UNIVERSITA' DI PISA
Facoltà di Medicina e Chirurgia
Scuola di specializzazione in Farmacologia

Ruolo del sistema ubiquitina-proteasoma (UPS) nella disfunzione beta cellulare del diabete di tipo 2 e possibili opzioni terapeutiche

Relatori	**Candidato**
Prof. Piero Marchetti	**Dr. Marco Bugliani**
Prof. Giovanni Umberto Corsini	

ANNO ACCADEMICO
2010-2011

Indice

Riassunto

Sebbene la disfunzione beta cellulare rivesta un ruolo di primaria importanza nel diabete di tipo 2, le informazioni ad oggi disponibili riguardanti il loro fenotipo molecolare in tale tipo di diabete, sono ancora piuttosto limitate. In questo lavoro, dapprima sono state valutate le differenze di espressione tra il trascrittoma di isole purificate da donatori affetti da diabete di tipo 2 (T2D) e quello di isole di donatori non diabetici (ND) mentre in seguito l'attenzione è stata focalizzata sul sistema ubiquitina-proteasoma (UPS), il principale pathway intracellulare deputato alla degradazione delle proteine. L'analisi microarray mostrava che 1230 geni risultavano differenzialmente espressi nelle isole diabetiche e che questi influenzavano sia la struttura che la funzione di tale tessuto. In seguito a questa ed ad altre analisi emergeva in maniera decisa una riduzione dell'UPS nel T2D.

Gli esperimenti di RT-PCR quantitativa mostravano una riduzione dell'espressione di UBE2K, PSMB7 e UCHL1 (geni dell'UPS). Studi di immunoistochimica rivelavano un maggior accumulo di ubiquitina accompagnato ad una riduzione dell'attività del proteasoma in T2D. L'inibizione diretta del proteasoma e l'esposizione ad acido palmitico riducevano l' attività del proteasoma e a questo si accompagnava una riduzione della secrezione insulinica indotta da glucosio. L'esposizione a metformina o a GLP-1, due molecole utilizzate nel trattamento del diabete di tipo 2 in grado di ripristinare un corretto rilascio insulinico in risposta a glucosio era associata ad un aumento dell'attività del proteasoma. In questo studio si mostra la presenza di numerose alterazioni nel trascrittoma delle isole diabetiche e si sottolinea l'importanza delle alterazioni a carico del sistema UPS come meccanismo associato alla disfunzione beta cellulare nel diabete di tipo 2.

Introduzione

Il diabete di tipo 2 rappresenta la forma più comune di diabete e risulta da una combinazione di fattori genetici e ambientali che da un lato riducono la sensibilità all'insulina e dall'altro danneggiano il turnover e la funzione beta cellulare (Stumvoll et al., 2008; American Diabetes Association, 2011). Un numero sempre maggiore di evidenze sperimentali indica le alterazioni beta cellulari come centrali per lo sviluppo e la progressione del diabete di tipo 2 (Donath et al., 2004; Stumvoll et al., 2008; American Diabetes Association, 2011), infatti alcuni autori hanno osservato come in questa forma di diabete ci sia una riduzione del volume delle isole e/o della massa delle cellule contenenti insulina (Donath et al., 2004; Meier JJ, 2008; Stumvoll et al., 2008; Marchetti et al., 2009;). In aggiunta a questi, numerosi altri studi condotti in vivo e/o in vitro su pazienti e/o isole pancreatiche umane isolate da donatori affetti da diabete di tipo 2 hanno consistentemente mostrato difetti della secrezione insulinica indotta da glucosio sia in termini qualitativi che quantitativi (Butler et al., 2003; Del Guerra et al., 2005; Ferrannini et al., 2005). Sebbene molti geni siano stati associati al diabete di tipo 2 (Doria et al., 2008; Staiger et al., 2009; McCarthy, 2010), e sebbene siano stati descritti numerosi meccanismi in grado di spiegare la disfunzione cellulare in questa forma di diabete (Butler et al., 2003; Del Guerra et al., 2005; Ferrannini et al., 2005; Wajchenberg, 2007; Doria et al., 2008; Marchetti et al., 2009; Staiger et al., 2009; McCarthy, 2010), ancora poche sono le informazioni attualmente disponibili che siano in grado di descrivere appieno il fenotipo delle isole pancreatiche a livello molecolare. Pochi, infatti, sono gli autori che hanno riportato dati sulle caratteristiche del trascrittoma di isole isolate dai pancreas di pazienti affetti da diabete di tipo 2 (Gunton et al., 2005; Ostenson et al., 2006; MacDonald et al., 2009). Gunton et al hanno studiato l'intera espressione genica in isole di 7 donatori non diabetici e 5 diabetici di tipo 2 (Gunton et al., 2005) trovando alterazioni significative ($p<0.01$) nell'espressione di 370 dei 44,298 geni e EST analizzati; dei quali 243 risultavano upregolati e 137 downregolati nelle isole diabetiche. I risultati di un'analisi ottenuta con isole di 4 donatori di controllo e 4 di donatore di tipo 2 sono stati parzialmente riportati da Ostenson et al e MacDonald et al (Ostenson et al., 2006; MacDonald et al., 2009); in particolare, essi mostravano una riduzione dell'espressione di geni implicati nel processo esocitotico e nella funzione mitocondriale.

In questo studio, abbiamo effettuato l'analisi microarray di isole pancreatiche umane isolate da 6 donatori con diabete di tipo 2 e 7 individui non diabetici e sono stati trovati differenze significative nell'espressione dei geni di entrambi i gruppi. Tutte le analisi effettuate mostravano come tra le varie alterazioni, l'espressione di geni relativi al sistema ubiquitina-proteasoma (UPS) risultasse alterata in maniera consistente nelle isole di diabete di tipo 2. Il sistema UPS è il principale pathway intracellulare per la degradazione delle proteine (Jung et al., 2009; Wong et al., 2010). Inizialmente, la proteina substrato viene marcata per la degradazione tramite il legame covalente ad una piccola molecola proteica di 76 KDa denominata ubiquitina, attraverso 3 steps principali (attivazione, coniugazione e ligazione) mediati da tre diverse classi di enzimi denominate E1, E2 e E3 (Petroski, 2008; Clague et al., 2010). In seguito, la proteina ubiquitinata viene riconosciuta dal proteasoma che la degrada in piccoli peptidi e amminoacidi. Il proteasoma che degrada le proteine poliubiquitinate è conosciuto come proteasoma 26S, ed è costituito da un core catalitico 20S chiuso alle estremità da due subunità regolatorie 19S (Bedford et al., 2010; Xie, 2010). L'UPS è implicato nella degradazione proteolitica di proteine ossidate, nella regolazione della durata della vita delle proteine, nel loro controllo qualità, nella regolazione del ciclo cellulare, nell'espressione genica e nella risposta immunitaria e agli stress (Petroski, 2008; Jung et al., 2009; Bedford et al., 2010; Clague et al., 2010; Wong et al., 2010; Xie, 2010); in tal modo, il sistema riveste un ruolo importante nella fisiologia e nella patologia cellulare, tanto che le sue alterazioni sono state associate a varie patologie incluso il cancro e il diabete (Petroski, 2008; Jung et al., 2009; Bedford et al., 2010; Clague et al., 2010; Wong et al., 2010; Xie, 2010). In questo studio, mostriamo che i cambiamenti dell'UPS possono essere implicati nella disfunzione beta cellulare del diabete di tipo 2, e che gli effetti dell'inibizione del proteasoma sono correlati anche alla secrezione insulinica; inoltre si esplora il ruolo giocato dalla lipotossicità. In ultima analisi, poi, si osserva come l'uso di alcune molecole correntemente utilizzate in terapia nel trattamento del diabete mellito di tipo 2, metformina e GLP-1, possa modulare l'attività del suddetto sistema (Schwanstecher C et al, 2011; Ahrén B, 2011) aprendo così la strada allo studio del sistema UPS come possibile target per il trattamento del diabete.

Finalità della tesi

Come già anticipato, nonostante la percentuale di persone affette da diabete di tipo 2 sia in costane aumento in tutto il mondo, ancora poche sono le informazioni attualmente in grado di evidenziare tutti i difetti presenti nella disfunzione beta cellulare di tale forma di diabete. Scopo di questo studio è stato quindi, quello di confrontare tramite analisi microarray il trascrittoma di isole isolate da donatori diabetici con quello di isole ottenute da donatori non diabetici, allo scopo di valutarne le alterazioni e possibilmente trovare target per lo sviluppo di nuove opzioni terapeutiche. Per tale motivo, una volta evidenziate le suddette alterazioni, si è cercato prima di tutto di verificare se queste potessero spiegare il fenotipo diabetico, in seguito si è valutato se queste potevano essere indotte da fattori ambientali; infine per cercare di capire se tali alterazioni potevano rappresentare un target per lo sviluppo opzioni terapeutiche si è studiato se alcune delle molecole attualmente utilizzate in terapia nel trattamento del diabete di tipo 2 fossero in grado di correggerle.

Risultati

Secrezione insulinica

I risultati della secrezione acuta di insulina stimolata da glucosio e altri secretagoghi sono riportate in tabella 1. Come aspettato la secrezione dell'ormone stimolata da glucosio e sulfonilurea risultava ridotta in maniera significativa nelle isole di donatore diabetico di tipo 2 rispetto a quelle di donatore non diabetico, sia in termini di secrezione assoluta (μU/isola/min) sia quando espresso come indice di stimolazione (rapporto tra il rilascio insulinico in risposta a 16.7 mmol/l di glucosio o secretagogo e il rilascio insulinico in risposta a glucosio 3.3 mmol/l). Questi risultati confermano dati pubblicati precedentemente sia dal nostro che da altri gruppi (Deng et al., 2004; Del Guerra et al., 2005).

	3.3 mM glucosio	**16.7 mM glucosio**	**SI glucosio**	**100 μM glibenclamide**	**SI glibenclamide**	**20 mM arginina**	**SI arginina**
ND	0.04±0.02	0.10±0.06	2.8±1.2	0.09±0.06	2.7±1.4	0.06±0.04	2.0±0.5
T2D	0.03±0.01	0.04±0.02	1.6±0.4	0.04±0.02	1.6±0.4	0.05±0.02	1.8±0.5
P value	NS	0.007	0.007	0.038	0.047	NS	NS

Tabella 1: Secrezione insulinica (μU/isola/min) in risposta a differenti secretagoghi e relative indici di stimolazione (IS: rilascio di insulina in seguito a stimolo rispetto al rilascio basale).

ND: non diabetici; T2D: diabetici tipo 2

Esperimenti di microarray: risultati globali

L’analisi microarray mostrava 1,345 probe sets differentemente espressi tra le isole diabetiche e quelle di controllo; di questi 59 risultavano upregulati e 1,286 downregulati. I vari trascritti e varianti identificavano un totale di 1,230 geni (Dati supplementari, tabella 1), che rivestono un ruolo nella struttura e nella funzionalità insulare, tra cui il metabolismo del glucosio, alcuni canali ionici, l’esocitosi dell’insulina e il segnale insulinico, l’apoptosi, lo stress ossidativo, la rigenerazione e il ciclo cellulare (Tabella supplementare 1). I risultati ottenuti utilizzando i database della gene ontology (GO), e della KEGG e della gene set enrichment analysis (GSEA) sono riportati nelle tabelle 2 e 3 dei dati supplementari. I risultati della GO e della KEGG identificavano rispettivamente 22 processi biologici e 15 pathways, relativi ai geni down regolati nel diabete di tipo 2 (Dati supplementari, tabella 2). L'analisi GSEA, invece, che tiene conto anche dei geni non alterati, mostrava che dei 1,419 gene sets analizzati, rispettivamente 195 e 46 risultavano arricchiti positivamente e negativamente nelle isole di diabetico di tipo 2 (Dati supplementari, tabella 3). Tutte le suddette analisi avevano un punto in comune, e cioè, indicavano che il sistema ubiquitina-proteasoma risultava essere consistentemente alterato nelle isole diabetiche, e ciò ci induceva ad investigare più dettagliatamente questo aspetto.

Il sistema ubiquitina-proteasoma: risultati di microarray

Come riportato in precedenza, l'ubiquitinazione è un processo multistep catalizzato da 3 diverse serie di enzimi (E1 o ubiquitina-attivante, E2 o ubiquitino-coniugante, e E3 o ubiquitino-legante), che porta alla formazione di una catena di poliubiquitina sulla proteina che deve essere degradata. I risultati di microarray dei geni implicati in questo processo (Dati supplementari, tabella 4) non mostravano differenze nell'espressione del gene *UBE1* (conosciuto anche come *UBA1*), che codifica per E1. Tuttavia, parecchi geni degli enzimi delle famiglie E2 e E3 risultavano downregolati. Nelle nostre serie, solo 3 geni ubiquitinanti risultavano invece upregolati e appartenevano alla famiglia E3.

Nella normale fisiologia, il processo di ubiquitinazione può essere risolto dall'azione di enzimi deubiquitinanti, che sono proteasi specifiche per l'ubiquitina. Si stima che tali proteasi siano circa un centinaio nelle cellule di mammifero (Petroski, 2008; Clague et al., 2010). Noi abbiamo trovato che nelle isole diabetiche gli enzimi deubiquitinanti *UCHL1*, *USP 1*, *16*, *46*, e *COPS 2*, *3*, *4* e *5* erano marcatamente ridotti (Dati supplementari, tabella 4).

Una volta formatosi, il complesso poliubiquitina-proteina viene riconosciuto dal proteasoma, dove avviene la proteolisi. Il proteasoma è costituito da un core catalitico (20S) e da due parti regolatorie (19S), che vanno a formare il cosiddetto complesso proteasoma 26S. Il core catalitico ha una forma a barra ed è composto da 4 anelli impilati: i due più esterni, gli anelli α, formano uno stretto canale attraverso cui le proteine che devono essere degradate raggiungono i due anelli β più interni; questi contengono tre siti attivi identificati a seconda del loro comportamento enzimatico in caspasi-simile (β1), tripsino-simile (β2) e chimotripsino-simile (β5). La particella regolatoria 19S è localizzata alle due estremità del complesso 20S, consiste di circa 20 subunità ed è capace di riconoscere le proteine poliubiquitinate, rimuovere le catene di ubiquitina, sfogliare le proteine e trasferirle al core catalitico per la degradazione. Grazie all'analisi di microarray abbiamo osservato una marcata riduzione nell'espressione di vari geni codificanti le subunità del core [*PSMA1* (*α6*), *PSMA3 (α7*), *PSMB7* (*β2*), *PSMB5* (*β5*), e *PSMB1* (*β6*)] e della componente regolatoria [*PSMD12* (*Rpn5*), *PSMD11* (*Rpn6*), *PSMD6* (*Rpn7*), *PSMD7* (*Rpn8*), *PSMD14* (*Rpn11*), *PSMD8* (*Rpn12*), *PSMC2* (*Rpt1*), *PSMC6* (*Rpt4*), e *PSMC3* (*Rpt5*)] (Dati supplemetari, tabella 4).

Il sistema ubiquitina-proteasoma: RT-PCR quantitativa

In seguito, allo scopo di studiare l'espressione di pochi geni selezionati del sistema ubiquitina-proteasoma che risultavano alterati nell'analisi microarray sono stati effettuati alcuni esperimenti di RT-PCR quantitativa. I geni presi in esame erano: *SAE-1* della famiglia E1, *UBE2K* e*UBE3C* delle famiglie E2 e E3, *UCHL1* che codifica per un enzima deubiquitinante e *PSMB7*, una delle subunità catalitiche del proteasoma (quella con attività tripsino-simile). Tali risultati confermavano che c'erano differenze significative tra il gruppo di controllo e quello diabetico, con una riduzione di 3 dei 5 geni studiati, nel gruppo delle isole di diabetico tipo 2 (figura 1).

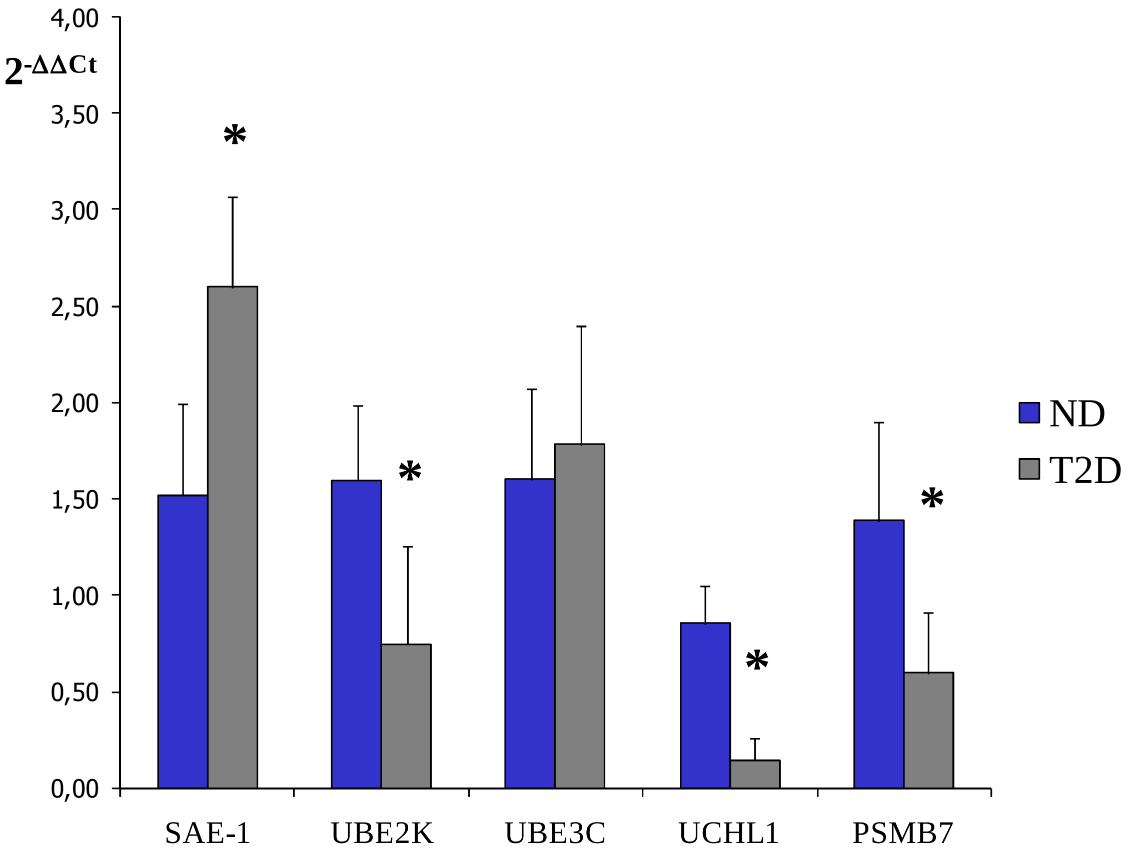

Figura 1. Espressione genica quantitativa di alcuni geni implicati nel sistema ubiquitina-proteasoma (n=5 per ogni gruppo) *p<0.02 vs ND.
SAE-1 = SUMO1 activating enzyme subunit 1; UBE2K = ubiquitin-conjugating enzyme E2K; UBE3C = ubiquitin protein ligase E3C; UCHL1 = ubiquitin carboxyl-terminal esterase L1; PSMB7 = proteasome (prosome, macropain) subunit, beta type, 7. I dati sono rappresentati come media±DS.

Immunoistochimica e attività del proteasoma

Per valutare se i cambiamenti di espressione genica del proteasoma erano accompagnati da alterazioni della rimozione di proteine e dell'attività del proteasoma, abbiamo determinato la presenza di proteine poliubiquitinate e l'attività del proteasoma nelle isole umane, rispettivamente mediante immunoistochimica e grazie ad un saggio luminometrico. Come mostrato in figura 2, sia le isole che le beta cellule risultavano positive per l'ubiquitinazione, tuttavia la quantificazione rilevava che le isole di diabetico tipo 2 avevano una maggior quantità di beta cellule positive per l'ubiquitina rispetto ai campioni non diabetici (figura 2).

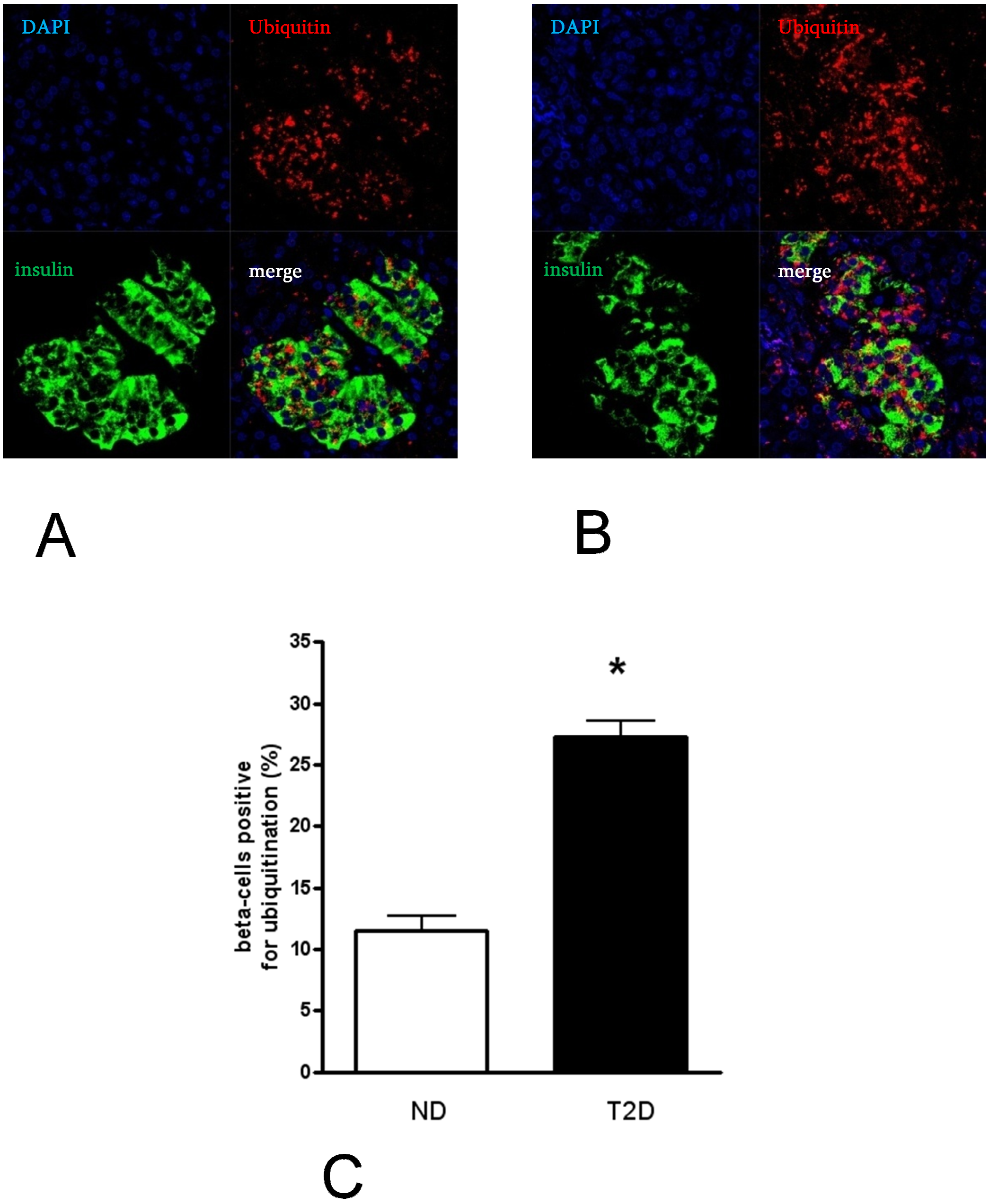

Figura 2. Localizzazione delle protein poliubiquitinate nelle beta cellule di campioni di isole isolate da donatori non diabetici (A) e donatori diabetici di tipo 2 (B). La quantificazione della percentuale di beta cellule positive per l’ubiquitina è fornita nel pannello C. * $p<0.01$

L’attività proteolitica tripsino-simile di isole non-diabetiche e diabetiche di tipo 2 è stata valutata grazie ad un metodo chemiluminescente e normalizzata per il contenuto di DNA. Come mostrato in figura 3, l’attività del proteasoma nelle isole di diabetico risultava essere inferiore al 50% di quella osservata nei soggetti non diabetici.

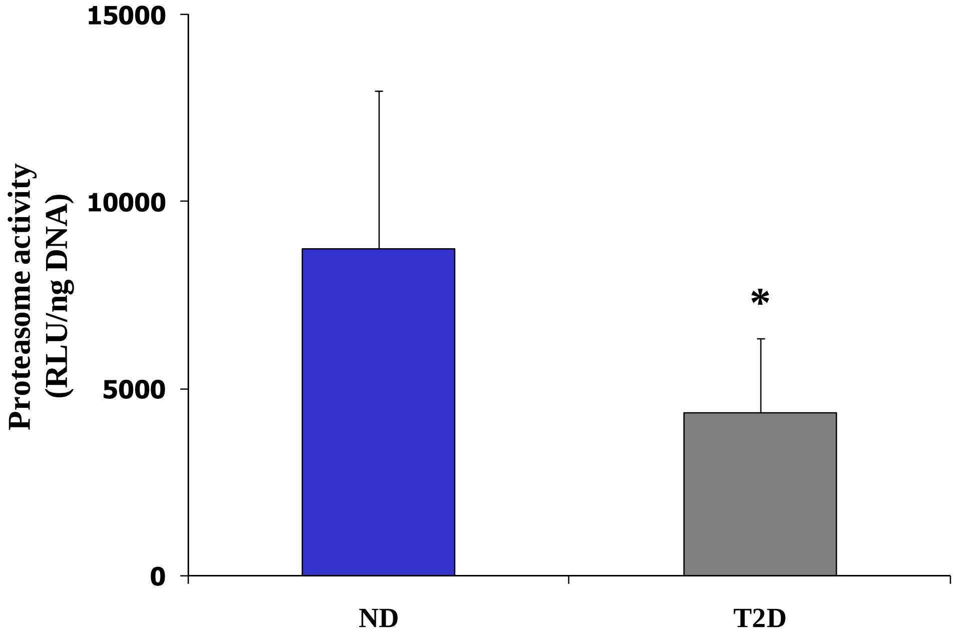

Figura 3. Attività del proteasoma (tripsino-simile) in isole umane non diabetiche (ND) e diabetiche di tipo 2 (T2D) *p<0.05 vs ND. I dati sono rappresentati come media±DS.

Ruolo dell'inibizione dell'attività del proteasoma e della lipotossicità nelle isole pancreatiche umane

Per meglio capire le relazioni tra l'attività del proteasoma e la secrezione insulinica, e per esplorare il ruolo di alterazioni metaboliche (lipotossicità), abbiamo incubato le isole per 24hr in presenza di un inibitore del proteasoma (10 µmol/l Z-Leu-Leu-Leu-al) o di 0.5 mmol/l palmitato. Come aspettato, l'inibitore Z-Leu-Leu-Leu-al era in grado di ridurre l'attività del proteasoma di quasi il 90%, ma sorprendentemente, anche il palmitato, seppur in grado minore, era in grado di indurre una diminuzione di circa il 20% rispetto all'attività proteolitica osservata nelle isole non trattate (figura 4a). Queste riduzioni dell'attività erano accompagnate ad una diversa ma significativa diminuzione del rilascio insulinico in seguito a stimolo acuto di glucosio (figura 4b). La riduzione della secrezione era apparentemente correlata al grado di inibizione del proteasoma (figura 4c).

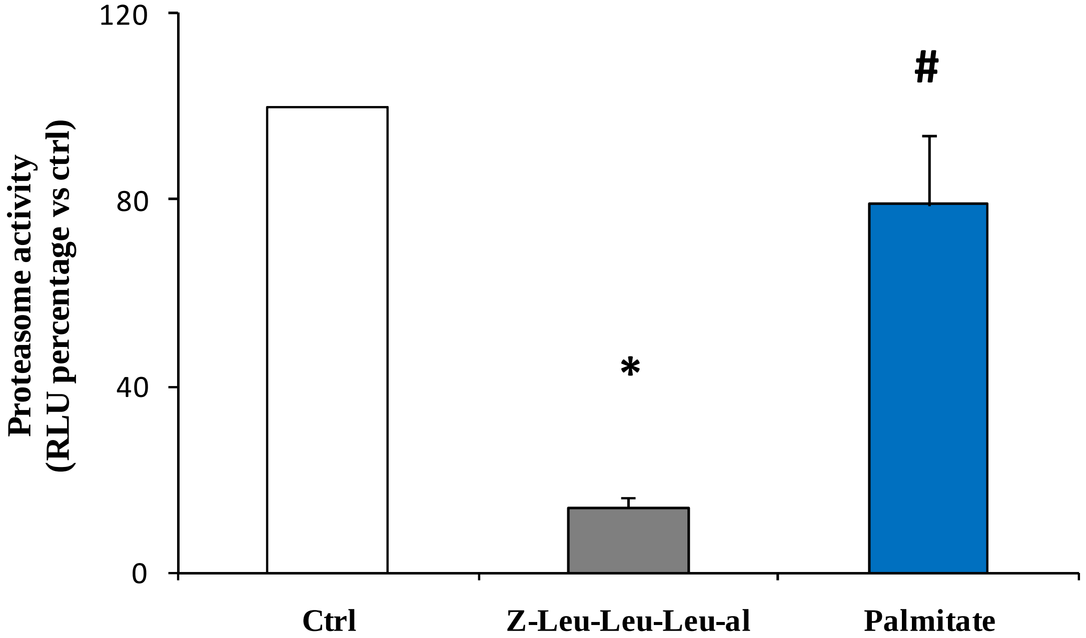

Figura 4a: Attività del proteasoma (tripsino-simile) in isole di controllo non trattate (Ctrl), isole esposte per 24hr a 10 µM Z-Leu-Leu-Leu-al (un inibitore dell'attività del proteasoma) e isole esposte per 24hr a 0.5 mM palmitato. (n=4 per ogni gruppo).
Dal test ANOVA risultava che i 3 gruppi differivano in maniera significativa ($p<0.01$).
*$p<0.05$ vs Ctrl e palmitato, e #$p<0.05$ vs Ctrl e Z-Leu-Leu-Leu-al dopo correzione di Bonferroni.

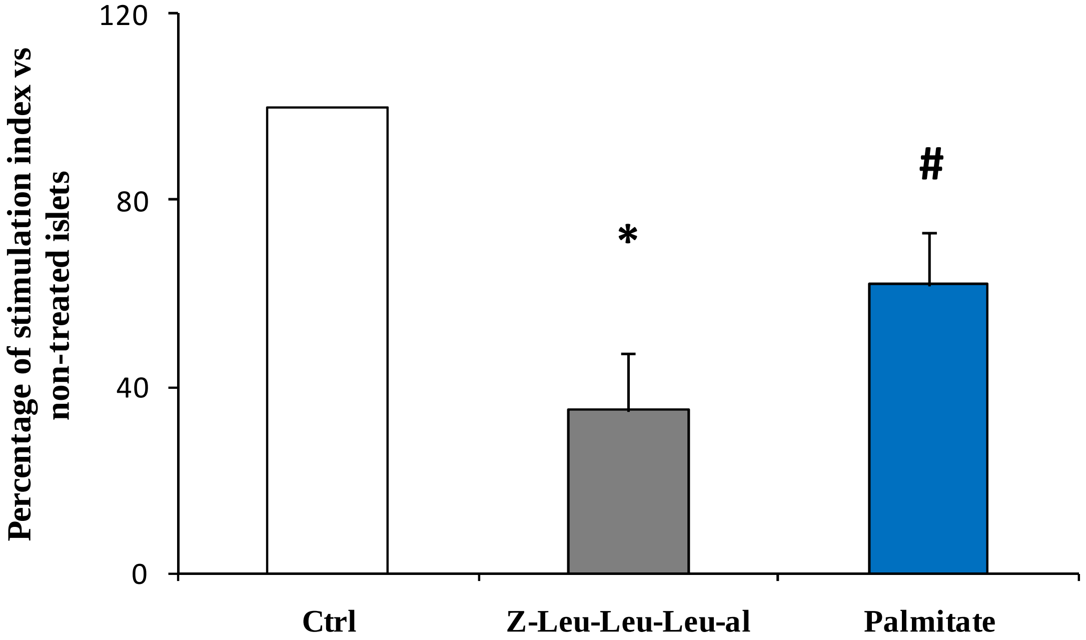

Figura 4b: Percentuale dell'indice di stimolazione vs le isole di controllo non trattate, dopo 24hr di esposizione a 10 µM dell'inibitore Z-Leu-Leu-Leu-al o a 0.5 mM palmitato (n=4 per ogni gruppo).
Dal test ANOVA risultava che i 3 gruppi differivano in maniera significativa ($p<0.01$).
*$p<0.05$ vs Ctrl e palmitato, e #$p<0.05$ vs Ctrl e Z-Leu-Leu-Leu-al dopo correzione di Bonferroni.

