RLD 5 |
| **HEXB** | -2.04 | 0.0000 | hexosaminidase B (beta polypeptide) |
| **HFE** | -1.22 | 0.0000 | hemochromatosis |
| **HIC1** | 1.34 | 0.0000 | hypermethylated in cancer 1 |
| **HIF1A** | 1.29 | 0.0000 | hypoxia inducible factor 1, alpha subunit (basic helix-loop-helix transcription factor) |
| **HIP1R** | 1.63 | 0.0000 | huntingtin interacting protein 1 related |
| **HIPK2** | 1.79 | 0.0000 | homeodomain interacting protein kinase 2; similar to homeodomain interacting protein kinase 2 |
| **HK1** | -1.10 | 0.0000 | hexokinase 1 |
| **HKDC1** | -3.75 | 0.0000 | hexokinase domain containing 1 |
| **HLA-A** | -2.75 | 0.0000 | major histocompatibility complex, class I, A |
| **HLA-B** | -2.50 | 0.0000 | major histocompatibility complex, class I, C; major histocompatibility complex, class I, B |
| **HLA-C** | -4.21 | 0.0000 | major histocompatibility complex, class I, C; major histocompatibility complex, class I, B |
| **HLA-DMA** | -5.07 | 0.0000 | major histocompatibility complex, class II, DM alpha |
| **HLA-DMB** | -4.75 | 0.0000 | major histocompatibility complex, class II, DM beta |
| **HLA-DOA** | -3.93 | 0.0000 | major histocompatibility complex, class II, DO alpha |
| **HLA-DPA1** | -4.20 | 0.0000 | major histocompatibility complex, class II, DP alpha 1 |
| **HLA-DPB1** | -2.52 | 0.0000 | major histocompatibility complex, class II, DP beta 1 |
| **HLA-DPB2** | -2.77 | 0.0000 | major histocompatibility complex, class II, DP beta 2 (pseudogene) |
| **HLA-DRA** | -4.97 | 0.0000 | major histocompatibility complex, class II, DR alpha |
| **HLA-DRB1** | -3.30 | 0.0000 | major histocompatibility complex, class II, DR beta 4; major histocompatibility complex, class II, DR beta 1 |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **HLA-DRB3** | -3.83 | 0.0000 | major histocompatibility complex, class II, DR beta 3 |
| **HLA-DRB4** | -3.96 | 0.0000 | major histocompatibility complex, class II, DR beta 4; major histocompatibility complex, class II, DR beta 1 |
| **HLA-DRB5** | -3.64 | 0.0000 | major histocompatibility complex, class II, DR beta 5 |
| **HLA-E** | -2.61 | 0.0000 | major histocompatibility complex, class I, E |
| **HLA-F** | -2.54 | 0.0000 | major histocompatibility complex, class I, F |
| **HLA-G** | -2.85 | 0.0000 | major histocompatibility complex, class I, G |
| **HLA-H** | -3.02 | 0.0000 | major histocompatibility complex, class I, H (pseudogene) |
| **HLA-J** | -2.57 | 0.0000 | major histocompatibility complex, class I, J (pseudogene) |
| **HLTF** | 1.52 | 0.0000 | helicase-like transcription factor |
| **HMBOX1** | -1.76 | 0.0000 | homeobox containing 1 |
| **HMG20B** | -2.35 | 0.0000 | high-mobility group 20B |
| **HMGB2** | 1.33 | 0.0000 | high-mobility group box 2 |
| **HMGN2** | 0.93 | 0.0000 | hypothetical LOC729505; similar to hCG2040565; high-mobility group nucleosomal binding domain 2; similar to high-mobility group nucleosomal binding domain 2 |
| **HN1** | 2.08 | 0.0000 | hematological and neurological expressed 1 |
| **HN1L** | 1.13 | 0.0000 | hematological and neurological expressed 1-like |
| **HNRNPA1L2** | 0.77 | 0.0000 | heterogeneous nuclear ribonucleoprotein A1-like 2 |
| **HNRNPA3** | 1.56 | 0.0000 | heterogeneous nuclear ribonucleoprotein A3 |
| **HNRNPH1** | 1.41 | 0.0000 | heterogeneous nuclear ribonucleoprotein H1 (H) |
| **HNRNPH2** | -1.22 | 0.0000 | ribosomal protein L36a pseudogene 51; ribosomal protein L36a pseudogene 37; ribosomal protein L36a pseudogene 49; heterogeneous nuclear ribonucleoprotein H2 (H'); ribosomal protein L36a |
| **HNRNPUL2** | -1.98 | 0.0000 | heterogeneous nuclear ribonucleoprotein U-like 2 |
| **HOOK3** | -2.09 | 0.0000 | hook homolog 3 (Drosophila) |
| **HOPX** | 4.46 | 0.0000 | HOP homeobox |
| **HOXA13** | 3.44 | 0.0000 | homeobox A13 |
| **HOXA3** | 2.09 | 0.0000 | homeobox A3 |
| **HOXA5** | 1.57 | 0.0000 | homeobox A5 |
| **HOXA9** | 2.17 | 0.0000 | homeobox A9 |
| **HOXB13** | 3.90 | 0.0000 | homeobox B13 |
| **HOXB9** | 2.85 | 0.0000 | homeobox B9 |
| **HOXC13** | 3.43 | 0.0000 | homeobox C13 |
| **HOXD3** | 1.93 | 0.0000 | homeobox D3 |
| **HPCAL1** | -1.87 | 0.0000 | hippocalcin-like 1 |
| **HPS1** | -2.51 | 0.0000 | Hermansky-Pudlak syndrome 1 |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **HPS5** | -1.01 | 0.0000 | Hermansky-Pudlak syndrome 5 |
| **HR** | -1.03 | 0.0000 | hairless homolog (mouse) |
| **HRASLS** | 3.06 | 0.0000 | HRAS-like suppressor |
| **HRASLS2** | -1.78 | 0.0000 | HRAS-like suppressor 2 |
| **HRH1** | 2.20 | 0.0000 | histamine receptor H1 |
| **HS1BP3** | -1.69 | 0.0000 | HCLS1 binding protein 3 |
| **HS3ST3A1** | 3.05 | 0.0000 | heparan sulfate (glucosamine) 3-O-sulfotransferase 3A1 |
| **HS6ST2** | 5.95 | 0.0000 | heparan sulfate 6-O-sulfotransferase 2 |
| **HSBP1** | -1.76 | 0.0000 | heat shock factor binding protein 1 |
| **HSD17B10** | -0.84 | 0.0000 | hydroxysteroid (17-beta) dehydrogenase 10 |
| **HSD17B11** | -1.50 | 0.0000 | hydroxysteroid (17-beta) dehydrogenase 11 |
| **HSD17B12** | -1.68 | 0.0000 | hydroxysteroid (17-beta) dehydrogenase 12 |
| **HSPA12A** | -2.95 | 0.0000 | heat shock 70kDa protein 12A |
| **HSPA1L** | 1.44 | 0.0000 | heat shock 70kDa protein 1-like |
| **HSPA4L** | 1.69 | 0.0000 | heat shock 70kDa protein 4-like |
| **HSPA5** | -1.57 | 0.0000 | hypothetical gene supported by AF216292; NM_005347; heat shock 70kDa protein 5 (glucose-regulated protein, 78kDa) |
| **HSPA6** | -2.18 | 0.0000 | heat shock 70kDa protein 7 (HSP70B); heat shock 70kDa protein 6 (HSP70B') |
| **HSPA9** | 0.73 | 0.0000 | heat shock 70kDa protein 9 (mortalin) |
| **HSPBAP1** | 0.77 | 0.0000 | HSPB (heat shock 27kDa) associated protein 1 |
| **HSPC157** | 1.73 | 0.0000 | hypothetical LOC29092 |
| **HSPC159** | 2.92 | 0.0000 | galectin-related protein |
| **HSPD1** | 1.56 | 0.0000 | heat shock 60kDa protein 1 (chaperonin) pseudogene 5; heat shock 60kDa protein 1 (chaperonin) pseudogene 6; heat shock 60kDa protein 1 (chaperonin) pseudogene 1; heat shock 60kDa protein 1 (chaperonin) pseudogene 4; heat shock 60kDa protein 1 (chaperonin) |
| **HSPG2** | -1.30 | 0.0000 | heparan sulfate proteoglycan 2 |
| **HTATIP2** | -2.29 | 0.0000 | HIV-1 Tat interactive protein 2, 30kDa |
| **HTR7** | 3.24 | 0.0000 | 5-hydroxytryptamine (serotonin) receptor 7 (adenylate cyclase-coupled) |
| **HTRA3** | 2.84 | 0.0000 | HtrA serine peptidase 3 |
| **HUWE1** | -1.97 | 0.0000 | HECT, UBA and WWE domain containing 1 |
| **HYAL1** | -3.11 | 0.0000 | hyaluronoglucosaminidase 1 |
| **IBTK** | -1.24 | 0.0000 | inhibitor of Bruton agammaglobulinemia tyrosine kinase |
| **ICAM1** | -2.22 | 0.0000 | intercellular adhesion molecule 1 |
| **IER5** | 1.63 | 0.0000 | immediate early response 5 |
| **IFI27L2** | -1.78 | 0.0000 | interferon, alpha-inducible protein 27-like 2 |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **IFI30** | -1.68 | 0.0000 | interferon, gamma-inducible protein 30 |
| **IFI6** | -1.33 | 0.0000 | interferon, alpha-inducible protein 6 |
| **IFIT2** | -1.96 | 0.0000 | interferon-induced protein with tetratricopeptide repeats 2 |
| **IFIT3** | -3.04 | 0.0000 | interferon-induced protein with tetratricopeptide repeats 3 |
| **IFITM3** | -1.37 | 0.0000 | interferon induced transmembrane protein 3 (1-8U) |
| **IFNE** | 2.18 | 0.0000 | interferon, epsilon |
| **IFRD1** | 1.49 | 0.0000 | interferon-related developmental regulator 1 |
| **IFT88** | -1.55 | 0.0000 | intraflagellar transport 88 homolog (Chlamydomonas) |
| **IGDCC4** | 4.12 | 0.0000 | immunoglobulin superfamily, DCC subclass, member 4 |
| **IGF2** | 3.10 | 0.0000 | insulin-like growth factor 2 (somatomedin A); insulin; INS-IGF2 readthrough transcript |
| **IGF2BP1** | 5.22 | 0.0000 | insulin-like growth factor 2 mRNA binding protein 1 |
| **IGFBP3** | 4.14 | 0.0000 | insulin-like growth factor binding protein 3 |
| **IGFBP5** | -3.53 | 0.0000 | insulin-like growth factor binding protein 5 |
| **IGFBPL1** | 4.59 | 0.0000 | insulin-like growth factor binding protein-like 1 |
| **IGHD** | -1.87 | 0.0000 | immunoglobulin heavy constant delta |
| **IGSF11** | -3.13 | 0.0000 | immunoglobulin superfamily, member 11 |
| **IGSF9** | 2.61 | 0.0000 | immunoglobulin superfamily, member 9 |
| **IKBKB** | -1.28 | 0.0000 | inhibitor of kappa light polypeptide gene enhancer in B-cells, kinase beta |
| **IKZF4** | -1.48 | 0.0000 | IKAROS family zinc finger 4 (Eos) |
| **IL12A** | 1.47 | 0.0000 | interleukin 12A (natural killer cell stimulatory factor 1, cytotoxic lymphocyte maturation factor 1, p35) |
| **IL13RA1** | -2.08 | 0.0000 | interleukin 13 receptor, alpha 1 |
| **IL17RD** | 2.42 | 0.0000 | interleukin 17 receptor D |
| **IL1RAP** | -1.53 | 0.0000 | interleukin 1 receptor accessory protein |
| **IL28RA** | 3.76 | 0.0000 | interleukin 28 receptor, alpha (interferon, lambda receptor) |
| **IL6** | -3.63 | 0.0000 | interleukin 6 (interferon, beta 2) |
| **IL7** | 2.85 | 0.0000 | interleukin 7 |
| **ILK** | -1.67 | 0.0000 | integrin-linked kinase |
| **IMP4** | 1.19 | 0.0000 | IMP4, U3 small nucleolar ribonucleoprotein, homolog (yeast) |
| **IMPAD1** | -1.80 | 0.0000 | inositol monophosphatase domain containing 1 |
| **INPP4B** | -1.61 | 0.0000 | inositol polyphosphate-4-phosphatase, type II, 105kDa |
| **INPP5F** | -3.31 | 0.0000 | inositol polyphosphate-5-phosphatase F |
| **INPP5K** | -2.11 | 0.0000 | inositol polyphosphate-5-phosphatase K |
| **INTS2** | 1.24 | 0.0000 | integrator complex subunit 2 |
| **IP6K2** | 1.47 | 0.0000 | inositol hexakisphosphate kinase 2 |
| **IQCA1** | 2.58 | 0.0000 | IQ motif containing with AAA domain 1 |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **IQCC** | 1.23 | 0.0000 | IQ motif containing C |
| **IQSEC1** | -1.18 | 0.0000 | IQ motif and Sec7 domain 1 |
| **IRAK1** | 1.65 | 0.0000 | interleukin-1 receptor-associated kinase 1 |
| **IRF9** | -1.35 | 0.0000 | interferon regulatory factor 9 |
| **IRS1** | 2.66 | 0.0000 | insulin receptor substrate 1 |
| **IRS2** | -1.73 | 0.0000 | insulin receptor substrate 2 |
| **IRX3** | 4.04 | 0.0000 | iroquois homeobox 3 |
| **IRX4** | 3.66 | 0.0000 | iroquois homeobox 4 |
| **IRX5** | 3.39 | 0.0000 | iroquois homeobox 5 |
| **ISG20** | -2.09 | 0.0000 | interferon stimulated exonuclease gene 20kDa |
| **ISOC1** | 1.46 | 0.0000 | isochorismatase domain containing 1 |
| **ITFG1** | -1.62 | 0.0000 | integrin alpha FG-GAP repeat containing 1 |
| **ITGB1** | -1.65 | 0.0000 | integrin, beta 1 (fibronectin receptor, beta polypeptide, antigen CD29 includes MDF2, MSK12) |
| **ITGB2** | 1.91 | 0.0000 | integrin, beta 2 (complement component 3 receptor 3 and 4 subunit) |
| **ITGB3** | -3.39 | 0.0000 | integrin, beta 3 (platelet glycoprotein IIIa, antigen CD61) |
| **ITGB3BP** | 1.32 | 0.0000 | integrin beta 3 binding protein (beta3-endonexin) |
| **ITGB8** | -5.83 | 0.0000 | integrin, beta 8 |
| **ITIH5** | -4.30 | 0.0000 | inter-alpha (globulin) inhibitor H5 |
| **ITPK1** | -3.05 | 0.0000 | inositol 1,3,4-triphosphate 5/6 kinase |
| **ITPKB** | -1.91 | 0.0000 | inositol 1,4,5-trisphosphate 3-kinase B |
| **ITPR1** | -2.01 | 0.0000 | inositol 1,4,5-triphosphate receptor, type 1 |
| **ITPR3** | -3.03 | 0.0000 | inositol 1,4,5-triphosphate receptor, type 3 |
| **JAGN1** | -0.91 | 0.0000 | jagunal homolog 1 (Drosophila) |
| **JAKMIP2** | -1.15 | 0.0000 | Janus kinase and microtubule interacting protein 2 |
| **JAM2** | 3.39 | 0.0000 | junctional adhesion molecule 2 |
| **JARID2** | -2.12 | 0.0000 | jumonji, AT rich interactive domain 2 |
| **JMJD7** | -1.02 | 0.0000 | JMJD7-PLA2G4B readthrough transcript; phospholipase A2, group IVB (cytosolic); jumonji domain containing 7 |
| **JMJD8** | -1.62 | 0.0000 | jumonji domain containing 8 |
| **JUN** | -1.66 | 0.0000 | jun oncogene |
| **JUNB** | -1.93 | 0.0000 | jun B proto-oncogene |
| **KALRN** | 2.73 | 0.0000 | kalirin, RhoGEF kinase |
| **KAT2A** | 1.78 | 0.0000 | K(lysine) acetyltransferase 2A |
| **KAT2B** | -4.03 | 0.0000 | K(lysine) acetyltransferase 2B |
| **KATNAL1** | -1.55 | 0.0000 | katanin p60 subunit A-like 1 |
| **KBTBD10** | -1.63 | 0.0000 | kelch repeat and BTB (POZ) domain containing 10 |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **KBTBD11** | 3.09 | 0.0000 | kelch repeat and BTB (POZ) domain containing 11 |
| **KCNAB1** | -2.99 | 0.0000 | potassium voltage-gated channel, shaker-related subfamily, beta member 1 |
| **KCNG1** | 2.14 | 0.0000 | potassium voltage-gated channel, subfamily G, member 1 |
| **KCNG3** | 2.42 | 0.0000 | potassium voltage-gated channel, subfamily G, member 3 |
| **KCNIP3** | 3.25 | 0.0000 | Kv channel interacting protein 3, calsenilin |
| **KCNK1** | 4.40 | 0.0000 | potassium channel, subfamily K, member 1 |
| **KCNMA1** | 3.05 | 0.0000 | potassium large conductance calcium-activated channel, subfamily M, alpha member 1 |
| **KCNN2** | 3.08 | 0.0000 | potassium intermediate/small conductance calcium-activated channel, subfamily N, member 2 |
| **KCNN4** | -3.91 | 0.0000 | potassium intermediate/small conductance calcium-activated channel, subfamily N, member 4 |
| **KCNQ2** | 5.20 | 0.0000 | potassium voltage-gated channel, KQT-like subfamily, member 2 |
| **KCNS3** | -3.37 | 0.0000 | potassium voltage-gated channel, delayed-rectifier, subfamily S, member 3 |
| **KCTD11** | -0.69 | 0.0000 | potassium channel tetramerisation domain containing 11 |
| **KCTD12** | -3.15 | 0.0000 | potassium channel tetramerisation domain containing 12 |
| **KCTD20** | -2.30 | 0.0000 | potassium channel tetramerisation domain containing 20 |
| **KCTD3** | -1.20 | 0.0000 | potassium channel tetramerisation domain containing 3 |
| **KDELR3** | -1.36 | 0.0000 | KDEL (Lys-Asp-Glu-Leu) endoplasmic reticulum protein retention receptor 3 |
| **KDM4D** | 2.01 | 0.0000 | lysine (K)-specific demethylase 4D |
| **KDSR** | -1.62 | 0.0000 | 3-ketodihydrosphingosine reductase |
| **KHDRBS1** | 0.79 | 0.0000 | KH domain containing, RNA binding, signal transduction associated 1 |
| **KIAA0101** | 1.98 | 0.0000 | KIAA0101 |
| **KIAA0174** | -0.78 | 0.0000 | similar to CG10103; KIAA0174 |
| **KIAA0232** | -1.02 | 0.0000 | KIAA0232 |
| **KIAA0247** | -1.11 | 0.0000 | KIAA0247 |
| **KIAA0391** | -1.10 | 0.0000 | KIAA0391 |
| **KIAA0494** | -1.21 | 0.0000 | KIAA0494 |
| **KIAA0513** | -2.16 | 0.0000 | KIAA0513 |
| **KIAA0802** | 1.87 | 0.0000 | KIAA0802 |
| **KIAA1012** | -1.29 | 0.0000 | KIAA1012 |
| **KIAA1033** | -2.01 | 0.0000 | KIAA1033 |
| **KIAA1147** | 1.36 | 0.0000 | KIAA1147 |
| **KIAA1199** | 3.09 | 0.0000 | KIAA1199 |
| **KIAA1244** | -1.15 | 0.0000 | KIAA1244 |
| **KIAA1274** | 3.02 | 0.0000 | KIAA1274 |
| **KIAA1279** | -1.12 | 0.0000 | KIAA1279 |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **KIAA1430** | -0.93 | 0.0000 | KIAA1430 |
| **KIAA1468** | -0.97 | 0.0000 | KIAA1468 |
| **KIAA1539** | -0.95 | 0.0000 | KIAA1539 |
| **KIAA1549** | 2.08 | 0.0000 | KIAA1549 |
| **KIAA1598** | -3.53 | 0.0000 | KIAA1598 |
| **KIAA1731** | 1.07 | 0.0000 | KIAA1731 |
| **KIAA1804** | 2.76 | 0.0000 | mixed lineage kinase 4 |
| **KIAA1826** | 1.06 | 0.0000 | KIAA1826 |
| **KIAA1841** | -1.22 | 0.0000 | KIAA1841 |
| **KIAA1919** | -1.05 | 0.0000 | KIAA1919 |
| **KIF13A** | -2.11 | 0.0000 | kinesin family member 13A |
| **KIF13B** | -4.42 | 0.0000 | kinesin family member 13B |
| **KIF16B** | -1.76 | 0.0000 | kinesin family member 16B |
| **KIF1B** | -1.05 | 0.0000 | kinesin family member 1B |
| **KIF26A** | 2.84 | 0.0000 | kinesin family member 26A |
| **KIF2A** | 1.18 | 0.0000 | kinesin heavy chain member 2A |
| **KIF5B** | -1.47 | 0.0000 | kinesin family member 5B |
| **KIF5C** | 4.32 | 0.0000 | kinesin family member 5C |
| **KIFAP3** | -1.59 | 0.0000 | kinesin-associated protein 3 |
| **KIT** | 4.20 | 0.0000 | similar to Mast/stem cell growth factor receptor precursor (SCFR) (Proto-oncogene tyrosine-protein kinase Kit) (c-kit) (CD117 antigen); v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog |
| **KITLG** | 2.03 | 0.0000 | KIT ligand |
| **KLC1** | 1.51 | 0.0000 | kinesin light chain 1 |
| **KLF13** | -1.22 | 0.0000 | Kruppel-like factor 13 |
| **KLF5** | 1.77 | 0.0000 | Kruppel-like factor 5 (intestinal) |
| **KLF6** | -1.74 | 0.0000 | Kruppel-like factor 6 |
| **KLF9** | -3.42 | 0.0000 | Kruppel-like factor 9 |
| **KLHL12** | 0.70 | 0.0000 | kelch-like 12 (Drosophila) |
| **KLHL22** | -0.90 | 0.0000 | kelch-like 22 (Drosophila) |
| **KLHL23** | 4.04 | 0.0000 | kelch-like 23 (Drosophila) |
| **KLHL35** | 2.12 | 0.0000 | kelch-like 35 (Drosophila) |
| **KLHL5** | 1.77 | 0.0000 | kelch-like 5 (Drosophila) |
| **KNTC1** | 1.38 | 0.0000 | kinetochore associated 1 |
| **KPNA5** | -1.26 | 0.0000 | karyopherin alpha 5 (importin alpha 6) |
| **KRAS** | -1.07 | 0.0000 | v-Ki-ras2 Kirsten rat sarcoma viral oncogene homolog |
| **KRCC1** | -1.22 | 0.0000 | lysine-rich coiled-coil 1 |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **KRT10** | -1.04 | 0.0000 | keratin 10 |
| **KRT18** | 5.60 | 0.0000 | keratin 18; keratin 18 pseudogene 26; keratin 18 pseudogene 19 |
| **KRT8** | 2.29 | 0.0000 | keratin 8 pseudogene 9; similar to keratin 8; keratin 8 |
| **KRT80** | 1.53 | 0.0000 | keratin 80 |
| **KRTAP6-3** | -3.03 | 0.0000 | keratin associated protein 6-3 |
| **KYNU** | -1.85 | 0.0000 | kynureninase (L-kynurenine hydrolase) |
| **LAGE3** | 1.13 | 0.0000 | L antigen family, member 3 |
| **LAMA1** | 4.20 | 0.0000 | laminin, alpha 1 |
| **LAMA2** | -2.22 | 0.0000 | laminin, alpha 2 |
| **LAMA4** | -2.55 | 0.0000 | laminin, alpha 4 |
| **LAMB2** | -2.20 | 0.0000 | laminin, beta 2 (laminin S) |
| **LAMC1** | -2.20 | 0.0000 | laminin, gamma 1 (formerly LAMB2) |
| **LAMC3** | 2.01 | 0.0000 | laminin, gamma 3 |
| **LAMP1** | -2.00 | 0.0000 | lysosomal-associated membrane protein 1 |
| **LAMP2** | -4.26 | 0.0000 | lysosomal-associated membrane protein 2 |
| **LAMP3** | 2.31 | 0.0000 | lysosomal-associated membrane protein 3 |
| **LANCL3** | 1.28 | 0.0000 | LanC lantibiotic synthetase component C-like 3 (bacterial) |
| **LAPTM4B** | 1.05 | 0.0000 | lysosomal protein transmembrane 4 beta |
| **LARGE** | -3.08 | 0.0000 | like-glycosyltransferase |
| **LARP7** | -1.23 | 0.0000 | La ribonucleoprotein domain family, member 7 |
| **LARS** | 0.87 | 0.0000 | leucyl-tRNA synthetase |
| **LAT** | 2.47 | 0.0000 | linker for activation of T cells |
| **LATS2** | -1.41 | 0.0000 | LATS, large tumor suppressor, homolog 2 (Drosophila) |
| **LCP1** | -2.04 | 0.0000 | lymphocyte cytosolic protein 1 (L-plastin) |
| **LDLRAP1** | -1.65 | 0.0000 | low density lipoprotein receptor adaptor protein 1 |
| **LEF1** | -2.50 | 0.0000 | lymphoid enhancer-binding factor 1 |
| **LEPREL1** | 3.95 | 0.0000 | leprecan-like 1 |
| **LEPROT** | -1.20 | 0.0000 | leptin receptor overlapping transcript |
| **LGALS1** | -2.54 | 0.0000 | lectin, galactoside-binding, soluble, 1 |
| **LGALS3** | -4.61 | 0.0000 | lectin, galactoside-binding, soluble, 3 |
| **LGALS8** | -0.95 | 0.0000 | lectin, galactoside-binding, soluble, 8 |
| **LHX2** | 5.37 | 0.0000 | LIM homeobox 2 |
| **LIFR** | 1.92 | 0.0000 | leukemia inhibitory factor receptor alpha |
| **LIG4** | -1.64 | 0.0000 | ligase IV, DNA, ATP-dependent |
| **LIMK2** | -1.69 | 0.0000 | LIM domain kinase 2 |
| **LIN52** | 1.25 | 0.0000 | lin-52 homolog (C. elegans) |
| **LIPA** | -1.67 | 0.0000 | lipase A, lysosomal acid, cholesterol esterase |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **LIPG** | 2.99 | 0.0000 | lipase, endothelial |
| **LMAN1** | -1.27 | 0.0000 | lectin, mannose-binding, 1 |
| **LMBRD1** | -3.30 | 0.0000 | LMBR1 domain containing 1 |
| **LMO2** | 2.63 | 0.0000 | LIM domain only 2 (rhombotin-like 1) |
| **LNX1** | 1.98 | 0.0000 | ligand of numb-protein X 1 |
| **LOC100126784** | -2.40 | 0.0000 | hypothetical LOC100126784 |
| **LOC100127980** | 1.69 | 0.0000 | hypothetical protein LOC100127980 |
| **LOC100128164** | 2.83 | 0.0000 | four and a half LIM domains 1 pseudogene |
| **LOC100129113** | -1.56 | 0.0000 | hypothetical protein LOC100129113 |
| **LOC100130175** | -1.00 | 0.0000 | hypothetical protein LOC100130175 |
| **LOC100130890** | -1.23 | 0.0000 | similar to hCG2030844 |
| **LOC100132244** | -2.19 | 0.0000 | hypothetical protein LOC100132244 |
| **LOC100190939** | -1.41 | 0.0000 | hypothetical LOC100190939 |
| **LOC100271840** | 4.22 | 0.0000 | hypothetical LOC100271840 |
| **LOC100288144** | 2.08 | 0.0000 | hypothetical protein LOC100288144 |
| **LOC145783** | -0.85 | 0.0000 | hypothetical LOC145783 |
| **LOC149501** | 2.22 | 0.0000 | keratin 8 pseudogene 9; similar to keratin 8; keratin 8 |
| **LOC151009** | 1.63 | 0.0000 | hypothetical LOC151009 |
| **LOC254057** | 2.14 | 0.0000 | hypothetical protein LOC254057 |
| **LOC257396** | 2.00 | 0.0000 | hypothetical protein LOC257396 |
| **LOC283658** | 2.32 | 0.0000 | hypothetical protein LOC283658 |
| **LOC284542** | -2.10 | 0.0000 | hypothetical protein LOC284542 |
| **LOC375010** | 2.61 | 0.0000 | ankyrin repeat domain 20 family, member A pseudogene |
| **LOC388152** | 0.81 | 0.0000 | hypothetical LOC388152 |
| **LOC388796** | 1.43 | 0.0000 | hypothetical LOC388796 |
| **LOC389634** | -1.36 | 0.0000 | hypothetical LOC389634 |
| **LOC389641** | 0.89 | 0.0000 | hypothetical gene supported by AK124295 |
| **LOC390414** | 0.92 | 0.0000 | hypothetical LOC390414 |
| **LOC392288** | -1.96 | 0.0000 | similar to microtubule-associated proteins 1A/1B light chain 3 |
| **LOC399959** | 2.96 | 0.0000 | hypothetical LOC399959 |
| **LOC400236** | 1.50 | 0.0000 | hypothetical LOC400236 |
| **LOC401022** | 2.24 | 0.0000 | hypothetical LOC401022 |
| **LOC407835** | -1.24 | 0.0000 | mitogen-activated protein kinase kinase 2 pseudogene; mitogen-activated protein kinase kinase 2 |
| **LOC439949** | 3.31 | 0.0000 | hypothetical protein LOC439949 |
| **LOC440104** | -1.51 | 0.0000 | hypothetical LOC440104 |
| **LOC442249** | 6.06 | 0.0000 | similar to keratin 18 |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **LOC442421** | -0.91 | 0.0000 | hypothetical LOC442421 |
| **LOC550643** | -1.01 | 0.0000 | hypothetical LOC550643 |
| **LOC554202** | 1.58 | 0.0000 | hypothetical LOC554202 |
| **LOC572558** | 2.60 | 0.0000 | hypothetical locus LOC572558 |
| **LOC644563** | -0.86 | 0.0000 | similar to general transcription factor IIIC, polypeptide 6, alpha 35kDa |
| **LOC645249** | 3.32 | 0.0000 | hypothetical protein LOC645249 |
| **LOC653071** | -1.59 | 0.0000 | similar to CG32820-PA, isoform A |
| **LOC654433** | -3.32 | 0.0000 | hypothetical LOC654433 |
| **LOC728142** | -1.81 | 0.0000 | hypothetical LOC728142 |
| **LOC728705** | 1.19 | 0.0000 | hypothetical protein LOC728705 |
| **LOC729082** | -1.66 | 0.0000 | hypothetical protein LOC729082 |
| **LOC729683** | 2.19 | 0.0000 | hypothetical protein LOC729683 |
| **LOC730091** | 1.80 | 0.0000 | hypothetical protein LOC730091 |
| **LOC730144** | -1.01 | 0.0000 | similar to eukaryotic translation initiation factor 1; eukaryotic translation initiation factor 1 |
| **LOC80154** | 2.26 | 0.0000 | hypothetical LOC80154 |
| **LOH12CR1** | -2.05 | 0.0000 | loss of heterozygosity, 12, chromosomal region 1 |
| **LONRF2** | 3.63 | 0.0000 | LON peptidase N-terminal domain and ring finger 2 |
| **LOXL3** | -3.39 | 0.0000 | lysyl oxidase-like 3 |
| **LPCAT4** | 1.12 | 0.0000 | lysophosphatidylcholine acyltransferase 4 |
| **LPGAT1** | -1.72 | 0.0000 | lysophosphatidylglycerol acyltransferase 1 |
| **LPHN3** | 1.61 | 0.0000 | latrophilin 3 |
| **LPIN1** | -1.43 | 0.0000 | lipin 1 |
| **LPL** | 3.31 | 0.0000 | lipoprotein lipase |
| **LPP** | -1.87 | 0.0000 | LIM domain containing preferred translocation partner in lipoma |
| **LRAT** | -4.14 | 0.0000 | lecithin retinol acyltransferase (phosphatidylcholine--retinol O-acyltransferase) |
| **LRIG1** | -1.83 | 0.0000 | leucine-rich repeats and immunoglobulin-like domains 1 |
| **LRP1** | -1.16 | 0.0000 | low density lipoprotein-related protein 1 (alpha-2-macroglobulin receptor) |
| **LRP10** | -2.49 | 0.0000 | low density lipoprotein receptor-related protein 10 |
| **LRP4** | 3.33 | 0.0000 | low density lipoprotein receptor-related protein 4 |
| **LRP5** | 2.08 | 0.0000 | low density lipoprotein receptor-related protein 5 |
| **LRP6** | -1.06 | 0.0000 | low density lipoprotein receptor-related protein 6 |
| **LRP8** | -1.38 | 0.0000 | low density lipoprotein receptor-related protein 8, apolipoprotein e receptor |
| **LRPPRC** | 1.06 | 0.0000 | leucine-rich PPR-motif containing |
| **LRRC1** | 1.93 | 0.0000 | leucine rich repeat containing 1 |
| **LRRC15** | -4.36 | 0.0000 | leucine rich repeat containing 15 |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **LRRC17** | 4.59 | 0.0000 | leucine rich repeat containing 17 |
