A plasma-derived extracellular vesicle mRNA classifier for the detection of breast cancer

Geng-Xi Cai^{1,2#^}, Li Lin^{3#}, Xiang-Ming Zhai^{3#}, Zhi-Wei Guo³, Ying-Song Wu³, Guo-Lin Ye², Qing Liu², Lu-Shi Chen², Guan-Yu Xing², Qiao-Hong Zhao², Li-Ling Tang², Shun-He Mai², Bo-Jian Ye²

¹Breast Tumor Center, Sun Yat-Sen Memorial Hospital, Sun Yat-Sen University, Guangzhou, China; ²Department of Breast Surgery, The First People's Hospital of Foshan, Foshan, China; ³Key Laboratory of Antibody Engineering of Guangdong Higher Education Institutes, School of Laboratory Medical and Biotechnology, Southern Medical University, Guangzhou, China

Contributions: (I) Conception and design: GX Cai; (II) Administrative support: GX Cai; (III) Provision of study materials or patients: GL Ye, Q Liu, LS Chen, GY Xing, QH Zhao, LL Tang, SH Mai, BJ Ye; (IV) Collection and assembly of data: Q Liu, LS Chen, GY Xing, QH Zhao, LL Tang, SH Mai, BJ Ye; (V) Data analysis and interpretation: L Lin, XM Zhai, GL Ye, Q Liu, LS Chen, GY Xing, QH Zhao, LL Tang, SH Mai, BJ Ye, ZW Guo, YS Wu; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

[#]These authors contributed equally to this work.

Correspondence to: Geng-Xi Cai. Sun Yat-Sen Memorial Hospital, Sun Yat-Sen University, 107 West Yanjiang Road, Guangzhou 510120, China; The First People's Hospital of Foshan, 81 North Lingnan Avenue, Foshan 528000, China. Email: caigengxi2021@126.com.

Background: According to the global cancer burden data released in 2020, breast cancer (BC) has become the most common cancer in the world. Similar to those of other cancers, the present methods used in clinic for diagnosing early BC are invasive, inaccurate, and insensitive. Hence, new non-invasive methods capable of early diagnosis are needed.

Methods: We applied next-generation sequencing and analyzed the messenger RNA (mRNA) profiles of plasma extracellular vesicles (EVs) derived from 14 BC patients and 6 patients with benign breast lesions. We used 3 regression models, namely support vector machine (SVM), linear discriminate analysis (LDA), and logistic regression (LR), to develop classifiers for use in making predictive BC diagnoses; and used 259 plasma samples, including those obtained from 144 patients with BC, 72 patients with benign breast lesions, and 43 healthy women, which were divided into training groups and validation groups to verify their performances as classifiers by quantitative reverse transcription polymerase chain reaction (RT-qPCR). The area under the curve (AUC) and accuracy, sensitivity, and specificity of the classifiers were cross-validated with the leave-1-out cross-validation (LOOCV) method.

Results: Among all combinations assessed with the 3 different regression models, an 8-mRNA combination, named EXOB_{mRNA}, exhibited high performance [accuracy =71.9% and AUC =0.718, 95% confidence interval (CI): 0.652 to 0.784] in the training cohort after LOOCV was performed, showing the largest AUC in the SVM model. The mRNAs in EXOB_{mRNA} were HLA-DRB1, HAVCR1, ENPEP, TIMP1, CD36, MARCKS, DAB2, and CXCL14. In the validation cohort, the AUC of EXOB_{mRNA} was 0.737 (95% CI: 0.636 to 0.837). In addition, gene function and pathway analyses revealed that different levels of gene expression were associated with cancer.

Conclusions: We developed a high-performing predictive classifiers including 8 mRNAs from plasma extracellular vesicles for diagnosing breast cancer.

Keywords: Breast cancer (BC); messenger RNAs (mRNAs); extracellular vesicles (EVs); diagnosis; predictive classifier

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[^] ORCID: 0000-0003-0575-4314.

Introduction

According to the latest global cancer burden data released by the World Health Organization (WHO) in 2020, the number of new cases of breast cancer (BC) has increased rapidly, replacing lung cancer as the most common cancer, and comprising 11.7% of all cancer cases. Among women, BC is the most frequently diagnosed cancer, accounting for approximately 25% of cancer cases and is the main cause of cancer death (1). Similar to other types of cancer, early diagnosis can reduce the incidence and mortality rates of BC, and is the key to improving the survival rate. Therefore, early diagnosis of BC has become an important aspect in the treatment of BC.

In various platforms, imaging techniques are major diagnostic methods and include ultrasound scanning, mammography, magnetic resonance imaging (MRI), and positron-emission tomography (PET), which can provide valuable data for the treatment of BC patients. However, some of these techniques are expensive, lack sensitivity for detecting early BC, and/or expose the patient to radiation, which adds an extra risk factor. In addition, some of the most studied and established BC biomarkers, such as CEA, CA125, and CA15-3, have been used to detect and monitor the diagnosis of BC in patients; however, low sensitivity limits their applications in early BC detection (2). Moreover, the currently available diagnostic technologies for use with BC have certain limitations, and the probability of false-positive results is 20–50% (3). Therefore, there is an urgent need for non-invasive methods that can more sensitively and specifically identify BC in the early stage.

Extracellular vesicles (EVs) produced by cells are mainly divided into three types according to their size and biogenesis: exosomes (40–200 nm), microvesicles (200–1,000 nm) and apoptotic bodies (500–2,000 nm) (4). EVs play an important role in breast physiology and pathophysiology including carcinogenesis, tumor progression, molding the tumor microenvironment, and immune modulation. Exosomes, as a class of EVs, are nano-vesicles related to the physiologic regulation of breast development (such as lactation), but they are also significant mediators of breast tumors, endowing them with great potential as new molecular markers for the diagnosis and prognosis of BC (5). Exosomes are considered to be important mediators of cell-to-cell communication, through the horizontal transfer of bioactive substances, such as proteins (6), messenger RNA (mRNA) and non-coding RNA (7). Considerable evidence has suggested that mRNAs enriched in serum exosomes can

be effectively internalized recipient cells (8,9). Therefore, the mRNA in exosomes is a potential biomarker for use in liquid biopsy, and the use of exosomal profiling without tissue has obvious prospects for the early diagnosis of diseases. Up to now, there is no research on developing BC diagnosis model by detecting multiple plasma-derived EV mRNAs.

In this study, we exploited a non-invasive method for the diagnosis of BC. First, we employed next-generation sequencing to determine the RNA profiles of plasma EVs derived from 14 patients with BC and 6 patients with benign breast lesions serving as controls. Next, we compared these RNA profiles to identify the mRNAs of plasma EVs at significantly different levels. Finally, we developed predictive classifiers with multiple machine learning models to discriminate patients with BC from individuals without cancer. In summary, our study may provide some new suggestions for the diagnosis of BC.

We present the following article in accordance with the STARD reporting checklist (available at <https://dx.doi.org/10.21037/gs-21-275>).

Methods

Sample characteristics

A total of 259 plasma samples were derived from 3 groups of participants enrolled at The First People's Hospital of Foshan, including 144 with BC, 72 benign with breast lesions, and 43 healthy women. All the plasma samples of cancer patients were prospectively collected during the discovery stage and before cancer therapy was initiated. The plasma samples of the discovery cohort were prospectively collected between January 2018 and July 2018. The samples comprising the training and validation cohorts were prospectively collected between August 2018 and May 2019. With the informed consent of all participants, all plasma samples were collected for research according to the protocols approved by the Ethics Committee of the First People's Hospital of Foshan (ID: L[2021]-7). All procedures performed in this study involving human participants were in accordance with the Declaration of Helsinki (as revised in 2013). Details regarding the clinical information of the participants involved in this study are listed in [Table S1](#).

RNA isolation from Plasma EVs

Total RNA was isolated using an exoRNeasy Serum/Plasma

Maxi Kit (Qiagen, Valencia, CA, USA) according to the manufacturer's protocol. We purified exosomes and other EVs and isolated total vesicular RNA, including mRNA, non-coding RNA, miRNA and other small RNAs, from 2–4 mL serum. In brief, the plasma was prefiltered, then was mixed with 2× binding buffer. The mixture is added to the exoEasy membrane affinity to bind the EVs to the membrane. After centrifugation, the wash buffer was added to wash off non-specific material in the column. After enriching EVs, QIAzol was added to the column to lyse the vesicles and chloroform was added to the lysate collected after centrifugation. The aqueous phases were recovered and mixed with ethanol, and the sample-ethanol mixture is added to the RNeasy MinElute spin column and centrifuged. Wash the column with buffer RWT, then wash twice with buffer RPE. And finally elute RNA in water.