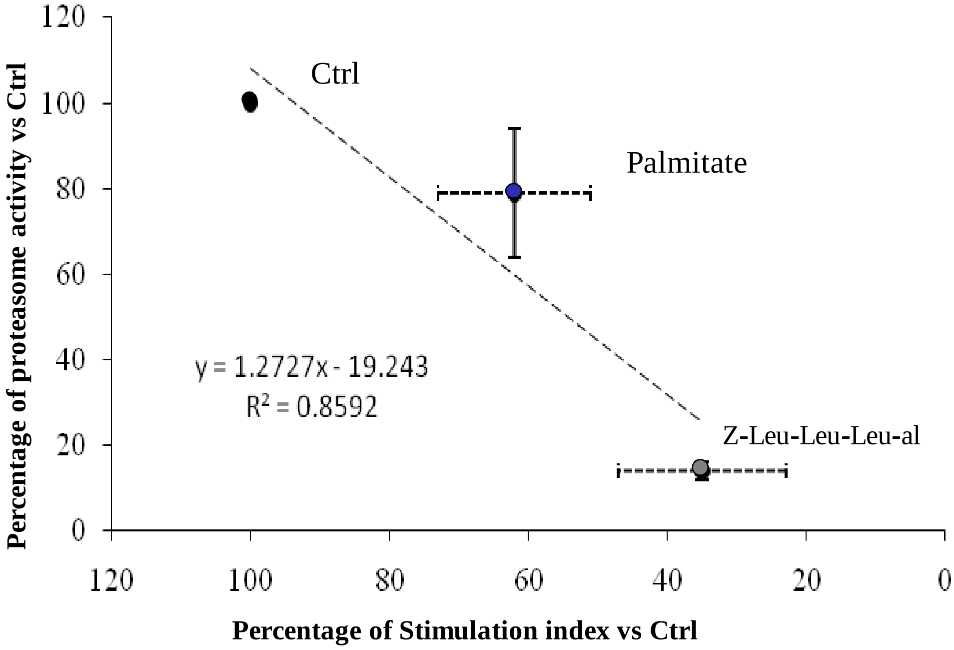

Figura 4c: Correlazione tra l’attività media tripsino-simile del proteasoma e la relativa percentuale dell’indice di stimolazione di isole esposte a Z-leu-Leu-Leu-al e palmitato verso le isole di controllo.

Ruolo di concentrazioni terapeutiche di metformina e GLP-1 sull’attività del proteasoma di isole pancreatiche umane.

In seguito per indagare gli effetti di due farmaci utilizzati nel trattamento terapeutico dei pazienti con diabete tipo 2 abbiamo incubato le isole diabetiche per 24hr in presenza di 2.4 μg/ml metformina cloridrato e 10 ng/ml di GLP-1. Sorprendentemente, l’esposizione a tali farmaci era in grado di aumentare in maniera significativa (+27% metformina e +41% GLP-1) l’attività proteolitica del proteasoma (figura 5a). Al contrario, nessuna alterazione significativa si osservava nell’attività del proteasoma di isole non diabetiche esposte alle medesime condizioni (figura 5b).

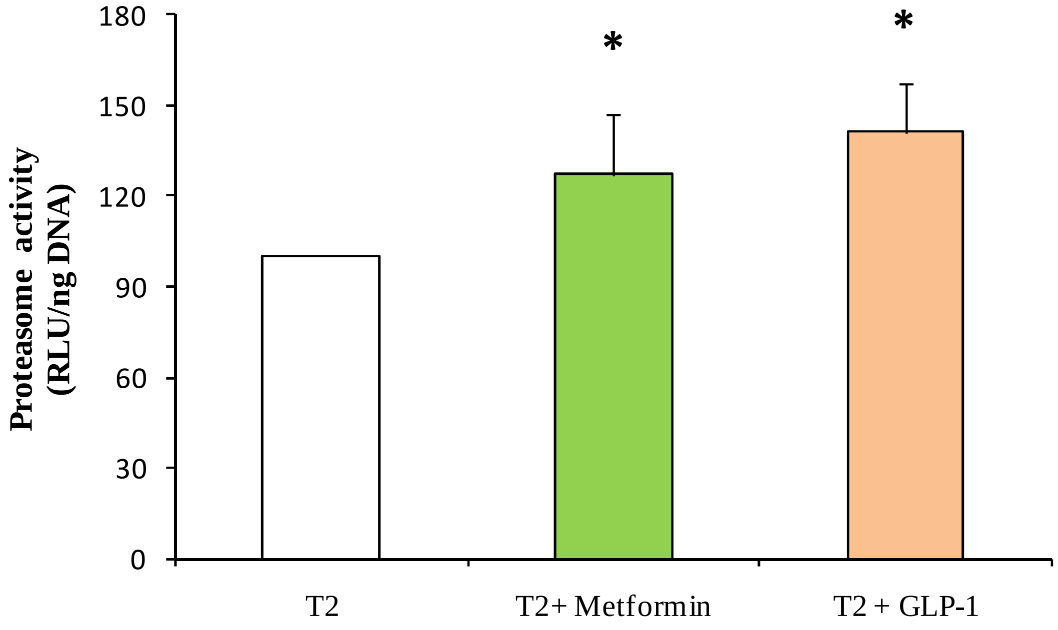

Figura 5a: Attività del proteasoma (tripsino-simile) in isole isolate da donatori affetti da diabete tipo 2 non trattate (T2), e isole diabetiche trattate per 24hr con 2.4µg/ml metformina o 10 nM GLP-1.
(n=6 per ogni gruppo).
Dal test ANOVA risultava che i 3 gruppi differivano in maniera significativa ($p<0.01$).
*$p<0.05$ vs T2 dopo correzione di Bonferroni.

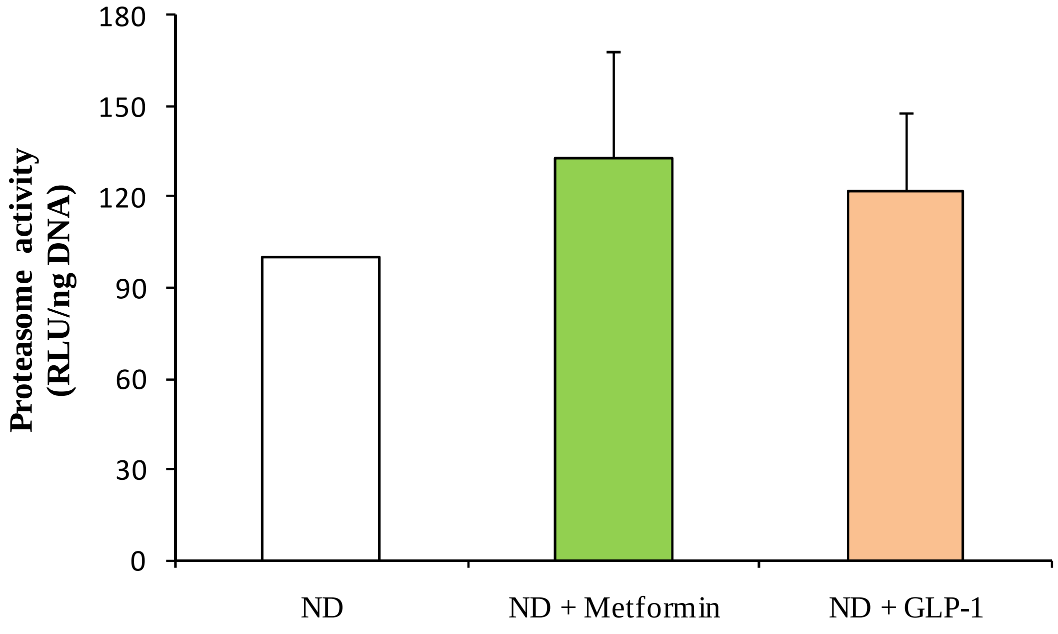

Figura 5b: Attività del proteasoma (tripsino-simile) in isole isolate di controllo non trattate (ND), e isole trattate per 24hr con 2.4µg/ml metformina o 10 nM GLP-1.
(n=6 per ogni gruppo).
Dal test ANOVA risultava che i 3 gruppi non differivano in maniera significativa.

Discussione

Il presente studio mostra come esistano numerose alterazioni nel trascrittoma di isole pancreatiche isolate dalle ghiandole di donatori affetti da diabete di tipo 2 rispetto a quelle di soggetti non diabetici. I geni alterati sono implicati in molte strutture e funzioni proprie delle cellule che costituiscono l'isola pancreatica, e la loro alterazione plausibilmente contribuisce ai difetti di sopravvivenza e di secrezione insulinica che sono stati evidenziati da numerosi studi sia in-vivo che ex-vivo negli individui affetti da diabetici tipo 2 (Del Guerra et al., 2005; Ferrannini et al., 2005; Marchetti et al., 2008; Marchetti et al., 2009). Simili conclusioni erano state definite da alcuni autori che negli anni passati hanno trattato di questo aspetto (Gunton et al., 2005; Ostenson et al., 2006; MacDonald et al., 2009). Tuttavia, i risultati osservati differiscono tra i vari gruppi. In questo studio, circa il 5% dei geni valutati nell'analisi microarray delle isole diabetiche risultavano alterati mentre la stessa proporzione nei dati riportati da Gunton e colleghi (Gunton et al., 2005) era inferiore all'1%. Altri autori, invece, sempre valutando le variazioni del trascrittoma delle isole diabetiche, hanno evidenziato una riduzione dell'espressione di vari geni implicati nell'esocitosi dei granuli di insulina e della funzione mitocondriale (Ostenson et al., 2006; MacDonald et al., 2009). Le suddette discrepanze possono essere dovute a variazioni biologiche tra i gruppi studiati, differenze dei protocolli sperimentali e variazioni del metodo di analisi; ciononostante, per valutare se alcune alterazioni siano consistentemente osservate nei vari studi, abbiamo comparato i risultati di questo studio con quelli di Gunton et al, 2005. In aggiunta, abbiamo tenuto conto anche delle osservazioni pubblicate da Marselli et al, che ha valutato il trascrittoma delle beta cellule di donatori diabetici e non, acquisite mediante tecnica di cattura laser (Marselli et al., 2008). Così facendo, abbiamo evidenziato alcuni geni che risultavano alterati nei soggetti diabetici in tutti e 3 i gruppi di analisi (tabella 3). Questi riguardavano geni del ciclo cellulare, della funzione del reticolo endoplasmatico, della regolazione dell'omeostasi del Ca^{++}, della trascrizione genica, della distribuzione dei metalli ossido riducenti e dello splicing dell'mRNA (tabella 3). Questi geni e i processi in cui sono coinvolti possono quindi essere considerati come potenziali target per un possibile intervento terapeutico.

Symbol	**Description**	**Gene Id**	**Involved in:**
PSMG1	Proteasome (prosome, macropain) assembly chaperone 1	8624	20S proteasome assembly
CDK10	cyclin-dependent kinase 10	8558	Cell cycle
ALAS1	aminolevulinate, delta-, synthase 1	211	Redox metal distribution
CANX	calnexin	821	Endoplasmic reticulum function
PRKRA	protein kinase, interferon-inducible double stranded RNA dependent activator	8575	Endoplasmic reticulum function
ASPH	aspartate beta-hydroxylase	444	Ca^{++} regulation
SFRS18	splicing factor, arginine/serine-rich 18	25957	mRNA splicing
GTF3C2	general transcription factor IIIC, polypeptide 2, beta 110kDa	2976	Gene transcription
TASP1	taspase, threonine aspartase, 1	55617	Cell cycle

Tabella 3: Geni differenzialmente espresso dopo analisi di microarray di isole umane isolate (presente studio e Gunton et al., 2005) e beta cellule ottenute mediante LCM (Marselli et al., 2008). I dati di Gunton et al., sono stati recuperate e analizzati come descritto per i dati di microarray di questo studio. I dati di Marselli et al. sono stati utilizzati come presentati nello studio originale (Marselli et al., 2008).

D’altro canto, se tali differenze del trascrittoma debbano essere considerate causa o conseguenza della condizione diabetica è ancora materia di dibattito. L’espressione di geni che conferiscono suscettibilità al diabete tipo 2 possono essere influenzati dal fenotipo, come dimostrato per il *TCF7L2* (Lyssenko et al., 2007), tuttavia, dati preliminari del nostro gruppo mostrano che le isole di diabetici e di non diabetici con un simile numero di polimorfismi nei geni associati al diabete, mostrano ancora numerose differenze nell’espressione genica (Del Guerra et al., 2011). D’altra parte, una prolungata esposizione delle isole umane ad concentrazioni elevate di glucosio e/o acidi grassi porta a numerose modifiche dell’espressione genica (Poitout et al., 2002; Weir et al., 2009). In uno studio pubblicato di recente, è stato mostrato che le beta cellule di isole trapiantate nei topi e quindi esposte a livelli di glicemia moderatamente elevati sviluppano alterazioni geniche (Kennedy et al., 2010). Ovviamente, allo scopo di sviluppare strategie adatte alle varie fasi della storia naturale del diabete, risulta cruciale chiarire le relazioni tra i difetti primari e secondari delle beta cellule nel diabete tipo 2.

Le varie analisi effettuate in questo studio mostrano che i geni dell’UPS, uno dei principali sistemi per la degradazione intracelluare delle proteine, erano diversamente espressi nelle isole diabetiche rispetto alle non diabetiche; queste alterazioni sono state confermate anche dalla RT-PCR quantitativa di alcuni geni selezionati. In aggiunta, è stato confermato anche un significativo aumento di proteine ubiquitinate associate ad una significativa riduzione dell’attività del proteasoma delle isole diabetiche. In vari modelli sperimentali di diabete sono stati osservati sia riduzione dell’attività del proteasoma che la capacità di degradare le proteine ossidate danneggiate (Kitiphongspattana et al., 2005; Kawaguchi et al., 2006). L’esposizione di isole di ratto ad alte concentrazioni di glucosio per 24hr induceva una riduzione dell’espressione di numerosi geni del sistema UPS, inclusa la proteina de-ubiquitinante *UCHL1*; questo dato è stato confermato in un modello di ratti pancreatotomizzati al 90% (Lòpez-Avalos et al., 2006). In aggiunta, in isole in cui è stato alterato il processo autofagico, si sono osservati aggregati di proteine ubiquitinate accumulati nelle beta cellule di modelli di roditore (Jung et al., 2008). Più recentemente, sono stati dimostrati un aumento delle proteine ubiquitinate e una riduzione dei livelli di *UCHL1* nelle beta cellule di individui diabetici tipo 2 (Costes et al., 2011). Per la prima volta, il nostro studio fornisce ulteriore evidenza del ruolo del proteasoma, mostrando riduzione dell’attività proteolitica in isole preparate da individui diabetici per tipo 2; tale aspetto può per sé influenzare la secrezione insulinica. Infatti, quando abbiamo inibito l’attività del proteasoma con l’esposizione per 24hr all’inibitore dell’attività, si osservava una significativa riduzione della secrezione insulinica indotta da glucosio delle isole umane (Figura 4b). Risultati simili sono stati riportati inibendo l’attività del proteasoma in isole di topo (Kitiphongspattana et al., 2005) e cellule MIN6 (Kawaguchi et al., 2006); tuttavia, lo stesso effetto non è stato osservato con isole di ratto (Lòpez-Avalos et al., 2006).

Il meccanismo attraverso cui l'UPS controlla la secrezione insulinica è probabilmente complesso ed implica diversi processi. Alcuni autori hanno mostrato che l'espressione di alcune delle molecole della superficie cellulare implicate nella secrezione insulinica come il canale del potassio sensibile all'ATP (K_{ATP}) (Yan et al., 2005) e l'attività del canale del calcio voltaggio-dipendente (Kawaguchi et al., 2006) così come anche la biosintesi dell'insulina (Kitiphongspattana et al., 2005), vengono regolati dal sistema ubiquitina-proteasoma. In aggiunta, la riduzione dell'attività del proteasoma può amplificare gli effetti dello stress del reticolo endoplasmatico, attraverso la mancata rimozione delle proteine malripiegate (Hoseki et al., 2010).

Alcuni degli indizi descritti in precedenza, erano parzialmente riprodotti in questo studio dalla pre-esposizione delle isole a 0.5 mmol/l di palmitato, un acido grasso saturo che è noto essere capace di indurre danneggiamento delle beta cellule (Cnop et al., 2010; Igoillo-Esteve et al., 2010). I meccanismi alla base della tossicità beta cellulare indotta da palmitato, inclusa l'induzione dello stress del reticolo endoplasmatico (Cnop et al., 2010) sono vari. Ora noi mostriamo che questo acido grasso può causare anche riduzione dell'attività del proteasoma.Recentemente, è stato dimostrato su miotubuli umani che il palmitato può indurre l'espressione delle citochine e la loro secrezione attraverso un meccanismo proteasoma-dipendente in grado di portare ad una rapida e cronica attivazione del fattore nucleare kappaB, che non si osserva con alte concentrazioni di glucosio o acidi grassi insaturi (Weigert et al., 2004). Mentre maggiori studi sono necessari in tal proposito, è interessante notare che il fenomeno della lipotossicità beta cellulare, che probabilmente gioca un ruolo importante nella disfunzione beta cellulare nel diabete di tipo 2, può anche essere mediato, almeno in parte, dal sistema UPS.

Alcune molecole comunemente utilizzate nel trattamento della disfunzione beta-cellulare nel diabete di tipo 2, GLP1 e metformina, che sono in grado di ripristinare un corretto rilascio di insulina in risposta a stimolo con glucosio, al contempo sono state viste essere in grado di aumentare l'attività del proteasoma nelle isole isolate da donatori diabetici dove invece tale attività risultava essere ridotta rispetto alle isole non diabetiche; tuttavia, tale aumento non sembrava verificarsi nelle isole non diabetiche, facendo quindi ipotizzare che i due farmaci vadano a correggere una disfunzione piuttosto che agire per sé. Il meccanismo d’azione delle suddette molecole non è ancora ben definito quindi attualmente non è possibile capire se esista una via di attivazione comune o meno.

In conclusione, il presente studio contribuisce ad identificare aspetti del trascrittoma delle isole umane diabetiche di tipo 2 che possono essere cruciali per l’insorgenza e la progressione del diabete. In aggiunta, viene sottolineata l’importanza del sistema UPS per la funzione della beta cellula, e vengono dimostrati i suoi difetti nelle isole diabetiche. Ad oggi sono allo sviluppo parecchie strategie terapeutiche per modulare l’attività dell’UPS in molte malattie sono allo sviluppo (Huang et al., 2009; Bedford et al., 2011). Se tale concetto possa essere applicato anche al diabete di tipo 2 richiederà ulteriori studi finalizzati allo scopo.

Materiali e Metodi

Isolamento delle isole e studi di secrezione insulinica

Le isole pancreatiche umane sono state isolate, con l’approvazione del comitato etico locale, da un totale di 15 donatori affetti da diabetici di tipo 2 e 25 donatori non diabetici, tramite un protocollo di digestione enzimatica con collage nasi e purificazione su gradiente di densità. Una volta isolate sono state tenute in coltura in terreno M199 supplementato con 10% siero bovino e antibiotici in un incubatore a CO_2 fino al giorno dell’esperimento (Del Guerra et al., 2005; Marchetti et al., 2007). Tutti i reagenti sono stati forniti dalla Sigma-Aldrich s.r.l. La tabella 2 riporta le principali caratteristiche cliniche dei donatori e alcuni aspetti dei preparati di isole.

La secrezione insulinica in risposta ad un bolo acuto di glucosio è stata studiata come descritto in precedenza (Del Guerra et al., 2005; Marchetti et al., 2007). In breve, gruppi di isole pescate a mano sono state tenute a 37°C per 45 min in soluzione di Krebs–Ringer bicarbonate (KRB), 0.5%

(peso/vol) di albumina, pH 7.4, contenente 3.3 mmol/l di glucosio (fase di lavaggio). Il mezzo, poi, è stato rimpiazzato con KRB contenente 3.3 mmol/l di glucosio allo scopo di valutare la secrezione insulinica basale durante 45 min; al termine di tale periodo le isole venivano esposte per ulteriori 45 min a 16.7 mmol/l di glucosio, 100 µmol/l di glibenclamide o 20 mmol/l di arginina. L'insulina è stata poi quantificata grazie ad un dosaggio radioimmunometrico (Pantec Forniture Biomediche, Torino, Italia).

	Età (anni)	**Genere**	**IMC (Kg/m^2)**	**Causa del decesso**	**Ischemia fredda (hrs)**	**Purezza del preparato (%)**
ND	65±16	10M/15F	25.7±3.1	18CVD/6Trauma	15±6	73±16
T2D	72±7	10M/5F	27.2±2.5	10CVD/5Trauma5	16±5	60±23
P value	NS	NS	NS	NS	NS	NS

Tabella 2: Principali caratteristiche cliniche dei donatori e aspetti peculiari delle preparazioni di isole.
ND: non-diabetic; T2D: type 2 diabetic

Studi di espressione genica (analisi di microarray e RT-PCR quantitativa)

L'RNA totale è stato estratto utilizzando l'RNeasy mini Kit (Qiagen, Milano, Italia) in accordo alle raccomandazioni del fornitore e quantificato valutando l'assorbanza a A260/A280 nm (ratio >1.9) in uno spettrofotometro Perkin-Elmer. L'integrità dell'RNA è stata valutata misurandola in un Agilent 2100 Bioanalyzer (Agilent Technologies, Palo Alto, CA).

Per gli studi di microarray 100 ng di RNA totale è stato preparato e ibridizzato su chips HG U133A di Affymetrix, contenenti 22,283 trascritti e varianti, in accordo al protocollo riportato nell'Affymetrix GeneChip® Expression Analysis Manual (Affymetrix, Santa Clara, CA). I lavaggi e lo staining sono stati effettuati in una Fluidic Station 400 (Affymetrix) usando il protocollo EukGEWS2v4. I chips sono stati poi scannerizzati in un Affymetrix GeneChip® Scanner 3000. La qualità degli arrays è stata verificata con il software Microarray Analysis Suite 5.0 (Affymetrix) e con i pacchetti *affy* e *affyPLM* disponibili su R/Bioconductor (www.bioconductor.org; R version

2.8.0; Bioconductor version 2.3) (Irizarry et al., 2003; Gautier et al., 2004; Bolstad et al., 2005). Una volta normalizzati gli array tramite *robust multiarray analysis* (RMA), l'analisi di espressione genica è stata valutata usando il pacchetto *limma* di R/Bioconductor. I dati degli array sono stati depositati in un database seguendo le indicazioni MIAME (GEO, numero di accesso: GSE25724). Al termine dell'analisi, sono stati scartati probe sets non specifici (probe sets che avevano l'estensione _x_at), a meno che non fossero stati gli unici in grado di identificare un determinato gene. Sono stati considerati differentemente espressi quei geni che mostravano sia un valore di p inferior allo 0.01 e un fold change (rapporto tra espressione nei T2D ed espressione nei ND) superiore a 2.0 o inferior a 0.5. Utilizzando il software *GeneCoDis* (disponibile all'indirizzo http://genecodis.dacya.ucm.es/) e il software Gene Set Enrichment Analysis (GSEA) (scaricabile dal sito www.broadinstitute.org/gsea/) (Subramanian et al., 2005; Carmona-Saez et al., 2007), sono stati identificati i processi metabolici influenzati dal diabete di tipo 2. Riguardo l'analisi con Genecodis, è stata applicata la correzione FDR e un valore di p ipergeometrico corretto inferior allo 0.01 è stato considerato per la significatività; riguardo la GSEA, sono stati analizzati un totale di 1419 gene sets (con una dimesione compresa tra 15 e 500 geni) appartenenti alla collezione C2 dei gene sets del Molecular Signature Database (MSigDB). Questi gene sets sono stati recuperati da varie fonti come pathway online, database, pubblicazioni di PubMed e conoscenze di esperti. Nell'analisi, sono state effettuate 1000 permutazioni per ottenere il valore di p nominale, mentre un valore FDR inferiore allo 0.25 è stata considerate come soglia per la significatività dell'arricchimento. Queste analisi sono state precedentemente usate dal nostro gruppo in un altro set di esperimenti (Bugliani et al., 2009).

Per gli esperimenti di RT-PCR quantitativa, 1 μg di RNA totale è stato retrotrascritto con l'iScript cDNA Synthesis Kit (Bio-Rad Laboratories, Hercules, CA). Gli oligonucleotidi per i geni di interesse sono stati scelti dai prodotti per l'espressione genica della serie assay-on-demand (Applied Biosystems, Foster City, CA). I livelli di mRNA dei geni bersaglio sono stati quantificati e normalizzati per la beta actina come descritto in precedenza con un bioanalizzatore Applied Biosystem 7700 (Applied Biosystems) (Marchetti et al., 2007; Cauchi et al., 2010).

Valutazione immunoistochimica delle proteine poliubiquitinate

Per l'analisi immunoistochimica con doppia immunofluorescenza, sezioni deparaffinizzate sono state incubate con anticorpo primario anti-insulina (Dako, Carpinteria, CA), poi con anticorpo secondario FITC-coniugato (Zymed, San Francisco, CA) per evidenziare le beta cellule pancreatiche. Le sezioni sono state poi ulteriormente incubate con anticorpo anti-ubiquitina (Dako), e quindi con anticorpo Alexa Fluor 568-coniugato (Molecular probes, Eugene, OR) per evidenziare la presenza delle molecole di ubiquitina. I nuclei sono stati evidenziati usando il DAPI (Vector Laboratories, Burlingame, CA). Le immagini sono state recuperate da un microscopio confocale (Zeiss LSM 700, Carl Zeiss, Thornwood, NY) e analizzate usando il software Zen (Carl Zeiss) allo scopo di contare il numero delle cellule insulino-positive colocalizzanti con l'ubiquitina.

Misurazione dell'attività del proteasoma

L'attività enzimatica proteolitica del proteasoma è stata misurata come attività tripsino-simile con il kit Proteasome-Glo™ Trypsin-Like Cell-Based Assay (Promega, Madison, Wisconsin, USA) (Groll eta al., 2008). In questo saggio, un particolare substrato viene fatto entrare all'interno delle cellule dove viene degradato dal proteasoma, liberando in tal modo amino-luciferina che viene rilevata da un luminometro come unità di luce relative (RLU). In questi esperimenti, 75 µl di una soluzione di lavoro costituita da un reagente per il rilevamento di amino-luciferina, la molecola substrato per il proteasoma e due inibitori di proteasi specifiche del siero e altre non specifiche, sono stati aggiunti, in triplicato, ad una eguale quantità di mezzo di coltura contenente 15 isole. Dopo 2 minuti di agitazione, la miscela è stata tenuta 15 min a temperatura ambiente e prima di rilevare la luminosità con un apposito luminometro [Lumino (Stratec Electronic GMBH, Birkenfeld, Germany)]. I dati sono stati normalizzati con la quantità di DNA. Il DNA è stato dapprima estratto con il PicoPure™

DNA Extraction Kit seguendo le indicazioni del produttore e in seguito quantificato con il Quant-iT^{TM} dsDNA BR Assay kit in un fluorometro Qubit^{TM} (Invitrogen^{TM}, Paisley PA4 9RF, UK).

Ruolo dell'inibizione del proteasoma, effetto della lipotossicità ed effetto di farmaci per il trattamento del diabete.

L'attività del proteasoma e la secrezione insulinica stimolata da glucosio sono state valutate anche in isole esposte per 24hr a 10 μM Z-Leu-Leu-Leu-al (conosciuto anche come MG132), un inibitore dell'attività del proteasoma (Lee et al., 1998) (Sigma-Aldrich, St. Louis, MO); questa molecola è stata sciolta in DMSO per ottenere una concentrazione finale nel mezzo di 0.1%. In aggiunta, sono stati valutati anche gli effetti di una esposizione cronica (24hr) a 0.5 mol/l di palmitato. Il palmitato (Sigma-Aldrich) è stato sciolto in etanolo 90%. Per questo tipo di studio, le isole sono state incubate in mezzo M199 serum-free contenente esclusivamente un 2% di albumina umana (Kedrion, Lucca, Italy) per una concentrazione finale di etanolo 90% nel mezzo dell'1% (Igoillo-Esteve et al., 2010). Infine, allo scopo di valutare se molecole utilizzate nel trattamento del diabete di tipo 2 e in grado di ripristinare un corretto rilascio insulinico in risposta a stimolo con glucosio fossero in grado di modulare anche l'attività del proteasoma, le isole sono state trattate per 24hr con 2.4 μg/ml metformina o 10 nM GLP.

Analisi statistica

L'analisi dei dati di microarray sono state discusse in precedenza. Tutti gli altri dati sono stati rappresentati come media ± deviazione standard. Il test t di Student è stato usato per valutare la differenza tra due gruppi. Mentre quando sono stati presi in esame più di due gruppi, è stato utilizzato il test ANOVA seguito dalla correzione di Bonferroni.

Bibliografia

Ahrén B. (2011). GLP-1 for type 2 diabetes. Exp Cell Res. 15:1239-45.

American Diabetes Association. (2011). Diagnosis and classification of diabetes mellitus. Diabetes Care. 34 Suppl 1, S62-9.

Bedford L, Lowe J, Dick LR, Mayer RJ, Brownell JE. (2011). Ubiquitin-like protein conjugation and the ubiquitin-proteasome system as drug targets. Nat Rev Drug Discov. 10, 29-46.

Bedford L, Paine S, Sheppard PW, Mayer RJ, Roelofs J. (2010). Assembly, structure, and function of the 26S proteasome. Trends Cell Biol. 20, 391-401.

Bolstad BM, Collin F, Brettschneider J, Simpson K, Cope L, Irizarry RA, Speed TP. (2005). Quality Assessment of Affymetrix GeneChip Data. In Bioinformatics and Computational Biology Solutions Using R and Bioconductor, Gentleman R, Carey V, Huber W, Irizarry R, Dudoit S, eds.. (New York, USA: Springer) pp 33-47.

Bugliani M, Masini M, Liechti R, Marselli L, Xenarios I, Boggi U, Filipponi F, Masiello P, Marchetti P. (2009). The direct effects of tacrolimus and cyclosporin A on isolated human islets: A functional, survival and gene expression study. Islets. 1, 106-110.

Butler AE, Janson J, Bonner-Weir S, Ritzel R, Rizza RA, Butler PC. (2003). Beta-cell deficit and increased beta-cell apoptosis in humans with type 2 diabetes. Diabetes. 52, 102-110.

Carmona-Saez P, Chagoyen M, Tirado F, Carazo JM, Pascual-Montano A. (2007) GENECODIS: a web-based tool for finding significant concurrent annotations in gene lists. Genome Biol. 8, R3.

Cauchi S, Del Guerra S, Choquet H, D'Aleo V, Groves CJ, Lupi R, McCarthy MI, Froguel P, Marchetti P. (2010). Meta-analysis and functional effects of the SLC30A8 rs13266634 polymorphism on isolated human pancreatic islets. Mol Genet Metab. 100, 77-82.

Clague MJ, Urbé S. (2010). Ubiquitin: same molecule, different degradation pathways. Cell. 143, 682-685.

Cnop M, Ladrière L, Igoillo-Esteve M, Moura RF, Cunha DA. (2010). Causes and cures for endoplasmic reticulum stress in lipotoxic β-cell dysfunction. Diabetes Obes Metab. Suppl 2, 76-82.

Costes S, Huang CJ, Gurlo T, Daval M, Matveyenko AV, Rizza RA, Butler AE, Butler PC. (2011). β-cell dysfunctional ERAD/ubiquitin/proteasome system in type 2 diabetes mediated by islet amyloid polypeptide-induced UCH-L1 deficiency. Diabetes. 60, 227-238.

Del Guerra S, Lupi R, Marselli L, Masini M, Bugliani M, Sbrana S, Torri S, Pollera M, Boggi U, Mosca F et al. (2005). Functional and molecular defects of pancreatic islets in human type 2 diabetes. Diabetes. 54, 727-735.

Del Guerra S, Groves C, D’Aleo V, Lupi R, McCarthy M, Marchetti P. (2011). Type 2 diabetes (T2D) susceptibility loci and beta cell defects in islets from non-diabetic (ND) and T2D subjects Diabetes. 60 Suppl 1, A387.

Deng S, Vatamaniuk M, Huang X, Doliba N, Lian MM, Frank A, Velidedeoglu E, Desai NM, Koeberlein B, Wolf B et al. (2004). Structural and functional abnormalities in the islets isolated from type 2 diabetic subjects. Diabetes. 53, 624-632.

Donath MY, Halban PA. (2004). Decreased beta-cell mass in diabetes: significance, mechanisms and therapeutic implications. Diabetologia. 47, 581-589.

Doria A, Patti ME, Kahn CR. (2008). The emerging genetic architecture of type 2 diabetes. Cell Metab. 8, 186-200.

Ferrannini E, Gastaldelli A, Miyazaki Y, Matsuda M, Mari A, DeFronzo RA. (2005). Beta-cell function in subjects spanning the range from normal glucose tolerance to overt diabetes: a new analysis. J Clin Endocrinol Metab. 90, 493-500.