| **LRRC4** | -1.71 | 0.0000 | leucine rich repeat containing 4 |
| **LRRC42** | 0.93 | 0.0000 | leucine rich repeat containing 42 |
| **LRRC47** | 1.21 | 0.0000 | leucine rich repeat containing 47 |
| **LRRC8D** | -0.75 | 0.0000 | leucine rich repeat containing 8 family, member D |
| **LRRFIP1** | 2.78 | 0.0000 | leucine rich repeat (in FLII) interacting protein 1 |
| **LRRK1** | -2.25 | 0.0000 | leucine-rich repeat kinase 1 |
| **LRRN3** | 2.90 | 0.0000 | leucine rich repeat neuronal 3 |
| **LSM14A** | 1.27 | 0.0000 | LSM14A, SCD6 homolog A (S. cerevisiae) |
| **LSM14B** | 0.96 | 0.0000 | LSM14B, SCD6 homolog B (S. cerevisiae) |
| **LSM5** | 0.91 | 0.0000 | LSM5 homolog, U6 small nuclear RNA associated (S. cerevisiae) |
| **LTBR** | -1.66 | 0.0000 | lymphotoxin beta receptor (TNFR superfamily, member 3) |
| **LUC7L** | 0.96 | 0.0000 | LUC7-like (S. cerevisiae) |
| **LUC7L3** | 1.91 | 0.0000 | cisplatin resistance-associated overexpressed protein |
| **LY6K** | 6.39 | 0.0000 | lymphocyte antigen 6 complex, locus K |
| **LYN** | 1.34 | 0.0000 | v-yes-1 Yamaguchi sarcoma viral related oncogene homolog |
| **LYPD6** | 2.03 | 0.0000 | LY6/PLAUR domain containing 6 |
| **LYPD6B** | 3.50 | 0.0000 | LY6/PLAUR domain containing 6B |
| **LYRM2** | -1.56 | 0.0000 | LYR motif containing 2 |
| **LYRM5** | -2.03 | 0.0000 | LYR motif containing 5 |
| **LYZ** | -2.85 | 0.0000 | lysozyme (renal amyloidosis) |
| **LZTFL1** | -1.03 | 0.0000 | leucine zipper transcription factor-like 1 |
| **MAD2L1BP** | -1.06 | 0.0000 | MAD2L1 binding protein |
| **MAF** | -5.89 | 0.0000 | v-maf musculoaponeurotic fibrosarcoma oncogene homolog (avian) |
| **MAGEA1** | 2.09 | 0.0000 | melanoma antigen family A, 1 (directs expression of antigen MZ2-E) |
| **MAGEA6** | 1.32 | 0.0000 | melanoma antigen family A, 6 |
| **MAGOHB** | 1.08 | 0.0000 | mago-nashi homolog B (Drosophila) |
| **MAGT1** | -1.96 | 0.0000 | magnesium transporter 1 |
| **MAL** | -3.77 | 0.0000 | mal, T-cell differentiation protein |
| **MALT1** | 1.65 | 0.0000 | mucosa associated lymphoid tissue lymphoma translocation gene 1 |
| **MAN1A2** | -1.08 | 0.0000 | mannosidase, alpha, class 1A, member 2 |
| **MAN2A2** | -2.46 | 0.0000 | mannosidase, alpha, class 2A, member 2 |
| **MAN2B1** | -1.62 | 0.0000 | mannosidase, alpha, class 2B, member 1 |
| **MANEA** | -2.17 | 0.0000 | mannosidase, endo-alpha |
| **MANEAL** | 3.43 | 0.0000 | mannosidase, endo-alpha-like |
| **MANF** | -1.05 | 0.0000 | mesencephalic astrocyte-derived neurotrophic factor |
| **MAP1LC3B** | -2.14 | 0.0000 | microtubule-associated protein 1 light chain 3 beta |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **MAP2K2** | -1.06 | 0.0000 | mitogen-activated protein kinase kinase 2 pseudogene; mitogen-activated protein kinase kinase 2 |
| **MAP3K14** | 2.23 | 0.0000 | mitogen-activated protein kinase kinase kinase 14 |
| **MAP3K6** | -1.69 | 0.0000 | mitogen-activated protein kinase kinase kinase 6 |
| **MAP3K9** | 1.74 | 0.0000 | mitogen-activated protein kinase kinase kinase 9 |
| **MAP4** | -2.44 | 0.0000 | microtubule-associated protein 4 |
| **MAPK1** | -1.50 | 0.0000 | mitogen-activated protein kinase 1 |
| **MAPK14** | -1.07 | 0.0000 | mitogen-activated protein kinase 14 |
| **MAPKAPK2** | -1.04 | 0.0000 | mitogen-activated protein kinase-activated protein kinase 2 |
| **MAPKAPK5** | 0.80 | 0.0000 | mitogen-activated protein kinase-activated protein kinase 5 |
| **MAPRE2** | -1.82 | 0.0000 | microtubule-associated protein, RP/EB family, member 2 |
| **MAPRE3** | -0.95 | 0.0000 | microtubule-associated protein, RP/EB family, member 3 |
| **MARCH2** | -0.94 | 0.0000 | membrane-associated ring finger (C3HC4) 2 |
| **MAX** | -1.17 | 0.0000 | MYC associated factor X |
| **MBD4** | 0.85 | 0.0000 | methyl-CpG binding domain protein 4 |
| **MBOAT1** | -2.17 | 0.0000 | membrane bound O-acyltransferase domain containing 1 |
| **MBP** | -4.50 | 0.0000 | myelin basic protein |
| **MC1R** | -2.89 | 0.0000 | tubulin, beta 3; melanocortin 1 receptor (alpha melanocyte stimulating hormone receptor) |
| **MCAM** | -2.10 | 0.0000 | melanoma cell adhesion molecule |
| **MCM2** | 1.03 | 0.0000 | minichromosome maintenance complex component 2 |
| **MCM6** | 1.32 | 0.0000 | minichromosome maintenance complex component 6 |
| **MCM9** | -1.17 | 0.0000 | minichromosome maintenance complex component 9 |
| **MDC1** | 0.86 | 0.0000 | mediator of DNA-damage checkpoint 1 |
| **MDFI** | 0.93 | 0.0000 | MyoD family inhibitor |
| **MDGA1** | -2.26 | 0.0000 | MAM domain containing glycosylphosphatidylinositol anchor 1 |
| **MDK** | 3.33 | 0.0000 | midkine (neurite growth-promoting factor 2) |
| **MDM4** | -1.42 | 0.0000 | Mdm4 p53 binding protein homolog (mouse) |
| **ME2** | -3.21 | 0.0000 | malic enzyme 2, NAD(+)-dependent, mitochondrial |
| **MED1** | -0.65 | 0.0000 | mediator complex subunit 1 |
| **MED10** | 0.70 | 0.0000 | mediator complex subunit 10 |
| **MED11** | -1.14 | 0.0000 | mediator complex subunit 11 |
| **MED14** | -1.01 | 0.0000 | mediator complex subunit 14 |
| **MED28** | 1.16 | 0.0000 | mediator complex subunit 28 |
| **MEF2C** | -3.56 | 0.0000 | myocyte enhancer factor 2C |
| **MEG3** | -1.03 | 0.0000 | maternally expressed 3 (non-protein coding) |
| **MEGF10** | 3.80 | 0.0000 | multiple EGF-like-domains 10 |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **MEGF6** | 2.20 | 0.0000 | multiple EGF-like-domains 6 |
| **MEIS2** | 4.49 | 0.0000 | Meis homeobox 2 |
| **MEST** | 6.80 | 0.0000 | mesoderm specific transcript homolog (mouse) |
| **METTL2B** | 0.82 | 0.0000 | methyltransferase like 2B |
| **MEX3A** | 2.83 | 0.0000 | mex-3 homolog A (C. elegans) |
| **MFI2** | -0.93 | 0.0000 | antigen p97 (melanoma associated) identified by monoclonal antibodies 133.2 and 96.5 |
| **MFSD1** | -1.60 | 0.0000 | major facilitator superfamily domain containing 1 |
| **MFSD10** | -0.88 | 0.0000 | major facilitator superfamily domain containing 10 |
| **MFSD6** | -2.45 | 0.0000 | major facilitator superfamily domain containing 6 |
| **MFSD8** | -1.42 | 0.0000 | major facilitator superfamily domain containing 8 |
| **MGAT5B** | 4.42 | 0.0000 | mannosyl (alpha-1,6-)-glycoprotein beta-1,6-N-acetyl-glucosaminyltransferase, isozyme B |
| **MGC16025** | -2.05 | 0.0000 | hypothetical LOC85009 |
| **MGC16275** | -1.08 | 0.0000 | hypothetical protein MGC16275 |
| **MGC27345** | 1.53 | 0.0000 | hypothetical protein MGC27345 |
| **MGC42105** | -3.86 | 0.0000 | serine/threonine-protein kinase NIM1 |
| **MIA** | -6.47 | 0.0000 | melanoma inhibitory activity |
| **MICA** | -1.16 | 0.0000 | MHC class I polypeptide-related sequence A |
| **MICAL3** | -0.84 | 0.0000 | microtubule associated monoxygenase, calponin and LIM domain containing 3 |
| **MICALL2** | -1.76 | 0.0000 | MICAL-like 2 |
| **MICB** | 1.53 | 0.0000 | MHC class I polypeptide-related sequence B |
| **MID1IP1** | -0.91 | 0.0000 | MID1 interacting protein 1 (gastrulation specific G12 homolog (zebrafish)) |
| **MIOS** | 1.13 | 0.0000 | missing oocyte, meiosis regulator, homolog (Drosophila) |
| **MIR17HG** | 2.00 | 0.0000 | microRNA host gene 1 (non-protein coding) |
| **MKNK2** | -1.53 | 0.0000 | MAP kinase interacting serine/threonine kinase 2 |
| **MKRN1** | -1.17 | 0.0000 | makorin ring finger protein pseudogene 6; makorin ring finger protein 1 |
| **MKS1** | 1.15 | 0.0000 | Meckel syndrome, type 1 |
| **MLF1** | 1.48 | 0.0000 | myeloid leukemia factor 1 |
| **MLL3** | -1.14 | 0.0000 | myeloid/lymphoid or mixed-lineage leukemia 3 |
| **MLL4** | 1.46 | 0.0000 | myeloid/lymphoid or mixed-lineage leukemia 4 |
| **MLLT10** | -1.07 | 0.0000 | myeloid/lymphoid or mixed-lineage leukemia (trithorax homolog, Drosophila); translocated to, 10 |
| **MLPH** | 4.41 | 0.0000 | melanophilin |
| **MLXIP** | -0.96 | 0.0000 | MLX interacting protein |
| **MLYCD** | -1.14 | 0.0000 | malonyl-CoA decarboxylase |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **MMAA** | -1.40 | 0.0000 | methylmalonic aciduria (cobalamin deficiency) cblA type |
| **MMGT1** | -1.19 | 0.0000 | membrane magnesium transporter 1 |
| **MMP1** | 6.74 | 0.0000 | matrix metallopeptidase 1 (interstitial collagenase) |
| **MMP14** | -2.60 | 0.0000 | matrix metallopeptidase 14 (membrane-inserted) |
| **MMP15** | -2.85 | 0.0000 | matrix metallopeptidase 15 (membrane-inserted) |
| **MMP17** | -2.35 | 0.0000 | matrix metallopeptidase 17 (membrane-inserted) |
| **MMP19** | -4.71 | 0.0000 | matrix metallopeptidase 19 |
| **MMP28** | -1.80 | 0.0000 | matrix metallopeptidase 28 |
| **MMS19** | -0.62 | 0.0000 | MMS19 nucleotide excision repair homolog (S. cerevisiae) |
| **MNAT1** | 0.93 | 0.0000 | menage a trois homolog 1, cyclin H assembly factor (Xenopus laevis) |
| **MNX1** | 3.35 | 0.0000 | motor neuron and pancreas homeobox 1 |
| **MON1A** | -1.21 | 0.0000 | MON1 homolog A (yeast) |
| **MON1B** | -0.98 | 0.0000 | MON1 homolog B (yeast) |
| **MORF4L1** | -1.21 | 0.0000 | mortality factor 4; mortality factor 4 like 1 |
| **MOSPD2** | -1.87 | 0.0000 | motile sperm domain containing 2 |
| **MPP3** | 2.61 | 0.0000 | membrane protein, palmitoylated 3 (MAGUK p55 subfamily member 3) |
| **MPP4** | 2.85 | 0.0000 | membrane protein, palmitoylated 4 (MAGUK p55 subfamily member 4) |
| **MPP6** | 1.12 | 0.0000 | membrane protein, palmitoylated 6 (MAGUK p55 subfamily member 6) |
| **MPZL1** | 0.99 | 0.0000 | myelin protein zero-like 1 |
| **MRAS** | -1.78 | 0.0000 | muscle RAS oncogene homolog |
| **MRPL21** | 1.15 | 0.0000 | mitochondrial ribosomal protein L21 |
| **MRPL3** | 0.97 | 0.0000 | mitochondrial ribosomal protein L3 |
| **MRPL32** | 0.98 | 0.0000 | mitochondrial ribosomal protein L32 |
| **MRPL36** | 0.85 | 0.0000 | mitochondrial ribosomal protein L36 |
| **MRPL39** | 1.11 | 0.0000 | mitochondrial ribosomal protein L39 |
| **MRPL42P5** | -1.50 | 0.0000 | mitochondrial ribosomal protein L42 pseudogene 5 |
| **MRPL43** | -0.88 | 0.0000 | mitochondrial ribosomal protein L43 |
| **MRPL54** | -1.32 | 0.0000 | mitochondrial ribosomal protein L54 |
| **MRPS27** | 0.75 | 0.0000 | mitochondrial ribosomal protein S27 |
| **MRRF** | 0.77 | 0.0000 | mitochondrial ribosome recycling factor |
| **MSH2** | 1.10 | 0.0000 | mutS homolog 2, colon cancer, nonpolyposis type 1 (E. coli) |
| **MSH3** | 0.97 | 0.0000 | mutS homolog 3 (E. coli) |
| **MSH6** | 1.08 | 0.0000 | mutS homolog 6 (E. coli) |
| **MSL1** | -0.99 | 0.0000 | male-specific lethal 1 homolog (Drosophila) |
| **MSL3L2** | 1.48 | 0.0000 | male-specific lethal 3-like 2 (Drosophila) |
| **MSN** | -1.22 | 0.0000 | moesin |
| **MSRA** | -2.22 | 0.0000 | methionine sulfoxide reductase A |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **MSX2** | 2.99 | 0.0000 | msh homeobox 2 |
| **MSX2P1** | 1.96 | 0.0000 | msh homeobox 2 pseudogene 1 |
| **MT1A** | -1.76 | 0.0000 | metallothionein 1A |
| **MT1E** | -2.40 | 0.0000 | metallothionein 1L (gene/pseudogene); metallothionein 1E; metallothionein 1 pseudogene 3; metallothionein 1J (pseudogene) |
| **MT1F** | -4.95 | 0.0000 | metallothionein 1F |
| **MT1G** | -1.75 | 0.0000 | metallothionein 1G |
| **MT1H** | -1.57 | 0.0000 | metallothionein 1H |
| **MT1L** | -1.45 | 0.0000 | metallothionein 1L (gene/pseudogene); metallothionein 1E; metallothionein 1 pseudogene 3; metallothionein 1J (pseudogene) |
| **MT1X** | -1.80 | 0.0000 | metallothionein 1X |
| **MTBP** | 1.55 | 0.0000 | Mdm2, transformed 3T3 cell double minute 2, p53 binding protein (mouse) binding protein, 104kDa |
| **MTCH2** | -1.61 | 0.0000 | mitochondrial carrier homolog 2 (C. elegans) |
| **MTERFD1** | 1.30 | 0.0000 | MTERF domain containing 1 |
| **MTF1** | -1.27 | 0.0000 | metal-regulatory transcription factor 1 |
| **MTHFD1L** | 1.40 | 0.0000 | methylenetetrahydrofolate dehydrogenase (NADP+ dependent) 1-like |
| **MTIF3** | -1.40 | 0.0000 | mitochondrial translational initiation factor 3 |
| **MTMR1** | 1.65 | 0.0000 | myotubularin related protein 1 |
| **MTMR14** | -1.28 | 0.0000 | myotubularin related protein 14 |
| **MTMR4** | 1.14 | 0.0000 | myotubularin related protein 4 |
| **MTSS1** | 3.42 | 0.0000 | metastasis suppressor 1 |
| **MUM1** | 1.40 | 0.0000 | melanoma associated antigen (mutated) 1 |
| **MUT** | -1.55 | 0.0000 | methylmalonyl Coenzyme A mutase |
| **MVP** | -1.65 | 0.0000 | major vault protein |
| **MXI1** | -1.48 | 0.0000 | MAX interactor 1 |
| **MYB** | 2.12 | 0.0000 | v-myb myeloblastosis viral oncogene homolog (avian) |
| **MYBBP1A** | 0.96 | 0.0000 | MYB binding protein (P160) 1a |
| **MYBL2** | 1.91 | 0.0000 | v-myb myeloblastosis viral oncogene homolog (avian)-like 2 |
| **MYCBP** | 1.58 | 0.0000 | c-myc binding protein |
| **MYD88** | -1.60 | 0.0000 | myeloid differentiation primary response gene (88) |
| **MYL12A** | -1.21 | 0.0000 | myosin, light chain 12A, regulatory, non-sarcomeric |
| **MYL12B** | -0.86 | 0.0000 | myosin, light chain 12B, regulatory |
| **MYL6** | -1.65 | 0.0000 | myosin, light chain 6, alkali, smooth muscle and non-muscle |
| **MYL9** | -4.56 | 0.0000 | myosin, light chain 9, regulatory |
| **MYO1B** | 1.77 | 0.0000 | myosin IB |
| **MYO1E** | -2.44 | 0.0000 | myosin IE |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **MYO5A** | -1.83 | 0.0000 | myosin VA (heavy chain 12, myoxin) |
| **MYO5B** | 4.07 | 0.0000 | similar to acetyl-Coenzyme A acyltransferase 2 (mitochondrial 3-oxoacyl-Coenzyme A thiolase); similar to KIAA1119 protein; myosin VB |
| **MYO5C** | 2.39 | 0.0000 | myosin VC |
| **MYO6** | 1.48 | 0.0000 | myosin VI |
| **MYO9A** | -1.14 | 0.0000 | myosin IXA |
| **MYRIP** | 2.75 | 0.0000 | myosin VIIA and Rab interacting protein |
| **MYST1** | 1.45 | 0.0000 | MYST histone acetyltransferase 1 |
| **N4BP2L2** | -2.21 | 0.0000 | NEDD4 binding protein 2-like 2 |
| **NAAA** | -1.86 | 0.0000 | N-acylethanolamine acid amidase |
| **NAB1** | 2.09 | 0.0000 | NGFI-A binding protein 1 (EGR1 binding protein 1) |
| **NACC2** | -2.28 | 0.0000 | NACC family member 2, BEN and BTB (POZ) domain containing |
| **NASP** | 1.41 | 0.0000 | nuclear autoantigenic sperm protein (histone-binding) |
| **NAT8L** | 2.33 | 0.0000 | N-acetyltransferase 8-like (GCN5-related, putative) |
| **NAT9** | 1.33 | 0.0000 | N-acetyltransferase 9 (GCN5-related, putative) |
| **NAV1** | -1.83 | 0.0000 | neuron navigator 1 |
| **NAV3** | -3.05 | 0.0000 | neuron navigator 3; similar to neuron navigator 3 |
| **NCBP1** | 0.82 | 0.0000 | nuclear cap binding protein subunit 1, 80kDa |
| **NCL** | 0.79 | 0.0000 | nucleolin |
| **NCRNA00189** | 1.81 | 0.0000 | chromosome 21 open reading frame 109 |
| **NCSTN** | -1.36 | 0.0000 | nicastrin |
| **NDNL2** | 1.01 | 0.0000 | necdin-like 2 |
| **NDP** | -2.51 | 0.0000 | Norrie disease (pseudoglioma) |
| **NDUFA1** | -1.10 | 0.0000 | NADH dehydrogenase (ubiquinone) 1 alpha subcomplex, 1, 7.5kDa |
| **NDUFA7** | -1.21 | 0.0000 | NADH dehydrogenase (ubiquinone) 1 alpha subcomplex, 7, 14.5kDa |
| **NDUFAF3** | -1.21 | 0.0000 | NADH dehydrogenase (ubiquinone) 1 alpha subcomplex, assembly factor 3 |
| **NDUFB9** | 1.12 | 0.0000 | NADH dehydrogenase (ubiquinone) 1 beta subcomplex, 9, 22kDa |
| **NDUFC1** | -0.85 | 0.0000 | NADH dehydrogenase (ubiquinone) 1, subcomplex unknown, 1, 6kDa |
| **NDUFV2** | -0.90 | 0.0000 | NADH dehydrogenase (ubiquinone) flavoprotein 2, 24kDa |
| **NEFH** | 5.45 | 0.0000 | neurofilament, heavy polypeptide |
| **NEK1** | -2.11 | 0.0000 | NIMA (never in mitosis gene a)-related kinase 1 |
| **NEK11** | 0.67 | 0.0000 | NIMA (never in mitosis gene a)- related kinase 11 |
| **NELL2** | 2.95 | 0.0000 | NEL-like 2 (chicken) |
| **NET1** | 1.25 | 0.0000 | neuroepithelial cell transforming 1 |
| **NEU1** | -1.96 | 0.0000 | sialidase 1 (lysosomal sialidase) |
| **NEXN** | 2.15 | 0.0000 | nexilin (F actin binding protein) |
| **NF1** | -2.25 | 0.0000 | neurofibromin 1 |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **NFATC1** | 3.72 | 0.0000 | nuclear factor of activated T-cells, cytoplasmic, calcineurin-dependent 1 |
| **NFE2L2** | -1.55 | 0.0000 | nuclear factor (erythroid-derived 2)-like 2 |
| **NFIB** | 3.85 | 0.0000 | nuclear factor I/B |
| **NFIC** | -1.84 | 0.0000 | nuclear factor I/C (CCAAT-binding transcription factor) |
| **NFIL3** | -2.64 | 0.0000 | nuclear factor, interleukin 3 regulated |
| **NFKBIA** | -2.07 | 0.0000 | nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, alpha |
| **NFKBIL2** | 1.16 | 0.0000 | nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor-like 2 |
| **NFS1** | 1.57 | 0.0000 | NFS1 nitrogen fixation 1 homolog (S. cerevisiae) |
| **NFYB** | 1.17 | 0.0000 | nuclear transcription factor Y, beta |
| **NGFR** | -3.64 | 0.0000 | nerve growth factor receptor (TNFR superfamily, member 16) |
| **NGFRAP1** | -1.79 | 0.0000 | nerve growth factor receptor (TNFRSF16) associated protein 1 |
| **NHLRC2** | -1.08 | 0.0000 | NHL repeat containing 2 |
| **NICN1** | -1.76 | 0.0000 | nicolin 1 |
| **NIN** | 1.57 | 0.0000 | ninein (GSK3B interacting protein) |
| **NKAIN1** | 2.44 | 0.0000 | Na+/K+ transporting ATPase interacting 1 |
| **NKD2** | 2.22 | 0.0000 | naked cuticle homolog 2 (Drosophila) |
| **NKX2-1** | 1.67 | 0.0000 | NK2 homeobox 1 |
| **NKX2-5** | 2.40 | 0.0000 | NK2 transcription factor related, locus 5 (Drosophila) |
| **NKX3-2** | 2.04 | 0.0000 | NK3 homeobox 2 |
| **NLRP3** | 1.96 | 0.0000 | NLR family, pyrin domain containing 3 |
| **NLRX1** | -3.06 | 0.0000 | NLR family member X1 |
| **NME1** | 1.00 | 0.0000 | non-metastatic cells 1, protein (NM23A) expressed in; NME1-NME2 readthrough transcript; non-metastatic cells 2, protein (NM23B) expressed in |
| **NME2** | 0.90 | 0.0000 | non-metastatic cells 1, protein (NM23A) expressed in; NME1-NME2 readthrough transcript; non-metastatic cells 2, protein (NM23B) expressed in |
| **NME2P1** | 1.14 | 0.0000 | non-metastatic cells 2, protein (NM23B) expressed in, pseudogene 1 |
| **NME3** | -1.97 | 0.0000 | non-metastatic cells 3, protein expressed in |
| **NMT2** | 1.65 | 0.0000 | N-myristoyltransferase 2 |
| **NMU** | 2.64 | 0.0000 | neuromedin U |
| **NOC2L** | 1.30 | 0.0000 | nucleolar complex associated 2 homolog (S. cerevisiae) |
| **NOC3L** | 0.98 | 0.0000 | nucleolar complex associated 3 homolog (S. cerevisiae) |
| **NOL10** | 1.02 | 0.0000 | nucleolar protein 10 |
| **NOL11** | 1.50 | 0.0000 | nucleolar protein 11 |
| **NOL9** | 1.50 | 0.0000 | nucleolar protein 9 |
| **NOM1** | 0.96 | 0.0000 | nucleolar protein with MIF4G domain 1 |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **NONO** | -0.79 | 0.0000 | non-POU domain containing, octamer-binding |
| **NOP2** | 1.03 | 0.0000 | NOP2 nucleolar protein homolog (yeast) |
| **NOTCH1** | -0.96 | 0.0000 | Notch homolog 1, translocation-associated (Drosophila) |
| **NOV** | -1.53 | 0.0000 | nephroblastoma overexpressed gene |
| **NPAS3** | 1.88 | 0.0000 | neuronal PAS domain protein 3 |
| **NPC1** | -1.28 | 0.0000 | Niemann-Pick disease, type C1 |
| **NPC2** | -1.44 | 0.0000 | Niemann-Pick disease, type C2 |
| **NPL** | -3.15 | 0.0000 | N-acetylneuraminate pyruvate lyase (dihydrodipicolinate synthase) |
| **NPM1** | 1.23 | 0.0000 | nucleophosmin 1 (nucleolar phosphoprotein B23, numatrin) pseudogene 21; hypothetical LOC100131044; similar to nucleophosmin 1; nucleophosmin (nucleolar phosphoprotein B23, numatrin) |
| **NPPB** | 4.02 | 0.0000 | natriuretic peptide precursor B |
| **NPR3** | 1.48 | 0.0000 | natriuretic peptide receptor C/guanylate cyclase C (atrionatriuretic peptide receptor C) |
| **NPTX1** | 4.14 | 0.0000 | neuronal pentraxin I |
| **NQO2** | -1.31 | 0.0000 | NAD(P)H dehydrogenase, quinone 2 |
| **NR0B1** | 3.23 | 0.0000 | nuclear receptor subfamily 0, group B, member 1 |
| **NR4A1** | -3.89 | 0.0000 | nuclear receptor subfamily 4, group A, member 1 |
| **NR4A2** | -2.74 | 0.0000 | nuclear receptor subfamily 4, group A, member 2 |
| **NRBF2** | -1.36 | 0.0000 | nuclear receptor binding factor 2 |
| **NRBP2** | -1.24 | 0.0000 | nuclear receptor binding protein 2 |
| **NRCAM** | -3.02 | 0.0000 | neuronal cell adhesion molecule |
| **NRG1** | 2.69 | 0.0000 | neuregulin 1 |
| **NRN1** | -3.44 | 0.0000 | neuritin 1 |
| **NRP1** | 1.71 | 0.0000 | neuropilin 1 |
| **NSF** | 1.46 | 0.0000 | N-ethylmaleimide-sensitive factor |
| **NSUN2** | 0.97 | 0.0000 | NOL1/NOP2/Sun domain family, member 2 |
| **NTN4** | 3.07 | 0.0000 | netrin 4 |
| **NTNG1** | -3.38 | 0.0000 | netrin G1 |
| **NUAK2** | 1.93 | 0.0000 | NUAK family, SNF1-like kinase, 2 |
| **NUCB2** | -2.34 | 0.0000 | nucleobindin 2 |
| **NUDT10** | 2.28 | 0.0000 | nudix (nucleoside diphosphate linked moiety X)-type motif 10 |
| **NUDT21** | 2.14 | 0.0000 | nudix (nucleoside diphosphate linked moiety X)-type motif 21 |
| **NUDT3** | -1.84 | 0.0000 | nudix (nucleoside diphosphate linked moiety X)-type motif 3 |
| **NUDT4** | -1.91 | 0.0000 | nudix (nucleoside diphosphate linked moiety X)-type motif 4; nudix (nucleoside diphosphate linked moiety X)-type motif 4 pseudogene 1 |
| **NUDT9** | -1.30 | 0.0000 | nudix (nucleoside diphosphate linked moiety X)-type motif 9 |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **NUP107** | 1.43 | 0.0000 | nucleoporin 107kDa |
| **NUP155** | 1.28 | 0.0000 | nucleoporin 155kDa |
| **NUP205** | 1.26 | 0.0000 | nucleoporin 205kDa |
| **NUP85** | 1.22 | 0.0000 | nucleoporin 85kDa |
| **NXT1** | 1.54 | 0.0000 | NTF2-like export factor 1 |
| **OAF** | -3.04 | 0.0000 | OAF homolog (Drosophila) |
| **OAT** | -2.17 | 0.0000 | ornithine aminotransferase (gyrate atrophy) |
| **OAZ1** | -1.74 | 0.0000 | ornithine decarboxylase antizyme 1 |
| **OBFC2A** | 1.65 | 0.0000 | oligonucleotide/oligosaccharide-binding fold containing 2A |
| **OCA2** | 4.12 | 0.0000 | oculocutaneous albinism II |
| **OCIAD2** | -6.62 | 0.0000 | OCIA domain containing 2 |
| **ODC1** | 1.75 | 0.0000 | ornithine decarboxylase 1 |
| **ODZ4** | 2.00 | 0.0000 | odz, odd Oz/ten-m homolog 4 (Drosophila) |
| **OGDHL** | 2.71 | 0.0000 | oxoglutarate dehydrogenase-like |
| **OGFOD1** | 0.83 | 0.0000 | 2-oxoglutarate and iron-dependent oxygenase domain containing 1 |
| **OLA1** | 1.79 | 0.0000 | Obg-like ATPase 1 |
| **OLFML2A** | -3.60 | 0.0000 | olfactomedin-like 2A |
| **OLFML2B** | -2.40 | 0.0000 | olfactomedin-like 2B |
| **OLFML3** | -2.58 | 0.0000 | olfactomedin-like 3 |
| **OLIG1** | 3.87 | 0.0000 | oligodendrocyte transcription factor 1 |
| **OPA1** | 0.85 | 0.0000 | optic atrophy 1 (autosomal dominant) |
| **OPHN1** | -2.19 | 0.0000 | oligophrenin 1 |
| **OPLAH** | -2.44 | 0.0000 | 5-oxoprolinase (ATP-hydrolysing) |
| **OPN3** | -1.85 | 0.0000 | opsin 3 |
| **OR7E5P** | -0.71 | 0.0000 | olfactory receptor, family 7, subfamily E, member 5 pseudogene |
| **ORC5L** | 0.88 | 0.0000 | origin recognition complex, subunit 5-like (yeast) |
| **ORMDL2** | -1.07 | 0.0000 | ORM1-like 2 (S. cerevisiae) |
| **OSBPL8** | -2.21 | 0.0000 | oxysterol binding protein-like 8 |
| **OSGIN2** | -0.75 | 0.0000 | oxidative stress induced growth inhibitor family member 2 |
| **OSR2** | 2.69 | 0.0000 | odd-skipped related 2 (Drosophila) |
| **OSTF1** | -1.31 | 0.0000 | osteoclast stimulating factor 1 |
| **OSTM1** | -3.31 | 0.0000 | osteopetrosis associated transmembrane protein 1 |
| **OTUD1** | -1.05 | 0.0000 | OTU domain containing 1 |
| **OTUD7B** | -1.18 | 0.0000 | OTU domain containing 7B |
| **OVOS2** | -5.37 | 0.0000 | ovostatin; ovostatin 2 |
| **OXSR1** | -1.17 | 0.0000 | oxidative-stress responsive 1 |
| **P2RX7** | -2.68 | 0.0000 | purinergic receptor P2X, ligand-gated ion channel, 7 |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **P4HA2** | -2.02 | 0.0000 | prolyl 4-hydroxylase, alpha polypeptide II |
| **PAAF1** | 1.05 | 0.0000 | proteasomal ATPase-associated factor 1 |
| **PABPC1** | 1.06 | 0.0000 | poly(A) binding protein, cytoplasmic pseudogene 5; poly(A) binding protein, cytoplasmic 1 |
| **PABPC3** | 0.96 | 0.0000 | poly(A) binding protein, cytoplasmic 3 |
| **PABPC4L** | 3.37 | 0.0000 | poly(A) binding protein, cytoplasmic 4-like |
| **PAFAH1B3** | 0.91 | 0.0000 | platelet-activating factor acetylhydrolase, isoform Ib, subunit 3 (29kDa) |
| **PAIP1** | 4.05 | 0.0000 | poly(A) binding protein interacting protein 1; similar to poly(A) binding protein interacting protein 1 |
| **PALM** | 1.57 | 0.0000 | paralemmin |
| **PANK2** | 0.61 | 0.0000 | pantothenate kinase 2 |
| **PAPOLG** | 1.12 | 0.0000 | poly(A) polymerase gamma |
| **PAQR6** | -1.84 | 0.0000 | progestin and adipoQ receptor family member VI |
| **PAQR8** | -2.48 | 0.0000 | progestin and adipoQ receptor family member VIII |
