

Altered integrin expression patterns revealed by microarray in human cutaneous melanoma

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Abstract

A large variety of molecular pathways in melanoma progression suggests that no individual molecular alteration is crucial itself. Our aim was to define the molecular alterations underlying metastasis formation. Gene expression profiling was performed using microarray and qRT-PCR to define alterations between matched primary and metastatic melanoma cell lines. These data were integrated with publicly available unmatched tissue data. The invasiveness of cell lines was determined by Matrigel invasion assays, and invasive clones from primary melanoma derived cell lines were also selected. Two metastatic cell line models were created: the regional lymph node WM983A-WM983A^{INV}-WM983B and the distant lung WM793B-WM793B^{INV}-1205Lu metastatic models. The majority of metastasis genes were downregulated and enriched in adhesion and ITGA6-B4 pathways. Upregulation of immune pathways was characteristic of distant metastases, whereas increased Rap1 signalling was specific for regional (sub)cutaneous metastases. qRT-PCR analysis of selected integrins (A2, A3, A4, A9, B5, B8, A6, B1 and B3) highlighted the possible importance of ITGA3/4 and B8 in metastatic process, distinguishing regional and distant metastases. We identified functionally relevant gene clusters that influenced metastasis formation. Our data provide further evidence that integrin expression patterns may be important in distant metastasis formation.

Key words: melanoma metastasis, gene expression microarray, integrins, cell line invasivity

Introduction

Melanocyte-derived malignant melanoma is among the most challenging malignancies to treat, with an increasing incidence and high mortality worldwide [1]. The metastatic process is the predominant cause of melanoma-specific death, dramatically decreasing survival rates. Effective treatments that substantially extend the life expectancy of patients with advanced stage melanoma are still not available [2]. Recent efforts have revealed that a large variety of molecular pathways are associated with disease development and progression, thus suggesting that no individual molecular alteration is crucial in these processes. Therefore, the identification of novel metastasis-specific biomarkers is essential to improving both tumor prognosis and disease management [3, 4].

The rapid development of microarray technology provides a great opportunity to discover prognosis-related genetic and gene expression signatures [5-7]. These high-throughput screening technologies have been extensively used in cancer research to identify tumor subclasses, predict disease outcomes and define genes associated with drug resistance. However, these studies face several obstacles, including the scarcity of samples, the heterogeneous nature of this malignancy and the wide variety of platforms and statistical methods used, thus making the prediction of the clinical-biological outcome and efficacy of these patterns relative to current clinical practices uncertain [8-10]. In contrast to breast cancer, in which the breakthrough MammaPrint 70 gene signature provides an opportunity to enhance tumor classification, prognosis and outcome prediction [11, 12], such a set of prognosis-related genes does not exist for melanoma. Surgical resection and sentinel lymph node monitoring remain the leading treatment option. Classical prognostic markers for melanoma have only limited predictive power at the individual level and do not directly aid in decision making between the limited treatment options [8, 13]. In recent years, efforts have been made to evaluate and standardize methodical approaches to allow comparison of results derived from different microarray studies [14-16].

Because of the limited availability of cryopreserved tissue samples, relatively few genetic and gene expression studies in matched primary and metastatic melanomas have been conducted [17-20]. In the present study, our aim was to define molecular alterations underlying metastasis formation and to determine the extent to which the profiles of primary melanoma and the corresponding metastasis are similar or distinct. We used gene expression profiling with Affymetrix Human Gene 1.0 ST arrays on paired human melanoma cell lines with different invasive properties. These experiments were also completed with RNAseq data of unmatched primary and metastatic melanoma tissue samples (SKCM) from the TCGA (The Cancer Genome Atlas) data portal.

As both primary and metastatic tumors are genetically heterogeneous and could be evolved parallelly [21], analysis of paired samples might be helpful in identifying molecular pathways that influence the biological behaviour of melanoma, highlighting the progression-related genes [22]. These candidate genes may be used as targets in combination therapies or in the prevention of advanced human melanomas in the future.

Materials and methods

Cell lines

Human melanoma cell line pairs [WM983A and WM983B, WM115 and WM266-4, WM278 and WM1617, WM793B and 1205Lu] were maintained in RPMI medium supplemented with 10% foetal bovine serum, 300 mg/l L-glutamine and antibiotics. All cell lines were obtained from Coriell Cell Repositories of the Coriell Institute for Medical Research (Camden, New Jersey, USA), and all chemicals were obtained from Sigma-Aldrich (Sigma-Aldrich Inc., St. Louis, MO, USA).

Melanoma tissue samples used for qRT-PCR

Fresh/frozen melanoma tissues were obtained from the Department of Dermatology at the University of Debrecen (Debrecen, Hungary) from patients who did not undergo therapy prior to surgical removal of their primary lesions. This study was approved by the Regional and Institutional Ethics Committee of the University of Debrecen [document no.: 25364-1/2012/EKU (449/PI/12.)] and was performed according to all relevant regulations. Lesions were diagnosed on the basis of formalin-fixed paraffin-embedded (FFPE) tissue sections stained with haematoxylin-eosin. A total of 19 primary and 17 metastatic melanoma samples were used for the qRT-PCR of integrins. Clinical-pathological parameters of the tumors are summarized in Table 1.

RNA extraction, quality control and microarray hybridization

An RNeasy Plus Mini Kit (Qiagen GmbH, Hilden, Germany) was used to isolate the total RNA from melanoma cell lines. The obtained RNA was quantified using a NanoDrop ND-1000 UV-Vis Spectrophotometer (NanoDrop Technologies, Wilmington, DE), and only samples with a 260/280 ratio of greater than 1.8 were included in the analysis. Sample quality was checked using an Agilent 2100 Bioanalyzer (Agilent Technologies, Inc., Santa Clara, CA, USA), and samples with an RNA Integrity Number (RIN) of greater than 7.5 were considered for labelling and hybridization to Affymetrix Human Gene 1.0 microarrays (Affymetrix, Inc., Santa Clara, CA, USA). Labelling, hybridization and imaging setup were performed by UD-GenoMed Medical Genomic Technologies Ltd. (University of Debrecen, Clinical Genomic Center, Debrecen, Hungary) according to the recent laboratory protocol using 500 ng of sample RNA. The microarray data were deposited in the Gene Expression Omnibus (GEO) repository under accession number GSE65570.

Analysis of Microarray Experiments

Gene Expression Microarrays

RMA (Robust Microarray Analysis) analysis was performed on raw chip data (CEL files) using conditions summarized in the Supplementary Methods. Melanocyte was used as reference array. Using

stringent criteria a total of 7542 out of the 33297 genes were passed the filtering criteria and were taken on further analysis using the Bioconductor BRB-ArrayTools 4.3.0 (Richard Simon and Amy Peng Lam, National Cancer Institute, Bethesda, USA) software as described in the Supplementary Methods.

Gene expression analysis was completed with RNAseq data on melanoma tissue samples (SKCM) from the TCGA (The Cancer Genome Atlas) data portal, using batches 180, 198, 206, 240, 262, 277, 291, 316, 332, 358, 388, 393, 408 and 416. Dataset was consisted of 109 primary tumors and 352 melanoma metastases with the following distribution of their location: 18.8% distant organ, 60.8% regional lymph node and 20.4% regional (sub)cutaneous. Normalized, level 3 data were downloaded and after \log_2 transformation, submitted to analysis using the same criteria as the cell line experiments. Except for that univariate test was two-sample t-test, considering p-value ≤ 0.01 as statistically significant.

Pathway Analysis of the Gene Expression Data

Functional characterization of differentially expressed genes ($p \leq 0.05$) that showed alteration of greater than 2-fold between the primary and metastatic melanomas was performed using GO-Elite 1.2.5 [23] and the web-accessible program of the Transcriptome, ontology, phenotype, proteome, and pharmacome annotations based gene list functional enrichment analysis (ToppFun) [24]. We applied Bonferroni correction using a p-value ≤ 0.01 , and only classes with at least 5 observations in the selected subset were considered as altered pathway. Genes, identified using the GO-Elite program, were categorized according to their reported biological and molecular functions.

Real-Time qRT-PCR analysis

Microarray results were confirmed for ITGA2, ITGA3, ITGA4, ITGA9, ITGB5 and ITGB8 using TaqMan real-time qPCR analysis. Additional integrins (ITGA6, ITGB1 and ITGB3) were also analyzed. The primers and UPL probes were designed with the ProbeFinder Software 2.50 (Universal ProbeLibrary Assay Design Center web service, Roche Diagnostics, Basel, Switzerland), and purchased from Roche Magyarország Ltd. (Roche Magyarország Ltd., Budaörs, Hungary). Primer sequences and the corresponding UPL probes are summarized in Supplementary Table 1. Reverse transcription and qRT-PCR workflow is summarized in the Supplementary Methods. Raw PCR data were analyzed using the Livak method ($2^{-\Delta\Delta C_t}$) with glyceraldehyde-3-phosphate dehydrogenase (GAPDH) and beta-actin (ACTB) as internal control genes and cultured melanocyte or pooled nevi (N=8) and pooled normal skin tissues (N=5) as calibrator samples. Two-sided Mann-Whitney-Wilcoxon exact test was used to reveal significant differences between primary melanomas and regional or distant organ metastases at the 0.05 nominal level of p-value. [Spearman correlation was applied to assess coexpression of different ITG subunits.](#)

Matrigel Invasion Assay

Invasive potential of melanoma cells was analyzed using 24-well BD Biocoat Matrigel invasion chambers (pore size: 8µm; BD Biosciences, Bedford, MA, USA). Assay conditions and evaluation are summarized in the Supplementary Methods. Parallel experiments were also run to separate invasive cell populations. After removing non-invading cells with a cotton swab, invasive cell clones were treated with 0.5% trypsin/0.2% EDTA solution (Sigma-Aldrich Inc., St. Louis, MO, USA) to extract from the membrane and were cultured following standard protocol in a T25 flask till 90% confluence before subjected to RNA isolation. Besides, invasive clones were also subjected to reanalysis to check whether they keep their invasive property.

Results

Altered gene expression patterns of primary and metastatic human melanoma cell line pairs

Tumor cell lines can be effective *in vitro* models for obtaining an overview of the processes involved in cancer development and progression. A total of four melanoma-derived cell line pairs were included in the study to investigate the differences between primary tumors and their corresponding metastases. The characteristics of the examined cell lines are summarized in the ‘Materials and Methods’ section.

After normalization, quality control and filtering steps of the microarray data, 7542 genes were used in further analyses. Gene expression profiles displayed a medium to high correlation between all matched cell line pairs (Pearson correlation 0.504-0.953, $p \leq 0.001$). Univariate t-tests with a random variance model were performed on log-transformed expression values of the probes to identify the differentially expressed genes (p-value cut-off 0.05, greater than 2-fold change). The analysis identified 438 genes that were differentially expressed between primary samples and metastases. The results are represented with a Volcano plot (Figure 1A). The transition from the vertical growth phase (VGT) to metastatic melanoma (MM) was typically accompanied by the loss of gene expression. The majority of the differentially expressed genes (Supplementary Table 2) were downregulated (413 genes), and only 25 genes were significantly upregulated in metastases compared to primary melanomas. The HLA-DPA1 gene exhibited the lowest expression, and histatin 1 (HTN1) showed the highest mRNA level. Multivariate tests with a false discovery rate (FDR) of less than 10% revealed no significant alterations between metastases and primary-derived cell lines; however, this test handles genes as independent units and does not consider the possible interactions between the genes.

To determine how primary and metastasis melanoma groups could be distinguished on the basis of the 438 altered genes, class prediction was performed using the nearest centroid algorithm with bootstrap cross-validation method to compute the misclassification rate. As shown in Figure 1B, 6 out of 8 melanoma cell lines were classified 100% correctly into the given group based on the preselected gene subset. The performance and precision of the classifier are shown in Figure 1C.

Pathway analysis of the gene expression data

Genes with decreased expression in metastasis were significantly enriched in the cell-cell and cell-matrix interaction, antigen processing and presentation (mainly HLA antigens), PI3K-Akt signalling and p53 signalling pathways (Supplementary Figure 1A) and belong to 7 molecular functional groups (Supplementary Figure 1B). The genes, including their molecular pathways and functional groups, are summarized in Supplementary Tables 3 and 4, respectively.

Of the 25 overexpressed genes, 24 were identified by DAVID, and 10 of these genes belonged to the well-known KEGG (Kyoto Encyclopedia of Genes and Genomes) pathways. The overexpressed genes in the metastasis-derived cell lines included genes with reported functional roles in the regulation of transcription, such as the nuclear receptor RORA, ATP-binding (e.g., MERTK or CKB) and integral membrane proteins (e.g., CD52 or GABRA5).

Altered gene expression patterns of unmatched primary and metastatic human melanoma tissues based on the TCGA RNAseq v2.0 data of SKCM

The cell line pair experiments were completed with tissue sample data from the TCGA Database. Because only a few data describing matched primary and metastasis melanoma are available, we used RNAseq v2.0 data to compare the expression patterns of unmatched metastatic primary lesions (N=109) and melanoma metastases with known location (N=352). Metastatic samples were subdivided into 3 groups based on their organ location: distant organ metastasis (N=66), regional lymph node metastasis (N=214) and regional (sub)cutaneous metastasis (N=72). Multivariate analysis revealed that out of 14,134 filtered transcripts and variants, 1065 unique genes showed altered expression with a greater than 2-fold change between primary samples and at least one of the 3 metastasis subgroups (Supplementary Table 5). A total of 212 genes were common in the gene lists of metastasis groups. Similarly to the cell line results, these genes were primarily downregulated and significantly enriched in cell adhesion (cell-cell and cell-matrix interactions) and ITGA6-B4 signalling pathways (Figure 2A). Regarding integrin expression, a decreased ITGB4 mRNA level was the most remarkable alteration in the metastatic lesions. In comparison to the cell line results, regional metastatic tissue samples were characterized by increased ITGA4 and decreased ITGA3 levels, but the change in ITG3 was less than 2-fold (Supplementary Table 5). The main difference between distant organ and regional (both lymph node and (sub)cutaneous) metastases was the significant upregulation of different immunoregulatory pathways. Furthermore, upregulation of the Rap1 signalling cascade was unique for the regional (sub)cutaneous metastasis (Supplementary Table 6).

Examination of integrin expression in metastasis formation

The mRNA levels of several integrins (ITGA2, ITGA3, ITGA4, ITGA6, ITGA9, ITGB1, ITGB3, ITGB5 and ITGB8; Supplementary Table 2) were also decreased in the metastatic cell lines relative to their primary pairs. These molecules play an important role in the switch between the two invasion

mechanisms through the loss of the cell-matrix interaction, resulting in a higher invasive capacity. Partly as a validation of the array results, we performed a real-time qRT-PCR analysis of integrin expression in the cell line pairs in addition to the examination of single-cell invasion ability. A similar integrin expression pattern was detected in primary cell lines with local metastasis (Supplementary Figure 2). These results confirmed our microarray results. WM983A and B were mildly invasive, whereas the other cell lines and their regional metastases were only slightly or noninvasive in our Matrigel system (Supplementary Table 7). However, the lung metastasis-derived 1205Lu showed an elevated ITGA3 level (Supplementary Figure 2), which was associated with greater invasiveness (average of 33 ± 2.5 invasive clones per well; Supplementary Table 7). Because only a small proportion of cells were invasive, we also investigated whether the invasive clones were similar to or distinct from the original cell line and the metastatic pairs. Therefore, we extracted invasive clones from the gel (WM983A^{INV} and WM793B^{INV}) and compared ITG expression to that in the original cell lines (WM983A or WM793B) and the corresponding metastases (WM983B or 1205Lu). WM983A^{INV} cells exhibited a lower expression of the most of examined integrins than did both the original cell line and its lymph node metastasis (Supplementary Figure 2-3). However, WM793B^{INV} cells showed a completely different ITG profile, with a remarkable reduction in ITGA3, ITGB1 and ITGB8 levels and an increase in ITGA4, ITGA6, ITGA9 and ITGB5 mRNA expression- (Supplementary Figure 2 and Figure 3). With the exception of ITGA3, these changes in ITG expression in metastatic samples returned to or were close to the original WM793B levels (Supplementary Figure 2). Examining co-expression of the possible ITG heterodimers' median, significant co-expression of $\alpha 3\beta 1$ and $\alpha 9\beta 1$ subunits was found (correlation coefficient: 0.673, $p=0.033$ and correlation coefficient: 0.701, $p=0.024$, respectively).

Analysis of integrin levels in tissue samples revealed that ITGA3 exhibited significant downregulation in both regional and distant organ metastases compared to the metastatic primary melanoma cohort ($p=0.032$ and $p=0.021$, respectively; Figure 2B), whereas ITGA4 was upregulated only in the regional metastases ($p=0.021$; Figure 2B). Distant organ metastases were exclusively characterized by increased ITGB8 expression in contrast to both the primary samples and regional metastases ($p=0.030$ and $p=0.047$, respectively).

Discussion

Human malignant melanoma arises from the malignant transformation of melanocytes in the basal epidermal layer and is among the most challenging malignancies to treat, exhibiting a constantly increasing incidence worldwide [25]. Although several new melanoma predisposition genes have been reported and somatic events (e.g., BRAF^{V600} mutation) have been implemented in therapeutic treatment, surgery and sentinel lymph-node biopsy still form the bases of primary care [25, 26]. The high mortality associated with the disease is primarily due to early resistance to chemotherapy and aggressive

metastatic capacity of melanomas [27]. Therefore, early detection and precise diagnosis are both important in disease outcome. Malignant melanoma can be divided into two basic biological forms: metastatic and non-metastatic melanoma [10]. However, these groups cannot be accurately predicted by the classical clinical and pathological parameters, thus creating a need for the identification of useful biomarkers. Several studies have aimed at identifying these biomarkers but did not produce satisfying results, and the list of potential novel markers is still very short [3, 8, 10, 28, 29]. In recent decades, microarray technology has become a reasonable choice for the identification of cancer-related genes responsible for the biological behaviour of malignancies. In recent years, concerted efforts to methodically standardize and evaluate of microarray data have been implemented [14-16]. Only a limited number of studies have used matched primary and metastasis sample pairs, mainly because of the lack of availability of paired tissues [17-20]. Therefore, cell lines can be effective models with which to obtain an overview of the changes involved during cancer progression. Because the heterogeneity of melanomas may be caused by both alterations in gene expression and genomic changes [10, 30], the present study sought to define the gene expression profiles in 4 human melanoma cell line pairs ~~and to correlate these data with alterations in DNA copy number~~ completed with melanoma RNASeq data from the TCGA Database.

We identified 438 genes with altered expression values in metastatic melanoma cell lines. Similarly to Koh et al. (2012) the majority of metastasis correlated genes (94%) were downregulated, including many genes involved in signalling in the immune system (HLA antigens), cell adhesion and cell motility networks [20]. These networks involve genes such as integrins (ITGA2, ITGA3, ITGA4, ITGA9, ITGB5 or ITGB8), which play a role in the flexible modification of the tumor cell migration strategy, depending on the environmental conditions [31-33]. Rounded cells are morphologically flexible, providing a faster dissemination of tumor cells and higher resistance against elevated pressure in the blood vessels [32, 34]. Our functional analysis also revealed a differential expression of distinct components of the PI3K-Akt signalling cascade, which mediates extracellular signalling by integrins and other ECM proteins such as laminins.

To determine whether these gene expression changes also occur *in vivo*, cell line pair experiments were conducted with unmatched tissue data from the TCGA Database. The tissue included metastatic primary tumors and melanoma metastases from different locations (regional lymph node or (sub)cutaneous and distant organ). Commonly altered genes in metastases were mainly downregulated and enriched in ECM degradation and ITGA6-B4 signalling pathways, including decreased ITGB4 levels as one of the most prominent alterations. ITGB4 can be overexpressed in side populations of human primary melanoma [35]. However, Mishra et al. (2015) have recently observed in a 4D lung cancer model that circulating tumor cells downregulate ITGB4 and that this process is linked to metastatic property [36]. In contrast to the cell line results, the ITGA4 mRNA level was increased in regional metastases, whereas ITGA3 was downregulated in both regional and distant organ metastases, but less than 2-fold. Furthermore, upregulation of the immune pathways was shown to represent an important difference between distant

organ and regional metastases. The opposite findings were observed in cell lines, possibly because of the lack of a tissue microenvironment. Upregulation of the Rap1 cascade was exclusive for the regional (sub)cutaneous metastasis with a possible role in this type of metastatic process. Because Rap1 is the closest relative of Ras, there is a possibility that Ras-mediated signalling regulation may be activated through extracellular signals. Therefore, Rap1 has an important function in diverse processes, including the modulation of growth, ITG-mediated cell adhesion and morphogenesis [37, 38].

Flexible transition between the mesenchymal and amoeboid invasion strategies (MAT vs. AMT) has great importance in invasiveness and metastasis formation [32, 33]. It is well known that melanoma cells can use both strategies, which provides the tumor cells with a great degree of plasticity [31, 33]. Our microarray data revealed that the mRNA levels of several integrins were decreased in the regional metastatic cell lines. These molecules have a central role in the MAT/AMT mechanism, by acting through the loss of ECM-cell interaction [31]. Partly as a validation of the array results, we performed real-time qRT-PCR analysis on the matched cell line pairs in parallel with the determination of invasion capacity. We also evaluated the extent to which the invasive clones within a cell line were different. To this end, we extracted the invasive clones (WM983A^{INV} and WM793B^{INV}) and determined ITG expression. Primary cell lines with regional metastasis showed similar integrin expression patterns. However, with the exception of the mildly invasive WM983A and B, neither of the clones was invasive in our Matrigel system. The mRNA levels of the examined ITGs were also decreased in WM983A^{INV} cells compared to both WM983A and WM983B, with the exception of ITGA4, which continuously decreased towards metastasis. One reason for this pattern might be that in the process of lymphatic metastasis, the collective invasion strategy and/or the passive lymphatic transport can be expedient, and the presence of single cells is not a prerequisite. The main task is to evade the activity of immunoeffector cells [39]. In contrast, lung metastasis 1205Lu was characterized by a higher ITGA3 level, which was associated with an increased invasiveness. WM793B^{INV} cells also exhibited a different ITG expression pattern relative to the original primary cell line. Tissue qRT-PCR results also highlighted the possible importance of ITGA3, ITGA4 and ITGB8. Similarly to the results of the cell line data, ITGA3 was downregulated in both regional and distant melanoma metastases. Contois et al. (2015) have demonstrated that ITGA3 positively regulates the angiogenic switch in melanoma via the suppression of IGFBP-4, a negative regulator of IGF1 signalling [40]. Therefore, ITGA3 may promote the growth activation of small dormant tumors. Our results suggest that ITGA3 is important primarily for the progression of primary tumors, but these data must be studied further. ITGA4 was upregulated in regional metastases both in TCGA and our tissue PCR experiments. ITGA4 in complex with ITGB1 promotes the transendothelial migration of highly metastatic melanoma cell lines through its interaction with VCAM1 on the activated endothelial cells [41]. This migration velocity depends on the concentration of VCAM1, with which the tumor cells can optimize their motile activity to distinct targets in response to the different physical microenvironments [42]. Although the sample number was relatively low in the present study, the role of ITGB8 in the formation of distant metastasis should be

examined in a larger cohort of tissue samples. Our PCR experiments revealed that ITGB8 was upregulated only in distant metastases, in this case to the brain. It has recently been shown that ITGB8 can be regulated by EPHB4 in prostate cancer, facilitating *in vitro* cell migration and invasion [43].

Each of the existing mammalian ITGs has specific, nonredundant function [44]. Evolutionary relationships, ligand specificity, and in case of some integrins (e.g. B2, B7 or AL) cell type-specificity reduce the possible number of functional heterodimers formed by different α and β subunits. Regarding the examined ITGs, co-expression of $\alpha 3\beta 1$ and $\alpha 9\beta 1$ subunits was found. Newham et al. showed in leukocytes that $\alpha 9\beta 1$ heterodimer is a receptor for both cell surface ligands and ECM components, therefore mediates their migration from vessels to inflammation sites [45]. Based on this, the receptor may contribute to the dissemination of cancer cells to distant organs (in that case lung) as well. In case of $\alpha 9$ a marked increase was observed in WM793B^{INV} cells without increase of $\beta 1$. As the cytoplasmic domain of $\beta 1$ has several alternatively spliced variants, changes of their distribution within tumor cells may occur [46]. $\alpha 3\beta 1$ has both pro-junction and pro-migratory activities in collective invasion. Zevian et al. revealed that rapid single cell motility is $\alpha 3\beta 1$ -dependent and promoted by CD151 [47]. Besides, the lack of $\alpha 3\beta 1$ was correlated with poor survival in invasive lobular, but not in ductal breast cancers [48]. This dual role should be further investigated in melanoma, as in our model decreased ITGA3 was observed in both invasive primary clones (independently from the type of metastasis) and regional metastasis, but not in the lung metastatic 1205Lu cell line. To get additional valuable information about the presence of ITG subunit combinations, and to validate whether the above mentioned co-expressions have an effect on protein level, translational studies would be useful.

This study has provided preliminary insight into the diverse molecular regulation of the metastatic process by using high-throughput microarrays on matched primary and metastatic melanoma cell lines and confirming these results with RNAseq data of unmatched primary and metastatic melanomas from the TCGA Database. We determined groups of genes, mainly enriched in cell adhesion, motility and antigen presentation pathways, whose deregulation was primarily associated with metastasis and invasion and which may be candidates involved in melanomagenesis. Focusing on integrins, we also showed that different integrin expression patterns might play a role in the formation of site-specific metastasis and dynamically change throughout the metastatic process. Based on these results, we believe that analysis of the metastatic melanoma, and not only the primary melanoma, may be of great importance in the future therapeutic decision-making process.

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Figure legends

Figure 1. Gene expression patterns of the primary and metastatic melanoma cell line pairs revealed by cDNA microarray analyses. **(A)** Volcano plot analysis of the 7542 filtered unique genes. Blue dots represent significantly (paired t-test, $p \leq 0.05$) altered genes with at least a two-fold expression change in the metastatic cell lines. The majority of genes (94%; 413/438) showed decreased expression level in metastases. **(B)** Results of the class prediction analysis on the preselected gene subset. The nearest centroid algorithm was used with the bootstrap cross-validation method. **(C)** Performance and precision of the prediction classifiers (primary vs. metastasis).

Figure 2. Summary of tissue melanoma sample results. **(A)** Venn diagram representing the number of altered genes in different metastasis subgroups (DM – distant metastasis, rLN – regional lymph node metastasis and rSC/C – regional (sub)cutaneous metastasis) compared to unmatched metastatic primary samples (P) based on the TCGA RNAseq v2.0 data. A total of 212 genes were commonly altered in all 3 subgroups. These mainly downregulated genes were significantly enriched in cell adhesion and ITGA6-B4 signalling pathways. **(B)** Box plots representing the results of qRT-PCR analysis of integrin

expression in unmatched metastatic primary melanomas and melanoma metastases (regional and distant organ). Significant differences ($p \leq 0.05$; two-sided Mann-Whitney-Wilcoxon exact test) are indicated by asterisks.