Gautier L, Cope L, Bolstad BM, Irizarry RA. (2004). Affy—analysis of Affymetrix GeneChip data at the probe level. Bioinformatics. 20, 307-315

Groll, M., Schellenberg, B., Bachmann, A.S., Archer, C.R., Huber, R., Powell, T.K., Lindow, S., Kaiser, M. and Duler, R. (2008). A plant pathogen virulence factor inhibits the eukaryotic proteasome by a novel mechanism. Nature. 452, 755-758

Gunton JE, Kulkarni RN, Yim S, Okada T, Hawthorne WJ, Tseng YH, Roberson RS, Ricordi C, O'Connell PJ, Gonzalez FJ et al. (2005). Loss of ARNT/HIF1beta mediates altered gene expression and pancreatic-islet dysfunction in human type 2 diabetes. Cell. 122, 337-349.

Hoseki J, Ushioda R, Nagata K. (2010). Mechanism and components of endoplasmic reticulum-associated degradation. J Biochem. 147, 19-25.

Huang L, Chen CH. (2009). Proteasome regulators: activators and inhibitors. Curr Med Chem.;16, 931-939.

Igoillo-Esteve M, Marselli L, Cunha DA, Ladrière L, Ortis F, Grieco FA, Dotta F, Weir GC, Marchetti P, Eizirik DL et al. (2010). Palmitate induces a pro-inflammatoryresponse in human pancreatic islets that mimics CCL2 expression by beta cells in type 2 diabetes. Diabetologia. 53, 1395-1405.

Irizarry RA, Hobbs B, Collin F, Beazer-Barclay YD, Antonellis KJ, Scherf U, Speed TP. (2003) Exploration, normalization and summaries of high density oligonucleotide array probe level data. Biostatistics. 4, 249-264.

Jung HS, Chung KW, Won Kim J, Kim J, Komatsu M, Tanaka K, Nguyen YH, Kang TM, Yoon KH, Kim JW et al. (2008). Loss of autophagy diminishes pancreatic beta cell mass and function with resultant hyperglycemia. Cell Metab. 8, 318-324.

Jung T, Catalgol B, Grune T. (2009). The proteasomal system. Mol Aspects Med. 30, 191-296.

Kawaguchi M, Minami K, Nagashima K, Seino S. (2006). Essential role of ubiquitin-proteasome system in normal regulation of insulin secretion. J Biol Chem. 281, 13015-13020.

Kennedy J, Katsuta H, Jung MH, Marselli L, Goldfine AB, Balis UJ, Sgroi D, Bonner-Weir S, Weir GC. (2010). Protective unfolded protein response in human pancreatic beta cells transplanted into mice. PLoS One. 5, e11211.

Kitiphongspattana K, Mathews CE, Leiter EH, Gaskins HR. (2005). Proteasome inhibition alters glucose-stimulated (pro)insulin secretion and turnover in pancreatic {beta}-cells. J Biol Chem. 280, 15727-15734.

Lee, D.H., and Goldberg, A.L. (1998). Proteasome inhibitors: valuable new tools for cell biologists. Trends Cell Biol 8, 397-403,
López-Avalos MD, Duvivier-Kali VF, Xu G, Bonner-Weir S, Sharma A, Weir GC. (2006). Evidence for a role of the ubiquitin-proteasome pathway in pancreatic islets. Diabetes. 55, 1223-1231.

Lyssenko V, Lupi R, Marchetti P, Del Guerra S, Orho-Melander M, Almgren P, Sjögren M, Ling C, Eriksson KF, Lethagen AL et al. (2007). Mechanisms by which common variants in the TCF7L2 gene increase risk of type 2 diabetes. J Clin Invest. 117, 2155-2163.

MacDonald MJ, Longacre MJ, Langberg EC, Tibell A, Kendrick MA, Fukao T, Ostenson CG. (2009). Decreased levels of metabolic enzymes in pancreatic islets of patients with type 2 diabetes. Diabetologia. 52, 1087-1091.

Marchetti P, Bugliani M, Lupi R, Marselli L, Masini M, Boggi U, Filipponi F, Weir GC, Eizirik DL, Cnop M. (2007). The endoplasmic reticulum in pancreatic beta cells of type 2 diabetes patients. Diabetologia. 50, 2486-2494.

Marchetti P, Dotta F, Lauro D, Purrello F. (2008). An overview of pancreatic beta-cell defects in human type 2 diabetes: implications for treatment. Regul Pept. 146, 4-11.

Marchetti P, Lupi R, Del Guerra S, Bugliani M, D'Aleo V, Occhipinti M, Boggi U, Marselli L, Masini M. (2009). Goals of treatment for type 2 diabetes: beta-cell preservation for glycemic control. Diabetes Care. 32 Suppl 2, S178-S183.

Marselli L, Thorne J, Ahn YB, Omer A, Sgroi DC, Libermann T, Otu HH, Sharma A, Bonner-Weir S, Weir GC. (2008). Gene expression of purified beta-cell tissue obtained from human pancreas with laser capture microdissection. J Clin Endocrinol Metab. 93, 1046-1053.

McCarthy MI. (2010). Genomics, type 2 diabetes, and obesity. N Engl J Med. 363, 2339-2350.

Mejer JJ. (2008). Beta cell mass in diabetes: a realistic therapeutic target? Diabetologia. 51, 703-713.

Ostenson CG, Gaisano H, Sheu L, Tibell A, Bartfai T. (2006). Impaired gene and protein expression of exocytotic soluble N-ethylmaleimide attachment protein receptor complex proteins in pancreatic islets of type 2 diabetic patients. Diabetes. 55, 435-440.

Petroski MD. (2008). The ubiquitin system, disease, and drug discovery. BMC Biochem. 9 Suppl 1, S7.

Poitout V, Robertson RP. Minireview: (2002). Secondary beta-cell failure in type 2 diabetes--a convergence of glucotoxicity and lipotoxicity. Endocrinology. 143, 339-342.

Schwanstecher C, Schwanstecher M. (2011) Targeting type 2 diabetes. Handb Exp Pharmacol. 203:1-33.

Staiger H, Machicao F, Fritsche A, Häring HU. (2009). Pathomechanisms of type 2 diabetes genes. Endocr Rev. 30, 557-585.

Stumvoll M, Goldstein BJ, van Haeften TW. (2008). Type 2 diabetes: pathogenesis and treatment. Lancet. 371, 2153-2156.

Subramanian A, Tamayo P, Mootha VK, Mukherjee S, Ebert BL, Gillette MA, et al. (2005) Gene set enrichment analysis: a knowledge-based approach for interpreting genome-wide expression profiles. Proc Natl Acad Sci USA. 102, 15545-15550.

Wajchenberg BL. (2007). Beta-cell failure in diabetes and preservation by clinical treatment. Endocr Rev. 28, 187-218.

Weigert C, Brodbeck K, Staiger H, Kausch C, Machicao F, Häring HU, Schleicher ED. (2004). Palmitate, but not unsaturated fatty acids, induces the expression of interleukin-6 in human myotubes through proteasome-dependent activation of nuclear factor-kappaB. J Biol Chem. 279, 23942-23952.

Weir GC, Marselli L, Marchetti P, Katsuta H, Jung MH, Bonner-Weir S. (2009). Towards better understanding of the contributions of overwork and glucotoxicity to the beta-cell inadequacy of type 2 diabetes. Diabetes Obes Metab. 11 Suppl 4, 82-90.

Wong E, Cuervo AM. (2010). Integration of clearance mechanisms: the proteasome and autophagy. Cold Spring Harb Perspect Biol. 2, a006734.

Xie Y. (2010). Structure, assembly and homeostatic regulation of the 26S proteasome. J Mol Cell Biol. 2, 308-317.

Yan FF, Lin CW, Cartier EA, Shyng SL. (2005). Role of ubiquitin-proteasome degradation pathway in biogenesis efficiency of {beta}-cell ATP-sensitive potassium channels. Am J Physiol Cell Physiol. 289, C1351-C1359.

Dati supplementari, tabella 1. Probe sets differenzialmente espressi (upregulati e downregolati) nelle isole isolate diabetiche di tipo 2 vs isole non diabetiche

External ID	**Symbol**	**Description**	**Gene Id**
Upregolati			
201416_at	SOX4	SRY (sex determining region Y)-box 4	6659
201418_s_at	SOX4	SRY (sex determining region Y)-box 4	6659
201641_at	BST2	bone marrow stromal cell antigen 2	684
201820_at	KRT5	keratin 5 (epidermolysis bullosa simplex, Dowling-Meara/Kobner/Weber-Cockayne types)	3852
202102_s_at	BRD4	bromodomain containing 4	23476
202219_at	SLC6A8	solute carrier family 6 (neurotransmitter transporter, creatine), member 8	6535
202935_s_at	SOX9	SRY (sex determining region Y)-box 9 (campomelic dysplasia, autosomal sex-reversal)	6662
203021_at	SLPI	secretory leukocyte peptidase inhibitor	6590
203240_at	FCGBP /// LOC100133944	Fc fragment of IgG binding protein /// similar to IgGFc-binding protein precursor (FcgammaBP) (Fcgamma-binding protein antigen)	8857
203255_at	FBXO11	F-box protein 11	80204
203468_at	CDK10	cyclin-dependent kinase 10	8558
203652_at	MAP3K11	mitogen-activated protein kinase kinase kinase 11	4296
203687_at	CX3CL1	chemokine (C-X3-C motif) ligand 1	6376
203892_at	WFDC2	WAP four-disulfide core domain 2	10406
204647_at	HOMER3	homer homolog 3 (Drosophila)	9454
205367_at	SH2B2	SH2B adaptor protein 2	10603
205434_s_at	AAK1	AP2 associated kinase 1	22848
206548_at	hCG_1776259	hypothetical protein FLJ23556	79938
207076_s_at	ASS1	argininosuccinate synthetase 1	445
207953_at	RP5-886K2.1	neuronal thread protein AD7c-NTP	27308
208306_x_at	HLA-DRB1	Major histocompatibility complex, class II, DR beta 3	3123
208436_s_at	IRF7	interferon regulatory factor 7	3665
209381_x_at	SF3A2	splicing factor 3a, subunit 2, 66kDa	8175
209546_s_at	APOL1	apolipoprotein L, 1	8542
209619_at	CD74	CD74 molecule, major histocompatibility complex, class II invariant chain	972
210069_at	CHKB /// CPT1B	choline kinase beta /// carnitine palmitoyltransferase 1B (muscle)	1120 /// 1375 /// 9411
210835_s_at	CTBP2	C-terminal binding protein 2	1488
210981_s_at	GRK6	G protein-coupled receptor kinase 6	2870
211465_x_at	FUT6	fucosyltransferase 6 (alpha (1,3) fucosyltransferase)	2528
212089_at	LMNA	lamin A/C	4000
212285_s_at	AGRN	agrin	375790
212492_s_at	JMJD2B	jumonji domain containing 2B	23030
213178_s_at	MAPK8IP3	mitogen-activated protein kinase 8 interacting protein 3	23162
213311_s_at	TCF25	transcription factor 25 (basic helix-loop-helix)	22980 /// 439921
213665_at	SOX4	SRY (sex determining region Y)-box 4	6659
213716_s_at	SECTM1	secreted and transmembrane 1	6398
214022_s_at	IFITM1	interferon induced transmembrane protein 1 (9-27)	8519
214235_at	CYP3A5	cytochrome P450, family 3, subfamily A, polypeptide 5	1577
214594_x_at	ATP8B1	ATPase, class I, type 8B, member 1	5205
214715_x_at	ZNF160	zinc finger protein 160	90338
215235_at	SPTAN1	spectrin, alpha, non-erythrocytic 1 (alpha-fodrin)	6709
215373_x_at	FLJ12151	hypothetical protein FLJ12151	80047
215600_x_at	FBXW12	F-box and WD repeat domain containing 12	285231
215978_x_at	LOC152719	hypothetical protein LOC152719	152719
216310_at	TAOK1	TAO kinase 1	57551
216867_s_at	PDGFA	platelet-derived growth factor alpha polypeptide	5154
217875_s_at	PMEPA1	prostate transmembrane protein, androgen induced 1	56937
218847_at	IGF2BP2	insulin-like growth factor 2 mRNA binding protein 2	10644
219186_at	ZBTB7A	zinc finger and BTB domain containing 7A	51341
219392_x_at	PRR11	proline rich 11	55771
220071_x_at	CEP27	centrosomal protein 27kDa	55142
220113_x_at	POLR1B	polymerase (RNA) I polypeptide B, 128kDa	84172
220411_x_at	PODNL1	podocan-like 1	79883
220720_x_at	FAM128B	family with sequence similarity 128, member B	80097
221829_s_at	TNPO1	transportin 1	3842
222024_s_at	AKAP13	A kinase (PRKA) anchor protein 13	11214
222104_x_at	GTF2H3	general transcription factor IIH, polypeptide 3, 34kDa	2967

823_at	CX3CL1	chemokine (C-X3-C motif) ligand 1	6376
91617_at	DGCR8	DiGeorge syndrome critical region gene 8	54487
Downregolati			
200004_at	EIF4G2	eukaryotic translation initiation factor 4 gamma, 2	1982
200030_s_at	SLC25A3	solute carrier family 25 (mitochondrial carrier; phosphate carrier), member 3	5250
200033_at	DDX5	DEAD (Asp-Glu-Ala-Asp) box polypeptide 5	1655
200036_s_at	RPL10A	ribosomal protein L10a	4736
200038_s_at	RPL17	ribosomal protein L17	6139
200042_at	C22orf28	chromosome 22 open reading frame 28	51493
200046_at	DAD1	defender against cell death 1	1603
200052_s_at	ILF2	interleukin enhancer binding factor 2, 45kDa	3608
200056_s_at	C1D	nuclear DNA-binding protein	10438
200059_s_at	RHOA	ras homolog gene family, member A	387
200062_s_at	RPL30	ribosomal protein L30	6156
200064_at	HSP90AB1	heat shock protein 90kDa alpha (cytosolic), class B member 1	3326
200067_x_at	SNX3	sorting nexin 3	8724
200074_s_at	RPL14 /// RPL14L	ribosomal protein L14 /// ribosomal protein L14-like	144581///649821///9045
200078_s_at	ATP6V0B	ATPase, H+ transporting, lysosomal 21kDa, V0 subunit b	533
200082_s_at	LOC644315 /// RPS7	ribosomal protein S7 /// similar to ribosomal protein S7	6201
200084_at	C11orf58	chromosome 11 open reading frame 58	10944
200087_s_at	TMED2	transmembrane emp24 domain trafficking protein 2	10959
200093_s_at	HINT1	histidine triad nucleotide binding protein 1	3094
200096_s_at	ATP6V0E1	ATPase, H+ transporting, lysosomal 9kDa, V0 subunit e1	8992
200097_s_at	HNRNPK	heterogeneous nuclear ribonucleoprotein K	3190
200099_s_at	LOC439992 /// RPS3A	ribosomal protein S3A /// similar to v-fos transformation effector protein	439992 /// 6189
200597_at	EIF3A	eukaryotic translation initiation factor 3, subunit A	8661
200599_s_at	HSP90B1	heat shock protein 90kDa beta (Grp94), member 1	7184
200603_at	PRKAR1A	protein kinase, cAMP-dependent, regulatory, type I, alpha (tissue specific extinguisher 1)	5573
200605_s_at	PRKAR1A	protein kinase, cAMP-dependent, regulatory, type I, alpha (tissue specific extinguisher 1)	5573
200608_s_at	RAD21	RAD21 homolog (S. pombe)	5885
200613_at	AP2M1	adaptor-related protein complex 2, mu 1 subunit	1173
200620_at	TMEM59	transmembrane protein 59	9528
200626_s_at	MATR3	matrin 3	9782
200627_at	PTGES3	prostaglandin E synthase 3 (cytosolic)	10728
200631_s_at	SET	SET nuclear oncogene	6418
200651_at	GNB2L1	guanine nucleotide binding protein (G protein), beta polypeptide 2-like 1	10399
200655_s_at	CALM1 /// CALM2 /// CALM3	calmodulin 1 (phosphorylase kinase, delta) /// calmodulin 2 (phosphorylase kinase, delta) /// calmodulin 3 (phosphorylase kinase, delta)	801
200656_s_at	P4HB	procollagen-proline, 2-oxoglutarate 4-dioxygenase (proline 4-hydroxylase), beta polypeptide	5034
200657_at	SLC25A5	solute carrier family 25 (mitochondrial carrier; adenine nucleotide translocator), member 5	292
200658_s_at	PHB	prohibitin	5245
200662_s_at	TOMM20	translocase of outer mitochondrial membrane 20 homolog (yeast)	9804
200670_at	XBP1	X-box binding protein 1	7494
200681_at	GLO1	glyoxalase I	2739
200693_at	YWHAQ	tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, theta polypeptide	10971
200698_at	KDELR2	KDEL (Lys-Asp-Glu-Leu) endoplasmic reticulum protein retention receptor 2	11014
200700_s_at	KDELR2	KDEL (Lys-Asp-Glu-Leu) endoplasmic reticulum protein retention receptor 2	11014
200705_s_at	EEF1B2	eukaryotic translation elongation factor 1 beta 2	1933
200712_s_at	MAPRE1	microtubule-associated protein, RP/EB family, member 1	22919
200713_s_at	MAPRE1	microtubule-associated protein, RP/EB family, member 1	22919
200723_s_at	CAPRIN1	cell cycle associated protein 1	4076
200726_at	PPP1CC	protein phosphatase 1, catalytic subunit, gamma isoform	5501
200735_x_at	NACA	nascent polypeptide-associated complex alpha subunit	4666
200745_s_at	GNB1	guanine nucleotide binding protein (G protein), beta polypeptide 1	2782
200751_s_at	HNRNPC	heterogeneous nuclear ribonucleoprotein C (C1/C2)	3183
200786_at	PSMB7	proteasome (prosome, macropain) subunit, beta type, 7	5695
200790_at	ODC1	ornithine decarboxylase 1	4953
200792_at	XRCC6	X-ray repair complementing defective repair in Chinese hamster cells 6 (Ku	2547

		autoantigen, 70kDa)	
200802_at	SARS	seryl-tRNA synthetase	6301
200806_s_at	HSPD1	heat shock 60kDa protein 1 (chaperonin)	3329
200811_at	CIRBP	cold inducible RNA binding protein	1153
200816_s_at	PAFAH1B1	platelet-activating factor acetylhydrolase, isoform Ib, alpha subunit 45kDa	5048
200820_at	PSMD8	proteasome (prosome, macropain) 26S subunit, non-ATPase, 8	5714
200828_s_at	ZNF207	zinc finger protein 207	7756
200833_s_at	hCG_1757335 /// RAP1B	RAP1B, member of RAS oncogene family /// hCG1757335	5908 /// 643752
200853_at	H2AFZ	H2A histone family, member Z	3015
200864_s_at	RAB11A	RAB11A, member RAS oncogene family	8766
200866_s_at	PSAP	prosaposin (variant Gaucher disease and variant metachromatic leukodystrophy)	5660 /// 57048
200870_at	STRAP	serine/threonine kinase receptor associated protein	11171
200876_s_at	PSMB1	proteasome (prosome, macropain) subunit, beta type, 1	5689
200877_at	CCT4	chaperonin containing TCP1, subunit 4 (delta)	10575
200883_at	UQCRC2	ubiquinol-cytochrome c reductase core protein II	7385
200892_s_at	SFRS10	splicing factor, arginine/serine-rich 10 (transformer 2 homolog, Drosophila)	6434
200901_s_at	M6PR	mannose-6-phosphate receptor (cation dependent)	4074
200902_at	SEPT15	15 kDa selenoprotein	9403
200903_s_at	AHCY	S-adenosylhomocysteine hydrolase	191
200918_s_at	SRPR	signal recognition particle receptor ('docking protein')	6734
200927_s_at	RAB14	RAB14, member RAS oncogene family	51552
200929_at	TMED10	transmembrane emp24-like trafficking protein 10 (yeast)	10972
200934_at	DEK	DEK oncogene (DNA binding)	7913
200950_at	ARPC1A	actin related protein 2/3 complex, subunit 1A, 41kDa	10552
200967_at	PPIB	peptidylprolyl isomerase B (cyclophilin B)	5479
200968_s_at	PPIB	peptidylprolyl isomerase B (cyclophilin B)	5479
200970_s_at	SERP1	stress-associated endoplasmic reticulum protein 1	27230
200973_s_at	TSPAN3	tetraspanin 3	10099
200975_at	PPT1	palmitoyl-protein thioesterase 1 (ceroid-lipofuscinosis, neuronal 1, infantile)	5538
200978_at	MDH1	malate dehydrogenase 1, NAD (soluble)	4190
200993_at	IPO7	importin 7	10527
201013_s_at	PAICS	phosphoribosylaminoimidazole carboxylase, phosphoribosylaminoimidazole succinocarboxamide synthetase	10606
201014_s_at	PAICS	phosphoribosylaminoimidazole carboxylase, phosphoribosylaminoimidazole succinocarboxamide synthetase	10606
201017_at	EIF1AX	eukaryotic translation initiation factor 1A, X-linked	1964
201018_at	EIF1AX	eukaryotic translation initiation factor 1A, X-linked	1964
201023_at	TAF7	TAF7 RNA polymerase II, TATA box binding protein (TBP)-associated factor, 55kDa	6879
201028_s_at	CD99	CD99 molecule	4267
201036_s_at	HADH	hydroxyacyl-Coenzyme A dehydrogenase	3033
201038_s_at	ANP32A	Acidic (leucine-rich) nuclear phosphoprotein 32 family, member A	8125
201051_at	ANP32A	acidic (leucine-rich) nuclear phosphoprotein 32 family, member A	8125
201054_at	HNRNPA0	heterogeneous nuclear ribonucleoprotein A0	10949
201066_at	CYC1	cytochrome c-1	1537
201068_s_at	PSMC2	proteasome (prosome, macropain) 26S subunit, ATPase, 2	5701
201078_at	TM9SF2	transmembrane 9 superfamily member 2	9375
201084_s_at	BCLAF1	BCL2-associated transcription factor 1	9774
201089_at	ATP6V1B2	ATPase, H+ transporting, lysosomal 56/58kDa, V1 subunit B2	526
201095_at	DAP	death-associated protein	1611
201096_s_at	ARF4	ADP-ribosylation factor 4	378
201097_s_at	ARF4	ADP-ribosylation factor 4	378
201098_at	COPB2	coatomer protein complex, subunit beta 2 (beta prime)	9276
201099_at	USP9X	ubiquitin specific peptidase 9, X-linked	8239
201112_s_at	CSE1L	CSE1 chromosome segregation 1-like (yeast)	1434
201116_s_at	CPE	carboxypeptidase E	1363
201117_s_at	CPE	carboxypeptidase E	1363
201118_at	PGD	phosphogluconate dehydrogenase	5226 /// 7358
201121_s_at	PGRMC1	progesterone receptor membrane component 1	10857
201123_s_at	EIF5A	eukaryotic translation initiation factor 5A	1984
201128_s_at	ACLY	ATP citrate lyase	47
201132_at	HNRNPH2	heterogeneous nuclear ribonucleoprotein H2 (H')	3188
201133_s_at	PJA2	praja 2, RING-H2 motif containing	9867
201136_at	PLP2	proteolipid protein 2 (colonic epithelium-enriched)	5355
201142_at	EIF2S1	eukaryotic translation initiation factor 2, subunit 1 alpha, 35kDa	1965
201146_at	NFE2L2	nuclear factor (erythroid-derived 2)-like 2	4780

201157_s_at	NMT1	N-myristoyltransferase 1	4836
201176_s_at	ARCN1	archain 1	372
201177_s_at	UBA2	ubiquitin-like modifier activating enzyme 2	10054
201190_s_at	PITPNA	phosphatidylinositol transfer protein, alpha	5306
201191_at	PITPNA	phosphatidylinositol transfer protein, alpha	5306
201196_s_at	AMD1	adenosylmethionine decarboxylase 1	262
201197_at	AMD1	adenosylmethionine decarboxylase 1	262
201198_s_at	PSMD1	proteasome (prosome, macropain) 26S subunit, non-ATPase, 1	5707
201202_at	PCNA	proliferating cell nuclear antigen	5111
201210_at	DDX3X	DEAD (Asp-Glu-Ala-Asp) box polypeptide 3, X-linked	1654
201222_s_at	RAD23B	RAD23 homolog B (S. cerevisiae)	5887
201225_s_at	SRRM1	serine/arginine repetitive matrix 1	10250
201237_at	CAPZA2	capping protein (actin filament) muscle Z-line, alpha 2	830
201238_s_at	CAPZA2	capping protein (actin filament) muscle Z-line, alpha 2	830
201239_s_at	SPCS2	signal peptidase complex subunit 2 homolog (S. cerevisiae)	653566 /// 9789
201240_s_at	SPCS2	signal peptidase complex subunit 2 homolog (S. cerevisiae)	9789
201241_at	DDX1	DEAD (Asp-Glu-Ala-Asp) box polypeptide 1	1653
201259_s_at	SYPL1	synaptophysin-like 1	6856
201260_s_at	SYPL1	synaptophysin-like 1	6856
201263_at	TARS	threonyl-tRNA synthetase	6897
201267_s_at	PSMC3	proteasome (prosome, macropain) 26S subunit, ATPase, 3	5702
201272_at	AKR1B1	aldo-keto reductase family 1, member B1 (aldose reductase)	231
201273_s_at	hCG_1781062 /// SRP9	signal recognition particle 9kDa /// hCG1781062	6726
201303_at	EIF4A3	eukaryotic translation initiation factor 4A, isoform 3	9775
201304_at	NDUFA5	NADH dehydrogenase (ubiquinone) 1 alpha subcomplex, 5, 13kDa	4698
201312_s_at	SH3BGRL	SH3 domain binding glutamic acid-rich protein like	6451
201322_at	ATP5B	ATP synthase, H+ transporting, mitochondrial F1 complex, beta polypeptide	506
201339_s_at	SCP2	sterol carrier protein 2	6342
201343_at	UBE2D2	ubiquitin-conjugating enzyme E2D 2 (UBC4/5 homolog, yeast)	7322
201348_at	GPX3	glutathione peroxidase 3 (plasma)	2878
201368_at	ZFP36L2	zinc finger protein 36, C3H type-like 2	678
201371_s_at	CUL3	cullin 3	8452
201375_s_at	PPP2CB	protein phosphatase 2 (formerly 2A), catalytic subunit, beta isoform	5516
201376_s_at	HNRNPF	heterogeneous nuclear ribonucleoprotein F	3185
201385_at	DHX15	DEAH (Asp-Glu-Ala-His) box polypeptide 15	1665
201386_s_at	DHX15	DEAH (Asp-Glu-Ala-His) box polypeptide 15	1665
201387_s_at	UCHL1	ubiquitin carboxyl-terminal esterase L1 (ubiquitin thiolesterase)	7345
201398_s_at	LOC100130862 /// TRAM1	translocation associated membrane protein 1 /// PRO1292	23471
201410_at	PLEKHB2	pleckstrin homology domain containing, family B (evectins) member 2	55041
201426_s_at	VIM	vimentin	7431
201432_at	CAT	catalase	847
201435_s_at	EIF4E	eukaryotic translation initiation factor 4E	1977
201437_s_at	EIF4E	eukaryotic translation initiation factor 4E	1977
201443_s_at	ATP6AP2	ATPase, H+ transporting, lysosomal accessory protein 2	10159
201444_s_at	ATP6AP2	ATPase, H+ transporting, lysosomal accessory protein 2	10159
201455_s_at	NPEPPS	aminopeptidase puromycin sensitive	9520
201458_s_at	BUB3	BUB3 budding uninhibited by benzimidazoles 3 homolog (yeast)	9184
201472_at	VBP1	von Hippel-Lindau binding protein 1	7411
201478_s_at	DKC1	dyskeratosis congenita 1, dyskerin	1736
201485_s_at	RCN2	reticulocalbin 2, EF-hand calcium binding domain	5955
201486_at	RCN2	reticulocalbin 2, EF-hand calcium binding domain	5955
201487_at	CTSC	cathepsin C	1075
201501_s_at	GRSF1	G-rich RNA sequence binding factor 1	2926
201515_s_at	TSN	translin	7247
201517_at	NCBP2	nuclear cap binding protein subunit 2, 20kDa	22916
201518_at	CBX1	chromobox homolog 1 (HP1 beta homolog Drosophila)	10951
201520_s_at	GRSF1	G-rich RNA sequence binding factor 1	2926
201528_at	RPA1	replication protein A1, 70kDa	6117
201529_s_at	RPA1	replication protein A1, 70kDa	6117
201532_at	PSMA3	proteasome (prosome, macropain) subunit, alpha type, 3	5684
201535_at	UBL3	ubiquitin-like 3	5412
201540_at	FHL1	four and a half LIM domains 1	2273
201542_at	SAR1A	SAR1 gene homolog A (S. cerevisiae)	56681
201552_at	LAMP1	lysosomal-associated membrane protein 1	3916
201567_s_at	GOLGA4	golgi autoantigen, golgin subfamily a, 4	2803

201569_s_at	LOC100131861 /// SAMM50	sorting and assembly machinery component 50 homolog (S. cerevisiae) /// hypothetical protein LOC100131861	25813
201574_at	ETF1	eukaryotic translation termination factor 1	2107
201576_s_at	GLB1	galactosidase, beta 1	2720
201577_at	NME1 /// NME2	non-metastatic cells 1, protein (NM23A) expressed in /// non-metastatic cells 2, protein (NM23B) expressed in	4830
201579_at	FAT	FAT tumor suppressor homolog 1 (Drosophila)	2195
201581_at	TXNDC13	thioredoxin domain containing 13	56255
201583_s_at	SEC23B	Sec23 homolog B (S. cerevisiae)	10483
201586_s_at	SFPQ	splicing factor proline/glutamine-rich (polypyrimidine tract binding protein associated)	6421
201595_s_at	ZC3H15	zinc finger CCCH-type containing 15	55854
201599_at	OAT	ornithine aminotransferase (gyrate atrophy)	4942
201603_at	PPP1R12A	protein phosphatase 1, regulatory (inhibitor) subunit 12A	4659
201619_at	PRDX3	peroxiredoxin 3	10935
201628_s_at	RRAGA	Ras-related GTP binding A	10670
201630_s_at	ACP1	acid phosphatase 1, soluble	52
201632_at	EIF2B1	eukaryotic translation initiation factor 2B, subunit 1 alpha, 26kDa	1967
201634_s_at	CYB5B	cytochrome b5 type B (outer mitochondrial membrane)	80777
201646_at	SCARB2	scavenger receptor class B, member 2	950
201652_at	COPS5	COP9 constitutive photomorphogenic homolog subunit 5 (Arabidopsis)	10987
201653_at	CNIH	cornichon homolog (Drosophila)	10175
201659_s_at	ARL1	ADP-ribosylation factor-like 1	400
201681_s_at	DLG5	discs, large homolog 5 (Drosophila)	9231
201687_s_at	API5	apoptosis inhibitor 5	8539
201688_s_at	TPD52	tumor protein D52	7163
201689_s_at	TPD52	tumor protein D52	7163
201690_s_at	TPD52	tumor protein D52	7163
201698_s_at	SFRS9	splicing factor, arginine/serine-rich 9	8683
201699_at	PSMC6	proteasome (prosome, macropain) 26S subunit, ATPase, 6	5706
201705_at	PSMD7	proteasome (prosome, macropain) 26S subunit, non-ATPase, 7	5713
201713_s_at	RANBP2	RAN binding protein 2	5903
201714_at	TUBG1	tubulin, gamma 1	7283
201725_at	CDC123	cell division cycle 123 homolog (S. cerevisiae)	8872
201734_at	CLCN3	Chloride channel 3	1182
201735_s_at	CLCN3	chloride channel 3	1182
201736_s_at	MARCH6	membrane-associated ring finger (C3HC4) 6	10299
201738_at	EIF1B	eukaryotic translation initiation factor 1B	10289
201745_at	TWF1	twinfilin, actin-binding protein, homolog 1 (Drosophila)	5756
201751_at	JOSD1	Josephin domain containing 1	9929
201754_at	COX6C	cytochrome c oxidase subunit VIc	1345
201760_s_at	WSB2	WD repeat and SOCS box-containing 2	55884
201769_at	CLINT1	clathrin interactor 1	9685
201772_at	AZIN1	antizyme inhibitor 1	51582
201773_at	ADNP	activity-dependent neuroprotector homeobox	23394
201779_s_at	RNF13	ring finger protein 13	11342
201780_s_at	RNF13	ring finger protein 13	11342
201784_s_at	C11orf58	chromosome 11 open reading frame 58	10944
201790_s_at	DHCR7	7-dehydrocholesterol reductase	1717
201807_at	VPS26A	vacuolar protein sorting 26 homolog A (S. pombe)	9559
201817_at	UBE3C	ubiquitin protein ligase E3C	9690
201821_s_at	TIMM17A	translocase of inner mitochondrial membrane 17 homolog A (yeast)	10440
201823_s_at	RNF14	ring finger protein 14	9604
201830_s_at	NET1	neuroepithelial cell transforming gene 1	10276
201832_s_at	USO1	USO1 homolog, vesicle docking protein (yeast)	5058 /// 8615
201847_at	LIPA	lipase A, lysosomal acid, cholesterol esterase (Wolman disease)	3988
201855_s_at	ATMIN	ATM interactor	23300
201857_at	ZFR	zinc finger RNA binding protein	51663
201873_s_at	ABCE1	ATP-binding cassette, sub-family E (OABP), member 1	6059
201877_s_at	PPP2R5C	protein phosphatase 2, regulatory subunit B', gamma isoform	5527
201894_s_at	SSR1	signal sequence receptor, alpha (translocon-associated protein alpha)	6745
201899_s_at	UBE2A	ubiquitin-conjugating enzyme E2A (RAD6 homolog)	7319
201912_s_at	GSPT1	G1 to S phase transition 1	2935
201916_s_at	SEC63	SEC63 homolog (S. cerevisiae)	11231
201919_at	SLC25A36	solute carrier family 25, member 36	55186
201920_at	SLC20A1	solute carrier family 20 (phosphate transporter), member 1	6574
201923_at	PRDX4	peroxiredoxin 4	10549