| **PAQR9** | 3.26 | 0.0000 | progestin and adipoQ receptor family member IX |
| **PARD6B** | 1.35 | 0.0000 | par-6 partitioning defective 6 homolog beta (C. elegans) |
| **PARP2** | 1.13 | 0.0000 | poly (ADP-ribose) polymerase 2 |
| **PARP4** | -1.03 | 0.0000 | poly (ADP-ribose) polymerase family, member 4 |
| **PARVA** | -0.77 | 0.0000 | parvin, alpha |
| **PASK** | 1.18 | 0.0000 | PAS domain containing serine/threonine kinase |
| **PAX3** | -1.32 | 0.0000 | paired box 3 |
| **PAX8** | -2.03 | 0.0000 | paired box 8 |
| **PBRM1** | -1.20 | 0.0000 | polybromo 1 |
| **PC** | -2.05 | 0.0000 | pyruvate carboxylase |
| **PCBD2** | 0.95 | 0.0000 | pterin-4 alpha-carbinolamine dehydratase/dimerization cofactor of hepatocyte nuclear factor 1 alpha (TCF1) 2 |
| **PCBP1** | -0.95 | 0.0000 | poly(rC) binding protein 1 |
| **PCBP4** | -2.20 | 0.0000 | poly(rC) binding protein 4 |
| **PCCA** | -0.94 | 0.0000 | propionyl Coenzyme A carboxylase, alpha polypeptide |
| **PCDH9** | -2.42 | 0.0000 | protocadherin 9 |
| **PCDHB12** | 2.01 | 0.0000 | protocadherin beta 12 |
| **PCDHB5** | 3.26 | 0.0000 | protocadherin beta 5 |
| **PCDHB7** | 2.65 | 0.0000 | protocadherin beta 7 |
| **PCDHB9** | 2.16 | 0.0000 | protocadherin beta 10; protocadherin beta 9 |
| **PCDHGA2** | -1.14 | 0.0000 | protocadherin gamma subfamily A, 2 |
| **PCMT1** | -2.32 | 0.0000 | protein-L-isoaspartate (D-aspartate) O-methyltransferase |
| **PCMTD1** | -1.14 | 0.0000 | protein-L-isoaspartate (D-aspartate) O-methyltransferase domain containing |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| | | | 1 |
| **PCNA** | 1.48 | 0.0000 | proliferating cell nuclear antigen |
| **PCOLCE** | 2.48 | 0.0000 | procollagen C-endopeptidase enhancer |
| **PCOLCE2** | 2.96 | 0.0000 | procollagen C-endopeptidase enhancer 2 |
| **PCSK1** | 7.06 | 0.0000 | proprotein convertase subtilisin/kexin type 1 |
| **PCSK1N** | 1.20 | 0.0000 | proprotein convertase subtilisin/kexin type 1 inhibitor |
| **PCSK6** | 1.46 | 0.0000 | proprotein convertase subtilisin/kexin type 6 |
| **PCYT1A** | -0.89 | 0.0000 | phosphate cytidylyltransferase 1, choline, alpha |
| **PDCD2L** | 2.33 | 0.0000 | programmed cell death 2-like |
| **PDCD6IP** | -1.07 | 0.0000 | programmed cell death 6 interacting protein |
| **PDE4DIP** | -1.89 | 0.0000 | hypothetical protein LOC100134230; similar to KIAA0454 protein; similar to phosphodiesterase 4D interacting protein isoform 2; phosphodiesterase 4D interacting protein |
| **PDE7A** | 1.57 | 0.0000 | phosphodiesterase 7A |
| **PDE8B** | 3.08 | 0.0000 | phosphodiesterase 8B |
| **PDE9A** | 3.35 | 0.0000 | phosphodiesterase 9A |
| **PDGFD** | 2.69 | 0.0000 | platelet derived growth factor D |
| **PDGFRA** | 3.55 | 0.0000 | platelet-derived growth factor receptor, alpha polypeptide |
| **PDGFRL** | 3.07 | 0.0000 | platelet-derived growth factor receptor-like |
| **PDHB** | -1.48 | 0.0000 | pyruvate dehydrogenase (lipoamide) beta |
| **PDK3** | -0.84 | 0.0000 | pyruvate dehydrogenase kinase, isozyme 3 |
| **PDLIM4** | -1.51 | 0.0000 | PDZ and LIM domain 4 |
| **PDPN** | -4.51 | 0.0000 | podoplanin |
| **PDZRN3** | -2.03 | 0.0000 | PDZ domain containing ring finger 3 |
| **PEA15** | -1.18 | 0.0000 | phosphoprotein enriched in astrocytes 15 |
| **PEBP1** | -2.57 | 0.0000 | phosphatidylethanolamine binding protein 1 |
| **PEG10** | 2.33 | 0.0000 | paternally expressed 10 |
| **PEPD** | -1.94 | 0.0000 | peptidase D |
| **PER2** | 2.54 | 0.0000 | period homolog 2 (Drosophila) |
| **PEX13** | 1.46 | 0.0000 | peroxisomal biogenesis factor 13 |
| **PEX14** | -1.13 | 0.0000 | peroxisomal biogenesis factor 14 |
| **PFDN4** | 1.24 | 0.0000 | prefoldin subunit 4 |
| **PFKFB4** | -3.35 | 0.0000 | 6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 4 |
| **PGBD1** | -1.06 | 0.0000 | piggyBac transposable element derived 1 |
| **PGM3** | -2.47 | 0.0000 | phosphoglucomutase 3 |
| **PGPEP1** | -0.84 | 0.0000 | pyroglutamyl-peptidase I |
| **PHB** | 0.72 | 0.0000 | prohibitin |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **PHF11** | -4.82 | 0.0000 | PHD finger protein 11 |
| **PHF14** | 1.01 | 0.0000 | PHD finger protein 14 |
| **PHF15** | -1.21 | 0.0000 | PHD finger protein 15 |
| **PHF16** | 0.99 | 0.0000 | PHD finger protein 16 |
| **PHF17** | -1.34 | 0.0000 | PHD finger protein 17 |
| **PHF20L1** | 1.70 | 0.0000 | PHD finger protein 20-like 1 |
| **PHF21B** | 2.07 | 0.0000 | PHD finger protein 21B |
| **PHKA1** | 1.51 | 0.0000 | phosphorylase kinase, alpha 1 pseudogene 1; phosphorylase kinase, alpha 1 (muscle) |
| **PHTF1** | -0.80 | 0.0000 | putative homeodomain transcription factor 1 |
| **PHTF2** | 0.77 | 0.0000 | putative homeodomain transcription factor 2 |
| **PHYHIPL** | 2.11 | 0.0000 | phytanoyl-CoA 2-hydroxylase interacting protein-like |
| **PI4K2A** | -0.89 | 0.0000 | phosphatidylinositol 4-kinase type 2 alpha |
| **PID1** | 3.38 | 0.0000 | phosphotyrosine interaction domain containing 1 |
| **PIGB** | -1.46 | 0.0000 | phosphatidylinositol glycan anchor biosynthesis, class B |
| **PIGK** | -1.12 | 0.0000 | phosphatidylinositol glycan anchor biosynthesis, class K |
| **PIGN** | -1.32 | 0.0000 | phosphatidylinositol glycan anchor biosynthesis, class N |
| **PIK3C3** | -1.09 | 0.0000 | phosphoinositide-3-kinase, class 3 |
| **PIK3R1** | -2.12 | 0.0000 | phosphoinositide-3-kinase, regulatory subunit 1 (alpha) |
| **PIM1** | 2.57 | 0.0000 | pim-1 oncogene |
| **PIP4K2A** | -0.71 | 0.0000 | phosphatidylinositol-5-phosphate 4-kinase, type II, alpha |
| **PITPNA** | -1.93 | 0.0000 | phosphatidylinositol transfer protein, alpha |
| **PITPNC1** | -2.00 | 0.0000 | phosphatidylinositol transfer protein, cytoplasmic 1 |
| **PITX2** | 4.75 | 0.0000 | paired-like homeodomain 2 |
| **PJA1** | -1.25 | 0.0000 | praja ring finger 1 |
| **PKIG** | 1.00 | 0.0000 | protein kinase (cAMP-dependent, catalytic) inhibitor gamma |
| **PKNOX2** | -4.62 | 0.0000 | PBX/knotted 1 homeobox 2 |
| **PLA2G16** | -2.92 | 0.0000 | phospholipase A2, group XVI |
| **PLA2G4C** | -2.10 | 0.0000 | phospholipase A2, group IVC (cytosolic, calcium-independent) |
| **PLA2G7** | 3.00 | 0.0000 | phospholipase A2, group VII (platelet-activating factor acetylhydrolase, plasma) |
| **PLAGL1** | -2.59 | 0.0000 | pleiomorphic adenoma gene-like 1 |
| **PLAGL2** | 2.10 | 0.0000 | pleiomorphic adenoma gene-like 2; similar to pleiomorphic adenoma gene-like 2 |
| **PLAU** | 4.02 | 0.0000 | plasminogen activator, urokinase |
| **PLBD2** | -1.37 | 0.0000 | phospholipase B domain containing 2 |
| **PLCB4** | 3.32 | 0.0000 | phospholipase C, beta 4 |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **PLCE1** | -1.52 | 0.0000 | phospholipase C, epsilon 1 |
| **PLCG1** | 1.75 | 0.0000 | phospholipase C, gamma 1 |
| **PLCH2** | 1.61 | 0.0000 | phospholipase C, eta 2 |
| **PLCL2** | 1.29 | 0.0000 | phospholipase C-like 2 |
| **PLD6** | 1.85 | 0.0000 | phospholipase D family, member 6 |
| **PLEK2** | -2.44 | 0.0000 | pleckstrin 2 |
| **PLEKHA1** | -2.05 | 0.0000 | pleckstrin homology domain containing, family A (phosphoinositide binding specific) member 1 |
| **PLEKHA4** | -4.16 | 0.0000 | pleckstrin homology domain containing, family A (phosphoinositide binding specific) member 4 |
| **PLEKHA5** | -1.27 | 0.0000 | pleckstrin homology domain containing, family A member 5 |
| **PLEKHB2** | -1.72 | 0.0000 | pleckstrin homology domain containing, family B (evectins) member 2 |
| **PLEKHF1** | -1.60 | 0.0000 | pleckstrin homology domain containing, family F (with FYVE domain) member 1 |
| **PLEKHG3** | 1.25 | 0.0000 | pleckstrin homology domain containing, family G (with RhoGef domain) member 3 |
| **PLEKHH2** | 3.51 | 0.0000 | pleckstrin homology domain containing, family H (with MyTH4 domain) member 2 |
| **PLEKHM1** | -1.13 | 0.0000 | pleckstrin homology domain containing, family M (with RUN domain) member 1 |
| **PLEKHM3** | -1.13 | 0.0000 | pleckstrin homology domain containing, family M, member 3 |
| **PLEKHO1** | -1.46 | 0.0000 | pleckstrin homology domain containing, family O member 1 |
| **PLIN3** | -1.23 | 0.0000 | mannose-6-phosphate receptor binding protein 1 |
| **PLOD1** | -1.82 | 0.0000 | procollagen-lysine 1, 2-oxoglutarate 5-dioxygenase 1 |
| **PLOD3** | -1.63 | 0.0000 | procollagen-lysine, 2-oxoglutarate 5-dioxygenase 3 |
| **PLP1** | -6.68 | 0.0000 | proteolipid protein 1 |
| **PLP2** | -2.02 | 0.0000 | proteolipid protein 2 (colonic epithelium-enriched) |
| **PLSCR3** | -1.26 | 0.0000 | phospholipid scramblase 3 |
| **PLXNA2** | 2.29 | 0.0000 | plexin A2 |
| **PLXNA4** | -1.42 | 0.0000 | plexin A4 |
| **PLXNB3** | -2.08 | 0.0000 | plexin B3 |
| **PLXND1** | -2.22 | 0.0000 | plexin D1 |
| **PM20D2** | 2.18 | 0.0000 | peptidase M20 domain containing 2 |
| **PMAIP1** | 4.29 | 0.0000 | phorbol-12-myristate-13-acetate-induced protein 1 |
| **PMEPA1** | -2.20 | 0.0000 | prostate transmembrane protein, androgen induced 1 |
| **PMP22** | -5.20 | 0.0000 | peripheral myelin protein 22 |
| **PMS2L2** | 1.22 | 0.0000 | postmeiotic segregation increased 2-like 5; postmeiotic segregation |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| | | | increased 2-like 5-like; similar to postmeiotic segregation increased 2-like 2; postmeiotic segregation increased 2-like 2 pseudogene |
| **PMS2L3** | 1.03 | 0.0000 | postmeiotic segregation increased 2-like 3; zinc finger protein 12 |
| **PMS2L5** | 0.91 | 0.0000 | postmeiotic segregation increased 2-like 5; postmeiotic segregation increased 2-like 5-like; similar to postmeiotic segregation increased 2-like 2; postmeiotic segregation increased 2-like 2 pseudogene |
| **PNMA1** | -1.01 | 0.0000 | paraneoplastic antigen MA1 |
| **PNMA2** | 4.01 | 0.0000 | paraneoplastic antigen MA2 |
| **PNMA3** | 2.35 | 0.0000 | paraneoplastic antigen MA3 |
| **PNMA5** | 1.62 | 0.0000 | paraneoplastic antigen like 5 |
| **PNPLA3** | -2.25 | 0.0000 | patatin-like phospholipase domain containing 3 |
| **PNPLA4** | -2.19 | 0.0000 | patatin-like phospholipase domain containing 4 |
| **PNPLA6** | -1.94 | 0.0000 | patatin-like phospholipase domain containing 6 |
| **PNPO** | 1.13 | 0.0000 | pyridoxamine 5'-phosphate oxidase |
| **PNPT1** | 1.01 | 0.0000 | polyribonucleotide nucleotidyltransferase 1 |
| **PODXL** | 1.92 | 0.0000 | podocalyxin-like |
| **POLD3** | 1.05 | 0.0000 | polymerase (DNA-directed), delta 3, accessory subunit |
| **POLD4** | -1.36 | 0.0000 | polymerase (DNA-directed), delta 4 |
| **POLG2** | 1.67 | 0.0000 | polymerase (DNA directed), gamma 2, accessory subunit |
| **POLK** | -1.77 | 0.0000 | polymerase (DNA directed) kappa |
| **POLR2C** | 0.91 | 0.0000 | polymerase (RNA) II (DNA directed) polypeptide C, 33kDa |
| **POLR2I** | 1.38 | 0.0000 | polymerase (RNA) II (DNA directed) polypeptide I, 14.5kDa |
| **POMZP3** | -0.77 | 0.0000 | POM (POM121 homolog, rat) and ZP3 fusion |
| **PON2** | -1.54 | 0.0000 | paraoxonase 2 |
| **PON3** | -2.09 | 0.0000 | paraoxonase 3 |
| **POPDC3** | -2.40 | 0.0000 | popeye domain containing 3 |
| **POU4F1** | 4.62 | 0.0000 | POU class 4 homeobox 1 |
| **PPAPDC3** | -2.59 | 0.0000 | phosphatidic acid phosphatase type 2 domain containing 3 |
| **PPARA** | -2.62 | 0.0000 | peroxisome proliferator-activated receptor alpha |
| **PPARG** | 3.18 | 0.0000 | peroxisome proliferator-activated receptor gamma |
| **PPARGC1A** | 2.96 | 0.0000 | peroxisome proliferator-activated receptor gamma, coactivator 1 alpha |
| **PPFIA1** | -1.25 | 0.0000 | protein tyrosine phosphatase, receptor type, f polypeptide (PTPRF), interacting protein (liprin), alpha 1 |
| **PPIB** | -2.42 | 0.0000 | peptidylprolyl isomerase B (cyclophilin B) |
| **PPIL1** | 1.00 | 0.0000 | peptidylprolyl isomerase (cyclophilin)-like 1 |
| **PPM1E** | 3.18 | 0.0000 | protein phosphatase 1E (PP2C domain containing) |
| **PPP1R12A** | -1.70 | 0.0000 | protein phosphatase 1, regulatory (inhibitor) subunit 12A |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **PPP1R12B** | -1.53 | 0.0000 | protein phosphatase 1, regulatory (inhibitor) subunit 12B |
| **PPP1R13B** | 2.12 | 0.0000 | protein phosphatase 1, regulatory (inhibitor) subunit 13B |
| **PPP1R14C** | 1.78 | 0.0000 | protein phosphatase 1, regulatory (inhibitor) subunit 14C |
| **PPP1R1C** | -2.17 | 0.0000 | protein phosphatase 1, regulatory (inhibitor) subunit 1C |
| **PPP1R3D** | -1.06 | 0.0000 | protein phosphatase 1, regulatory (inhibitor) subunit 3D |
| **PPP2CB** | -1.49 | 0.0000 | protein phosphatase 2 (formerly 2A), catalytic subunit, beta isoform |
| **PPP2R2A** | -1.29 | 0.0000 | protein phosphatase 2 (formerly 2A), regulatory subunit B, alpha isoform |
| **PPP2R2D** | -0.95 | 0.0000 | protein phosphatase 2, regulatory subunit B, delta isoform |
| **PPP2R3A** | -1.77 | 0.0000 | protein phosphatase 2 (formerly 2A), regulatory subunit B'', alpha |
| **PPP2R5A** | -1.51 | 0.0000 | protein phosphatase 2, regulatory subunit B', alpha isoform |
| **PPP3CB** | -1.71 | 0.0000 | protein phosphatase 3 (formerly 2B), catalytic subunit, beta isoform |
| **PPP4R2** | -1.31 | 0.0000 | protein phosphatase 4, regulatory subunit 2 |
| **PPRC1** | 0.93 | 0.0000 | peroxisome proliferator-activated receptor gamma, coactivator-related 1 |
| **PPT2** | -2.88 | 0.0000 | palmitoyl-protein thioesterase 2 |
| **PRAME** | 3.29 | 0.0000 | preferentially expressed antigen in melanoma |
| **PRDM11** | 1.52 | 0.0000 | PR domain containing 11 |
| **PRDX2** | -1.87 | 0.0000 | peroxiredoxin 2 |
| **PREP** | -1.77 | 0.0000 | prolyl endopeptidase |
| **PRIM1** | 2.07 | 0.0000 | primase, DNA, polypeptide 1 (49kDa) |
| **PRIM2** | 0.83 | 0.0000 | primase, DNA, polypeptide 2 (58kDa) |
| **PRKCD** | -1.49 | 0.0000 | protein kinase C, delta |
| **PRKCDBP** | -3.28 | 0.0000 | protein kinase C, delta binding protein |
| **PRKCH** | 3.85 | 0.0000 | protein kinase C, eta |
| **PRKCZ** | 1.62 | 0.0000 | protein kinase C, zeta |
| **PRKRA** | -1.19 | 0.0000 | protein kinase, interferon-inducible double stranded RNA dependent activator |
| **PRKRIP1** | 0.90 | 0.0000 | PRKR interacting protein 1 (IL11 inducible) |
| **PRMT2** | -1.37 | 0.0000 | protein arginine methyltransferase 2 |
| **PRMT5** | 1.02 | 0.0000 | protein arginine methyltransferase 5 |
| **PRMT6** | -1.24 | 0.0000 | protein arginine methyltransferase 6 |
| **PROCR** | 1.94 | 0.0000 | protein C receptor, endothelial (ERT-PCR) |
| **PROS1** | -3.58 | 0.0000 | protein S (alpha) |
| **PRPF3** | 0.92 | 0.0000 | PRP3 pre-mRNA processing factor 3 homolog (S. cerevisiae) |
| **PRR3** | 1.35 | 0.0000 | proline rich 3 |
| **PRR5** | 1.37 | 0.0000 | Rho GTPase activating protein 8; proline rich 5 (renal); PRR5-ARHGAP8 fusion |
| **PRR5L** | 2.15 | 0.0000 | proline rich 5 like |
| **PRR7** | -1.01 | 0.0000 | proline rich 7 (synaptic) |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **PRRG4** | -1.67 | 0.0000 | proline rich Gla (G-carboxyglutamic acid) 4 (transmembrane) |
| **PRRT1** | -1.61 | 0.0000 | proline-rich transmembrane protein 1 |
| **PRRX1** | 1.79 | 0.0000 | paired related homeobox 1 |
| **PRRX2** | 4.07 | 0.0000 | paired related homeobox 2 |
| **PRSS12** | -2.39 | 0.0000 | protease, serine, 12 (neurotrypsin, motopsin) |
| **PRUNE2** | -3.93 | 0.0000 | prune homolog 2 (Drosophila) |
| **PSAP** | -2.22 | 0.0000 | prosaposin |
| **PSCA** | 1.54 | 0.0000 | prostate stem cell antigen |
| **PSD3** | -2.85 | 0.0000 | pleckstrin and Sec7 domain containing 3 |
| **PSIP1** | 1.74 | 0.0000 | PC4 and SFRS1 interacting protein 1 |
| **PSMD12** | 0.88 | 0.0000 | proteasome (prosome, macropain) 26S subunit, non-ATPase, 12 |
| **PSMD9** | -0.80 | 0.0000 | proteasome (prosome, macropain) 26S subunit, non-ATPase, 9 |
| **PSME1** | -0.98 | 0.0000 | proteasome (prosome, macropain) activator subunit 1 (PA28 alpha) |
| **PSME3** | 1.04 | 0.0000 | proteasome (prosome, macropain) activator subunit 3 (PA28 gamma; Ki) |
| **PSMF1** | 1.19 | 0.0000 | proteasome (prosome, macropain) inhibitor subunit 1 (PI31) |
| **PSMG2** | -0.99 | 0.0000 | proteasome (prosome, macropain) assembly chaperone 2 |
| **PSTPIP2** | 1.93 | 0.0000 | proline-serine-threonine phosphatase interacting protein 2 |
| **PTCD1** | 1.11 | 0.0000 | pentatricopeptide repeat domain 1 |
| **PTEN** | -2.15 | 0.0000 | phosphatase and tensin homolog; phosphatase and tensin homolog pseudogene 1 |
| **PTGR1** | -1.60 | 0.0000 | prostaglandin reductase 1 |
| **PTGS2** | 3.24 | 0.0000 | prostaglandin-endoperoxide synthase 2 (prostaglandin G/H synthase and cyclooxygenase) |
| **PTK2** | 1.34 | 0.0000 | PTK2 protein tyrosine kinase 2 |
| **PTP4A1** | -0.92 | 0.0000 | protein tyrosine phosphatase type IVA, member 1 |
| **PTP4A3** | 1.37 | 0.0000 | protein tyrosine phosphatase type IVA, member 3 |
| **PTPLB** | -2.75 | 0.0000 | protein tyrosine phosphatase-like (proline instead of catalytic arginine), member b |
| **PTPMT1** | -1.08 | 0.0000 | protein tyrosine phosphatase, mitochondrial 1 |
| **PTPRE** | -4.25 | 0.0000 | protein tyrosine phosphatase, receptor type, E |
| **PTPRG** | 1.62 | 0.0000 | protein tyrosine phosphatase, receptor type, G |
| **PTPRS** | -1.79 | 0.0000 | protein tyrosine phosphatase, receptor type, S |
| **PURB** | -0.97 | 0.0000 | purine-rich element binding protein B |
| **PUS1** | 0.98 | 0.0000 | pseudouridylate synthase 1 |
| **PUS7** | 1.34 | 0.0000 | pseudouridylate synthase 7 homolog (S. cerevisiae) |
| **PXMP2** | 2.14 | 0.0000 | hypothetical LOC100129532; peroxisomal membrane protein 2, 22kDa |
| **PYCR1** | 2.26 | 0.0000 | pyrroline-5-carboxylate reductase 1 |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **PYCRL** | 1.66 | 0.0000 | pyrroline-5-carboxylate reductase-like |
| **PYGL** | -1.11 | 0.0000 | phosphorylase, glycogen, liver |
| **PYROXD1** | -1.66 | 0.0000 | pyridine nucleotide-disulphide oxidoreductase domain 1 |
| **PZP** | -3.05 | 0.0000 | pregnancy-zone protein |
| **QDPR** | -1.41 | 0.0000 | quinoid dihydropteridine reductase |
| **QPCT** | -2.91 | 0.0000 | glutaminyl-peptide cyclotransferase |
| **QRSL1** | -1.53 | 0.0000 | glutaminyl-tRNA synthase (glutamine-hydrolyzing)-like 1 |
| **QSER1** | -0.79 | 0.0000 | glutamine and serine rich 1 |
| **RAB11FIP4** | 2.54 | 0.0000 | RAB11 family interacting protein 4 (class II) |
| **RAB14** | -1.05 | 0.0000 | RAB14, member RAS oncogene family |
| **RAB18** | -1.67 | 0.0000 | RAB18, member RAS oncogene family |
| **RAB2A** | -1.29 | 0.0000 | RAB2A, member RAS oncogene family |
| **RAB31** | -2.37 | 0.0000 | RAB31, member RAS oncogene family |
| **RAB33A** | -3.44 | 0.0000 | RAB33A, member RAS oncogene family |
| **RAB36** | -1.45 | 0.0000 | RAB36, member RAS oncogene family |
| **RAB39B** | 2.56 | 0.0000 | RAB39B, member RAS oncogene family |
| **RAB3D** | 2.14 | 0.0000 | RAB3D, member RAS oncogene family |
| **RAB5A** | -2.49 | 0.0000 | RAB5A, member RAS oncogene family |
| **RAB6A** | -1.21 | 0.0000 | RAB6C, member RAS oncogene family; RAB6A, member RAS oncogene family; hypothetical LOC100130819; RAB6C-like |
| **RAB6B** | 1.93 | 0.0000 | RAB6B, member RAS oncogene family |
| **RAB6C** | -1.27 | 0.0000 | RAB6C, member RAS oncogene family; RAB6A, member RAS oncogene family; hypothetical LOC100130819; RAB6C-like |
| **RAB7B** | -4.02 | 0.0000 | RAB7B, member RAS oncogene family |
| **RAB9A** | -2.35 | 0.0000 | RAB9A, member RAS oncogene family |
| **RAB9B** | -1.07 | 0.0000 | RAB9B, member RAS oncogene family |
| **RAB9P1** | -2.30 | 0.0000 | RAB9, member RAS oncogene family, pseudogene 1 |
| **RABEP1** | -1.93 | 0.0000 | rabaptin, RAB GTPase binding effector protein 1 |
| **RABEPK** | 0.87 | 0.0000 | Rab9 effector protein with kelch motifs |
| **RAD50** | 1.17 | 0.0000 | RAD50 homolog (S. cerevisiae) |
| **RAD51C** | 1.68 | 0.0000 | RAD51 homolog C (S. cerevisiae) |
| **RAD51L3** | -0.88 | 0.0000 | RAD51-like 3 (S. cerevisiae) |
| **RAE1** | 1.44 | 0.0000 | RAE1 RNA export 1 homolog (S. pombe) |
| **RAI14** | 1.80 | 0.0000 | retinoic acid induced 14 |
| **RANBP1** | 0.77 | 0.0000 | similar to RAN binding protein 1; RAN binding protein 1 |
| **RANBP17** | 2.11 | 0.0000 | RAN binding protein 17 |
| **RANBP9** | -1.34 | 0.0000 | RAN binding protein 9 |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **RAP1A** | -2.32 | 0.0000 | RAP1A, member of RAS oncogene family |
| **RAP1GDS1** | -2.33 | 0.0000 | RAP1, GTP-GDP dissociation stimulator 1 |
| **RAPH1** | -1.34 | 0.0000 | Ras association (RalGDS/AF-6) and pleckstrin homology domains 1 |
| **RASA4** | 1.85 | 0.0000 | RAS p21 protein activator 4; RAS p21 protein activator 4 pseudogene |
| **RASD1** | -3.53 | 0.0000 | RAS, dexamethasone-induced 1 |
| **RASD2** | -1.03 | 0.0000 | RASD family, member 2 |
| **RASL10A** | 2.48 | 0.0000 | RAS-like, family 10, member A |
| **RASL10B** | 1.37 | 0.0000 | RAS-like, family 10, member B |
| **RASSF2** | 3.78 | 0.0000 | Ras association (RalGDS/AF-6) domain family member 2 |
| **RASSF4** | -2.92 | 0.0000 | Ras association (RalGDS/AF-6) domain family member 4 |
| **RASSF5** | 2.34 | 0.0000 | Ras association (RalGDS/AF-6) domain family member 5 |
| **RAVER2** | 1.71 | 0.0000 | ribonucleoprotein, PTB-binding 2 |
| **RB1** | -1.73 | 0.0000 | retinoblastoma 1 |
| **RBBP7** | -1.04 | 0.0000 | retinoblastoma binding protein 7 |
| **RBBP9** | 1.09 | 0.0000 | retinoblastoma binding protein 9 |
| **RBM12** | 1.46 | 0.0000 | RNA binding motif protein 12; copine I |
| **RBM47** | -1.79 | 0.0000 | RNA binding motif protein 47 |
| **RBMS1** | -0.94 | 0.0000 | RNA binding motif, single stranded interacting protein 1 |
| **RBPMS2** | 4.89 | 0.0000 | RNA binding protein with multiple splicing 2 |
| **RBX1** | -0.60 | 0.0000 | ring-box 1 |
| **RCAN1** | -3.18 | 0.0000 | regulator of calcineurin 1 |
| **RCAN2** | 3.41 | 0.0000 | regulator of calcineurin 2 |
| **RCC2** | 1.13 | 0.0000 | regulator of chromosome condensation 2 |
| **RCL1** | 2.04 | 0.0000 | RNA terminal phosphate cyclase-like 1 |
| **RDH11** | -1.14 | 0.0000 | retinol dehydrogenase 11 (all-trans/9-cis/11-cis) |
| **RDX** | -2.29 | 0.0000 | radixin |
| **REC8** | -2.64 | 0.0000 | REC8 homolog (yeast) |
| **REEP1** | 2.74 | 0.0000 | receptor accessory protein 1 |
| **REEP3** | -1.33 | 0.0000 | receptor accessory protein 3 |
| **REEP5** | -1.02 | 0.0000 | receptor accessory protein 5 |
| **RELL1** | 1.56 | 0.0000 | RELT-like 1 |
| **RELN** | 2.56 | 0.0000 | reelin |
| **RFC2** | 1.11 | 0.0000 | replication factor C (activator 1) 2, 40kDa |
| **RFC4** | 1.42 | 0.0000 | replication factor C (activator 1) 4, 37kDa |
| **RFESD** | 1.55 | 0.0000 | Rieske (Fe-S) domain containing |
| **RFX5** | -0.98 | 0.0000 | regulatory factor X, 5 (influences HLA class II expression) |
| **RGS2** | 3.89 | 0.0000 | regulator of G-protein signaling 2, 24kDa |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **RGS9BP** | 1.26 | 0.0000 | regulator of G protein signaling 9 binding protein |
| **RHOA** | -2.23 | 0.0000 | ras homolog gene family, member A |
| **RHOB** | -1.71 | 0.0000 | ras homolog gene family, member B |
| **RHOJ** | -1.92 | 0.0000 | ras homolog gene family, member J |
| **RHOQ** | -2.74 | 0.0000 | ras homolog gene family, member Q; similar to small GTP binding protein TC10 |
| **RILP** | -1.24 | 0.0000 | Rab interacting lysosomal protein |
| **RILPL1** | -1.09 | 0.0000 | Rab interacting lysosomal protein-like 1 |
| **RIMBP3** | 1.25 | 0.0000 | RIMS binding protein 3B; RIMS binding protein 3C; RIMS binding protein 3 |
| **RIMKLA** | 3.61 | 0.0000 | ribosomal modification protein rimK-like family member A |
| **RIMS3** | 2.03 | 0.0000 | regulating synaptic membrane exocytosis 3 |
| **RINT1** | 1.03 | 0.0000 | RAD50 interactor 1 |
| **RIOK2** | 1.09 | 0.0000 | RIO kinase 2 (yeast) |
| **RIPK1** | -0.90 | 0.0000 | receptor (TNFRSF)-interacting serine-threonine kinase 1 |
| **RIT1** | -1.22 | 0.0000 | Ras-like without CAAX 1 |
| **RLN2** | 2.63 | 0.0000 | relaxin 2 |
| **RMI1** | 1.50 | 0.0000 | RMI1, RecQ mediated genome instability 1, homolog (S. cerevisiae) |
| **RNASE1** | -4.16 | 0.0000 | ribonuclease, RNase A family, 1 (pancreatic) |
| **RNASEK** | -2.16 | 0.0000 | ribonuclease, RNase K |
| **RNASEN** | 1.18 | 0.0000 | ribonuclease type III, nuclear |
| **RNF114** | 1.62 | 0.0000 | ring finger protein 114 |
| **RNF128** | -5.93 | 0.0000 | ring finger protein 128 |
| **RNF13** | -1.78 | 0.0000 | ring finger protein 13 |
| **RNF141** | -0.89 | 0.0000 | ring finger protein 141 |
| **RNF149** | 0.82 | 0.0000 | ring finger protein 149 |
| **RNF175** | 2.91 | 0.0000 | ring finger protein 175 |
| **RNF2** | 1.06 | 0.0000 | ring finger protein 2 |
| **RNF217** | -1.49 | 0.0000 | ring finger protein 217 |