Supporting information

Supplementary Methods

Normalization, filtering and statistical analysis of gene expression microarray data: After background correction and \log_2 transformation of signal intensities normalization was carried out using quantile normalization by arithmetical mean of the distribution and Tukey's median polish. The acquired CHP files containing background corrected, \log_2 transformed and normalized intensity data were then transformed to TXT files using Affymetrix APT-1.15.0 software (Affymetrix, Inc., Santa Clara, CA, USA) and inserted to Bioconductor BRB-ArrayTools 4.3.0 (Richard Simon and Amy Peng Lam, National Cancer Institute, Bethesda, USA). Genes were excluded if less than 20% of expression data have at least a 1.5-fold change in either direction from gene's median value; p-value of the log-ratio variation was greater than 0.05 or at least 50% of data was missing or filtered out. Multiple probes or probe sets were reduced to one per gene symbol by using maximally expressed probe or probe set measured by average intensity across arrays.

Volcano plot filtering and paired t-test with random variance model was applied to reveal differentially expressed genes between primary and metastatic cell lines, considering significant at the nominal 0.05 level with at least 2 fold-change. Exact multivariate permutation test was computed based on 1000 random permutations. The maximum allowed proportion of false-positive genes (FDR) was less than 0.1 and the confidence level of false discovery rate assessment was 80%.

Reverse transcription and qRT-PCR analysis workflow: Reverse transcription was carried out with High Capacity cDNA Reverse Transcription Kit, according to the protocol of the supplier (Life Technologies Corporation, Carlsbad, CA, USA), using 1000 ng total RNA. We used primers in 0.4 μM and UPL probes in 0.2 μM final concentrations per reaction. Each reaction (20 μl in volume) contained 50 ng cDNA and was run in triplicate on LightCycler 480 instrument (Roche Magyarország Kft., Budaörs, Hungary) with the following thermal profile: (1) activation at 95°C for 10 min, (2) amplification (45 cycles): denaturation at 95°C for 10 sec, annealing at 60°C for 30 sec, extension at 72°C for 1 sec, and (3) cooling at 40°C for 30 sec.

Matrigel invasion assay: Before invasion assay the chambers were rehydrated for 2h at 37°C with serum-free RPMI1640 medium. During incubation cell lines with 50-70% confluence were harvested, counted and resuspended with 500 μl serum-free medium. The upper chamber of insert was filled with

500µl of cell suspension in serum-free medium (5×10^4 cells/well). Medium supplemented with 10% FBS (750µl) was applied as chemoattractant. Tumor cells were incubated for 24h at 37°C. After non-invading cells have been removed with a sterile cotton swab, the invading cells at the lower layer were fixed with 500µl 100% methanol for 15 min at -20°C and stained with hematoxylin-eosin. The average number of invaded cells was counted using light microscope in 7 different visual fields at 200X magnification. Data were presented as mean \pm SD of three independent experiments. To select invasive clones, parallel experiments were run with the same conditions. After 24h incubation at 37°C the invading cells at the lower layer were extracted from the membrane using 50µl 0.5% trypsin/0.2% EDTA solution (Sigma-Aldrich Inc., St. Louis, MO, USA) for 1 min at 37°C. Blocking trypsin solution with 1ml serum supplemented medium, cells were incubated for 4h at 37°C till adhesion. Cells were then cultured following standard protocol till 90% confluence and passed to a T25 flask. The selected invasive clones were checked whether they maintain the invasive property comparing to the original cell line and increased invasiveness was observed (Supplementary Figure 3).

Supplementary Figure 1 – Pathway analysis of the 413 significantly downregulated genes in metastases. Bonferroni correction was applied with a p-value ≤ 0.01 . (A) Altered molecular pathways with at least 5 observations in the selected gene subset. Columns represent the number of genes included in the given pathway, whereas lines represent the significance of the given pathway. (B) Molecular functional characterization of the altered genes based on the GO classification.

Supplementary Figure 2 – Different expression patterns of selected integrins (ITG) in matched melanoma cell lines: (A) WM278 (primary; black dots) and WM1617 (lymph node metastasis; empty dots) cell line pair, (B) WM115 (primary; black dots) and WM266-4 (cutaneous metastasis; empty dots) cell line pair, (C) WM983A (primary; black dots), WM983A^{INV} (selected invasive primary; gray dots) and WM983B (lymph node metastasis; empty dots) cell line trio, and (D) WM793B (primary; black dots), WM793B^{INV} (selected invasive primary; gray dots) and 1205Lu (lung metastasis; empty dots) cell line trio. Sectors of polar charts represent different ITGs, ~~whose~~ The relative log₂ transformed expression levels increase from the centre towards the outer edge of the ~~formation chart~~ Every dot represents the exact relative mRNA level of the corresponding integrin on a log₂ scale. The ITG pattern based on the combined expression changes of the 9 selected ITGs (A2, A3, A4, A6, A9, B1, B3, B5 and B8) was similar in primary samples with regional lymph node and cutaneous metastasis compared to the WM793B forming distant organ metastasis- (lung). GAPDH and ACTB were used as internal control genes, and melanocyte was used as a calibrator sample. Relative mRNA levels are based on the average of three replicates.

Supplementary Figure 3 – ~~Matrigel~~ Result of matrigel invasion analysis of extracted invasive clones (WM983A^{INV} and WM793B^{INV}) comparing to the original cell lines. Both WM983A^{INV} and WM793B^{INV} clones acquire an increased rate of invasion potential- (Invasive capacity was

approximately 5-fold and 6-fold higher than the original WM983A and WM793B cell lines, respectively. Invasion rate was provided as the ratio of average number of selected clones and original cell lines. Invaded cells were stained with hematoxylin-eosin, and counted using light microscope in 7 different visual fields at 200X magnification. In the table below the diagram, fold-change values of mRNA levels of the selected ITGs between invasive primary clones vs. corresponding original primary cell lines were represented. Fold-change values were acquired using the following equation: the relative ITG mRNA level of (invasive clones) divided by the relative ITG mRNA level of (original cell line). In case of lymph node metastatic WM983A primary melanoma cell line all the examined ITGs were downregulated in the selected invasive clones, in contrast to the lung metastatic primary melanoma cell line WM793B.

Supplementary Table 1 - Primer sequences and UPL probes used in RT-qPCR experiments.

Supplementary Table 2 - Differentially expressed genes in cell lines derived from melanoma metastases compared to their primary pairs (N=438). Melanocyte was used as a reference array to normalize expression intensity. Genes are significant at the nominal level of $p \leq 0.05$ with a greater than two-fold change in their expression.

Supplementary Table 3 - Biological processes affected in the metastatic melanoma cell lines. Biological processes are significant at the nominal level of $p \leq 0.01$ using Bonferroni correction and containing at least 5 observations in the selected downregulated gene subset.

Supplementary Table 4 - Significantly altered molecular pathways in the metastatic melanoma cell lines. Pathways are significant at the nominal level of $p \leq 0.01$ using Bonferroni correction and containing at least 5 observations in the selected downregulated gene subset.

Supplementary Table 5 - Downregulated genes in the metastatic melanoma cell lines are included in 4 molecular functional groups. Pathways are significant at the nominal level of $p \leq 0.01$ using Bonferroni correction and containing at least 5 observations in the selected gene subset.

Supplementary Table 6 - Class comparison analysis results of TCGA SKCM RNAseq v2.0 data. A total of 1065 differentially expressed genes were revealed between primary melanomas and at least one of the metastasis subgroups (regional lymph node, (sub)cutaneous metastases or distant organ metastases). A multivariate permutation test was computed based on 1000 random permutations. The maximum allowed proportion of false-positive genes (FDR) was less than 0.1, and the confidence level of false-discovery rate assessment was 80%. The univariate test was a two-sample t-test, considering $p < 0.01$ as statistically significant, and the fold-change was greater than 2.

Supplementary Table 7 - Pathway analysis of the 1065 altered genes between primary melanomas and different metastatic subgroups (regional lymph node, (sub)cutaneous metastases or distant organ metastases) based on TCGA RNAseq v2.0 data. Bonferroni correction was applied using a p-value ≤ 0.05 , and classes with at least 5 observations in the selected subset were considered as altered pathways.

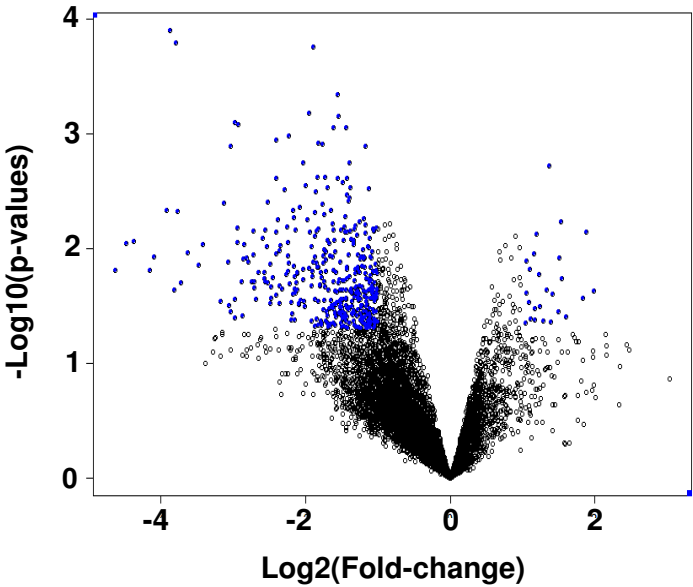
Table 1 - Clinical-pathological data of melanoma tissue samples used in qRT-PCR analysis of different integrins.

Sample no.	Gender ¹	Age at initial diagnosis (years)	Location	Histological subtype ²	Breslow thickness (mm)	TNM stage at initial diagnosis	Ulceration
<i>Metastatic primary melanoma</i>							
1	M	74	trunk	NM	7	T4bN2aM0	yes
2	M	69	trunk	SSM/NM	8	T4bN0M0	yes
3	M	65	trunk	NM	4	T3bN0M1c	yes
4	M	74	head	SSM	5	T4bN0M0	yes
5	M	44	head	NM	25	T4bN0M0	yes
6	M	38	trunk	NM	12	T4bN0M0	yes
7	M	75	extremities	NM	11	T4bN2cM0	yes
8	F	74	extremities	NM	4	T3aN0M0	no
9	M	67	extremities	SSM	7	T4bN0M0	yes
10	M	41	extremities	SSM	14	T4bN2bM3	yes
11	M	57	n.d. ³	NM	n.d.	T4NxMx	n.d.
12	M	n.d.	trunk	SSM	9	T4bN1M0	yes
13	F	40	trunk	SSM	7	T4bN0M0	yes
14	M	71	trunk	SSM	2.3	T1aNxM1c	no
15	M	76	trunk	NM	4	T3bN0M0	yes
16	F	71	head	NM	7	T4bN0M0	yes
17	M	63	trunk	NM	8	T4bN0M0	yes
18	F	54	extremities	n.d.	11	T4aN1M0	no
19	M	33	trunk	NM	3	T3aN2M0	no
<i>Melanoma metastasis</i>							
20	M	57	distant				
21	F	12	distant				
22	F	48	distant				
23	M	75	rLN ⁴				
24	F	51	rLN				
25	M	63	rLN				
26	M	n.d.	rLN				
27	F	74	rLN				
28	M	81	rSC/C ⁵				
29	F	n.d.	rLN				
30	F	30	rLN				
31	M	84	rSC/C				
32	F	n.d.	rLN				
33	M	44	rLN				
34	M	72	rLN				
35	M	52	rLN				
36	F	11	rSC/C				

¹M-male, F-female; ²NM-nodular melanoma, SSM-superficial spreading melanoma; ³n.d.-no data available;⁴rLN-regional lymph node; ⁵rSC/C-regional (sub)cutaneous

Figure 1

A



B

Cell line	Class label	Mean no. of genes in classifier	Nearest Centroid*
WM266-4	metastasis	280	100
WM983B	metastasis	303	67
1205Lu	metastasis	238	100
WM1617	metastasis	271	100
WM115	primary	262	100
WM278	primary	229	100
WM793B	primary	270	100
WM983A	primary	356	0
Mean percent of correct classification			85%

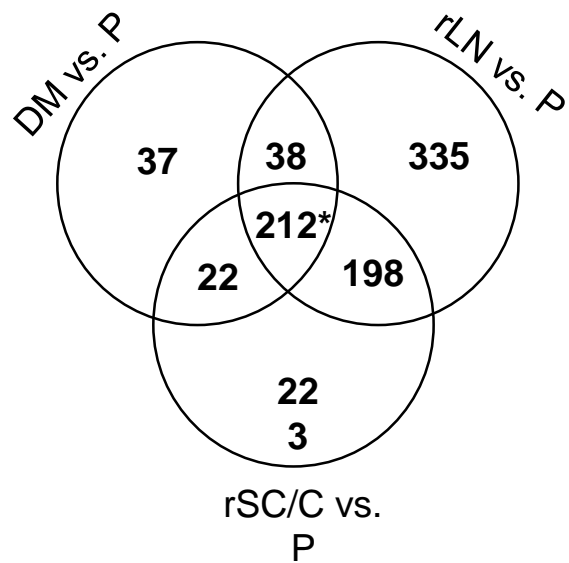
*presented are percents of correct predictions among all cross-validation predictions for each sample

C

Class	Sensitivity	Specificity	PPV*	NPV§
primary	0.917	0.750	0.786	0.900
metastasis	0.750	0.917	0.900	0.786

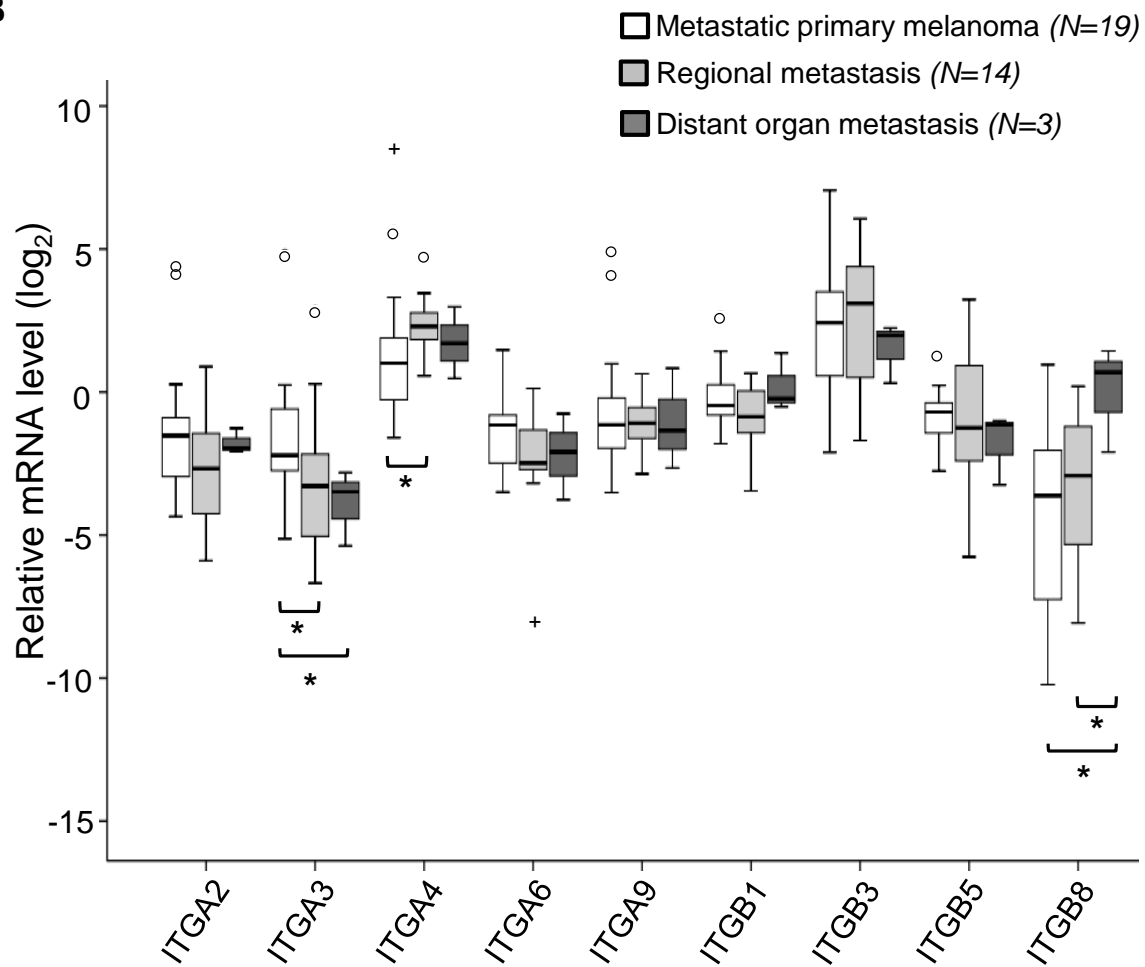
*positive predictive value; §negative predictive value

A



***downregulation of cell adhesion and ITGA6-B4 signaling pathways**

B



Supplementary Table 1. Primer sequences and UPL probes used in RT-qPCR experiments.

Gene	Primer sequence (5'-3') ¹	UPL ² probe no.	Amplicon size (bp) ³
ITGA2	F: TCGTGCACAGTTTTGAAGATG	7	71
	R: TGGAACACTTCCTGTTGTTACC		
ITGA3	F: GAGGACATGTGGCTTGGAGT	13	75
	R: GTAGCGGTGGGCACAGAC		
ITGA4	F: GATGAAAATGAGCCTGAAACG	22	80
	R: GCCATACTATTGCCAGTGTTGA		
ITGA6	F: TTTGAAGATGGGCCTTATGAA	22	102
	R: CCCTGAGTCCAAAGAAAAACC		
ITGA9	F: TTGTTGGTGGGAATCCTCAT	18	73
	R: ACCTTCGGCGAAAGAAGC		
ITGB1	F: CGATGCCATCATGCAAGT	65	71
	R: ACACCAGCAGCCGTGTAAC		
ITGB3	F: CGCTAAATTTGAGGAAGAACG	76	82
	R: GAAGGTAGACGTGGCCTCTTT		
ITGB5	F: GGGAGTTTGCAAAGTTTCAGAG	81	90
	R: TGTGCGTGGAGATAGGCTTT		
ITGB8	F: GCATTATGTCGACCAAACCTCA	19	95
	R: GCAACCCAATCAAGAATGTAACT		
GAPDH	F: AGCCACATCGCTCAGACAC	60	66
	R: GCCCAATACGACCAAATCC		
ACTB	F: CCAACCGCGAGAAGATGA	64	97
	R: CCAGAGGCGTACAGGGATAG		

¹F: forward, R: reverse²Universal Probe Library probes 5'-labeled with 6-FAM and 3'-labeled with TAMRA quencher dye³bp: base pair

Supplementary Table 2. Differentially expressed genes in cell lines derived from melanoma metastases comparing to their primary pairs (N=438). Melanocyte was used as reference array.

	ProbeSet	Gene symbol	Gene name	Alteration
1	8180100	HLA-DPA1	major histocompatibility complex, class II, DP alpha 1	DOWN
2	8115147	CD74	CD74 molecule, major histocompatibility complex, class II invariant chain	DOWN
3	8150428	SFRP1	secreted frizzled-related protein 1	DOWN
4	8107897	PDLIM4	PDZ and LIM domain 4	DOWN
5	8135594	CAV1	caveolin 1, caveolae protein, 22kDa	DOWN
6	7984569	LRRC49	leucine rich repeat containing 49	DOWN
7	8105302	FST	folliculin	DOWN
8	8095697	CXCL1	chemokine (C-X-C motif) ligand 1 (melanoma growth stimulating activity, alpha)	DOWN
9	8077270	CHL1	cell adhesion molecule with homology to L1CAM (close homolog of L1)	DOWN
10	7931097	HTRA1	HtrA serine peptidase 1	DOWN
11	8147461	SDC2	syndecan 2	DOWN
12	8121712	SLC35F1	solute carrier family 35, member F1	DOWN
13	8088560	ADAMTS9	ADAM metalloproteinase with thrombospondin type 1 motif, 9	DOWN
14	7951397	CASP1	caspase 1, apoptosis-related cysteine peptidase (interleukin 1, beta, convertase)	DOWN
15	8065612	C20orf112	chromosome 20 open reading frame 112	DOWN
16	8134257	GNG11	guanine nucleotide binding protein (G protein), gamma 11	DOWN
17	8040458	KCNS3	potassium voltage-gated channel, delayed-rectifier, subfamily S, member 3	DOWN
18	8084165	SOX2	SOX (sex determining region Y)-box 2	DOWN
19	8103520	TRIM61	tripartite motif containing 61	UP
20	8031632	ZNF542	zinc finger protein 542	DOWN
21	7974341	GNG2	guanine nucleotide binding protein (G protein), gamma 2	DOWN
22	8082797	TF	transferrin	DOWN
23	7968678	FREM2	FRAS1 related extracellular matrix protein 2	DOWN
24	8065071	FLRT3	fibronectin leucine rich transmembrane protein 3	DOWN
25	8161964	FRMD3	FERM domain containing 3	DOWN
26	7916609	JUN	jun proto-oncogene	DOWN
27	8091306	PLSCR4	phospholipid scramblase 4	DOWN
28	8093858	STK32B	serine/threonine kinase 32B	DOWN
29	8018966	TIMP2	TIMP metalloproteinase inhibitor 2	DOWN
30	8111998	HCN1	hyperpolarization activated cyclic nucleotide-gated potassium channel 1	DOWN
31	8145470	DPYSL2	dihydropyrimidinase-like 2	DOWN
32	7976012	NRXN3	neurexin 3	DOWN
33	8100994	CXCL2	chemokine (C-X-C motif) ligand 2	DOWN
34	8103415	FAM198B	family with sequence similarity 198, member B	DOWN
35	8138337	AGMO	alkylglycerol monooxygenase	DOWN
36	8081564	CD96	CD96 molecule	DOWN
37	8135587	CAV2	caveolin 2	DOWN
38	8105267	ITGA2	integrin, alpha 2 (CD49B, alpha 2 subunit of VLA-2 receptor)	DOWN

39	8081657	CD200	CD200 molecule	DOWN
40	7986385	SYNM	synemin, intermediate filament protein	DOWN
41	8127051	TRAM2	translocation associated membrane protein 2	DOWN
42	8108217	TGFB1	transforming growth factor, beta-induced, 68kDa	DOWN
43	8047926	MAP2	microtubule-associated protein 2	DOWN
44	7927202	ZNF22	zinc finger protein 22 (KOX 15)	DOWN
45	7947599	CHST1	carbohydrate (keratan sulfate Gal-6) sulfotransferase 1	DOWN
46	8106743	VCAN	versican	DOWN
47	7939546	CD82	CD82 molecule	DOWN
48	8134098	CDK14	cyclin-dependent kinase 14	DOWN
49	8106098	MAP1B	microtubule-associated protein 1B	DOWN
50	8067955	CXADR	coxsackie virus and adenovirus receptor	UP
51	8138718	HOXA2	homeobox A2	DOWN
52	7920552	KCNN3	potassium intermediate/small conductance calcium-activated channel, subfamily N, member 3	DOWN
53	7917946	LPPR5	lipid phosphate phosphatase-related protein type 5	DOWN
54	8060854	PLCB1	phospholipase C, beta 1 (phosphoinositide-specific)	DOWN
55	8058063	RFTN2	raftlin family member 2	DOWN
56	8131957	SNX10	sorting nexin 10	DOWN
57	8175696	GABRA3	gamma-aminobutyric acid (GABA) A receptor, alpha 3	DOWN
58	7986446	ALDH1A3	aldehyde dehydrogenase 1 family, member A3	DOWN
59	8035838	ZNF724P	zinc finger protein 724, pseudogene	DOWN
60	8139500	TNS3	tensin 3	DOWN
61	8175177	MBNL3	muscleblind-like 3 (Drosophila)	DOWN
62	7954631	FAR2	fatty acyl CoA reductase 2	DOWN
63	8178811	HLA-DRB4	major histocompatibility complex, class II, DR beta 4	DOWN
64	8140534	SEMA3C	sema domain, immunoglobulin domain (Ig), short basic domain, secreted, (semaphorin) 3C	DOWN
65	7899075	EXTL1	exostoses (multiple)-like 1	DOWN
66	8094550	C4orf19	chromosome 4 open reading frame 19	DOWN
67	7940565	FADS2	fatty acid desaturase 2	DOWN
68	8047738	NRP2	neuropilin 2	DOWN
69	7983157	TMEM62	transmembrane protein 62	DOWN
70	7957338	SYT1	synaptotagmin I	DOWN
71	8180003	HLA-DRB3	major histocompatibility complex, class II, DR beta 3	DOWN
72	8105908	OCLN	occludin	DOWN
73	8034210	TMEM205	transmembrane protein 205	DOWN
74	8170119	FHL1	four and a half LIM domains 1	DOWN
75	8154951	GLUL	glutamate-ammonia ligase	UP
76	7939150	PRRG4	proline rich Gla (G-carboxyglutamic acid) 4 (transmembrane)	DOWN
77	8144656	C8orf49	chromosome 8 open reading frame 49	UP
78	7929047	IFIT2	interferon-induced protein with tetratricopeptide repeats 2	DOWN
79	8008237	ITGA3	integrin, alpha 3 (antigen CD49C, alpha 3 subunit of VLA-3 receptor)	DOWN
80	7945245	NTM	neurotrimin	DOWN
81	8049299	SCARNA6	small Cajal body-specific RNA 6	DOWN
82	7976698	EML1	echinoderm microtubule associated protein like 1	DOWN
83	8108697	PCDHB5	protocadherin beta 5	DOWN

84	8071036	S100B	S100 calcium binding protein B	DOWN
85	7944869	SPA17	sperm autoantigenic protein 17	DOWN
86	8030925	ZNF880	zinc finger protein 880	DOWN
87	7962516	SLC38A1	solute carrier family 38, member 1	DOWN
88	7927186	RASSF4	Ras association (RalGDS/AF-6) domain family member 4	DOWN
89	8094301	SLIT2	slit homolog 2 (Drosophila)	DOWN
90	8063536	TFAP2C	transcription factor AP-2 gamma (activating enhancer binding protein 2 gamma)	DOWN
91	7942957	PRSS23	protease, serine, 23	DOWN
92	8178193	HLA-DRA	major histocompatibility complex, class II, DR alpha	DOWN
93	7953291	CD9	CD9 molecule	DOWN
94	8122222	PDE7B	phosphodiesterase 7B	DOWN
95	8118594	HLA-DPB1	major histocompatibility complex, class II, DP beta 1	DOWN
96	8038967	ZNF83	zinc finger protein 83	DOWN
97	8103226	TMEM154	transmembrane protein 154	DOWN
98	7972239	SLITRK6	SLIT and NTRK-like family, member 6	DOWN
99	8078529	STAC	SH3 and cysteine rich domain	DOWN
100	8046695	ITGA4	integrin, alpha 4 (antigen CD49D, alpha 4 subunit of VLA-4 receptor)	DOWN
101	8078650	CTDSPL	CTD (carboxy-terminal domain, RNA polymerase II, polypeptide A) small phosphatase-like	DOWN
102	8016841	TMEM100	transmembrane protein 100	DOWN
103	8138824	SCRN1	secernin 1	DOWN
104	8108713	PCDHB8	protocadherin beta 8	DOWN
105	7934970	HTR7	5-hydroxytryptamine (serotonin) receptor 7 (adenylate cyclase-coupled)	DOWN
106	8034342	ZNF625-ZNF20	ZNF625-ZNF20 readthrough	DOWN
107	8095680	IL8	interleukin 8	DOWN
108	7899160	CD52	CD52 molecule	UP
109	7936968	ADAM12	ADAM metallopeptidase domain 12	DOWN
110	8045776	GALNT13	UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 13 (GalNAc-T13)	DOWN
111	8070182	RCAN1	regulator of calcineurin 1	DOWN
112	8113130	MCTP1	multiple C2 domains, transmembrane 1	DOWN
113	8169174	RNF128	ring finger protein 128	DOWN
114	8102862	MAML3	mastermind-like 3 (Drosophila)	DOWN
115	8113358	ST8SIA4	ST8 alpha-N-acetyl-neuraminide alpha-2,8-sialyltransferase 4	DOWN
116	8113103	KIAA0825	KIAA0825	DOWN
117	8122265	TNFAIP3	tumor necrosis factor, alpha-induced protein 3	DOWN
118	8112731	F2RL2	coagulation factor II (thrombin) receptor-like 2	DOWN
119	8008802	GDPD1	glycerophosphodiester phosphodiesterase domain containing 1	DOWN
120	8112615	ENC1	ectodermal-neural cortex 1 (with BTB-like domain)	DOWN
121	8048926	SP140L	SP140 nuclear body protein-like	DOWN
122	8135774	PTPRZ1	protein tyrosine phosphatase, receptor-type, Z polypeptide 1	DOWN
123	8088636	LOC100508226	HHSL751	UP
124	8074286	MICAL3	microtubule associated monooxygenase, calponin and LIM domain containing 3	DOWN
125	8072710	APOL6	apolipoprotein L, 6	DOWN