Library preparation and next-generation sequencing

A high-throughput sequencing service, transcriptome high-throughput sequencing, and subsequent bioinformatics analysis were provided by Cloud-Seq Biotech (Shanghai, China). Briefly, total RNA was used to remove ribosomal RNA (rRNA) prior to the construction of the RNA-seq libraries with Ribo-Zero rRNA Removal Kits (Illumina, San Diego, CA, USA) following the manufacturer's instructions. The RNA libraries were prepared using a TruSeq Stranded Total RNA Library Prep Kit (Illumina) with rRNA-depleted RNAs following the manufacturer's instructions. A BioAnalyzer 2100 system (Agilent Technologies, Santa Clara, CA, USA) was used to quantify and control the quality of the libraries. According to the manufacturer's instructions, 10 pM libraries were denatured as single-stranded DNA molecules, captured in Illumina flow cells, and amplified into clusters *in situ*. Finally, each nucleic acid sequence was sequenced for 150 cycles on an Illumina HiSeq Sequencer.

Data analysis of RNA-sequencing

Paired-end reads were obtained from an Illumina HiSeq 4000 sequencer, and quality control was performed by Q30. Low-quality reads were filtered by Cutadapt software (v1.9.3) after 3' adaptor trimming (9). The high-quality trimmed reads were used to analyze mRNAs and were aligned to the human reference genome (UCSC hg19) using HISAT2 software v2.0.4 (<http://www.ccb.jhu.edu/software/hisat/index.shtml>) (10). The FPKM was obtained by using

Cuffdiff software (v2.2.1, in the Cufflinks package) (10) and used for the mRNA expression profiles as guided by the Ensembl gtf gene annotation file. Then, fold change and P value were determined based on the FPKM to identify the differentially expressed mRNAs. We performed GO and pathway enrichment analyses with the clusterProfiler package on the mRNAs expressed at differential levels.

Quantitative real-time polymerase chain reaction

Complementary DNA was synthesized using a PrimeScript RT reagent Kit (Takara, Bio Inc., Kusatsu, Shiga, Japan) after RNA isolation. mRNA quantification was obtained with qPCR using SYBR Premix Ex Taq (Takara, Bio Inc.) and an ABI7500 Real-Time PCR system (Applied Biosystems, Foster City, CA, USA) with the primers and complementary DNA (cDNA) template recommended by the manufacturer. The primers are listed in Table S2.

Classifier construction

To develop classifiers for BC diagnosis, 13 candidate mRNAs with significantly elevated levels in BC patients were selected and assessed using quantitative real-time polymerase chain reaction (qRT-PCR). A total of 259 participants were divided into training and validation cohorts at a ratio of 7:3. The training cohort contained 182 participants, including 101 patients with BC and 81 without cancer serving as controls (51 individuals with benign breast lesions and 30 healthy women). The validation cohort contained 77 participants, including 43 patients with BC and 34 without cancer serving as controls (21 individuals with benign breast lesions and 13 healthy women). To construct predictive classifiers that can be used to differentiate individuals with BC from those serving as controls, we used 3 regression models: support vector machine (SVM), logistic regression (LR), and linear discriminate analysis (LDA). As numerous studies have reported that discrete data may improve classifier performance (11), continuous variables were discretized before classifier construction according to the optimal cut-off point, which was selected according to the maximum value of (sensitivity + specificity)/2 in the training cohort. Then, the continuous value was set to 1 when it was higher than the corresponding optimal cut-off for each subject; otherwise, it was set to 0 (Table S3). Using the stepwise method, the optimal classifier with the largest AUC was selected. The leave-1-out cross-validation (LOOCV) method was used to estimate the robustness and

prediction error of the selected classifiers. In the validation cohort, the relative levels of the mRNAs in the selected classifiers were determined, and the predictive efficacy of the classifiers was evaluated in the test cohort.

Statistical analysis

We used R software (version 3.4; <https://www.R-project.org/>) for statistical analyses. Mann-Whitney U test or Kruskal-Wallis test was used to compare the differences in patient characteristics in 2 or more groups, respectively, and Pearson chi-square was used to compare sample compositions. The diagnostic accuracy of the candidate mRNAs or their combinations was evaluated by receiver operating characteristic (ROC) curve analysis with the area under the ROC curve (AUC). A P value <0.05 was considered significant.

Results

Significantly differential mRNAs identification

To identify different levels of plasma EV mRNAs between patients with BC and those without cancer, we first generated the mRNA profiles of the exosomes obtained from the plasma of 14 participants with BC and 6 with benign lesions during the discovery stage. We found that the levels of 1,156 mRNAs were significantly different, including 183 mRNAs at higher levels and 973 mRNAs at lower levels (*Figure 1A*, *Table S4*, $|\log_2\text{-fold change}| > 2$, P value <0.05). By implementing unsupervised clustering analysis, we found distinct patterns between the participants with and without cancer, and the samples in each group clustered together in separate groups (*Figure 1B*), which indicated the potential of using mRNAs from EVs for screening BC.

Gene function and pathway enrichment analyses

To reveal the potential roles of mRNAs as indicated by their different levels in cases of tumorigenesis, we performed a gene function enrichment analysis. The results indicated that the terms associated with these mRNAs were enriched in multiple processes, such as multiple biological pathways and processes related to immunity (*Figure 1C*). For example, HCK participates in a variety of biological processes by mediating immune response regulation signaling pathways and multiple signaling pathways [including epithelial to mesenchymal transition (EMT), the PI3K/AKT signaling pathway, and focal adhesion] in BC (12). In addition, AXL

is involved in a variety of processes that promote tumor formation and metastasis, and is considered an effective biomarker for BC. Especially in triple negative (TN)BC tumors, AXL is considered a key factor in promoting EMT associated with mesenchymal and invasive phenotypes (13). In addition, we performed a pathway enrichment analysis and found that some of the mRNAs in BC are closely related to ribosomes (*Figure 1D*). These mRNAs may play important roles in the translation process.

Classifier construction

For clinical practice and detection convenience, we focused on the mRNAs of plasma EVs with elevated levels. According to fold change, the false discovery rate (FDR) value and mean levels, we selected 12 mRNAs for further qRT-PCR identification and predictive classifier construction. To develop predictive classifiers for BC diagnosis, the samples were split into training and validation cohorts. Using qRT-PCR, we assessed the relative levels of 12 mRNAs in the training group that were at higher levels in the 182 plasma samples obtained from 101 BC participants and 81 patients without cancer serving as controls (51 participants with benign breast lesions and 30 healthy women). We used 3 regression models, SVM, LDA, and LR, to construct mRNA classifiers that could be used to differentiate individuals with BC from those without cancer serving as controls. The AUC and accuracy, sensitivity, and specificity of the classifiers were cross-validated with the LOOCV method (*Figure 2*). Among all combinations assessed with the 3 different regression models, an 8-mRNA combination, named EXOB_{mRNA}, achieved high performance [AUC =0.718, 95% confidence interval (CI): 0.652 to 0.784, and accuracy =71.9%] in the training cohort after LOOCV was performed, showing the largest AUC with the SVM model (*Figure 2A*). The mRNAs in EXOB_{mRNA} were HLA-DRB1, HAVCR1, ENPEP, TIMP1, CD36, MARCKS, DAB2, and CXCL14. Then, the performance of EXOB_{mRNA} was subsequently studied and verified in the validation cohort. In the validation cohort, the AUC for the EXOB_{mRNA} group was 0.737 (95% CI: 0.636 to 0.837, *Figure 2E,F*). In contrast with that of the training cohort, the AUC of the validation cohort was similar to that of the training cohort (P=0.764).