| **RNF44** | 1.32 | 0.0000 | ring finger protein 44 |
| **RNF5** | -1.45 | 0.0000 | ring finger protein 5; ring finger protein 5 pseudogene 1 |
| **ROPN1** | -4.34 | 0.0000 | ropporin, rhophilin associated protein 1 |
| **ROPN1B** | -4.86 | 0.0000 | ropporin, rhophilin associated protein 1B |
| **ROPN1L** | 1.51 | 0.0000 | ropporin 1-like |
| **RPA2** | 1.23 | 0.0000 | replication protein A2, 32kDa |
| **RPA3** | 1.33 | 0.0000 | replication protein A3, 14kDa |
| **RPAP3** | 1.19 | 0.0000 | RNA polymerase II associated protein 3 |
| **RPIA** | 1.43 | 0.0000 | ribose 5-phosphate isomerase A |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **RPL10** | 0.70 | 0.0000 | ribosomal protein L10; ribosomal protein L10 pseudogene 15; ribosomal protein L10 pseudogene 6; ribosomal protein L10 pseudogene 16; ribosomal protein L10 pseudogene 9 |
| **RPL13** | -1.02 | 0.0000 | ribosomal protein L13 pseudogene 12; ribosomal protein L13 |
| **RPL13P5** | -1.28 | 0.0000 | ribosomal protein L13 pseudogene 5 |
| **RPL23** | -0.80 | 0.0000 | ribosomal protein L23 pseudogene 6; ribosomal protein L23 |
| **RPL23AP82** | -1.58 | 0.0000 | ribosomal protein L23a pseudogene 25; ribosomal protein L23a pseudogene 82 |
| **RPL28** | -1.01 | 0.0000 | ribosomal protein L28 |
| **RPL37** | 1.09 | 0.0000 | ribosomal protein L37 |
| **RPL8** | 0.94 | 0.0000 | ribosomal protein L8; ribosomal protein L8 pseudogene 2 |
| **RPN1** | -0.92 | 0.0000 | ribophorin I |
| **RPP38** | -0.68 | 0.0000 | ribonuclease P/MRP 38kDa subunit |
| **RPRD1A** | -1.11 | 0.0000 | regulation of nuclear pre-mRNA domain containing 1A |
| **RPRD1B** | 1.76 | 0.0000 | regulation of nuclear pre-mRNA domain containing 1B |
| **RPS21** | 1.47 | 0.0000 | ribosomal protein S21 |
| **RPS28** | -1.41 | 0.0000 | ribosomal protein S28 pseudogene 6; ribosomal protein S28 pseudogene 9; ribosomal protein S28 |
| **RPS2P32** | 1.04 | 0.0000 | ribosomal protein S2 pseudogene 32 |
| **RPS6KA1** | -1.48 | 0.0000 | ribosomal protein S6 kinase, 90kDa, polypeptide 1 |
| **RPS6KA3** | -2.11 | 0.0000 | ribosomal protein S6 kinase, 90kDa, polypeptide 3 |
| **RPS6KB1** | 1.40 | 0.0000 | ribosomal protein S6 kinase, 70kDa, polypeptide 1 |
| **RPS6KC1** | -1.27 | 0.0000 | ribosomal protein S6 kinase, 52kDa, polypeptide 1 |
| **RRAGA** | -0.90 | 0.0000 | Ras-related GTP binding A |
| **RRAGB** | -1.37 | 0.0000 | Ras-related GTP binding B |
| **RRAGC** | -2.20 | 0.0000 | Ras-related GTP binding C |
| **RRAS** | -1.06 | 0.0000 | related RAS viral (r-ras) oncogene homolog |
| **RRP15** | 0.82 | 0.0000 | ribosomal RNA processing 15 homolog (S. cerevisiae) |
| **RRP1B** | 1.47 | 0.0000 | ribosomal RNA processing 1 homolog B (S. cerevisiae) |
| **RSBN1L** | 0.98 | 0.0000 | round spermatid basic protein 1-like |
| **RSL1D1** | 1.61 | 0.0000 | ribosomal L1 domain containing 1 |
| **RSPH9** | -1.37 | 0.0000 | radial spoke head 9 homolog (Chlamydomonas) |
| **RSRC1** | 1.05 | 0.0000 | arginine/serine-rich coiled-coil 1 |
| **RSU1** | -1.76 | 0.0000 | Ras suppressor protein 1 |
| **RTKN** | -1.74 | 0.0000 | rhotekin |
| **RTN4R** | 2.77 | 0.0000 | reticulon 4 receptor |
| **RUNX1** | -2.49 | 0.0000 | runt-related transcription factor 1 |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **RUNX3** | 4.03 | 0.0000 | runt-related transcription factor 3 |
| **RYBP** | -1.24 | 0.0000 | RING1 and YY1 binding protein |
| **S100A11** | -1.75 | 0.0000 | S100 calcium binding protein A11; S100 calcium binding protein A11 pseudogene |
| **S100A16** | -1.23 | 0.0000 | S100 calcium binding protein A16 |
| **S100A2** | 1.65 | 0.0000 | S100 calcium binding protein A2 |
| **S100A6** | -2.02 | 0.0000 | S100 calcium binding protein A6 |
| **S100B** | -8.24 | 0.0000 | S100 calcium binding protein B |
| **S100PBP** | 0.92 | 0.0000 | S100P binding protein |
| **SAE1** | 0.85 | 0.0000 | SUMO1 activating enzyme subunit 1 |
| **SALL1** | 3.65 | 0.0000 | sal-like 1 (Drosophila) |
| **SAMD13** | 2.10 | 0.0000 | sterile alpha motif domain containing 13 |
| **SAMD8** | -1.01 | 0.0000 | sterile alpha motif domain containing 8 |
| **SAMD9** | -1.56 | 0.0000 | sterile alpha motif domain containing 9 |
| **SAMHD1** | -1.33 | 0.0000 | SAM domain and HD domain 1 |
| **SAP30** | -0.94 | 0.0000 | Sin3A-associated protein, 30kDa |
| **SASH1** | -3.74 | 0.0000 | SAM and SH3 domain containing 1 |
| **SATB1** | -2.57 | 0.0000 | SATB homeobox 1 |
| **SCAND3** | 2.42 | 0.0000 | SCAN domain containing 3 |
| **SCARA3** | 2.40 | 0.0000 | scavenger receptor class A, member 3 |
| **SCARB2** | -3.92 | 0.0000 | scavenger receptor class B, member 2 |
| **SCCPDH** | -1.72 | 0.0000 | saccharopine dehydrogenase (putative) |
| **SCD5** | 2.13 | 0.0000 | stearoyl-CoA desaturase 5 |
| **SCG2** | 1.82 | 0.0000 | secretogranin II (chromogranin C) |
| **SCG5** | -3.21 | 0.0000 | secretogranin V (7B2 protein) |
| **SCHIP1** | -0.83 | 0.0000 | schwannomin interacting protein 1 |
| **SCN4B** | 2.88 | 0.0000 | sodium channel, voltage-gated, type IV, beta |
| **SCPEP1** | -0.65 | 0.0000 | serine carboxypeptidase 1 |
| **SDC1** | 1.43 | 0.0000 | syndecan 1 |
| **SDC3** | -1.46 | 0.0000 | syndecan 3 |
| **SDCCAG3** | 0.91 | 0.0000 | serologically defined colon cancer antigen 3; similar to Serologically defined colon cancer antigen 3 |
| **SDF2** | -1.23 | 0.0000 | stromal cell-derived factor 2 |
| **SDF2L1** | -1.33 | 0.0000 | stromal cell-derived factor 2-like 1 |
| **SDF4** | -0.94 | 0.0000 | stromal cell derived factor 4 |
| **SDHAF1** | 1.32 | 0.0000 | succinate dehydrogenase complex assembly factor 1 |
| **SDSL** | 1.42 | 0.0000 | serine dehydratase-like |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **SEC14L1** | 0.78 | 0.0000 | SEC14-like 1 (S. cerevisiae); SEC14-like 1 pseudogene |
| **SEC14L2** | -1.37 | 0.0000 | SEC14-like 2 (S. cerevisiae) |
| **SEC31A** | 2.07 | 0.0000 | SEC31 homolog A (S. cerevisiae) |
| **SECISBP2L** | -3.00 | 0.0000 | SECIS binding protein 2-like |
| **SEL1L** | -2.18 | 0.0000 | sel-1 suppressor of lin-12-like (C. elegans) |
| **SELENBP1** | -2.60 | 0.0000 | selenium binding protein 1 |
| **SELK** | -1.42 | 0.0000 | selenoprotein K; similar to HSPC297 |
| **SELM** | -1.88 | 0.0000 | selenoprotein M |
| **SELPLG** | -1.22 | 0.0000 | selectin P ligand |
| **SELS** | -1.81 | 0.0000 | selenoprotein S |
| **SEMA3A** | 3.46 | 0.0000 | sema domain, immunoglobulin domain (Ig), short basic domain, secreted, (semaphorin) 3A |
| **SEMA3B** | -4.88 | 0.0000 | sema domain, immunoglobulin domain (Ig), short basic domain, secreted, (semaphorin) 3B |
| **SEMA3D** | 4.95 | 0.0000 | sema domain, immunoglobulin domain (Ig), short basic domain, secreted, (semaphorin) 3D |
| **SEMA4F** | -0.90 | 0.0000 | sema domain, immunoglobulin domain (Ig), transmembrane domain (TM) and short cytoplasmic domain, (semaphorin) 4F |
| **SEMA6A** | -2.80 | 0.0000 | sema domain, transmembrane domain (TM), and cytoplasmic domain, (semaphorin) 6A |
| **SENP1** | 1.27 | 0.0000 | SUMO1/sentrin specific peptidase 1 |
| **SEP15** | -0.97 | 0.0000 | 15 kDa selenoprotein |
| **SEPHS2** | 1.30 | 0.0000 | selenophosphate synthetase 2 |
| **SEPP1** | -4.55 | 0.0000 | selenoprotein P, plasma, 1 |
| **SEPT11** | 1.02 | 0.0000 | septin 11 |
| **SEPT5** | 1.56 | 0.0000 | septin 5 |
| **SEPW1** | -1.68 | 0.0000 | selenoprotein W, 1 |
| **SERF1B** | 1.09 | 0.0000 | small EDRK-rich factor 1A (telomeric); small EDRK-rich factor 1B (centromeric) |
| **SERINC1** | -1.85 | 0.0000 | serine incorporator 1 |
| **SERPINE2** | -2.10 | 0.0000 | serpin peptidase inhibitor, clade E (nexin, plasminogen activator inhibitor type 1), member 2 |
| **SERTAD4** | 3.93 | 0.0000 | SERTA domain containing 4 |
| **SESN1** | 1.10 | 0.0000 | sestrin 1 |
| **SETD7** | -1.09 | 0.0000 | SET domain containing (lysine methyltransferase) 7 |
| **SETDB2** | -1.21 | 0.0000 | SET domain, bifurcated 2 |
| **SF3A3** | 0.73 | 0.0000 | splicing factor 3a, subunit 3, 60kDa |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **SFRP1** | -1.59 | 0.0000 | secreted frizzled-related protein 1 |
| **SFRS1** | 1.40 | 0.0000 | splicing factor, arginine/serine-rich 1 |
| **SFRS2B** | -1.33 | 0.0000 | splicing factor, arginine/serine-rich 2B |
| **SFT2D1** | -1.34 | 0.0000 | SFT2 domain containing 1 |
| **SFT2D2** | -1.60 | 0.0000 | SFT2 domain containing 2 |
| **SFXN1** | 0.81 | 0.0000 | sideroflexin 1 |
| **SFXN2** | 1.60 | 0.0000 | sideroflexin 2 |
| **SFXN4** | 1.53 | 0.0000 | sideroflexin 4 |
| **SGCB** | -2.65 | 0.0000 | sarcoglycan, beta (43kDa dystrophin-associated glycoprotein) |
| **SGCE** | -1.31 | 0.0000 | sarcoglycan, epsilon |
| **SGSM3** | -1.62 | 0.0000 | small G protein signaling modulator 3 |
| **SH2D5** | 3.01 | 0.0000 | SH2 domain containing 5 |
| **SH3BGRL2** | 2.20 | 0.0000 | SH3 domain binding glutamic acid-rich protein like 2 |
| **SH3BGRL3** | -1.13 | 0.0000 | SH3 domain binding glutamic acid-rich protein like 3 |
| **SH3GL1** | -2.46 | 0.0000 | SH3-domain GRB2-like 1 |
| **SH3GL3** | 2.15 | 0.0000 | SH3-domain GRB2-like 3 |
| **SH3GLB1** | -1.83 | 0.0000 | SH3-domain GRB2-like endophilin B1 |
| **SH3KBP1** | -1.95 | 0.0000 | SH3-domain kinase binding protein 1 |
| **SH3PXD2A** | -4.90 | 0.0000 | SH3 and PX domains 2A |
| **SHC1** | 1.50 | 0.0000 | SHC (Src homology 2 domain containing) transforming protein 1 |
| **SHC4** | -3.12 | 0.0000 | SHC (Src homology 2 domain containing) family, member 4 |
| **SHISA2** | 2.53 | 0.0000 | shisa homolog 2 (Xenopus laevis) |
| **SHISA4** | -1.74 | 0.0000 | shisa homolog 4 (Xenopus laevis) |
| **SHROOM1** | 1.48 | 0.0000 | shroom family member 1 |
| **SHROOM3** | 3.79 | 0.0000 | shroom family member 3 |
| **SIDT2** | -1.99 | 0.0000 | SID1 transmembrane family, member 2 |
| **SIGIRR** | -1.69 | 0.0000 | single immunoglobulin and toll-interleukin 1 receptor (TIR) domain |
| **SIGMAR1** | 0.85 | 0.0000 | sigma non-opioid intracellular receptor 1 |
| **SIP1** | 1.22 | 0.0000 | survival of motor neuron protein interacting protein 1 |
| **SIRPA** | 3.27 | 0.0000 | signal-regulatory protein alpha |
| **SIRT2** | -1.79 | 0.0000 | sirtuin (silent mating type information regulation 2 homolog) 2 (S. cerevisiae) |
| **SIX1** | 2.09 | 0.0000 | SIX homeobox 1 |
| **SIX4** | 4.16 | 0.0000 | SIX homeobox 4 |
| **SKIV2L2** | 0.78 | 0.0000 | superkiller viralicidic activity 2-like 2 (S. cerevisiae) |
| **SKP2** | 1.77 | 0.0000 | S-phase kinase-associated protein 2 (p45) |
| **SLC12A4** | -1.46 | 0.0000 | solute carrier family 12 (potassium/chloride transporters), member 4 |
| **SLC12A7** | 4.24 | 0.0000 | solute carrier family 12 (potassium/chloride transporters), member 7 |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **SLC15A3** | -3.99 | 0.0000 | solute carrier family 15, member 3 |
| **SLC15A4** | -1.93 | 0.0000 | solute carrier family 15, member 4 |
| **SLC16A9** | 4.12 | 0.0000 | solute carrier family 16, member 9 (monocarboxylic acid transporter 9) |
| **SLC19A2** | -2.08 | 0.0000 | solute carrier family 19 (thiamine transporter), member 2 |
| **SLC1A1** | 3.76 | 0.0000 | solute carrier family 1 (neuronal/epithelial high affinity glutamate transporter, system Xag), member 1 |
| **SLC1A4** | -1.75 | 0.0000 | solute carrier family 1 (glutamate/neutral amino acid transporter), member 4 |
| **SLC1A5** | 1.15 | 0.0000 | solute carrier family 1 (neutral amino acid transporter), member 5 |
| **SLC20A2** | -1.54 | 0.0000 | solute carrier family 20 (phosphate transporter), member 2 |
| **SLC22A17** | -0.79 | 0.0000 | solute carrier family 22, member 17 |
| **SLC22A18** | -1.98 | 0.0000 | solute carrier family 22, member 18 |
| **SLC23A2** | -1.12 | 0.0000 | solute carrier family 23 (nucleobase transporters), member 2 |
| **SLC25A12** | 1.27 | 0.0000 | solute carrier family 25 (mitochondrial carrier, Aralar), member 12 |
| **SLC25A20** | -3.61 | 0.0000 | solute carrier family 25 (carnitine/acylcarnitine translocase), member 20 |
| **SLC25A36** | 0.81 | 0.0000 | solute carrier family 25, member 36 |
| **SLC26A10** | 1.75 | 0.0000 | RhoA/RAC/CDC42 exchange factor; solute carrier family 26, member 10 |
| **SLC26A11** | 1.14 | 0.0000 | solute carrier family 26, member 11 |
| **SLC27A2** | 2.20 | 0.0000 | solute carrier family 27 (fatty acid transporter), member 2 |
| **SLC27A4** | -1.89 | 0.0000 | solute carrier family 27 (fatty acid transporter), member 4 |
| **SLC29A1** | 1.26 | 0.0000 | solute carrier family 29 (nucleoside transporters), member 1 |
| **SLC2A4RG** | 1.95 | 0.0000 | SLC2A4 regulator |
| **SLC30A4** | -0.91 | 0.0000 | solute carrier family 30 (zinc transporter), member 4 |
| **SLC35A1** | -1.27 | 0.0000 | solute carrier family 35 (CMP-sialic acid transporter), member A1 |
| **SLC35A2** | -1.56 | 0.0000 | solute carrier family 35 (UDP-galactose transporter), member A2 |
| **SLC35B2** | -1.67 | 0.0000 | solute carrier family 35, member B2 |
| **SLC35F2** | 3.34 | 0.0000 | solute carrier family 35, member F2 |
| **SLC35F3** | 2.43 | 0.0000 | solute carrier family 35, member F3 |
| **SLC37A2** | -2.28 | 0.0000 | solute carrier family 37 (glycerol-3-phosphate transporter), member 2 |
| **SLC38A1** | 5.52 | 0.0000 | solute carrier family 38, member 1 |
| **SLC39A4** | -2.42 | 0.0000 | solute carrier family 39 (zinc transporter), member 4 |
| **SLC39A7** | -0.91 | 0.0000 | solute carrier family 39 (zinc transporter), member 7 |
| **SLC39A8** | 1.83 | 0.0000 | solute carrier family 39 (zinc transporter), member 8 |
| **SLC41A2** | -1.40 | 0.0000 | solute carrier family 41, member 2 |
| **SLC45A4** | 1.71 | 0.0000 | solute carrier family 45, member 4 |
| **SLC48A1** | 1.52 | 0.0000 | solute carrier family 48 (heme transporter), member 1 |
| **SLC4A4** | 3.20 | 0.0000 | solute carrier family 4, sodium bicarbonate cotransporter, member 4 |
| **SLC5A6** | 1.27 | 0.0000 | solute carrier family 5 (sodium-dependent vitamin transporter), member 6 |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **SLC6A19** | -1.20 | 0.0000 | solute carrier family 6 (neutral amino acid transporter), member 19 |
| **SLC7A8** | -2.09 | 0.0000 | solute carrier family 7 (cationic amino acid transporter, y+ system), member 8 |
| **SLC8A1** | 3.09 | 0.0000 | solute carrier family 8 (sodium/calcium exchanger), member 1 |
| **SLC9A7** | -1.52 | 0.0000 | solute carrier family 9 (sodium/hydrogen exchanger), member 7 |
| **SLITRK4** | 5.03 | 0.0000 | SLIT and NTRK-like family, member 4 |
| **SLK** | -0.92 | 0.0000 | STE20-like kinase (yeast) |
| **SMAD2** | -1.15 | 0.0000 | SMAD family member 2 |
| **SMARCA5** | -0.95 | 0.0000 | SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily a, member 5 |
| **SMN1** | 0.88 | 0.0000 | survival of motor neuron 1, telomeric; survival of motor neuron 2, centromeric |
| **SMO** | 2.03 | 0.0000 | smoothened homolog (Drosophila) |
| **SMPD1** | -2.20 | 0.0000 | sphingomyelin phosphodiesterase 1, acid lysosomal |
| **SMPD4** | 0.77 | 0.0000 | sphingomyelin phosphodiesterase 4, neutral membrane (neutral sphingomyelinase-3) |
| **SMYD3** | -1.53 | 0.0000 | SET and MYND domain containing 3 |
| **SNAPC1** | 1.50 | 0.0000 | small nuclear RNA activating complex, polypeptide 1, 43kDa |
| **SNHG1** | 1.88 | 0.0000 | small nucleolar RNA host gene 1 (non-protein coding) |
| **SNHG10** | 1.25 | 0.0000 | small Cajal body-specific RNA 13; small nucleolar RNA host gene 10 (non-protein coding) |
| **SNHG11** | 1.51 | 0.0000 | small nucleolar RNA host gene 11 (non-protein coding) |
| **SNHG12** | 1.40 | 0.0000 | small nucleolar RNA host gene 12 (non-protein coding) |
| **SNHG3-RCC1** | 1.47 | 0.0000 | regulator of chromosome condensation 1; SNHG3-RCC1 readthrough transcript |
| **SNORD22** | 1.99 | 0.0000 | small nucleolar RNA, C/D box 22 |
| **SNRNP25** | 1.63 | 0.0000 | small nuclear ribonucleoprotein 25kDa (U11/U12) |
| **SNRNP35** | -0.96 | 0.0000 | ATP-binding cassette, sub-family B (MDR/TAP), member 5; small nuclear ribonucleoprotein 35kDa (U11/U12) |
| **SNRPE** | 0.92 | 0.0000 | small nuclear ribonucleoprotein polypeptide E-like 1; small nuclear ribonucleoprotein polypeptide E; similar to hCG23490 |
| **SNRPF** | 1.22 | 0.0000 | small nuclear ribonucleoprotein polypeptide F |
| **SNTB2** | -1.57 | 0.0000 | syntrophin, beta 2 (dystrophin-associated protein A1, 59kDa, basic component 2) |
| **SNX10** | 3.22 | 0.0000 | sorting nexin 10 |
| **SNX12** | -1.21 | 0.0000 | sorting nexin 12 |
| **SNX14** | -1.45 | 0.0000 | sorting nexin 14 |
| **SNX18** | -2.12 | 0.0000 | sorting nexin 18 |
| **SNX25** | -0.75 | 0.0000 | sorting nexin 25 |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **SNX27** | -1.61 | 0.0000 | sorting nexin family member 27 |
| **SNX3** | -1.56 | 0.0000 | sorting nexin 3 |
| **SNX5** | 1.32 | 0.0000 | sorting nexin 5 |
| **SOCS3** | 2.04 | 0.0000 | suppressor of cytokine signaling 3 |
| **SOCS6** | -1.32 | 0.0000 | suppressor of cytokine signaling 6 |
| **SON** | 0.85 | 0.0000 | SON DNA binding protein |
| **SORL1** | 4.13 | 0.0000 | sortilin-related receptor, L(DLR class) A repeats-containing |
| **SORT1** | -2.31 | 0.0000 | sortilin 1 |
| **SOX10** | -3.28 | 0.0000 | SRY (sex determining region Y)-box 10 |
| **SOX2OT** | -4.10 | 0.0000 | SOX2 overlapping transcript (non-protein coding) |
| **SOX3** | 3.62 | 0.0000 | SRY (sex determining region Y)-box 3 |
| **SOX4** | -3.14 | 0.0000 | SRY (sex determining region Y)-box 4 |
| **SOX8** | -2.68 | 0.0000 | SRY (sex determining region Y)-box 8 |
| **SPATA13** | -1.70 | 0.0000 | spermatogenesis associated 13 |
| **SPATA6** | -1.72 | 0.0000 | spermatogenesis associated 6 |
| **SPATS2** | 1.37 | 0.0000 | spermatogenesis associated, serine-rich 2 |
| **SPCS3** | -1.32 | 0.0000 | signal peptidase complex subunit 3 homolog (S. cerevisiae) |
| **SPEG** | 2.70 | 0.0000 | SPEG complex locus |
| **SPHK1** | -2.52 | 0.0000 | sphingosine kinase 1 |
| **SPOCK1** | 2.63 | 0.0000 | sparc/osteonectin, cwcv and kazal-like domains proteoglycan (testican) 1 |
| **SPON1** | 4.86 | 0.0000 | spondin 1, extracellular matrix protein |
| **SPON2** | -2.61 | 0.0000 | spondin 2, extracellular matrix protein |
| **SPP1** | -4.13 | 0.0000 | secreted phosphoprotein 1 |
| **SPPL2A** | -2.36 | 0.0000 | signal peptide peptidase-like 2A |
| **SPRY1** | 2.25 | 0.0000 | sprouty homolog 1, antagonist of FGF signaling (Drosophila) |
| **SPTBN1** | -3.36 | 0.0000 | spectrin, beta, non-erythrocytic 1 |
| **SQRDL** | -3.30 | 0.0000 | sulfide quinone reductase-like (yeast) |
| **SR140** | 1.44 | 0.0000 | U2-associated SR140 protein |
| **SRBD1** | -1.07 | 0.0000 | S1 RNA binding domain 1 |
| **SRF** | -0.72 | 0.0000 | serum response factor (c-fos serum response element-binding transcription factor) |
| **SRGAP1** | 2.02 | 0.0000 | SLIT-ROBO Rho GTPase activating protein 1 |
| **SRGAP2P1** | -3.16 | 0.0000 | SLIT-ROBO Rho GTPase activating protein 2 pseudogene 1 |
| **SRI** | -1.82 | 0.0000 | sorcin |
| **SRPK1** | 0.94 | 0.0000 | SFRS protein kinase 1 |
| **SRPX** | -2.59 | 0.0000 | sushi-repeat-containing protein, X-linked |
| **SRPX2** | -1.92 | 0.0000 | sushi-repeat-containing protein, X-linked 2 |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **SRR** | -1.43 | 0.0000 | serine racemase |
| **SS18L1** | 1.01 | 0.0000 | synovial sarcoma translocation gene on chromosome 18-like 1 |
| **SSBP4** | 1.53 | 0.0000 | single stranded DNA binding protein 4 |
| **SSH3** | -2.36 | 0.0000 | slingshot homolog 3 (Drosophila) |
| **SSR1** | -1.19 | 0.0000 | signal sequence receptor, alpha |
| **SSR2** | -1.23 | 0.0000 | signal sequence receptor, beta (translocon-associated protein beta) |
| **SSR3** | 1.30 | 0.0000 | signal sequence receptor, gamma (translocon-associated protein gamma) |
| **SSTR1** | 5.24 | 0.0000 | somatostatin receptor 1 |
| **SSTR2** | 2.02 | 0.0000 | somatostatin receptor 2 |
| **ST3GAL2** | -1.19 | 0.0000 | ST3 beta-galactoside alpha-2,3-sialyltransferase 2 |
| **ST3GAL3** | -1.05 | 0.0000 | ST3 beta-galactoside alpha-2,3-sialyltransferase 3 |
| **ST3GAL4** | -2.25 | 0.0000 | ST3 beta-galactoside alpha-2,3-sialyltransferase 4 |
| **ST3GAL5** | 2.28 | 0.0000 | ST3 beta-galactoside alpha-2,3-sialyltransferase 5 |
| **ST5** | -1.51 | 0.0000 | suppression of tumorigenicity 5 |
| **ST6GAL1** | -2.74 | 0.0000 | ST6 beta-galactosamide alpha-2,6-sialyltranferase 1 |
| **ST6GALNAC2** | -4.10 | 0.0000 | ST6 (alpha-N-acetyl-neuraminyl-2,3-beta-galactosyl-1,3)-N-acetylgalactosaminide alpha-2,6-sialyltransferase 2 |
| **ST8SIA5** | -1.80 | 0.0000 | ST8 alpha-N-acetyl-neuraminide alpha-2,8-sialyltransferase 5 |
| **STAC** | 3.37 | 0.0000 | SH3 and cysteine rich domain |
| **STAG3L4** | 1.39 | 0.0000 | stromal antigen 3-like 4 |
| **STAM** | -1.08 | 0.0000 | signal transducing adaptor molecule (SH3 domain and ITAM motif) 1 |
| **STAMBP** | -1.51 | 0.0000 | STAM binding protein |
| **STARD13** | -1.57 | 0.0000 | StAR-related lipid transfer (START) domain containing 13 |
| **STARD3** | -1.49 | 0.0000 | StAR-related lipid transfer (START) domain containing 3 |
| **STARD8** | -1.81 | 0.0000 | StAR-related lipid transfer (START) domain containing 8 |
| **STAT5B** | 1.52 | 0.0000 | signal transducer and activator of transcription 5B |
| **STAU1** | 1.17 | 0.0000 | staufen, RNA binding protein, homolog 1 (Drosophila) |
| **STBD1** | -2.50 | 0.0000 | starch binding domain 1 |
| **STEAP2** | 1.82 | 0.0000 | six transmembrane epithelial antigen of the prostate 2 |
| **STK10** | -1.24 | 0.0000 | serine/threonine kinase 10 |
| **STK11IP** | -1.39 | 0.0000 | serine/threonine kinase 11 interacting protein |
| **STK17B** | 1.52 | 0.0000 | serine/threonine kinase 17b |
| **STK39** | 1.32 | 0.0000 | serine threonine kinase 39 (STE20/SPS1 homolog, yeast) |
| **STK40** | -1.20 | 0.0000 | serine/threonine kinase 40 |
| **STMN2** | 2.45 | 0.0000 | stathmin-like 2 |
| **STMN3** | 2.57 | 0.0000 | stathmin-like 3 |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **STOM** | 1.26 | 0.0000 | stomatin |
| **STOX2** | -2.50 | 0.0000 | storkhead box 2 |
| **STRA13** | 1.65 | 0.0000 | stimulated by retinoic acid 13 homolog (mouse) |
| **STRAP** | -1.58 | 0.0000 | serine/threonine kinase receptor associated protein |
| **STRBP** | 2.00 | 0.0000 | spermatid perinuclear RNA binding protein |
| **STX12** | -1.13 | 0.0000 | syntaxin 12 |
| **STX2** | -1.91 | 0.0000 | syntaxin 2 |
| **STX7** | -1.62 | 0.0000 | syntaxin 7 |
| **STXBP3** | -1.50 | 0.0000 | syntaxin binding protein 3 |
| **STXBP5** | -1.91 | 0.0000 | syntaxin binding protein 5 (tomosyn) |
| **STXBP6** | 1.82 | 0.0000 | syntaxin binding protein 6 (amisyn) |
| **STYK1** | 1.60 | 0.0000 | serine/threonine/tyrosine kinase 1 |
| **SUB1** | 0.71 | 0.0000 | SUB1 homolog (S. cerevisiae) |
| **SULF2** | 4.83 | 0.0000 | sulfatase 2 |
| **SUSD1** | -1.53 | 0.0000 | sushi domain containing 1 |
| **SUZ12** | -4.20 | 0.0000 | suppressor of zeste 12 homolog (Drosophila) |
| **SVIL** | -2.73 | 0.0000 | supervillin |
| **SYCP1** | 1.58 | 0.0000 | synaptonemal complex protein 1 |
| **SYCP2** | 2.88 | 0.0000 | synaptonemal complex protein 2 |
| **SYNJ2** | 2.75 | 0.0000 | synaptojanin 2 |
| **SYNM** | -1.34 | 0.0000 | synemin, intermediate filament protein |
| **SYNRG** | -0.83 | 0.0000 | AP1 gamma subunit binding protein 1 |
| **SYT11** | -1.21 | 0.0000 | synaptotagmin XI |
| **SYT12** | 1.10 | 0.0000 | synaptotagmin XII |
| **SYT13** | 4.33 | 0.0000 | synaptotagmin XIII |
| **SYTL5** | 2.13 | 0.0000 | synaptotagmin-like 5 |
| **TACC1** | -2.20 | 0.0000 | transforming, acidic coiled-coil containing protein 1 |
| **TAF12** | 0.72 | 0.0000 | TAF12 RNA polymerase II, TATA box binding protein (TBP)-associated factor, 20kDa |
| **TAF1A** | 1.68 | 0.0000 | TATA box binding protein (TBP)-associated factor, RNA polymerase I, A, 48kDa |
| **TAF4** | 1.88 | 0.0000 | TAF4 RNA polymerase II, TATA box binding protein (TBP)-associated factor, 135kDa |
| **TAF7** | 1.01 | 0.0000 | TAF7 RNA polymerase II, TATA box binding protein (TBP)-associated factor, 55kDa |
| **TAF7L** | 2.83 | 0.0000 | TAF7-like RNA polymerase II, TATA box binding protein (TBP)-associated factor, 50kDa |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **TAF8** | -1.20 | 0.0000 | TAF8 RNA polymerase II, TATA box binding protein (TBP)-associated factor, 43kDa |
| **TAGLN3** | 2.68 | 0.0000 | transgelin 3 |
| **TAL1** | 3.33 | 0.0000 | T-cell acute lymphocytic leukemia 1 |
| **TALDO1** | -2.15 | 0.0000 | transaldolase 1 |
| **TAOK2** | 1.10 | 0.0000 | TAO kinase 2 |
| **TAOK3** | -1.95 | 0.0000 | TAO kinase 3 |
| **TAP1** | -2.29 | 0.0000 | transporter 1, ATP-binding cassette, sub-family B (MDR/TAP) |
| **TAPBP** | -1.67 | 0.0000 | TAP binding protein (tapasin) |