126	8103399	PDGFC	platelet derived growth factor C	DOWN
127	8014241	SLFN12	schlafen family member 12	DOWN
128	8108378	CTNNA1	catenin (cadherin-associated protein), alpha 1, 102kDa	DOWN
129	8103166	SH3D19	SH3 domain containing 19	DOWN
130	7989365	RORA	RAR-related orphan receptor A	UP
131	8035779	ZNF253	zinc finger protein 253	DOWN
132	8139832	ZNF117	zinc finger protein 117	DOWN
133	7985809	ABHD2	abhydrolase domain containing 2	DOWN
134	8068100	LINC00189	long intergenic non-protein coding RNA 189	DOWN
135	8091867	BCHE	butyrylcholinesterase	DOWN
136	8039006	ZNF320	zinc finger protein 320	DOWN
137	7957260	GLIPR1	GLI pathogenesis-related 1	DOWN
138	8172022	TMEM47	transmembrane protein 47	DOWN
139	7913787	C1orf201	chromosome 1 open reading frame 201	DOWN
140	8163637	TNC	tenascin C	DOWN
141	8023121	ST8SIA5	ST8 alpha-N-acetyl-neuraminide alpha-2,8-sialyltransferase 5	DOWN
142	7919326	ACP6	acid phosphatase 6, lysophosphatidic	DOWN
143	8114938	JAKMIP2	janus kinase and microtubule interacting protein 2	DOWN
144	7951807	CADM1	cell adhesion molecule 1	DOWN
145	8106962	ARSK	arylsulfatase family, member K	DOWN
146	7919800	CTSS	cathepsin S	DOWN
147	7977507	RPPH1	ribonuclease P RNA component H1	DOWN
148	8016468	HOXB7	homeobox B7	DOWN
149	8034344	ZNF625	zinc finger protein 625	DOWN
150	7957417	TMTC2	transmembrane and tetratricopeptide repeat containing 2	DOWN
151	7902227	GADD45A	growth arrest and DNA-damage-inducible, alpha	DOWN
152	8142981	PODXL	podocalyxin-like	DOWN
153	8154100	VLDLR	very low density lipoprotein receptor	UP
154	8037579	ERCC1	excision repair cross-complementing rodent repair deficiency, complementation group 1 (includes overlapping antisense sequence)	DOWN
155	8016476	HOXB9	homeobox B9	DOWN
156	8111670	GDNF	glial cell derived neurotrophic factor	DOWN
157	7939215	C11orf41	chromosome 11 open reading frame 41	DOWN
158	8006433	CCL2	chemokine (C-C motif) ligand 2	DOWN
159	8054712	IL1A	interleukin 1, alpha	DOWN
160	8079966	SEMA3B	sema domain, immunoglobulin domain (Ig), short basic domain, secreted, (semaphorin) 3B	DOWN
161	8027674	ZNF302	zinc finger protein 302	DOWN
162	8088180	WNT5A	wingless-type MMTV integration site family, member 5A	DOWN
163	8138888	PDE1C	phosphodiesterase 1C, calmodulin-dependent 70kDa	DOWN
164	8155898	PCSK5	proprotein convertase subtilisin/kexin type 5	DOWN
165	7964631	FAM19A2	family with sequence similarity 19 (chemokine (C-C motif)-like), member A2	DOWN
166	8029006	AXL	AXL receptor tyrosine kinase	DOWN
167	7922001	FAM78B	family with sequence similarity 78, member B	DOWN
168	8150509	PLAT	plasminogen activator, tissue	DOWN
169	7956658	SLC16A7	solute carrier family 16, member 7 (monocarboxylic acid transporter 2)	DOWN

170	8171205	NLGN4X	neuroligin 4, X-linked	DOWN
171	8027260	ZNF486	zinc finger protein 486	DOWN
172	8127234	DST	dystonin	DOWN
173	7949971	CPT1A	carnitine palmitoyltransferase 1A (liver)	DOWN
174	8032509	GNG7	guanine nucleotide binding protein (G protein), gamma 7	DOWN
175	8010967	NXN	nucleoredoxin	UP
176	8140967	SAMD9	sterile alpha motif domain containing 9	DOWN
177	8120501	COL19A1	collagen, type XIX, alpha 1	DOWN
178	8021081	SLC14A1	solute carrier family 14 (urea transporter), member 1 (Kidd blood group)	DOWN
179	8155460	CNTNAP3	contactin associated protein-like 3	DOWN
180	8100393	KDR	kinase insert domain receptor (a type III receptor tyrosine kinase)	DOWN
181	8069676	ADAMTS1	ADAM metalloproteinase with thrombospondin type 1 motif, 1	DOWN
182	8137670	PDGFA	platelet-derived growth factor alpha polypeptide	DOWN
183	8014233	SLFN11	schlafen family member 11	DOWN
184	7977397	CRIP2	cysteine-rich protein 2	DOWN
185	7925672	ZNF670	zinc finger protein 670	DOWN
186	8044391	MERTK	c-mer proto-oncogene tyrosine kinase	UP
187	8107133	PAM	peptidylglycine alpha-amidating monooxygenase	DOWN
188	7910923	FMN2	formin 2	DOWN
189	7934570	KCNMA1	potassium large conductance calcium-activated channel, subfamily M, alpha member 1	DOWN
190	8127767	ELOVL4	ELOVL fatty acid elongase 4	DOWN
191	8163257	LPAR1	lysophosphatidic acid receptor 1	DOWN
192	8108703	PCDHB6	protocadherin beta 6	DOWN
193	8028213	ZNF568	zinc finger protein 568	DOWN
194	8035795	ZNF626	zinc finger protein 626	DOWN
195	8045688	TNFAIP6	tumor necrosis factor, alpha-induced protein 6	DOWN
196	7936494	GFRA1	GDNF family receptor alpha 1	DOWN
197	8112980	EDIL3	EGF-like repeats and discoidin I-like domains 3	DOWN
198	8131600	TSPAN13	tetraspanin 13	DOWN
199	7938880	HTATIP2	HIV-1 Tat interactive protein 2, 30kDa	DOWN
200	8139840	ERV3-1	endogenous retrovirus group 3, member 1	DOWN
201	7917503	GBP3	guanylate binding protein 3	DOWN
202	8133770	CCDC146	coiled-coil domain containing 146	DOWN
203	7902687	CYR61	cysteine-rich, angiogenic inducer, 61	DOWN
204	8101086	NAAA	N-acyl ethanolamine acid amidase	DOWN
205	8056257	FAP	fibroblast activation protein, alpha	DOWN
206	8054722	IL1B	interleukin 1, beta	DOWN
207	7943413	BIRC3	baculoviral IAP repeat containing 3	DOWN
208	8050007	PXDN	peroxidasin homolog (Drosophila)	DOWN
209	7966234	TRPV4	transient receptor potential cation channel, subfamily V, member 4	DOWN
210	8037408	KCNN4	potassium intermediate/small conductance calcium-activated channel, subfamily N, member 4	DOWN
211	8083978	NAALADL2	N-acetylated alpha-linked acidic dipeptidase-like 2	DOWN
212	7910387	RHOU	ras homolog gene family, member U	DOWN
213	8106393	F2R	coagulation factor II (thrombin) receptor	DOWN
214	7969613	GPC6	glypican 6	DOWN

215	8162533	PTCH1	patched 1	DOWN
216	8102440	ARSJ	arylsulfatase family, member J	DOWN
217	7977447	LINC00221	long intergenic non-protein coding RNA 221	DOWN
218	7913357	ECE1	endothelin converting enzyme 1	DOWN
219	7997504	CDH13	cadherin 13, H-cadherin (heart)	DOWN
220	8152297	ANGPT1	angiopoietin 1	DOWN
221	8090433	MGLL	monoglyceride lipase	DOWN
222	8034390	ZNF799	zinc finger protein 799	DOWN
223	8087337	LAMB2	laminin, beta 2 (laminin S)	DOWN
224	7990309	STRA6	stimulated by retinoic acid gene 6 homolog (mouse)	DOWN
225	8140955	CDK6	cyclin-dependent kinase 6	DOWN
226	8103025	ZNF827	zinc finger protein 827	DOWN
227	8058869	TNS1	tensin 1	UP
228	7898939	NIPAL3	NIPA-like domain containing 3	DOWN
229	8071044	TEKT4P2	tektin 4 pseudogene 2	DOWN
230	7984079	TPM1	tropomyosin 1 (alpha)	DOWN
231	8084206	B3GNT5	UDP-GlcNAc:betaGal beta-1,3-N-acetylglucosaminyltransferase 5	DOWN
232	7968577	NBEA	neurobeachin	DOWN
233	8045539	KYNU	kynureninase	DOWN
234	8056837	GPR155	G protein-coupled receptor 155	DOWN
235	8125436	HLA-DRB5	major histocompatibility complex, class II, DR beta 5	DOWN
236	8072626	TIMP3	TIMP metalloproteinase inhibitor 3	DOWN
237	8122464	UTRN	utrophin	DOWN
238	8112107	PPAP2A	phosphatidic acid phosphatase type 2A	DOWN
239	8039017	ZNF816	zinc finger protein 816	DOWN
240	8095435	HTN1	histatin 1	UP
241	8100109	GABRA2	gamma-aminobutyric acid (GABA) A receptor, alpha 2	DOWN
242	7968035	SPATA13	spermatogenesis associated 13	DOWN
243	7935180	PDLIM1	PDZ and LIM domain 1	DOWN
244	7989493	RPS27L	ribosomal protein S27-like	DOWN
245	7951554	RDX	radixin	DOWN
246	8105229	PELO	pelota homolog (Drosophila)	DOWN
247	8019486	SECTM1	secreted and transmembrane 1	DOWN
248	7943075	FAT3	FAT tumor suppressor homolog 3 (Drosophila)	DOWN
249	8078350	TGFBR2	transforming growth factor, beta receptor II (70/80kDa)	DOWN
250	7961532	ARHGDIB	Rho GDP dissociation inhibitor (GDI) beta	UP
251	8024660	HMG20B	high mobility group 20B	DOWN
252	8071051	LOC100233156	tektin 4 pseudogene	DOWN
253	8161353	LOC554249	hypothetical LOC554249	DOWN
254	8068024	JAM2	junctional adhesion molecule 2	DOWN
255	7921852	MPZ	myelin protein zero	DOWN
256	8175933	RENBP	renin binding protein	UP
257	8069880	TIAM1	T-cell lymphoma invasion and metastasis 1	DOWN
258	8090162	ITGB5	integrin, beta 5	DOWN
259	8044933	GLI2	GLI family zinc finger 2	DOWN
260	8019074	NPTX1	neuronal pentraxin I	DOWN
261	8078619	ITGA9	integrin, alpha 9	DOWN

262	8173673	ATRX	alpha thalassemia/mental retardation syndrome X-linked	DOWN
263	8071420	SERPIND1	serpin peptidase inhibitor, clade D (heparin cofactor), member 1	DOWN
264	8180411	ELMO1	engulfment and cell motility 1	DOWN
265	8098006	GLRB	glycine receptor, beta	DOWN
266	8083594	PTX3	pentraxin 3, long	DOWN
267	8041447	CRIM1	cysteine rich transmembrane BMP regulator 1 (chordin-like)	DOWN
268	8174201	BEX1	brain expressed, X-linked 1	DOWN
269	7999562	PARN	poly(A)-specific ribonuclease	DOWN
270	7931977	ITIH5	inter-alpha (globulin) inhibitor H5	DOWN
271	8131339	FSCN1	fascin homolog 1, actin-bundling protein (Strongylocentrotus purpuratus)	DOWN
272	8103244	RNF175	ring finger protein 175	DOWN
273	8148304	TRIB1	tribbles homolog 1 (Drosophila)	DOWN
274	8027247	ZNF93	zinc finger protein 93	DOWN
275	8155754	MAMDC2	MAM domain containing 2	UP
276	7970763	FLT1	fms-related tyrosine kinase 1 (vascular endothelial growth factor/vascular permeability factor receptor)	DOWN
277	8068202	C21orf63	chromosome 21 open reading frame 63	DOWN
278	8130739	RPS6KA2	ribosomal protein S6 kinase, 90kDa, polypeptide 2	DOWN
279	8140971	SAMD9L	sterile alpha motif domain containing 9-like	DOWN
280	8139699	FLJ45974	hypothetical LOC401337	DOWN
281	8030128	PPP1R15A	protein phosphatase 1, regulatory (inhibitor) subunit 15A	DOWN
282	8017964	ABCA6	ATP-binding cassette, sub-family A (ABC1), member 6	DOWN
283	8084742	LPP	LIM domain containing preferred translocation partner in lipoma	DOWN
284	7902452	AK5	adenylate kinase 5	DOWN
285	8098021	GRIA2	glutamate receptor, ionotropic, AMPA 2	DOWN
286	8098441	ODZ3	odz, odd Oz/ten-m homolog 3 (Drosophila)	DOWN
287	8165947	WWC3	WWC family member 3	DOWN
288	8145365	DOCK5	dedicator of cytokinesis 5	DOWN
289	8050302	ROCK2	Rho-associated, coiled-coil containing protein kinase 2	DOWN
290	8032608	C19orf28	chromosome 19 open reading frame 28	DOWN
291	8168868	ARMCX1	armadillo repeat containing, X-linked 1	DOWN
292	8163775	MEGF9	multiple EGF-like-domains 9	DOWN
293	8067233	PMEPA1	prostate transmembrane protein, androgen induced 1	DOWN
294	8078330	RBMS3	RNA binding motif, single stranded interacting protein 3	DOWN
295	8113039	MEF2C	myocyte enhancer factor 2C	DOWN
296	8097829	FHDC1	FH2 domain containing 1	DOWN
297	7912537	DHRS3	dehydrogenase/reductase (SDR family) member 3	DOWN
298	8140752	ABCB4	ATP-binding cassette, sub-family B (MDR/TAP), member 4	DOWN
299	8104492	ROPN1L	rhophilin associated tail protein 1-like	DOWN
300	7912706	EPHA2	EPH receptor A2	DOWN
301	8138489	CDCA7L	cell division cycle associated 7-like	UP
302	8066214	TGM2	transglutaminase 2 (C polypeptide, protein-glutamine-gamma-glutamyltransferase)	DOWN

303	8130993	FAM20C	family with sequence similarity 20, member C	DOWN
304	7939173	DEPDC7	DEP domain containing 7	DOWN
305	8132503	STK17A	serine/threonine kinase 17a	DOWN
306	8153002	NDRG1	N-myc downstream regulated 1	DOWN
307	7906307	KIRREL	kin of IRRE like (Drosophila)	DOWN
308	8108724	PCDHB10	protocadherin beta 10	DOWN
309	7918379	GSTM3	glutathione S-transferase mu 3 (brain)	DOWN
310	8038998	ZNF468	zinc finger protein 468	DOWN
311	8037363	CADM4	cell adhesion molecule 4	DOWN
312	8131666	ITGB8	integrin, beta 8	DOWN
313	8008151	IGF2BP1	insulin-like growth factor 2 mRNA binding protein 1	DOWN
314	8108744	PCDHB14	protocadherin beta 14	DOWN
315	7951408	CARD16	caspase recruitment domain family, member 16	DOWN
316	8069744	RWDD2B	RWD domain containing 2B	DOWN
317	8042416	ARHGAP25	Rho GTPase activating protein 25	UP
318	8135734	C7orf58	chromosome 7 open reading frame 58	DOWN
319	8177788	HLA-E	major histocompatibility complex, class I, E	DOWN
320	8039010	ZNF765	zinc finger protein 765	DOWN
321	7952341	CLMP	CXADR-like membrane protein	DOWN
322	7925062	SIPA1L2	signal-induced proliferation-associated 1 like 2	DOWN
323	8170648	BGN	biglycan	DOWN
324	8014066	EVI2A	ecotropic viral integration site 2A	DOWN
325	7908409	RGS2	regulator of G-protein signaling 2, 24kDa	DOWN
326	8155849	ANXA1	annexin A1	DOWN
327	8163839	C5	complement component 5	DOWN
328	7950128	C11orf51	chromosome 11 open reading frame 51	UP
329	8122909	SCAF8	SR-related CTD-associated factor 8	DOWN
330	8136347	CALD1	caldesmon 1	DOWN
331	7956878	IRAK3	interleukin-1 receptor-associated kinase 3	DOWN
332	7928291	CHST3	carbohydrate (chondroitin 6) sulfotransferase 3	DOWN
333	8123044	TULP4	tubby like protein 4	DOWN
334	8027254	ZNF90	zinc finger protein 90	DOWN
335	8113796	C5orf63	chromosome 5 open reading frame 63	DOWN
336	8088776	FOXP1	forkhead box P1	UP
337	8030931	ZNF528	zinc finger protein 528	DOWN
338	7917912	DPYD	dihydropyrimidine dehydrogenase	DOWN
339	8124901	HLA-C	major histocompatibility complex, class I, C	DOWN
340	8068570	DSCR8	Down syndrome critical region gene 8	DOWN
341	8141882	DPY19L2P2	dpy-19-like 2 pseudogene 2 (C. elegans)	DOWN
342	8151890	TP53INP1	tumor protein p53 inducible nuclear protein 1	DOWN
343	7945371	IFITM3	interferon induced transmembrane protein 3	DOWN
344	7908459	CFH	complement factor H	DOWN
345	8083233	ZIC1	Zic family member 1	DOWN
346	8112202	PLK2	polo-like kinase 2	DOWN
347	8099259	AFAP1	actin filament associated protein 1	DOWN
348	7943263	AMOTL1	angiominin like 1	DOWN
349	8138613	OSBPL3	oxysterol binding protein-like 3	DOWN
350	8081235	COL8A1	collagen, type VIII, alpha 1	DOWN
351	8036324	ZNF260	zinc finger protein 260	DOWN
352	7923034	B3GALT2	UDP-Gal:betaGlcNAc beta 1,3-galactosyltransferase, polypeptide 2	DOWN

353	8113709	LOX	lysyl oxidase	DOWN
354	8173106	ITIH5L	inter-alpha (globulin) inhibitor H5-like	DOWN
355	8005225	LOC162632	ubiquitin specific peptidase 6 (Tre-2 oncogene) pseudogene	DOWN
356	8075462	SELM	selenoprotein M	DOWN
357	8068022	MIR155	microRNA 155	DOWN
358	8175393	ARHGEF6	Rac/Cdc42 guanine nucleotide exchange factor (GEF) 6	DOWN
359	8139488	IGFBP3	insulin-like growth factor binding protein 3	DOWN
360	8139820	ZNF680	zinc finger protein 680	DOWN
361	8040238	HPCAL1	hippocalcin-like 1	DOWN
362	8107632	SNX24	sorting nexin 24	DOWN
363	8130674	PDE10A	phosphodiesterase 10A	DOWN
364	8088602	MAGI1	membrane associated guanylate kinase, WW and PDZ domain containing 1	UP
365	7971922	PCDH9	protocadherin 9	DOWN
366	8067279	CTSZ	cathepsin Z	DOWN
367	8039054	ZNF347	zinc finger protein 347	DOWN
368	8012605	GAS7	growth arrest-specific 7	DOWN
369	7903586	TMEM167B	transmembrane protein 167B	DOWN
370	7952313	MIRLET7A2	microRNA let-7a-2	DOWN
371	7930682	FAM160B1	family with sequence similarity 160, member B1	DOWN
372	8120967	NT5E	5'-nucleotidase, ecto (CD73)	DOWN
373	8121257	PRDM1	PR domain containing 1, with ZNF domain	DOWN
374	8039044	ZNF415	zinc finger protein 415	DOWN
375	7944623	TBCEL	tubulin folding cofactor E-like	DOWN
376	8043197	VAMP8	vesicle-associated membrane protein 8 (endobrevin)	DOWN
377	8127563	COL12A1	collagen, type XII, alpha 1	DOWN
378	8029856	ARHGAP35	Rho GTPase activating protein 35	DOWN
379	8160260	BNC2	basonuclin 2	UP
380	7958253	C12orf75	chromosome 12 open reading frame 75	DOWN
381	8141374	AZGP1	alpha-2-glycoprotein 1, zinc-binding	DOWN
382	8092230	ZMAT3	zinc finger, matrin-type 3	DOWN
383	8133233	AUTS2	autism susceptibility candidate 2	UP
384	7929032	FAS	Fas (TNF receptor superfamily, member 6)	DOWN
385	8051573	CDC42EP3	CDC42 effector protein (Rho GTPase binding) 3	DOWN
386	8040113	ASAP2	ArfGAP with SH3 domain, ankyrin repeat and PH domain 2	DOWN
387	7943715	ZC3H12C	zinc finger CCCH-type containing 12C	DOWN
388	7981427	CKB	creatine kinase, brain	UP
389	8152606	SNTB1	syntrophin, beta 1 (dystrophin-associated protein A1, 59kDa, basic component 1)	DOWN
390	8108683	PCDHB2	protocadherin beta 2	DOWN
391	8176375	RPS4Y1	ribosomal protein S4, Y-linked 1	DOWN
392	8146633	UG0898H09	hypothetical LOC643763	DOWN
393	8033754	ZNF266	zinc finger protein 266	DOWN
394	8159900	GLIS3	GLIS family zinc finger 3	DOWN
395	8036420	ZFP30	zinc finger protein 30 homolog (mouse)	DOWN
396	7982102	GABRA5	gamma-aminobutyric acid (GABA) A receptor, alpha 5	UP
397	8166593	IL1RAPL1	interleukin 1 receptor accessory protein-like 1	DOWN
398	7924636	TMEM63A	transmembrane protein 63A	DOWN

399	8067836	LINC00314	long intergenic non-protein coding RNA 314	DOWN
400	8139656	GRB10	growth factor receptor-bound protein 10	DOWN
401	8128991	LAMA4	laminin, alpha 4	DOWN
402	8160274	MGC24103	hypothetical MGC24103	UP
403	8035793	ZNF737	zinc finger protein 737	DOWN
404	8104035	SORBS2	sorbin and SH3 domain containing 2	DOWN
405	7945666	CTSD	cathepsin D	DOWN
406	8105585	RNF180	ring finger protein 180	DOWN
407	8179731	HLA-B	major histocompatibility complex, class I, B	DOWN
408	8147756	BAALC	brain and acute leukemia, cytoplasmic	DOWN
409	8100318	SGCB	sarcoglycan, beta (43kDa dystrophin-associated glycoprotein)	DOWN
410	8111101	ANKH	ankylosis, progressive homolog (mouse)	DOWN
411	7951133	MAML2	mastermind-like 2 (Drosophila)	DOWN
412	8033667	ZNF558	zinc finger protein 558	DOWN
413	7911017	SDCCAG8	serologically defined colon cancer antigen 8	DOWN
414	8131944	NFE2L3	nuclear factor (erythroid-derived 2)-like 3	DOWN
415	8016390	COPZ2	coatamer protein complex, subunit zeta 2	DOWN
416	8114797	SPRY4	sprouty homolog 4 (Drosophila)	DOWN
417	8102800	SLC7A11	solute carrier family 7 (anionic amino acid transporter light chain, xc- system), member 11	DOWN
418	8115196	ZNF300	zinc finger protein 300	DOWN
419	8025998	ZNF136	zinc finger protein 136	DOWN
420	8122334	CCRL1	chemokine (C-C motif) receptor-like 1	DOWN
421	7998978	ZNF597	zinc finger protein 597	DOWN
422	8030946	ZNF808	zinc finger protein 808	DOWN
423	7947425	CD59	CD59 molecule, complement regulatory protein	DOWN
424	8179049	HLA-J	major histocompatibility complex, class I, J (pseudogene)	DOWN
425	7999387	EMP2	epithelial membrane protein 2	DOWN
426	8169473	PLS3	plastin 3	DOWN
427	8103736	SCRG1	stimulator of chondrogenesis 1	DOWN
428	8108729	PCDHB11	protocadherin beta 11	DOWN
429	8143188	CREB3L2	cAMP responsive element binding protein 3-like 2	DOWN
430	7929072	IFIT5	interferon-induced protein with tetratricopeptide repeats 5	DOWN
431	8054395	UXS1	UDP-glucuronate decarboxylase 1	DOWN
432	8090715	ACAD11	acyl-CoA dehydrogenase family, member 11	DOWN
433	8085689	TBC1D5	TBC1 domain family, member 5	DOWN
434	8124040	ATXN1	ataxin 1	DOWN
435	7929065	IFIT1	interferon-induced protein with tetratricopeptide repeats 1	DOWN
436	8052872	TGFA	transforming growth factor, alpha	DOWN
437	7924207	PTPN14	protein tyrosine phosphatase, non-receptor type 14	DOWN
438	7919139	LOC375010	ankyrin repeat domain 20 family, member A pseudogene	DOWN

Supplementary Table 3. Significantly altered molecular pathways in metastatic melanoma cell lines.