Discussion

Our study found 1,156 mRNAs at different levels between

Figure 1 mRNA with differential levels between breast cancer and non-cancer controls. (A) Volcano plots of the mRNA profiles of plasma EVs derived from 14 patients with BC and 6 without cancer ($|\log_2\text{fold change}| \geq 2$ and $\text{FDR} \leq 0.2$). (B) Heat map of the mRNAs with differential read coverages. (C) Top 10 enriched GO biological processes. (D) Top 10 enriched pathway analysis. EVs, extracellular vesicles; mRNA, messenger RNA; BC, breast cancer; GO, Gene Ontology; FDR, false discovery rate.

14 participants with BC and 6 participants with benign breast lesions by comparing the mRNA profiles using next-generation sequencing. In addition, gene function and pathway analyses showed that the genes expressed at differential levels were related to cancer. Finally, we developed predictive classifiers to assess their potential for BC diagnosis, and we found that the AUC of the EXOB_{mRNA}

group was 0.724 (0.669 to 0.779).

Our method is non-invasive, and detection is not confounded by the heterogeneity of a tumor. At the same time, it does not expose patients to the effects of radiation and shows high sensitivity and specificity, highlighting great potential for use in the early screening of BC. However, this method has certain limitations. The cost of extracting

Figure 2 The performance of predictive classifiers. The roc curves of the predictive classifiers in the training (A), testing (C), and all (E) cohorts. The predictive efficacy of the classifiers the training (B), testing (D), and all (F) cohorts. The performance of classifiers in training cohort was cross-validated using LOOCV. P = the P value of the comparison of 2 AUCs. LOOCV, leave-1-out cross-validation; ROC, receiver operating characteristic; Acc, accuracy; Sen, sensitivity; Spe, specificity; AUC, area under the curve.

exosomes is still very high, kits are expensive, and an ultracentrifuge is often lacking in the clinic; therefore, this method is still difficult to use extensively in the clinic. In addition, the classifier model needs to be further optimized, and the biological function of each mRNA and the relationship between them need to be further studied. With optimization and further characterization, the possibility that this method will be used in clinical applications will be increased.

We searched the literature for the genes that we identified and discovered that many of the mRNAs and their translated proteins are closely related to BC (14). For instance, DAB2 can be used as a novel marker and therapeutic target for BC (15), MARCKS is closely related to poor prognosis of BC, and knockdown of ENPEP can inhibit the invasion of BC (16). In addition, there have been many research reports on these genes in other tumors. First, they can be used as tumor risk genes or prognostic genes, and their expression levels in tumor patients are significantly increased. For example, HLA-DRB1 is considered a risk gene for cervical cancer (17), and TIMP1 may be related to the metastasis of uveal melanoma (UM), possibly playing an important role in identifying patients with high metastatic risk and predicting the prognosis of UM (18). Second, these

genes are important for the occurrence and development of tumors. For instance, CD36 upregulates DEK transcription and promotes cell migration and invasion and EMT in gastric cancer (19). Overexpression of HAVCR1 can reduce cell adhesion and invasion in colorectal cancer (8). Finally, these genes can play important roles in tumor immunity and the tumor microenvironment and are potential targets for future immunotherapy. For instance, the chemokine CXCL14 is often dysregulated in several types of cancer, and its destructive effect limits key antitumor immune regulator function and is closely related to poor patient prognosis.

Therefore, we expect that the biological functions and characteristics of these mRNAs can be combined to construct different classifiers for use in early tumor diagnosis or subtype classification of tumors.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. With the informed consent of all participants, all plasma samples were collected for research according to the protocols approved by the Ethics Committee of the First People's Hospital of Foshan (ID: L[2021]-7). All procedures performed in this study involving human participants were in accordance with the Declaration of Helsinki (as revised in 2013).

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Table S1 Clinical characteristics of the patients and control individuals in this study

	Breast cancer pat (n=144)	Benign breast lesion (n=72)	Healthy women (n=43)
Age			
<40	27 (18.75%)	45 (62.5%)	25 (58.1%)
>40	117 (71.25%)	27 (37.5%)	18 (41.9%)
TNM stage			
0	16 (11.11%)		
I	41 (28.47%)		
II	70 (48.61%)		
III	14 (9.72%)		
IV	3 (2.09%)		
Molecular Subtype			
ER/PR+ Her2+	94 (65.28%)		
ER/PR+ Her2-	19 (13.19%)		
ER/PR- Her2+	26 (18.06%)		
ER/PR- Her-	5 (3.47%)		

Data are n, n (%). Benign breast= patients with benign breast lesions. ER= estrogen receptor. PR= progesterone receptor. Her2= human epidermal growth factor receptor-2.

Table S2 Primers of the candidate mRNAs

ID	Gene name	Direction	Sequence
ENSG00000196126	HLA-DRB1	F	CGGGGTTGGTGAGAGCTTC
ENSG00000196126	HLA-DRB1	R	AACCACCTGACTTCAATGCTG
ENSG00000113249	HAVCR1	F	TGGCAGATTCTGTAGCTGGTT
ENSG00000113249	HAVCR1	R	AGAGAACATGAGCCTCTATTCCA
ENSG00000101336	HCK	F	AGGGCTACATCCCAAGCAAC
ENSG00000101336	HCK	R	GGTCTCGCTATCCCGGATCA
ENSG00000159189	C1QC	F	AGGATGGGTACGACGGACTG
ENSG00000159189	C1QC	R	GTAAGCCGGTTCTCCCTTC
ENSG00000138792	ENPEP	F	CTTGACCAGATCGTGTGACTC
ENSG00000138792	ENPEP	R	GGCAGTCGAAAGTTTTTCCAC
ENSG00000102265	TIMP1	F	AGAGTGTCTGCGGATACTTCC
ENSG00000102265	TIMP1	R	CCAACAGTGTAGGTCTTGGTG
ENSG00000135218	CD36	F	CTTTGGCTTAATGAGACTGGGAC
ENSG00000135218	CD36	R	GCAACAAACATCACCACACCA
ENSG00000167601	AXL	F	CCGTGGACCTACTCTGGCT
ENSG00000167601	AXL	R	CCTTGGCGTTATGGGCTTC
ENSG00000162692	VCAM1	F	CAGTAAGGCAGGCTGTAAAAGA
ENSG00000162692	VCAM1	R	TGGAGCTGGTAGACCCTCG
ENSG00000277443	MARCKS	F	AGCCCGGTAGAGAAGGAGG
ENSG00000277443	MARCKS	R	TTGGGCGAAGAAGTCGAGGA
ENSG00000153071	DAB2	F	GTAGAAACAAGTGCAACCAATGG
ENSG00000153071	DAB2	R	GCCTTTGAACCTTGCTAAGAGA
ENSG00000145824	CXCL14	F	CGCTACAGCGACGTGAAGAA
ENSG00000145824	CXCL14	R	GTTCCAGCGTTGTACCAC
ENSG00000124564	SLC17A3	F	TTCCGGCTATATCACAGCAACT
ENSG00000124564	SLC17A3	R	AAAACCTGGAATACCTTGGAGCAA

F, forward; R, reverse.

Table S3 The information of the candidate mRNAs

ID	Gene symbol	Threshold
ENSG00000196126	HLA-DRB1	0.0761
ENSG00000113249	HAVCR1	0.0087
ENSG00000101336	HCK	0.1857
ENSG00000159189	C1QC	0.0320
ENSG00000138792	ENPEP	0.8527
ENSG00000102265	TIMP1	4.0924
ENSG00000135218	CD36	0.1564
ENSG00000167601	AXL	0.5521
ENSG00000162692	VCAM1	0.3120
ENSG00000277443	MARCKS	23.635
ENSG00000153071	DAB2	0.3238
ENSG00000145824	CXCL14	1.5475

Threshold, threshold for discretization.