| **TARBP1** | 1.06 | 0.0000 | TAR (HIV-1) RNA binding protein 1 |
| **TARDBP** | 1.60 | 0.0000 | TAR DNA binding protein |
| **TARSL2** | -3.24 | 0.0000 | threonyl-tRNA synthetase-like 2 |
| **TATDN1** | 1.36 | 0.0000 | TatD DNase domain containing 1 |
| **TBC1D10A** | -1.87 | 0.0000 | TBC1 domain family, member 10A |
| **TBC1D23** | -0.88 | 0.0000 | TBC1 domain family, member 23 |
| **TBC1D24** | 1.41 | 0.0000 | TBC1 domain family, member 24 |
| **TBC1D4** | 1.49 | 0.0000 | TBC1 domain family, member 4 |
| **TBC1D7** | -1.43 | 0.0000 | TBC1 domain family, member 7 |
| **TBC1D9B** | -1.17 | 0.0000 | TBC1 domain family, member 9B (with GRAM domain) |
| **TBL1Y** | -1.06 | 0.0000 | transducin (beta)-like 1Y-linked |
| **TBL2** | 1.00 | 0.0000 | transducin (beta)-like 2 |
| **TBRG4** | 1.29 | 0.0000 | transforming growth factor beta regulator 4 |
| **TBX1** | 6.46 | 0.0000 | T-box 1 |
| **TBX2** | -2.80 | 0.0000 | T-box 2 |
| **TBX3** | 2.47 | 0.0000 | T-box 3 |
| **TBXA2R** | -3.09 | 0.0000 | thromboxane A2 receptor |
| **TBXAS1** | 2.31 | 0.0000 | thromboxane A synthase 1 (platelet) |
| **TCEA3** | 3.22 | 0.0000 | transcription elongation factor A (SII), 3 |
| **TCEAL3** | -1.59 | 0.0000 | transcription elongation factor A (SII)-like 3 |
| **TCEAL4** | -1.62 | 0.0000 | transcription elongation factor A (SII)-like 4 |
| **TCEAL5** | -1.07 | 0.0000 | transcription elongation factor A (SII)-like 5 |
| **TCEAL6** | -1.47 | 0.0000 | transcription elongation factor A (SII)-like 6 |
| **TCEAL8** | -1.07 | 0.0000 | transcription elongation factor A (SII)-like 8 |
| **TCF15** | 4.86 | 0.0000 | transcription factor 15 (basic helix-loop-helix) |
| **TCF25** | -1.81 | 0.0000 | transcription factor 25 (basic helix-loop-helix) |
| **TCF3** | 0.93 | 0.0000 | transcription factor 3 (E2A immunoglobulin enhancer binding factors E12/E47) |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **TCFL5** | 1.39 | 0.0000 | transcription factor-like 5 (basic helix-loop-helix) |
| **TCIRG1** | -3.37 | 0.0000 | T-cell, immune regulator 1, ATPase, H+ transporting, lysosomal V0 subunit A3 |
| **TCOF1** | 1.27 | 0.0000 | Treacher Collins-Franceschetti syndrome 1 |
| **TCTA** | -1.19 | 0.0000 | T-cell leukemia translocation altered gene |
| **TCTN3** | -0.93 | 0.0000 | tectonic family member 3 |
| **TDRD3** | -0.81 | 0.0000 | tudor domain containing 3 |
| **TET3** | -1.05 | 0.0000 | tet oncogene family member 3 |
| **TEX10** | 0.92 | 0.0000 | testis expressed 10 |
| **TEX15** | 1.61 | 0.0000 | testis expressed 15 |
| **TEX2** | -1.70 | 0.0000 | testis expressed 2 |
| **TFAP2A** | -2.48 | 0.0000 | transcription factor AP-2 alpha (activating enhancer binding protein 2 alpha) |
| **TFAP2B** | -3.25 | 0.0000 | transcription factor AP-2 beta (activating enhancer binding protein 2 beta) |
| **TFPI** | 2.71 | 0.0000 | tissue factor pathway inhibitor (lipoprotein-associated coagulation inhibitor) |
| **TGFA** | -4.50 | 0.0000 | transforming growth factor, alpha |
| **TGFB1** | 1.69 | 0.0000 | transforming growth factor, beta 1 |
| **TGFBR2** | -2.27 | 0.0000 | transforming growth factor, beta receptor II (70/80kDa) |
| **TGIF1** | -1.29 | 0.0000 | TGFB-induced factor homeobox 1 |
| **TGIF2** | 1.23 | 0.0000 | TGFB-induced factor homeobox 2 |
| **TGOLN2** | -1.56 | 0.0000 | trans-golgi network protein 2 |
| **THAP10** | 1.11 | 0.0000 | THAP domain containing 10 |
| **THBS2** | -3.69 | 0.0000 | thrombospondin 2 |
| **THBS4** | 4.42 | 0.0000 | thrombospondin 4 |
| **THOC3** | 1.24 | 0.0000 | similar to THO complex 3; THO complex 3 |
| **THOC4** | 1.91 | 0.0000 | THO complex 4 |
| **THSD1** | 1.46 | 0.0000 | thrombospondin, type I, domain containing 1 |
| **THSD4** | 2.69 | 0.0000 | thrombospondin, type I, domain containing 4 |
| **THUMPD2** | 0.94 | 0.0000 | THUMP domain containing 2 |
| **THUMPD3** | -4.50 | 0.0000 | THUMP domain containing 3 |
| **THY1** | 2.31 | 0.0000 | Thy-1 cell surface antigen |
| **TIGD1** | 1.50 | 0.0000 | tigger transposable element derived 1 |
| **TIGD3** | 1.44 | 0.0000 | tigger transposable element derived 3 |
| **TIGD7** | 1.68 | 0.0000 | tigger transposable element derived 7 |
| **TIMELESS** | 1.56 | 0.0000 | timeless homolog (Drosophila) |
| **TIMM10** | 1.22 | 0.0000 | translocase of inner mitochondrial membrane 10 homolog (yeast) |
| **TIMM50** | 1.30 | 0.0000 | translocase of inner mitochondrial membrane 50 homolog (S. cerevisiae) |
| **TIMP1** | -2.06 | 0.0000 | TIMP metallopeptidase inhibitor 1 |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **TIMP3** | -6.00 | 0.0000 | TIMP metallopeptidase inhibitor 3 |
| **TINF2** | -0.98 | 0.0000 | TERF1 (TRF1)-interacting nuclear factor 2 |
| **TIPRL** | -0.98 | 0.0000 | TIP41, TOR signaling pathway regulator-like (S. cerevisiae) |
| **TJP2** | 1.67 | 0.0000 | tight junction protein 2 (zona occludens 2) |
| **TK1** | 1.91 | 0.0000 | thymidine kinase 1, soluble |
| **TKTL1** | -3.10 | 0.0000 | transketolase-like 1 |
| **TLE4** | 2.73 | 0.0000 | transducin-like enhancer of split 4 (E(sp1) homolog, Drosophila) |
| **TLR1** | -4.61 | 0.0000 | toll-like receptor 1 |
| **TLR6** | -2.67 | 0.0000 | toll-like receptor 6 |
| **TM4SF1** | 2.04 | 0.0000 | transmembrane 4 L six family member 1 |
| **TM9SF2** | -1.00 | 0.0000 | transmembrane 9 superfamily member 2 |
| **TM9SF3** | -0.92 | 0.0000 | transmembrane 9 superfamily member 3 |
| **TMBIM1** | -2.18 | 0.0000 | transmembrane BAX inhibitor motif containing 1 |
| **TMBIM6** | -1.63 | 0.0000 | transmembrane BAX inhibitor motif containing 6 |
| **TMC7** | -3.31 | 0.0000 | transmembrane channel-like 7 |
| **TMCO6** | 1.09 | 0.0000 | transmembrane and coiled-coil domains 6 |
| **TMED10** | -1.94 | 0.0000 | transmembrane emp24-like trafficking protein 10 (yeast) |
| **TMED10P** | -1.90 | 0.0000 | transmembrane emp24-like trafficking protein 10 (yeast) pseudogene |
| **TMED5** | -1.96 | 0.0000 | transmembrane emp24 protein transport domain containing 5 |
| **TMEFF2** | 3.88 | 0.0000 | transmembrane protein with EGF-like and two follistatin-like domains 2 |
| **TMEM100** | -1.80 | 0.0000 | transmembrane protein 100 |
| **TMEM102** | -1.90 | 0.0000 | transmembrane protein 102 |
| **TMEM107** | -1.56 | 0.0000 | transmembrane protein 107 |
| **TMEM108** | 2.67 | 0.0000 | transmembrane protein 108 |
| **TMEM111** | -0.99 | 0.0000 | transmembrane protein 111 |
| **TMEM116** | 0.96 | 0.0000 | transmembrane protein 116 |
| **TMEM127** | -1.11 | 0.0000 | transmembrane protein 127 |
| **TMEM140** | -1.86 | 0.0000 | transmembrane protein 140 |
| **TMEM154** | 2.58 | 0.0000 | transmembrane protein 154 |
| **TMEM158** | 2.02 | 0.0000 | transmembrane protein 158 |
| **TMEM169** | -2.86 | 0.0000 | transmembrane protein 169 |
| **TMEM173** | 1.51 | 0.0000 | transmembrane protein 173 |
| **TMEM178** | 2.18 | 0.0000 | transmembrane protein 178 |
| **TMEM184B** | -1.65 | 0.0000 | transmembrane protein 184B |
| **TMEM184C** | -1.84 | 0.0000 | transmembrane protein 184C |
| **TMEM186** | 1.61 | 0.0000 | transmembrane protein 186 |
| **TMEM2** | -1.84 | 0.0000 | transmembrane protein 2 |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **TMEM200A** | 4.53 | 0.0000 | transmembrane protein 200A |
| **TMEM208** | -1.46 | 0.0000 | transmembrane protein 208 |
| **TMEM209** | 1.46 | 0.0000 | transmembrane protein 209 |
| **TMEM216** | 1.30 | 0.0000 | transmembrane protein 216 |
| **TMEM220** | -2.14 | 0.0000 | transmembrane protein 220 |
| **TMEM35** | 2.08 | 0.0000 | transmembrane protein 35 |
| **TMEM47** | -2.71 | 0.0000 | transmembrane protein 47 |
| **TMEM50A** | -1.08 | 0.0000 | transmembrane protein 50A |
| **TMEM51** | 3.49 | 0.0000 | transmembrane protein 51 |
| **TMEM62** | -1.18 | 0.0000 | transmembrane protein 62 |
| **TMEM71** | -3.43 | 0.0000 | transmembrane protein 71 |
| **TMEM87A** | -2.15 | 0.0000 | transmembrane protein 87A |
| **TMEM87B** | -1.12 | 0.0000 | transmembrane protein 87B |
| **TMEM8B** | -1.10 | 0.0000 | transmembrane protein 8B |
| **TMEM97** | 1.10 | 0.0000 | transmembrane protein 97 |
| **TMEM9B** | -1.92 | 0.0000 | TMEM9 domain family, member B |
| **TMOD1** | 4.18 | 0.0000 | tropomodulin 1 |
| **TMOD2** | -3.58 | 0.0000 | tropomodulin 2 (neuronal) |
| **TMPRSS5** | -3.57 | 0.0000 | transmembrane protease, serine 5 |
| **TMTC1** | 5.43 | 0.0000 | transmembrane and tetratricopeptide repeat containing 1 |
| **TMTC2** | -5.28 | 0.0000 | transmembrane and tetratricopeptide repeat containing 2 |
| **TMX3** | -1.21 | 0.0000 | thioredoxin-related transmembrane protein 3 |
| **TNC** | -2.50 | 0.0000 | tenascin C |
| **TNFAIP1** | -1.46 | 0.0000 | tumor necrosis factor, alpha-induced protein 1 (endothelial) |
| **TNFAIP2** | 2.32 | 0.0000 | tumor necrosis factor, alpha-induced protein 2 |
| **TNFAIP6** | -4.40 | 0.0000 | tumor necrosis factor, alpha-induced protein 6 |
| **TNFRSF11B** | 4.49 | 0.0000 | tumor necrosis factor receptor superfamily, member 11b |
| **TNFRSF14** | -3.05 | 0.0000 | tumor necrosis factor receptor superfamily, member 14 (herpesvirus entry mediator) |
| **TNFRSF25** | 2.79 | 0.0000 | tumor necrosis factor receptor superfamily, member 25 |
| **TNFSF12** | -3.04 | 0.0000 | TNFSF12-TNFSF13 readthrough transcript; tumor necrosis factor (ligand) superfamily, member 12; tumor necrosis factor (ligand) superfamily, member 13 |
| **TNRC6B** | -1.50 | 0.0000 | trinucleotide repeat containing 6B |
| **TNS3** | -1.80 | 0.0000 | tensin 3 |
| **TOLLIP** | -1.93 | 0.0000 | toll interacting protein |
| **TOMM5** | 1.04 | 0.0000 | translocase of outer mitochondrial membrane 5 homolog (yeast) |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **TOP1P2** | 1.51 | 0.0000 | topoisomerase (DNA) I pseudogene 2 |
| **TOX2** | 1.78 | 0.0000 | TOX high mobility group box family member 2 |
| **TP53RK** | 0.78 | 0.0000 | TP53 regulating kinase |
| **TPBG** | 2.37 | 0.0000 | trophoblast glycoprotein |
| **TPD52L2** | 1.26 | 0.0000 | tumor protein D52-like 2 |
| **TPM4** | -1.72 | 0.0000 | tropomyosin 4 |
| **TPMT** | -1.37 | 0.0000 | thiopurine S-methyltransferase |
| **TPT1** | -1.48 | 0.0000 | similar to tumor protein, translationally-controlled 1; tumor protein, translationally-controlled 1 |
| **TRADD** | -1.44 | 0.0000 | TNFRSF1A-associated via death domain |
| **TRAF1** | -3.33 | 0.0000 | TNF receptor-associated factor 1 |
| **TRAF3IP3** | 1.02 | 0.0000 | TRAF3 interacting protein 3 |
| **TRAK1** | -1.03 | 0.0000 | trafficking protein, kinesin binding 1 |
| **TRAM1** | -1.10 | 0.0000 | translocation associated membrane protein 1 |
| **TRAM2** | -0.93 | 0.0000 | translocation associated membrane protein 2 |
| **TRAP1** | 1.84 | 0.0000 | TNF receptor-associated protein 1 |
| **TRAPPC2P1** | -0.90 | 0.0000 | trafficking protein particle complex 2; trafficking protein particle complex 2 pseudogene 1 |
| **TRIB1** | 2.72 | 0.0000 | tribbles homolog 1 (Drosophila) |
| **TRIM2** | -3.64 | 0.0000 | tripartite motif-containing 2 |
| **TRIM6** | 1.58 | 0.0000 | TRIM6-TRIM34 readthrough transcript; tripartite motif-containing 6; tripartite motif-containing 34 |
| **TRIM63** | -1.73 | 0.0000 | tripartite motif-containing 63 |
| **TRIO** | -1.15 | 0.0000 | triple functional domain (PTPRF interacting) |
| **TRIT1** | 0.95 | 0.0000 | tRNA isopentenyltransferase 1 |
| **TRMT12** | 0.97 | 0.0000 | tRNA methyltransferase 12 homolog (S. cerevisiae) |
| **TRPC3** | 2.17 | 0.0000 | transient receptor potential cation channel, subfamily C, member 3 |
| **TRPM7** | -1.85 | 0.0000 | transient receptor potential cation channel, subfamily M, member 7 |
| **TRPV2** | -1.37 | 0.0000 | transient receptor potential cation channel, subfamily V, member 2 |
| **TRUB2** | -1.74 | 0.0000 | TruB pseudouridine (psi) synthase homolog 2 (E. coli) |
| **TSEN54** | 1.48 | 0.0000 | tRNA splicing endonuclease 54 homolog (S. cerevisiae) |
| **TSGA14** | 3.41 | 0.0000 | testis specific, 14 |
| **TSHZ3** | 1.74 | 0.0000 | teashirt zinc finger homeobox 3 |
| **TSKU** | 1.67 | 0.0000 | tsukushin |
| **TSPAN8** | 3.61 | 0.0000 | tetraspanin 8 |
| **TSPYL1** | -1.41 | 0.0000 | TSPY-like 1 |
| **TTC19** | -1.51 | 0.0000 | tetratricopeptide repeat domain 19 |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **TTC39C** | -1.17 | 0.0000 | tetratricopeptide repeat domain 39C |
| **TTC9C** | 0.89 | 0.0000 | tetratricopeptide repeat domain 9C |
| **TTLL7** | -2.16 | 0.0000 | tubulin tyrosine ligase-like family, member 7 |
| **TTPAL** | 1.52 | 0.0000 | tocopherol (alpha) transfer protein-like |
| **TUBD1** | 1.49 | 0.0000 | tubulin, delta 1 |
| **TUBGCP4** | 0.86 | 0.0000 | tubulin, gamma complex associated protein 4 |
| **TULP3** | -1.24 | 0.0000 | tubby like protein 3 |
| **TWIST2** | 2.45 | 0.0000 | twist homolog 2 (Drosophila) |
| **TWSG1** | -1.79 | 0.0000 | twisted gastrulation homolog 1 (Drosophila) |
| **TXNDC15** | -1.16 | 0.0000 | thioredoxin domain containing 15 |
| **TXNDC16** | -0.99 | 0.0000 | thioredoxin domain containing 16 |
| **TXNL1** | -0.64 | 0.0000 | thioredoxin-like 1 |
| **TXNL4B** | -1.11 | 0.0000 | thioredoxin-like 4B |
| **TYMS** | 1.56 | 0.0000 | thymidylate synthetase |
| **UAP1L1** | -1.66 | 0.0000 | UDP-N-acteylglucosamine pyrophosphorylase 1-like 1 |
| **UBA1** | -1.13 | 0.0000 | ubiquitin-like modifier activating enzyme 1 |
| **UBA2** | 2.01 | 0.0000 | ubiquitin-like modifier activating enzyme 2 |
| **UBA5** | 0.74 | 0.0000 | ubiquitin-like modifier activating enzyme 5 |
| **UBA7** | -1.21 | 0.0000 | ubiquitin-like modifier activating enzyme 7 |
| **UBC** | -1.49 | 0.0000 | ubiquitin C |
| **UBE2A** | -1.44 | 0.0000 | ubiquitin-conjugating enzyme E2A (RAD6 homolog) |
| **UBE2J1** | -1.14 | 0.0000 | ubiquitin-conjugating enzyme E2, J1 (UBC6 homolog, yeast) |
| **UBL3** | -2.82 | 0.0000 | ubiquitin-like 3 |
| **UBL5** | -0.82 | 0.0000 | ubiquitin-like 5 |
| **UBXN8** | -1.33 | 0.0000 | UBX domain protein 8 |
| **UFC1** | -0.93 | 0.0000 | ubiquitin-fold modifier conjugating enzyme 1 |
| **UGGT2** | -1.33 | 0.0000 | UDP-glucose ceramide glucosyltransferase-like 2 |
| **UGT8** | -1.85 | 0.0000 | UDP glycosyltransferase 8 |
| **UHRF1BP1L** | -1.41 | 0.0000 | UHRF1 binding protein 1-like |
| **UMPS** | 1.07 | 0.0000 | uridine monophosphate synthetase |
| **UNC13B** | -0.79 | 0.0000 | unc-13 homolog B (C. elegans) |
| **UPF1** | 1.14 | 0.0000 | UPF1 regulator of nonsense transcripts homolog (yeast) |
| **UPF3B** | 0.89 | 0.0000 | UPF3 regulator of nonsense transcripts homolog B (yeast) |
| **UPRT** | -1.25 | 0.0000 | uracil phosphoribosyltransferase (FUR1) homolog (S. cerevisiae) |
| **URB2** | 1.69 | 0.0000 | URB2 ribosome biogenesis 2 homolog (S. cerevisiae) |
| **USO1** | -1.07 | 0.0000 | USO1 homolog, vesicle docking protein (yeast) |
| **USP10** | -1.78 | 0.0000 | ubiquitin specific peptidase 10 |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **USP3** | 1.41 | 0.0000 | ubiquitin specific peptidase 3 |
| **USP53** | -2.01 | 0.0000 | ubiquitin specific peptidase 53 |
| **USP54** | -1.53 | 0.0000 | ubiquitin specific peptidase 54 |
| **USP7** | 1.37 | 0.0000 | ubiquitin specific peptidase 7 (herpes virus-associated) |
| **USP9X** | -1.89 | 0.0000 | ubiquitin specific peptidase 9, X-linked |
| **UTP15** | 1.22 | 0.0000 | UTP15, U3 small nucleolar ribonucleoprotein, homolog (S. cerevisiae) |
| **UTP3** | -0.92 | 0.0000 | UTP3, small subunit (SSU) processome component, homolog (S. cerevisiae) |
| **UTRN** | -2.67 | 0.0000 | utrophin |
| **UXS1** | -1.16 | 0.0000 | UDP-glucuronate decarboxylase 1 |
| **UXT** | -1.23 | 0.0000 | ubiquitously-expressed transcript |
| **VAMP5** | -2.58 | 0.0000 | vesicle-associated membrane protein 5 (myobrevin) |
| **VAT1** | -1.33 | 0.0000 | vesicle amine transport protein 1 homolog (T. californica) |
| **VAT1L** | 3.44 | 0.0000 | vesicle amine transport protein 1 homolog (T. californica)-like |
| **VGLL4** | -1.74 | 0.0000 | vestigial like 4 (Drosophila) |
| **VHL** | -1.27 | 0.0000 | von Hippel-Lindau tumor suppressor |
| **VIM** | -1.85 | 0.0000 | vimentin |
| **VKORC1** | -1.05 | 0.0000 | vitamin K epoxide reductase complex, subunit 1 |
| **VMA21** | -1.21 | 0.0000 | VMA21 vacuolar H+-ATPase homolog (S. cerevisiae) |
| **VMAC** | -1.27 | 0.0000 | vimentin-type intermediate filament associated coiled-coil protein |
| **VOPP1** | 1.89 | 0.0000 | similar to EGFR-coamplified and overexpressed protein; EGFR-coamplified and overexpressed protein |
| **VPS13C** | -1.35 | 0.0000 | vacuolar protein sorting 13 homolog C (S. cerevisiae) |
| **VPS24** | -1.07 | 0.0000 | vacuolar protein sorting 24 homolog (S. cerevisiae); ring finger protein 103 |
| **VPS26A** | -1.18 | 0.0000 | vacuolar protein sorting 26 homolog A (S. pombe) |
| **VPS35** | -1.11 | 0.0000 | hypothetical protein LOC100133770; vacuolar protein sorting 35 homolog (S. cerevisiae) |
| **VPS36** | -1.13 | 0.0000 | vacuolar protein sorting 36 homolog (S. cerevisiae) |
| **VPS37B** | -0.99 | 0.0000 | vacuolar protein sorting 37 homolog B (S. cerevisiae) |
| **VSNL1** | 3.11 | 0.0000 | visinin-like 1 |
| **VWA1** | -3.59 | 0.0000 | von Willebrand factor A domain containing 1 |
| **VWF** | -1.06 | 0.0000 | von Willebrand factor |
| **WARS** | -1.30 | 0.0000 | tryptophanyl-tRNA synthetase |
| **WASF1** | 1.17 | 0.0000 | WAS protein family, member 1 |
| **WASF3** | 0.97 | 0.0000 | WAS protein family, member 3 |
| **WBP5** | -2.66 | 0.0000 | WW domain binding protein 5 |
| **WDFY3** | -1.48 | 0.0000 | WD repeat and FYVE domain containing 3 |
| **WDR1** | -0.88 | 0.0000 | WD repeat domain 1 |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **WDR19** | -1.96 | 0.0000 | WD repeat domain 19 |
| **WDR4** | 2.05 | 0.0000 | WD repeat domain 4 |
| **WDR43** | 1.59 | 0.0000 | WD repeat domain 43 |
| **WDR44** | -1.18 | 0.0000 | WD repeat domain 44 |
| **WDR45** | -1.58 | 0.0000 | WD repeat domain 45 |
| **WDR67** | 1.23 | 0.0000 | WD repeat domain 67 |
| **WDR7** | -1.65 | 0.0000 | WD repeat domain 7 |
| **WDR72** | -2.33 | 0.0000 | WD repeat domain 72 |
| **WDR74** | 1.16 | 0.0000 | WD repeat domain 74 |
| **WDR75** | 1.25 | 0.0000 | WD repeat domain 75 |
| **WDR81** | -1.43 | 0.0000 | WD repeat domain 81 |
| **WDR90** | 1.75 | 0.0000 | WD repeat domain 90 |
| **WDYHV1** | 1.37 | 0.0000 | WDYHV motif containing 1 |
| **WIPF1** | -1.78 | 0.0000 | WAS/WASL interacting protein family, member 1 |
| **WIPF2** | -1.45 | 0.0000 | WAS/WASL interacting protein family, member 2 |
| **WNK4** | 2.31 | 0.0000 | WNK lysine deficient protein kinase 4 |
| **WNT10B** | 1.21 | 0.0000 | wingless-type MMTV integration site family, member 10B |
| **WNT3** | 2.37 | 0.0000 | wingless-type MMTV integration site family, member 3 |
| **WNT5A** | 3.62 | 0.0000 | wingless-type MMTV integration site family, member 5A |
| **WSB2** | -1.92 | 0.0000 | WD repeat and SOCS box-containing 2 |
| **WT1** | 1.43 | 0.0000 | Wilms tumor 1 |
| **WWC1** | 2.52 | 0.0000 | WW and C2 domain containing 1 |
| **WWC3** | -1.63 | 0.0000 | WWC family member 3 |
| **WWOX** | -1.50 | 0.0000 | WW domain containing oxidoreductase |
| **YBX2** | 3.61 | 0.0000 | Y box binding protein 2 |
| **YEATS2** | 1.02 | 0.0000 | YEATS domain containing 2 |
| **YIPF6** | -1.39 | 0.0000 | Yip1 domain family, member 6 |
| **YTHDF1** | 1.26 | 0.0000 | YTH domain family, member 1 |
| **YTHDF2** | -0.86 | 0.0000 | YTH domain family, member 2 |
| **ZADH2** | -1.08 | 0.0000 | zinc binding alcohol dehydrogenase domain containing 2 |
| **ZAK** | 1.97 | 0.0000 | sterile alpha motif and leucine zipper containing kinase AZK |
| **ZBTB20** | -1.86 | 0.0000 | zinc finger and BTB domain containing 20 |
| **ZBTB24** | -1.13 | 0.0000 | zinc finger and BTB domain containing 24 |
| **ZBTB38** | -2.32 | 0.0000 | zinc finger and BTB domain containing 38 |
| **ZBTB4** | -1.58 | 0.0000 | zinc finger and BTB domain containing 4 |
| **ZBTB44** | -2.00 | 0.0000 | zinc finger and BTB domain containing 44 |
| **ZBTB46** | 1.67 | 0.0000 | zinc finger and BTB domain containing 46 |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **ZBTB7A** | -2.04 | 0.0000 | zinc finger and BTB domain containing 7A |
| **ZC3H8** | 1.56 | 0.0000 | zinc finger CCCH-type containing 8 |
| **ZC3HAV1L** | 2.35 | 0.0000 | zinc finger CCCH-type, antiviral 1-like |
| **ZCCHC17** | -1.16 | 0.0000 | zinc finger, CCHC domain containing 17 |
| **ZCCHC3** | 1.98 | 0.0000 | zinc finger, CCHC domain containing 3 |
| **ZDHHC17** | -1.51 | 0.0000 | zinc finger, DHHC-type containing 17 |
| **ZDHHC20** | -0.90 | 0.0000 | zinc finger, DHHC-type containing 20 |
| **ZDHHC23** | 2.08 | 0.0000 | zinc finger, DHHC-type containing 23 |
| **ZDHHC7** | -1.77 | 0.0000 | zinc finger, DHHC-type containing 7 |
| **ZEB2** | -2.89 | 0.0000 | zinc finger E-box binding homeobox 2 |
| **ZFP2** | -1.42 | 0.0000 | zinc finger protein 2 homolog (mouse) |
| **ZFP41** | 1.18 | 0.0000 | zinc finger protein 41 homolog (mouse) |
| **ZFP62** | 0.93 | 0.0000 | zinc finger protein 62 homolog (mouse) |
| **ZFP64** | 3.17 | 0.0000 | zinc finger protein 64 homolog (mouse) |
| **ZFYVE16** | -1.26 | 0.0000 | zinc finger, FYVE domain containing 16 |
| **ZFYVE27** | -1.54 | 0.0000 | zinc finger, FYVE domain containing 27 |
| **ZIC5** | 4.15 | 0.0000 | Zic family member 5 (odd-paired homolog, Drosophila) |
| **ZMAT2** | 0.97 | 0.0000 | zinc finger, matrin type 2 |
| **ZMAT4** | 2.01 | 0.0000 | zinc finger, matrin type 4 |
| **ZMIZ1** | -2.46 | 0.0000 | zinc finger, MIZ-type containing 1 |
| **ZNF101** | 0.99 | 0.0000 | zinc finger protein 101 |
| **ZNF107** | 2.08 | 0.0000 | zinc finger protein 107 |
| **ZNF121** | -1.49 | 0.0000 | zinc finger protein 121 |
| **ZNF138** | 2.71 | 0.0000 | zinc finger protein 138 |
| **ZNF146** | 1.99 | 0.0000 | zinc finger protein 146 |
| **ZNF181** | 1.18 | 0.0000 | zinc finger protein 181 |
| **ZNF185** | 2.51 | 0.0000 | zinc finger protein 185 (LIM domain) |
| **ZNF195** | 1.42 | 0.0000 | zinc finger protein 195 |
| **ZNF202** | 1.52 | 0.0000 | zinc finger protein 202 |
| **ZNF211** | -0.74 | 0.0000 | zinc finger protein 211 |
| **ZNF217** | 1.97 | 0.0000 | zinc finger protein 217 |
| **ZNF226** | -1.92 | 0.0000 | zinc finger protein 226 |
| **ZNF236** | -1.48 | 0.0000 | zinc finger protein 236 |
| **ZNF24** | -2.32 | 0.0000 | zinc finger protein 24 |
| **ZNF25** | -0.91 | 0.0000 | zinc finger protein 25 |
| **ZNF250** | 1.61 | 0.0000 | zinc finger protein 250 |
| **ZNF251** | 1.23 | 0.0000 | zinc finger protein 251 |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **ZNF26** | 1.24 | 0.0000 | zinc finger protein 26 |
| **ZNF266** | -1.00 | 0.0000 | zinc finger protein 266 |
| **ZNF273** | 1.96 | 0.0000 | zinc finger protein 273 |
| **ZNF280C** | 1.36 | 0.0000 | zinc finger protein 280C |
| **ZNF280D** | -1.78 | 0.0000 | zinc finger protein 280D |
| **ZNF30** | 1.68 | 0.0000 | zinc finger protein 30 |
| **ZNF302** | 1.58 | 0.0000 | zinc finger protein 302 |
| **ZNF334** | 2.16 | 0.0000 | zinc finger protein 334 |
| **ZNF337** | 1.37 | 0.0000 | zinc finger protein 337 |
| **ZNF34** | 0.64 | 0.0000 | zinc finger protein 34 |
| **ZNF343** | 0.85 | 0.0000 | zinc finger protein 343 |
| **ZNF382** | 1.56 | 0.0000 | zinc finger protein 382 |
| **ZNF433** | -1.25 | 0.0000 | zinc finger protein 433 |
| **ZNF436** | 0.96 | 0.0000 | zinc finger protein 436 |
| **ZNF44** | -1.31 | 0.0000 | zinc finger protein 44 |
| **ZNF440** | -1.60 | 0.0000 | zinc finger protein 440 |
| **ZNF461** | 1.61 | 0.0000 | zinc finger protein 461 |
| **ZNF462** | -1.04 | 0.0000 | zinc finger protein 462 |
| **ZNF48** | 1.91 | 0.0000 | zinc finger protein 48 |
| **ZNF490** | -0.91 | 0.0000 | zinc finger protein 490 |
| **ZNF507** | 1.05 | 0.0000 | zinc finger protein 507 |
| **ZNF512B** | 1.36 | 0.0000 | zinc finger protein 512B |
| **ZNF513** | -1.43 | 0.0000 | zinc finger protein 513 |
| **ZNF521** | 4.27 | 0.0000 | zinc finger protein 521 |
| **ZNF524** | -1.59 | 0.0000 | zinc finger protein 524 |
| **ZNF529** | 2.66 | 0.0000 | zinc finger protein 529 |
| **ZNF561** | -0.92 | 0.0000 | zinc finger protein 561; zinc finger protein 812 |
| **ZNF562** | -1.07 | 0.0000 | zinc finger protein 562 |
| **ZNF563** | -1.39 | 0.0000 | zinc finger protein 563 |
| **ZNF565** | 1.16 | 0.0000 | zinc finger protein 565 |
| **ZNF567** | 2.14 | 0.0000 | zinc finger protein 567 |
| **ZNF598** | 0.96 | 0.0000 | zinc finger protein 598 |
| **ZNF599** | 1.26 | 0.0000 | zinc finger protein 599 |
| **ZNF618** | 4.20 | 0.0000 | zinc finger protein 618 |
| **ZNF623** | 0.82 | 0.0000 | zinc finger protein 623 |
| **ZNF643** | 1.55 | 0.0000 | zinc finger protein 643 |
| **ZNF644** | -1.61 | 0.0000 | zinc finger protein 644 |