201931_at	ETFA	electron-transfer-flavoprotein, alpha polypeptide (glutaric aciduria II)	2108
201941_at	CPD	carboxypeptidase D	1362
201943_s_at	CPD	carboxypeptidase D	1362
201963_at	ACSL1	acyl-CoA synthetase long-chain family member 1	2180
201972_at	ATP6V1A	ATPase, H+ transporting, lysosomal 70kDa, V1 subunit A	523
202003_s_at	ACAA2	acetyl-Coenzyme A acyltransferase 2	10449
202006_at	PTPN12	protein tyrosine phosphatase, non-receptor type 12	5782
202016_at	MEST	mesoderm specific transcript homolog (mouse)	4232
202020_s_at	LANCL1	LanC lantibiotic synthetase component C-like 1 (bacterial)	10314
202026_at	SDHD	succinate dehydrogenase complex, subunit D, integral membrane protein	6392
202033_s_at	RB1CC1	RB1-inducible coiled-coil 1	9821
202038_at	UBE4A	ubiquitination factor E4A (UFD2 homolog, yeast)	9354
202060_at	CTR9	Ctr9, Paf1/RNA polymerase II complex component, homolog (S. cerevisiae)	9646
202061_s_at	SEL1L	sel-1 suppressor of lin-12-like (C. elegans)	6400
202069_s_at	IDH3A	isocitrate dehydrogenase 3 (NAD+) alpha	3419
202078_at	COPS3	COP9 constitutive photomorphogenic homolog subunit 3 (Arabidopsis)	8533
202088_at	SLC39A6	solute carrier family 39 (zinc transporter), member 6	25800
202089_s_at	SLC39A6	solute carrier family 39 (zinc transporter), member 6	25800
202097_at	NUP153	nucleoporin 153kDa	9972
202113_s_at	SNX2	sorting nexin 2	6643
202116_at	DPF2	D4, zinc and double PHD fingers family 2	5977
202119_s_at	CPNE3	copine III	8895
202136_at	ZMYND11	zinc finger, MYND domain containing 11	10771
202147_s_at	IFRD1	interferon-related developmental regulator 1	3475
202164_s_at	CNOT8	CCR4-NOT transcription complex, subunit 8	9337
202165_at	PPP1R2	protein phosphatase 1, regulatory (inhibitor) subunit 2	5504
202166_s_at	PPP1R2	protein phosphatase 1, regulatory (inhibitor) subunit 2	5504
202168_at	TAF9	TAF9 RNA polymerase II, TATA box binding protein (TBP)-associated factor, 32kDa	6880
202169_s_at	AASDHPPT	aminoadipate-semialdehyde dehydrogenase-phosphopantetheinyl transferase	60496
202171_at	VEZF1	vascular endothelial zinc finger 1	7716
202174_s_at	PCM1	pericentriolar material 1	5108 /// 7179
202194_at	TMED5	transmembrane emp24 protein transport domain containing 5	50999
202195_s_at	TMED5	transmembrane emp24 protein transport domain containing 5	50999
202211_at	ARFGAP3	ADP-ribosylation factor GTPase activating protein 3	26286
202220_at	KIAA0907	KIAA0907	22889
202228_s_at	NPTN	neuroplastin	27020
202232_s_at	EIF3M	eukaryotic translation initiation factor 3, subunit M	10480
202242_at	TSPAN7	tetraspanin 7	7102
202243_s_at	PSMB4	proteasome (prosome, macropain) subunit, beta type, 4	5692
202246_s_at	CDK4	cyclin-dependent kinase 4	1019
202260_s_at	STXBP1	syntaxin binding protein 1	6812
202263_at	CYB5R1	cytochrome b5 reductase 1	51706
202265_at	BMI1	BMI1 polycomb ring finger oncogene	648
202266_at	TTRAP	TRAF and TNF receptor associated protein	51567
202268_s_at	NAE1	NEDD8 activating enzyme E1 subunit 1	8883
202271_at	FBXO28	F-box protein 28	23219
202277_at	SPTLC1	serine palmitoyltransferase, long chain base subunit 1	10558
202296_s_at	RER1	RER1 retention in endoplasmic reticulum 1 homolog (S. cerevisiae)	11079
202300_at	HBXIP	hepatitis B virus x interacting protein	10542
202302_s_at	RSRC2	arginine/serine-rich coiled-coil 2	65117
202304_at	FNDC3A	fibronectin type III domain containing 3A	22862
202318_s_at	SENP6	SUMO1/sentrin specific peptidase 6	26054
202324_s_at	ACBD3	acyl-Coenzyme A binding domain containing 3	64746
202336_s_at	PAM	peptidylglycine alpha-amidating monooxygenase	5066
202342_s_at	TRIM2	tripartite motif-containing 2	23321
202346_at	UBE2K	ubiquitin-conjugating enzyme E2K (UBC1 homolog, yeast)	3093
202347_s_at	UBE2K	ubiquitin-conjugating enzyme E2K (UBC1 homolog, yeast)	3093
202353_s_at	PSMD12	proteasome (prosome, macropain) 26S subunit, non-ATPase, 12	5718
202365_at	UNC119B	unc-119 homolog B (C. elegans)	84747
202370_s_at	CBFB	core-binding factor, beta subunit	865
202375_at	SEC24D	SEC24 related gene family, member D (S. cerevisiae)	9871
202395_at	NSF	N-ethylmaleimide-sensitive factor	4905
202396_at	TCERG1	transcription elongation regulator 1	10915
202413_s_at	USP1	ubiquitin specific peptidase 1	7398
202427_s_at	BRP44	brain protein 44	25874
202429_s_at	PPP3CA	protein phosphatase 3 (formerly 2B), catalytic subunit, alpha isoform	5530
202432_at	PPP3CB	protein phosphatase 3 (formerly 2B), catalytic subunit, beta isoform	5532

202433_at	SLC35B1	solute carrier family 35, member B1	10237
202453_s_at	GTF2H1	general transcription factor IIH, polypeptide 1, 62kDa	2965
202462_s_at	DDX46	DEAD (Asp-Glu-Ala-Asp) box polypeptide 46	9879
202467_s_at	COPS2	COP9 constitutive photomorphogenic homolog subunit 2 (Arabidopsis)	9318
202491_s_at	IKBKAP	inhibitor of kappa light polypeptide gene enhancer in B-cells, kinase complex-associated protein	8518
202502_at	ACADM	acyl-Coenzyme A dehydrogenase, C-4 to C-12 straight chain	34
202508_s_at	SNAP25	synaptosomal-associated protein, 25kDa	6616
202512_s_at	ATG5	ATG5 autophagy related 5 homolog (S. cerevisiae)	9474
202515_at	DLG1	discs, large homolog 1 (Drosophila)	1739
202520_s_at	MLH1	mutL homolog 1, colon cancer, nonpolyposis type 2 (E. coli)	4292
202539_s_at	HMGCR	3-hydroxy-3-methylglutaryl-Coenzyme A reductase	3156
202540_s_at	HMGCR	3-hydroxy-3-methylglutaryl-Coenzyme A reductase	3156
202541_at	SCYE1	small inducible cytokine subfamily E, member 1 (endothelial monocyte-activating)	9255
202543_s_at	GMFB	glia maturation factor, beta	2764
202544_at	GMFB	glia maturation factor, beta	2764
202557_at	STCH	stress 70 protein chaperone, microsome-associated, 60kDa	6782
202561_at	TNKS	tankyrase, TRF1-interacting ankyrin-related ADP-ribose polymerase	8658
202567_at	SNRPD3	small nuclear ribonucleoprotein D3 polypeptide 18kDa	6634
202591_s_at	SSBP1	single-stranded DNA binding protein 1	6742
202606_s_at	TLK1	tousled-like kinase 1	9874
202614_at	SLC30A9	solute carrier family 30 (zinc transporter), member 9	10463
202623_at	EAPP	E2F-associated phosphoprotein	55837
202635_s_at	POLR2K	polymerase (RNA) II (DNA directed) polypeptide K, 7.0kDa	5440
202636_at	RNF103	ring finger protein 103	7844
202641_at	ARL3	ADP-ribosylation factor-like 3	403
202653_s_at	MARCH7	membrane-associated ring finger (C3HC4) 7	64844
202658_at	PEX11B	peroxisomal biogenesis factor 11B	8799
202670_at	MAP2K1	mitogen-activated protein kinase kinase 1	5604
202673_at	DPM1	dolichyl-phosphate mannosyltransferase polypeptide 1, catalytic subunit	8813
202675_at	SDHB	succinate dehydrogenase complex, subunit B, iron sulfur (Ip)	6390
202680_at	GTF2E2	general transcription factor IIE, polypeptide 2, beta 34kDa	2961
202691_at	SNRPD1	small nuclear ribonucleoprotein D1 polypeptide 16kDa	6632
202696_at	OXSR1	oxidative-stress responsive 1	9943
202704_at	TOB1	transducer of ERBB2, 1	10140
202710_at	BET1	blocked early in transport 1 homolog (S. cerevisiae)	10282
202717_s_at	CDC16	cell division cycle 16 homolog (S. cerevisiae)	8881
202722_s_at	GFPT1	glutamine-fructose-6-phosphate transaminase 1	2673
202731_at	PDCD4	programmed cell death 4 (neoplastic transformation inhibitor)	27250
202741_at	PRKACB	protein kinase, cAMP-dependent, catalytic, beta	5567
202749_at	WRB	tryptophan rich basic protein	7485
202753_at	PSMD6	proteasome (prosome, macropain) 26S subunit, non-ATPase, 6	9861
202759_s_at	AKAP2 /// PALM2 /// PALM2-AKAP2	A kinase (PRKA) anchor protein 2 /// paralemmin 2 /// PALM2-AKAP2	11217 /// 445815
202777_at	SHOC2	soc-2 suppressor of clear homolog (C. elegans)	8036
202794_at	INPP1	inositol polyphosphate-1-phosphatase	3628
202798_at	SEC24B	SEC24 related gene family, member B (S. cerevisiae)	10427
202829_s_at	VAMP7	vesicle-associated membrane protein 7	6845
202832_at	GCC2	GRIP and coiled-coil domain containing 2	9648
202836_s_at	TXNL4A	thioredoxin-like 4A	10907
202838_at	FUCA1	fucosidase, alpha-L- 1, tissue	2517
202842_s_at	DNAJB9	DnaJ (Hsp40) homolog, subfamily B, member 9	4189
202843_at	DNAJB9	DnaJ (Hsp40) homolog, subfamily B, member 9	4189
202850_at	ABCD3	ATP-binding cassette, sub-family D (ALD), member 3	5825
202854_at	HPRT1	hypoxanthine phosphoribosyltransferase 1 (Lesch-Nyhan syndrome)	3251
202868_s_at	POP4	processing of precursor 4, ribonuclease P/MRP subunit (S. cerevisiae)	10775
202890_at	MAP7	microtubule-associated protein 7	9053
202892_at	CDC23	cell division cycle 23 homolog (S. cerevisiae)	8697
202911_at	MSH6	mutS homolog 6 (E. coli)	2956
202918_s_at	MOBKL3	MOB1, Mps One Binder kinase activator-like 3 (yeast)	25843
202930_s_at	SUCLA2	succinate-CoA ligase, ADP-forming, beta subunit	8803
202932_at	YES1	v-yes-1 Yamaguchi sarcoma viral oncogene homolog 1	7525
202946_s_at	BTBD3	BTB (POZ) domain containing 3	22903
202950_at	CRYZ	crystallin, zeta (quinone reductase)	1429
202967_at	GSTA4	glutathione S-transferase A4	2941
202969_at	DYRK2	dual-specificity tyrosine-(Y)-phosphorylation regulated kinase 2	---

202975_s_at	RHOBTB3	Rho-related BTB domain containing 3	22836
202976_s_at	RHOBTB3	Rho-related BTB domain containing 3	22836
202982_s_at	ACOT1 /// ACOT2	acyl-CoA thioesterase 2 /// acyl-CoA thioesterase 1	10965 /// 641371 /// 653878
202983_at	HLTF	helicase-like transcription factor	6596
202993_at	ILVBL	ilvB (bacterial acetolactate synthase)-like	10994
203000_at	STMN2	stathmin-like 2	11075
203008_x_at	TXNDC9	thioredoxin domain containing 9	10190
203011_at	IMPA1	inositol(myo)-1(or 4)-monophosphatase 1	3612
203029_s_at	PTPRN2	protein tyrosine phosphatase, receptor type, N polypeptide 2	5799
203041_s_at	LAMP2	lysosomal-associated membrane protein 2	3920
203048_s_at	KIAA0372	KIAA0372	9652
203049_s_at	KIAA0372	KIAA0372	9652
203053_at	BCAS2	breast carcinoma amplified sequence 2	10286
203058_s_at	PAPSS2	3'-phosphoadenosine 5'-phosphosulfate synthase 2	9060
203060_s_at	PAPSS2	3'-phosphoadenosine 5'-phosphosulfate synthase 2	9060
203067_at	PDHX	pyruvate dehydrogenase complex, component X	8050
203075_at	SMAD2	SMAD family member 2	4087
203087_s_at	KIF2A	kinesin heavy chain member 2A	3796
203097_s_at	RAPGEF2	Rap guanine nucleotide exchange factor (GEF) 2	9693
203102_s_at	MGAT2	mannosyl (alpha-1,6-)-glycoprotein beta-1,2-N-acetylglucosaminyltransferase	4247
203109_at	UBE2M	ubiquitin-conjugating enzyme E2M (UBC12 homolog, yeast)	9040
203124_s_at	SLC11A2	solute carrier family 11 (proton-coupled divalent metal ion transporters), member 2	4891
203130_s_at	KIF5C	kinesin family member 5C	3800
203138_at	HAT1	histone acetyltransferase 1	8520
203142_s_at	AP3B1	adaptor-related protein complex 3, beta 1 subunit	8546
203156_at	AKAP11	A kinase (PRKA) anchor protein 11	11215
203182_s_at	SRPK2	SFRS protein kinase 2	6733
203200_s_at	MTRR	5-methyltetrahydrofolate-homocysteine methyltransferase reductase	4552
203207_s_at	MTFR1	mitochondrial fission regulator 1	9650
203209_at	RFC5	replication factor C (activator 1) 5, 36.5kDa	5985
203211_s_at	MTMR2	myotubularin related protein 2	8898
203218_at	MAPK9	mitogen-activated protein kinase 9	5601
203253_s_at	HISPPD1	histidine acid phosphatase domain containing 1	23262
203259_s_at	HDDC2	HD domain containing 2	51020
203261_at	DCTN6	dynactin 6	10671
203266_s_at	MAP2K4	mitogen-activated protein kinase kinase 4	6416
203269_at	NSMAF	neutral sphingomyelinase (N-SMase) activation associated factor	8439
203284_s_at	HS2ST1	heparan sulfate 2-O-sulfotransferase 1	9653
203285_s_at	HS2ST1	heparan sulfate 2-O-sulfotransferase 1	9653
203302_at	DCK	deoxycytidine kinase	1633
203303_at	DYNLT3	dynein, light chain, Tctex-type 3	6990
203316_s_at	SNRPE	small nuclear ribonucleoprotein polypeptide E	6635
203327_at	IDE	insulin-degrading enzyme	3416
203336_s_at	ITGB1BP1	integrin beta 1 binding protein 1	9270
203355_s_at	PSD3	pleckstrin and Sec7 domain containing 3	23362
203356_at	CAPN7	calpain 7	23473
203376_at	CDC40	cell division cycle 40 homolog (S. cerevisiae)	51362
203403_s_at	RNF6	ring finger protein (C3H2C3 type) 6	6049
203404_at	ARMCX2	armadillo repeat containing, X-linked 2	9823
203405_at	PSMG1	proteasome (prosome, macropain) assembly chaperone 1	8624
203420_at	FAM8A1	family with sequence similarity 8, member A1	51439
203427_at	ASF1A	ASF1 anti-silencing function 1 homolog A (S. cerevisiae)	25842
203428_s_at	ASF1A	ASF1 anti-silencing function 1 homolog A (S. cerevisiae)	25842
203429_s_at	C1orf9	chromosome 1 open reading frame 9	51430
203447_at	PSMD5	proteasome (prosome, macropain) 26S subunit, non-ATPase, 5	5711
203465_at	MRPL19	mitochondrial ribosomal protein L19	9801
203485_at	RTN1	reticulon 1	6252
203511_s_at	TRAPPC3	trafficking protein particle complex 3	27095
203517_at	MTX2	metaxin 2	10651
203525_s_at	APC	adenomatous polyposis coli	324
203531_at	CUL5	cullin 5	8065
203537_at	PRPSAP2	phosphoribosyl pyrophosphate synthetase-associated protein 2	5636
203544_s_at	STAM	signal transducing adaptor molecule (SH3 domain and ITAM motif) 1	8027
203574_at	NFIL3	nuclear factor, interleukin 3 regulated	4783
203582_s_at	RAB4A	RAB4A, member RAS oncogene family	5867

203583_at	UNC50	unc-50 homolog (C. elegans)	25972
203584_at	TTC35	tetratricopeptide repeat domain 35	9694
203593_at	CD2AP	CD2-associated protein	23607
203594_at	RTCD1	RNA terminal phosphate cyclase domain 1	8634
203605_at	SRP54	signal recognition particle 54kDa	6729
203607_at	INPP5F	inositol polyphosphate-5-phosphatase F	22876
203613_s_at	NDUFB6	NADH dehydrogenase (ubiquinone) 1 beta subcomplex, 6, 17kDa	4712
203614_at	UTP14C	UTP14, U3 small nucleolar ribonucleoprotein, homolog C (yeast)	9724
203630_s_at	COG5	component of oligomeric golgi complex 5	10466
203646_at	FDX1	ferredoxin 1	2230
203654_s_at	COIL	coilin	8161
203659_s_at	TRIM13	tripartite motif-containing 13	10206
203675_at	NUCB2	nucleobindin 2	4925
203688_at	PKD2	polycystic kidney disease 2 (autosomal dominant)	5311
203721_s_at	UTP18	UTP18, small subunit (SSU) processome component, homolog (yeast)	51096
203724_s_at	RUFY3	RUN and FYVE domain containing 3	22902
203732_at	TRIP4	thyroid hormone receptor interactor 4	9325
203738_at	C5orf22	chromosome 5 open reading frame 22	55322
203743_s_at	TDG	thymine-DNA glycosylase	6996
203758_at	CTSO	cathepsin O	1519
203765_at	GCA	grancalcin, EF-hand calcium binding protein	25801
203774_at	MTR	5-methyltetrahydrofolate-homocysteine methyltransferase	4548
203791_at	DMXL1	Dmx-like 1	1657
203817_at	GUCY1B3	guanylate cyclase 1, soluble, beta 3	2983
203827_at	WIPI1	WD repeat domain, phosphoinositide interacting 1	55062
203843_at	RPS6KA3	ribosomal protein S6 kinase, 90kDa, polypeptide 3	6197
203869_at	USP46	ubiquitin specific peptidase 46	64854
203884_s_at	RAB11FIP2	RAB11 family interacting protein 2 (class I)	22841
203885_at	RAB21	RAB21, member RAS oncogene family	23011
203889_at	SCG5	secretogranin V (7B2 protein)	6447
203893_at	TAF9	TAF9 RNA polymerase II, TATA box binding protein (TBP)-associated factor, 32kDa	6880
203909_at	SLC9A6	solute carrier family 9 (sodium/hydrogen exchanger), member 6	10479
203935_at	ACVR1	activin A receptor, type I	90
203946_s_at	ARG2	arginase, type II	384
203961_at	NEBL	nebulette	10529
203962_s_at	NEBL	nebulette	10529
203966_s_at	PPM1A	protein phosphatase 1A (formerly 2C), magnesium-dependent, alpha isoform	5494
203970_s_at	PEX3	peroxisomal biogenesis factor 3	8504
203987_at	FZD6	frizzled homolog 6 (Drosophila)	8323
203997_at	PTPN3	protein tyrosine phosphatase, non-receptor type 3	5774
204004_at	PAWR	PRKC, apoptosis, WT1, regulator	5074
204026_s_at	ZWINT	ZW10 interactor	11130
204035_at	SCG2	secretogranin II (chromogranin C)	7857
204042_at	WASF3	WAS protein family, member 3	10810
204045_at	TCEAL1	transcription elongation factor A (SII)-like 1	9338
204048_s_at	PHACTR2	phosphatase and actin regulator 2	9749
204049_s_at	PHACTR2	phosphatase and actin regulator 2	9749
204058_at	ME1	malic enzyme 1, NADP(+)-dependent, cytosolic	4199
204072_s_at	FRY	furry homolog (Drosophila)	10129
204085_s_at	CLN5	ceroid-lipofuscinosis, neuronal 5	1203
204105_s_at	NRCAM	neuronal cell adhesion molecule	4897
204119_s_at	ADK	adenosine kinase	132
204127_at	RFC3	replication factor C (activator 1) 3, 38kDa	5983
204160_s_at	ENPP4	ectonucleotide pyrophosphatase/phosphodiesterase 4 (putative function)	22875
204224_s_at	GCH1	GTP cyclohydrolase 1 (dopa-responsive dystonia)	2643
204244_s_at	DBF4	DBF4 homolog (S. cerevisiae)	10926
204246_s_at	DCTN3	dynactin 3 (p22)	11258
204260_at	CHGB	chromogranin B (secretogranin 1)	1114 /// 23041
204274_at	EBAG9	estrogen receptor binding site associated, antigen, 9	9166
204299_at	FUSIP1 /// LOC642558	FUS interacting protein (serine/arginine-rich) 1 /// similar to FUS interacting protein (serine-arginine rich) 1	10772 /// 642558
204331_s_at	MRPS12	mitochondrial ribosomal protein S12	6183
204332_s_at	AGA	aspartylglucosaminidase	175
204337_at	RGS4	regulator of G-protein signaling 4	5999
204354_at	POT1	POT1 protection of telomeres 1 homolog (S. pombe)	25913
204369_at	PIK3CA	phosphoinositide-3-kinase, catalytic, alpha polypeptide	5290
204417_at	GALC	galactosylceramidase	2581

204465_s_at	INA	internexin neuronal intermediate filament protein, alpha	9118
204485_s_at	TOM1L1	target of myb1 (chicken)-like 1	10040
204500_s_at	AGTPBP1	ATP/GTP binding protein 1	23287
204516_at	ATXN7	ataxin 7	6314
204529_s_at	TOX	thymocyte selection-associated high mobility group box	9760
204605_at	CGRRF1	cell growth regulator with ring finger domain 1	10668
204634_at	NEK4	NIMA (never in mitosis gene a)-related kinase 4	6787
204688_at	SGCE	sarcoglycan, epsilon	8910
204720_s_at	DNAJC6	DnaJ (Hsp40) homolog, subfamily C, member 6	9829
204744_s_at	IARS	isoleucyl-tRNA synthetase	3376
204749_at	NAP1L3	nucleosome assembly protein 1-like 3	4675
204807_at	TMEM5	transmembrane protein 5	10329
204809_at	CLPX	ClpX caseinolytic peptidase X homolog (E. coli)	10845
204831_at	CDK8	cyclin-dependent kinase 8	1024
204869_at	PCSK2	proprotein convertase subtilisin/kexin type 2	5126
204892_x_at	EEF1A1	eukaryotic translation elongation factor 1 alpha 1	1915
204905_s_at	EEF1E1	eukaryotic translation elongation factor 1 epsilon 1	9521
204953_at	SNAP91	synaptosomal-associated protein, 91kDa homolog (mouse)	9892
204992_s_at	PFN2	profilin 2	5217
205042_at	GNE	glucosamine (UDP-N-acetyl)-2-epimerase/N-acetylmannosamine kinase	10020
205047_s_at	ASNS	asparagine synthetase	440
205052_at	AUH	AU RNA binding protein/enoyl-Coenzyme A hydratase	549
205055_at	ITGAE	integrin, alpha E (antigen CD103, human mucosal lymphocyte antigen 1; alpha polypeptide)	3682
205087_at	RWDD3	RWD domain containing 3	25950
205097_at	SLC26A2	solute carrier family 26 (sulfate transporter), member 2	1836
205113_at	NEFM	neurofilament, medium polypeptide 150kDa	4741
205133_s_at	HSPE1	heat shock 10kDa protein 1 (chaperonin 10)	3336
205174_s_at	QPCT	glutaminyl-peptide cyclotransferase (glutaminyl cyclase)	25797
205190_at	PLS1	plastin 1 (I isoform)	5357
205251_at	PER2	period homolog 2 (Drosophila)	8864
205260_s_at	ACYP1 /// C17orf13	acylphosphatase 1, erythrocyte (common) type /// chromosome 17 open reading frame 13	97
205281_s_at	PIGA	phosphatidylinositol glycan anchor biosynthesis, class A (paroxysmal nocturnal hemoglobinuria)	5277
205335_s_at	SRP19	signal recognition particle 19kDa	6728
205348_s_at	DYNC1I1	dynein, cytoplasmic 1, intermediate chain 1	1780
205352_at	SERPINI1	serpin peptidase inhibitor, clade I (neuroserpin), member 1	5274
205412_at	ACAT1	acetyl-Coenzyme A acetyltransferase 1 (acetoacetyl Coenzyme A thiolase)	38
205420_at	PEX7	peroxisomal biogenesis factor 7	5191
205429_s_at	MPP6	membrane protein, palmitoylated 6 (MAGUK p55 subfamily member 6)	51678
205480_s_at	UGP2	UDP-glucose pyrophosphorylase 2	7360
205548_s_at	BTG3	BTG family, member 3	10950
205571_at	LIPT1	lipoyltransferase 1	51601
205573_s_at	SNX7	sorting nexin 7	51375
205633_s_at	ALAS1	aminolevulinate, delta-, synthase 1	211
205697_at	SCGN	secretagogin, EF-hand calcium binding protein	10590
205751_at	SH3GL2	SH3-domain GRB2-like 2	6456
205825_at	PCSK1	proprotein convertase subtilisin/kexin type 1	5122
205830_at	CLGN	calmegin	1047
205979_at	SCGB2A1	secretoglobin, family 2A, member 1	4246
206052_s_at	SLBP	stem-loop binding protein	7884
206095_s_at	FUSIP1 /// LOC642558	FUS interacting protein (serine/arginine-rich) 1 /// similar to FUS interacting protein (serine-arginine rich) 1	10772 /// 642558
206158_s_at	CNBP	CCHC-type zinc finger, nucleic acid binding protein	7555
206172_at	IL13RA2	interleukin 13 receptor, alpha 2	3598
206191_at	ENTPD3	ectonucleoside triphosphate diphosphohydrolase 3	956
206302_s_at	NUDT4 /// NUDT4P1	nudix (nucleoside diphosphate linked moiety X)-type motif 4 /// nudix (nucleoside diphosphate linked moiety X)-type motif 4 pseudogene 1	11163 /// 440672
206422_at	GCG	glucagon	2641
206502_s_at	INSM1	insulinoma-associated 1	3642
206542_s_at	SMARCA2	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily a, member 2	6595
206587_at	CCT6B	chaperonin containing TCP1, subunit 6B (zeta 2)	10693
206598_at	INS	insulin	3630
206621_s_at	EIF4H	eukaryotic translation initiation factor 4H	7458
206645_s_at	NR0B1	nuclear receptor subfamily 0, group B, member 1	190
206710_s_at	EPB41L3	erythrocyte membrane protein band 4.1-like 3	23136

206780_at	GAD2	glutamate decarboxylase 2 (pancreatic islets and brain, 65kDa)	2572
206958_s_at	UPF3A	UPF3 regulator of nonsense transcripts homolog A (yeast)	65110
207000_s_at	PPP3CC	protein phosphatase 3 (formerly 2B), catalytic subunit, gamma isoform	5533
207002_s_at	PLAGL1	pleiomorphic adenoma gene-like 1	5325
207062_at	IAPP	islet amyloid polypeptide	3375
207098_s_at	MFN1	mitofusin 1	55669
207170_s_at	LETMD1	LETM1 domain containing 1	25875
207243_s_at	CALM1 /// CALM2 /// CALM3	calmodulin 1 (phosphorylase kinase, delta) /// calmodulin 2 (phosphorylase kinase, delta) /// calmodulin 3 (phosphorylase kinase, delta)	805
207275_s_at	ACSL1	acyl-CoA synthetase long-chain family member 1	2180
207332_s_at	TFRC	transferrin receptor (p90, CD71)	7037
207405_s_at	RAD17	RAD17 homolog (S. pombe)	5884
207483_s_at	CAND1	cullin-associated and neddylation-dissociated 1	55832
207507_s_at	ATP5G3	ATP synthase, H+ transporting, mitochondrial F0 complex, subunit C3 (subunit 9)	518
207508_at	ATP5G3	ATP synthase, H+ transporting, mitochondrial F0 complex, subunit C3 (subunit 9)	518
207621_s_at	PEMT	phosphatidylethanolamine N-methyltransferase	10400
207707_s_at	SEC13	SEC13 homolog (S. cerevisiae)	6396
207791_s_at	RAB1A	RAB1A, member RAS oncogene family	5861
207812_s_at	GORASP2	golgi reassembly stacking protein 2, 55kDa	26003
207845_s_at	ANAPC10	anaphase promoting complex subunit 10	10393
207941_s_at	RBM39	RNA binding motif protein 39	9584
207974_s_at	SKP1	S-phase kinase-associated protein 1	6500
207983_s_at	STAG2	stromal antigen 2	10735
208029_s_at	LAPTM4B	lysosomal associated protein transmembrane 4 beta	55353
208066_s_at	GTF2B	general transcription factor IIB	2959
208070_s_at	REV3L	REV3-like, catalytic subunit of DNA polymerase zeta (yeast)	5980
208097_s_at	TXNDC1	thioredoxin domain containing 1	81542
208152_s_at	DDX21	DEAD (Asp-Glu-Ala-Asp) box polypeptide 21	9188
208264_s_at	EIF3J	eukaryotic translation initiation factor 3, subunit J	8669
208290_s_at	EIF5	eukaryotic translation initiation factor 5	1983
208308_s_at	GPI /// LOC100133951	glucose phosphate isomerase /// similar to Glucose phosphate isomerase	2821
208310_s_at	C7orf28A /// C7orf28B	chromosome 7 open reading frame 28A /// chromosome 7 open reading frame 28B	221960 /// 51622
208319_s_at	RBM3	RNA binding motif (RNP1, RRM) protein 3	5935
208398_s_at	TBPL1	TBP-like 1	9519
208405_s_at	CD164	CD164 molecule, sialomucin	8763
208453_s_at	XPNPEP1	X-prolyl aminopeptidase (aminopeptidase P) 1, soluble	7511
208620_at	PCBP1	poly(rC) binding protein 1	5093
208627_s_at	YBX1	Y box binding protein 1	4904
208628_s_at	YBX1	Y box binding protein 1	4904
208631_s_at	HADHA	hydroxyacyl-Coenzyme A dehydrogenase/3-ketoacyl-Coenzyme A thiolase/enoyl-Coenzyme A hydratase (trifunctional protein), alpha subunit	3030
208635_x_at	NACA	nascent polypeptide-associated complex alpha subunit	4666
208638_at	PDIA6	protein disulfide isomerase family A, member 6	10130
208643_s_at	XRCC5	X-ray repair complementing defective repair in Chinese hamster cells 5 (double-strand-break rejoining; Ku autoantigen, 80kDa)	7520
208652_at	PPP2CA	protein phosphatase 2 (formerly 2A), catalytic subunit, alpha isoform	5515
208654_s_at	CD164	CD164 molecule, sialomucin	8763
208666_s_at	ST13	suppression of tumorigenicity 13 (colon carcinoma) (Hsp70 interacting protein)	6767
208667_s_at	ST13	suppression of tumorigenicity 13 (colon carcinoma) (Hsp70 interacting protein)	6767
208668_x_at	HMGN2	high-mobility group nucleosomal binding domain 2	3151
208669_s_at	EID1	EP300 interacting inhibitor of differentiation 1	23741
208671_at	SERINC1	serine incorporator 1	57515
208673_s_at	SFRS3	splicing factor, arginine/serine-rich 3	6428
208675_s_at	DDOST	dolichyl-diphosphooligosaccharide-protein glycosyltransferase	1650
208679_s_at	ARPC2	actin related protein 2/3 complex, subunit 2, 34kDa	10109
208692_at	RPS3	ribosomal protein S3	27127 /// 6188
208697_s_at	EIF3E	eukaryotic translation initiation factor 3, subunit E	3646
208703_s_at	APLP2	amyloid beta (A4) precursor-like protein 2	334
208706_s_at	EIF5	eukaryotic translation initiation factor 5	1983
208720_s_at	RBM39	RNA binding motif protein 39	9584
208722_s_at	ANAPC5	anaphase promoting complex subunit 5	51433
208724_s_at	RAB1A	RAB1A, member RAS oncogene family	5861
208726_s_at	EIF2S2	eukaryotic translation initiation factor 2, subunit 2 beta, 38kDa	8894
208731_at	RAB2A	RAB2A, member RAS oncogene family	5862