Pathway ID	Pathway name	Source	P-value	Bonferroni	Genes included (at least 5)
83069	Cell adhesion molecules (CAMs)	KEGG	3.75E-10	4.78E-07	<i>HLA-B, HLA-C, HLA-DPA1, HLA-DPB1, HLA-DRA, HLA-DRB3, HLA-DRB4, HLA-DRB5, HLA-E, JAM2, NRXN3, CADM1, NLGN4X, SDC2, MPZ, VCAN, OCLN, ITGA4, ITGA9, ITGB8</i>
576262	Extracellular matrix organization	REACTOME	5.54E-09	7.05E-06	<i>PDGFA, JAM2, SDC2, COL8A1, COL12A1, COL19A1, ADAMTS1, TNC, VCAN, CTSD, CTSS, ITGA2, ITGA3, ITGA4, ITGA9, ITGB5, ITGB8, BGN, DST, ADAMTS9, KDR, LAMA4, LAMB2, TIMP2, LOX</i>
198795	Focal adhesion	WikiPathways	1.04E-07	1.32E-04	<i>PDGFA, ROCK2, FLT1, TNC, BIRC3, ITGA2, ITGA3, ITGA4, ITGA9, ITGB5, ITGB8, JUN, PELO, KDR, PDGFC, LAMA4, LAMB2, CAV1, CAV2</i>
83067	Focal adhesion	KEGG	6.12E-07	7.79E-04	<i>PDGFA, ROCK2, FLT1, TNC, BIRC3, ITGA2, ITGA3, ITGA4, ITGA9, ITGB5, ITGB8, JUN, KDR, PDGFC, LAMA4, LAMB2, CAV1, CAV2, ARHGAP35</i>
137939	Direct p53 effectors	Pathway Interaction Database	8.46E-07	1.08E-03	<i>TP53INP1, NDRG1, IGFBP3, VCAN, CTSD, GADD45A, PRDM1, JUN, CD82, CASP1, CAV1, RPS27L, TGFA, EPHA2</i>
83074	Antigen processing and presentation	KEGG	4.33E-06	5.51E-03	<i>HLA-B, HLA-C, HLA-DPA1, HLA-DPB1, HLA-DRA, HLA-DRB3, HLA-DRB4, HLA-DRB5, HLA-E, CTSS, CD74</i>
187106	Interferon gamma signaling	REACTOME	7.61E-06	9.69E-03	<i>HLA-B, HLA-C, HLA-DPA1, HLA-DPB1, HLA-DRA, HLA-DRB3, HLA-DRB4, HLA-DRB5, HLA-E, GBP3</i>
106416	Translocation of ZAP-70 to Immunological synapse	REACTOME	7.79E-06	9.92E-03	<i>HLA-DPA1, HLA-DPB1, HLA-DRA, HLA-DRB3, HLA-DRB4, HLA-DRB5</i>
106415	Phosphorylation of CD3 and TCR zeta chains	REACTOME	1.39E-05	1.77E-02	<i>HLA-DPA1, HLA-DPB1, HLA-DRA, HLA-DRB3, HLA-DRB4, HLA-DRB5</i>

106110	Integrin cell surface interactions	REACTOME	2.85E-05	3.63E-02	<i>JAM2, TNC, ITGA2, ITGA3, ITGA4, ITGA9, ITGB5, ITGB8, KDR</i>
692234	PI3K-Akt signaling pathway	KEGG	3.64E-05	4.63E-02	<i>PDGFA, GNG2, CREB3L2, FLT1, ANGPT1, TNC, ITGA2, ITGA3, ITGA4, ITGA9, ITGB5, ITGB8, KDR, PDGFC, GNG7, GNG11, LAMA4, LAMB2, LPAR1, EPHA2, CDK6</i>
119557	PD-1 signaling	REACTOME	3.76E-05	4.79E-02	<i>HLA-DPA1, HLA-DPB1, HLA-DRA, HLA-DRB3, HLA-DRB4, HLA-DRB5</i>

Supplementary Table 4. Downregulated genes in metastatic melanoma cell lines are included in 7 molecular functional groups.

GO term / Name	Entrez Gene ID	Gene Symbol	Gene Name
0050839 / Cell adhesion molecule binding	9369	NRXN3	neurexin 3
	23705	CADM1	cell adhesion molecule 1
	10397	NDRG1	N-myc downstream regulated 1
	57502	NLGN4X	neuroligin 4, X-linked
	7402	UTRN	utrophin
	3491	CYR61	cysteine-rich, angiogenic inducer, 61
	1495	CTNNA1	catenin (cadherin-associated protein), alpha 1, 102kDa
	3673	ITGA2	integrin, alpha 2 (CD49B, alpha 2 subunit of VLA-2 receptor)
	3675	ITGA3	integrin, alpha 3 (antigen CD49C, alpha 3 subunit of VLA-3 receptor)
	3676	ITGA4	integrin, alpha 4 (antigen CD49D, alpha 4 subunit of VLA-4 receptor)
	3693	ITGB5	integrin, beta 5
	2674	GFRA1	GDNF family receptor alpha 1
	667	DST	dystonin
	3791	KDR	kinase insert domain receptor
	3913	LAMB2	laminin, beta 2 (laminin S)
	10085	EDIL3	EGF-like repeats and discoidin I-like domains 3
	7045	TGFBI	transforming growth factor, beta-induced, 68kDa
	928	CD9	CD9 molecule
	7077	TIMP2	TIMP metalloproteinase inhibitor 2
0042605 / Peptide antigen binding	2013	EMP2	epithelial membrane protein 2
	1012	CDH13	cadherin 13
	3106	HLA-B	major histocompatibility complex, class I, B
	3107	HLA-C	major histocompatibility complex, class I, C
	3113	HLA-DPA1	major histocompatibility complex, class II, DP alpha 1
	3115	HLA-DPB1	major histocompatibility complex, class II, DP beta 1
	3122	HLA-DRA	major histocompatibility complex, class II, DR alpha
	3125	HLA-DRB3	major histocompatibility complex, class II, DR beta 3
	3126	HLA-DRB4	major histocompatibility complex, class II, DR beta 4
	3127	HLA-DRB5	major histocompatibility complex, class II, DR beta 5
	3133	HLA-E	major histocompatibility complex, class I, E
	563	AZGP1	alpha-2-glycoprotein 1, zinc-binding

0005178 / Integrin binding	7402	UTRN	utrophin
	3491	CYR61	cysteine-rich, angiogenic inducer, 61
	3673	ITGA2	integrin, alpha 2 (CD49B, alpha 2 subunit of VLA-2 receptor)
	3675	ITGA3	integrin, alpha 3 (antigen CD49C, alpha 3 subunit of VLA-3 receptor)
	3693	ITGB5	integrin, beta 5
	2674	GFRA1	GDNF family receptor alpha 1
	667	DST	dystonin
	3791	KDR	kinase insert domain receptor (a type III receptor tyrosine kinase)
	3913	LAMB2	laminin, beta 2 (laminin S)
	10085	EDIL3	EGF-like repeats and discoidin I-like domains 3
	7045	TGFBI	transforming growth factor, beta-induced, 68kDa
	928	CD9	CD9 molecule
	7077	TIMP2	TIMP metalloproteinase inhibitor 2
	2013	EMP2	epithelial membrane protein 2
0050840 / Extracellular matrix binding	9353	SLIT2	slit homolog 2 (Drosophila)
	3491	CYR61	cysteine-rich, angiogenic inducer, 61
	1520	CTSS	cathepsin S
	3673	ITGA2	integrin, alpha 2 (CD49B, alpha 2 subunit of VLA-2 receptor)
	3675	ITGA3	integrin, alpha 3 (antigen CD49C, alpha 3 subunit of VLA-3 receptor)
	3680	ITGA9	integrin, alpha 9
	633	BGN	biglycan
	7045	TGFBI	transforming growth factor, beta-induced, 68kDa
0003823 / Antigen binding	3106	HLA-B	major histocompatibility complex, class I, B
	3107	HLA-C	major histocompatibility complex, class I, C
	3113	HLA-DPA1	major histocompatibility complex, class II, DP alpha 1
	3115	HLA-DPB1	major histocompatibility complex, class II, DP beta 1
	3122	HLA-DRA	major histocompatibility complex, class II, DR alpha
	3125	HLA-DRB3	major histocompatibility complex, class II, DR beta 3
	3126	HLA-DRB4	major histocompatibility complex, class II, DR beta 4
	3127	HLA-DRB5	major histocompatibility complex, class II, DR beta 5
	3133	HLA-E	major histocompatibility complex, class I, E
	563	AZGP1	alpha-2-glycoprotein 1, zinc-binding
	972	CD74	CD74 molecule, major histocompatibility complex, class II invariant chain
0042277 / Peptide binding	5125	PCSK5	proprotein convertase subtilisin/kexin type 5
	3106	HLA-B	major histocompatibility complex, class I, B
	3107	HLA-C	major histocompatibility complex, class I, C

	3113	HLA-DPA1	major histocompatibility complex, class II, DP alpha 1
	3115	HLA-DPB1	major histocompatibility complex, class II, DP beta 1
	3122	HLA-DRA	major histocompatibility complex, class II, DR alpha
	3125	HLA-DRB3	major histocompatibility complex, class II, DR beta 3
	3126	HLA-DRB4	major histocompatibility complex, class II, DR beta 4
	3127	HLA-DRB5	major histocompatibility complex, class II, DR beta 5
	3133	HLA-E	major histocompatibility complex, class I, E
	1509	CTSD	cathepsin D
	563	AZGP1	alpha-2-glycoprotein 1, zinc-binding
	590	BCHE	butyrylcholinesterase
	1889	ECE1	endothelin converting enzyme 1
	2947	GSTM3	glutathione S-transferase mu 3 (brain)
	972	CD74	CD74 molecule, major histocompatibility complex, class II invariant chain
0033218 / Amide binding	5125	PCSK5	proprotein convertase subtilisin/kexin type 5
	3106	HLA-B	major histocompatibility complex, class I, B
	3107	HLA-C	major histocompatibility complex, class I, C
	3113	HLA-DPA1	major histocompatibility complex, class II, DP alpha 1
	3115	HLA-DPB1	major histocompatibility complex, class II, DP beta 1
	3122	HLA-DRA	major histocompatibility complex, class II, DR alpha
	3125	HLA-DRB3	major histocompatibility complex, class II, DR beta 3
	3126	HLA-DRB4	major histocompatibility complex, class II, DR beta 4
	3127	HLA-DRB5	major histocompatibility complex, class II, DR beta 5
	3133	HLA-E	major histocompatibility complex, class I, E
	1509	CTSD	cathepsin D
	563	AZGP1	alpha-2-glycoprotein 1, zinc-binding
	590	BCHE	butyrylcholinesterase
	1889	ECE1	endothelin converting enzyme 1
	2947	GSTM3	glutathione S-transferase mu 3 (brain)
	972	CD74	CD74 molecule, major histocompatibility complex, class II invariant chain

Supplementary Table 5. Differentially expressed genes between primary melanomas and at least one of the melanoma metastasis subgroups based on TCGA RNAseq v2.0 data (N=1065).

Gene Symbol / Gene ID	Official full name	Parametric p-value	DM ¹ vs. P ²	rLN ³ vs. P	rSC/C ⁴ vs. P
A2ML1 144568	Alpha-2-Macroglobulin-Like 1	< 1E-07	down	down	down
AATBC 284837	apoptosis associated transcript in bladder cancer	4.95E-05			down
ABCA12 26154	ATP-binding cassette, sub-family A (ABC1), member 12	< 1E-07	down	down	down
ABCA6 23460	ATP-binding cassette, sub-family A (ABC1), member 6	1.48E-05			up
ABCA8 10351	ATP-binding cassette, sub-family A (ABC1), member 8	1.52E-04		up	up
ABCB1 5243	ATP-binding cassette, sub-family B (MDR/TAP), member 1	< 1E-07		up	
ABCC2 1244	ATP-binding cassette, sub-family C (CFTR/MRP), member 2	1.69E-04	down	down	down
ABCC9 10060	ATP-binding cassette, sub-family C (CFTR/MRP), member 9	< 1E-07		up	up
ABI3BP 25890	ABI family, member 3 (NESH) binding protein	< 1E-07		up	up
ACAP1 9744	ArfGAP with coiled-coil, ankyrin repeat and PH domains 1	< 1E-07		up	
ACE 1636	angiotensin I converting enzyme	< 1E-07		up	
ACOX2 8309	acyl-CoA oxidase 2, branched chain	2.10E-04			up
ACSL5 51703	acyl-CoA synthetase long-chain family member 5	< 1E-07		up	
ADAM28 10863	ADAM metallopeptidase domain 28	< 1E-07		up	up
ADAM6 8755	ADAM metallopeptidase domain 6	< 1E-07		up	
ADAMDEC1 27299	ADAM-like, decysin 1	< 1E-07		up	
ADAMTS12 81792	ADAM metallopeptidase with thrombospondin type 1 motif, 12	2.00E-06			up
ADAMTS3 9508	ADAM metallopeptidase with thrombospondin type 1 motif, 3	7.21E-04			up
ADAMTS5 11096	ADAM metallopeptidase with thrombospondin type 1 motif, 5	< 1E-07			up
ADAMTS6 11174	ADAM metallopeptidase with thrombospondin type 1 motif, 6	2.00E-07			up
ADAMTS9 56999	ADAM metallopeptidase with thrombospondin type 1 motif, 9	1.00E-07			up
ADAMTSL1 92949	ADAMTS-like 1	< 1E-07			up
ADAMTSL3 57188	ADAMTS-like 3	< 1E-07	up	up	up
ADCY2 1108	adenylate cyclase 2 (brain)	9.26E-05	down	down	down
ADGRF5 221395	adhesion G protein-coupled receptor F5	< 1E-07		up	up
ADGRG5 221188	adhesion G protein-coupled receptor G5	< 1E-07		up	

ADGRL2 23266	adhesion G protein-coupled receptor L2	4.94E-03			up
ADGRL4 64123	adhesion G protein-coupled receptor L4	< 1E-07			up
ADH1B 125	alcohol dehydrogenase 1B (class I), beta polypeptide	1.00E-06		up	
ADIRF 10974	adipogenesis regulatory factor	< 1E-07	down	down	
ADORA2A 135	adenosine A2a receptor	< 1E-07		up	
ADRA2A 150	adrenoceptor alpha 2A	< 1E-07		up	
AHNAK2 113146	AHNAK nucleoprotein 2	3.80E-06	down	down	
AHRR 57491	aryl-hydrocarbon receptor repressor	< 1E-07	down		down
AIM2 9447	absent in melanoma 2	5.82E-05			up
AKAP12 9590	A kinase (PRKA) anchor protein 12	< 1E-07		up	up
AKAP5 9495	A kinase (PRKA) anchor protein 5	< 1E-07		up	
AKAP6 9472	A kinase (PRKA) anchor protein 6	4.67E-05			up
AKR1B10 57016	aldo-keto reductase family 1, member B10 (aldose reductase)	< 1E-07	down	down	down
ALDH3A1 218	aldehyde dehydrogenase 3 family, member A1	< 1E-07	down	down	down
ALDH3B2 222	aldehyde dehydrogenase 3 family, member B2	< 1E-07	down	down	down
ALOX5 240	arachidonate 5-lipoxygenase	< 1E-07		up	
ALS2CL 259173	ALS2 C-terminal like	< 1E-07		down	down
AMIGO2 347902	adhesion molecule with Ig-like domain 2	6.00E-07		up	
AMPH 273	amphiphysin	1.18E-04		down	
ANGPT1 284	angiopoietin 1	1.89E-03			up
ANGPT2 285	angiopoietin 2	8.75E-04			up
ANGPTL1 9068	angiopoietin-like 1	1.60E-06			up
ANKH 56172	ANKH inorganic pyrophosphate transport regulator	6.57E-04			up
ANKRD35 148741	ankyrin repeat domain 35	< 1E-07	down		
ANTXR2 118429	anthrax toxin receptor 2	< 1E-07			up
ANXA8 653145	annexin A8	< 1E-07	down	down	down
ANXA8L1 728113	annexin A8-like 1	< 1E-07	down	down	down
AOAH 313	acyloxyacyl hydrolase (neutrophil)	< 1E-07		up	up
AOC3 8639	amine oxidase, copper containing 3	< 1E-07		up	

APBB1IP154518	amyloid beta (A4) precursor protein-binding, family B, member 1 interacting protein	< 1E-07		up	up
APCDD1147495	adenomatosis polyposis coli down-regulated 1	< 1E-07	down	down	down
APOL3180833	apolipoprotein L, 3	1.00E-07		up	
AQP31360	aquaporin 3 (Gill blood group)	< 1E-07	down	down	down
ARHGAP15155843	Rho GTPase activating protein 15	< 1E-07		up	
ARHGAP2519938	Rho GTPase activating protein 25	< 1E-07		up	
ARHGAP2919411	Rho GTPase activating protein 29	< 1E-07			up
ARHGAP301257106	Rho GTPase activating protein 30	< 1E-07		up	
ARHGAP61395	Rho GTPase activating protein 6	5.00E-07			up
ARHGAP8123779	Rho GTPase activating protein 8	6.70E-06			down
ARHGAP9164333	Rho GTPase activating protein 9	< 1E-07		up	
ARHGDIB1397	Rho GDP dissociation inhibitor (GDI) beta	< 1E-07		up	
ARHGEF371389337	Rho guanine nucleotide exchange factor (GEF) 37	1.76E-04		down	
ARHGEF4150649	Rho guanine nucleotide exchange factor (GEF) 4	< 1E-07	down	down	down
ARHGEF619459	Rho guanine nucleotide exchange factor (GEF) 6	< 1E-07			up
ART31419	ADP-ribosyltransferase 3	2.16E-03			up
ASPN154829	asporin	1.40E-06			up
ASPRV11151516	aspartic peptidase, retroviral-like 1	< 1E-07	down	down	down
ATP2A31489	ATPase, Ca++ transporting, ubiquitous	2.00E-07		up	
ATP2B11490	ATPase, Ca++ transporting, plasma membrane 1	< 1E-07			up
ATP8A1110396	ATPase, aminophospholipid transporter (APLT), class I, type 8A, member 1	< 1E-07		up	up
AXL1558	AXL receptor tyrosine kinase	5.72E-05			up
B4GALNT31283358	beta-1,4-N-acetyl-galactosaminyl transferase 3	2.40E-06		down	
BAALC179870	brain and acute leukemia, cytoplasmic	1.94E-03	down		
BAG419530	BCL2-associated athanogene 4	< 1E-07			up
BAIAP2L1155971	BAI1-associated protein 2-like 1	1.06E-03			down
BAIAP2L2180115	BAI1-associated protein 2-like 2	1.80E-06		down	down
BANK1155024	B-cell scaffold protein with ankyrin repeats 1	< 1E-07		up	
BARX218538	BARX homeobox 2	< 1E-07	down	down	
BCAN163827	brevican	5.54E-04	down	down	down
BCAT11586	branched chain amino-acid transaminase 1, cytosolic	< 1E-07	up	up	up

BIN2 51411	bridging integrator 2	< 1E-07		up	
BIRC3 330	baculoviral IAP repeat containing 3	< 1E-07		up	
BLK 640	BLK proto-oncogene, Src family tyrosine kinase	< 1E-07		up	
BMP8B 656	bone morphogenetic protein 8b	4.89E-04			up
BMS1P20 96610	BMS1 ribosome biogenesis factor pseudogene 20	< 1E-07		up	
BNC1 646	basonuclin 1	< 1E-07	down	down	down
BSPRY 54836	B-box and SPRY domain containing	< 1E-07			down
BTK 695	Bruton agammaglobulinemia tyrosine kinase	< 1E-07		up	
BTLA 151888	B and T lymphocyte associated	< 1E-07		up	
C16orf54 283897	chromosome 16 open reading frame 54	< 1E-07		up	
C19orf71 100128569	chromosome 19 open reading frame 71	6.50E-06			down
C1orf106 55765	chromosome 1 open reading frame 106	4.15E-05		down	down
C1orf116 79098	chromosome 1 open reading frame 116	< 1E-07	down	down	down
C1QA 712	complement component 1, q subcomponent, A chain	7.00E-07		up	
C1QB 713	complement component 1, q subcomponent, B chain	< 1E-07		up	
C1QC 714	complement component 1, q subcomponent, C chain	< 1E-07		up	
C1QTNF3 114899	C1q and tumor necrosis factor related protein 3	4.64E-04		up	up
C3 718	complement component 3	< 1E-07		up	up
C3AR1 719	complement component 3a receptor 1	< 1E-07		up	up
C4A 720	complement component 4A (Rodgers blood group)	< 1E-07		up	
C5AR1 728	complement component 5a receptor 1	< 1E-07		up	
C7 730	complement component 7	< 1E-07	up	up	up
CA12 771	carbonic anhydrase XII	2.00E-07	down	down	
CA14 23632	carbonic anhydrase XIV	3.08E-04		down	down
CA8 767	carbonic anhydrase VIII	2.06E-03			down
CABLES1 91768	Cdk5 and Abl enzyme substrate 1	1.10E-06			down
CACNA2D4 93589	calcium channel, voltage-dependent, alpha 2/delta subunit 4	5.73E-05			up
CALCRL 10203	calcitonin receptor-like	< 1E-07			up
CALML3 810	calmodulin-like 3	< 1E-07	down	down	down
CALML5 51806	calmodulin-like 5	< 1E-07	down	down	down
CAMK4 814	calcium/calmodulin-dependent protein kinase IV	< 1E-07		up	
CAMSAP3 57662	calmodulin regulated spectrin-associated protein family, member 3	< 1E-07		down	down

CAPG 822	capping protein (actin filament), gelsolin-like	3.23E-03	down		
CARD11 84433	caspase recruitment domain family, member 11	< 1E-07		up	
CASC5 57082	cancer susceptibility candidate 5	< 1E-07			up
CCDC102B 79839	coiled-coil domain containing 102B	< 1E-07		up	
CCDC186 55088	coiled-coil domain containing 186	< 1E-07			up
CCL19 6363	chemokine (C-C motif) ligand 19	< 1E-07		up	
CCL21 6366	chemokine (C-C motif) ligand 21	< 1E-07	down	up	
CCL22 6367	chemokine (C-C motif) ligand 22	2.65E-04	down		
CCNT1 904	cyclin T1	< 1E-07			up
CCR1 1230	chemokine (C-C motif) receptor 1	< 1E-07		up	up
CCR2 729230	chemokine (C-C motif) receptor 2	< 1E-07		up	
CCR5 1234	chemokine (C-C motif) receptor 5	< 1E-07		up	
CCR6 1235	chemokine (C-C motif) receptor 6	< 1E-07		up	
CCR7 1236	chemokine (C-C motif) receptor 7	< 1E-07		up	
CCRL2 9034	chemokine (C-C motif) receptor-like 2	< 1E-07		up	
CD163 9332	CD163 molecule	< 1E-07		up	up
CD180 4064	CD180 molecule	< 1E-07		up	up
CD19 930	CD19 molecule	< 1E-07		up	
CD1D 912	CD1d molecule	< 1E-07		up	up
CD2 914	CD2 molecule	< 1E-07		up	
CD22 933	CD22 molecule	5.00E-07		up	
CD24 100133941	CD24 molecule	< 1E-07	down	down	down
CD247 919	CD247 molecule	< 1E-07		up	
CD27 939	CD27 molecule	< 1E-07		up	
CD28 940	CD28 molecule	< 1E-07		up	
CD300A 11314	CD300a molecule	< 1E-07		up	up
CD300C 10871	CD300c molecule	< 1E-07			up
CD300LF 146722	CD300 molecule-like family member f	< 1E-07		up	
CD33 945	CD33 molecule	1.00E-07			up
CD36 948	CD36 molecule	7.64E-04			up
CD37 951	CD37 molecule	< 1E-07		up	
CD38 952	CD38 molecule	< 1E-07		up	up
CD3D 915	CD3d molecule, delta (CD3-TCR complex)	< 1E-07		up	

CD3E 916	CD3e molecule, epsilon (CD3-TCR complex)	< 1E-07		up	
CD3G 917	CD3g molecule, gamma (CD3-TCR complex)	< 1E-07		up	
CD4 920	CD4 molecule	< 1E-07		up	
CD48 962	CD48 molecule	< 1E-07		up	
CD5 921	CD5 molecule	< 1E-07		up	
CD52 1043	CD52 molecule	< 1E-07		up	
CD53 963	CD53 molecule	< 1E-07		up	up
CD5L 922	CD5 molecule-like	< 1E-07		up	
CD6 923	CD6 molecule	< 1E-07		up	
CD69 969	CD69 molecule	< 1E-07		up	
CD7 924	CD7 molecule	< 1E-07		up	
CD72 971	CD72 molecule	< 1E-07		up	
CD79A 973	CD79a molecule, immunoglobulin-associated alpha	< 1E-07		up	
CD79B 974	CD79b molecule, immunoglobulin-associated beta	< 1E-07		up	
CD84 8832	CD84 molecule	< 1E-07		up	up
CD86 942	CD86 molecule	< 1E-07		up	
CD8A 925	CD8a molecule	< 1E-07		up	
CD8B 926	CD8b molecule	< 1E-07		up	
CD96 10225	CD96 molecule	< 1E-07		up	up
CDA 978	cytidine deaminase	< 1E-07	down	down	down
CDH1 999	cadherin 1, type 1, E-cadherin (epithelial)	4.71E-04	down	down	down
CDH11 1009	cadherin 11, type 2, OB-cadherin (osteoblast)	1.07E-05			up
CDH3 1001	cadherin 3, type 1, P-cadherin (placental)	< 1E-07	down	down	down
CDH6 1004	cadherin 6, type 2, K-cadherin (fetal kidney)	5.79E-05			up
CDHR1 92211	cadherin-related family member 1	< 1E-07	down	down	down
CDK14 5218	cyclin-dependent kinase 14	< 1E-07	up	up	up
CDKL5 6792	cyclin-dependent kinase-like 5	< 1E-07			up
CDS1 1040	CDP-diacylglycerol synthase (phosphatidate cytidyltransferase) 1	1.00E-07			down
CDSN 1041	corneodesmosin	< 1E-07	down	down	down
CEACAM19 56971	carcinoembryonic antigen-related cell adhesion molecule 19	< 1E-07	down	down	down
CEACAM6 4680	carcinoembryonic antigen-related cell adhesion molecule 6	< 1E-07		down	down
CECR1 51816	cat eye syndrome chromosome region, candidate 1	< 1E-07		up	
CEMIP 57214	cell migration inducing protein, hyaluronan binding	2.48E-03			up

CENPE 1062	centromere protein E, 312kDa	4.80E-06			up
CEP290 80184	centrosomal protein 290kDa	5.00E-07			up
CEP85L 387119	centrosomal protein 85kDa-like	< 1E-07		up	up
CEP97 79598	centrosomal protein 97kDa	< 1E-07			up
CETP 1071	cholesteryl ester transfer protein, plasma	< 1E-07		up	
CFH 3075	complement factor H	< 1E-07		up	up
CFI 3426	complement factor I	5.80E-06		up	up
CHAC1 79094	ChaC glutathione-specific gamma-glutamylcyclotransferase 1	2.14E-04			down
CHADL 150356	chondroadherin-like	3.16E-04		down	down
CHL1 10752	cell adhesion molecule L1-like	4.28E-03			up
CHRD1 91851	chordin-like 1	5.00E-07		up	up
CHRM1 1128	cholinergic receptor, muscarinic 1	2.50E-04			down
CHST15 51363	carbohydrate (N-acetylgalactosamine 4-sulfate 6-O) sulfotransferase 15	< 1E-07		up	
CILP 8483	cartilage intermediate layer protein, nucleotide pyrophosphohydrolase	< 1E-07		up	up
CKMT1A 548596	creatine kinase, mitochondrial 1A	< 1E-07	down	down	down
CKMT1B 1159	creatine kinase, mitochondrial 1B	< 1E-07	down	down	down
CLCA2 9635	chloride channel accessory 2	< 1E-07	down	down	down
CLDN1 9076	claudin 1	2.61E-03	down	down	
CLDN11 5010	claudin 11	1.24E-05		up	up
CLDN4 1364	claudin 4	< 1E-07		down	down
CLEC10A 10462	C-type lectin domain family 10, member A	1.00E-07		up	
CLEC1A 51267	C-type lectin domain family 1, member A	1.20E-06			up
CLEC2B 9976	C-type lectin domain family 2, member B	2.30E-06			up
CLIC2 1193	chloride intracellular channel 2	< 1E-07		up	up
CLIC3 9022	chloride intracellular channel 3	< 1E-07	down	down	down
CLIC5 53405	chloride intracellular channel 5	< 1E-07	up	up	up
CLMP 79827	CXADR-like membrane protein	< 1E-07		up	up
CLU 1191	clusterin	< 1E-07		up	
CNDP1 84735	carnosine dipeptidase 1 (metallopeptidase M20 family)	4.46E-03		up	
CNFN 84518	cornifelin	< 1E-07	down	down	down
CNTN4 152330	contactin 4	5.83E-04			up
COCH 1690	cochlin	7.14E-05	up		
COL10A1 1300	collagen, type X, alpha 1	3.04E-04			up