| Gene In DS-9 | ST88 vs HSC .logFC | adjPVal | Description |
|---|---|---|---|
| **ZNF646** | 1.20 | 0.0000 | zinc finger protein 646 |
| **ZNF658B** | 1.26 | 0.0000 | zinc finger protein 658 pseudogene; zinc finger protein 658B |
| **ZNF670** | 1.38 | 0.0000 | zinc finger protein 670 |
| **ZNF671** | -2.53 | 0.0000 | zinc finger protein 671 |
| **ZNF678** | 1.32 | 0.0000 | zinc finger protein 678 |
| **ZNF681** | 2.57 | 0.0000 | zinc finger protein 681 |
| **ZNF689** | 1.59 | 0.0000 | zinc finger protein 689 |
| **ZNF69** | -1.43 | 0.0000 | zinc finger protein 69 |
| **ZNF696** | 1.27 | 0.0000 | zinc finger protein 696 |
| **ZNF7** | 1.18 | 0.0000 | zinc finger protein 7 |
| **ZNF706** | -1.36 | 0.0000 | zinc finger protein 706 |
| **ZNF764** | 0.99 | 0.0000 | zinc finger protein 764 |
| **ZNF783** | 1.53 | 0.0000 | zinc finger family member 783 |
| **ZNF791** | -1.20 | 0.0000 | zinc finger protein 791 |
| **ZNF850P** | 1.27 | 0.0000 | zinc finger protein 850 pseudogene |
| **ZNF853** | 2.51 | 0.0000 | zinc finger protein 853 |
| **ZNF92** | 1.30 | 0.0000 | zinc finger protein 92 |
| **ZNRD1** | 0.92 | 0.0000 | zinc ribbon domain containing 1 |
| **ZRANB3** | 0.78 | 0.0000 | zinc finger, RAN-binding domain containing 3 |
| **ZSCAN18** | -4.17 | 0.0000 | zinc finger and SCAN domain containing 18 |
| **ZSCAN21** | 0.71 | 0.0000 | zinc finger and SCAN domain containing 21 |
| **ZSWIM5** | 2.78 | 0.0000 | zinc finger, SWIM-type containing 5 |