208732_at	RAB2A	RAB2A, member RAS oncogene family	5862
208739_x_at	SUMO2	SMT3 suppressor of mif two 3 homolog 2 (S. cerevisiae)	6613
208745_at	ATP5L	ATP synthase, H+ transporting, mitochondrial F0 complex, subunit G	10632
208750_s_at	ARF1	ADP-ribosylation factor 1	375
208761_s_at	SUMO1	SMT3 suppressor of mif two 3 homolog 1 (S. cerevisiae)	7341
208764_s_at	ATP5G2	ATP synthase, H+ transporting, mitochondrial F0 complex, subunit C2 (subunit 9)	517
208773_s_at	ANKHD1 /// ANKHD1-EIF4EBP3 /// EIF4EBP3	eukaryotic translation initiation factor 4E binding protein 3 /// ankyrin repeat and KH domain containing 1 /// ANKHD1-EIF4EBP3	404734 /// 54882
208775_at	XPO1	exportin 1 (CRM1 homolog, yeast)	7514
208777_s_at	PSMD11	proteasome (prosome, macropain) 26S subunit, non-ATPase, 11	5717
208778_s_at	TCP1	t-complex 1	6950
208781_x_at	SNX3	sorting nexin 3	8724
208786_s_at	MAP1LC3B	microtubule-associated protein 1 light chain 3 beta	81631
208787_at	MRPL3	mitochondrial ribosomal protein L3	11222
208788_at	ELOVL5	ELOVL family member 5, elongation of long chain fatty acids (FEN1/Elo2, SUR4/Elo3-like, yeast)	60481
208796_s_at	CCNG1	cyclin G1	900
208799_at	PSMB5	proteasome (prosome, macropain) subunit, beta type, 5	5693
208800_at	SRP72	signal recognition particle 72kDa	6731
208801_at	SRP72	signal recognition particle 72kDa	6731
208802_at	SRP72	signal recognition particle 72kDa	6731
208804_s_at	SFRS6	splicing factor, arginine/serine-rich 6	6431
208808_s_at	HMGB2	high-mobility group box 2	3148
208821_at	SNRPB	small nuclear ribonucleoprotein polypeptides B and B1	6628
208822_s_at	DAP3	death associated protein 3	7818
208828_at	POLE3	polymerase (DNA directed), epsilon 3 (p17 subunit)	54107
208833_s_at	ATXN10	ataxin 10	25814
208837_at	TMED3	transmembrane emp24 protein transport domain containing 3	23423
208841_s_at	G3BP2	GTPase activating protein (SH3 domain) binding protein 2	9908
208843_s_at	GORASP2	golgi reassembly stacking protein 2, 55kDa	26003
208846_s_at	VDAC3	voltage-dependent anion channel 3	3709 /// 7419
208848_at	ADH5	alcohol dehydrogenase 5 (class III), chi polypeptide	128
208852_s_at	CANX	calnexin	821
208860_s_at	ATRX	alpha thalassemia/mental retardation syndrome X-linked (RAD54 homolog, S. cerevisiae)	546 /// 642995
208863_s_at	SFRS1	splicing factor, arginine/serine-rich 1 (splicing factor 2, alternate splicing factor)	6426
208865_at	CSNK1A1	casein kinase 1, alpha 1	1452
208896_at	DDX18	DEAD (Asp-Glu-Ala-Asp) box polypeptide 18	8886
208905_at	CYCS	cytochrome c, somatic	54205
208909_at	UQCRFS1	ubiquinol-cytochrome c reductase, Rieske iron-sulfur polypeptide 1	7386
208910_s_at	C1QBP	complement component 1, q subcomponent binding protein	708
208924_at	RNF11	ring finger protein 11	26994
208937_s_at	ID1	inhibitor of DNA binding 1, dominant negative helix-loop-helix protein	3397
208939_at	SEPHS1	selenophosphate synthetase 1	22929
208943_s_at	SEC62	SEC62 homolog (S. cerevisiae)	7095
208944_at	TGFBR2	transforming growth factor, beta receptor II (70/80kDa)	7048
208959_s_at	TXNDC4	thioredoxin domain containing 4 (endoplasmic reticulum)	23071
208985_s_at	EIF3J	eukaryotic translation initiation factor 3, subunit J	8669
208990_s_at	HNRNPH3	heterogeneous nuclear ribonucleoprotein H3 (2H9)	3189
209001_s_at	ANAPC13	anaphase promoting complex subunit 13	25847
209004_s_at	FBXL5	F-box and leucine-rich repeat protein 5	26234
209009_at	ESD	esterase D/formylglutathione hydrolase	2098
209027_s_at	ABI1	abl-interactor 1	10006
209028_s_at	ABI1	abl-interactor 1	10006
209036_s_at	MDH2	malate dehydrogenase 2, NAD (mitochondrial)	4191
209043_at	PAPSS1	3'-phosphoadenosine 5'-phosphosulfate synthase 1	9061
209046_s_at	GABARAPL2	GABA(A) receptor-associated protein-like 2	11345
209056_s_at	CDC5L	CDC5 cell division cycle 5-like (S. pombe)	988
209089_at	RAB5A	RAB5A, member RAS oncogene family	5868
209090_s_at	SH3GLB1	SH3-domain GRB2-like endophilin B1	51100
209091_s_at	SH3GLB1	SH3-domain GRB2-like endophilin B1	51100
209092_s_at	GLOD4	glyoxalase domain containing 4	51031
209095_at	DLD	dihydrolipoamide dehydrogenase	1738
209106_at	NCOA1	nuclear receptor coactivator 1	8648
209112_at	CDKN1B	cyclin-dependent kinase inhibitor 1B (p27, Kip1)	1027

209115_at	UBA3	ubiquitin-like modifier activating enzyme 3	9039
209139_s_at	PRKRA	protein kinase, interferon-inducible double stranded RNA dependent activator	8575
209142_s_at	UBE2G1	ubiquitin-conjugating enzyme E2G 1 (UBC7 homolog, yeast)	7326
209150_s_at	TM9SF1	transmembrane 9 superfamily member 1	10548
209157_at	DNAJA2	DnaJ (Hsp40) homolog, subfamily A, member 2	10294
209175_at	SEC23IP	SEC23 interacting protein	11196
209180_at	RABGGTB	Rab geranylgeranyltransferase, beta subunit	5876
209181_s_at	RABGGTB	Rab geranylgeranyltransferase, beta subunit	5876
209187_at	DR1	down-regulator of transcription 1, TBP-binding (negative cofactor 2)	1810
209218_at	SQLE	squalene epoxidase	6713
209226_s_at	TNPO1	transportin 1	3842
209240_at	OGT	O-linked N-acetylglucosamine (GlcNAc) transferase (UDP-N-acetylglucosamine:polypeptide-N-acetylglucosaminyl transferase)	8473
209242_at	PEG3	paternally expressed 3	5178
209248_at	GHITM	growth hormone inducible transmembrane protein	27069
209249_s_at	GHITM	growth hormone inducible transmembrane protein	27069
209259_s_at	SMC3	structural maintenance of chromosomes 3	9126
209274_s_at	ISCA1	iron-sulfur cluster assembly 1 homolog (S. cerevisiae)	81689
209284_s_at	C3orf63	chromosome 3 open reading frame 63	23272
209288_s_at	CDC42EP3	CDC42 effector protein (Rho GTPase binding) 3	10602
209291_at	ID4	inhibitor of DNA binding 4, dominant negative helix-loop-helix protein	3400
209292_at	ID4	Inhibitor of DNA binding 4, dominant negative helix-loop-helix protein	3400
209300_s_at	NECAP1	NECAP endocytosis associated 1	25977
209311_at	BCL2L2	BCL2-like 2	599
209316_s_at	HBS1L	HBS1-like (S. cerevisiae)	10767
209323_at	PRKRIR	protein-kinase, interferon-inducible double stranded RNA dependent inhibitor, repressor of (P58 repressor)	5612
209330_s_at	HNRNPD	heterogeneous nuclear ribonucleoprotein D (AU-rich element RNA binding protein 1, 37kDa)	3184
209340_at	UAP1	UDP-N-acteylglucosamine pyrophosphorylase 1	6675
209362_at	MED21	mediator complex subunit 21	9412
209379_s_at	KIAA1128	KIAA1128	54462
209384_at	PROSC	proline synthetase co-transcribed homolog (bacterial)	11212
209392_at	ENPP2	ectonucleotide pyrophosphatase/phosphodiesterase 2 (autotaxin)	5168
209397_at	ME2	malic enzyme 2, NAD(+)-dependent, mitochondrial	4200
209430_at	BTAF1	BTAF1 RNA polymerase II, B-TFIID transcription factor-associated, 170kDa (Mot1 homolog, S. cerevisiae)	9044
209440_at	PRPS1	phosphoribosyl pyrophosphate synthetase 1	5631
209444_at	RAP1GDS1	RAP1, GTP-GDP dissociation stimulator 1	5910
209459_s_at	ABAT	4-aminobutyrate aminotransferase	18
209460_at	ABAT	4-aminobutyrate aminotransferase	18
209471_s_at	FNTA	farnesyltransferase, CAAX box, alpha	2339
209472_at	CCBL2	cysteine conjugate-beta lyase 2	56267
209476_at	TXNDC1	thioredoxin domain containing 1	81542
209510_at	RNF139	ring finger protein 139	11236
209523_at	TAF2	TAF2 RNA polymerase II, TATA box binding protein (TBP)-associated factor, 150kDa	6873
209560_s_at	DLK1	delta-like 1 homolog (Drosophila)	8788
209572_s_at	EED	embryonic ectoderm development	8726
209576_at	GNAI1	guanine nucleotide binding protein (G protein), alpha inhibiting activity polypeptide 1	2770
209580_s_at	MBD4	methyl-CpG binding domain protein 4	8930
209583_s_at	CD200	CD200 molecule	4345
209598_at	PNMA2	paraneoplastic antigen MA2	10687
209630_s_at	FBXW2	F-box and WD repeat domain containing 2	26190
209647_s_at	SOCS5	suppressor of cytokine signaling 5	9655
209662_at	CETN3	centrin, EF-hand protein, 3 (CDC31 homolog, yeast)	1070
209666_s_at	CHUK	conserved helix-loop-helix ubiquitous kinase	1147
209674_at	CRY1	cryptochrome 1 (photolyase-like)	1407
209694_at	PTS	6-pyruvoyltetrahydropterin synthase	5805
209737_at	MAGI2	membrane associated guanylate kinase, WW and PDZ domain containing 2	9863
209780_at	PHTF2	putative homeodomain transcription factor 2	57157
209786_at	HMGN4	high mobility group nucleosomal binding domain 4	10473
209814_at	ZNF330	zinc finger protein 330	27309
209817_at	PPP3CB	protein phosphatase 3 (formerly 2B), catalytic subunit, beta isoform	5532
209822_s_at	VLDLR	very low density lipoprotein receptor	7436
209825_s_at	UCK2	uridine-cytidine kinase 2	7371
209838_at	COPS2	COP9 constitutive photomorphogenic homolog subunit 2 (Arabidopsis)	9318
209860_s_at	ANXA7	annexin A7	310

209861_s_at	METAP2	methionyl aminopeptidase 2	10988
209902_at	ATR	ataxia telangiectasia and Rad3 related	545 /// 648152
209994_s_at	ABCB1 /// ABCB4	ATP-binding cassette, sub-family B (MDR/TAP), member 1 /// ATP-binding cassette, sub-family B (MDR/TAP), member 4	5243 /// 5244
210024_s_at	UBE2E3	ubiquitin-conjugating enzyme E2E 3 (UBC4/5 homolog, yeast)	10477
210027_s_at	APEX1	APEX nuclease (multifunctional DNA repair enzyme) 1	328
210028_s_at	ORC3L	origin recognition complex, subunit 3-like (yeast)	23595
210041_s_at	PGM3	phosphoglucomutase 3	5238
210092_at	MAGOH	mago-nashi homolog, proliferation-associated (Drosophila)	4116
210137_s_at	DCTD	dCMP deaminase	1635
210156_s_at	PCMT1	protein-L-isoaspartate (D-aspartate) O-methyltransferase	5110
210222_s_at	RTN1	reticulon 1	6252
210296_s_at	PXMP3	peroxisomal membrane protein 3, 35kDa (Zellweger syndrome)	5828
210338_s_at	HSPA8	heat shock 70kDa protein 8	3312
210371_s_at	RBBP4	retinoblastoma binding protein 4	5928
210406_s_at	RAB6A /// RAB6C	RAB6A, member RAS oncogene family /// RAB6C, member RAS oncogene family	5870 /// 84084
210418_s_at	IDH3B	isocitrate dehydrogenase 3 (NAD+) beta	3420
210621_s_at	RASA1	RAS p21 protein activator (GTPase activating protein) 1	5921
210648_x_at	SNX3	sorting nexin 3	8724
210665_at	TFPI	tissue factor pathway inhibitor (lipoprotein-associated coagulation inhibitor)	7035
210681_s_at	USP15	ubiquitin specific peptidase 15	9958
210759_s_at	PSMA1	proteasome (prosome, macropain) subunit, alpha type, 1	5682
210774_s_at	NCOA4	nuclear receptor coactivator 4	8031
210788_s_at	DHRS7	dehydrogenase/reductase (SDR family) member 7	51635
210830_s_at	PON2	paraoxonase 2	5445
210839_s_at	ENPP2	ectonucleotide pyrophosphatase/phosphodiesterase 2 (autotaxin)	5168
210896_s_at	ASPH	aspartate beta-hydroxylase	444
210907_s_at	PDCD10	programmed cell death 10	11235
210962_s_at	AKAP9	A kinase (PRKA) anchor protein (yotiao) 9	10142
210970_s_at	IBTK	inhibitor of Bruton agammaglobulinemia tyrosine kinase	25998
210976_s_at	PFKM	phosphofructokinase, muscle	5213
210980_s_at	ASAH1	N-acylsphingosine amidohydrolase (acid ceramidase) 1	427
211023_at	PDHB	pyruvate dehydrogenase (lipoamide) beta	5162
211061_s_at	MGAT2	mannosyl (alpha-1,6-)-glycoprotein beta-1,2-N-acetylglucosaminyltransferase	4247
211063_s_at	NCK1	NCK adaptor protein 1	4690
211071_s_at	MLLT11	myeloid/lymphoid or mixed-lineage leukemia (trithorax homolog, Drosophila); translocated to, 11	10962
211185_s_at	SF3B1	splicing factor 3b, subunit 1, 155kDa	23451
211297_s_at	CDK7	cyclin-dependent kinase 7	1022
211423_s_at	SC5DL	sterol-C5-desaturase (ERG3 delta-5-desaturase homolog, S. cerevisiae)-like	6309
211569_s_at	HADH	hydroxyacyl-Coenzyme A dehydrogenase	3033
211666_x_at	RPL3	ribosomal protein L3	6122
211671_s_at	NR3C1	nuclear receptor subfamily 3, group C, member 1 (glucocorticoid receptor)	2908
211676_s_at	IFNGR1	interferon gamma receptor 1	3459
211698_at	EID1	EP300 interacting inhibitor of differentiation 1	23741
211727_s_at	COX11	COX11 homolog, cytochrome c oxidase assembly protein (yeast)	1353
211755_s_at	ATP5F1	ATP synthase, H+ transporting, mitochondrial F0 complex, subunit B1	515
211758_x_at	TXNDC9	thioredoxin domain containing 9	10190
211762_s_at	KPNA2 /// LOC728860	karyopherin alpha 2 (RAG cohort 1, importin alpha 1) /// karyopherin alpha-2 subunit like	3838 /// 643995
211763_s_at	UBE2B	ubiquitin-conjugating enzyme E2B (RAD6 homolog)	7320
211941_s_at	PEBP1	phosphatidylethanolamine binding protein 1	5037
211953_s_at	IPO5	importin 5	3843
211954_s_at	IPO5	importin 5	3843
211963_s_at	ARPC5	actin related protein 2/3 complex, subunit 5, 16kDa	10092
211972_x_at	RPLP0	ribosomal protein, large, P0	6175
211984_at	CALM1 /// CALM2 /// CALM3	calmodulin 1 (phosphorylase kinase, delta) /// calmodulin 2 (phosphorylase kinase, delta) /// calmodulin 3 (phosphorylase kinase, delta)	801
211985_s_at	CALM1 /// CALM2 /// CALM3	calmodulin 1 (phosphorylase kinase, delta) /// calmodulin 2 (phosphorylase kinase, delta) /// calmodulin 3 (phosphorylase kinase, delta)	801
211988_at	SMARCE1	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily e, member 1	6605
211994_at	WNK1	WNK lysine deficient protein kinase 1	65125
212006_at	UBXD2	UBX domain containing 2	23190

212036_s_at	PNN	pinin, desmosome associated protein	5411
212038_s_at	VDAC1	voltage-dependent anion channel 1	7416
212060_at	SR140	U2-associated SR140 protein	23350
212074_at	UNC84A	unc-84 homolog A (C. elegans)	23353
212085_at	SLC25A6	solute carrier family 25 (mitochondrial carrier; adenine nucleotide translocator), member 6	293
212131_at	LSM14A	LSM14A, SCD6 homolog A (S. cerevisiae)	26065
212148_at	PBX1	Hypothetical LOC100131938	5087
212149_at	EFR3A	EFR3 homolog A (S. cerevisiae)	23167
212154_at	SDC2	syndecan 2	6383
212158_at	SDC2	syndecan 2	6383
212160_at	XPOT	exportin, tRNA (nuclear export receptor for tRNAs)	11260
212163_at	KIDINS220	kinase D-interacting substrate of 220 kDa	57498
212168_at	RBM12	RNA binding motif protein 12	10137
212175_s_at	AK2	adenylate kinase 2	204
212179_at	SFRS18	splicing factor, arginine/serine-rich 18	25957
212180_at	CRKL	v-crk sarcoma virus CT10 oncogene homolog (avian)-like	1399
212199_at	MRFAP1L1	Morf4 family associated protein 1-like 1	114932
212205_at	H2AFV	H2A histone family, member V	94239
212206_s_at	H2AFV	H2A histone family, member V	94239
212215_at	PREPL	prolyl endopeptidase-like	9581
212222_at	PSME4	proteasome (prosome, macropain) activator subunit 4	23198
212224_at	ALDH1A1	aldehyde dehydrogenase 1 family, member A1	216
212229_s_at	FBXO21	F-box protein 21	23014
212233_at	MAP1B	microtubule-associated protein 1B	---
212246_at	MCFD2	multiple coagulation factor deficiency 2	90411
212250_at	MTDH	metadherin	92140
212293_at	HIPK1	homeodomain interacting protein kinase 1	204851
212296_at	PSMD14	proteasome (prosome, macropain) 26S subunit, non-ATPase, 14	10213
212298_at	NRP1	neuropilin 1	8829
212321_at	SGPL1	sphingosine-1-phosphate lyase 1	---
212330_at	TFDP1	transcription factor Dp-1	7027
212331_at	RBL2	retinoblastoma-like 2 (p130)	5934
212333_at	FAM98A	family with sequence similarity 98, member A	25940
212335_at	GNS	glucosamine (N-acetyl)-6-sulfatase (Sanfilippo disease IIID)	2799
212341_at	YIPF6	Yip1 domain family, member 6	286451
212345_s_at	CREB3L2	cAMP responsive element binding protein 3-like 2	64764
212352_s_at	TMED10	transmembrane emp24-like trafficking protein 10 (yeast)	10972
212361_s_at	ATP2A2	ATPase, Ca++ transporting, cardiac muscle, slow twitch 2	488
212364_at	MYO1B	myosin IB	4430
212371_at	FAM152A	family with sequence similarity 152, member A	51029
212397_at	RDX	radixin	5962
212402_at	ZC3H13	zinc finger CCCH-type containing 13	23091
212408_at	TOR1AIP1	torsin A interacting protein 1	26092
212416_at	SCAMP1	secretory carrier membrane protein 1	9522
212418_at	ELF1	E74-like factor 1 (ets domain transcription factor)	1997
212429_s_at	GTF3C2	general transcription factor IIIC, polypeptide 2, beta 110kDa	2976
212433_x_at	RPS2	ribosomal protein S2	6187
212440_at	RY1	putative nucleic acid binding protein RY-1	11017
212449_s_at	LYPLA1	lysophospholipase I	10434
212453_at	KIAA1279	KIAA1279	26128
212458_at	SPRED2	sprouty-related, EVH1 domain containing 2	200734
212460_at	C14orf147	chromosome 14 open reading frame 147	171546
212461_at	AZIN1	antizyme inhibitor 1	51582
212470_at	SPAG9	sperm associated antigen 9	9043
212476_at	CENTB2	centaurin, beta 2	23527
212485_at	GPATCH8	G patch domain containing 8	23131
212507_at	TMEM131	transmembrane protein 131	23505
212508_at	MOAP1	modulator of apoptosis 1	64112
212509_s_at	MXRA7	matrix-remodelling associated 7	439921
212515_s_at	DDX3X	DEAD (Asp-Glu-Ala-Asp) box polypeptide 3, X-linked	1654
212519_at	UBE2E1	ubiquitin-conjugating enzyme E2E 1 (UBC4/5 homolog, yeast)	7324
212530_at	NEK7	NIMA (never in mitosis gene a)-related kinase 7	140609
212532_s_at	LSM12	LSM12 homolog (S. cerevisiae)	124801 /// 653122
212535_at	MEF2A	myocyte enhancer factor 2A	4205
212544_at	ZNHIT3	zinc finger, HIT type 3	9326

212560_at	SORL1	sortilin-related receptor, L(DLR class) A repeats-containing	442871
212573_at	ENDOD1	endonuclease domain containing 1	23052
212582_at	OSBPL8	oxysterol binding protein-like 8	114882
212585_at	OSBPL8	oxysterol binding protein-like 8	114882
212589_at	RRAS2	related RAS viral (r-ras) oncogene homolog 2	6342
212600_s_at	UQCRC2	ubiquinol-cytochrome c reductase core protein II	7385
212610_at	PTPN11	protein tyrosine phosphatase, non-receptor type 11 (Noonan syndrome 1)	5781
212612_at	RCOR1	REST corepressor 1	23186
212614_at	ARID5B	AT rich interactive domain 5B (MRF1-like)	84159
212615_at	CHD9	chromodomain helicase DNA binding protein 9	80205
212623_at	TMEM41B	transmembrane protein 41B	440026
212628_at	PKN2	protein kinase N2	5586
212633_at	KIAA0776	KIAA0776	23376
212635_at	TNPO1	transportin 1	3842
212641_at	HIVEP2	human immunodeficiency virus type I enhancer binding protein 2	3097
212648_at	DHX29	DEAH (Asp-Glu-Ala-His) box polypeptide 29	54505
212652_s_at	SNX4	sorting nexin 4	8723
212653_s_at	EHBP1	EH domain binding protein 1	23301
212655_at	ZCCHC14	zinc finger, CCHC domain containing 14	23174
212690_at	DDHD2	DDHD domain containing 2	23259
212692_s_at	LRBA	LPS-responsive vesicle trafficking, beach and anchor containing	987
212694_s_at	PCCB	propionyl Coenzyme A carboxylase, beta polypeptide	5096
212698_s_at	SEPT10	septin 10	151011
212714_at	LARP4	La ribonucleoprotein domain family, member 4	113251
212718_at	PAPOLA	poly(A) polymerase alpha	10914
212731_at	ANKRD46	ankyrin repeat domain 46	157567
212740_at	PIK3R4	phosphoinositide-3-kinase, regulatory subunit 4	30849
212749_s_at	RCHY1	ring finger and CHY zinc finger domain containing 1	25898
212751_at	UBE2N	ubiquitin-conjugating enzyme E2N (UBC13 homolog, yeast)	7334
212795_at	KIAA1033	KIAA1033	23325
212798_s_at	ANKMY2	ankyrin repeat and MYND domain containing 2	57037
212805_at	LOC100129762 /// PRUNE2	prune homolog 2 (Drosophila) /// similar to KIAA0367	23273
212815_at	ASCC3	activating signal cointegrator 1 complex subunit 3	10973
212833_at	SLC25A46	solute carrier family 25, member 46	91137
212847_at	FUBP1	Far upstream element (FUSE) binding protein 1	8880
212848_s_at	C9orf3	chromosome 9 open reading frame 3	84909
212854_x_at	NBPF10	neuroblastoma breakpoint family, member 10	440673
212855_at	DCUN1D4	DCN1, defective in cullin neddylation 1, domain containing 4 (S. cerevisiae)	23142
212878_s_at	KLC1	kinesin light chain 1	3831
212887_at	SEC23A	Sec23 homolog A (S. cerevisiae)	10484
212893_at	ZZZ3	zinc finger, ZZ-type containing 3	26009
212896_at	SKIV2L2	superkiller viralicidic activity 2-like 2 (S. cerevisiae)	23517
212902_at	SEC24A	SEC24 related gene family, member A (S. cerevisiae)	10802
212907_at	SLC30A1	Solute carrier family 30 (zinc transporter), member 1	7779
212918_at	RECQL	RecQ protein-like (DNA helicase Q1-like)	5965
212928_at	TSPYL4	TSPY-like 4	23270
212943_at	KIAA0528	KIAA0528	9847
212956_at	TBC1D9	TBC1 domain family, member 9 (with GRAM domain)	23158
212961_x_at	CXorf40A /// CXorf40B	chromosome X open reading frame 40A /// chromosome X open reading frame 40B	541578
212978_at	LRRC8B	leucine rich repeat containing 8 family, member B	23507
212987_at	FBXO9	F-box protein 9	26268
212989_at	SGMS1	sphingomyelin synthase 1	259230
213009_s_at	TRIM37	tripartite motif-containing 37	4591
213019_at	RANBP6	RAN binding protein 6	26953
213049_at	GARNL1	GTPase activating Rap/RanGAP domain-like 1	253959
213077_at	YTHDC2	YTH domain containing 2	64848
213086_s_at	CSNK1A1	casein kinase 1, alpha 1	1452
213088_s_at	DNAJC9	DnaJ (Hsp40) homolog, subfamily C, member 9	23234
213111_at	PIP5K3	phosphatidylinositol-3-phosphate/phosphatidylinositol 5-kinase, type III	200576
213118_at	UHRF1BP1L	UHRF1 (ICBP90) binding protein 1-like	23074
213122_at	TSPYL5	TSPY-like 5	85453
213128_s_at	UBE3A	ubiquitin protein ligase E3A (human papilloma virus E6-associated protein, Angelman syndrome)	7337
213129_s_at	GCSH /// LOC730107	glycine cleavage system protein H (aminomethyl carrier) /// similar to Glycine cleavage system H protein, mitochondrial	2653 /// 653763 ///

			654085
213140_s_at	SS18L1	synovial sarcoma translocation gene on chromosome 18-like 1	26039
213165_at	CEP350	centrosomal protein 350kDa	9857
213169_at	SEMA5A	sema domain, seven thrombospondin repeats (type 1 and type 1-like), transmembrane domain (TM) and short cytoplasmic domain, (semaphorin) 5A	---
213175_s_at	SNRPB	small nuclear ribonucleoprotein polypeptides B and B1	6628
213187_x_at	FTL	ferritin, light polypeptide	2512
213194_at	ROBO1	roundabout, axon guidance receptor, homolog 1 (Drosophila)	6091
213222_at	PLCB1	phospholipase C, beta 1 (phosphoinositide-specific)	23236
213224_s_at	LOC92482	hypothetical LOC92482	92482
213225_at	PPM1B	protein phosphatase 1B (formerly 2C), magnesium-dependent, beta isoform	5495
213227_at	PGRMC2	progesterone receptor membrane component 2	10424
213246_at	C14orf109	chromosome 14 open reading frame 109	26175
213251_at	SMARCA5	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily a, member 5	8467
213285_at	TMEM30B	transmembrane protein 30B	161291
213287_s_at	KRT10	keratin 10 (epidermolytic hyperkeratosis; keratosis palmaris et plantaris)	3858
213291_s_at	UBE3A	ubiquitin protein ligase E3A (human papilloma virus E6-associated protein, Angelman syndrome)	7337
213304_at	KIAA0423	KIAA0423	23116
213315_x_at	CXorf40A	chromosome X open reading frame 40A	91966
213320_at	PRMT3	protein arginine methyltransferase 3	10196
213325_at	PVRL3	poliovirus receptor-related 3	25945
213359_at	HNRNPD	Heterogeneous nuclear ribonucleoprotein D (AU-rich element RNA binding protein 1, 37kDa)	3184
213376_at	ZBTB1	zinc finger and BTB domain containing 1	22890
213404_s_at	RHEB	Ras homolog enriched in brain	6009
213405_at	RAB22A	RAB22A, member RAS oncogene family	57403
213465_s_at	PPP1R7	protein phosphatase 1, regulatory (inhibitor) subunit 7	5510
213545_x_at	SNX3	sorting nexin 3	8724
213555_at	RWDD2A	RWD domain containing 2A	112611
213624_at	SMPDL3A	sphingomyelin phosphodiesterase, acid-like 3A	10924
213687_s_at	RPL35A	ribosomal protein L35a	6165
213694_at	RSBN1	round spermatid basic protein 1	54665
213704_at	RABGGTB	Rab geranylgeranyltransferase, beta subunit	5876
213738_s_at	ATP5A1	ATP synthase, H+ transporting, mitochondrial F1 complex, alpha subunit 1, cardiac muscle	498
213750_at	RSL1D1	ribosomal L1 domain containing 1	---
213822_s_at	UBE3B	ubiquitin protein ligase E3B	89910
213838_at	NOL7	nucleolar protein 7, 27kDa	51406
213878_at	PYROXD1	Pyridine nucleotide-disulphide oxidoreductase domain 1	3375
213911_s_at	H2AFZ	H2A histone family, member Z	3015
213995_at	ATP5S	ATP synthase, H+ transporting, mitochondrial F0 complex, subunit s (factor B)	27109
214079_at	DHRS2	dehydrogenase/reductase (SDR family) member 2	10202
214091_s_at	GPX3	glutathione peroxidase 3 (plasma)	2878
214141_x_at	SFRS7	splicing factor, arginine/serine-rich 7, 35kDa	6432
214151_s_at	CCPG1	cell cycle progression 1	9236
214157_at	GNAS	GNAS complex locus	2778
214167_s_at	RPLP0 /// RPLP0-like	ribosomal protein, large, P0 /// ribosomal protein P0-like	220717 /// 6175
214214_s_at	C1QBP	complement component 1, q subcomponent binding protein	708
214281_s_at	RCHY1	ring finger and CHY zinc finger domain containing 1	25898
214323_s_at	UPF3A	UPF3 regulator of nonsense transcripts homolog A (yeast)	65110
214359_s_at	HSP90AB1	heat shock protein 90kDa alpha (cytosolic), class B member 1	3326
214429_at	MTMR6	myotubularin related protein 6	9107
214527_s_at	PQBP1	polyglutamine binding protein 1	10084
214658_at	TMED7	transmembrane emp24 protein transport domain containing 7	51014
214665_s_at	CHP	calcium binding protein P22	11261
214683_s_at	CLK1	CDC-like kinase 1	1195
214709_s_at	KTN1	kinectin 1 (kinesin receptor)	10130 /// 3895
214741_at	ZNF131	zinc finger protein 131	7690
214774_x_at	TOX3	TOX high mobility group box family member 3	27324
214835_s_at	SUCLG2	succinate-CoA ligase, GDP-forming, beta subunit	8801
214855_s_at	GARNL1	GTPase activating Rap/RanGAP domain-like 1	253959
214882_s_at	SFRS2	splicing factor, arginine/serine-rich 2	6427