COL17A1 1308	collagen, type XVII, alpha 1	< 1E-07	down	down	down
COL7A1 1294	collagen, type VII, alpha 1	< 1E-07	down	down	down
COL8A1 1295	collagen, type VIII, alpha 1	1.00E-07	up	up	up
COLEC12 81035	collectin sub-family member 12	< 1E-07			up
COMP 1311	cartilage oligomeric matrix protein	6.26E-05	down		
CORO1A 11151	coronin, actin binding protein, 1A	< 1E-07		up	
CPI 1356	ceruloplasmin (ferroxidase)	< 1E-07		up	
CPA4 51200	carboxypeptidase A4	< 1E-07	down	down	down
CPE 1363	carboxypeptidase E	2.00E-07			up
CPED1 79974	cadherin-like and PC-esterase domain containing 1	< 1E-07		up	up
CR1 1378	complement component (3b/4b) receptor 1 (Knops blood group)	< 1E-07		up	up
CR2 1380	complement component (3d/Epstein Barr virus) receptor 2	< 1E-07		up	
CRABP2 1382	cellular retinoic acid binding protein 2	< 1E-07	down	down	down
CRACR2A 84766	calcium release activated channel regulator 2A	< 1E-07		up	up
CRTAC1 55118	cartilage acidic protein 1	1.69E-04		down	down
CRTAM 56253	cytotoxic and regulatory T cell molecule	< 1E-07		up	
CRYM 1428	crystallin, mu	1.30E-06	down		down
CSF1R 1436	colony stimulating factor 1 receptor	< 1E-07		up	up
CSF2RB 1439	colony stimulating factor 2 receptor, beta, low-affinity (granulocyte-macrophage)	< 1E-07		up	
CSRP2 1466	cysteine and glycine-rich protein 2	1.36E-04	down		down
CST6 1474	cystatin E/M	< 1E-07	down	down	down
CSTA 1475	cystatin A (stefin A)	< 1E-07	down	down	down
CTLA4 1493	cytotoxic T-lymphocyte-associated protein 4	4.90E-06		up	
CTSV 1515	cathepsin V	< 1E-07		down	down
CXCL1 2919	chemokine (C-X-C motif) ligand 1 (melanoma growth stimulating activity, alpha)	6.00E-07		down	down
CXCL10 3627	chemokine (C-X-C motif) ligand 10	8.10E-06		up	
CXCL13 10563	chemokine (C-X-C motif) ligand 13	< 1E-07		up	
CXCL14 9547	chemokine (C-X-C motif) ligand 14	< 1E-07	down	down	down
CXCL9 4283	chemokine (C-X-C motif) ligand 9	3.00E-07		up	
CXCR2P1 3580	chemokine (C-X-C motif) receptor 2 pseudogene 1	< 1E-07		up	up
CXCR3 2833	chemokine (C-X-C motif) receptor 3	9.10E-06		up	

CXCR4 7852	chemokine (C-X-C motif) receptor 4	< 1E-07		up	
CXCR5 643	chemokine (C-X-C motif) receptor 5	< 1E-07		up	
CXCR6 10663	chemokine (C-X-C motif) receptor 6	3.00E-07		up	
CXorf21 80231	chromosome X open reading frame 21	< 1E-07		up	
CYBB 1536	cytochrome b-245, beta polypeptide	< 1E-07		up	up
CYP1B1 1545	cytochrome P450, family 1, subfamily B, polypeptide 1	< 1E-07		up	up
CYP26B1 56603	cytochrome P450, family 26, subfamily B, polypeptide 1	< 1E-07		down	down
CYTIP 9595	cytohesin 1 interacting protein	< 1E-07		up	
DAPL1 92196	death associated protein-like 1	< 1E-07	down	down	down
DAPP1 27071	dual adaptor of phosphotyrosine and 3-phosphoinositides	< 1E-07		up	
DCSTAMP 81501	dendrocyte expressed seven transmembrane protein	3.40E-06			up
DDAH1 23576	dimethylarginine dimethylaminohydrolase 1	2.40E-06			up
DDR2 4921	discoidin domain receptor tyrosine kinase 2	4.80E-06			up
DENND1B 163486	DENN/MADD domain containing 1B	< 1E-07			up
DERL3 91319	derlin 3	2.83E-05		up	
DIO2 1734	deiodinase, iodothyronine, type II	< 1E-07	down	down	
DMKN 93099	dermokine	< 1E-07	down	down	down
DMRTA1 63951	DMRT-like family A1	1.91E-04			up
DNAJA4 55466	DnaJ (Hsp40) homolog, subfamily A, member 4	1.50E-03			down
DOCK1 1139818	dedicator of cytokinesis 11	< 1E-07		up	up
DOCK2 1794	dedicator of cytokinesis 2	< 1E-07		up	up
DOCK4 9732	dedicator of cytokinesis 4	< 1E-07			up
DOCK8 81704	dedicator of cytokinesis 8	< 1E-07		up	
DPYD 1806	dihydropyrimidine dehydrogenase	< 1E-07		up	up
DSC2 1824	desmocollin 2	< 1E-07	down	down	down
DSC3 1825	desmocollin 3	< 1E-07	down	down	down
DSG1 1828	desmoglein 1	< 1E-07	down	down	down
DSG3 1830	desmoglein 3	< 1E-07	down	down	down
DSP 1832	desmoplakin	< 1E-07	down	down	down
DUOX1 53905	dual oxidase 1	< 1E-07	down	down	down
DUOXA1 90527	dual oxidase maturation factor 1	< 1E-07	down	down	down
EAF2 55840	ELL associated factor 2	< 1E-07		up	
EBF3 253738	early B-cell factor 3	< 1E-07		up	up

EBI3 10148	Epstein-Barr virus induced 3	< 1E-07		up	
ECM2 1842	extracellular matrix protein 2, female organ and adipocyte specific	5.90E-06			up
EDN3 1908	endothelin 3	2.24E-04			up
EFHD1 80303	EF-hand domain family, member D1	5.11E-03			down
EFNA3 1944	ephrin-A3	< 1E-07		down	
EGFL8 80864	EGF-like-domain, multiple 8	1.05E-04			down
EHF 26298	ets homologous factor	< 1E-07	down	down	down
ELF3 1999	E74-like factor 3 (ets domain transcription factor, epithelial-specific)	< 1E-07		down	down
ELMO1 9844	engulfment and cell motility 1	< 1E-07		up	
ELMO3 79767	engulfment and cell motility 3	< 1E-07	down	down	down
EMB 133418	embigin	1.00E-06		up	
EMCN 51705	endomucin	1.52E-04			up
EMILIN1 111117	elastin microfibril interfacier 1	3.09E-04			up
ENPP4 22875	ectonucleotide pyrophosphatase/phosphodiesterase 4 (putative)	< 1E-07	up	up	up
EPB41L4B 54566	erythrocyte membrane protein band 4.1 like 4B	< 1E-07		down	
EPHA1 2041	EPH receptor A1	< 1E-07	down		down
EPHA3 2042	EPH receptor A3	< 1E-07		up	up
EPHB6 2051	EPH receptor B6	3.72E-04	down		down
EPHX3 79852	epoxide hydrolase 3	< 1E-07	down	down	down
EPPK1 83481	epiplakin 1	< 1E-07	down	down	down
EPS8L1 54869	EPS8-like 1	< 1E-07		down	down
EPS8L2 64787	EPS8-like 2	< 1E-07		down	down
ERCC6L2 375748	excision repair cross-complementation group 6-like 2	< 1E-07			up
ERRFI1 54206	ERBB receptor feedback inhibitor 1	5.88E-04			up
ESM1 11082	endothelial cell-specific molecule 1	< 1E-07	up	up	up
ESRP1 54845	epithelial splicing regulatory protein 1	< 1E-07	down	down	down
ETV1 2115	ets variant 1	4.11E-05			up
EVI2A 2123	ecotropic viral integration site 2A	< 1E-07		up	up
EVI2B 2124	ecotropic viral integration site 2B	< 1E-07		up	
EVPL 2125	envoplakin	< 1E-07	down	down	down
EYA1 2138	EYA transcriptional coactivator and phosphatase 1	7.72E-04		up	up
F12 2161	coagulation factor XII (Hageman factor)	1.40E-06		down	
F2R 2149	coagulation factor II (thrombin) receptor	1.59E-04			up

F2RL2 2151	coagulation factor II (thrombin) receptor-like 2	< 1E-07	down	down	
F5 2153	coagulation factor V (proaccelerin, labile factor)	3.06E-03			up
FAAH 2166	fatty acid amide hydrolase	< 1E-07			down
FABP4 2167	fatty acid binding protein 4, adipocyte	4.50E-06			up
FABP5 2171	fatty acid binding protein 4, adipocyte	< 1E-07	down	down	down
FAM105A 54491	family with sequence similarity 105, member A	< 1E-07		up	up
FAM107B 83641	family with sequence similarity 107, member B	< 1E-07		up	
FAM113B 91523	family with sequence similarity 113, member B	< 1E-07		up	
FAM129C 199786	family with sequence similarity 129, member C	< 1E-07		up	
FAM131B 9715	family with sequence similarity 131, member B	1.07E-03			up
FAM171B 165215	family with sequence similarity 171, member B	1.87E-04			up
FAM184A 79632	family with sequence similarity 184, member A	3.00E-07	up		
FAM189A2 9413	family with sequence similarity 189, member A2	5.70E-06			down
FAM198B 51313	family with sequence similarity 198, member B	1.04E-05			up
FAM26F 441168	family with sequence similarity 26, member F	< 1E-07		up	up
FAM46B 115572	family with sequence similarity 46, member B	1.86E-05		down	down
FAM46C 54855	family with sequence similarity 46, member C	< 1E-07		up	up
FAM49A 81553	family with sequence similarity 49, member A	< 1E-07		up	up
FAM63B 54629	family with sequence similarity 63, member B	< 1E-07		up	up
FAM69C 125704	family with sequence similarity 69, member C	< 1E-07	down	down	down
FAM83A 84985	family with sequence similarity 83, member A	< 1E-07	down	down	down
FAM83C 128876	family with sequence similarity 83, member C	< 1E-07	down	down	down
FAM83G 644815	family with sequence similarity 83, member G	3.00E-07		down	
FAM83H 286077	family with sequence similarity 83, member H	< 1E-07		down	down
FAM84A 151354	family with sequence similarity 84, member A	< 1E-07	down	down	down
FAM84B 157638	family with sequence similarity 84, member B	3.85E-04		up	
FAT2 2196	FAT atypical cadherin 2	< 1E-07	down	down	down
FAT4 79633	FAT atypical cadherin 4	1.80E-06			up
FBLN2 2199	fibulin 2	4.59E-05	down		
FBN1 2200	fibrillin 1	< 1E-07			up
FBP1 2203	fructose-1,6-bisphosphatase 1	1.93E-05		up	
FCER2 2208	Fc fragment of IgE, low affinity II, receptor for (CD23)	< 1E-07		up	
FCGR2C 9103	Fc fragment of IgG, low affinity IIc, receptor for (CD32) (gene/pseudogene)	6.03E-05			up

FCGR3A 2214	Fc fragment of IgG, low affinity IIIa, receptor (CD16a)	< 1E-07		up	up
FCN1 2219	ficolin (collagen/fibrinogen domain containing) 1	2.11E-05		up	
FCRL1 115350	Fc receptor-like 1	< 1E-07		up	
FCRL2 79368	Fc receptor-like 2	< 1E-07		up	
FCRL3 115352	Fc receptor-like 3	< 1E-07		up	
FCRL5 83416	Fc receptor-like 5	< 1E-07		up	
FDCSP 260436	follicular dendritic cell secreted protein	2.99E-04	down		
FERMT1 55612	fermitin family member 1	< 1E-07	down	down	down
FGD2 221472	FYVE, RhoGEF and PH domain containing 2	< 1E-07		up	
FGF7 2252	fibroblast growth factor 7	< 1E-07		up	up
FGFBP1 9982	fibroblast growth factor binding protein 1	< 1E-07	down	down	down
FGFR2 2263	fibroblast growth factor receptor 2	5.00E-07		down	
FGFR3 2261	fibroblast growth factor receptor 3	< 1E-07	down	down	down
FGL2 10875	fibrinogen-like 2	< 1E-07		up	up
FHAD1 114827	forkhead-associated (FHA) phosphopeptide binding domain 1	2.30E-06			up
FHL1 2273	four and a half LIM domains 1	1.60E-06		up	up
FHOD3 80206	formin homology 2 domain containing 3	1.00E-07	down	down	
FILIP1 27145	filamin A interacting protein 1	< 1E-07		up	up
FLG 2312	filaggrin	< 1E-07	down	down	down
FLG2 388698	filaggrin family member 2	< 1E-07	down	down	down
FLI1 2313	Fli-1 proto-oncogene, ETS transcription factor	< 1E-07		up	
FLJ16779 100192386		9.22E-04			down
FLRT2 23768	fibronectin leucine rich transmembrane protein 2	5.02E-04			up
FLT1 2321	fms-related tyrosine kinase 1	< 1E-07		up	up
FMNL2 114793	formin-like 2	< 1E-07		up	
FMO1 2326	flavin containing monooxygenase 1	2.00E-07	down		
FMO2 2327	flavin containing monooxygenase 2	< 1E-07		up	
FOLH1 2346	folate hydrolase (prostate-specific membrane antigen) 1	1.59E-04		up	
FOXF2 2295	forkhead box F2	1.35E-05		down	
FPR3 2359	formyl peptide receptor 3	< 1E-07		up	up
FREM1 158326	FRAS1 related extracellular matrix 1	2.96E-05	up		up
FUT2 2524	fucosyltransferase 2 (secretor status included)	< 1E-07	down	down	down

FYB12533	FYN binding protein	< 1E-07		up	
FZD9 8326	frizzled class receptor 9	7.10E-06		down	down
GAB3 139716	GRB2-associated binding protein 3	< 1E-07		up	
GALNT16 57452	polypeptide N-acetylgalactosaminyltransferase 16	< 1E-07		up	
GALNT3 2591	polypeptide N-acetylgalactosaminyltransferase 3	1.74E-03			down
GALNT5 11227	polypeptide N-acetylgalactosaminyltransferase 5	7.20E-06			up
GAP43 2596	growth associated protein 43	3.02E-03			up
GAPDHS 26330	glyceraldehyde-3-phosphate dehydrogenase, spermatogenic	8.90E-06	down	down	down
GBP1 2633	guanylate binding protein 1, interferon-inducible	2.80E-06		up	
GBP4 115361	guanylate binding protein 4	< 1E-07		up	
GBP5 115362	guanylate binding protein 5	< 1E-07		up	up
GCNT1 2650	glucosaminyl (N-acetyl) transferase 1, core 2	< 1E-07		up	
GDPD3 79153	glycerophosphodiester phosphodiesterase domain containing 3	< 1E-07	down	down	down
GIMAP1 170575	GTPase, IMAP family member 1	< 1E-07		up	
GIMAP2 26157	GTPase, IMAP family member 2	< 1E-07		up	
GIMAP4 55303	GTPase, IMAP family member 4	< 1E-07		up	
GIMAP5 55340	GTPase, IMAP family member 5	< 1E-07		up	
GIMAP6 474344	GTPase, IMAP family member 6	< 1E-07		up	
GIMAP7 168537	GTPase, IMAP family member 7	< 1E-07		up	
GIMAP8 155038	GTPase, IMAP family member 8	< 1E-07		up	
GJA1 2697	gap junction protein, alpha 1	4.92E-05	down		
GJB2 2706	gap junction protein, beta 2, 26kDa	< 1E-07	down	down	down
GJB3 2707	gap junction protein, beta 3, 31kDa	< 1E-07	down	down	down
GJB6 10804	gap junction protein, beta 6, 30kDa	< 1E-07	down	down	down
GLB1L2 89944	galactosidase, beta 1-like 2	1.53E-03		down	down
GLDC 2731	glycine dehydrogenase (decarboxylating)	4.01E-04	down		
GLIPR1 11010	GLI pathogenesis-related 1	< 1E-07		up	up
GMPR 2766	guanosine monophosphate reductase	< 1E-07	down	down	down
GNAL 2774	guanine nucleotide binding protein (G protein), alpha activating activity polypeptide, olfactory type	3.05E-05	down		down
GNAO1 2775	guanine nucleotide binding protein (G protein), alpha activating activity polypeptide O	1.66E-03			down
GOLGA7B 401647	golgin A7 family, member B	2.60E-06	down	down	down

GP1BA 2811	glycoprotein Ib (platelet), alpha polypeptide	< 1E-07		up	down
GPC1 2817	glypican 1	2.34E-05		down	
GPC6 10082	glypican 6	< 1E-07		up	up
GPR132 29933	G protein-coupled receptor 132	< 1E-07		up	
GPR143 4935	G protein-coupled receptor 143	1.16E-05	down	down	down
GPR171 29909	G protein-coupled receptor 171	< 1E-07		up	
GPR183 1880	G protein-coupled receptor 183	< 1E-07		up	
GPR34 2857	G protein-coupled receptor 34	< 1E-07		up	up
GPR65 8477	G protein-coupled receptor 65	< 1E-07		up	up
GPR68 8111	G protein-coupled receptor 68	2.98E-04	down		
GPRC5A 9052	G protein-coupled receptor, class C, group 5, member A	4.17E-03			down
GPRIN3 285513	GPRIN family member 3	< 1E-07	up	up	up
GPX3 2878	glutathione peroxidase 3	2.64E-03	down		
GRHL1 29841	grainyhead-like 1 (Drosophila)	< 1E-07	down	down	down
GRHL3 57822	grainyhead-like 3 (Drosophila)	< 1E-07	down	down	down
GSDMA 284110	gasdermin A	< 1E-07	down	down	down
GVIN1 387751	GTPase, very large interferon inducible pseudogene 1	< 1E-07		up	up
GYG2 8908	glycogenin 2	7.98E-04			down
GZMA 3001	granzyme A (granzyme 1, cytotoxic T-lymphocyte-associated serine esterase 3)	1.60E-06		up	
GZMK 3003	granzyme K (granzyme 3; tryptase II)	< 1E-07		up	
H2AFJ 55766	H2A histone family, member J	< 1E-07	down	down	
HACD1 9200	3-hydroxyacyl-CoA dehydratase 1	1.62E-04			down
HAS3 3038	hyaluronan synthase 3	< 1E-07	down	down	down
HAVCR2 84868	hepatitis A virus cellular receptor 2	< 1E-07		up	up
HBA2 3040	hemoglobin, alpha 2	8.85E-04	up		
HBB 3043	hemoglobin, beta	1.35E-05	up		
HCAR2 338442	hydroxycarboxylic acid receptor 2	< 1E-07		down	
HCLS1 3059	hematopoietic cell-specific Lyn substrate 1	< 1E-07		up	
HDAC9 9734	histone deacetylase 9	< 1E-07		up	up
HECW2 57520	HECT, C2 and WW domain containing E3 ubiquitin protein ligase 2	< 1E-07			up
HES2 54626	hes family bHLH transcription factor 2	< 1E-07	down	down	down
HES6 55502	hes family bHLH transcription factor 6	1.03E-03			down
HEYL 26508	hes-related family bHLH transcription factor with YRPW motif-like	5.64E-04			up

HFE 3077	hemochromatosis	1.18E-04			up
HGF 3082	hepatocyte growth factor (hepapoietin A; scatter factor)	< 1E-07		up	up
HIPK3 10114	homeodomain interacting protein kinase 3	< 1E-07			up
HK3 3101	hexokinase 3 (white cell)	< 1E-07		up	up
HLA-DMB 3109	major histocompatibility complex, class II, DM beta	< 1E-07		up	
HLA-DOA 3111	major histocompatibility complex, class II, DO alpha	< 1E-07		up	
HLA-DOB 3112	major histocompatibility complex, class II, DO beta	< 1E-07		up	
HMGA2 8091	high mobility group AT-hook 2	4.20E-05	up	up	up
HOMER2 9455	homer scaffolding protein 2	4.78E-05			down
HOPX 84525	HOP homeobox	2.16E-04			down
HR 55806	hair growth associated	1.43E-05	down	down	
HRNR 388697	hornerin	< 1E-07		down	down
HS6ST2 90161	heparan sulfate 6-O-sulfotransferase 2	1.37E-03	up		
HSBP1L 440498	heat shock factor binding protein 1-like 1	< 1E-07			down
HSD11B1 3290	hydroxysteroid (11-beta) dehydrogenase 1	< 1E-07		up	
HSH2D 84941	hematopoietic SH2 domain containing	< 1E-07		up	
HSPA2 3306	heat shock 70kDa protein 2	6.20E-06	down		down
HSPB8 26353	heat shock 22kDa protein 8	3.33E-05		down	down
HVCN1 84329	hydrogen voltage gated channel 1	< 1E-07		up	
ICOS 29851	inducible T-cell co-stimulator	< 1E-07		up	
ID1 3397	inhibitor of DNA binding 1, dominant negative helix-loop-helix protein	< 1E-07		down	
IDO1 3620	indoleamine 2,3-dioxygenase 1	2.00E-07		up	
IGFBP5 3488	insulin-like growth factor binding protein 5	1.11E-03			up
IGSF6 10261	immunoglobulin superfamily, member 6	< 1E-07		up	up
IKZF1 10320	IKAROS family zinc finger 1 (Ikaros)	< 1E-07		up	
IKZF2 22807	IKAROS family zinc finger 2 (Helios)	< 1E-07		up	
IKZF3 22806	IKAROS family zinc finger 3 (Aiolos)	< 1E-07		up	
IL10RA 3587	interleukin 10 receptor, alpha	< 1E-07		up	
IL13RA2 3598	interleukin 13 receptor, alpha 2	2.57E-03			up
IL17RE 132014	interleukin 17 receptor E	< 1E-07		down	
IL1RN 3557	interleukin 1 receptor antagonist	2.51E-05	down	down	
IL20RB 53833	interleukin 20 receptor beta	< 1E-07	down	down	down
IL21R 50615	interleukin 21 receptor	< 1E-07		up	

IL22RA1 58985	interleukin 22 receptor, alpha 1	< 1E-07	down	down	
IL2RA 3559	interleukin 2 receptor, alpha	< 1E-07		up	
IL2RB 3560	interleukin 2 receptor, beta	2.00E-07		up	
IL2RG 3561	interleukin 2 receptor, gamma	< 1E-07		up	
IL33 90865	interleukin 33	< 1E-07		up	
IL36RN 26525	interleukin 36 receptor antagonist	< 1E-07	down	down	down
IL6ST 3572	interleukin 6 signal transducer	< 1E-07		up	up
IL7R 3575	interleukin 7 receptor	< 1E-07		up	up
IMPA2 3613	inositol(myo)-1(or 4)-monophosphatase 2	< 1E-07		down	
INMT1 1185	indolethylamine N-methyltransferase	< 1E-07		up	
INPP5D 3635	inositol polyphosphate-5-phosphatase, 145kDa	< 1E-07		up	
IPCEF1 26034	interaction protein for cytohesin exchange factors 1	< 1E-07		up	
IQGAP2 10788	IQ motif containing GTPase activating protein 2	< 1E-07		up	
IRF4 3662	interferon regulatory factor 4	3.00E-06	down	down	down
IRF6 3664	interferon regulatory factor 6	< 1E-07	down	down	down
IRF8 3394	interferon regulatory factor 8	< 1E-07		up	
IRX2 153572	iroquois homeobox 2	< 1E-07	down	down	down
IRX3 79191	iroquois homeobox 3	2.00E-07		down	down
IRX5 10265	iroquois homeobox 5	< 1E-07		down	
IRX6 79190	iroquois homeobox 6	3.80E-06		down	down
ITGA1 3672	integrin, alpha 1	< 1E-07		up	up
ITGA4 3676	integrin, alpha 4 (antigen CD49D, alpha 4 subunit of VLA-4 receptor)	< 1E-07		up	up
ITGAL 3683	integrin, alpha L (antigen CD11A (p180), lymphocyte function-associated antigen 1; alpha polypeptide)	< 1E-07		up	
ITGAM 3684	integrin, alpha M (complement component 3 receptor 3 subunit)	< 1E-07		up	up
ITGB2 3689	integrin, beta 2 (complement component 3 receptor 3 and 4 subunit)	< 1E-07		up	up
ITGB3 3690	integrin, beta 3 (platelet glycoprotein IIIa, antigen CD61)	4.77E-03			up
ITGB4 3691	integrin, beta 4	8.00E-07	down	down	down
ITIH5 80760	inter-alpha-trypsin inhibitor heavy chain family, member 5	2.53E-05			up
ITK 3702	IL2-inducible T-cell kinase	< 1E-07		up	
ITM2A 9452	integral membrane protein 2A	< 1E-07		up	up
ITPR1 3708	inositol 1,4,5-trisphosphate receptor, type 1	< 1E-07		up	up
IVL 3713	involucrin	< 1E-07	down	down	down

JAK3 3718	Janus kinase 3	< 1E-07		up	
JCHAIN 3512	joining chain of multimeric IgA and IgM	< 1E-07	up	up	up
JUP 3728	junction plakoglobin	< 1E-07		down	down
KBTBD8 84541	kelch repeat and BTB (POZ) domain containing 8	< 1E-07		up	
KCNA3 3738	potassium channel, voltage gated shaker related subfamily A, member 3	< 1E-07		up	
KCNE3 10008	potassium channel, voltage gated subfamily E regulatory beta subunit 3	< 1E-07		up	
KCNJ10 3766	potassium channel, inwardly rectifying subfamily J, member 10	1.34E-04		up	
KCNJ13 3769	potassium channel, inwardly rectifying subfamily J, member 13	2.05E-03			down
KCNJ8 3764	potassium channel, inwardly rectifying subfamily J, member 8	< 1E-07		up	up
KCNMA1 3778	potassium channel, calcium activated large conductance subfamily M alpha, member 1	7.60E-06		up	up
KCNMB4 27345	potassium channel, calcium activated large conductance subfamily M beta, member 4	9.18E-04			up
KCNN2 3781	potassium channel, calcium activated intermediate/small conductance subfamily N alpha, member 2	4.90E-04	down		down
KCTD12 115207	potassium channel tetramerization domain containing 12	< 1E-07			up
KIAA0040 9674	KIAA0040	2.81E-05			up
KIAA0125 9834	KIAA0125	< 1E-07		up	
KIAA0754 643314	KIAA0754	6.00E-07			up
KIAA1324L 222223	KIAA1324-like	5.15E-05			up
KIF21B 23046	kinesin family member 21B	< 1E-07		up	
KIT 3815	v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog	3.60E-06	down	down	down
KLC3 147700	kinesin light chain 3	< 1E-07	down	down	down
KLF12 11278	Kruppel-like factor 12	< 1E-07		up	
KLF5 688	Kruppel-like factor 5	< 1E-07		down	
KLHL13 90293	kelch-like family member 13	3.82E-05	up		up
KLHL6 89857	kelch-like family member 6	< 1E-07		up	
KLK10 5655	kallikrein-related peptidase 10	< 1E-07	down	down	down
KLK11 11012	kallikrein-related peptidase 11	< 1E-07	down	down	down
KLK13 26085	kallikrein-related peptidase 13	< 1E-07	down	down	down
KLK5 25818	kallikrein-related peptidase 5	< 1E-07	down	down	down