**Suppl. Table 7: DS-10**

DS-10, intersection of DS-9 and DS-1(siNf1VsSC), is hypothetically under the regulation of neurofibromin but independent from NRAS and MEK1/2, with matching the patterns: 1) increase in DS-9 and in DS-1, or 2) decreased in DS-9 and in DS-1

| Gene In DS-10 | si*Nf1* vs Ctrl (DS-1) | Adj PVal | ST88 vs HSC (DS-4) | Adj PVal | Descriptions |
|---|---|---|---|---|---|
| **ABCC4** | 0.74 | 0.0091 | 0.90 | 0.0000 | ATP-binding cassette, sub-family C (CFTR/MRP), member 4 |
| **ACP1** | 0.67 | 0.0001 | 0.69 | 0.0000 | acid phosphatase 1, soluble |
| **ACTG2** | -1.79 | 0.0008 | -3.96 | 0.0000 | actin, gamma 2, smooth muscle, enteric |
| **ADAL** | 0.69 | 0.0029 | 0.99 | 0.0000 | adenosine deaminase-like |
| **ADAM10** | -0.73 | 0.0046 | -2.86 | 0.0000 | ADAM metallopeptidase domain 10 |
| **ADAM17** | -0.99 | 0.0000 | -1.66 | 0.0000 | ADAM metallopeptidase domain 17 |
| **ADRB2** | 0.63 | 0.0051 | 2.01 | 0.0000 | adrenergic, beta-2-, receptor, surface |
| **AIP** | -0.71 | 0.0079 | -0.74 | 0.0005 | aryl hydrocarbon receptor interacting protein |
| **AKR1B10** | -0.81 | 0.0057 | -2.78 | 0.0000 | aldo-keto reductase family 1, member B10 (aldose reductase); aldo-keto reductase family 1, member B10-like |
| **ALS2** | 0.60 | 0.0087 | 0.76 | 0.0000 | amyotrophic lateral sclerosis 2 (juvenile) |
| **ANKHD1** | 0.65 | 0.0096 | 1.01 | 0.0000 | ankyrin repeat and KH domain containing 1; ANKHD1-EIF4EBP3 readthrough transcript; eukaryotic translation initiation factor 4E binding protein 3 |
| **ASB1** | 0.59 | 0.0028 | 1.20 | 0.0000 | ankyrin repeat and SOCS box-containing 1 |
| **ATAD2** | 0.99 | 0.0057 | 2.24 | 0.0000 | ATPase family, AAA domain containing 2 |
| **B3GALT4** | -0.96 | 0.0042 | -4.85 | 0.0000 | UDP-Gal:betaGlcNAc beta 1,3-galactosyltransferase, polypeptide 4 |
| **BACE1** | -0.99 | 0.0009 | -2.15 | 0.0000 | beta-site APP-cleaving enzyme 1 |
| **BAT5** | -0.74 | 0.0018 | -0.93 | 0.0000 | HLA-B associated transcript 5 |
| **BBS7** | -0.64 | 0.0001 | -1.13 | 0.0000 | Bardet-Biedl syndrome 7 |
| **BDH2** | -1.30 | 0.0000 | -0.82 | 0.0001 | 3-hydroxybutyrate dehydrogenase, type 2 |
| **BMP2** | 1.25 | 0.0006 | 1.77 | 0.0000 | bone morphogenetic protein 2 |
| **C10orf114** | -1.83 | 0.0000 | -2.44 | 0.0000 | chromosome 10 open reading frame 114 |
| **C15orf38** | -0.72 | 0.0007 | -0.71 | 0.0000 | chromosome 15 open reading frame 38 |
| **C17orf58** | 0.59 | 0.0075 | 1.91 | 0.0000 | chromosome 17 open reading frame 58 |
| **C1orf103** | 1.01 | 0.0025 | 1.97 | 0.0000 | chromosome 1 open reading frame 103 |

| Gene In DS-10 | si*Nf1* vs Ctrl (DS-1) | Adj PVal | ST88 vs HSC (DS-4) | Adj PVal | Descriptions |
|---|---|---|---|---|---|
| **C1orf27** | 0.68 | 0.0067 | 0.93 | 0.0000 | chromosome 1 open reading frame 27 |
| **C22orf9** | -0.82 | 0.0054 | -1.64 | 0.0000 | chromosome 22 open reading frame 9 |
| **C6orf105** | 1.79 | 0.0042 | 2.02 | 0.0001 | chromosome 6 open reading frame 105 |
| **C6orf125** | -0.60 | 0.0047 | -0.85 | 0.0000 | chromosome 6 open reading frame 125 |
| **C8orf46** | -0.98 | 0.0002 | -1.50 | 0.0000 | chromosome 8 open reading frame 46 |
| **CALHM2** | -1.31 | 0.0033 | -3.99 | 0.0000 | calcium homeostasis modulator 2 |
| **CAMK2N1** | 1.08 | 0.0025 | 1.07 | 0.0003 | calcium/calmodulin-dependent protein kinase II inhibitor 1 |
| **CARD6** | -0.79 | 0.0007 | -1.92 | 0.0000 | caspase recruitment domain family, member 6 |
| **CCDC80** | -0.70 | 0.0031 | -1.47 | 0.0000 | coiled-coil domain containing 80 |
| **CCL2** | -2.48 | 0.0007 | -2.09 | 0.0004 | chemokine (C-C motif) ligand 2 |
| **CCNL1** | 0.71 | 0.0075 | 0.93 | 0.0000 | cyclin L1 |
| **CD151** | -1.00 | 0.0022 | -0.93 | 0.0005 | CD151 molecule (Raph blood group) |
| **CDK2AP1** | -0.84 | 0.0001 | -1.46 | 0.0000 | cyclin-dependent kinase 2 associated protein 1 |
| **CDK2AP2** | -0.85 | 0.0011 | -0.94 | 0.0000 | cyclin-dependent kinase 2 associated protein 2 |
| **CDKN2A** | -0.66 | 0.0031 | -3.86 | 0.0000 | cyclin-dependent kinase inhibitor 2A (melanoma, p16, inhibits CDK4) |
| **CFI** | -3.13 | 0.0000 | -1.82 | 0.0000 | complement factor I |
| **CNOT6** | 0.59 | 0.0049 | 0.63 | 0.0003 | CCR4-NOT transcription complex, subunit 6 |
| **CNP** | -0.65 | 0.0024 | -2.68 | 0.0000 | 2',3'-cyclic nucleotide 3' phosphodiesterase |
| **COL4A2** | -0.67 | 0.0084 | -0.73 | 0.0005 | collagen, type IV, alpha 2 |
| **CREBZF** | 0.70 | 0.0037 | 2.16 | 0.0000 | CREB/ATF bZIP transcription factor |
| **CRNDE** | 0.79 | 0.0019 | 3.53 | 0.0000 | hCG1815491 |
| **CXXC5** | -1.59 | 0.0060 | -1.12 | 0.0004 | CXXC finger 5 |
| **CYBRD1** | -1.73 | 0.0007 | -1.17 | 0.0000 | cytochrome b reductase 1 |
| **DCP2** | 1.55 | 0.0000 | 1.09 | 0.0000 | DCP2 decapping enzyme homolog (S. cerevisiae) |
| **DCPS** | -0.67 | 0.0038 | -1.22 | 0.0000 | decapping enzyme, scavenger |
| **DDR1** | -1.12 | 0.0000 | -2.96 | 0.0000 | discoidin domain receptor tyrosine kinase 1 |
| **DIDO1** | 0.59 | 0.0060 | 1.97 | 0.0000 | death inducer-obliterator 1 |
| **DNAJB12** | -0.75 | 0.0058 | -1.23 | 0.0000 | DnaJ (Hsp40) homolog, subfamily B, member 12 |
| **DOCK4** | 1.49 | 0.0000 | 1.55 | 0.0000 | dedicator of cytokinesis 4 |
| **DOK1** | -0.66 | 0.0061 | -1.15 | 0.0000 | docking protein 1-like protein; docking protein 1, 62kDa (downstream of tyrosine kinase 1) |
| **DUT** | 0.60 | 0.0044 | 0.80 | 0.0000 | deoxyuridine triphosphatase |
| **EHD2** | -1.04 | 0.0057 | -1.63 | 0.0000 | EH-domain containing 2 |
| **ELMOD2** | -1.09 | 0.0000 | -1.27 | 0.0000 | ELMO/CED-12 domain containing 2 |
| **EXT2** | -0.85 | 0.0030 | -1.38 | 0.0000 | exostoses (multiple) 2 |
| **FADS2** | -1.95 | 0.0000 | -2.65 | 0.0000 | fatty acid desaturase 2 |