214961_at	KIAA0774	KIAA0774	23281
215017_s_at	FNBP1L	formin binding protein 1-like	54874
215108_x_at	TOX3	TOX high mobility group box family member 3	27324
215380_s_at	C7orf24	chromosome 7 open reading frame 24	79017
215416_s_at	STOML2	stomatin (EPB72)-like 2	30968
215440_s_at	BEX4	BEX family member 4	56271
215596_s_at	ZNF294	zinc finger protein 294	26046
215952_s_at	OAZ1	ornithine decarboxylase antizyme 1	4946
216064_s_at	AGA	aspartylglucosaminidase	175
216241_s_at	TCEA1	transcription elongation factor A (SII), 1	6917
216274_s_at	SEC11A	SEC11 homolog A (S. cerevisiae)	23478
216623_x_at	TOX3	TOX high mobility group box family member 3	27324
216640_s_at	PDIA6	protein disulfide isomerase family A, member 6	10130
217168_s_at	HERPUD1	homocysteine-inducible, endoplasmic reticulum stress-inducible, ubiquitin-like domain member 1	9709
217356_s_at	PGK1	phosphoglycerate kinase 1	5230
217724_at	SERBP1	SERPINE1 mRNA binding protein 1	26135
217732_s_at	ITM2B	integral membrane protein 2B	9445
217738_at	NAMPT	nicotinamide phosphoribosyltransferase	10135 /// 646309
217743_s_at	TMEM30A	transmembrane protein 30A	55754
217745_s_at	NAT13	N-acetyltransferase 13	80218
217746_s_at	PDCD6IP	programmed cell death 6 interacting protein	10015
217759_at	TRIM44	tripartite motif-containing 44	54765
217766_s_at	TMEM50A	transmembrane protein 50A	23585
217770_at	PIGT	phosphatidylinositol glycan anchor biosynthesis, class T	51604
217772_s_at	MTCH2	mitochondrial carrier homolog 2 (C. elegans)	23788
217779_s_at	LOC100132235 /// PNRC2	proline-rich nuclear receptor coactivator 2 /// hypothetical protein LOC100132235	55629 /// 644047 /// 653105
217786_at	PRMT5	protein arginine methyltransferase 5	10419
217790_s_at	SSR3	signal sequence receptor, gamma (translocon-associated protein gamma)	6747
217797_at	UFC1	ubiquitin-fold modifier conjugating enzyme 1	51506
217803_at	GOLPH3	golgi phosphoprotein 3 (coat-protein)	64083
217811_at	SELT	selenoprotein T	51714
217814_at	CCDC47	coiled-coil domain containing 47	57003
217816_s_at	PCNP	PEST proteolytic signal containing nuclear protein	57092
217819_at	GOLGA7	golgi autoantigen, golgin subfamily a, 7	51125
217821_s_at	WBP11	WW domain binding protein 11	51729
217823_s_at	UBE2J1	ubiquitin-conjugating enzyme E2, J1 (UBC6 homolog, yeast)	51465
217827_s_at	SPG21	spastic paraplegia 21 (autosomal recessive, Mast syndrome)	51324
217828_at	SLTM	SAFB-like, transcription modulator	79811
217832_at	SYNCRIP	synaptotagmin binding, cytoplasmic RNA interacting protein	10492
217833_at	SYNCRIP	synaptotagmin binding, cytoplasmic RNA interacting protein	10492
217837_s_at	VPS24	vacuolar protein sorting 24 homolog (S. cerevisiae)	51652
217848_s_at	PPA1	pyrophosphatase (inorganic) 1	5464
217850_at	GNL3	guanine nucleotide binding protein-like 3 (nucleolar)	26354
217851_s_at	SLMO2	slowmo homolog 2 (Drosophila)	51012
217852_s_at	ARL8B	ADP-ribosylation factor-like 8B	55207
217869_at	HSD17B12	hydroxysteroid (17-beta) dehydrogenase 12	51144
217883_at	C2orf25	chromosome 2 open reading frame 25	27249
217886_at	EPS15	epidermal growth factor receptor pathway substrate 15	2060
217894_at	KCTD3	potassium channel tetramerisation domain containing 3	51133
217898_at	C15orf24	chromosome 15 open reading frame 24	56851
217900_at	IARS2	isoleucyl-tRNA synthetase 2, mitochondrial	55699
217906_at	KLHDC2	kelch domain containing 2	23588
217915_s_at	C15orf15	chromosome 15 open reading frame 15	51187
217927_at	SPCS1	signal peptidase complex subunit 1 homolog (S. cerevisiae)	28972
217940_s_at	FLJ10769	hypothetical protein FLJ10769	55739
217941_s_at	ERBB2IP	erbb2 interacting protein	55914
217955_at	BCL2L13	BCL2-like 13 (apoptosis facilitator)	23786
217956_s_at	ENOPH1	enolase-phosphatase 1	58478
217957_at	C16orf80	chromosome 16 open reading frame 80	29105
217959_s_at	TRAPPC4	trafficking protein particle complex 4	51399
217964_at	TTC19	tetratricopeptide repeat domain 19	54902
217971_at	MAP2K1IP1	mitogen-activated protein kinase kinase 1 interacting protein 1	8649
217976_s_at	DYNC1LI1	dynein, cytoplasmic 1, light intermediate chain 1	51143

217978_s_at	UBE2Q1	ubiquitin-conjugating enzyme E2Q family member 1	55585
217982_s_at	MORF4L1	mortality factor 4 like 1	10933
217987_at	ASNSD1	asparagine synthetase domain containing 1	54529
217988_at	CCNB1IP1	cyclin B1 interacting protein 1	57820
217989_at	HSD17B11	hydroxysteroid (17-beta) dehydrogenase 11	51170
217993_s_at	MAT2B	methionine adenosyltransferase II, beta	27430
217995_at	SQRDL	sulfide quinone reductase-like (yeast)	58472
218008_at	C7orf42	chromosome 7 open reading frame 42	55069
218024_at	BRP44L	brain protein 44-like	51660
218025_s_at	PECI	peroxisomal D3,D2-enoyl-CoA isomerase	10455
218027_at	MRPL15	mitochondrial ribosomal protein L15	29088
218034_at	FIS1	fission 1 (mitochondrial outer membrane) homolog (S. cerevisiae)	51024
218042_at	COPS4	COP9 constitutive photomorphogenic homolog subunit 4 (Arabidopsis)	51138
218047_at	OSBPL9	oxysterol binding protein-like 9	114883
218049_s_at	MRPL13	mitochondrial ribosomal protein L13	28998
218059_at	ZNF706	zinc finger protein 706	51123
218067_s_at	ARGLU1	arginine and glutamate rich 1	55082
218079_s_at	GGNBP2	gametogenetin binding protein 2	79893
218092_s_at	HRB	HIV-1 Rev binding protein	3267 /// 649094
218095_s_at	TMEM165	transmembrane protein 165	55858
218098_at	ARFGEF2	ADP-ribosylation factor guanine nucleotide-exchange factor 2 (brefeldin A-inhibited)	---
218102_at	DERA	2-deoxyribose-5-phosphate aldolase homolog (C. elegans)	51071
218108_at	C14orf130	chromosome 14 open reading frame 130	55148
218111_s_at	CMAS	cytidine monophosphate N-acetylneuraminic acid synthetase	55907
218135_at	ERGIC2	ERGIC and golgi 2	51290
218137_s_at	SMAP1	stromal membrane-associated GTPase-activating protein 1	60682
218138_at	MKKS	McKusick-Kaufman syndrome	8195
218139_s_at	C14orf108	chromosome 14 open reading frame 108	55745
218140_x_at	SRPRB	signal recognition particle receptor, B subunit	58477
218147_s_at	GLT8D1	glycosyltransferase 8 domain containing 1	55830
218152_at	HMG20A	high-mobility group 20A	10363
218156_s_at	TSR1	TSR1, 20S rRNA accumulation, homolog (S. cerevisiae)	55720
218160_at	NDUFA8	NADH dehydrogenase (ubiquinone) 1 alpha subcomplex, 8, 19kDa	4702
218165_at	C1orf149	chromosome 1 open reading frame 149	64769
218167_at	AMZ2	archaelysin family metallopeptidase 2	51321
218170_at	ISOC1	isochorismatase domain containing 1	51015
218172_s_at	DERL1	Der1-like domain family, member 1	79139
218191_s_at	LMBRD1	LMBR1 domain containing 1	55788
218194_at	REXO2	REX2, RNA exonuclease 2 homolog (S. cerevisiae)	25996
218195_at	C6orf211	chromosome 6 open reading frame 211	79624
218196_at	OSTM1	osteopetrosis associated transmembrane protein 1	28962
218203_at	ALG5	asparagine-linked glycosylation 5 homolog (S. cerevisiae, dolichyl-phosphate beta-glucosyltransferase)	29880
218224_at	PNMA1	paraneoplastic antigen MA1	9240
218229_s_at	POGK	pogo transposable element with KRAB domain	57645
218230_at	ARFIP1	ADP-ribosylation factor interacting protein 1 (arfaptin 1)	27236
218236_s_at	PRKD3	protein kinase D3	23683
218238_at	GTPBP4	GTP binding protein 4	23560
218241_at	GOLGA5	golgi autoantigen, golgin subfamily a, 5	9950
218250_s_at	CNOT7	CCR4-NOT transcription complex, subunit 7	29883
218254_s_at	SAR1B	SAR1 gene homolog B (S. cerevisiae)	51128
218256_s_at	NUP54	nucleoporin 54kDa	53371
218259_at	MKL2	MKL/myocardin-like 2	57496
218263_s_at	ZBED5	zinc finger, BED-type containing 5	58486
218277_s_at	DHX40	DEAH (Asp-Glu-Ala-His) box polypeptide 40	79665
218286_s_at	RNF7	ring finger protein 7	9616
218289_s_at	UBA5	ubiquitin-like modifier activating enzyme 5	79876
218303_x_at	KRCC1	lysine-rich coiled-coil 1	51315
218311_at	MAP4K3	mitogen-activated protein kinase kinase kinase kinase 3	8491
218326_s_at	LGR4	leucine-rich repeat-containing G protein-coupled receptor 4	55366
218331_s_at	C10orf18	chromosome 10 open reading frame 18	54906
218332_at	BEX1	brain expressed, X-linked 1	55859
218339_at	MRPL22	mitochondrial ribosomal protein L22	29093
218341_at	PPCS	phosphopantothenoylcysteine synthetase	79717
218343_s_at	GTF3C3	general transcription factor IIIC, polypeptide 3, 102kDa	9330
218346_s_at	SESN1	sestrin 1	27244
218351_at	COMMD8	COMM domain containing 8	54951

218360_at	RAB22A	RAB22A, member RAS oncogene family	57403
218375_at	NUDT9	nudix (nucleoside diphosphate linked moiety X)-type motif 9	53343
218380_at	NLRP1	NLR family, pyrin domain containing 1	22861
218386_x_at	USP16	ubiquitin specific peptidase 16	10600
218395_at	ACTR6	ARP6 actin-related protein 6 homolog (yeast)	64431
218398_at	MRPS30	mitochondrial ribosomal protein S30	10884
218432_at	FBXO3	F-box protein 3	26273
218437_s_at	LZTFL1	leucine zipper transcription factor-like 1	54585
218446_s_at	FAM18B	family with sequence similarity 18, member B	51030
218449_at	UFSP2	UFM1-specific peptidase 2	55325
218462_at	BXDC5	brix domain containing 5	80135
218465_at	TMEM33	transmembrane protein 33	55161
218468_s_at	GREM1	gremlin 1, cysteine knot superfamily, homolog (Xenopus laevis)	26585
218469_at	GREM1	gremlin 1, cysteine knot superfamily, homolog (Xenopus laevis)	26585
218472_s_at	PELO	pelota homolog (Drosophila)	53918
218477_at	TMEM14A	transmembrane protein 14A	28978
218512_at	WDR12	WD repeat domain 12	55759
218518_at	C5orf5	chromosome 5 open reading frame 5	51306
218519_at	SLC35A5	solute carrier family 35, member A5	55032
218520_at	TBK1	TANK-binding kinase 1	29110
218528_s_at	RNF38	ring finger protein 38	152006
218535_s_at	RIOK2	RIO kinase 2 (yeast)	55781
218538_s_at	MRS2	MRS2 magnesium homeostasis factor homolog (S. cerevisiae)	57380
218558_s_at	MRPL39	mitochondrial ribosomal protein L39	54148
218559_s_at	MAFB	v-maf musculoaponeurotic fibrosarcoma oncogene homolog B (avian)	9935
218576_s_at	DUSP12	dual specificity phosphatase 12	11266
218577_at	LRRC40	leucine rich repeat containing 40	55631
218605_at	TFB2M	transcription factor B2, mitochondrial	64216
218613_at	PSD3	pleckstrin and Sec7 domain containing 3	653754
218616_at	INTS12	integrator complex subunit 12	57117
218622_at	NUP37	nucleoporin 37kDa	79023
218640_s_at	PLEKHF2	pleckstrin homology domain containing, family F (with FYVE domain) member 2	79666
218645_at	ZNF277	zinc finger protein 277	11179
218669_at	RAP2C	RAP2C, member of RAS oncogene family	57826
218683_at	PTBP2	polypyrimidine tract binding protein 2	58155
218692_at	GOLSYN	Golgi-localized protein	55638
218694_at	ARMCX1	armadillo repeat containing, X-linked 1	51309
218696_at	EIF2AK3	eukaryotic translation initiation factor 2-alpha kinase 3	9451
218698_at	APIP	APAF1 interacting protein	51074
218721_s_at	C1orf27	chromosome 1 open reading frame 27	54953
218738_s_at	RNF138	ring finger protein 138	51444
218750_at	JOSD3	Josephin domain containing 3	79101
218764_at	PRKCH	protein kinase C, eta	5583
218768_at	NUP107	nucleoporin 107kDa	57122
218820_at	C14orf132 /// LOC100132684	chromosome 14 open reading frame 132 /// hypothetical protein LOC100132684	56967
218823_s_at	KCTD9	potassium channel tetramerisation domain containing 9	54793
218852_at	PPP2R3C	protein phosphatase 2 (formerly 2A), regulatory subunit B", gamma	55012
218877_s_at	TRMT11	tRNA methyltransferase 11 homolog (S. cerevisiae)	60487
218885_s_at	GALNT12	UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 12 (GalNAc-T12)	79695
218889_at	NOC3L	nucleolar complex associated 3 homolog (S. cerevisiae)	64318
218905_at	INTS8	integrator complex subunit 8	55656
218917_s_at	ARID1A	AT rich interactive domain 1A (SWI-like)	8289
218919_at	ZFAND1	zinc finger, AN1-type domain 1	79752
218932_at	C1orf181	chromosome 1 open reading frame 181	54680
218970_s_at	CUTC	cutC copper transporter homolog (E. coli)	51076
218976_at	DNAJC12	DnaJ (Hsp40) homolog, subfamily C, member 12	56521
218989_x_at	SLC30A5	solute carrier family 30 (zinc transporter), member 5	64924
219017_at	ETNK1	ethanolamine kinase 1	55500
219029_at	C5orf28	chromosome 5 open reading frame 28	64417
219030_at	TPRKB	TP53RK binding protein	51002
219037_at	RRP15	ribosomal RNA processing 15 homolog (S. cerevisiae)	51018
219043_s_at	LOC285359 /// PDCL3	phosducin-like 3 /// phosducin-like 3 pseudogene	285359 /// 644850 /// 79031
219060_at	C8orf32	chromosome 8 open reading frame 32	55093

219069_at	ANKRD49	ankyrin repeat domain 49	54851
219079_at	CYB5R4	cytochrome b5 reductase 4	51167
219083_at	SHQ1	SHQ1 homolog (S. cerevisiae)	55164
219099_at	C12orf5	chromosome 12 open reading frame 5	57103
219133_at	OXSM	3-oxoacyl-ACP synthase, mitochondrial	54995
219137_s_at	C2orf33	chromosome 2 open reading frame 33	56947
219140_s_at	RBP4	retinol binding protein 4, plasma	5950
219147_s_at	C9orf95	chromosome 9 open reading frame 95	54981
219176_at	C2orf47	chromosome 2 open reading frame 47	79568
219196_at	SCG3	secretogranin III	29106
219200_at	FASTKD3	FAST kinase domains 3	79072
219212_at	HSPA14	heat shock 70kDa protein 14	51182
219242_at	CEP63	centrosomal protein 63kDa	80254
219274_at	TSPAN12	tetraspanin 12	23554
219283_at	C1GALT1C1	C1GALT1-specific chaperone 1	29071
219288_at	C3orf14	chromosome 3 open reading frame 14	57415
219303_at	RNF219	ring finger protein 219	79596
219329_s_at	C2orf28	chromosome 2 open reading frame 28	51374
219342_at	CASD1	CAS1 domain containing 1	64921
219343_at	CDC37L1	cell division cycle 37 homolog (S. cerevisiae)-like 1	55664
219355_at	CXorf57	chromosome X open reading frame 57	55086
219356_s_at	CHMP5	chromatin modifying protein 5	51510
219368_at	NAP1L2	nucleosome assembly protein 1-like 2	4674
219443_at	TASP1	taspase, threonine aspartase, 1	55617
219449_s_at	TMEM70	transmembrane protein 70	54968
219467_at	GIN1	gypsy retrotransposon integrase 1	54826
219485_s_at	PSMD10	proteasome (prosome, macropain) 26S subunit, non-ATPase, 10	5716
219553_at	NME7	non-metastatic cells 7, protein expressed in (nucleoside-diphosphate kinase)	29922
219569_s_at	TMEM22	transmembrane protein 22	80723
219598_s_at	RWDD1	RWD domain containing 1	51389
219603_s_at	ZNF226	zinc finger protein 226	7769
219816_s_at	RBM23	RNA binding motif protein 23	55147
219819_s_at	MRPS28	mitochondrial ribosomal protein S28	28957
219939_s_at	CSDE1	cold shock domain containing E1, RNA-binding	7812
220012_at	ERO1LB	ERO1-like beta (S. cerevisiae)	56605
220099_s_at	LUC7L2	LUC7-like 2 (S. cerevisiae)	51631
220175_s_at	CBWD1 /// CBWD2 /// CBWD3 /// CBWD5 /// CBWD6 /// CBWD7 /// LOC100132072 /// LOC100133216	COBW domain containing 1 /// COBW domain containing 2 /// COBW domain containing 5 /// COBW domain containing 3 /// COBW domain containing 6 /// COBW domain containing 7 /// hypothetical protein LOC100132072 /// hypothetical protein LOC100133216	150472 /// 220869 /// 389760 /// 445571 /// 55871 /// 644019 /// 653165
220495_s_at	TXNDC15	thioredoxin domain containing 15	79770
220607_x_at	TH1L	TH1-like (Drosophila)	51497
220643_s_at	FAIM	Fas apoptotic inhibitory molecule	55179
220690_s_at	DHRS7B	dehydrogenase/reductase (SDR family) member 7B	25979
220890_s_at	DDX47	DEAD (Asp-Glu-Ala-Asp) box polypeptide 47	51202
220939_s_at	DPP8	dipeptidyl-peptidase 8	54878
220990_s_at	MIRN21 /// TMEM49	transmembrane protein 49 /// microRNA 21	406991 /// 81671
221020_s_at	SLC25A32	solute carrier family 25, member 32	81034
221245_s_at	FZD5	frizzled homolog 5 (Drosophila)	7855
221253_s_at	MUTED /// TXNDC5	muted homolog (mouse) /// thioredoxin domain containing 5	81567
221264_s_at	LOC100128223 /// TARDBP	TAR DNA binding protein /// hypothetical protein LOC100128223	23435
221381_s_at	MORF4 /// MORF4L1	mortality factor 4 like 1 /// mortality factor 4	10933 /// 10934
221449_s_at	ITFG1	integrin alpha FG-GAP repeat containing 1	81533
221452_s_at	TMEM14B	transmembrane protein 14B	79133 /// 81853
221476_s_at	RPL15	ribosomal protein L15	6138

221482_s_at	ARPP-19	cyclic AMP phosphoprotein, 19 kD	10776
221486_at	ENSA	endosulfine alpha	2029
221492_s_at	ATG3	ATG3 autophagy related 3 homolog (S. cerevisiae)	64422
221493_at	TSPYL1	TSPY-like 1	7259
221502_at	KPNA3	karyopherin alpha 3 (importin alpha 4)	3839
221504_s_at	ATP6V1H	ATPase, H+ transporting, lysosomal 50/57kDa, V1 subunit H	51606
221505_at	ANP32E	acidic (leucine-rich) nuclear phosphoprotein 32 family, member E	81611
221510_s_at	GLS	glutaminase	2744
221523_s_at	RRAGD	Ras-related GTP binding D	58528
221532_s_at	WDR61	WD repeat domain 61	80349
221547_at	PRPF18	PRP18 pre-mRNA processing factor 18 homolog (S. cerevisiae)	8559
221556_at	CDC14B /// CDC14C	CDC14 cell division cycle 14 homolog B (S. cerevisiae) /// CDC14 cell division cycle 14 homolog C (S. cerevisiae)	8555
221568_s_at	LIN7C	lin-7 homolog C (C. elegans)	55327
221580_s_at	JOSD3	Josephin domain containing 3	79101
221584_s_at	KCNMA1	potassium large conductance calcium-activated channel, subfamily M, alpha member 1	3778
221726_at	RPL22	ribosomal protein L22	6146
221727_at	SUB1	SUB1 homolog (S. cerevisiae)	---
221751_at	SLC2A3P1	Solute carrier family 2 (facilitated glucose transporter), member 3 pseudogene 1	6516
221760_at	MAN1A1	Mannosidase, alpha, class 1A, member 1	4121
221761_at	ADSS	adenylosuccinate synthase	159
221763_at	JMJD1C	jumonji domain containing 1C	221037
221781_s_at	DNAJC10	DnaJ (Hsp40) homolog, subfamily C, member 10	54431
221786_at	C6orf120	chromosome 6 open reading frame 120	387263
221787_at	C6orf120	chromosome 6 open reading frame 120	387263
221824_s_at	MARCH8	membrane-associated ring finger (C3HC4) 8	220972
221896_s_at	HIGD1A	HIG1 domain family, member 1A	25994
221911_at	ETV1	ets variant gene 1	2115
221952_x_at	TRMT5	TRM5 tRNA methyltransferase 5 homolog (S. cerevisiae)	57570 /// 653695
221972_s_at	stromal cell derived factor 4	chr1:1142200-1153967 (-) // 94.65 // p36.33	ENSG00000078808
222035_s_at	PAPOLA	poly(A) polymerase alpha	10914
222044_at	PCIF1	PDX1 C-terminal inhibiting factor 1	---
222103_at	ATF1	activating transcription factor 1	466
222127_s_at	EXOC1	exocyst complex component 1	55763
222140_s_at	GPR89A /// GPR89B /// GPR89C	G protein-coupled receptor 89B /// G protein-coupled receptor 89A /// G protein-coupled receptor 89C	51463 /// 653519
222150_s_at	tcag7.1314	hypothetical protein LOC54103	54103
222204_s_at	RRN3	RRN3 RNA polymerase I transcription factor homolog (S. cerevisiae)	54700
222209_s_at	TMEM135	transmembrane protein 135	65084
222230_s_at	ACTR10	actin-related protein 10 homolog (S. cerevisiae)	55860
222231_s_at	LRRC59	leucine rich repeat containing 59	55379
222235_s_at	CSGALNACT2	chondroitin sulfate N-acetylgalactosaminyltransferase 2	55454 /// 644504
40189_at	SET	SET nuclear oncogene	6418
AFFX-HUMGAPDH/M33197_5_at	GAPDH	glyceraldehyde-3-phosphate dehydrogenase	2597
AFFX-HUMGAPDH/M33197_M_at	GAPDH	glyceraldehyde-3-phosphate dehydrogenase	2597

Dati supplementari, tabella 2. Risultati delle analisi dei processi di gene ontology (GO) e KEGG.

Geni downregolati

GOID	Term	Count	Size	Pvalue
GO:0051436	negative regulation of ubiquitin-protein ligase activity during mitotic cell cycle	24	62	7,13E-11
GO:0031145	anaphase-promoting complex-dependent proteasomal ubiquitin-dependent protein catabolic process	24	63	5,43E-11
GO:0051437	positive regulation of ubiquitin-protein ligase activity during mitotic cell cycle	24	65	8,17E-11
GO:0008380	RNA splicing	44	264	3,03E-07
GO:0006886	intracellular protein transport	34	180	7,64E-07
GO:0015031	protein transport	54	400	6,13E-06
GO:0016192	vesicle-mediated transport	31	171	7,42E-06
GO:0006888	ER to Golgi vesicle-mediated transport	14	41	1,13E-05
GO:0006511	ubiquitin-dependent protein catabolic process	27	144	2,13E-05
GO:0006397	mRNA processing	37	245	3,63E-05
GO:0016044	cellular membrane organization	15	58	0,000166
GO:0006413	translational initiation	12	38	0,000174
GO:0044419	interspecies interaction between organisms	40	300	0,000249
GO:0006099	tricarboxylic acid cycle	9	22	0,00027
GO:0006613	cotranslational protein targeting to membrane	6	9	0,000343
GO:0051028	mRNA transport	13	56	0,002071
GO:0007049	cell cycle	50	459	0,003543
GO:0051603	proteolysis involved in cellular protein catabolic process	8	24	0,00443
GO:0006457	protein folding	22	149	0,00709
GO:0015992	proton transport	12	57	0,009403
GO:0051301	cell division	30	240	0,009164
GO:0045454	cell redox homeostasis	13	66	0,009281

GOID: Gene Ontology ID dei Processi Biologici del database AmiGO. Size: numero dei geni del genoma in grado di identificare il termine dell'ontology. Count: numero dei geni differenzialmente espresso in grado di identificare questo termine.

Geni downregolati

KEGGID	Term	Count	Size	Pvalue
3040	Spliceosome	31	124	1,35E-09
3050	Proteasome	17	44	2,17E-08
4120	Ubiquitin mediated proteolysis	27	134	1,56E-06
3060	Protein export	10	23	1,52E-05
20	Citrate cycle (TCA cycle)	11	30	2,47E-05
4142	Lysosome	22	120	7,90E-05
4110	Cell cycle	22	123	0,000103
4114	Oocyte meiosis	20	109	0,000164
190	Oxidative phosphorylation	22	128	0,000157
5010	Alzheimer's disease	25	160	0,000201
5012	Parkinson's disease	21	125	0,000294
5016	Huntington's disease	25	176	0,000866
620	Pyruvate metabolism	10	40	0,001348
3430	Mismatch repair	7	23	0,003756
62	Fatty acid elongation in mitochondria	4	8	0,008878

KEGGID: KEGG ID delle mappe del database KEGG. Size: numero dei geni del genoma in grado di identificare il termine dell'ontology. Count: numero dei geni differenzialmente espresso in grado di identificare questo termine

Dati supplementari, tabella 3. GSEA dei processi arricchiti positivamente o negativamente nelle isole diabetiche tipo 2 vs isole non diabetiche

Arricchiti positivamente

NAME	**SIZE**	**ES**	**NES**	**NOM p-val**	**FDR q-val**
MOREAUX_TACI_HI_VS_LOW_UP	392	0,41	2,83	0,00000	0,00000
SANA_IFNG_ENDOTHELIAL_UP	60	0,51	2,78	0,00000	0,00000
HEARTFAILURE_ATRIA_UP	25	0,61	2,67	0,00000	0,00000
RIBAVIRIN_RSV_UP	22	0,59	2,53	0,00000	0,00000
HSA04080_NEUROACTIVE_LIGAND_RECEPTOR_INTERACTION	228	0,35	2,31	0,00000	0,00002
GH_EXOGENOUS_MIDDLE_UP	104	0,37	2,27	0,00000	0,00003
CMV_HCMV_TIMECOURSE_12HRS_UP	26	0,50	2,21	0,00000	0,00006
BENNETT_SLE_UP	28	0,55	2,48	0,00000	0,00018
HSA04340_HEDGEHOG_SIGNALING_PATHWAY	45	0,42	2,11	0,00000	0,00021
HSA04020_CALCIUM_SIGNALING_PATHWAY	162	0,33	2,11	0,00000	0,00021
HSA04640_HEMATOPOIETIC_CELL_LINEAGE	84	0,36	2,07	0,00000	0,00032
TAKEDA_NUP8_HOXA9_6H_DN	32	0,44	2,08	0,00000	0,00035
MOREAUX_TACI_HI_IN_BMPC	95	0,42	2,47	0,00000	0,00045
IFN_ALPHA_UP	40	0,41	2,01	0,00000	0,00054
HSA04612_ANTIGEN_PROCESSING_AND_PRESENTATION	74	0,35	2,01	0,00000	0,00055
HSA04730_LONG_TERM_DEPRESSION	73	0,35	2,00	0,00000	0,00060
HSA04360_AXON_GUIDANCE	113	0,33	1,97	0,00000	0,00079
DAC_PANC_UP	363	0,29	1,98	0,00000	0,00080
HSA05217_BASAL_CELL_CARCINOMA	45	0,38	1,94	0,00000	0,00108
HSA04060_CYTOKINE_CYTOKINE_RECEPTOR_INTERACTION	225	0,29	1,89	0,00000	0,00173
HSA04514_CELL_ADHESION_MOLECULES	115	0,30	1,80	0,00000	0,00400
HSA04916_MELANOGENESIS	90	0,31	1,79	0,00000	0,00425
HEMATOPOESIS_RELATED_TRANSCRIPTION_FACTORS	83	0,31	1,80	0,00000	0,00595
HSA04810_REGULATION_OF_ACTIN_CYTOSKELETON	180	0,27	1,72	0,00000	0,00774
HSA04650_NATURAL_KILLER_CELL_MEDIATED_CYTOTOXICITY	119	0,28	1,71	0,00000	0,00839
ZHAN_PCS_MULTIPLE_MYELOMA_SPKD	23	0,51	2,21	0,00000	0,00951
REFRACTORY_GASTRIC_UP	87	0,38	2,22	0,00000	0,01019
TARTE_MATURE_PC	382	0,32	2,21	0,00000	0,01047
NF90_UP	25	0,49	2,16	0,00000	0,01377
ICHIBA_GVHD	216	0,26	1,69	0,00000	0,01470
SANA_TNFA_ENDOTHELIAL_UP	75	0,38	2,13	0,00000	0,01670
DAC_BLADDER_UP	28	0,46	2,10	0,00000	0,01671
GPCRS_CLASS_A_RHODOPSIN_LIKE	130	0,34	2,11	0,00000	0,01728
BASSO_GERMINAL_CENTER_CD40_UP	97	0,34	2,07	0,00000	0,02016
IFNA_HCMV_6HRS_UP	53	0,39	2,06	0,00000	0,02178
GPCRDB_CLASS_A_RHODOPSIN_LIKE	160	0,32	2,04	0,00000	0,02248
HSA04010_MAPK_SIGNALING_PATHWAY	237	0,24	1,57	0,00000	0,02318
PEPTIDE_GPCRS	70	0,37	2,05	0,00000	0,02321
FALT_BCLL_UP	44	0,40	2,02	0,00000	0,02591
WIELAND_HEPATITIS_B_INDUCED	106	0,33	2,02	0,00000	0,02615
ST_GAQ_PATHWAY	27	0,44	1,98	0,00000	0,03451
DIAB_NEPH_UP	60	0,36	1,98	0,00000	0,03508
CROMER_HYPOPHARYNGEAL_MET_VS_NON_DN	80	0,34	1,95	0,00000	0,04062
GH_EXOGENOUS_ANY_UP	231	0,29	1,91	0,00000	0,05368
RADAEVA_IFNA_UP	50	0,36	1,90	0,00000	0,05397
ROSS_PML_RAR	80	0,33	1,89	0,00000	0,05769
MANALO_HYPOXIA_UP	92	0,32	1,89	0,00000	0,05898
GALINDO_ACT_UP	73	0,33	1,86	0,00000	0,06991
CELL_SURFACE_RECEPTOR_LINKED_SIGNAL_TRANSDUCTION	128	0,30	1,83	0,00000	0,08026