Table S4 mRNAs with significantly different levels

Gene name	Cancer_FPKM	Non-cancer_FPKM	log2(fold change)	FDR	Trend
<i>MGST1</i>	34.5897	7.7859	2.15141	0.04090	UP
<i>IL32</i>	115.7640	26.1449	2.14658	0.00387	UP
<i>TYROBP</i>	74.3656	6.6454	3.48420	0.05503	UP
<i>NR1H4</i>	21.5002	4.9453	2.12022	0.02336	UP
<i>CD74</i>	1,299.6700	234.3350	2.47150	0.00387	UP
<i>BIRC3</i>	36.1028	5.9446	2.60245	0.01979	UP
<i>ABCC2</i>	17.1771	3.3030	2.37864	0.03281	UP
<i>TYMP</i>	139.0980	18.6753	2.89690	0.00387	UP
<i>VIM</i>	774.3680	129.8420	2.57626	0.17049	UP
<i>RNASET2</i>	160.0510	32.7181	2.29037	0.03042	UP
<i>TNFRSF1B</i>	34.0887	5.0395	2.75794	0.04966	UP
<i>TMSB10</i>	1,215.1100	171.8940	2.82149	0.04691	UP
<i>CP</i>	194.8690	10.1819	4.25842	0.00387	UP
<i>COL23A1</i>	45.6279	4.1415	3.46168	0.02953	UP
<i>CYBA</i>	223.5060	36.4210	2.61747	0.00387	UP
<i>SPAG4</i>	21.7187	4.3063	2.33441	0.05329	UP
<i>VMP1</i>	245.0230	49.6675	2.30255	0.01081	UP
<i>SCARB1</i>	52.7990	8.6930	2.60258	0.00387	UP
<i>CST7</i>	7.2377	1.1294	2.67994	0.08862	UP

Table S4 (continued)

Table S4 (continued)

Gene name	Cancer_FPKM	Non-cancer_FPKM	log2(fold change)	FDR	Trend
<i>LRP2</i>	121.4210	26.8485	2.17711	0.00387	UP
<i>SLC13A1</i>	10.0110	1.1220	3.15748	0.00880	UP
<i>PTHLH</i>	35.8913	8.1662	2.13590	0.13504	UP
<i>RGS1</i>	92.5057	13.0560	2.82483	0.00387	UP
<i>LYZ</i>	74.2059	6.6488	3.48038	0.15323	UP
<i>ANGPT2</i>	16.7873	4.1744	2.00772	0.18836	UP
<i>TREM2</i>	12.1972	2.2135	2.46214	0.18519	UP
<i>SCD</i>	38.7496	4.4269	3.12981	0.00387	UP
<i>HSD3B7</i>	33.1037	5.7032	2.53715	0.04691	UP
<i>HMOX1</i>	65.8378	7.2898	3.17497	0.00655	UP
<i>APOL1</i>	64.0178	10.8307	2.56335	0.00655	UP
<i>TRIB3</i>	11.4874	2.3127	2.31239	0.03797	UP
<i>HCK</i>	13.5973	1.5610	3.12280	0.00387	UP
<i>SAMHD1</i>	32.0403	6.2232	2.36416	0.13040	UP
<i>PGK1</i>	376.8790	81.8157	2.20365	0.03857	UP
<i>TIMP1</i>	195.7460	30.0243	2.70478	0.05077	UP
<i>FLT1</i>	90.9207	12.1466	2.90406	0.01399	UP
<i>SLC39A14</i>	102.0160	18.0885	2.49565	0.00387	UP
<i>IL27RA</i>	6.5332	1.6080	2.02254	0.01847	UP
<i>RPS19</i>	873.0180	210.2250	2.05408	0.01399	UP
<i>TFEC</i>	20.7651	4.8100	2.11004	0.00387	UP
<i>SERPINE1</i>	50.3593	4.6348	3.44167	0.00387	UP
<i>DDX58</i>	24.4537	4.3609	2.48735	0.04691	UP
<i>CUBN</i>	80.2910	16.9641	2.24275	0.02839	UP
<i>CCND1</i>	206.9760	41.8340	2.30672	0.00387	UP
<i>VWF</i>	122.6810	14.2104	3.10990	0.13066	UP
<i>OAS2</i>	48.1845	8.3937	2.52119	0.05784	UP
<i>GAPDH</i>	950.8090	191.5090	2.31175	0.01081	UP
<i>SOD2</i>	404.4800	75.9547	2.41286	0.00387	UP
<i>VEGFA</i>	630.8220	134.3110	2.23165	0.00387	UP
<i>LOX</i>	72.3050	4.1616	4.11887	0.00387	UP
<i>SPARC</i>	770.9060	140.2420	2.45864	0.00387	UP
<i>HAVCR1</i>	38.1773	2.7356	3.80277	0.00387	UP
<i>CDH6</i>	112.4060	18.9697	2.56694	0.00387	UP
<i>HHLA2</i>	22.8002	2.3831	3.25814	0.00387	UP
<i>FN1</i>	267.0040	65.2055	2.03379	0.00387	UP
<i>STAT1</i>	178.0350	41.4442	2.10292	0.03493	UP
<i>CD2</i>	10.8305	2.2044	2.29662	0.04758	UP
<i>SPP1</i>	812.8540	90.5374	3.16641	0.00387	UP
<i>NEK6</i>	47.4071	9.6699	2.29353	0.00387	UP
<i>IFIT3</i>	43.8293	8.9774	2.28752	0.16260	UP
<i>TGFBI</i>	373.7460	43.1515	3.11457	0.00387	UP
<i>TNFSF10</i>	98.9841	21.1184	2.22869	0.00387	UP
<i>CXCR4</i>	50.6256	10.3437	2.29111	0.00387	UP
<i>PRDX4</i>	55.1117	13.1479	2.06752	0.07979	UP
<i>F13A1</i>	36.1219	8.6722	2.05841	0.00655	UP
<i>SLC17A3</i>	101.0000	6.4453	3.96995	0.00387	UP
<i>SLC17A1</i>	27.5621	4.5971	2.58389	0.05285	UP
<i>C3</i>	378.1060	25.2771	3.90289	0.00387	UP
<i>IFI6</i>	603.1450	34.4075	4.13171	0.04654	UP
<i>YEATS4</i>	5.6763	1.2113	2.22844	0.17163	UP
<i>KDR</i>	55.5592	13.3704	2.05498	0.01560	UP
<i>BBOX1</i>	43.8473	10.6625	2.03994	0.07588	UP
<i>CD68</i>	57.9979	8.7557	2.72771	0.10405	UP
<i>EGLN3</i>	155.8510	18.4840	3.07582	0.00387	UP
<i>APOE</i>	686.9700	140.1040	2.29375	0.00387	UP
<i>ACE2</i>	20.3463	4.0708	2.32137	0.06906	UP
<i>PNCK</i>	100.9930	21.3009	2.24527	0.04379	UP
<i>IDO1</i>	14.0941	3.4760	2.01960	0.13096	UP
<i>ACLY</i>	80.4375	18.0181	2.15842	0.04758	UP
<i>TOP2A</i>	5.1601	1.2244	2.07535	0.02109	UP
<i>LRRC41</i>	71.1989	13.7816	2.36911	0.00655	UP
<i>TRIM22</i>	131.7450	27.5914	2.25546	0.04889	UP
<i>IGJ</i>	125.3110	23.6890	2.40322	0.16472	UP
<i>XAF1</i>	174.3120	34.6746	2.32973	0.00387	UP
<i>EPSTI1</i>	43.5537	7.2816	2.58048	0.02439	UP
<i>POSTN</i>	70.4546	7.0390	3.32325	0.06247	UP
<i>LDHA</i>	334.3750	61.5788	2.44096	0.01399	UP
<i>CYP2J2</i>	22.2407	3.5815	2.63457	0.04691	UP
<i>HAVCR2</i>	37.5046	5.5127	2.76624	0.01399	UP
<i>CD36</i>	48.2074	7.1444	2.75436	0.00387	UP
<i>UGT2A3</i>	28.1931	4.1780	2.75446	0.00387	UP
<i>HILPDA</i>	96.2785	10.8342	3.15161	0.05609	UP

Table S4 (continued)

Table S4 (continued)