KLK6 5653	kallikrein-related peptidase 6	< 1E-07	down	down	down
KLK7 5650	kallikrein-related peptidase 7	< 1E-07	down	down	down
KLK8 11202	kallikrein-related peptidase 8	< 1E-07	down	down	down
KLRK1 22914	killer cell lectin-like receptor subfamily K, member 1	2.00E-07		up	
KMO 8564	kynurenine 3-monooxygenase (kynurenine 3-hydroxylase)	< 1E-07		up	
KRT1 3848	keratin 1, type II	< 1E-07	down	down	down
KRT10 3858	keratin 10, type I	< 1E-07	down	down	down
KRT14 3861	keratin 14, type I	< 1E-07	down	down	down
KRT15 3866	keratin 15, type I	< 1E-07	down	down	down
KRT16 3868	keratin 16, type I	< 1E-07	down	down	down
KRT17 3872	keratin 17, type I	< 1E-07	down	down	down
KRT23 25984	keratin 23, type I	< 1E-07	down	down	down
KRT5 3852	keratin 5, type II	< 1E-07	down	down	down
KRT6A 3853	keratin 6A, type II	< 1E-07	down	down	down
KRT6B 3854	keratin 6B, type II	< 1E-07	down	down	down
KRT6C 286887	keratin 6C, type II	< 1E-07	down	down	down
KRT75 9119	keratin 75, type II	< 1E-07	down	down	down
KRT80 144501	keratin 80, type II	< 1E-07	down	down	down
KRTDAP 388533	keratinocyte differentiation-associated protein	< 1E-07	down	down	down
LAD1 3898	ladinin 1	< 1E-07	down	down	down
LAG3 3902	lymphocyte-activation gene 3	1.50E-05		up	
LAIR1 3903	leukocyte-associated immunoglobulin-like receptor 1	< 1E-07		up	
LAMA3 3909	laminin, alpha 3	5.00E-06	down		down
LAMA4 3910	laminin, alpha 4	4.30E-06			up
LAMC2 3918	laminin, gamma 2	< 1E-07	down	down	down
LAMC3 10319	laminin, gamma 3	< 1E-07		down	down
LAPTM5 7805	lysosomal protein transmembrane 5	< 1E-07		up	
LAX1 54900	lymphocyte transmembrane adaptor 1	< 1E-07		up	
LCA5 167691	Leber congenital amaurosis 5	< 1E-07			up
LCE2A 353139	late cornified envelope 2A	< 1E-07	down	down	down
LCK 3932	LCK proto-oncogene, Src family tyrosine kinase	< 1E-07		up	
LCN2 3934	lipocalin 2	< 1E-07	down	down	down
LCOR 84458	ligand dependent nuclear receptor corepressor	< 1E-07			up

LCP1 3936	lymphocyte cytosolic protein 1 (L-plastin)	< 1E-07		up	
LGALS3 3958	lectin, galactoside-binding, soluble, 3	8.50E-06	down		
LGALS7 3963	lectin, galactoside-binding, soluble, 7	< 1E-07	down	down	down
LGALS7B 653499	lectin, galactoside-binding, soluble, 7B	< 1E-07	down	down	down
LGI2 55203	leucine-rich repeat LGI family, member 2	< 1E-07		up	up
LGI3 203190	leucine-rich repeat LGI family, member 3	1.90E-06	down	down	down
LIFR 3977	leukemia inhibitory factor receptor alpha	< 1E-07	up	up	up
LILRB1 10859	leukocyte immunoglobulin-like receptor, subfamily B (with TM and ITIM domains), member 1	< 1E-07		up	up
LILRB2 10288	leukocyte immunoglobulin-like receptor, subfamily B (with TM and ITIM domains), member 2	< 1E-07		up	
LILRB4 11006	leukocyte immunoglobulin-like receptor, subfamily B (with TM and ITIM domains), member 4	< 1E-07		up	up
LIMS1 3987	LIM and senescent cell antigen-like domains 1	< 1E-07			up
LINC01140 339524	long intergenic non-protein coding RNA 1140	< 1E-07			up
LOR 4014	loricrin	< 1E-07	down	down	down
LOXL3 84695	lysyl oxidase-like 3	1.41E-04			up
LPAR1 1902	lysophosphatidic acid receptor 1	4.67E-04			up
LPPR4 9890	lipid phosphate phosphatase-related protein type 4	1.34E-03	down		
LRCH2 57631	leucine-rich repeats and calponin homology (CH) domain containing 2	3.20E-06		up	up
LRFN5 145581	leucine rich repeat and fibronectin type III domain containing 5	5.50E-06			up
LRMP 4033	lymphoid-restricted membrane protein	< 1E-07		up	
LRRC15 131578	leucine rich repeat containing 15	< 1E-07	down	down	
LRRC17 10234	leucine rich repeat containing 17	3.19E-05			up
LRRC8E 80131	leucine rich repeat containing 8 family, member E	3.70E-06	down	down	
LRRCC1 85444	leucine rich repeat and coiled-coil centrosomal protein 1	2.73E-04			up
LRRN4CL 221091	LRRN4 C-terminal like	3.41E-03		down	down
LTB 4050	lymphotoxin beta (TNF superfamily, member 3)	< 1E-07		up	
LTB4R1 1241	leukotriene B4 receptor	< 1E-07		down	down
LTB4R2 56413	leukotriene B4 receptor 2	< 1E-07		down	
LY6D 8581	lymphocyte antigen 6 complex, locus D	< 1E-07	down	down	down
LY75 4065	lymphocyte antigen 75	< 1E-07		up	
LY9 4063	lymphocyte antigen 9	< 1E-07		up	

LYNX1 66004	Ly6/neurotoxin 1	5.00E-07	down	down	down
LYPD3 27076	LY6/PLAUR domain containing 3	< 1E-07	down	down	down
LYPD5 284348	LY6/PLAUR domain containing 5	8.80E-06	down		down
LYZ 4069	lysozyme	< 1E-07		up	up
MAGEA1 4100	melanoma antigen family A1	1.03E-03		up	up
MAGEA10 4109	melanoma antigen family A10	1.85E-04			up
MAL 4118	mal, T-cell differentiation protein	2.00E-07	down	down	down
MAL2 114569	mal, T-cell differentiation protein 2 (gene/pseudogene)	< 1E-07	down	down	down
MAN1A1 4121	mannosidase, alpha, class 1A, member 1	< 1E-07		up	up
MAN1A2 10905	mannosidase, alpha, class 1A, member 2	< 1E-07			up
MAOB 4129	monoamine oxidase B	2.60E-03	down		down
MAP4K1 11184	mitogen-activated protein kinase kinase kinase 1	2.00E-07		up	
MARCH1 55016	membrane-associated ring finger (C3HC4) 1, E3 ubiquitin protein ligase	< 1E-07		up	up
MARCO 8685	macrophage receptor with collagenous structure	3.00E-07	up	up	up
MASP1 5648	mannan-binding lectin serine peptidase 1 (C4/C2 activating component of Ra-reactive factor)	< 1E-07	down	down	down
MBNL3 55796	muscleblind-like splicing regulator 3	< 1E-07			up
MBP 4155	myelin basic protein	1.80E-06	down		down
MC1R 4157	melanocortin 1 receptor (alpha melanocyte stimulating hormone receptor)	< 1E-07	down	down	
MCOLN3 55283	mucolipin 3	2.76E-04	down	down	
MCTP1 79772	multiple C2 domains, transmembrane 1	< 1E-07		up	up
MECOM 2122	MDS1 and EVI1 complex locus	< 1E-07			up
MEGF6 1953	multiple EGF-like-domains 6	1.00E-07	down	down	
MEI1 150365	meiosis inhibitor 1	9.00E-07		up	
MEOX2 4223	mesenchyme homeobox 2	< 1E-07		up	up
MERTK 10461	MER proto-oncogene, tyrosine kinase	< 1E-07		up	up
MFAP2 4237	microfibrillar-associated protein 2	1.54E-04		down	
MFAP5 8076	microfibrillar-associated protein 5	1.60E-06	down		
MFSD12 126321	major facilitator superfamily domain containing 12	< 1E-07			down
MGAT4A 11320	mannosyl (alpha-1,3-)-glycoprotein beta-1,4-N-acetylglucosaminyltransferase, isozyme A	< 1E-07		up	
MGAT5B 146664	mannosyl (alpha-1,6-)-glycoprotein beta-1,6-N-acetyl-glucosaminyltransferase, isozyme B	6.34E-05			down

MGP 4256	matrix Gla protein	4.03E-04	up	up	up
MIR100HG 399959	mir-100-let-7a-2 cluster host gene	6.00E-06		up	up
MLANA 2315	melan-A	3.69E-04	down	down	down
MLPH 79083	melanophilin	2.86E-05	down	down	down
MMP1 4312	matrix metalloproteinase 1	< 1E-07	down	down	down
MMP12 4321	matrix metalloproteinase 12	3.00E-07		up	
MMP13 4322	matrix metalloproteinase 13	3.00E-07			up
MMP16 4325	matrix metalloproteinase 16 (membrane-inserted)	6.01E-05			up
MMP17 4326	matrix metalloproteinase 17 (membrane-inserted)	2.40E-06		down	
MMP3 4314	matrix metalloproteinase 3	< 1E-07	down	down	down
MMP9 4318	matrix metalloproteinase 9	< 1E-07		up	up
MNDA 4332	myeloid cell nuclear differentiation antigen	< 1E-07		up	up
MPEG1 219972	macrophage expressed 1	< 1E-07		up	
MPZL2 10205	myelin protein zero-like 2	3.93E-05	down		
MRC1 4360	mannose receptor, C type 1	8.00E-07		up	
MS4A1 931	membrane-spanning 4-domains, subfamily A, member 1	< 1E-07		up	
MS4A4A 51338	membrane-spanning 4-domains, subfamily A, member 4A	< 1E-07		up	
MS4A6A 64231	membrane-spanning 4-domains, subfamily A, member 6A	< 1E-07		up	
MSR1 4481	macrophage scavenger receptor 1	< 1E-07		up	up
MSX2 4488	msh homeobox 2	< 1E-07		down	
MXRA5 25878	matrix-remodelling associated 5	4.40E-05			up
MYO7A 4647	myosin VIIA	2.00E-07		up	
MZB1 51237	marginal zone B and B1 cell-specific protein	< 1E-07		up	
N4BP2 55728	NEDD4 binding protein 2	< 1E-07		up	up
NAPSB 256236	napsin B aspartic peptidase, pseudogene	< 1E-07		up	
NAT16 375607	N-acetyltransferase 16 (GCN5-related, putative)	2.99E-04			down
NBEA 26960	neurobeachin	1.23E-04			up
NBEAL1 65065	neurobeachin-like 1	< 1E-07			up
NCCRP1 342897	non-specific cytotoxic cell receptor protein 1 homolog (zebrafish)	< 1E-07	down	down	down
NCF1 653361	neutrophil cytosolic factor 1	< 1E-07		up	
NCF1B 654816	neutrophil cytosolic factor 1B pseudogene	< 1E-07		up	
NCF1C 654817	neutrophil cytosolic factor 1C pseudogene	< 1E-07		up	

NCKAP1L3071	NCK-associated protein 1-like	< 1E-07		up	up
NCR3LG11374383	natural killer cell cytotoxicity receptor 3 ligand 1	1.84E-04			up
NDUFA4L2156901	NADH dehydrogenase (ubiquinone) 1 alpha subcomplex, 4-like 2	5.00E-07		down	
NEGR11257194	neuronal growth regulator 1	1.18E-05			up
NEXN191624	nexilin (F actin binding protein)	< 1E-07		up	
NFATC214773	nuclear factor of activated T-cells, cytoplasmic, calcineurin-dependent 2	5.11E-05			up
NID2122795	nidogen 2 (osteonidogen)	< 1E-07			up
NIPAL41348938	NIPA-like domain containing 4	< 1E-07	down	down	down
NKG714818	natural killer cell granule protein 7	8.80E-06		up	
NLGN4X157502	neuroligin 4, X-linked	9.00E-07			up
NLRC4158484	NLR family, CARD domain containing 4	< 1E-07		up	
NOV14856	nephroblastoma overexpressed	< 1E-07	down	down	down
NOX4150507	NADPH oxidase 4	4.40E-04			up
NQO111728	NAD(P)H dehydrogenase, quinone 1	6.61E-04			down
NRP118829	neuropilin 1	< 1E-07			up
NSG1127065	neuron specific gene family member 1	2.95E-04		down	down
NTN119423	netrin 1	3.80E-05		down	down
OCA214948	oculocutaneous albinism II	9.00E-07		down	down
OGN14969	osteoglycin	2.92E-05			up
OLFM1110439	olfactomedin 1	5.43E-05	down	down	down
OLFM2193145	olfactomedin 2	1.80E-05		down	down
OLFML3156944	olfactomedin-like 3	2.69E-05			up
OLR114973	oxidized low density lipoprotein (lectin-like) receptor 1	< 1E-07		up	up
OR7A5126659	olfactory receptor, family 7, subfamily A, member 5	2.31E-03			down
OSMR19180	oncostatin M receptor	< 1E-07		up	up
OVOL115017	ovo-like zinc finger 1	< 1E-07	down	down	down
P2RX515026	purinergic receptor P2X, ligand gated ion channel, 5	< 1E-07		up	
P2RY10127334	purinergic receptor P2Y, G-protein coupled, 10	< 1E-07		up	
P2RY13153829	purinergic receptor P2Y, G-protein coupled, 13	< 1E-07		up	
P2RY81286530	purinergic receptor P2Y, G-protein coupled, 8	< 1E-07		up	
PAK6156924	p21 protein (Cdc42/Rac)-activated kinase 6	< 1E-07	down	down	down
PARM1125849	prostate androgen-regulated mucin-like protein 1	< 1E-07		up	
PARP151165631	poly (ADP-ribose) polymerase family, member 15	< 1E-07		up	

PARVG 64098	parvin, gamma	< 1E-07		up	
PAX5 5079	paired box 5	< 1E-07		up	
PAX8-AS1 654433	PAX8 antisense RNA 1	9.87E-04			up
PCDH17 27253	protocadherin 17	< 1E-07		up	up
PCDH18 54510	protocadherin 18	3.60E-06			up
PCDH9 5101	protocadherin 9	2.93E-03			up
PCDHGA12 26025	protocadherin gamma subfamily A, 12	1.82E-03	down		
PCSK1 5122	proprotein convertase subtilisin/kexin type 1	3.63E-05		up	up
PCSK2 5126	proprotein convertase subtilisin/kexin type 2	3.53E-04	down	down	down
PDCD1 5133	programmed cell death 1	1.00E-07		up	
PDCD1LG2 80380	programmed cell death 1 ligand 2	< 1E-07		up	
PDE1A 5136	phosphodiesterase 1A, calmodulin-dependent	1.80E-06		up	
PDE7B 27115	phosphodiesterase 7B	5.43E-05			up
PDGFC 56034	platelet derived growth factor C	5.00E-06			up
PDGFRL 5157	platelet-derived growth factor receptor-like	< 1E-07			up
PDK4 5166	pyruvate dehydrogenase kinase, isozyme 4	< 1E-07	up	up	up
PDPN 10630	podoplanin	1.02E-03	down		
PDZK1IP1 10158	PDZK1 interacting protein 1	< 1E-07	down	down	down
PEAR1 375033	platelet endothelial aggregation receptor 1	2.70E-06			up
PERP 64065	PERP, TP53 apoptosis effector	< 1E-07	down	down	down
PI15 51050	peptidase inhibitor 15	3.79E-03		up	up
PI16 221476	peptidase inhibitor 16	8.15E-04			up
PI3 5266	peptidase inhibitor 3, skin-derived	< 1E-07	down	down	down
PIK3AP1 118788	phosphoinositide-3-kinase adaptor protein 1	< 1E-07		up	up
PIK3CG 5294	phosphatidylinositol-4,5-bisphosphate 3-kinase, catalytic subunit gamma	< 1E-07		up	up
PIK3R6 146850	phosphoinositide-3-kinase, regulatory subunit 6	< 1E-07		up	
PITPNM3 83394	PITPNM family member 3	< 1E-07		down	
PITX1 5307	paired-like homeodomain 1	< 1E-07		down	down
PKDCC 91461	protein kinase domain containing, cytoplasmic	< 1E-07	up	up	up
PKHD1 5314	polycystic kidney and hepatic disease 1 (autosomal recessive)	1.50E-06	down		down
PKP1 5317	plakophilin 1	< 1E-07	down	down	down
PKP3 11187	plakophilin 3	< 1E-07	down	down	down

PLA2G2A 5320	phospholipase A2, group IIA (platelets, synovial fluid)	2.95E-03			up
PLA2G2D 26279	phospholipase A2, group IID	< 1E-07		up	up
PLA2G7 7941	phospholipase A2, group VII (platelet-activating factor acetylhydrolase, plasma)	< 1E-07		up	
PLAC8 51316	placenta-specific 8	< 1E-07		up	
PLCB1 23236	phospholipase C, beta 1 (phosphoinositide-specific)	2.20E-04			up
PLCB4 5332	phospholipase C, beta 4	2.07E-03	up	up	up
PLCE1 51196	phospholipase C, epsilon 1	1.38E-05			up
PLCH2 9651	phospholipase C, eta 2	4.30E-06	down		down
PLCL2 23228	phospholipase C-like 2	< 1E-07		up	up
PLCXD2 257068	phosphatidylinositol-specific phospholipase C, X domain containing 2	< 1E-07		up	
PLD4 122618	phospholipase D family, member 4	< 1E-07		up	
PLEK 5341	pleckstrin	< 1E-07		up	up
PLEKHH2 130271	pleckstrin homology domain containing, family H (with MyTH4 domain) member 2	2.00E-04			up
PLN 5350	phospholamban	1.11E-05			up
PMEL 6490	premelanosome protein	1.17E-04	down	down	down
PNMA6A 84968	paraneoplastic Ma antigen family member 6A	6.78E-05		down	down
POMK 84197	protein-O-mannose kinase	< 1E-07			up
POSTN 10631	periostin, osteoblast specific factor	6.00E-07			up
POU2AF1 5450	POU class 2 associating factor 1	< 1E-07		up	
POU2F2 5452	POU class 2 homeobox 2	< 1E-07		up	
POU3F1 5453	POU class 3 homeobox 1	9.10E-06	down	down	down
PPAP2B 8613	phosphatidic acid phosphatase type 2B	6.00E-07			up
PPAPDC1A 196051	phosphatidic acid phosphatase type 2 domain containing 1A	2.61E-05	down	down	
PPL 5493	periplakin	< 1E-07	down	down	down
PPP1R14C 81706	protein phosphatase 1, regulatory (inhibitor) subunit 14C	1.42E-05	down	down	
PPP1R16B 26051	protein phosphatase 1, regulatory (inhibitor) subunit 16B	< 1E-07		up	
PPP1R9A 55607	protein phosphatase 1, regulatory (inhibitor) subunit 9A	4.48E-03			up
PPP2R2C 5522	protein phosphatase 2, regulatory subunit B, gamma	< 1E-07	down	down	down
PRDM8 56978	PR domain containing 8	< 1E-07		up	up
PRF1 5551	perforin 1 (pore forming protein)	2.00E-07		up	

PRG2 5553	proteoglycan 2, bone marrow (natural killer cell activator, eosinophil granule major basic protein)	< 1E-07		down	
PRG4 10216	proteoglycan 4	3.40E-06			up
PRKAA2 5563	protein kinase, AMP-activated, alpha 2 catalytic subunit	2.54E-05	up		
PRKACB 5567	protein kinase, cAMP-dependent, catalytic, beta	< 1E-07			up
PRKCB 5579	protein kinase C, beta	< 1E-07		up	
PRKCQ 5588	protein kinase C, theta	1.00E-07		up	
PRKG1 5592	protein kinase, cGMP-dependent, type I	< 1E-07			up
PRLR 5618	prolactin receptor	1.33E-03			up
PRODHI 5625	proline dehydrogenase (oxidase) 1	< 1E-07	down	down	down
PROM2 150696	prominin 2	< 1E-07	down	down	down
PRRX1 5396	paired related homeobox 1	< 1E-07			up
PRRX2 51450	paired related homeobox 2	3.00E-07	down		
PRSS27 83886	protease, serine 27	< 1E-07	down	down	down
PRSS8 5652	protease, serine 8	< 1E-07	down	down	down
PSD3 23362	pleckstrin and Sec7 domain containing 3	3.51E-05			up
PTAFR 5724	platelet-activating factor receptor	< 1E-07		up	
PTGDS 5730	prostaglandin D2 synthase 21kDa (brain)	1.52E-03			down
PTGER4 5734	prostaglandin E receptor 4 (subtype EP4)	< 1E-07		up	
PTGIS 5740	prostaglandin I2 (prostacyclin) synthase	7.10E-04			up
PTK6 5753	protein tyrosine kinase 6	< 1E-07	down	down	down
PTNI 5764	pleiotrophin	8.26E-04			up
PTPN22 26191	protein tyrosine phosphatase, non-receptor type 22 (lymphoid)	< 1E-07		up	up
PTPN6 5777	protein tyrosine phosphatase, non-receptor type 6	< 1E-07		up	
PTPN7 5778	protein tyrosine phosphatase, non-receptor type 7	< 1E-07		up	
PTPRB 5787	protein tyrosine phosphatase, receptor type, B	1.00E-07			up
PTPRC 5788	protein tyrosine phosphatase, receptor type, C	< 1E-07		up	up
PTPRCAP 5790	protein tyrosine phosphatase, receptor type, C-associated protein	< 1E-07		up	
PTPRO 5800	protein tyrosine phosphatase, receptor type, O	< 1E-07		up	up
PVRL1 5818	poliovirus receptor-related 1 (herpesvirus entry mediator C)	< 1E-07	down	down	
PVRL3 25945	poliovirus receptor-related 3	1.36E-04			up
PVRL4 81607	poliovirus receptor-related 4	< 1E-07	down	down	down
PYHIN1 149628	pyrin and HIN domain family, member 1	1.00E-07		up	

RAB25 57111	RAB25, member RAS oncogene family	< 1E-07	down	down	down
RAB37 326624	RAB37, member RAS oncogene family	< 1E-07		up	
RAB3IP 117177	RAB3A interacting protein	3.00E-06		up	
RAC2 5880	ras-related C3 botulinum toxin substrate 2 (rho family, small GTP binding protein Rac2)	1.00E-07		up	
RAP1GAP 5909	RAP1 GTPase activating protein	1.21E-04			down
RAPGEF5 9771	Rap guanine nucleotide exchange factor (GEF) 5	< 1E-07			up
RAPGEFL1 51195	Rap guanine nucleotide exchange factor (GEF)-like 1	< 1E-07	down	down	down
RARB 5915	retinoic acid receptor, beta	< 1E-07		up	up
RARRES1 5918	retinoic acid receptor responder (tazarotene induced) 1	< 1E-07		up	up
RARRES3 5920	retinoic acid receptor responder (tazarotene induced) 3	2.82E-05		up	
RASAL3 64926	RAS protein activator like 3	< 1E-07		up	
RASGRP1 10125	RAS guanyl releasing protein 1 (calcium and DAG-regulated)	< 1E-07		up	
RASGRP2 10235	RAS guanyl releasing protein 2 (calcium and DAG-regulated)	< 1E-07		up	
RASGRP3 25780	RAS guanyl releasing protein 3 (calcium and DAG-regulated)	< 1E-07		up	
RBM20 282996	RNA binding motif protein 20	1.82E-04		up	
RBMS3 27303	RNA binding motif, single stranded interacting protein 3	1.40E-06			up
RBP5 83758	retinol binding protein 5, cellular	< 1E-07		up	
RCSD1 92241	RCSD domain containing 1	< 1E-07		up	up
RDH12 145226	retinol dehydrogenase 12 (all-trans/9-cis/11-cis)	< 1E-07	down	down	down
REEP6 92840	receptor accessory protein 6	< 1E-07		down	
RELN 5649	reelin	1.40E-06		up	up
REST 5978	RE1-silencing transcription factor	< 1E-07			up
RFX3 5991	regulatory factor X, 3 (influences HLA class II expression)	< 1E-07			up
RGPD5 84220	RANBP2-like and GRIP domain containing 5	< 1E-07			up
RGS18 64407	regulator of G-protein signaling 18	< 1E-07		up	
RGS4 5999	regulator of G-protein signaling 4	2.10E-06		up	up
RGS5 8490	regulator of G-protein signaling 5	7.20E-06			up
RHCG 51458	Rh family, C glycoprotein	< 1E-07	down	down	down
RHOD 29984	ras homolog family member D	< 1E-07	down	down	down
RHOF 54509	ras homolog family member F	2.00E-07		up	
RHOH 399	ras homolog family member H	< 1E-07		up	

RHOU158480	ras homolog family member U	< 1E-07		up	up
RHOV1171177	ras homolog family member V	< 1E-07	down	down	down
RIF1155183	replication timing regulatory factor 1	< 1E-07			up
RLTPR1146206	RGD motif, leucine rich repeats, tropomodulin domain and proline-rich containing	< 1E-07		up	
RNF39180352	ring finger protein 39	< 1E-07	down	down	down
ROCK219475	Rho-associated, coiled-coil containing protein kinase 2	< 1E-07			up
ROR114919	receptor tyrosine kinase-like orphan receptor 1	2.50E-06			up
RSAD2191543	radical S-adenosyl methionine domain containing 2	1.68E-05			up
RTN116252	reticulon 1	< 1E-07		up	up
RUNDC3A110900	RUN domain containing 3A	2.00E-07	down	down	
S100A14157402	S100 calcium binding protein A14	< 1E-07	down	down	down
S100A216273	S100 calcium binding protein A2	< 1E-07	down	down	down
S100A316274	S100 calcium binding protein A3	1.00E-06	down		
S100A416275	S100 calcium binding protein A4	1.33E-05	down		
S100A716278	S100 calcium binding protein A7	< 1E-07	down	down	down
S100A7A1338324	S100 calcium binding protein A7A	< 1E-07	down	down	down
S100A816279	S100 calcium binding protein A8	< 1E-07	down	down	down
S100A916280	S100 calcium binding protein A9	< 1E-07	down	down	down
S1PR311903	sphingosine-1-phosphate receptor 3	< 1E-07			up
S1PR418698	sphingosine-1-phosphate receptor 4	1.00E-07		up	
SALL216297	spalt-like transcription factor 2	2.49E-05	up		
SAMD9L1219285	sterile alpha motif domain containing 9-like	< 1E-07		up	up
SAMHD1125939	SAM domain and HD domain 1	< 1E-07		up	up
SAMSN1164092	SAM domain, SH3 domain and nuclear localization signals 1	< 1E-07		up	up
SASH3154440	SAM and SH3 domain containing 3	< 1E-07		up	
SATB116304	SATB homeobox 1	4.00E-07			up
SBSN1374897	suprabasin	< 1E-07	down	down	down
SCARA51286133	scavenger receptor class A, member 5	1.86E-04			up
SCEL18796	sciellin	< 1E-07		down	down
SCIMP1388325	SLP adaptor and CSK interacting membrane protein	< 1E-07		up	
SCML2110389	sex comb on midleg-like 2 (Drosophila)	4.70E-06	up		
SCN9A16335	sodium channel, voltage gated, type IX alpha subunit	9.60E-06			up