CALCIUM_REGULATION_IN_CARDIAC_CELLS	127	0,30	1,82	0,00000	0,08384
TAKEDA_NUP8_HOXA9_10D_UP	152	0,29	1,80	0,00000	0,09112
FLECHNER_KIDNEY_TRANSPLANT_REJECTION_UP	86	0,30	1,78	0,00000	0,09770
INTEGRIN_MEDIATED_CELL_ADHESION_KEGG	84	0,30	1,78	0,00000	0,10414
TAKEDA_NUP8_HOXA9_3D_UP	150	0,28	1,74	0,00000	0,12376
BRENTANI_TRANSCRIPTION_FACTORS	64	0,32	1,73	0,00000	0,12535
HSA04310_WNT_SIGNALING_PATHWAY	130	0,28	1,70	0,00100	0,00896
BCNU_GLIOMA_MGMT_48HRS_DN	157	0,26	1,68	0,00100	0,01077
HSA04510_FOCAL_ADHESION	187	0,25	1,59	0,00100	0,02020
VERHAAK_AML_NPM1_MUT_VS_WT_UP	189	0,27	1,73	0,00100	0,12639
CELL_ADHESION	167	0,27	1,74	0,00100	0,12672
TAKEDA_NUP8_HOXA9_16D_UP	135	0,28	1,70	0,00100	0,14557
HSA04630_JAK_STAT_SIGNALING_PATHWAY	138	0,27	1,71	0,00100	0,00804
HSA04912_GNRH_SIGNALING_PATHWAY	92	0,31	1,78	0,00100	0,00458
YAO_P4_KO_VS_WT_UP	65	0,34	1,88	0,00101	0,05977
IGF_VS_PDGF_UP	57	0,32	1,75	0,00101	0,12218
HSA00590_ARACHIDONIC_ACID_METABOLISM	50	0,36	1,87	0,00103	0,00204
ADIP_VS_PREADIP_DN	37	0,38	1,84	0,00104	0,08045
MONOAMINE_GPCRS	30	0,42	1,91	0,00105	0,05429
HSA00591_LINOLEIC_ACID_METABOLISM	27	0,45	2,05	0,00106	0,00039
IFNA_UV-CMV_COMMON_HCMV_6HRS_UP	29	0,46	2,12	0,00107	0,01673
WNT_TARGETS	25	0,48	2,13	0,00108	0,01617
IFNALPHA_NL_UP	27	0,44	1,98	0,00108	0,00064
JNK_UP	28	0,46	2,07	0,00109	0,02054
SHIPP_DLBCL_CURED_UP	28	0,43	1,93	0,00109	0,04741
LIAN_MYELOID_DIFF_RECEPTORS	27	0,41	1,84	0,00109	0,07888
MARTINELLI_IFNS_DIFF	21	0,47	1,98	0,00110	0,03606
HUMAN_TISSUE_PLACENTA	19	0,47	1,91	0,00113	0,00148
STATIN_PATHWAY_PHARMGKB	17	0,51	1,96	0,00114	0,03936
DAC_IFN_BLADDER_UP	16	0,59	2,17	0,00117	0,01390
HSA04512_ECM_RECEPTOR_INTERACTION	81	0,31	1,81	0,00201	0,00364
DER_IFNA_UP	65	0,33	1,84	0,00202	0,07893
HTERT_DN	61	0,31	1,68	0,00203	0,15797
JECHLINGER_EMT_DN	40	0,37	1,83	0,00205	0,00413
NUCLEAR_RECEPTORS	40	0,39	1,93	0,00207	0,04786
DAC_PANC50_UP	42	0,36	1,82	0,00207	0,08445
YU_CMYC_DN	39	0,38	1,86	0,00208	0,00309
INFLAMMATORY_RESPONSE_PATHWAY	29	0,42	1,95	0,00211	0,04190
IFNALPHA_NL_HCC_UP	18	0,52	2,10	0,00228	0,01748
FERRANDO_T_CELL_DIFFERENTIATION_PATHWAY	18	0,46	1,81	0,00229	0,08677
HSA04540_GAP_JUNCTION	85	0,29	1,65	0,00300	0,01330
HSA04720_LONG_TERM_POTENTIATION	66	0,31	1,74	0,00302	0,00622
GUO_HEX_UP	76	0,29	1,65	0,00302	0,18096
BASSO_GERMINAL_CENTER_CD40_DN	69	0,33	1,80	0,00302	0,09160
HSA05214_GLIOMA	62	0,32	1,75	0,00303	0,00603
HSA04742_TASTE_TRANSDUCTION	34	0,38	1,81	0,00313	0,00366
IFNALPHA_HCC_UP	29	0,40	1,82	0,00323	0,08367
ST_MYOCYTE_AD_PATHWAY	24	0,44	1,89	0,00327	0,00249
ABRAHAM_AL_VS_MM_UP	23	0,43	1,84	0,00333	0,00363
EICOSANOID_SYNTHESIS	17	0,50	1,96	0,00338	0,03834
G_PROTEIN_SIGNALING	86	0,27	1,58	0,00402	0,03220
HSA04070_PHOSPHATIDYLINOSITOL_SIGNALING_SYSTEM	67	0,32	1,74	0,00402	0,00647
DNMT1_KO_UP	70	0,30	1,72	0,00404	0,00922
CMV_8HRS_UP	31	0,40	1,88	0,00429	0,00230
HSA01430_CELL_COMMUNICATION	109	0,27	1,66	0,00500	0,01220

HOX_GENES	53	0,34	1,75	0,00515	0,11661
TSA_HEPATOMA_CANCER_UP	39	0,37	1,81	0,00525	0,08543
CHESLER_BRAIN_ONLY_SUBSET	23	0,41	1,76	0,00541	0,11463
GPCRS_CLASS_B_SECRETIN_LIKE	23	0,42	1,80	0,00545	0,08976
ABRAHAM_MM_VS_AL_DN	22	0,45	1,89	0,00556	0,05838
CHESLER_BRAIN_NEURAL_HIGH_GENES	21	0,44	1,83	0,00560	0,08185
TGFBETA_ALL_UP	80	0,29	1,68	0,00603	0,16171
RESISTANCE_XENOGRAFTS_UP	27	0,41	1,82	0,00658	0,08518
HSA04350_TGF_BETA_SIGNALING_PATHWAY	81	0,28	1,60	0,00701	0,01861
FETAL_LIVER_VS_ADULT_LIVER_GNF2	69	0,30	1,70	0,00704	0,15148
EMT_DN	53	0,32	1,68	0,00712	0,01225
GILDEA_BLADDER_UP	30	0,39	1,77	0,00743	0,10663
HSA05210_COLORECTAL_CANCER	81	0,27	1,58	0,00802	0,02185
BRENTANI_CELL_ADHESION	91	0,27	1,59	0,00802	0,03017
YANG_OSTECLASTS_SIG	38	0,36	1,74	0,00832	0,12538
HSA00760_NICOTINATE_AND_NICOTINAMIDE_METABOLISM	16	0,48	1,84	0,00833	0,00283
ST_G_ALPHA_I_PATHWAY	34	0,36	1,73	0,00843	0,12612
ZHAN_MMPC_PC	22	0,41	1,75	0,00880	0,12091
MYOD_NIH3T3_UP	75	0,29	1,66	0,00905	0,01505
RAY_P210_DIFF	53	0,31	1,68	0,00920	0,15709
ST_ADRENERGIC	33	0,37	1,74	0,00946	0,12516
GPCRDB_CLASS_B_SECRETIN_LIKE	23	0,42	1,79	0,00994	0,09430
AMIPATHWAY	21	0,41	1,73	0,01001	0,12546
RADMACHER_AMLNORMALKARYTYPE_SIG	78	0,29	1,66	0,01003	0,17211
LIN_WNT_UP	53	0,31	1,67	0,01021	0,16984
HSA05215_PROSTATE_CANCER	84	0,27	1,58	0,01103	0,02218
GPCRDB_OTHER	49	0,31	1,65	0,01124	0,01788
STEFFEN_AML_PML_PLZF_TRGT	42	0,33	1,69	0,01126	0,15756
GH_EXOGENOUS_ALL_UP	46	0,31	1,65	0,01128	0,01351
HOHENKIRK_MONOCYTE_DEND_UP	106	0,26	1,55	0,01200	0,03624
HADDAD_CD45CD7_PLUS_VS_MINUS_UP	64	0,30	1,64	0,01212	0,19322
HALMOS_CEBP_DN	43	0,33	1,67	0,01253	0,16923
ATRIA_UP	195	0,22	1,42	0,01300	0,08218
TFF2_KO_UP	22	0,40	1,70	0,01330	0,15018
HPV31_DN	44	0,33	1,69	0,01333	0,15567
HSA00512_O_GLYCAN_BIOSYNTHESIS	20	0,41	1,65	0,01359	0,01318
NAKAJIMA_MCSMBP_EOS	27	0,39	1,72	0,01376	0,13456
MYOD_BRG1_UP	27	0,38	1,68	0,01384	0,01257
WNT_SIGNALING	58	0,30	1,60	0,01417	0,24181
IL1_CORNEA_UP	62	0,30	1,61	0,01423	0,01651
CMV_8HRS_DN	42	0,33	1,69	0,01448	0,15462
TSADAC_PANC50_UP	42	0,33	1,66	0,01452	0,17027
CSKPATHWAY	21	0,41	1,73	0,01532	0,12366
ST_DIFFERENTIATION_PATHWAY_IN_PC12_CELLS	43	0,33	1,65	0,01660	0,17903
HSA04330_NOTCH_SIGNALING_PATHWAY	37	0,35	1,70	0,01684	0,00863
APPEL_IMATINIB_UP	31	0,35	1,66	0,01700	0,17089
JNK_DN	31	0,35	1,65	0,01793	0,01562
HSA05222_SMALL_CELL_LUNG_CANCER	87	0,27	1,55	0,01906	0,02585
MAMMARY_DEV_UP	50	0,31	1,60	0,02047	0,23976
HADDAD_HSC_CD7_UP	64	0,30	1,60	0,02119	0,24145
TGFBETA_C2_UP	18	0,41	1,64	0,02154	0,19588
INFLAMPATHWAY	29	0,35	1,63	0,02215	0,19742
HSA04012_ERBB_SIGNALING_PATHWAY	84	0,26	1,51	0,02302	0,03408
O6BG_RESIST_MEDULLOBLASTOMA_UP	23	0,39	1,64	0,02313	0,01435
PARK_RARALPHA_UP	37	0,33	1,59	0,02316	0,24887

SIG_PIP3_SIGNALING_IN_B_LYMPHOCYTES	34	0,33	1,60	0,02355	0,24156
ST_GA13_PATHWAY	35	0,34	1,64	0,02396	0,19454
TCELL_ANERGIC_UP	76	0,26	1,50	0,02412	0,03777
HSA05218_MELANOMA	67	0,28	1,52	0,02417	0,03184
CROONQUIST_RAS_STROMA_UP	23	0,39	1,64	0,02450	0,19275
ST_GA12_PATHWAY	21	0,39	1,65	0,02544	0,18281
SIG_BCR_SIGNALING_PATHWAY	44	0,31	1,59	0,02661	0,24227
TSA_CD4_DN	18	0,40	1,58	0,02697	0,02491
IFN_ANY_UP	81	0,26	1,47	0,02714	0,05447
TGFBETA_LATE_UP	33	0,33	1,54	0,02748	0,03329
UV-4NQO_FIBRO_DN	28	0,35	1,58	0,02823	0,02217
UCALPAINPATHWAY	15	0,44	1,61	0,02857	0,22170
ADIP_VS_FIBRO_DN	27	0,36	1,63	0,03024	0,19870
BRG1_SW13_UP	43	0,31	1,56	0,03080	0,02945
HSA04664_FC_EPSILON_RI_SIGNALING_PATHWAY	73	0,27	1,49	0,03119	0,03934
AGUIRRE_PANCREAS_CHR22	60	0,28	1,49	0,03122	0,05367
GAMMA_ESR_WS_UNREG	26	0,35	1,57	0,03205	0,02745
VEGF_MMMEC_3HRS_UP	64	0,27	1,49	0,03245	0,03541
UV_UNIQUE_FIBRO_UP	20	0,39	1,59	0,03277	0,02456
STRESS_GENOTOXIC_SPECIFIC_UP	33	0,33	1,55	0,03415	0,03124
HSA05212_PANCREATIC_CANCER	71	0,26	1,46	0,03427	0,04782
HSA04940_TYPE_I_DIABETES_MELLITUS	41	0,32	1,57	0,03441	0,02292
ST_T_CELL_SIGNAL_TRANSDUCTION	42	0,30	1,53	0,03509	0,04453
ST_WNT_CA2_CYCLIC_GMP_PATHWAY	19	0,39	1,57	0,03634	0,03502
HSA05223_NON_SMALL_CELL_LUNG_CANCER	52	0,29	1,52	0,03662	0,03152
HSA00562_INOSITOL_PHOSPHATE_METABOLISM	40	0,30	1,51	0,03731	0,03414
HSA04930_TYPE_II_DIABETES_MELLITUS	40	0,31	1,49	0,03770	0,03890
AS3_FIBRO_DN	31	0,33	1,54	0,03793	0,03340
HSA04520_ADHERENS_JUNCTION	72	0,26	1,46	0,03835	0,04624
TOB1PATHWAY	17	0,40	1,55	0,04070	0,03838
DRUG_RESISTANCE_AND_METABOLISM	95	0,24	1,43	0,04104	0,07927
BREAST_CANCER_ESTROGEN_SIGNALING	93	0,24	1,42	0,04204	0,08943
HSA04670_LEUKOCYTE_TRANSENDOTHELIAL_MIGRATION	101	0,23	1,41	0,04213	0,06613
HSA04662_B_CELL_RECEPTOR_SIGNALING_PATHWAY	59	0,27	1,48	0,04273	0,04114
ADIP_HUMAN_DN	25	0,36	1,57	0,04428	0,02365
HSA05220_CHRONIC_MYELOID_LEUKEMIA	74	0,25	1,42	0,04523	0,06082

Arricchiti negativamente

NAME	**SIZE**	**ES**	**NES**	**NOM p-val**	**FDR q-val**
ELECTRON_TRANSPORT_CHAIN	89	-0,31	-3,32	0,00000	0,00000
HSA03050_PROTEASOME	22	-0,63	-3,50	0,00000	0,00000
MOOTHA_VOXPHOS	76	-0,30	-2,43	0,00000	0,00004
ET743_SARCOMA_24HRS_DN	95	-0,17	-2,30	0,00000	0,00007
HSA03010_RIBOSOME	61	-0,24	-2,28	0,00000	0,00008
HSA00190_OXIDATIVE_PHOSPHORYLATION	99	-0,22	-1,91	0,00000	0,00071
HBX_HCC_UP	16	-0,39	-1,90	0,00000	0,00083
HDACI_COLON_CUR24HRS_UP	36	-0,26	-1,87	0,00000	0,00087
CITRATE_CYCLE_TCA_CYCLE	20	-0,36	-1,93	0,00000	0,00094
AGED_MOUSE_HYPOTH_UP	43	-0,21	-1,82	0,00000	0,00118
SMITH_HTERT_UP	102	-0,20	-2,67	0,00000	0,00323
UVB_SCC_UP	86	-0,21	-1,66	0,00000	0,00336
TRANSLATION_FACTORS	45	-0,30	-2,48	0,00000	0,00429
PROTEASOMEPATHWAY	21	-0,44	-2,45	0,00000	0,00470
RNA_TRANSCRIPTION_REACTOME	34	-0,35	-2,52	0,00000	0,00472

PROTEASOME	17	-0,49	-2,44	0,00000	0,00519
HSA00500_STARCH_AND_SUCROSE_METABOLISM	60	-0,15	-1,54	0,00000	0,00578
HSC_INTERMEDIATEPROGENITORS_ADULT	113	-0,14	-1,56	0,00000	0,00596
TRNA_SYNTHETASES	17	-0,47	-2,40	0,00000	0,00718
HYPOXIA_RCC_NOVHL_UP	57	-0,17	-1,51	0,00000	0,00776
SCHUMACHER_MYC_UP	50	-0,26	-2,24	0,00000	0,01505
UVB_NHEK2_UP	68	-0,21	-2,08	0,00000	0,02493
UVB_NHEK3_C0	82	-0,20	-2,13	0,00000	0,02503
CANTHARIDIN_DN	49	-0,27	-2,09	0,00000	0,02677
IDX_TSA_UP_CLUSTER5	88	-0,18	-2,09	0,00000	0,02843
HYPOPHYSECTOMY_RAT_UP	33	-0,28	-2,00	0,00000	0,04000
BRCA_PROGNOSIS_NEG	94	-0,11	-1,19	0,00000	0,04008
CHESLER_HIGHEST_FOLD_RANGE_GENES	33	-0,27	-1,94	0,00000	0,05052
CMV_HCMV_TIMECOURSE_18HRS_UP	74	-0,18	-1,93	0,00000	0,05093
AGUIRRE_PANCREAS_CHR6	32	-0,26	-1,84	0,00000	0,07708
NOUZOVA_CPG_H4_UP	95	-0,16	-1,74	0,00000	0,11952
RIBOSOMAL_PROTEINS	92	-0,13	-1,73	0,00000	0,12191
MRNA_SPLICING	47	-0,22	-1,76	0,00000	0,12399
SANA_IFNG_ENDOTHELIAL_DN	80	-0,16	-1,74	0,00000	0,12544
OXIDATIVE_PHOSPHORYLATION	55	-0,20	-1,67	0,00000	0,16148
HEARTFAILURE_ATRIA_DN	110	-0,22	-1,65	0,00000	0,17127
CANCER_NEOPLASTIC_META_UP	60	-0,17	-1,63	0,00000	0,17217
PYRUVATE_METABOLISM	35	-0,24	-1,64	0,00000	0,17218
MOREAUX_TACI_HI_VS_LOW_DN	143	-0,16	-1,60	0,00000	0,18594
ROME_INSULIN_2F_UP	166	-0,15	-1,60	0,00000	0,19246
GALE_FLT3ANDAPL_UP	59	-0,18	-1,57	0,00000	0,21757
HSA00020_CITRATE_CYCLE	25	-0,34	-2,05	0,01282	0,00031
AMINOACYL_TRNA_BIOSYNTHESIS	20	-0,30	-1,65	0,02459	0,16547
HDACI_COLON_SUL12HRS_DN	22	-0,27	-1,54	0,04124	0,00725
HSA04130_SNARE_INTERACTIONS_IN_VESICULAR_TRANSPORT	30	-0,26	-1,61	0,04615	0,00390
UVB_NHEK3_C6	29	-0,23	-1,51	0,04762	0,00850

Size: numero di geni inclusi nello specifico gene set; ES: enrichment score (riflette il grado a cui il gene set è sovrarappresentato); NES: ES normalizzato per tutti I gene set analizzati; P value: significativo se < 0.05; FDR q-value: probabilità di falsa positività (se < 0.25il valore di P è accettato)

Dati supplementari, tabella 4. Risultati di microarray dei geni coinvolti nel sistema UPS

UBIQUITINATION SYSTEM

External ID	Symbol	Description	Gene Id	FC	P.Value
Ubiquitin-activating enzymes (E1)					
218673_s_at	ATG7	ATG7 autophagy related 7 homolog (S. cerevisiae)	10533	1,23	0,06204
206141_at	MOCS3	molybdenum cofactor synthesis 3	27304	1,19	0,12990
202268_s_at	**NAE1**	**NEDD8 activating enzyme E1 subunit 1**	**8883**	**0,21**	**0,00683**
217946_s_at	SAE1	SUMO1 activating enzyme subunit 1	10055	0,52	0,00307
200964_at	UBA1	ubiquitin-like modifier activating enzyme 1	7317	1,30	0,32594
201177_s_at	**UBA2**	**ubiquitin-like modifier activating enzyme 2**	**10054**	**0,49**	**0,00207**
209115_at	**UBA3**	**ubiquitin-like modifier activating enzyme 3**	**9039**	**0,44**	**0,00806**
218289_s_at	**UBA5**	**ubiquitin-like modifier activating enzyme 5**	**79876**	**0,46**	**0,00105**
218340_s_at	UBA6	ubiquitin-like modifier activating enzyme 6	55236	0,82	0,03242
203281_s_at	UBA7	ubiquitin-like modifier activating enzyme 7	7318	1,33	0,27000
Ubiquitin-conjugating enzymes (E2)					
220237_at	ATG3	ATG3 autophagy related 3 homolog (S. cerevisiae)	64422	1,02	0,80452
212540_at	CDC34	cell division cycle 34 homolog (S. cerevisiae)	997	1,21	0,28261
202779_s_at	LOC731049///UBE2S	ubiquitin-conjugating enzyme E2S /// similar to Ubiquitin-conjugating enzyme E2S (Ubiquitin-conjugating enzyme E2-24 kDa) (Ubiquitin-protein ligase) (Ubiquitin carrier protein) (E2-EPF5)	27338///651816	0,83	0,07274
201899_s_at	**UBE2A**	**ubiquitin-conjugating enzyme E2A (RAD6 homolog)**	**7319**	**0,37**	**0,00102**
211763_s_at	**UBE2B**	**ubiquitin-conjugating enzyme E2B (RAD6 homolog)**	**7320**	**0,36**	**0,00049**
202954_at	UBE2C	ubiquitin-conjugating enzyme E2C	11065 /// 5063	1,52	0,01709
211764_s_at	UBE2D1	ubiquitin-conjugating enzyme E2D 1 (UBC4/5 homolog, yeast)	7321	0,57	0,00449
201345_s_at	UBE2D2	ubiquitin-conjugating enzyme E2D 2 (UBC4/5 homolog, yeast)	7322	0,56	0,00334
200668_s_at	UBE2D3	ubiquitin-conjugating enzyme E2D 3 (UBC4/5 homolog, yeast)	7323	0,39	0,02129
218837_s_at	UBE2D4	ubiquitin-conjugating enzyme E2D 4 (putative)	51619	1,01	0,93960
212519_at	**UBE2E1**	**ubiquitin-conjugating enzyme E2E 1 (UBC4/5 homolog, yeast)**	**7324**	**0,38**	**0,00691**
210024_s_at	**UBE2E3**	**ubiquitin-conjugating enzyme E2E 3 (UBC4/5 homolog, yeast)**	**10477**	**0,31**	**0,00018**
209142_s_at	**UBE2G1**	**ubiquitin-conjugating enzyme E2G 1 (UBC7 homolog, yeast)**	**7326**	**0,35**	**0,00056**
209042_s_at	UBE2G2	ubiquitin-conjugating enzyme E2G 2 (UBC7 homolog, yeast)	7327	0,74	0,07810
221962_s_at	UBE2H	ubiquitin-conjugating enzyme E2H (UBC8 homolog, yeast)	7328	0,94	0,70745
208760_at	UBE2I	Ubiquitin-conjugating enzyme E2I (UBC9 homolog, yeast)	7329	0,99	0,95166
217825_s_at	UBE2J1	ubiquitin-conjugating enzyme E2, J1 (UBC6 homolog, yeast)	51465	0,76	0,01429
202346_at	**UBE2K**	**ubiquitin-conjugating enzyme E2K (UBC1 homolog, yeast)**	**3093**	**0,34**	**0,00045**
200676_s_at	UBE2L3	ubiquitin-conjugating enzyme E2L 3	7332	0,95	0,73165
201649_at	UBE2L6	ubiquitin-conjugating enzyme E2L 6	9246	1,15	0,42460
203109_at	**UBE2M**	**ubiquitin-conjugating enzyme E2M (UBC12 homolog, yeast)**	**9040**	**0,48**	**0,00004**
212751_at	**UBE2N**	**ubiquitin-conjugating enzyme E2N (UBC13 homolog, yeast)**	**7334**	**0,38**	**0,00008**
217393_x_at	UBE2NL	ubiquitin-conjugating enzyme E2N-like	389898	1,34	0,00723

218141_at	UBE2O	ubiquitin-conjugating enzyme E2O	63893	1,24	0,06350
217978_s_at	**UBE2Q1**	**ubiquitin-conjugating enzyme E2Q family member 1**	**55585**	**0,49**	**0,00124**
218521_s_at	UBE2W	ubiquitin-conjugating enzyme E2W (putative)	55284	0,71	0,05783
217750_s_at	UBE2Z	ubiquitin-conjugating enzyme E2Z	65264	0,79	0,19745
212404_s_at	UBE3B	ubiquitin protein ligase E3B	89910	1,11	0,23003
217797_at	**UFC1**	**ubiquitin-fold modifier conjugating enzyme 1**	**51506**	**0,38**	**0,00087**

Ubiquitin ligases (E3)

219574_at	MARCH1	membrane-associated ring finger (C3HC4) 1	55016	1,09	0,23149
210075_at	MARCH2	membrane-associated ring finger (C3HC4) 2	51257	0,87	0,15426
218582_at	MARCH5	membrane-associated ring finger (C3HC4) 5	54708	0,62	0,02503
201737_s_at	MARCH6	membrane-associated ring finger (C3HC4) 6	10299	0,57	0,03887
202653_s_at	**MARCH7**	**membrane-associated ring finger (C3HC4) 7**	**64844**	**0,49**	**0,00989**
221824_s_at	**MARCH8**	**membrane-associated ring finger (C3HC4) 8**	**220972**	**0,38**	**0,00119**
215589_at	---	CDNA: FLJ21284 fis, clone COL01911	57154	1,49	0,00837
216444_at	---	CDNA FLJ14076 fis, clone HEMBB1001925	64750	1,27	0,01541
215587_x_at	***---***	***CDNA FLJ13829 fis, clone THYRO1000625***	***112939***	***2,48***	***0,00020***
214801_at	---	CDNA FLJ11392 fis, clone HEMBA1000575	64163	1,31	0,30507
213497_at	ABTB2	ankyrin repeat and BTB (POZ) domain containing 2	25841	1,13	0,44670
208090_s_at	AIRE	autoimmune regulator	326	1,23	0,12122
202204_s_at	AMFR	autocrine motility factor receptor	267	0,86	0,39647
218575_at	ANAPC1	anaphase promoting complex subunit 1	64682	0,87	0,22236
207845_s_at	**ANAPC10**	**anaphase promoting complex subunit 10**	**10393**	**0,48**	**0,00142**
209001_s_at	**ANAPC13**	**anaphase promoting complex subunit 13**	**25847**	**0,39**	**0,00024**
218555_at	ANAPC2	anaphase promoting complex subunit 2	29882	1,63	0,00461
208722_s_at	**ANAPC5**	**anaphase promoting complex subunit 5**	**51433**	**0,38**	**0,00009**
201881_s_at	ARIH1	ariadne homolog, ubiquitin-conjugating enzyme E2 binding protein, 1 (Drosophila)	25820	0,75	0,00319
201230_s_at	ARIH2	ariadne homolog 2 (Drosophila)	10425	0,59	0,00678
212818_s_at	ASB1	ankyrin repeat and SOCS box-containing 1	51665	1,23	0,07822
218862_at	ASB13	ankyrin repeat and SOCS box-containing 13	79754	0,82	0,12374
208481_at	ASB4	ankyrin repeat and SOCS box-containing 4	51666	1,12	0,10899
221657_s_at	ASB6	ankyrin repeat and SOCS box-containing 6	140459	1,09	0,39046
219996_at	ASB7	ankyrin repeat and SOCS box-containing 7	140460	1,14	0,32562
218841_at	ASB8	ankyrin repeat and SOCS box-containing 8	140461	1,07	0,53477
205673_s_at	ASB9	ankyrin repeat and SOCS box-containing 9	140462	0,72	0,24625
205345_at	BARD1	BRCA1 associated RING domain 1	580	1,03	0,83025
202076_at	BIRC2	baculoviral IAP repeat-containing 2	329	0,66	0,02766
210538_s_at	BIRC3	baculoviral IAP repeat-containing 3	330	0,81	0,55965
209923_s_at	BRAP	BRCA1 associated protein	8315	1,20	0,16524
204531_s_at	BRCA1	breast cancer 1, early onset	672	1,12	0,24155
214727_at	BRCA2	breast cancer 2, early onset	675	1,08	0,23643
216521_s_at	BRCC3	BRCA1/BRCA2-containing complex, subunit 3	79184	1,03	0,77401
205550_s_at	BRE	brain and reproductive organ-expressed (TNFRSF1A modulator)	9577	0,74	0,00880
219280_at	BRWD1	bromodomain and WD repeat domain containing 1	54014	1,17	0,18384
216091_s_at	BTRC	beta-transducin repeat containing	8945	1,40	0,01630
218108_at	**C14orf130**	**chromosome 14 open reading frame 130**	**55148**	**0,38**	**0,00014**
213386_at	C9orf125	chromosome 9 open reading frame 125	56254	0,76	0,03708
206607_at	CBL	Cas-Br-M (murine) ecotropic retroviral transforming sequence	867	1,36	0,02784
209682_at	CBLB	Cas-Br-M (murine) ecotropic retroviral transforming sequence b	868	1,10	0,68105
220638_s_at	CBLC	Cas-Br-M (murine) ecotropic retroviral transforming sequence c	23624	1,28	0,18272
206724_at	CBX4	chromobox homolog 4 (Pc class homolog, Drosophila)	8535	1,19	0,06112
217988_at	**CCNB1IP1**	**cyclin B1 interacting protein 1**	**57820**	**0,45**	**0,00116**
204826_at	CCNF	cyclin F	899	1,58	0,00057

209658_at	CDC16	cell division cycle 16 homolog (S. cerevisiae)	8881	0,79	0,33200
202870_s_at	CDC20	cell division cycle 20 homolog (S. cerevisiae)	991	1,27	0,03700
202892_at	**CDC23**	**cell division cycle 23 homolog (S. cerevisiae)**	**8697**	**0,48**	**0,00632**
217881_s_at	CDC27	cell division cycle 27 homolog (S. cerevisiae)	996	0,98	0,87450
218803_at	CHFR	checkpoint with forkhead and ring finger domains	55743	0,80	0,18078
221223_x_at	CISH	cytokine inducible SH2-containing protein	1154	1,32	0,06555
203291_at	CNOT4	CCR4-NOT transcription complex, subunit 4	4850	0,71	0,11274
218142_s_at	CRBN	cereblon	51185	0,97	0,80786
207614_s_at	CUL1	cullin 1	8454	0,52	0,00094
203078_at	CUL2	cullin 2	8453	0,94	0,44900
203079_s_at	CUL2	cullin 2	8453	0,70	0,06505
201372_s_at	CUL3	cullin 3	8452	1,00	0,98562
201424_s_at	CUL4A	cullin 4A	8451	0,55	0,00467
202213_s_at	CUL4B	cullin 4B	8450	0,64	0,01930
203533_s_at	CUL5	cullin 5	8065	0,91	0,58512
203558_at	CUL7	cullin 7	9820	1,18	0,35613
218260_at	DDA1	DET1 and DDB1 associated 1	79016	1,30	0,04035
208619_at	DDB1	damage-specific DNA binding protein 1, 127kDa	1642	0,80	0,09292
203409_at	DDB2	damage-specific DNA binding protein 2, 48kDa	1643	0,96	0,79506
219641_at	DET1	de-etiolated homolog 1 (Arabidopsis)	55070	0,86	0,19754
219350_s_at	DIABLO	diablo homolog (Drosophila)	56616	0,86	0,17612
218585_s_at	DTL	denticleless homolog (Drosophila)	51514	1,03	0,75108
207231_at	DZIP3	DAZ interacting protein 3, zinc finger	9666	0,96	0,72671
201341_at	ENC1	ectodermal-neural cortex (with BTB-like domain)	8507	0,73	0,13136
205162_at	ERCC8 /// FLJ12595	excision repair cross-complementing rodent repair deficiency, complementation group 8 /// guanine nucleotide binding protein-like 3 (nucleolar)-like pseudogene	1161	0,87	0,16015
218397_at	FANCL	Fanconi anemia, complementation group L	55120	0,59	0,14036
208987_s_at	FBXL11	F-box and leucine-rich repeat protein 11	22992	1,66	0,00329
220127_s_at	FBXL12	F-box and leucine-rich repeat protein 12	54850	1,05	0,48698
213145_at	FBXL14	F-box and leucine-rich repeat protein 14	144699	0,64	0,02268
218938_at	FBXL15	F-box and leucine-rich repeat protein 15	79176	0,70	0,02998
215068_s_at	FBXL18	F-box and leucine-rich repeat protein 18	80028	1,51	0,00906
214436_at	FBXL2	F-box and leucine-rich repeat protein 2	25827	0,91	0,47653
209943_at	FBXL4	F-box and leucine-rich repeat protein 4	26235	0,84	0,09810
209005_at	FBXL5	F-box and leucine-rich repeat protein 5	26234	0,82	0,08990
219189_at	FBXL6	F-box and leucine-rich repeat protein 6	26233	1,21	0,07221
213249_at	FBXL7	F-box and leucine-rich repeat protein 7	23194	1,14	0,34694
220080_at	FBXL8	F-box and leucine-rich repeat protein 8	55336	1,17	0,17857
203255_at	***FBXO11***	***F-box protein 11***	***80204***	***2,13***	***0,00161***
220233_at	FBXO17	F-box protein 17	115290	1,12	0,51544
219305_x_at	FBXO2	F-box protein 2	26232	1,12	0,60623
212231_at	FBXO21	F-box protein 21	23014	0,52	0,00491
219638_at	FBXO22	F-box protein 22	26263	1,05	0,56483
221157_s_at	FBXO24	F-box protein 24	26261	1,33	0,01288
202271_at	**FBXO28**	**F-box protein 28**	**23219**	**0,39**	**0,00514**
218432_at	**FBXO3**	**F-box protein 3**	**26273**	**0,37**	**0,00337**
219785_s_at	FBXO31	F-box protein 31	79791	0,84	0,19898
218539_at	FBXO34	F-box protein 34	55030	0,89	0,54818
219608_s_at	FBXO38	F-box protein 38	81545	1,06	0,50475
220550_at	FBXO4	F-box protein 4	26272	1,01	0,87272
220164_s_at	FBXO40	F-box protein 40	51725	1,43	0,00402
44040_at	FBXO41	F-box protein 41	150726	0,92	0,62411
221812_at	FBXO42	F-box protein 42	54455	1,01	0,91242
205310_at	FBXO46	F-box protein 46	23403	1,10	0,27937
218875_s_at	FBXO5	F-box protein 5	26271	0,87	0,10388