Gene name	Cancer_FPKM	Non-cancer_FPKM	log2(fold change)	FDR	Trend
AGT	22.2476	4.7454	2.22907	0.01241	UP
LCP1	60.6637	14.3829	2.07648	0.00387	UP
MYC	29.9008	7.0586	2.08273	0.01081	UP
DDX60	27.9295	5.8466	2.25612	0.16313	UP
MMP7	200.7670	16.7297	3.58504	0.11052	UP
IFI44L	117.8210	15.4851	2.92764	0.00387	UP
IFI44	105.6320	15.0976	2.80666	0.00387	UP
ENPEP	82.4968	8.7917	3.23012	0.00387	UP
CLEC18B	29.7152	6.4688	2.19964	0.05503	UP
IFITM3	251.9190	58.0880	2.11665	0.07426	UP
SLC2A5	52.8797	8.1676	2.69473	0.00387	UP
RGS5	601.9250	77.4167	2.95887	0.06298	UP
RIT1	25.8044	5.7346	2.16986	0.01712	UP
DEGS1	38.0363	8.7927	2.11300	0.10001	UP
NAT8	117.6200	23.4551	2.32615	0.00387	UP
IGFBP3	514.7070	95.0231	2.43740	0.00387	UP
TMEM27	26.8905	4.2198	2.67184	0.16585	UP
PLIN2	243.6360	15.5610	3.96872	0.00387	UP
ADM	112.9750	23.0466	2.29338	0.01712	UP
PDK1	31.2311	7.3189	2.09328	0.04889	UP
GJA1	34.8822	7.6521	2.18856	0.00387	UP
PLOD2	97.0631	17.6757	2.45715	0.00880	UP
ENPP3	80.3724	1.4419	5.80067	0.00387	UP
SLC16A1	26.0676	5.6168	2.21444	0.01847	UP
SLC28A1	54.6315	11.5184	2.24579	0.04829	UP
ARSE	20.2463	3.9607	2.35384	0.00387	UP
MX1	144.4400	25.5713	2.49788	0.00387	UP
FCER1G	32.3932	6.3239	2.35680	0.17569	UP
C1QC	154.9240	20.7497	2.90040	0.00387	UP
CCDC58	13.5701	2.9137	2.21954	0.18766	UP
LY6E	166.3090	30.0716	2.46740	0.01399	UP
VCAM1	156.3420	19.3755	3.01240	0.00387	UP
CTSS	114.5150	13.3406	3.10164	0.06727	UP
DTX3L	24.3202	5.0667	2.26304	0.08130	UP
CTSB	321.0000	76.5537	2.06803	0.00387	UP
ABCA1	45.3039	10.2325	2.14647	0.00387	UP
CYBB	42.1811	5.3641	2.97519	0.09977	UP
CLDN2	33.5532	8.2297	2.02754	0.14757	UP
FOLR2	17.5791	4.1882	2.06945	0.01560	UP
C2	27.0740	5.6498	2.26065	0.00655	UP
B2M	3,895.9300	950.3010	2.03551	0.10296	UP
NNMT	356.3260	17.6845	4.33264	0.00387	UP
AXL	30.4549	5.9746	2.34976	0.00387	UP
SERPINF2	76.1275	13.5064	2.49477	0.03336	UP
ANGPTL4	152.3840	3.0577	5.63914	0.00387	UP
FTH1	771.5220	192.6340	2.00185	0.05193	UP
COL3A1	134.2320	30.8072	2.12339	0.03431	UP
SLC16A4	32.4636	7.2820	2.15642	0.05609	UP
LGALS9	41.0111	9.6804	2.08288	0.01399	UP
CD52	24.5403	1.8522	3.72788	0.11660	UP
CD14	81.9753	16.0484	2.35276	0.00387	UP
UGT2B7	64.1100	15.1784	2.07853	0.00387	UP
FGG	129.9220	4.8828	4.73380	0.00387	UP
FGA	87.4698	9.4040	3.21743	0.03135	UP
FGB	173.7940	8.5157	4.35111	0.00387	UP
SMPDL3A	21.0100	3.7245	2.49595	0.00387	UP
PARP14	87.4088	20.3591	2.10211	0.02109	UP
C1QB	203.3510	19.9941	3.34633	0.00387	UP
C1QA	161.5500	15.1561	3.41402	0.00387	UP
KCNE3	34.8466	8.2107	2.08545	0.02336	UP
BNIP3	78.9625	12.9485	2.60839	0.10042	UP
SAMD9L	34.4323	8.3936	2.03640	0.00387	UP
C5orf46	49.1221	4.4939	3.45032	0.18606	UP
HLA-DQB1	66.0857	3.7285	4.14768	0.02336	UP
TMEM45A	15.0556	3.7100	2.02081	0.12693	UP
HIST1H1B	39.8999	5.8602	2.76736	0.00387	UP
MAP7D2	19.7461	1.5418	3.67886	0.06906	UP
PROS1	27.4218	5.1654	2.40838	0.03573	UP
USP18	10.8937	2.0081	2.43957	0.00387	UP
NDUFA4L2	224.3770	31.0639	2.85262	0.01847	UP
IFITM1	184.1950	29.0650	2.66388	0.03281	UP
ISG15	202.5720	12.7281	3.99235	0.00387	UP
RAB42	13.4298	1.8708	2.84368	0.14176	UP

Table S4 (continued)

Table S4 (continued)

Gene name	Cancer_FPKM	Non-cancer_FPKM	log2(fold change)	FDR	Trend
HLA-DRB1	160.2480	9.2275	4.11823	0.00387	UP
AKR1C3	39.7805	9.0105	2.14237	0.01081	UP
HLA-DQA1	65.7906	3.6522	4.17104	0.10644	UP
HIST1H2AI	24.5722	1.3992	4.13436	0.11101	UP
SERPINA1	417.0610	46.2690	3.17214	0.00387	UP
NMB	11.7954	2.3717	2.31426	0.07136	UP
HIST1H4K	29.9046	3.4400	3.11989	0.15371	UP
HLA-DRB5	80.5012	4.9194	4.03247	0.00387	UP
FCGR3A	45.7923	7.9537	2.52540	0.01399	UP
HLA-DRA	501.8820	99.8957	2.32885	0.05503	UP
C4orf47	6.9326	1.2848	2.43190	0.09874	UP
CFI	101.4710	17.9410	2.49974	0.00387	UP
HLA-A	564.7830	135.6480	2.05782	0.06343	UP
IFI30	129.4920	18.5807	2.80098	0.01560	UP
HLA-DPA1	279.3960	48.7119	2.51997	0.03135	UP
HLA-B	1,034.6100	223.9470	2.20785	0.02109	UP
ECSCR	24.8675	2.8480	3.12622	0.13220	UP
IGLL5	29.8796	5.3009	2.49484	0.06906	UP
CYP26B1	3.0910	18.7295	-2.59918	0.01241	DOWN
SLC22A16	1.3694	13.3725	-3.28765	0.00655	DOWN
HOXA11	2.0416	8.7784	-2.10427	0.19448	DOWN
MPO	1.3813	6.9210	-2.32496	0.09227	DOWN
SOX8	1.0108	6.3433	-2.64969	0.04517	DOWN
YBX2	1.7081	7.5189	-2.13813	0.06153	DOWN
ABCC8	5.6162	30.5069	-2.44148	0.00387	DOWN
TAC1	1.2663	8.2021	-2.69542	0.08011	DOWN
DLX6	1.6756	11.0378	-2.71972	0.03737	DOWN
DNAH9	2.8928	12.4486	-2.10546	0.01081	DOWN
SCN4A	2.3984	22.0327	-3.19950	0.06454	DOWN
PAX6	4.1243	33.3219	-3.01424	0.00387	DOWN
DLEC1	1.8712	9.4119	-2.33049	0.05960	DOWN
CELSR3	1.6305	8.1060	-2.31366	0.03042	DOWN
HHATL	1.1667	12.4337	-3.41373	0.03336	DOWN
PRSS3	1.0359	17.7452	-4.09848	0.00387	DOWN
DPF1	1.3298	6.8195	-2.35844	0.03857	DOWN
SYT7	1.4839	9.2377	-2.63819	0.01081	DOWN
STMN4	1.6734	10.9329	-2.70782	0.01081	DOWN
SRCIN1	1.7379	8.0918	-2.21914	0.05960	DOWN
ATP1A2	4.7962	27.1310	-2.49997	0.01241	DOWN
PLEKHB1	5.9779	33.4537	-2.48444	0.00387	DOWN
CPS1	3.4790	25.2046	-2.85694	0.02225	DOWN
KCNG1	1.8623	8.4383	-2.17988	0.05193	DOWN
CYP46A1	2.1301	9.0161	-2.08162	0.00880	DOWN
RTN4R	1.6590	9.7312	-2.55234	0.02225	DOWN
MYO16	1.6216	12.5611	-2.95352	0.04758	DOWN
ZBPB	2.1409	13.8069	-2.68913	0.10405	DOWN
TG	2.8836	23.0669	-2.99988	0.00387	DOWN
LMO3	4.4808	26.2613	-2.55110	0.00387	DOWN
CBLN4	1.3598	6.7726	-2.31630	0.01081	DOWN
KCNH2	1.3715	8.1734	-2.57522	0.04013	DOWN
ITIH1	1.6599	10.5544	-2.66870	0.06678	DOWN
CAMK2B	1.9588	11.6774	-2.57568	0.00387	DOWN
PSD	2.3896	15.0884	-2.65859	0.02109	DOWN
RIMBP2	3.4553	16.2699	-2.23532	0.03857	DOWN
DGAT2	2.0967	10.8469	-2.37109	0.02109	DOWN
SEZ6	2.3938	26.9105	-3.49079	0.03281	DOWN
SLC6A16	1.4369	6.4578	-2.16807	0.02839	DOWN
AHRR	2.2393	10.1016	-2.17345	0.03655	DOWN
ATP2C2	2.6490	23.7868	-3.16663	0.00387	DOWN
SNCAIP	3.1894	18.9072	-2.56760	0.02109	DOWN
BCAS1	2.0446	18.0461	-3.14180	0.00387	DOWN
NTN1	1.1803	6.2401	-2.40248	0.01979	DOWN
ROPN1	1.6090	14.1842	-3.14001	0.01241	DOWN
SNAP91	1.1722	6.7117	-2.51750	0.00880	DOWN
STAG3	3.2438	18.7223	-2.52898	0.00387	DOWN
SYT1	1.6259	7.3649	-2.17942	0.01241	DOWN
REEP1	2.3510	9.7789	-2.05640	0.08263	DOWN
PITX1	2.1058	11.4884	-2.44777	0.10296	DOWN
SPTB	2.7678	14.2011	-2.35917	0.04187	DOWN
FGF10	1.2978	10.5327	-3.02080	0.16675	DOWN
FRMPD1	1.1134	5.5981	-2.32995	0.12207	DOWN
TRIP13	1.2535	7.4873	-2.57845	0.15824	DOWN
MYO3B	2.0613	9.1637	-2.15236	0.09102	DOWN