| Gene In DS-10 | si*Nf1* vs Ctrl (DS-1) | Adj PVal | ST88 vs HSC (DS-4) | Adj PVal | Descriptions |
|---|---|---|---|---|---|
| **FAM116A** | -1.13 | 0.0001 | -1.35 | 0.0000 | family with sequence similarity 116, member A |
| **FAM20C** | -0.78 | 0.0019 | -2.47 | 0.0000 | family with sequence similarity 20, member C |
| **FAM45A** | -0.70 | 0.0055 | -0.72 | 0.0001 | family with sequence similarity 45, member A |
| **FEM1B** | -0.63 | 0.0075 | -0.89 | 0.0000 | fem-1 homolog b (C. elegans) |
| **FGD6** | 1.14 | 0.0000 | 2.07 | 0.0000 | FYVE, RhoGEF and PH domain containing 6 |
| **FKBP1B** | -1.14 | 0.0000 | -0.87 | 0.0000 | FK506 binding protein 1B, 12.6 kDa |
| **FLJ10357** | -1.17 | 0.0000 | -0.81 | 0.0001 | hypothetical protein FLJ10357 |
| **FLJ39632** | 1.24 | 0.0046 | 3.54 | 0.0000 | hypothetical LOC642477; hypothetical LOC400879 |
| **FLJ40330** | 0.78 | 0.0009 | 0.85 | 0.0000 | hypothetical LOC645784 |
| **FNTB** | -0.73 | 0.0062 | -2.63 | 0.0000 | farnesyltransferase, CAAX box, beta |
| **FZD4** | -0.86 | 0.0006 | -1.88 | 0.0000 | frizzled homolog 4 (Drosophila) |
| **GALC** | -0.98 | 0.0001 | -1.02 | 0.0000 | galactosylceramidase |
| **GALNT10** | 0.95 | 0.0029 | 1.32 | 0.0000 | UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 10 (GalNAc-T10) |
| **GAS5** | 0.86 | 0.0002 | 1.64 | 0.0000 | growth arrest-specific 5 (non-protein coding) |
| **GBP2** | -1.35 | 0.0001 | -2.05 | 0.0000 | guanylate binding protein 2, interferon-inducible |
| **GCA** | 1.14 | 0.0084 | 1.37 | 0.0002 | grancalcin, EF-hand calcium binding protein |
| **GCH1** | 1.02 | 0.0028 | 1.41 | 0.0000 | GTP cyclohydrolase 1 |
| **GFRA1** | -1.57 | 0.0010 | -3.74 | 0.0000 | GDNF family receptor alpha 1 |
| **GOSR2** | 0.73 | 0.0047 | 1.06 | 0.0000 | golgi SNAP receptor complex member 2 |
| **GSTT2** | -0.82 | 0.0082 | -5.59 | 0.0000 | glutathione S-transferase theta 2B (gene/pseudogene); glutathione S-transferase theta 2 |
| **H3F3A** | -1.41 | 0.0000 | -1.14 | 0.0000 | H3 histone, family 3B (H3.3B); H3 histone, family 3A pseudogene; H3 histone, family 3A; similar to H3 histone, family 3B; similar to histone H3.3B |
| **HEXIM1** | -0.60 | 0.0065 | -0.86 | 0.0000 | hexamethylene bis-acetamide inducible 1 |
| **HIPK2** | 1.46 | 0.0001 | 1.79 | 0.0000 | homeodomain interacting protein kinase 2; similar to homeodomain interacting protein kinase 2 |
| **HLA-DMA** | -0.73 | 0.0023 | -5.07 | 0.0000 | major histocompatibility complex, class II, DM alpha |
| **HSPA5** | -0.77 | 0.0023 | -1.57 | 0.0000 | hypothetical gene supported by AF216292; NM_005347; heat shock 70kDa protein 5 (glucose-regulated protein, 78kDa) |
| **IFI16** | -0.67 | 0.0042 | -0.94 | 0.0000 | interferon, gamma-inducible protein 16 |
| **IFRD1** | 0.80 | 0.0029 | 1.49 | 0.0000 | interferon-related developmental regulator 1 |
| **IRF9** | -0.95 | 0.0016 | -1.35 | 0.0000 | interferon regulatory factor 9 |
| **ITFG3** | -0.74 | 0.0069 | -0.95 | 0.0000 | integrin alpha FG-GAP repeat containing 3 |
| **KCNN4** | -1.08 | 0.0046 | -3.91 | 0.0000 | potassium intermediate/small conductance calcium-activated channel, subfamily N, member 4 |

| Gene In DS-10 | si*Nf1* vs Ctrl (DS-1) | Adj PVal | ST88 vs HSC (DS-4) | Adj PVal | Descriptions |
|---|---|---|---|---|---|
| **KIAA1609** | 0.65 | 0.0071 | 0.78 | 0.0001 | KIAA1609 |
| **KNTC1** | 0.69 | 0.0012 | 1.38 | 0.0000 | kinetochore associated 1 |
| **KRCC1** | -1.09 | 0.0000 | -1.22 | 0.0000 | lysine-rich coiled-coil 1 |
| **LAT2** | 1.92 | 0.0000 | 0.98 | 0.0001 | linker for activation of T cells family, member 2 |
| **LDB2** | 0.87 | 0.0000 | 0.63 | 0.0000 | LIM domain binding 2 |
| **LOC100132790** | 1.50 | 0.0003 | 1.15 | 0.0004 | hypothetical protein LOC100132790; hypothetical LOC100132670; hypothetical LOC100132263 |
| **LOC399959** | 1.04 | 0.0053 | 2.96 | 0.0000 | hypothetical LOC399959 |
| **LOC442421** | -0.61 | 0.0016 | -0.91 | 0.0000 | hypothetical LOC442421 |
| **LOC550643** | -0.84 | 0.0000 | -1.01 | 0.0000 | hypothetical LOC550643 |
| **LOC554202** | 0.59 | 0.0046 | 1.58 | 0.0000 | hypothetical LOC554202 |
| **LRRC41** | -0.72 | 0.0043 | -0.75 | 0.0003 | leucine rich repeat containing 41 |
| **LRRC8D** | -0.59 | 0.0010 | -0.75 | 0.0000 | leucine rich repeat containing 8 family, member D |
| **MAGED2** | -0.68 | 0.0058 | -1.27 | 0.0000 | melanoma antigen family D, 2 |
| **MANF** | -0.64 | 0.0012 | -1.05 | 0.0000 | mesencephalic astrocyte-derived neurotrophic factor |
| **MAP4** | -1.01 | 0.0009 | -2.44 | 0.0000 | microtubule-associated protein 4 |
| **MAPK14** | -0.61 | 0.0021 | -1.07 | 0.0000 | mitogen-activated protein kinase 14 |
| **MARCKS** | -1.15 | 0.0017 | -1.13 | 0.0002 | myristoylated alanine-rich protein kinase C substrate |
| **MCAM** | -0.69 | 0.0084 | -2.10 | 0.0000 | melanoma cell adhesion molecule |
| **MCTP1** | 1.13 | 0.0002 | 1.06 | 0.0001 | multiple C2 domains, transmembrane 1 |
| **MMP17** | -0.89 | 0.0035 | -2.35 | 0.0000 | matrix metallopeptidase 17 (membrane-inserted) |
| **MOCS1** | -0.77 | 0.0012 | -0.90 | 0.0000 | molybdenum cofactor synthesis 1 |
| **MPP4** | 1.80 | 0.0002 | 2.85 | 0.0000 | membrane protein, palmitoylated 4 (MAGUK p55 subfamily member 4) |
| **MTHFD1L** | 0.61 | 0.0075 | 1.40 | 0.0000 | methylenetetrahydrofolate dehydrogenase (NADP+ dependent) 1-like |
| **MXI1** | -0.67 | 0.0024 | -1.48 | 0.0000 | MAX interactor 1 |
| **MYL9** | -1.40 | 0.0002 | -4.56 | 0.0000 | myosin, light chain 9, regulatory |
| **MYO5B** | 1.12 | 0.0000 | 4.07 | 0.0000 | similar to acetyl-Coenzyme A acyltransferase 2 (mitochondrial 3-oxoacyl-Coenzyme A thiolase); similar to KIAA1119 protein; myosin VB |
| **NAB1** | 0.86 | 0.0000 | 2.09 | 0.0000 | NGFI-A binding protein 1 (EGR1 binding protein 1) |
| **NACC2** | -0.98 | 0.0039 | -2.28 | 0.0000 | NACC family member 2, BEN and BTB (POZ) domain containing |
| **NCSTN** | -0.75 | 0.0014 | -1.36 | 0.0000 | nicastrin |
| **NF1** | -1.15 | 0.0006 | -2.25 | 0.0000 | neurofibromin 1 |
| **NGFRAP1** | -0.77 | 0.0024 | -1.79 | 0.0000 | nerve growth factor receptor (TNFRSF16) associated protein 1 |

| Gene In DS-10 | si*Nf1* vs Ctrl (DS-1) | Adj PVal | ST88 vs HSC (DS-4) | Adj PVal | Descriptions |
|---|---|---|---|---|---|
| **NIPSNAP3A** | -0.84 | 0.0007 | -0.83 | 0.0000 | nipsnap homolog 3A (C. elegans) |
| **NME3** | -1.08 | 0.0028 | -1.97 | 0.0000 | non-metastatic cells 3, protein expressed in |
| **NRIP3** | 1.29 | 0.0008 | 1.26 | 0.0001 | nuclear receptor interacting protein 3 |
| **OLFML2A** | -2.60 | 0.0010 | -3.60 | 0.0000 | olfactomedin-like 2A |
| **OLFML2B** | -1.37 | 0.0014 | -2.40 | 0.0000 | olfactomedin-like 2B |
| **OPA1** | 0.61 | 0.0082 | 0.85 | 0.0000 | optic atrophy 1 (autosomal dominant) |
| **P4HB** | -0.71 | 0.0091 | -0.85 | 0.0002 | prolyl 4-hydroxylase, beta polypeptide |
| **PABPC1** | 0.61 | 0.0006 | 1.06 | 0.0000 | poly(A) binding protein, cytoplasmic pseudogene 5; poly(A) binding protein, cytoplasmic 1 |
| **PABPC3** | 0.71 | 0.0007 | 0.96 | 0.0000 | poly(A) binding protein, cytoplasmic 3 |
| **PARVA** | -0.61 | 0.0092 | -0.77 | 0.0000 | parvin, alpha |
| **PCDH7** | -1.35 | 0.0018 | -1.76 | 0.0000 | protocadherin 7 |
| **PCMTD2** | 0.96 | 0.0001 | 1.60 | 0.0000 | protein-L-isoaspartate (D-aspartate) O-methyltransferase domain containing 2 |
| **PDZRN3** | -1.88 | 0.0000 | -2.03 | 0.0000 | PDZ domain containing ring finger 3 |
| **PGM1** | -0.88 | 0.0000 | -0.83 | 0.0000 | phosphoglucomutase 1 |
| **PHTF2** | 0.67 | 0.0001 | 0.77 | 0.0000 | putative homeodomain transcription factor 2 |
| **PLEKHB2** | -0.68 | 0.0000 | -1.72 | 0.0000 | pleckstrin homology domain containing, family B (evectins) member 2 |
| **PLEKHO1** | -0.89 | 0.0049 | -1.46 | 0.0000 | pleckstrin homology domain containing, family O member 1 |
| **PLSCR3** | -0.62 | 0.0040 | -1.26 | 0.0000 | phospholipid scramblase 3 |
| **PLXND1** | -1.44 | 0.0012 | -2.22 | 0.0000 | plexin D1 |
| **PMP22** | -0.86 | 0.0077 | -5.20 | 0.0000 | peripheral myelin protein 22 |
| **PODXL** | 1.15 | 0.0006 | 1.92 | 0.0000 | podocalyxin-like |
| **POU4F1** | 0.93 | 0.0087 | 4.62 | 0.0000 | POU class 4 homeobox 1 |
| **PPAPDC1A** | -1.13 | 0.0028 | -1.47 | 0.0000 | phosphatidic acid phosphatase type 2 domain containing 1A |
| **PPAPDC3** | -1.86 | 0.0000 | -2.59 | 0.0000 | phosphatidic acid phosphatase type 2 domain containing 3 |
| **PPT1** | -0.85 | 0.0016 | -0.96 | 0.0000 | palmitoyl-protein thioesterase 1 |
| **PPT2** | -0.68 | 0.0085 | -2.88 | 0.0000 | palmitoyl-protein thioesterase 2 |
| **PRKCDBP** | -1.27 | 0.0000 | -3.28 | 0.0000 | protein kinase C, delta binding protein |
| **PRR7** | -0.61 | 0.0059 | -1.01 | 0.0000 | proline rich 7 (synaptic) |
| **PSAT1** | 0.84 | 0.0063 | 1.07 | 0.0001 | chromosome 8 open reading frame 62; phosphoserine aminotransferase 1 |
| **PTPLA** | -0.74 | 0.0011 | -0.93 | 0.0000 | protein tyrosine phosphatase-like (proline instead of |

| Gene In DS-10 | si*Nf1* vs Ctrl (DS-1) | Adj PVal | ST88 vs HSC (DS-4) | Adj PVal | Descriptions |
|---|---|---|---|---|---|
| | | | | | catalytic arginine), member A |
| **PXN** | 0.70 | 0.0011 | 0.65 | 0.0000 | paxillin |
| **RABAC1** | -0.65 | 0.0096 | -1.01 | 0.0000 | Rab acceptor 1 (prenylated) |
| **RBBP4** | 0.66 | 0.0060 | 1.70 | 0.0000 | hypothetical LOC642954; retinoblastoma binding protein 4 |
| **RDH11** | -0.61 | 0.0004 | -1.14 | 0.0000 | retinol dehydrogenase 11 (all-trans/9-cis/11-cis) |
| **RELL1** | 0.61 | 0.0046 | 1.56 | 0.0000 | RELT-like 1 |
| **RHOJ** | -1.09 | 0.0014 | -1.92 | 0.0000 | ras homolog gene family, member J |
| **RNF32** | 0.63 | 0.0074 | 0.71 | 0.0003 | ring finger protein 32 |
| **RUNX2** | -2.45 | 0.0000 | -1.99 | 0.0000 | runt-related transcription factor 2 |
| **SCD** | -1.81 | 0.0035 | -2.33 | 0.0000 | stearoyl-CoA desaturase (delta-9-desaturase) |
| **SELM** | -1.67 | 0.0000 | -1.88 | 0.0000 | selenoprotein M |
| **SEP15** | -0.61 | 0.0012 | -0.97 | 0.0000 | 15 kDa selenoprotein |
| **SERPINA5** | -0.91 | 0.0018 | -1.25 | 0.0000 | serpin peptidase inhibitor, clade A (alpha-1 antiproteinase, antitrypsin), member 5 |
| **SFRS1** | 0.64 | 0.0036 | 1.40 | 0.0000 | splicing factor, arginine/serine-rich 1 |
| **SFRS12IP1** | 0.75 | 0.0094 | 1.02 | 0.0000 | SFRS12-interacting protein 1; family with sequence similarity 159, member B |
| **SHISA4** | -0.70 | 0.0065 | -1.74 | 0.0000 | shisa homolog 4 (Xenopus laevis) |
| **SIAE** | -0.72 | 0.0025 | -0.76 | 0.0000 | sialic acid acetylesterase |
| **SIDT2** | -0.81 | 0.0069 | -1.99 | 0.0000 | SID1 transmembrane family, member 2 |
| **SLBP** | 0.63 | 0.0039 | 0.93 | 0.0000 | stem-loop binding protein |
| **SLC27A1** | -0.93 | 0.0060 | -0.99 | 0.0004 | solute carrier family 27 (fatty acid transporter), member 1 |
| **SLC35B2** | -0.69 | 0.0036 | -1.67 | 0.0000 | solute carrier family 35, member B2 |
| **SLC38A1** | 1.02 | 0.0013 | 5.52 | 0.0000 | solute carrier family 38, member 1 |
| **SLC38A10** | -0.60 | 0.0080 | -0.66 | 0.0004 | solute carrier family 38, member 10 |
| **SOCS2** | -1.00 | 0.0024 | -1.25 | 0.0000 | suppressor of cytokine signaling 2 |
| **SPATA2** | 0.65 | 0.0089 | 1.11 | 0.0000 | spermatogenesis associated 2 |
| **SPG20** | -1.43 | 0.0000 | -0.87 | 0.0000 | spastic paraplegia 20 (Troyer syndrome) |
| **SREBF1** | -1.46 | 0.0000 | -1.48 | 0.0000 | sterol regulatory element binding transcription factor 1 |
| **SRGAP1** | 0.96 | 0.0009 | 2.02 | 0.0000 | SLIT-ROBO Rho GTPase activating protein 1 |
| **SRPX2** | -1.00 | 0.0005 | -1.92 | 0.0000 | sushi-repeat-containing protein, X-linked 2 |
| **SSH3** | -1.11 | 0.0007 | -2.36 | 0.0000 | slingshot homolog 3 (Drosophila) |
| **SSR3** | 0.97 | 0.0000 | 1.30 | 0.0000 | signal sequence receptor, gamma (translocon-associated protein gamma) |
| **ST5** | -0.95 | 0.0006 | -1.51 | 0.0000 | suppression of tumorigenicity 5 |
| **STRBP** | 0.74 | 0.0000 | 2.00 | 0.0000 | spermatid perinuclear RNA binding protein |

| Gene In DS-10 | si*Nf1* vs Ctrl (DS-1) | Adj PVal | ST88 vs HSC (DS-4) | Adj PVal | Descriptions |
|---|---|---|---|---|---|
| **SUSD1** | -0.88 | 0.0036 | -1.53 | 0.0000 | sushi domain containing 1 |
| **SYNM** | -0.70 | 0.0093 | -1.34 | 0.0000 | synemin, intermediate filament protein |
| **SYT11** | -1.08 | 0.0000 | -1.21 | 0.0000 | synaptotagmin XI |
| **TCEAL3** | -0.66 | 0.0002 | -1.59 | 0.0000 | transcription elongation factor A (SII)-like 3 |
| **TCEAL5** | -0.76 | 0.0002 | -1.07 | 0.0000 | transcription elongation factor A (SII)-like 5 |
| **TCEAL6** | -0.69 | 0.0001 | -1.47 | 0.0000 | transcription elongation factor A (SII)-like 6 |
| **TCEAL8** | -0.59 | 0.0025 | -1.07 | 0.0000 | transcription elongation factor A (SII)-like 8 |
| **TEX15** | 0.83 | 0.0035 | 1.61 | 0.0000 | testis expressed 15 |
| **TK2** | -0.90 | 0.0004 | -0.98 | 0.0000 | thymidine kinase 2, mitochondrial |
| **TLR1** | -0.75 | 0.0055 | -4.61 | 0.0000 | toll-like receptor 1 |
| **TMEM117** | 1.14 | 0.0004 | 1.12 | 0.0000 | transmembrane protein 117 |
| **TMEM150A** | -0.93 | 0.0019 | -0.85 | 0.0005 | transmembrane protein 150A |
| **TMEM209** | 0.78 | 0.0042 | 1.46 | 0.0000 | transmembrane protein 209 |
| **TMEM50A** | -0.76 | 0.0007 | -1.08 | 0.0000 | transmembrane protein 50A |
| **TNFAIP1** | -0.69 | 0.0000 | -1.46 | 0.0000 | tumor necrosis factor, alpha-induced protein 1 (endothelial) |
| **TNFAIP6** | -1.92 | 0.0016 | -4.40 | 0.0000 | tumor necrosis factor, alpha-induced protein 6 |
| **TNFSF12** | -1.09 | 0.0017 | -3.04 | 0.0000 | TNFSF12-TNFSF13 readthrough transcript; tumor necrosis factor (ligand) superfamily, member 12; tumor necrosis factor (ligand) superfamily, member 13 |
| **TNS3** | -0.75 | 0.0076 | -1.80 | 0.0000 | tensin 3 |
| **TOLLIP** | -0.64 | 0.0024 | -1.93 | 0.0000 | toll interacting protein |
| **TOM1L2** | -0.96 | 0.0018 | -1.05 | 0.0000 | target of myb1-like 2 (chicken) |
| **TP53I3** | -0.87 | 0.0014 | -0.85 | 0.0001 | tumor protein p53 inducible protein 3 |
| **TWSG1** | -1.12 | 0.0008 | -1.79 | 0.0000 | twisted gastrulation homolog 1 (Drosophila) |
| **UBE2B** | -0.91 | 0.0036 | -0.65 | 0.0003 | ubiquitin-conjugating enzyme E2B (RAD6 homolog) |
| **UROS** | -0.69 | 0.0029 | -0.75 | 0.0001 | uroporphyrinogen III synthase |
| **USP3** | 0.62 | 0.0089 | 1.41 | 0.0000 | ubiquitin specific peptidase 3 |
| **VWA1** | -1.57 | 0.0076 | -3.59 | 0.0000 | von Willebrand factor A domain containing 1 |
| **WWC3** | -0.74 | 0.0014 | -1.63 | 0.0000 | WWC family member 3 |
| **ZBTB4** | -0.73 | 0.0014 | -1.58 | 0.0000 | zinc finger and BTB domain containing 4 |
| **ZDHHC20** | -0.60 | 0.0024 | -0.90 | 0.0000 | zinc finger, DHHC-type containing 20 |
| **ZEB2** | -0.78 | 0.0079 | -2.89 | 0.0000 | zinc finger E-box binding homeobox 2 |
| **ZNF185** | 1.51 | 0.0001 | 2.51 | 0.0000 | zinc finger protein 185 (LIM domain) |
| **ZNF26** | 0.77 | 0.0001 | 1.24 | 0.0000 | zinc finger protein 26 |
| **ZNF30** | 0.63 | 0.0036 | 1.68 | 0.0000 | zinc finger protein 30 |
| **ZNF643** | 0.72 | 0.0001 | 1.55 | 0.0000 | zinc finger protein 643 |

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# ABSTRACT

## IDENTIFICATION OF TRANSCRIPTIONAL MECHANISMS DOWNSTREAM OF NF1 GENE DEFICIENCY IN MALIGANT PERIPHERAL NERVE SHEATH TUMORS

by

**DAOCHUN SUN**

**December 2012**

**Advisor:** Michael A. Tainsky, Ph.D.

**Major:** Molecular Biology and Genetics

**Degree:** Doctor of Philosophy

Malignant peripheral nerve sheath tumor (MPNST) is a type of soft tissue sarcoma that occurs in carriers of mutations in the neurofibromatosis type I gene (*Nf1*) as well as sporadically. Plexiform neurofibromas in NF1 patients have a significant risk of developing into MPNSTs leading to increased morbidity and mortality from this syndrome. Surgery is the primary intervention but it is not always effective due to the tendency of MPNSTs to infiltrate the surrounding tissue or grow in an inoperable location. Neurofibromin, the protein coded by the *Nf1* gene, functions as a GTPase activating protein (GAP) whose mutation leads to constitutive activation of RAS and mitogen-activated protein kinase (MAPK) signaling in NF1 patients' tumors. However, therapeutic targeting of RAS and MAPK have had limited success.

In this study, we modulated NRAS, MEK1/2 and neurofibromin levels in MPNST cell lines and determined the global gene expression changes that were associated with each experimental condition. Gene expression changes due to neurofibromin deficiency but independent of NRAS and MEK1/2 regulation were characterized for the first time in MPNST cell lines and led me to focus on bone morphogenetic protein 2 (*Bmp2*) and its signaling pathway. The BMP2-SMAD1/5 pathway was activated in NF1-associated MPNST cells and inhibition of BMP2 signaling by LDN-193189 or shRNA to BMP2 decreased the motility and invasion of NF1-associated MPNST cells *in vitro* thus providing evidence of a critical function for BMP2 signaling in MPNST malignancy.

The stratification of gene changes according to pathway responses has provided a clarification of one mechanism within the complex effects of neurofibromin in MPNST pathology and some novel targets for future therapeutic intervention.

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## EDUCATION

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2. Kraniak JM, **Sun D** et al. *Mol Cell Biochem*. 2010 Nov; 344(1-2):267-76 The role of neurofibromin in N-Ras mediated AP-1 regulation in malignant peripheral nerve sheath tumors.
3. Sun Y, **Sun D**, et al. *Lung Cancer.* 2007 Oct; 58(1):21-9.
   Downregulation of Sirt1 by antisense oligonucleotides induces apoptosis and enhances radiation sensitization in A549 lung cancer cells.