201178_at	FBXO7	F-box protein 7	25793	0,66	0,00937
212991_at	FBXO9	F-box protein 9	26268	1,12	0,47691
209456_s_at	FBXW11	F-box and WD repeat domain containing 11	23291	1,45	0,00947
215600_x_at	***FBXW12***	***F-box and WD repeat domain containing 12***	***285231***	***2,51***	***0,00077***
218941_at	FBXW2	F-box and WD repeat domain containing 2	26190	0,63	0,01003
221519_at	FBXW4	F-box and WD repeat domain containing 4	6468	0,90	0,51077
218751_s_at	FBXW7	F-box and WD repeat domain containing 7	55294	1,03	0,85726
212374_at	FEM1B	fem-1 homolog b (C. elegans)	10116	0,76	0,13134
209416_s_at	FZR1	fizzy/cell division cycle 20 related 1 (Drosophila)	51343	1,49	0,00056
220124_at	GAN	giant axonal neuropathy (gigaxonin)	8139	0,98	0,81233
218458_at	GMCL1	germ cell-less homolog 1 (Drosophila)	64395	0,80	0,30737
218632_at	HECTD3	HECT domain containing 3	79654	1,42	0,05692
210331_at	HECW1	HECT, C2 and WW domain containing E3 ubiquitin protein ligase 1	23072	1,34	0,01868
218306_s_at	HERC1	hect (homologous to the E6-AP (UBE3A) carboxyl terminus) domain and RCC1 (CHC1)-like domain (RLD) 1	8925	0,66	0,05141
217902_s_at	HERC2	hect domain and RLD 2	8924	0,68	0,18504
206183_s_at	HERC3	hect domain and RLD 3	8916	0,88	0,09197
208054_at	HERC4	hect domain and RLD 4	26091	1,01	0,85270
208598_s_at	HUWE1	HECT, UBA and WWE domain containing 1	10075	0,59	0,00242
217908_s_at	IQWD1	IQ motif and WD repeats 1	55827	0,62	0,02133
220788_s_at	IRF9 /// RNF31	interferon regulatory factor 9 /// ring finger protein 31	55072	0,97	0,73549
217094_s_at	ITCH	itchy E3 ubiquitin protein ligase homolog (mouse)	83737	0,84	0,25084
219106_s_at	KBTBD10	kelch repeat and BTB (POZ) domain containing 10	10324	0,35	0,02385
204301_at	KBTBD11	kelch repeat and BTB (POZ) domain containing 11	9920	1,07	0,69253
212447_at	KBTBD2	kelch repeat and BTB (POZ) domain containing 2	25948	0,69	0,06766
218570_at	KBTBD4 /// PTPMT1	kelch repeat and BTB (POZ) domain containing 4 /// protein tyrosine phosphatase, mitochondrial 1	55709	0,47	0,01404
202417_at	KEAP1	kelch-like ECH-associated protein 1	9817	0,90	0,43323
216391_s_at	KLHL1	kelch-like 1 (Drosophila)	57626	1,32	0,03445
220657_at	KLHL11	kelch-like 11 (Drosophila)	55175	1,43	0,01856
219931_s_at	KLHL12	kelch-like 12 (Drosophila)	59349	1,05	0,64115
212882_at	KLHL18	kelch-like 18 (Drosophila)	23276	0,61	0,00030
219157_at	KLHL2	kelch-like 2, Mayven (Drosophila)	11275	0,63	0,13712
204177_s_at	KLHL20	kelch-like 20 (Drosophila)	27252	0,91	0,43743
203068_at	KLHL21	kelch-like 21 (Drosophila)	9903	0,93	0,80451
222141_at	KLHL22	kelch-like 22 (Drosophila)	84861	1,18	0,03732
213610_s_at	KLHL23	kelch-like 23 (Drosophila)	151230	1,02	0,83339
221985_at	KLHL24	kelch-like 24 (Drosophila)	54800	0,97	0,84749
210307_s_at	KLHL25 /// LOC100129082	kelch-like 25 (Drosophila) /// hypothetical protein LOC100129082	64410	1,26	0,02995
219354_at	KLHL26	kelch-like 26 (Drosophila)	55295	0,96	0,81030
220374_at	KLHL28	kelch-like 28 (Drosophila)	54813	1,61	0,00012
220348_at	KLHL29	kelch-like 29 (Drosophila)	114818	1,21	0,03367
221221_s_at	KLHL3	kelch-like 3 (Drosophila)	26249	0,85	0,20169
214591_at	KLHL4	kelch-like 4 (Drosophila)	56062	1,19	0,08502
220239_at	KLHL7	kelch-like 7 (Drosophila)	55975	0,49	0,06164
213117_at	KLHL9	kelch-like 9 (Drosophila)	55958	0,93	0,44401
202674_s_at	LMO7	LIM domain 7	4008	1,13	0,32610
213256_at	LOC100133609 /// MARCH3	membrane-associated ring finger (C3HC4) 3 /// similar to membrane-associated ring finger (C3HC4) 3	115123	0,69	0,12991
212879_x_at	LOC100134427 /// PIAS4	protein inhibitor of activated STAT, 4 /// similar to PIAS4 protein	51588	1,15	0,35112
211012_s_at	LOC161527	promyelocytic leukemia /// hypothetical protein	161527///	1,67	0,00059

	/// PML	LOC161527	5371///652671		
221851_at	LOC90379	hypothetical protein BC002926	90379	1,18	0,19021
201932_at	LRRC41	leucine rich repeat containing 41	10489	0,79	0,04013
214786_at	MAP3K1	mitogen-activated protein kinase kinase kinase 1	4214	1,20	0,06090
205386_s_at	MDM2	Mdm2 p53 binding protein homolog (mouse)	4193	1,03	0,69372
212576_at	MGRN1	mahogunin, ring finger 1	23295	1,20	0,29659
203637_s_at	MID1	midline 1 (Opitz/BBB syndrome)	4281	0,96	0,79658
208384_s_at	MID2	midline 2	11043	1,09	0,38196
201960_s_at	MYCBP2	MYC binding protein 2	23077	0,71	0,18543
220319_s_at	MYLIP	myosin regulatory light chain interacting protein	29116	0,91	0,35008
213012_at	NEDD4	neural precursor cell expressed, developmentally down-regulated 4	4734	0,80	0,08003
212448_at	NEDD4L	neural precursor cell expressed, developmentally down-regulated 4-like	23327	1,17	0,08391
204889_s_at	NEURL	neuralized homolog (Drosophila)	9148	1,10	0,19864
213204_at	PARC	p53-associated parkin-like cytoplasmic protein	23113	1,32	0,08278
207058_s_at	PARK2	Parkinson disease (autosomal recessive, juvenile) 2, parkin	5071	1,32	0,01021
215305_at	PDGFRA	platelet-derived growth factor receptor, alpha polypeptide	445372 /// 5156	1,06	0,47361
218319_at	PELI1	pellino homolog 1 (Drosophila)	57162	0,65	0,14685
219132_at	PELI2	pellino homolog 2 (Drosophila)	57161	0,62	0,02454
212542_s_at	PHIP	pleckstrin homology domain interacting protein	55023	0,74	0,28355
217864_s_at	PIAS1	protein inhibitor of activated STAT, 1	8554	0,64	0,00921
214442_s_at	PIAS2	protein inhibitor of activated STAT, 2	9063	0,79	0,19660
203035_s_at	PIAS3	protein inhibitor of activated STAT, 3	10401	0,74	0,02276
212881_at	PIAS4	protein inhibitor of activated STAT, 4	51588	0,94	0,57021
218667_at	PJA1	praja 1	64219	0,61	0,02997
201133_s_at	**PJA2**	**praja 2, RING-H2 motif containing**	**9867**	**0,27**	**0,00013**
211589_at	PML	promyelocytic leukemia	5371	1,64	0,00998
220741_s_at	PPA2	pyrophosphatase (inorganic) 2	140691///27068	0,51	0,02643
206064_s_at	PPIL2	peptidylprolyl isomerase (cyclophilin)-like 2	23759	1,47	0,00231
203103_s_at	PRPF19	PRP19/PSO4 pre-mRNA processing factor 19 homolog (S. cerevisiae)	27339	0,85	0,55162
217589_at	RAB40A	RAB40A, member RAS oncogene family	142684	1,12	0,14465
204547_at	RAB40B	RAB40B, member RAS oncogene family	10966	1,01	0,96678
213466_at	RAB40C	RAB40C, member RAS oncogene family	57799	1,33	0,09374
205023_at	RAD51	RAD51 homolog (RecA homolog, E. coli) (S. cerevisiae)	5888	1,12	0,13211
206591_at	RAG1	recombination activating gene 1	5896	1,11	0,08336
201712_s_at	RANBP2	RAN binding protein 2	5903	0,78	0,01245
207713_s_at	RBCK1	RanBP-type and C3HC4-type zinc finger containing 1	10616	1,49	0,01084
218117_at	RBX1	ring-box 1	9978	0,54	0,00594
212743_at	RCHY1	ring finger and CHY zinc finger domain containing 1	25898	1,09	0,33459
212651_at	RHOBTB1	Rho-related BTB domain containing 1	9886	0,86	0,58339
209441_at	RHOBTB2	Rho-related BTB domain containing 2	23221	1,10	0,27593
202976_s_at	**RHOBTB3**	**Rho-related BTB domain containing 3**	**22836**	**0,30**	**0,00382**
208371_s_at	RING1	ring finger protein 1	6015	0,89	0,22299
208924_at	**RNF11**	**ring finger protein 11**	**26994**	**0,41**	**0,00767**
221063_x_at	RNF123	ring finger protein 123	63891	1,08	0,52843
207735_at	RNF125	ring finger protein 125	54941	1,19	0,07563
205748_s_at	RNF126	ring finger protein 126	55658	1,00	0,98290
219263_at	RNF128	ring finger protein 128	79589	0,64	0,07891
218738_s_at	**RNF138**	**ring finger protein 138**	**51444**	**0,30**	**0,00028**
201824_at	RNF14	ring finger protein 14	9604	0,51	0,00007
204040_at	RNF144A	ring finger protein 144A	9781	0,91	0,40697
220483_s_at	RNF19A	ring finger protein 19A	25897	1,37	0,03009

36564_at	RNF19B	ring finger protein 19B	127544	1,11	0,45164
205215_at	RNF2	ring finger protein 2	6045	1,09	0,49514
218425_at	RNF216	ring finger protein 216	54476	1,31	0,06300
218861_at	RNF25	ring finger protein 25	64320	1,02	0,78968
206845_s_at	RNF40	ring finger protein 40	9810	0,98	0,87342
201962_s_at	RNF41	ring finger protein 41	10193	0,62	0,01272
209111_at	RNF5	ring finger protein 5	6048	0,53	0,00467
218286_s_at	**RNF7**	**ring finger protein 7**	**9616**	**0,49**	**0,00765**
203161_s_at	RNF8	ring finger protein 8	9025	1,31	0,01271
200051_at	SART1	squamous cell carcinoma antigen recognized by T cells	9092	1,05	0,58468
202980_s_at	SIAH1	seven in absentia homolog 1 (Drosophila)	6477	0,84	0,08313
209339_at	SIAH2	seven in absentia homolog 2 (Drosophila)	6478	0,91	0,44034
200711_s_at	SKP1	S-phase kinase-associated protein 1	6500	0,51	0,00340
203626_s_at	SKP2	S-phase kinase-associated protein 2 (p45)	6502	1,51	0,00390
212666_at	SMURF1	SMAD specific E3 ubiquitin protein ligase 1	57154	0,75	0,16143
205596_s_at	SMURF2	SMAD specific E3 ubiquitin protein ligase 2	64750	0,82	0,54422
210001_s_at	SOCS1	suppressor of cytokine signaling 1	8651	1,06	0,80342
203373_at	SOCS2	suppressor of cytokine signaling 2	8835	0,45	0,01648
206360_s_at	SOCS3	suppressor of cytokine signaling 3	9021	1,51	0,00990
208127_s_at	SOCS5	suppressor of cytokine signaling 5	9655	0,57	0,00893
206020_at	SOCS6	suppressor of cytokine signaling 6	9306	0,67	0,00710
214015_at	SOCS7	suppressor of cytokine signaling 7	30837	1,38	0,03520
204640_s_at	SPOP	speckle-type POZ protein	8405	1,02	0,85380
219677_at	SPSB1	splA/ryanodine receptor domain and SOCS box containing 1	80176	1,85	0,00943
221769_at	SPSB3	splA/ryanodine receptor domain and SOCS box containing 3	90864	1,08	0,39201
217934_x_at	STUB1	STIP1 homology and U-box containing protein 1	10273	0,89	0,37074
202824_s_at	TCEB1	transcription elongation factor B (SIII), polypeptide 1 (15kDa, elongin C)	6921	0,55	0,05077
200085_s_at	TCEB2	transcription elongation factor B (SIII), polypeptide 2 (18kDa, elongin B)	6923	0,88	0,57084
204071_s_at	TOPORS	topoisomerase I binding, arginine/serine-rich	10210	0,77	0,10738
212654_at	TPM2	tropomyosin 2 (beta)	122769 /// 7169	1,43	0,00935
201731_s_at	TPR	translocated promoter region (to activated MET oncogene)	7175///8945	0,82	0,14646
204413_at	TRAF2	TNF receptor-associated factor 2	7186	1,24	0,03812
204352_at	TRAF5	TNF receptor-associated factor 5	7188	0,82	0,37071
205558_at	TRAF6	TNF receptor-associated factor 6	7189	1,08	0,41617
205598_at	TRAIP	TRAF interacting protein	10293	1,29	0,00314
221627_at	TRIM10	tripartite motif-containing 10	10107	1,42	0,01153
203659_s_at	**TRIM13**	**tripartite motif-containing 13**	**10206**	**0,42**	**0,00155**
203148_s_at	TRIM14	tripartite motif-containing 14	9830	1,02	0,95445
210177_at	TRIM15	tripartite motif-containing 15	89870	1,72	0,00154
204341_at	TRIM16	tripartite motif-containing 16	10626///147166///653524	0,53	0,04720
220279_at	TRIM17	tripartite motif-containing 17	51127	1,32	0,05689
202342_s_at	**TRIM2**	**tripartite motif-containing 2**	**23321**	**0,25**	**0,00011**
204804_at	TRIM21	tripartite motif-containing 21	6737 /// 81025	1,00	0,98642
213293_s_at	TRIM22	tripartite motif-containing 22	10346	1,37	0,12345
210995_s_at	TRIM23	tripartite motif-containing 23	373	1,07	0,40957
204391_x_at	TRIM24	tripartite motif-containing 24	8805	1,05	0,74702
206911_at	TRIM25	tripartite motif-containing 25	7706	1,53	0,00444
202702_at	TRIM26	tripartite motif-containing 26	7726	1,35	0,00378
210541_s_at	TRIM27	tripartite motif-containing 27	5987	0,60	0,00733

200990_at	TRIM28	tripartite motif-containing 28	10155	1,01	0,96386
202504_at	TRIM29	tripartite motif-containing 29	23650	1,34	0,29551
204911_s_at	TRIM3	tripartite motif-containing 3	10612	1,20	0,06016
210159_s_at	TRIM31	tripartite motif-containing 31	11074	1,42	0,00329
203846_at	TRIM32	tripartite motif-containing 32	22954	0,92	0,35576
212435_at	TRIM33	tripartite motif-containing 33	51592	0,72	0,02638
221044_s_at	TRIM34///TRIM6///TRIM6-TRIM34	tripartite motif-containing 34 /// tripartite motif-containing 6 /// TRIM6-TRIM34	445372///53840	1,33	0,01500
213009_s_at	**TRIM37**	**tripartite motif-containing 37**	**4591**	**0,46**	**0,00278**
203568_s_at	TRIM38	tripartite motif-containing 38	10475	1,37	0,01740
217759_at	**TRIM44**	**tripartite motif-containing 44**	**54765**	**0,49**	**0,00208**
219923_at	TRIM45	tripartite motif-containing 45	80263	1,40	0,04080
220909_at	TRIM46	tripartite motif-containing 46	80128	1,15	0,23970
220534_at	TRIM48	tripartite motif-containing 48	79097	1,38	0,02118
221154_at	TRIM49	tripartite motif-containing 49	283116///57093///653111	1,09	0,28617
210705_s_at	TRIM5	tripartite motif-containing 5	85363	1,13	0,49801
221897_at	TRIM52	tripartite motif-containing 52	84851	0,78	0,01521
215047_at	TRIM58	tripartite motif-containing 58	25893	1,04	0,60176
219272_at	TRIM62	tripartite motif-containing 62	55223	1,63	0,00050
213748_at	TRIM66	tripartite motif-containing 66	9866	1,08	0,33183
219405_at	TRIM68	tripartite motif-containing 68	55128	0,64	0,03209
221012_s_at	TRIM8	tripartite motif-containing 8	81603	1,14	0,57391
209859_at	TRIM9	tripartite motif-containing 9	114088	0,46	0,02153
201546_at	TRIP12	thyroid hormone receptor interactor 12	9320	0,54	0,02775
212059_s_at	TRPC4AP	transient receptor potential cation channel, subfamily C, member 4 associated protein	26133	0,91	0,37798
202151_s_at	UBAC1	UBA domain containing 1	10422	0,70	0,02590
214980_at	UBE3A	Ubiquitin protein ligase E3A (human papilloma virus E6-associated protein, Angelman syndrome)	7337	1,37	0,01892
201817_at	**UBE3C**	**ubiquitin protein ligase E3C**	**9690**	**0,41**	**0,00486**
202038_at	**UBE4A**	**ubiquitination factor E4A (UFD2 homolog, yeast)**	**9354**	**0,40**	**0,00956**
202317_s_at	UBE4B	ubiquitination factor E4B (UFD2 homolog, yeast)	10277	0,80	0,18330
204598_at	UBOX5	U-box domain containing 5	22888	1,39	0,00530
212760_at	UBR2	ubiquitin protein ligase E3 component n-recognin 2	23304	0,62	0,02378
211950_at	UBR4	ubiquitin protein ligase E3 component n-recognin 4	23352	1,07	0,74711
208883_at	UBR5	ubiquitin protein ligase E3 component n-recognin 5	51366	0,65	0,00326
203844_at	VHL	von Hippel-Lindau tumor suppressor	7428	1,14	0,04834
204377_s_at	VPRBP	Vpr (HIV-1) binding protein	9730	1,10	0,48302
214758_at	WDR21A	WD repeat domain 21A	26094	1,43	0,00605
201886_at	WDR23	WD repeat domain 23	80344	0,87	0,34983
219001_s_at	WDR32	WD repeat domain 32	79269	0,94	0,64812
202250_s_at	WDR42A	WD repeat domain 42A	50717	0,83	0,36918
221744_at	WDR68	WD repeat domain 68	10238	0,92	0,29161
220843_s_at	WDSOF1	WD repeats and SOF1 domain containing	25879	1,02	0,79486
215497_s_at	WDTC1	WD and tetratricopeptide repeats 1	23038	1,40	0,01607
201296_s_at	WSB1	WD repeat and SOCS box-containing 1	26118	1,05	0,88000
201760_s_at	**WSB2**	**WD repeat and SOCS box-containing 2**	**55884**	**0,31**	**0,00132**
212637_s_at	WWP1	WW domain containing E3 ubiquitin protein ligase 1	11059	0,78	0,23480
210200_at	WWP2	WW domain containing E3 ubiquitin protein ligase 2	11060	1,19	0,11128
206536_s_at	XIAP	X-linked inhibitor of apoptosis	331	1,00	0,94050
213376_at	**ZBTB1**	**zinc finger and BTB domain containing 1**	**22890**	**0,33**	**0,00092**
219312_s_at	ZBTB10	zinc finger and BTB domain containing 10	65986	0,75	0,01620
204847_at	ZBTB11	zinc finger and BTB domain containing 11	27107	0,57	0,03810
205883_at	ZBTB16	zinc finger and BTB domain containing 16	7704	1,27	0,10760
203602_s_at	ZBTB17	zinc finger and BTB domain containing 17	7709	1,42	0,01116

205383_s_at	ZBTB20	zinc finger and BTB domain containing 20	26137	0,95	0,85036
213081_at	ZBTB22	zinc finger and BTB domain containing 22	9278	1,21	0,14572
205340_at	ZBTB24	zinc finger and BTB domain containing 24	9841	0,88	0,54734
214482_at	ZBTB25	zinc finger and BTB domain containing 25	7597	1,15	0,14030
220391_at	ZBTB3	zinc finger and BTB domain containing 3	79842	0,92	0,39180
220118_at	ZBTB32	zinc finger and BTB domain containing 32	27033	1,38	0,02402
214631_at	ZBTB33	zinc finger and BTB domain containing 33	10009	1,13	0,18199
219221_at	ZBTB38	zinc finger and BTB domain containing 38	253461	0,82	0,15415
205256_at	ZBTB39	zinc finger and BTB domain containing 39	9880	1,23	0,04082
203958_s_at	ZBTB40	zinc finger and BTB domain containing 40	9923	1,38	0,00470
204182_s_at	ZBTB43	zinc finger and BTB domain containing 43	23099	1,22	0,18012
220243_at	ZBTB44	zinc finger and BTB domain containing 44	29068	1,41	0,02428
205025_at	ZBTB48	zinc finger and BTB domain containing 48	3104	1,21	0,15256
203026_at	ZBTB5	zinc finger and BTB domain containing 5	9925	0,85	0,07131
206098_at	ZBTB6	zinc finger and BTB domain containing 6	10773	1,00	0,94891
219186_at	***ZBTB7A***	***zinc finger and BTB domain containing 7A***	***51341***	***2,09***	***0,00037***
205853_at	ZBTB7B	zinc finger and BTB domain containing 7B	51043	1,33	0,05670
217675_at	ZBTB7C	zinc finger and BTB domain containing 7C	201501	1,26	0,02336
202456_s_at	ZER1	zer-1 homolog (C. elegans)	10444	1,12	0,11794
212742_at	ZNF364	zinc finger protein 364	27246	0,55	0,00849

Deubiquitinating enzyme (DUB)

205416_s_at	ATXN3	ataxin 3	4287	1,13	0,24795
216539_at	ATXN3L	ataxin 3-like	92552	1,10	0,43534
201419_at	BAP1	BRCA1 associated protein-1 (ubiquitin carboxy-terminal hydrolase)	8314	1,01	0,90154
202467_s_at	**COPS2**	**COP9 constitutive photomorphogenic homolog subunit 2 (Arabidopsis)**	**9318**	**0,37**	**0,00092**
202078_at	**COPS3**	**COP9 constitutive photomorphogenic homolog subunit 3 (Arabidopsis)**	**8533**	**0,50**	**0,00162**
218042_at	**COPS4**	**COP9 constitutive photomorphogenic homolog subunit 4 (Arabidopsis)**	**51138**	**0,35**	**0,00842**
201652_at	**COPS5**	**COP9 constitutive photomorphogenic homolog subunit 5 (Arabidopsis)**	**10987**	**0,45**	**0,00067**
201405_s_at	COPS6	COP9 constitutive photomorphogenic homolog subunit 6 (Arabidopsis)	10980	0,52	0,00106
209029_at	COPS7A	COP9 constitutive photomorphogenic homolog subunit 7A (Arabidopsis)	50813	0,53	0,00110
219997_s_at	COPS7B	COP9 constitutive photomorphogenic homolog subunit 7B (Arabidopsis)	64708	0,95	0,58050
202142_at	COPS8	COP9 constitutive photomorphogenic homolog subunit 8 (Arabidopsis)	10920	0,71	0,00216
222142_at	CYLD	cylindromatosis (turban tumor syndrome)	1540	0,96	0,78154
217782_s_at	GPS1	G protein pathway suppressor 1	2873	0,84	0,13774
206624_at	LOC100130216 /// USP9Y	ubiquitin specific peptidase 9, Y-linked (fat facets-like, Drosophila) /// hypothetical protein LOC100130216	8287	0,91	0,47376
201246_s_at	OTUB1	OTU domain, ubiquitin aldehyde binding 1	55611	1,11	0,27587
219369_s_at	OTUB2	OTU domain, ubiquitin aldehyde binding 2	78990	1,14	0,33562
220031_at	OTUD7B	OTU domain containing 7B	56957	1,25	0,03542
218122_s_at	SENP2	SUMO1/sentrin/SMT3 specific peptidase 2	59343	0,99	0,91285
203871_at	SENP3	SUMO1/sentrin/SMT3 specific peptidase 3	26168	0,82	0,18913
222110_at	SENP5	SUMO1/sentrin specific peptidase 5	205564	1,32	0,00530
202319_at	SENP6	SUMO1/sentrin specific peptidase 6	26054	0,96	0,60019
220735_s_at	SENP7	SUMO1/sentrin specific peptidase 7	57337	1,01	0,83692
202811_at	STAMBP	STAM binding protein	10617	0,81	0,30577
220803_at	STAMBPL1	STAM binding protein-like 1	57559	1,20	0,01466
201387_s_at	**UCHL1**	**ubiquitin carboxyl-terminal esterase L1 (ubiquitin thiolesterase)**	**7345**	**0,26**	**0,00029**
204616_at	UCHL3	ubiquitin carboxyl-terminal esterase L3 (ubiquitin	7347	0,42	0,02587

		thiolesterase)			
219960_s_at	UCHL5	ubiquitin carboxyl-terminal hydrolase L5	51377	0,59	0,00118
202413_s_at	**USP1**	**ubiquitin specific peptidase 1**	**7398**	**0,24**	**0,00002**
209137_s_at	USP10	ubiquitin specific peptidase 10	9100	0,72	0,03641
208723_at	USP11	ubiquitin specific peptidase 11	8237	0,79	0,12994
213327_s_at	USP12	ubiquitin specific peptidase 12	219333	0,62	0,05806
205356_at	USP13	ubiquitin specific peptidase 13 (isopeptidase T-3)	8975	0,82	0,20380
201672_s_at	USP14	ubiquitin specific peptidase 14 (tRNA-guanine transglycosylase)	9097	0,48	0,02309
209475_at	USP15	ubiquitin specific peptidase 15	9958	0,67	0,01112
218386_x_at	**USP16**	**ubiquitin specific peptidase 16**	**10600**	**0,28**	**0,00010**
219211_at	USP18	ubiquitin specific peptidase 18	11274	1,12	0,31040
214674_at	USP19	ubiquitin specific peptidase 19	10869	1,19	0,06982
207213_s_at	USP2	ubiquitin specific peptidase 2	9099	1,28	0,09375
203965_at	USP20	ubiquitin specific peptidase 20	10868	1,15	0,32689
218367_x_at	USP21	ubiquitin specific peptidase 21	27005	1,20	0,05979
200083_at	USP22	ubiquitin specific peptidase 22	23326	0,86	0,37993
212388_at	USP24	ubiquitin specific peptidase 24	23358	0,61	0,00591
220419_s_at	USP25	ubiquitin specific peptidase 25	29761	0,52	0,00526
217605_at	USP27X	ubiquitin specific peptidase 27, X-linked	389856	1,24	0,10877
220895_at	USP29	ubiquitin specific peptidase 29	57663	1,40	0,08287
221654_s_at	USP3	ubiquitin specific peptidase 3	9960	0,51	0,01760
211702_s_at	USP32	ubiquitin specific peptidase 32	84669	1,10	0,50612
212513_s_at	USP33	ubiquitin specific peptidase 33	23032	0,57	0,08711
215013_s_at	USP34	ubiquitin specific peptidase 34	9736	1,08	0,26919
220370_s_at	USP36	ubiquitin specific peptidase 36	57602	1,61	0,12070
202682_s_at	USP4	ubiquitin specific peptidase 4 (proto-oncogene)	7375	1,67	0,00699
203869_at	**USP46**	**ubiquitin specific peptidase 46**	**64854**	**0,38**	**0,00075**
221518_s_at	USP47	ubiquitin specific peptidase 47	55031	1,10	0,50758
220078_at	USP48	ubiquitin specific peptidase 48	84196	1,12	0,30099
206031_s_at	USP5	ubiquitin specific peptidase 5 (isopeptidase T)	8078	1,49	0,00127
206405_x_at	USP6	ubiquitin specific peptidase 6 (Tre-2 oncogene)	9098	0,89	0,33213
201499_s_at	USP7	ubiquitin specific peptidase 7 (herpes virus-associated)	7874	0,83	0,13211
202745_at	USP8	ubiquitin specific peptidase 8	9101	0,62	0,02078
201100_s_at	USP9X	ubiquitin specific peptidase 9, X-linked	8239	0,80	0,07103
219810_at	VCPIP1	valosin containing protein (p97)/p47 complex interacting protein 1	80124	0,91	0,35293

PROTEASOME

PA 700 (Lid)

201388_at	PSMD3	proteasome (prosome, macropain) 26S subunit, non-ATPase, 3	5709	0,78	0,11709
202353_s_at	**PSMD12**	**proteasome (prosome, macropain) 26S subunit, non-ATPase, 12**	**5718**	**0,37**	**0,00122**
208777_s_at	**PSMD11**	**proteasome (prosome, macropain) 26S subunit, non-ATPase, 11**	**5717**	**0,40**	**0,00004**
202753_at	**PSMD6**	**proteasome (prosome, macropain) 26S subunit, non-ATPase, 6**	**9861**	**0,27**	**0,00019**
201705_at	**PSMD7**	**proteasome (prosome, macropain) 26S subunit, non-ATPase, 7**	**5713**	**0,48**	**0,00055**
201232_s_at	PSMD13	proteasome (prosome, macropain) 26S subunit, non-ATPase, 13	5719	0,77	0,17327
212296_at	**PSMD14**	**proteasome (prosome, macropain) 26S subunit, non-ATPase, 14**	**10213**	**0,30**	**0,00098**
200820_at	**PSMD8**	**proteasome (prosome, macropain) 26S subunit, non-ATPase, 8**	**5714**	**0,45**	**0,00030**
202276_at	SHFM1	split hand/foot malformation (ectrodactyly) type 1	7979	0,84	0,27711
200882_s_at	PSMD4	proteasome (prosome, macropain) 26S subunit, non-	5710	0,89	0,55327

		ATPase, 4			
200814_at	PSME1	proteasome (prosome, macropain) activator subunit 1 (PA28 alpha)	5720	0,87	0,41440
201762_s_at	PSME2	proteasome (prosome, macropain) activator subunit 2 (PA28 beta)	5721	1,26	0,36220
200988_s_at	PSME3	proteasome (prosome, macropain) activator subunit 3 (PA28 gamma; Ki)	10197	0,63	0,01216
PA 700 (Base)					
200830_at	PSMD2	proteasome (prosome, macropain) 26S subunit, non-ATPase, 2	5708	0,63	0,07546
201199_s_at	PSMD1	proteasome (prosome, macropain) 26S subunit, non-ATPase, 1	5707	0,67	0,05796
201068_s_at	**PSMC2**	**proteasome (prosome, macropain) 26S subunit, ATPase, 2**	**5701**	**0,38**	**0,00149**
204219_s_at	PSMC1	proteasome (prosome, macropain) 26S subunit, ATPase, 1	5700	0,69	0,09507
209503_s_at	PSMC5	proteasome (prosome, macropain) 26S subunit, ATPase, 5	5705	0,68	0,04825
201699_at	**PSMC6**	**proteasome (prosome, macropain) 26S subunit, ATPase, 6**	**5706**	**0,32**	**0,00876**
201267_s_at	**PSMC3**	**proteasome (prosome, macropain) 26S subunit, ATPase, 3**	**5702**	**0,39**	**0,00048**
201252_at	PSMC4	proteasome (prosome, macropain) 26S subunit, ATPase, 4	5704 /// 652826	0,59	0,01590
212219_at	PSME4	proteasome (prosome, macropain) activator subunit 4	23198	0,71	0,14167
Core particles (20S Proteasome)					
208805_at	KIAA0391 /// PSMA6	proteasome (prosome, macropain) subunit, alpha type, 6 /// KIAA0391	5687	0,49	0,02720
201317_s_at	PSMA2	proteasome (prosome, macropain) subunit, alpha type, 2	5683	0,36	0,01118
203396_at	PSMA4	proteasome (prosome, macropain) subunit, alpha type, 4	5685	0,53	0,19200
216088_s_at	PSMA7	proteasome (prosome, macropain) subunit, alpha type, 7	5688	0,61	0,01803
201274_at	PSMA5	proteasome (prosome, macropain) subunit, alpha type, 5	5686	0,56	0,02036
210759_s_at	**PSMA1**	**proteasome (prosome, macropain) subunit, alpha type, 1**	**5682**	**0,28**	**0,00044**
201532_at	**PSMA3**	**proteasome (prosome, macropain) subunit, alpha type, 3**	**5684**	**0,24**	**0,00264**
208827_at	PSMB6	proteasome (prosome, macropain) subunit, beta type, 6	5694	0,63	0,11133
200786_at	**PSMB7**	**proteasome (prosome, macropain) subunit, beta type, 7**	**5695**	**0,40**	**0,00045**
201400_at	PSMB3	proteasome (prosome, macropain) subunit, beta type, 3	5691	0,56	0,00145
200039_s_at	PSMB2	proteasome (prosome, macropain) subunit, beta type, 2	5690	0,82	0,28433
208799_at	**PSMB5**	**proteasome (prosome, macropain) subunit, beta type, 5**	**5693**	**0,32**	**0,00038**
200876_s_at	**PSMB1**	**proteasome (prosome, macropain) subunit, beta type, 1**	**5689**	**0,35**	**0,00159**
202244_at	PSMB4	proteasome (prosome, macropain) subunit, beta type, 4	5692	0,80	0,15209
204279_at	PSMB9	proteasome (prosome, macropain) subunit, beta type, 9 (large multifunctional peptidase 2)	5698	0,96	0,90485
202659_at	PSMB10	proteasome (prosome, macropain) subunit, beta type, 10	5699	1,27	0,32682
209040_s_at	PSMB8	proteasome (prosome, macropain) subunit, beta type, 8 (large multifunctional peptidase 7)	5696	0,67	0,28143
Accessories genes					
217769_s_at	POMP	proteasome maturation protein	51371	0,74	0,17751
201053_s_at	PSMF1	proteasome (prosome, macropain) inhibitor subunit 1 (PI31)	9491	0,63	0,02343

Nota: I probe sets upregolati in maniera significativa sono elencati in grassetto e corsivo, mentre quelli significativamente downregolati sono elencato solo in grassetto