SCNN1A 6337	sodium channel, non voltage gated 1 alpha subunit	< 1E-07	down	down	down
SCNN1B 6338	sodium channel, non voltage gated 1 beta subunit	< 1E-07		down	down
SCUBE2 57758	signal peptide, CUB domain, EGF-like 2	5.00E-07	down	down	down
SCUBE3 222663	signal peptide, CUB domain, EGF-like 3	1.63E-03			up
SDC1 6382	syndecan 1	< 1E-07	down	down	down
SDCBP2 27111	syndecan binding protein (syntenin) 2	< 1E-07	down	down	down
SDPRI 8436	serum deprivation response	< 1E-07	up	up	
SEL1L3 23231	sel-1 suppressor of lin-12-like 3 (C. elegans)	< 1E-07		up	up
SELL 6402	selectin L	< 1E-07		up	up
SEMA3A 10371	sema domain, immunoglobulin domain (Ig), short basic domain, secreted, (semaphorin) 3A	2.00E-07		up	up
SEPP1 6414	selenoprotein P, plasma, 1	< 1E-07		up	up
SEPT1 1731	sepin 1	< 1E-07		up	
SERPINB13 5275	serpin peptidase inhibitor, clade B (ovalbumin), member 13	< 1E-07	down	down	down
SERPINB2 5055	serpin peptidase inhibitor, clade B (ovalbumin), member 2	2.00E-07	down	down	
SERPINB3 6317	serpin peptidase inhibitor, clade B (ovalbumin), member 3	< 1E-07	down	down	down
SERPINB4 6318	serpin peptidase inhibitor, clade B (ovalbumin), member 4	< 1E-07	down	down	down
SERPINB5 5268	serpin peptidase inhibitor, clade B (ovalbumin), member 5	< 1E-07	down	down	down
SERPINB7 8710	serpin peptidase inhibitor, clade B (ovalbumin), member 7	< 1E-07	down	down	down
SESN3 143686	sestrin 3	2.80E-06			up
SFMBT2 57713	Scm-like with four mbt domains 2	< 1E-07		up	up
SFN 2810	stratifin	< 1E-07	down	down	down
SFRP2 6423	secreted frizzled-related protein 2	< 1E-07	down	down	
SFRP4 6424	secreted frizzled-related protein 4	< 1E-07	up	up	up
SGOL2 151246	shugoshin-like 2 (S. pombe)	< 1E-07			up
SH2D1A 4068	SH2 domain containing 1A	< 1E-07		up	
SH2D3A 10045	SH2 domain containing 3A	< 1E-07			down
SH3RF2 153769	SH3 domain containing ring finger 2	< 1E-07	down	down	down
SHISA3 152573	shisa family member 3	< 1E-07		up	
SHPRH 257218	SNF2 histone linker PHD RING helicase, E3 ubiquitin protein ligase	7.00E-07			up
SIGLEC10 89790	sialic acid binding Ig-like lectin 10	< 1E-07		up	
SIGLEC14 100049587	sialic acid binding Ig-like lectin 14	< 1E-07		up	
SIGLEC5 8778	sialic acid binding Ig-like lectin 5	< 1E-07		up	

SIGLEC7 27036	sialic acid binding Ig-like lectin 7	< 1E-07		up	up
SIGLEC8 27181	sialic acid binding Ig-like lectin 8	4.00E-07		up	
SIGLEC9 27180	sialic acid binding Ig-like lectin 9	< 1E-07		up	up
SIRPB2 284759	signal-regulatory protein beta 2	< 1E-07		up	up
SIRPG 55423	signal-regulatory protein gamma	< 1E-07		up	
SIT1 27240	signaling threshold regulating transmembrane adaptor 1	< 1E-07		up	
SKAP1 8631	src kinase associated phosphoprotein 1	< 1E-07		up	
SKIL 6498	SKI-like proto-oncogene	< 1E-07			up
SLA 6503	Src-like-adaptor	< 1E-07		up	
SLA2 84174	Src-like-adaptor 2	< 1E-07		up	
SLAMF1 6504	signaling lymphocytic activation molecule family member 1	< 1E-07		up	
SLAMF6 114836	signaling lymphocytic activation molecule family member 6	< 1E-07		up	
SLAMF7 57823	signaling lymphocytic activation molecule family member 7	3.00E-07		up	
SLC12A8 84561	solute carrier family 12, member 8	9.30E-06			up
SLC1A3 6507	solute carrier family 1 (glial high affinity glutamate transporter), member 3	1.40E-06		up	
SLC2A5 6518	solute carrier family 2 (facilitated glucose/fructose transporter), member 5	< 1E-07		up	up
SLC40A1 30061	solute carrier family 40 (iron-regulated transporter), member 1	< 1E-07		up	up
SLC41A2 84102	solute carrier family 41 (magnesium transporter), member 2	< 1E-07			up
SLC45A2 51151	solute carrier family 45, member 2	2.79E-04	down		down
SLC5A3 6526	solute carrier family 5 (sodium/myo-inositol cotransporter), member 3	1.23E-05			up
SLC6A9 6536	solute carrier family 6 (neurotransmitter transporter, glycine), member 9	3.00E-07		down	
SLC7A7 9056	solute carrier family 7 (amino acid transporter light chain, y+L system), member 7	< 1E-07		up	
SLC8A1 6546	solute carrier family 8 (sodium/calcium exchanger), member 1	< 1E-07		up	up
SLC9A7 84679	solute carrier family 9, subfamily A (NHE7, cation proton antiporter 7), member 7	< 1E-07		up	up
SLC9A9 285195	solute carrier family 9, subfamily A (NHE9, cation proton antiporter 9), member 9	< 1E-07		up	
SLCO2B1 11309	solute carrier organic anion transporter family, member 2B1	< 1E-07		up	
SLCO4A1-AS1 100127888	SLCO4A1 antisense RNA 1	1.20E-06		down	down
SLFN11 91607	schlafen family member 11	< 1E-07		up	up
SLIT2 9353	slit homolog 2 (Drosophila)	< 1E-07		up	up

SLPII6590	secretory leukocyte peptidase inhibitor	< 1E-07	down	down	down
SMPD3I55512	sphingomyelin phosphodiesterase 3, neutral membrane (neutral sphingomyelinase II)	2.00E-07	down		
SNX20I124460	sorting nexin 20	< 1E-07		up	
SORL1I6653	sortilin-related receptor, L(DLR class) A repeats containing	2.00E-07		up	up
SOX11I6664	SRY (sex determining region Y)-box 11	3.05E-03			up
SOX15I6665	SRY (sex determining region Y)-box 15	< 1E-07	down	down	down
SOX5I6660	SRY (sex determining region Y)-box 5	1.11E-04			up
SP140I11262	SP140 nuclear body protein	< 1E-07		up	
SPARCL1I8404	SPARC-like 1 (hevin)	1.00E-06			up
SPIBI6689	Spi-B transcription factor (Spi-1/PU.1 related)	< 1E-07		up	
SPINK5I11005	serine peptidase inhibitor, Kazal type 5	< 1E-07	down	down	down
SPINT1I6692	serine peptidase inhibitor, Kunitz type 1	3.85E-04		down	
SPINT2I10653	serine peptidase inhibitor, Kunitz type 2	3.02E-05	down		
SPNI6693	sialophorin	< 1E-07		up	
SPNS2I124976	spinstar homolog 2 (Drosophila)	1.94E-05	down		
SPOCK1I6695	sparc/osteonectin, cwcv and kazal-like domains proteoglycan (testican) 1	1.19E-03	down		
SPOCK2I9806	sparc/osteonectin, cwcv and kazal-like domains proteoglycan (testican) 2	< 1E-07		up	
SPP1I6696	secreted phosphoprotein 1	9.00E-07		up	up
SPRR1AI6698	small proline-rich protein 1A	< 1E-07	down	down	down
SPRR1BI6699	small proline-rich protein 1B	< 1E-07	down	down	down
SPRR2AI6700	small proline-rich protein 2A	< 1E-07	down	down	down
SPRR2DI6703	small proline-rich protein 2D	< 1E-07	down	down	down
SPRR2EI6704	small proline-rich protein 2E	< 1E-07	down	down	down
SPRR2GI6706	small proline-rich protein 2G	< 1E-07	down	down	down
SPRR3I6707	small proline-rich protein 3	4.64E-04			down
SPTBN2I6712	spectrin, beta, non-erythrocytic 2	9.00E-07		down	down
SRGNI5552	serglycin	< 1E-07		up	
SRPX2I27286	sushi-repeat containing protein, X-linked 2	7.52E-05			up
ST14I6768	suppression of tumorigenicity 14 (colon carcinoma)	2.53E-04	down		
ST8SIA4I7903	ST8 alpha-N-acetyl-neuraminide alpha-2,8-sialyltransferase 4	< 1E-07		up	up
STAP1I26228	signal transducing adaptor family member 1	< 1E-07		up	

STAT4 6775	signal transducer and activator of transcription 4	< 1E-07		up	
STC1 6781	stanniocalcin 1	< 1E-07		up	up
STK17B 9262	serine/threonine kinase 17b	< 1E-07		up	
STK26 51765	serine/threonine protein kinase 26	1.40E-06		up	
STRA6 64220	stimulated by retinoic acid 6	1.67E-04		up	up
SULF1 23213	sulfatase 1	< 1E-07		up	up
SULT1A1 6817	sulfotransferase family, cytosolic, 1A, phenol-preferring, member 1	6.00E-06		up	
SULT2B1 6820	sulfotransferase family, cytosolic, 2B, member 1	< 1E-07	down	down	down
SUSD3 203328	sushi domain containing 3	< 1E-07		up	
SV2B 9899	synaptic vesicle glycoprotein 2B	1.06E-05		up	
SVEP1 79987	sushi, von Willebrand factor type A, EGF and pentraxin domain containing 1	< 1E-07		up	up
SYNPO2 171024	synaptopodin 2	< 1E-07		up	up
SYT1 6857	synaptotagmin I	5.69E-04			up
SYT11 23208	synaptotagmin XI	4.30E-06			up
TACSTD2 4070	tumor-associated calcium signal transducer 2	< 1E-07	down	down	down
TAGAP1 17289	T-cell activation RhoGTPase activating protein	< 1E-07		up	
TAOK1 57551	TAO kinase 1	< 1E-07			up
TBC1D10C 374403	TBC1 domain family, member 10C	< 1E-07		up	
TBC1D4 9882	TBC1 domain family, member 4	< 1E-07		up	
TBC1D9 23158	TBC1 domain family, member 9 (with GRAM domain)	< 1E-07		up	up
TBXAS1 6916	thromboxane A synthase 1 (platelet)	< 1E-07		up	up
TCF4 6925	transcription factor 4	< 1E-07		up	up
TCL1A 8115	T-cell leukemia/lymphoma 1A	< 1E-07		up	
TCN1 6947	transcobalamin I (vitamin B12 binding protein, R binder family)	4.21E-03	down		down
TENM2 57451	teneurin transmembrane protein 2	< 1E-07	down	down	down
TESPA1 9840	thymocyte expressed, positive selection associated 1	< 1E-07		up	
TFAP2A 7020	transcription factor AP-2 alpha (activating enhancer binding protein 2 alpha)	4.80E-06		down	down
TFCP2L1 29842	transcription factor CP2-like 1	5.50E-06	down	down	down
TFEC 22797	transcription factor EC	< 1E-07		up	up
TFF3 7033	trefoil factor 3 (intestinal)	1.65E-04	down		down
TFPII 7035	tissue factor pathway inhibitor (lipoprotein-associated coagulation inhibitor)	< 1E-07		up	up
TGFB3 7043	transforming growth factor, beta 3	< 1E-07			up
TGM1 7051	transglutaminase 1	< 1E-07	down	down	down

TGM2 7052	transglutaminase 2	< 1E-07		up	
TGM3 7053	transglutaminase 3	< 1E-07	down	down	down
THBS2 7058	thrombospondin 2	1.23E-03			up
THBS4 7060	thrombospondin 4	6.07E-05			up
THEMIS 387357	thymocyte selection associated	< 1E-07		up	
TIGIT 201633	T cell immunoreceptor with Ig and ITIM domains	< 1E-07		up	
TINCR 257000	tissue differentiation-inducing non-protein coding RNA	< 1E-07	down	down	down
TLR10 81793	toll-like receptor 10	< 1E-07		up	
TLR4 7099	toll-like receptor 4	< 1E-07		up	up
TLR6 10333	toll-like receptor 6	< 1E-07		up	
TLR7 51284	toll-like receptor 7	< 1E-07		up	up
TLR8 51311	toll-like receptor 8	< 1E-07		up	up
TMEM108 66000	transmembrane protein 108	2.63E-03	up		
TMEM119 338773	transmembrane protein 119	3.30E-05	down		
TMEM156 80008	transmembrane protein 156	< 1E-07		up	
TMEM171 134285	transmembrane protein 171	2.90E-06	down	down	
TMEM195 392636	transmembrane protein 195	9.87E-04			up
TMEM200A 114801	transmembrane protein 200A	< 1E-07		up	up
TMEM45A 55076	transmembrane protein 45A	< 1E-07	down	down	
TMEM47 83604	transmembrane protein 47	< 1E-07		up	up
TMEM79 84283	transmembrane protein 79	< 1E-07		down	
TMOD1 7111	tropomodulin 1	2.00E-07			down
TMPRSS13 84000	transmembrane protease, serine 13	< 1E-07	down	down	down
TNFAIP8L3 388121	tumor necrosis factor, alpha-induced protein 8-like 3	1.34E-05	down		
TNFRSF11B 4982	tumor necrosis factor receptor superfamily, member 11b	8.00E-07		up	
TNFRSF17 608	tumor necrosis factor receptor superfamily, member 17	< 1E-07		up	
TNFRSF4 7293	tumor necrosis factor receptor superfamily, member 4	< 1E-07		up	
TNFRSF9 3604	tumor necrosis factor receptor superfamily, member 9	< 1E-07		up	
TNFSF11 8600	tumor necrosis factor (ligand) superfamily, member 11	< 1E-07		up	
TNFSF13B 10673	tumor necrosis factor (ligand) superfamily, member 13B	< 1E-07		up	up
TNFSF8 944	tumor necrosis factor (ligand) superfamily, member 8	< 1E-07		up	
TNS4 84951	tensin 4	< 1E-07	down	down	down

TOR4A 54863	torsin family 4, member A	2.20E-05			up
TOX 9760	thymocyte selection-associated high mobility group box	< 1E-07		up	
TOX2 84969	TOX high mobility group box family member 2	< 1E-07		up	
TP63 8626	tumor protein p63	< 1E-07	down	down	down
TPPP1 11076	tubulin polymerization promoting protein	1.11E-05	down		down
TPRXL 348825	tetra-peptide repeat homeobox-like	< 1E-07		down	
TPSAB1 7177	tryptase alpha/beta 1	6.50E-06	down	down	
TPSB2 64499	tryptase beta 2 (gene/pseudogene)	2.50E-06	down	down	
TRAF3IP3 80342	TRAF3 interacting protein 3	< 1E-07		up	
TRANK1 9881	tetratricopeptide repeat and ankyrin repeat containing 1	< 1E-07		up	
TRAT1 50852	T cell receptor associated transmembrane adaptor 1	< 1E-07		up	
TRIL 9865	TLR4 interactor with leucine-rich repeats	2.01E-03			up
TRIM29 23650	tripartite motif containing 29	< 1E-07	down	down	down
TRIM63 84676	tripartite motif containing 63, E3 ubiquitin protein ligase	1.76E-04	down	down	down
TRIM7 81786	tripartite motif containing 7	< 1E-07		down	
TRPM1 4308	transient receptor potential cation channel, subfamily M, member 1	2.06E-04	down	down	down
TSHZ2 128553	teashirt zinc finger homeobox 2	< 1E-07			up
TSPAN10 83882	tetraspanin 10	4.05E-04		down	down
TSPAN13 27075	tetraspanin 13	2.00E-07		up	up
TSPAN5 10098	tetraspanin 5	5.83E-04			up
TTBK2 146057	tau tubulin kinase 2	< 1E-07			up
TUBA4A 7277	tubulin, alpha 4a	< 1E-07	down	down	down
TUBB4 10382	tubulin, beta 4A class IVa	1.90E-06		down	down
TYR 7299	tyrosinase	1.68E-04	down	down	down
TYRP1 7306	tyrosinase-related protein 1	1.00E-07	down	down	down
UBASH3A 53347	ubiquitin associated and SH3 domain containing A	< 1E-07		up	
UCN2 90226	urocortin 2	3.67E-03	down	down	
UHMK1 127933	U2AF homology motif (UHM) kinase 1	< 1E-07		up	up
USP53 54532	ubiquitin specific peptidase 53	5.72E-05			up
VAT1L 57687	vesicle amine transport 1-like	4.60E-06			up
VAV1 7409	vav 1 guanine nucleotide exchange factor	< 1E-07		up	
VCAM1 7412	vascular cell adhesion molecule 1	< 1E-07		up	up
VCAN 1462	versican	7.10E-06			up

VNN2 8875	vanin 2	< 1E-07		up	
VPREB3 29802	pre-B lymphocyte 3	< 1E-07		up	
VSIG10L 147645	V-set and immunoglobulin domain containing 10 like	< 1E-07	down		down
VSIG4 11326	V-set and immunoglobulin domain containing 4	< 1E-07		up	up
VSNL1 7447	visinin-like 1	< 1E-07		down	
WAS 7454	Wiskott-Aldrich syndrome	< 1E-07		up	
WDFY4 57705	WDFY family member 4	< 1E-07		up	
WDR63 126820	WD repeat domain 63	2.10E-06	down	down	
WISP2 8839	WNT1 inducible signaling pathway protein 2	< 1E-07	down	down	
WNT4 54361	wingless-type MMTV integration site family, member 4	< 1E-07		down	down
WWC1 23286	WW and C2 domain containing 1	7.29E-05			down
XG 7499	Xg blood group	< 1E-07	down	down	
ZAP70 7535	zeta-chain (TCR) associated protein kinase 70kDa	< 1E-07		up	
ZBP1 81030	Z-DNA binding protein 1	< 1E-07		up	
ZBTB7C 201501	zinc finger and BTB domain containing 7C	< 1E-07	down	down	down
ZDBF2 57683	zinc finger, DBF-type containing 2	1.61E-04	up		up
ZDHHC20 253832	zinc finger, DHHC-type containing 20	< 1E-07			up
ZEB1 6935	zinc finger E-box binding homeobox 1	< 1E-07		up	up
ZFHX4 79776	zinc finger homeobox 4	5.15E-03			up
ZFPM2 23414	zinc finger protein, FOG family member 2	< 1E-07		up	up
ZNF750 79755	zinc finger protein 750	< 1E-07	down	down	down
ZNF827 152485	zinc finger protein 827	< 1E-07			up
ZNF831 128611	zinc finger protein 831	< 1E-07		up	
ZNHIT2 741	zinc finger, HIT-type containing 2	4.00E-06		down	down

¹distant metastasis, ²primary melanoma, ³regional lymph node metastasis, ⁴regional (sub)cutaneous metastasis

Supplementary Table 6. Pathway analysis of the 1.065 altered genes between primary melanomas and different metastatic subgroups based on TCGA RNAseq v2.0 data.

Pathway ID	Pathway name	Source	P-value	Bonferroni	Alteration in regulation	Genes included (at least 5)
<i>Common altered pathways in all three metastasis subgroups*</i>						
105680	Apoptotic cleavage of cell adhesion proteins	REACTOME	2.88E-08	1.68E-05	down	<i>PKP1, DSG1, DSG3, DSP, CDH1</i>
576263	Degradation of the extracellular matrix	REACTOME	1.88E-05	1.10E-02	down	<i>KLK7, MMP1, MMP3, COL17A1, LAMC2, BCAN, CDH1</i>
105678	Apoptotic cleavage of cellular proteins	REACTOME	2.92E-05	1.70E-02	down	<i>PKP1, DSG1, DSG3, DSP, CDH1</i>
198807	Alpha6-Beta4 Integrin Signaling Pathway	WikiPathways	4.69E-05	2.74E-02	down	<i>ITGB4, SFN, COL17A1, DSP, LAMC2, CLCA2</i>
<i>Common altered pathways in regional melanoma metastases</i>						
106028	Hemostasis	REACTOME	1.56E-08	1.16E-05	up	<i>DOCK2, SELL, HGF, DOCK11, ITGA1, ITGA4, ITGAM, ITGB2, OLR1, ZFPM2, TFPI, ITPR1, SIRPB2, CD84, SLC8A1, PIK3CG, KCNMA1, MERTK, PLEK, APBB1IP</i>
172846	Staphylococcus aureus infection	KEGG	1.02E-06	7.61E-04	up	<i>CFH, FPR3, CFI, ITGAM, ITGB2, C3, C3AR1</i>
83078	Hematopoietic cell lineage	KEGG	1.32E-06	9.88E-04	up	<i>ITGA1, ITGA4, CR1, ITGAM, CD1D, CSF1R, CD38, IL7R</i>
106413	Immunoregulatory interactions between a Lymphoid and a non-Lymphoid cell	REACTOME	2.38E-06	1.77E-03	up	<i>SELL, ITGA4, ITGB2, LILRB1, C3, CD96, VCAM1, LILRB4</i>
106062	Cell surface interactions at the vascular wall	REACTOME	3.01E-06	2.24E-03	up	<i>SELL, ITGA4, ITGAM, ITGB2, OLR1, SIRPB2, CD84, MERTK</i>

83083	Leukocyte transendothelial migration	KEGG	1.20E-05	8.97E-03	up	<i>CYBB, ITGA4, ITGAM, ITGB2, CLDN11, PIK3CG, MMP9, VCAM1</i>
692234	PI3K-Akt signaling pathway	KEGG	1.54E-05	1.15E-02	up	<i>PIK3API, HGF, FLT1, RELN, SPPI, ITGA1, ITGA4, CSF1R, PIK3CG, TLR4, FGF7, OSMR, IL7R</i>
PW:0000286	integrin signaling	Pathway Ontology	2.32E-05	1.73E-02	up	<i>ITGA1, ITGA4, ITGAM, ITGB2, APBB1IP</i>
106110	Integrin cell surface interactions	REACTOME	2.98E-05	2.23E-02	up	<i>SPP1, ITGA1, ITGA4, ITGAM, ITGB2, VCAM1</i>
83073	Complement and coagulation cascades	KEGG	3.85E-05	2.87E-02	up	<i>CFH, CFI, CR1, TFPI, C3, C3AR1</i>
144181	Leishmaniasis	KEGG	6.67E-05	4.97E-02	up	<i>ITGA4, CR1, ITGAM, ITGB2, TLR4, C3</i>
<i>Altered pathways in regional lymph node melanoma metastases</i>						
137998	TCR signaling in naive CD4+ T cells	Pathway Interaction Database	2.70E-21	2.46E-18	up	<i>ITK, PTPN6, SLA2, VAV1, WAS, LCK, ZAP70, RASGRP1, CD3D, CD3E, CD3G, CD247, CD4, CD28, MAP4K1, PRKCB, CARD11, PRKCQ, FYB, RASGRP2</i>
138055	TCR signaling in naive CD8+ T cells	Pathway Interaction Database	5.32E-19	4.85E-16	up	<i>PTPN6, VAV1, LCK, ZAP70, RASGRP1, CD3D, CD3E, CD3G, CD247, CD8A, CD8B, CD86, PRF1, PRKCB, CARD11, PRKCQ, RASGRP2</i>
198909	B Cell Receptor Signaling Pathway	WikiPathways	3.67E-17	3.35E-14	up	<i>INPP5D, ITK, BLK, PTPN6, CHST15, RASGRP3, BTK, SLA2, BANK1, VAV1, WAS, LCK, CR2, ZAP70, CD5, CD19, CD22, MAP4K1, DAPPI, CD72, PRKCB, CD79A, CD79B, CARD11, PRKCQ, HCLS1</i>
138018	Downstream signaling in naive CD8+ T cells	Pathway Interaction Database	6.66E-16	6.07E-13	up	<i>TNFRSF9, STAT4, TNFRSF4, PTPN7, CD3D, CD3E, CD3G, CD247, CD8A, CD8B, PRF1, PRKCB, PRKCQ, IL2RA, IL2RB, IL2RG</i>
198862	TCR Signaling Pathway	WikiPathways	1.06E-13	9.68E-11	up	<i>TNFRSF9, ITK, CCR5, VAV1, WAS, ZAP70, CD3D, CD3E, CD3G, CD247, CD4, CD8A, CD8B, MAP4K1, SKAP1, CARD11, PRKCQ, FYB</i>

83080	T cell receptor signaling pathway	KEGG	1.20E-12	1.09E-09	up	<i>PDCD1, ITK, PTPN6, VAV1, LCK, ZAP70, RASGRP1, CD3D, CD3E, CD3G, CD247, CD4, CD8A, CD8B, CD28, CARD11, PRKCQ, CTLA4</i>
83125	Primary immunodeficiency	KEGG	1.82E-12	1.65E-09	up	<i>JAK3, BTK, LCK, ZAP70, CD3D, CD3E, CD3G, CD247, CD4, CD8A, CD8B, CD19, CD79A, IL2RG</i>
366160	Adaptive Immune System	REACTOME	2.94E-12	2.68E-09	up	<i>PDCD1, HLA-DMB, HLA-DOA, HLA-DOB, LILRB2, INPP5D, ITGAL, ITK, BLK, PTPN6, TRAT1, RASGRP3, BTK, VAV1, MRC1, WAS, BTLA, LCK, ZAP70, KLRK1, RASGRP1, CD3D, CD3E, CD3G, CD247, CD4, CD8A, CD8B, CD19, CD28, CD86, CRTAM, DAPPI, PRKCB, CD79A, CD79B, CARD11, PRKCQ, CTLA4, FYB, RASGRP2, PDCD1LG2</i>
83081	B cell receptor signaling pathway	KEGG	5.82E-12	5.31E-09	up	<i>INPP5D, PTPN6, RASGRP3, BTK, VAV1, RAC2, CR2, CD19, CD22, DAPPI, CD72, PRKCB, CD79A, CD79B, CARD11</i>
M6231	NO2-dependent IL 12 Pathway in NK cells	BioCarta	7.26E-12	6.61E-09	up	<i>STAT4, CCR5, CXCR3, CD2, CD3D, CD3E, CD3G, CD247, CD4</i>
137922	IL12-mediated signaling events	Pathway Interaction Database	9.39E-12	8.56E-09	up	<i>STAT4, CCR5, LCK, CD3D, CD3E, CD3G, CD247, CD4, CD8A, CD8B, GZMA, IL2RA, IL2RB, IL2RG</i>
83078	Hematopoietic cell lineage	KEGG	1.02E-11	9.32E-09	up	<i>FCER2, CR2, CD2, CD3D, CD3E, CD3G, CD4, CD5, CD7, CD8A, CD8B, CD19, MS4A1, CD22, CD37, IL2RA</i>
106414	TCR signaling	REACTOME	1.49E-11	1.36E-08	up	<i>INPP5D, ITK, TRAT1, WAS, LCK, ZAP70, CD3D, CD3E, CD3G, CD247, CD4, CARD11, PRKCQ, FYB</i>
106359	Chemokine receptors bind chemokines	REACTOME	3.64E-11	3.31E-08	up	<i>CXCL10, CXCR5, CCR2, CXCR4, CXCL9, CCR5, CCR6, CCR7, CCL19, CXCR3, CXCL13, CCRL2, CXCR6</i>
M13247	T Cytotoxic Cell Surface Molecules	BioCarta	4.95E-11	4.51E-08	up	<i>ITGAL, CD2, CD3D, CD3E, CD3G, CD247, CD8A, CD28</i>