Table S4 (continued)

Table S4 (continued)

Gene name	Cancer_FPKM	Non-cancer_FPKM	log2(fold change)	FDR	Trend
ASIC4	1.1837	9.8864	-3.06211	0.00387	DOWN
SPEG	6.2169	32.2467	-2.37488	0.00387	DOWN
MOV10L1	1.5093	6.6611	-2.14185	0.05767	DOWN
PPP2R2C	1.8533	7.8806	-2.08823	0.02839	DOWN
SLC12A1	109.5020	529.6760	-2.27416	0.00387	DOWN
WSCD2	3.5772	15.9689	-2.15835	0.00387	DOWN
ADD2	1.9214	11.2586	-2.55083	0.00387	DOWN
CACNG5	1.7344	12.3678	-2.83405	0.16106	DOWN
AMPH	2.1427	10.3787	-2.27614	0.01560	DOWN
RBFOX1	1.3333	8.2257	-2.62512	0.00387	DOWN
MYH7B	2.8458	13.5848	-2.25507	0.06642	DOWN
TP73	2.1191	11.3227	-2.41767	0.03655	DOWN
KCNN2	1.4442	9.5661	-2.72762	0.00387	DOWN
TCF7	7.1703	31.8537	-2.15135	0.03493	DOWN
PKP1	2.3617	11.2197	-2.24816	0.03281	DOWN
PGR	1.7933	8.1755	-2.18868	0.00387	DOWN
SERTAD4	1.4107	7.1556	-2.34263	0.01241	DOWN
GRHL2	3.1650	15.9456	-2.33289	0.00880	DOWN
HAL	1.9254	16.5661	-3.10499	0.01241	DOWN
SLCO1A2	1.8682	9.5488	-2.35369	0.00387	DOWN
GCKR	1.4177	8.5367	-2.59013	0.13203	DOWN
IGSF9	1.1180	11.3487	-3.34352	0.02225	DOWN
HSD17B2	2.6034	14.9055	-2.51737	0.06454	DOWN
PHACTR3	1.5533	7.0366	-2.17957	0.05767	DOWN
SULT2B1	1.2391	6.8556	-2.46800	0.05710	DOWN
SLC4A11	2.3926	17.5294	-2.87313	0.03336	DOWN
F11	4.8720	23.2757	-2.25624	0.09481	DOWN
C20orf26	1.5857	8.6946	-2.45501	0.01847	DOWN
RPH3A	1.4390	9.1772	-2.67299	0.00387	DOWN
CHGB	1.6753	10.4980	-2.64760	0.13787	DOWN
NOS1	2.8431	12.9713	-2.18978	0.07087	DOWN
OTUB2	1.0897	8.0401	-2.88332	0.00655	DOWN
LAMB4	1.0852	5.9786	-2.46188	0.04437	DOWN
MYO15A	2.2216	14.9373	-2.74924	0.00387	DOWN
PITPNM3	1.7085	8.8208	-2.36821	0.00655	DOWN
ZFHX4	2.6046	14.7363	-2.50025	0.00387	DOWN
CPA1	1.0046	4.2923	-2.09512	0.03336	DOWN
TGM1	4.6901	29.7509	-2.66525	0.03493	DOWN
TBX15	1.0859	6.3469	-2.54711	0.02537	DOWN
GABRP	1.3165	6.5651	-2.31813	0.01847	DOWN
NXPE1	1.0773	6.0652	-2.49319	0.06153	DOWN
EPB41L4B	1.0017	4.0771	-2.02513	0.15744	DOWN
P2RX6	1.2233	8.8644	-2.85727	0.01847	DOWN
SEPT3	1.0069	5.5181	-2.45421	0.01560	DOWN
PVALB	2.1664	8.9013	-2.03873	0.17987	DOWN
KCTD17	7.3519	29.9049	-2.02419	0.00387	DOWN
KCNK10	1.1417	7.7489	-2.76283	0.01399	DOWN
COCH	2.3752	17.8996	-2.91383	0.13596	DOWN
C14orf166B	1.4759	14.9637	-3.34184	0.16675	DOWN
CHGA	3.1319	25.0115	-2.99748	0.03655	DOWN
ASB2	3.1718	17.1568	-2.43540	0.01081	DOWN
SLC8A3	1.8012	17.9564	-3.31744	0.00387	DOWN
TCL1A	1.6218	8.0747	-2.31584	0.05329	DOWN
DHRS2	1.8375	12.3589	-2.74971	0.00387	DOWN
CPNE6	3.5985	16.8268	-2.22530	0.02537	DOWN
VSX1	2.7529	14.5057	-2.39758	0.06298	DOWN
SALL4	1.1544	5.1732	-2.16396	0.02336	DOWN
BMP7	2.6634	13.2424	-2.31380	0.03573	DOWN
COL20A1	1.5632	18.1895	-3.54053	0.00387	DOWN
SNPH	2.3343	10.2750	-2.13805	0.01560	DOWN
BPI	1.1603	4.8070	-2.05064	0.13242	DOWN
EPPIN	1.0667	16.4687	-3.94846	0.00387	DOWN
CELF4	1.6587	8.7628	-2.40136	0.00387	DOWN
ST8SIA5	2.5903	12.3899	-2.25800	0.01847	DOWN
NOL4	1.9652	12.7326	-2.69581	0.01560	DOWN
VGLL1	1.1705	13.9529	-3.57538	0.05024	DOWN
CBLN1	1.2237	10.7122	-3.12996	0.07803	DOWN
CCDC113	3.3417	13.9269	-2.05920	0.03655	DOWN
NDRG4	5.9939	36.3870	-2.60186	0.00387	DOWN
HAS3	2.0123	12.3935	-2.62268	0.09506	DOWN
SMPD3	4.3455	25.1374	-2.53224	0.00387	DOWN
ACSBG1	2.8344	19.8809	-2.81025	0.00655	DOWN
IGDCC4	1.8913	13.1482	-2.79744	0.04517	DOWN

Table S4 (continued)

Table S4 (continued)