M6427	T Helper Cell Surface Molecules	BioCarta	4.95E-11	4.51E-08	up	<i>ITGAL, CD2, CD3D, CD3E, CD3G, CD247, CD4, CD28</i>
83051	Cytokine-cytokine receptor interaction	KEGG	5.44E-11	4.96E-08	up	<i>IL10RA, TNFRSF9, CXCL10, TNFRSF17, TNFRSF4, CXCR5, CCR2, CXCR4, CXCL9, CCR5, CCR6, CCR7, CCL19, CXCR3, CXCL13, TNFSF11, CSF2RB, CXCR6, CD27, TNFSF8, IL21R, LTB, IL2RA, IL2RB, IL2RG</i>
119552	Costimulation by the CD28 family	REACTOME	8.13E-11	7.41E-08	up	<i>PDCD1, PTPN6, VAV1, BTLA, LCK, CD3D, CD3E, CD3G, CD247, CD4, CD28, CD86, CTLA4, PDCD1LG2</i>
M1467	The Co-Stimulatory Signal During T-cell Activation	BioCarta	8.20E-11	7.47E-08	up	<i>ITK, LCK, CD3D, CD3E, CD3G, CD247, CD28, CD86, CTLA4</i>
99051	Chemokine signaling pathway	KEGG	9.94E-11	9.06E-08	up	<i>CXCL10, NCF1, ELMO1, ITK, CXCR5, CCR2, JAK3, CXCR4, CXCL9, CCR5, CCR6, CCR7, CCL19, VAV1, RAC2, CXCR3, WAS, CXCL13, CXCR6, PRKCB, RASGRP2</i>
M16519	HIV Induced T Cell Apoptosis	BioCarta	2.99E-10	2.72E-07	up	<i>CCR5, CD3D, CD3E, CD3G, CD247, CD4, CD28</i>
106417	Generation of second messenger molecules	REACTOME	5.56E-10	5.07E-07	up	<i>ITK, WAS, LCK, ZAP70, CD3D, CD3E, CD3G, CD247, CD4, FYB</i>
119557	PD-1 signaling	REACTOME	1.18E-09	1.08E-06	up	<i>PDCD1, PTPN6, LCK, CD3D, CD3E, CD3G, CD247, CD4, PDCD1LG2</i>
M10765	Lck and Fyn tyrosine kinases in initiation of TCR Activation	BioCarta	1.50E-09	1.37E-06	up	<i>LCK, ZAP70, CD3D, CD3E, CD3G, CD247, CD4</i>
137936	IL12 signaling mediated by STAT4	Pathway Interaction Database	1.71E-09	1.56E-06	up	<i>STAT4, CD3D, CD3E, CD3G, CD247, CD4, CD28, PRF1, IL2RA</i>
83069	Cell adhesion molecules (CAMs)	KEGG	3.55E-09	3.23E-06	up	<i>PDCD1, HLA-DMB, SPN, HLA-DOA, HLA-DOB, ITGAL, CD2, CD4, CD6, CD8A, CD8B, TIGIT, CD22, CD28, CD86, CTLA4, PDCD1LG2</i>

M9526	T Cell Signal Transduction	Signaling Transduction KE	1.12E-08	1.02E-05	up	<i>ITK, RASGRP3, VAV1, LCK, ZAP70, RASGRP1, CD3D, CD28, CTLA4, RASGRP2</i>
M19422	IL 17 Signaling Pathway	BioCarta	1.59E-08	1.45E-05	up	<i>CD2, CD3D, CD3E, CD3G, CD247, CD4, CD8A</i>
106418	Downstream TCR signaling	REACTOME	1.76E-08	1.60E-05	up	<i>INPP5D, TRAT1, LCK, CD3D, CD3E, CD3G, CD247, CD4, CARD11, PRKCQ</i>
P00053	T cell activation	PantherDB	2.27E-08	2.07E-05	up	<i>HLA-DOA, VAV1, WAS, LCK, ZAP70, CD3D, CD3E, CD3G, CD247, CD28, CD86, PRKCQ</i>
106357	Class A/1 (Rhodopsin-like receptors)	REACTOME	4.97E-08	4.53E-05	up	<i>CXCL10, P2RY13, PTAFR, PTGER4, CXCR5, CCR2, JAK3, ADORA2A, ADRA2A, CXCR4, CXCL9, P2RY10, CCR5, CCR6, CCR7, C5AR1, CCL19, GPR132, CXCR3, CXCL13, CCRL2, CXCR6, S1PR4</i>
138058	BCR signaling pathway	Pathway Interaction Database	4.98E-08	4.53E-05	up	<i>PTPN6, BTK, POU2F2, CD19, CD22, MAP4K1, DAPP1, CD72, CD79A, CD79B, CARD11</i>
106416	Translocation of ZAP-70 to Immunological synapse	REACTOME	8.91E-08	8.12E-05	up	<i>LCK, ZAP70, CD3D, CD3E, CD3G, CD247, CD4</i>
172846	Staphylococcus aureus infection	KEGG	1.74E-07	1.59E-04	up	<i>HLA-DMB, HLA-DOA, HLA-DOB, PTAFR, ITGAL, C1QA, C1QB, C1QC, C4A, C5AR1</i>
M4319	IL12 and Stat4 Dependent Signaling Pathway in Th1 Development	BioCarta	1.82E-07	1.66E-04	up	<i>STAT4, CCR5, CXCR3, CD3D, CD3E, CD3G, CD247</i>
M1462	CTL mediated immune response against target cells	BioCarta	2.21E-07	2.01E-04	up	<i>ITGAL, CD3D, CD3E, CD3G, CD247, PRF1</i>
M19784	T Cell Receptor Signaling Pathway	BioCarta	2.45E-07	2.23E-04	up	<i>PTPN7, VAV1, LCK, ZAP70, CD3D, CD3E, CD3G, CD247, PRKCB</i>
M6327	Activation of Csk by cAMP-dependent Protein Kinase Inhibits	BioCarta	2.52E-07	2.30E-04	up	<i>LCK, ZAP70, CD3D, CD3E, CD3G, CD247, CD4</i>

	Signaling through the T Cell Receptor					
187095	Interleukin receptor SHC signaling	REACTOME	1.05E-06	9.55E-04	up	<i>INPP5D, JAK3, PTPN6, CSFR2RB, IL2RA, IL2RB, IL2RG</i>
M4047	Selective expression of chemokine receptors during T-cell polarization	BioCarta	1.05E-06	9.55E-04	up	<i>CCR2, CXCR4, CCR5, CCR7, CXCR3, CD4, CD28</i>
M16966	Stathmin and breast cancer resistance to antimicrotubule agents	BioCarta	1.12E-06	1.02E-03	up	<i>CAMK4, CD2, CD3D, CD3E, CD3G, CD247</i>
205110	Interleukin-2 signaling	REACTOME	1.47E-06	1.34E-03	up	<i>INPP5D, JAK3, PTPN6, LCK, CSFR2RB, IL2RA, IL2RB, IL2RG</i>
P00010	B cell activation	PantherDB	1.59E-06	1.45E-03	up	<i>PTPN6, BTK, VAV1, RAC2, CD19, CD22, PRKCB, CD79A, CD79B</i>
137910	CXCR4-mediated signaling events	Pathway Interaction Database	1.98E-06	1.81E-03	up	<i>BLK, PTPN6, CXCR4, VAV1, LCK, CD3D, CD3E, CD3G, CD247, CD4</i>
198766	Inflammatory Response Pathway	WikiPathways	2.15E-06	1.96E-03	up	<i>LCK, ZAP70, CD28, CD86, IL2RA, IL2RB, IL2RG</i>
M18215	Role of Tob in T-cell activation	BioCarta	2.17E-06	1.98E-03	up	<i>CD3D, CD3E, CD3G, CD247, CD28, IL2RA</i>
106413	Immunoregulatory interactions between a Lymphoid and a non-Lymphoid cell	REACTOME	2.21E-06	2.01E-03	up	<i>LILRB2, ITGAL, KLRK1, CD3D, CD3E, CD3G, CD247, CD8A, CD8B, CD19, CRTAM</i>
106415	Phosphorylation of CD3 and TCR zeta chains	REACTOME	3.91E-06	3.56E-03	up	<i>LCK, CD3D, CD3E, CD3G, CD247, CD4</i>
119550	G alpha (i) signalling events	REACTOME	3.92E-06	3.57E-03	up	<i>CXCL10, P2RY13, CXCR5, CCR2, ADRA2A, CXCR4, CXCL9, CCR5, CCR6, CCR7, C5AR1, CCL19, CXCR3, CXCL13, RGS18, CXCR6, S1PR4</i>

106358	Peptide ligand-binding receptors	REACTOME	4.11E-06	3.75E-03	up	<i>CXCL10, CXCR5, CCR2, JAK3, CXCR4, CXCL9, CCR5, CCR6, CCR7, C5AR1, CCL19, CXCR3, CXCL13, CCRL2, CXCR6</i>
187094	Interleukin-3, 5 and GM-CSF signaling	REACTOME	4.13E-06	3.77E-03	up	<i>INPP5D, JAK3, PTPN6, VAV1, CSF2RB, IL2RA, IL2RB, IL2RG</i>
P00031	Inflammation mediated by chemokine and cytokine signaling pathway	PantherDB	4.68E-06	4.27E-03	up	<i>CXCL10, ITGAL, CXCR5, CCR2, CXCR4, CCR5, CCR6, CCR7, C5AR1, VAV1, RAC2, CXCR3, CCRL2, CXCR6, PRKCB</i>
920963	Allograft Rejection	WikiPathways	7.30E-06	6.65E-03	up	<i>HLA-DMB, HLA-DOA, HLA-DOB, CD4, CD28, CD86, PRF1</i>
634527	NF-kappa B signaling pathway	KEGG	1.04E-05	9.44E-03	up	<i>BTK, CCL19, BIRC3, LCK, ZAP70, TNFSF11, PRKCB, CARD11, LTB, PRKCQ</i>
83079	Natural killer cell mediated cytotoxicity	KEGG	1.24E-05	1.13E-02	up	<i>ITGAL, PTPN6, VAV1, RAC2, LCK, ZAP70, KLRK1, CD247, PRF1, CD48, PRKCB, SH2D1A</i>
106019	The role of Nef in HIV-1 replication and disease pathogenesis	REACTOME	1.67E-05	1.52E-02	up	<i>ELMO1, LCK, CD247, CD4, CD8B, CD28</i>
161020	GPCR ligand binding	REACTOME	1.83E-05	1.67E-02	up	<i>CXCL10, P2RY13, PTAFR, PTGER4, CXCR5, CCR2, JAK3, ADORA2A, ADRA2A, CXCR4, CXCL9, P2RY10, CCR5, CCR6, CCR7, C5AR1, CCL19, GPR132, CXCR3, CXCL13, CCRL2, CXCR6, SIPR4</i>
137988	IL2 signaling events mediated by STAT5	Pathway Interaction Database	2.05E-05	1.87E-02	up	<i>JAK3, LCK, PRF1, IL2RA, IL2RB, IL2RG</i>
576248	Signaling by the B Cell Receptor (BCR)	REACTOME	2.18E-05	1.99E-02	up	<i>BLK, TRAT1, RASGRP3, BTK, VAV1, LCK, RASGRP1, CD19, CD28, CD86, DAPPI, PRKCB, CD79A, CD79B, CARD11</i>
125138	Viral myocarditis	KEGG	2.50E-05	2.27E-02	up	<i>HLA-DMB, HLA-DOA, HLA-DOB, ITGAL, RAC2, CD28, CD86, PRF1</i>
M8626	Members of the BCR signaling pathway	Signaling Gateway	2.71E-05	2.47E-02	up	<i>INPP5D, BTK, VAV1, CR2, CD19, CD22, MAP4K1</i>

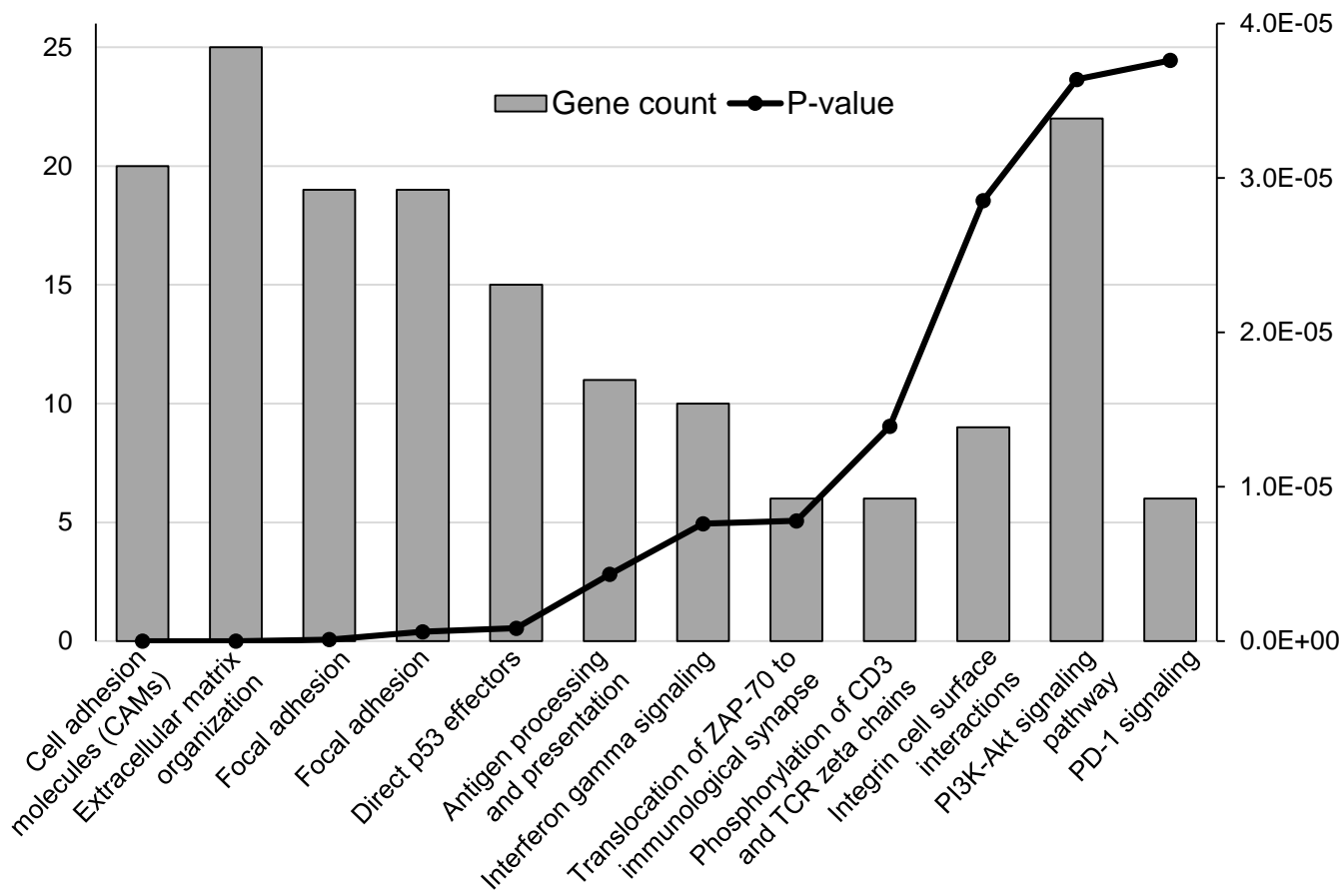
M7747	IL 2 signaling pathway	BioCarta	5.39E-05	4.91E-02	up	<i>JAK3, LCK, IL2RA, IL2RB, IL2RG</i>
128760	Intestinal immune network for IgA production	KEGG	5.41E-05	4.92E-02	up	<i>HLA-DMB, HLA-DOA, HLA-DOB, TNFRSF17, CXCR4, CD28, CD86</i>
<i>Altered pathways in regional (sub)cutaneous melanoma metastases</i>						
576262	Extracellular matrix organization	REACTOME	6.80E-08	5.04E-05	up	<i>NID2, COL10A1, ADAMTS3, ASPN, DDR2, LAMA4, ADAMTS5, ITGB3, TGFB3, FBN1, ADAMTS9, VCAN, LOXL3, MMP13, MMP16</i>
868086	Rap1 signaling pathway	KEGG	6.21E-05	4.61E-02	up	<i>DOCK4, ANGPT1, ANGPT2, RAPGEF5, F2R, ITGB3, LPAR1, PLCB1, PDGFC, PLCE1</i>

Supplementary Table 7. Single cell invasiveness of the melanoma cell line pairs revealed by Matrigel invasion assays.

Pair no.	Cell line	Type	Avg. no of invasive cells ¹	±SD ²
1	WM983A	primary	4.7	2
	WM983B	lymph node	3.3	2.4
2	WM278	primary	0	0
	WM1617	lymph node	0	0
3	WM115	primary	0	0
	WM266-4	cutaneous	0	0
4	WM793B	primary	1.5	0.8
	1205Lu	lung	33	2.5

¹average of three independent experiments; ²standard deviation

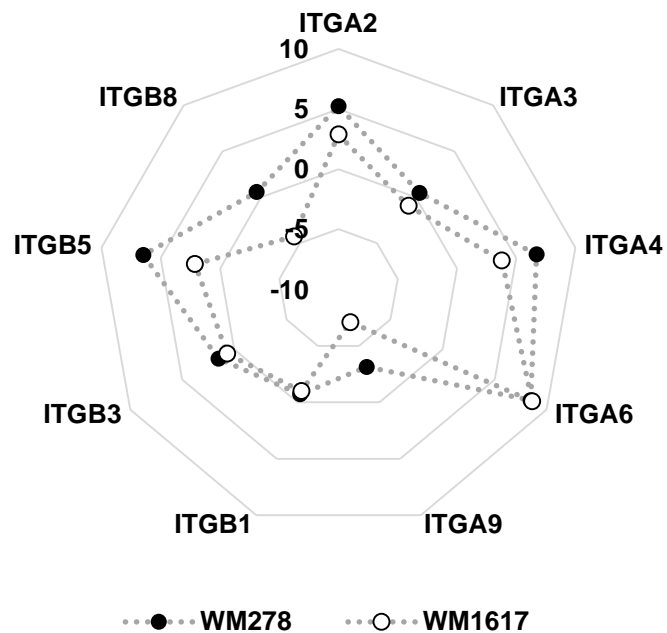
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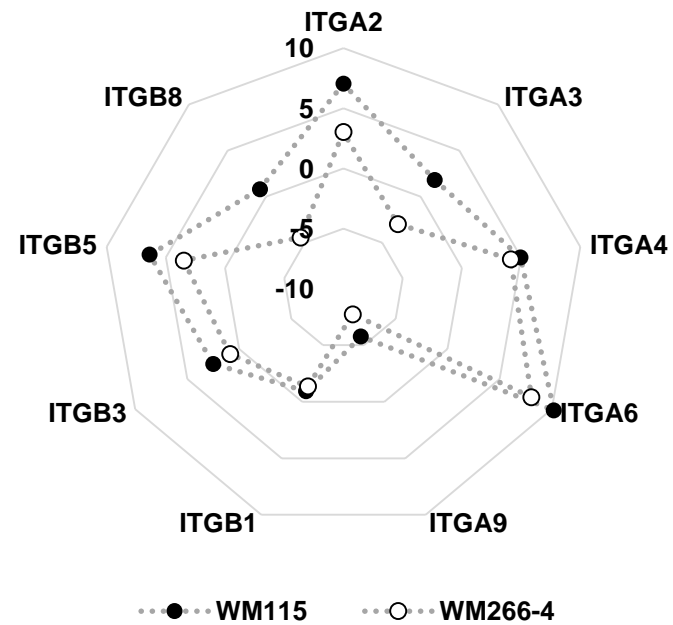
B

	GO ID	GO Pathway Name	P-value	No. of Genes Included
1	GO:0050839	cell adhesion molecule binding	1.25E-10	21
2	GO:0042605	peptide antigen binding	6.70E-10	10
3	GO:0005178	integrin binding	4.46E-08	14
4	GO:0050840	extracellular matrix binding	9.10E-06	8
5	GO:0003823	antigen binding	9.37E-06	11
6	GO:0042277	peptide binding	1.59E-05	16
7	GO:0033218	amide binding	2.62E-05	16

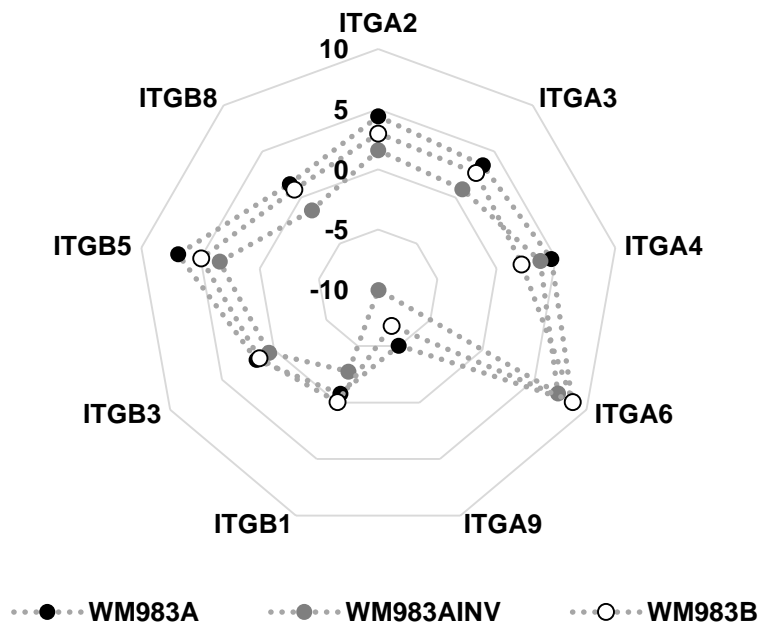
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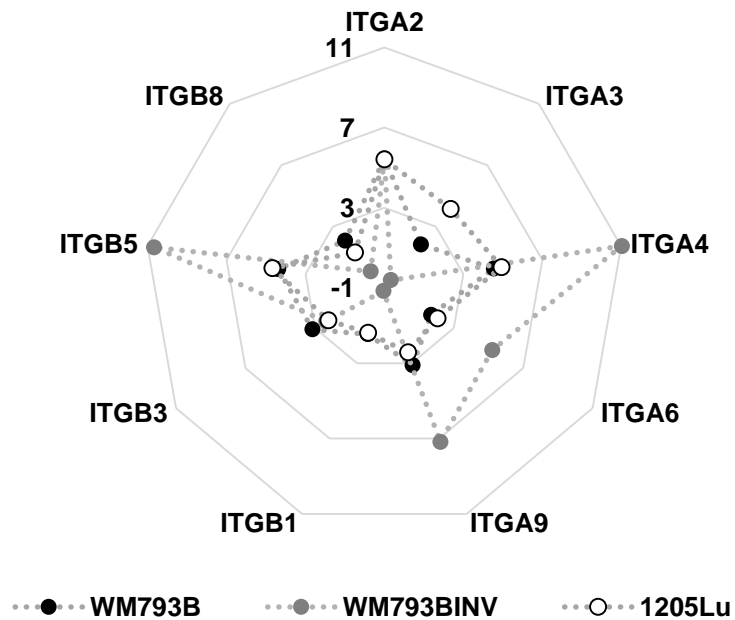
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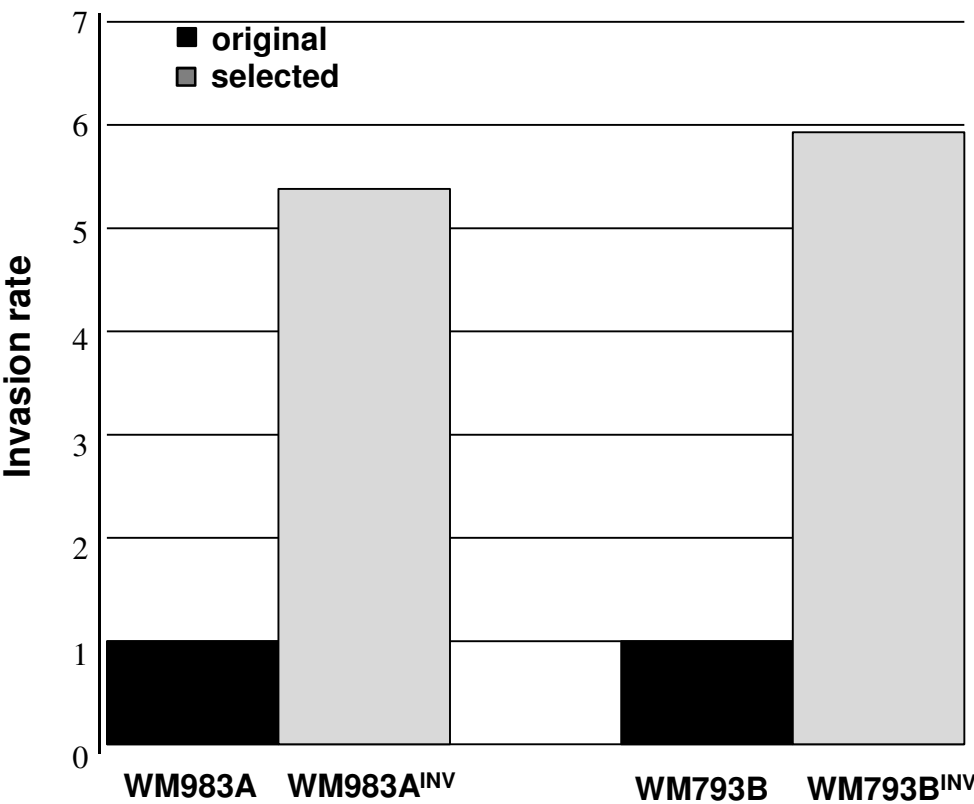
C



D



Supplementary Figure 3



Ratio	ITGA2	ITGA3	ITGA4	ITGA6	ITGA9	ITGB1	ITGB3	ITGB5	ITGB8
WM983A ^{INV} / WM983A	0.14	0.16	0.53	0.39	0.03	0.25	0.44	0.09	0.14
WM793B ^{INV} / WM793B	1.01	0.20	90.95	11.48	17.16	0.20	0.58	78.91	0.25