Gene name	Cancer_FPKM	Non-cancer_FPKM	log2(fold change)	FDR	Trend
FAM189A1	1.7313	9.5470	-2.46322	0.07588	DOWN
TRPA1	2.5965	12.9199	-2.31498	0.16726	DOWN
SLC17A7	1.1830	5.7142	-2.27208	0.08535	DOWN
SLC1A6	1.3937	7.1954	-2.36814	0.00880	DOWN
CRX	2.3051	14.7386	-2.67668	0.02109	DOWN
MAG	1.1945	5.0030	-2.06634	0.17581	DOWN
PON3	1.3881	9.8221	-2.82292	0.01560	DOWN
RNF32	2.2291	9.3946	-2.07536	0.00655	DOWN
VIPR2	1.1126	6.4818	-2.54251	0.08828	DOWN
EVX1	1.6654	16.6538	-3.32192	0.05024	DOWN
GCK	1.0033	6.6846	-2.73605	0.02439	DOWN
LHX6	1.8979	10.8063	-2.50943	0.00387	DOWN
TNFSF8	3.8578	15.6345	-2.01890	0.03042	DOWN
RLN2	1.0839	5.3215	-2.29567	0.14980	DOWN
TYRP1	3.3192	14.6539	-2.14239	0.07175	DOWN
CDH23	3.4339	14.2238	-2.05038	0.00655	DOWN
TLX1	2.7712	19.7351	-2.83220	0.04585	DOWN
KAZALD1	2.4044	13.1076	-2.44663	0.03493	DOWN
NEURL1	1.1953	8.5713	-2.84213	0.05548	DOWN
DKK1	2.7194	17.5987	-2.69409	0.08324	DOWN
SORCS1	1.6492	11.3797	-2.78665	0.01560	DOWN
KRT23	1.9558	17.4160	-3.15460	0.05329	DOWN
RUNDC3A	1.5347	6.3144	-2.04067	0.08571	DOWN
ALDH3A1	1.7514	8.2470	-2.23539	0.00880	DOWN
ASIC2	1.9295	9.2204	-2.25657	0.07543	DOWN
HSD17B1	1.2412	9.1455	-2.88131	0.03431	DOWN
DLX4	1.9551	21.0465	-3.42826	0.01560	DOWN
PPY	1.5227	19.2818	-3.66252	0.10109	DOWN
MPP2	2.2560	12.8531	-2.51031	0.00387	DOWN
VTN	1.4886	9.7736	-2.71492	0.05193	DOWN
CWH43	1.6644	9.9599	-2.58115	0.17937	DOWN
CPZ	2.5058	10.2586	-2.03347	0.07662	DOWN
GLRB	1.1574	6.0959	-2.39696	0.07175	DOWN
HGFAC	1.2056	6.1539	-2.35172	0.11269	DOWN
DDX25	1.8371	7.7307	-2.07317	0.14461	DOWN
TECTA	1.5405	7.6739	-2.31659	0.03281	DOWN
B3GAT1	3.2185	17.8649	-2.47267	0.01712	DOWN
CCKBR	1.5801	14.2872	-3.17662	0.04889	DOWN
HPX	2.9717	19.2018	-2.69189	0.03737	DOWN
PVRL1	3.9675	21.3114	-2.42533	0.00387	DOWN
C11orf21	3.3580	13.7685	-2.03568	0.08742	DOWN
PTPN5	2.2642	10.9707	-2.27660	0.04654	DOWN
ASIC1	1.5180	6.3586	-2.06653	0.02439	DOWN
TSPAN11	1.5624	10.4252	-2.73824	0.00387	DOWN
CYP27B1	5.4071	43.3834	-3.00421	0.02756	DOWN
GLI1	1.6937	8.2106	-2.27733	0.11729	DOWN
AKAP3	2.3294	15.0954	-2.69610	0.04305	DOWN
GPR133	3.9680	17.3906	-2.13182	0.02439	DOWN
GNB3	3.1877	20.6205	-2.69351	0.02225	DOWN
CDCA3	2.5949	11.3840	-2.13326	0.02439	DOWN
ST8SIA1	7.4267	32.0619	-2.11007	0.02225	DOWN
AICDA	1.1071	7.3120	-2.72345	0.12317	DOWN
RSPH4A	1.3133	5.5700	-2.08443	0.10001	DOWN
OPRM1	1.3901	13.0415	-3.22983	0.00387	DOWN
TULP1	1.8726	11.6949	-2.64281	0.05784	DOWN
SLC26A8	1.0385	5.7549	-2.47026	0.06393	DOWN
MDGA1	5.4986	22.2251	-2.01505	0.00387	DOWN
RBM24	1.4389	7.9709	-2.46980	0.06503	DOWN
HDGFL1	3.8513	19.8409	-2.36506	0.06873	DOWN
EYA4	2.4780	13.4675	-2.44223	0.01399	DOWN
PRPH2	1.2076	5.0632	-2.06796	0.01081	DOWN
PRSS16	5.0080	22.3533	-2.15817	0.00655	DOWN
TBX18	1.6055	9.9133	-2.62637	0.01081	DOWN
PCDHB7	2.1932	10.1851	-2.21535	0.03431	DOWN
GRM6	2.6070	13.0461	-2.32315	0.11234	DOWN
HRG	2.1675	11.5697	-2.41622	0.08904	DOWN
FGF12	2.5953	19.6215	-2.91846	0.01241	DOWN
ROPN1B	1.4841	16.2465	-3.45246	0.00387	DOWN
KIAA1257	1.5640	6.3923	-2.03109	0.09524	DOWN
PEX5L	2.4132	13.0085	-2.43047	0.04305	DOWN
ARHGEF26	1.7920	7.3565	-2.03746	0.10644	DOWN
VIPR1	3.2698	21.1596	-2.69406	0.00387	DOWN
SLC30A3	1.8057	7.3100	-2.01733	0.06393	DOWN

Table S4 (continued)

Table S4 (continued)

Gene name	Cancer_FPKM	Non-cancer_FPKM	log2(fold change)	FDR	Trend
TLX2	3.0187	17.7044	-2.55210	0.15362	DOWN
TACR1	1.1881	11.0960	-3.22327	0.00655	DOWN
KCNJ13	1.4961	7.1352	-2.25374	0.17633	DOWN
OTX1	1.8918	22.6628	-3.58250	0.00655	DOWN
SLC9A2	1.4050	7.3091	-2.37914	0.01081	DOWN
MLPH	3.7539	18.5709	-2.30659	0.00387	DOWN
KIAA1324	3.5714	20.5783	-2.52658	0.00655	DOWN
MYCL	3.2674	13.8523	-2.08391	0.07175	DOWN
ST6GALNAC5	1.3174	13.4860	-3.35575	0.05233	DOWN
MFAP2	2.0810	12.9023	-2.63227	0.02225	DOWN
PLA2G2D	1.3414	6.0283	-2.16800	0.04013	DOWN
ARTN	1.7037	11.9966	-2.81591	0.00880	DOWN
PTCH2	1.4983	7.1732	-2.25928	0.08442	DOWN
PROX1	3.0944	26.2106	-3.08242	0.01081	DOWN
CENPF	3.0876	13.6576	-2.14514	0.06819	DOWN
MUC5B	1.6494	17.3875	-3.39801	0.02109	DOWN
CA14	1.1448	7.1664	-2.64618	0.06393	DOWN
ATP10B	2.6125	24.5740	-3.23365	0.00387	DOWN
CNR1	2.1611	13.0003	-2.58870	0.03493	DOWN
TRPM6	1.0751	6.6481	-2.62850	0.00880	DOWN
PPP4R4	1.3387	6.3430	-2.24429	0.11234	DOWN
ESRRB	2.6412	16.5489	-2.64748	0.01560	DOWN
CRHR1	1.2838	12.0311	-3.22824	0.01241	DOWN
HOXB1	1.1317	7.3255	-2.69442	0.16140	DOWN
GRIA2	1.5235	9.5850	-2.65335	0.02537	DOWN
TP53AIP1	1.2891	9.2807	-2.84783	0.04187	DOWN
CHRNA2	1.0421	12.4937	-3.58370	0.00387	DOWN
ADRA1A	3.6376	20.3181	-2.48170	0.00880	DOWN
TNFRSF8	1.2974	5.5470	-2.09608	0.09506	DOWN
TSHZ3	5.6430	26.2028	-2.21518	0.00880	DOWN
LHX4	1.7595	7.8812	-2.16326	0.15857	DOWN
GJA8	2.3815	13.7966	-2.53437	0.02537	DOWN
CCRL2	4.1546	17.6842	-2.08966	0.02109	DOWN
CSMD2	1.5428	14.2744	-3.20979	0.00387	DOWN
HPCA	1.6793	6.7798	-2.01339	0.15857	DOWN
TBX22	1.2173	6.5946	-2.43761	0.19961	DOWN
LDB3	1.5266	8.5554	-2.48649	0.02336	DOWN
KIAA1045	1.6337	6.6800	-2.03167	0.04141	DOWN
SFTPA1	1.5541	15.5298	-3.32086	0.01712	DOWN
PLP1	2.8596	21.2227	-2.89173	0.00387	DOWN
FAM124B	1.6522	9.9380	-2.58856	0.05233	DOWN
CTCFL	1.0134	6.6880	-2.72240	0.00387	DOWN
WFDC3	1.2385	9.7831	-2.98169	0.00387	DOWN
KCNS1	1.1899	9.7758	-3.03837	0.02756	DOWN
SLC12A5	1.7113	7.6786	-2.16573	0.06678	DOWN
GDAP1L1	1.3788	7.1787	-2.38035	0.09328	DOWN
CHST8	1.4334	6.9560	-2.27888	0.17068	DOWN
PSG8	1.1794	12.2851	-3.38081	0.00387	DOWN
GRM4	1.7398	16.7494	-3.26716	0.00387	DOWN
PACSIN1	1.9015	15.2759	-3.00609	0.01081	DOWN
KLHL31	1.6047	6.6500	-2.05101	0.14461	DOWN
C1orf61	3.3538	25.5598	-2.93001	0.00387	DOWN
PAX1	1.5205	9.1687	-2.59213	0.06954	DOWN
BFSP1	1.0077	6.1079	-2.59967	0.07244	DOWN
F10	2.6213	11.0462	-2.07518	0.15149	DOWN
SIX1	1.1772	9.7699	-3.05303	0.02648	DOWN
AVPR2	2.2449	10.5280	-2.22952	0.16933	DOWN
BEST3	1.1173	12.1637	-3.44456	0.00387	DOWN
SYNGR3	1.2633	8.8668	-2.81119	0.06557	DOWN
PKMYT1	4.9335	22.8218	-2.20974	0.05077	DOWN
RASL11B	2.9672	12.6358	-2.09037	0.14501	DOWN
GNAZ	2.7866	12.5731	-2.17375	0.03573	DOWN
C22orf23	1.0953	5.0876	-2.21567	0.08504	DOWN
KRT17	2.7583	25.8195	-3.22659	0.07288	DOWN
KCNC1	1.3781	14.8700	-3.43169	0.00387	DOWN
AIPL1	1.0249	4.9249	-2.26465	0.09505	DOWN
FOXA1	2.4016	18.1722	-2.91964	0.05285	DOWN
CDO1	3.0122	21.8974	-2.86186	0.00387	DOWN
CHRNA10	2.2441	9.1800	-2.03236	0.19597	DOWN
SYT5	2.0525	9.1108	-2.15022	0.05819	DOWN
TNNI3	1.1990	7.9130	-2.72243	0.00655	DOWN
PRRG3	1.4845	10.0943	-2.76545	0.00655	DOWN
KCNA5	1.7083	8.1784	-2.25923	0.01241	DOWN

Table S4 (continued)

Table S4 (continued)

Gene name	Cancer_FPKM	Non-cancer_FPKM	log2(fold change)	FDR	Trend
DPP6	4.6969	25.6340	-2.44829	0.00387	DOWN
KIF1A	4.0325	33.4428	-3.05196	0.00387	DOWN
OLFM1	4.7566	21.0473	-2.14564	0.01712	DOWN
TNNT3	1.5253	7.3747	-2.27352	0.16066	DOWN
CYP2E1	3.5714	18.0379	-2.33646	0.03493	DOWN
MNX1	2.8898	15.2360	-2.39844	0.01712	DOWN
DUSP9	10.8989	44.8771	-2.04180	0.02225	DOWN
AOC2	1.2349	5.7629	-2.22236	0.04829	DOWN
TNS4	1.1484	6.3839	-2.47480	0.09527	DOWN
ABHD12B	1.4253	8.5695	-2.58797	0.03737	DOWN
C19orf57	2.4076	9.8930	-2.03884	0.06393	DOWN
SLC6A11	1.0407	9.3343	-3.16497	0.04141	DOWN
BCAN	1.4117	12.2677	-3.11934	0.02109	DOWN
CRP	1.2323	9.1689	-2.89544	0.01847	DOWN
HAPLN2	1.3365	5.7609	-2.10781	0.18026	DOWN
CHIT1	4.1886	21.1536	-2.33638	0.02109	DOWN
LGR6	1.4803	15.4746	-3.38598	0.00387	DOWN
TMCC2	1.8130	7.2575	-2.00108	0.02336	DOWN
UNC79	1.0639	4.9754	-2.22542	0.09661	DOWN
GSTM5	1.9951	15.6517	-2.97180	0.01399	DOWN
SYT6	2.5998	11.2324	-2.11119	0.02439	DOWN
CD101	2.0976	13.4868	-2.68471	0.05784	DOWN
CRB1	1.4409	8.2433	-2.51630	0.01081	DOWN
RAX	2.9534	22.9234	-2.95636	0.12028	DOWN
MTNR1B	1.1313	11.9263	-3.39807	0.07203	DOWN
SPOCD1	2.4917	12.3777	-2.31254	0.02336	DOWN
ELF5	1.8151	18.6713	-3.36273	0.05548	DOWN
PRPH	1.5892	7.5234	-2.24314	0.08862	DOWN
AMHR2	1.1524	7.1074	-2.62464	0.02839	DOWN
FAM186B	1.4815	9.1388	-2.62494	0.08862	DOWN
FAIM2	1.5631	9.1221	-2.54493	0.00387	DOWN
KCNH3	1.1557	5.6944	-2.30076	0.10529	DOWN
EGR4	1.0223	6.9752	-2.77037	0.07979	DOWN
SLC9A5	1.2194	5.6401	-2.20955	0.04691	DOWN
GPR55	1.2118	9.1052	-2.90952	0.00387	DOWN
PAX3	1.6292	11.8382	-2.86120	0.01241	DOWN
WNT10A	2.1429	8.7279	-2.02604	0.01241	DOWN
ARHGEF4	2.5924	23.6024	-3.18659	0.00387	DOWN
STAB2	1.5959	10.8391	-2.76382	0.05233	DOWN
USP44	1.8601	10.9929	-2.56311	0.01399	DOWN
NACAD	1.0641	4.8078	-2.17569	0.00880	DOWN
NKX2-1	1.0262	10.0430	-3.29079	0.07015	DOWN
ZFHX2	2.1674	9.6776	-2.15869	0.12362	DOWN
MYCBPAP	2.0527	9.0242	-2.13624	0.01979	DOWN
TBR1	1.0277	7.6811	-2.90187	0.02225	DOWN
ERMN	1.7316	7.4747	-2.10993	0.08230	DOWN
GATA4	2.6139	13.7017	-2.39009	0.01979	DOWN
IL36RN	1.4774	15.3358	-3.37576	0.05024	DOWN
LMX1B	1.3683	5.9877	-2.12967	0.10001	DOWN
TFAP2A	6.1128	31.6387	-2.37179	0.00387	DOWN
TRIM29	5.9229	47.7608	-3.01146	0.00387	DOWN
POU2F3	1.2640	5.6271	-2.15439	0.04654	DOWN
ARHGAP20	1.1767	6.8398	-2.53925	0.05329	DOWN
DUOX1	1.2547	8.0837	-2.68765	0.00387	DOWN
STRA6	3.7422	17.6031	-2.23388	0.00387	DOWN
CYP19A1	1.4324	10.4002	-2.86016	0.00387	DOWN
SEMA6D	7.2832	29.1548	-2.00110	0.02756	DOWN
GCOM1	1.4337	12.1360	-3.08144	0.00655	DOWN
TRIM54	2.8293	12.3398	-2.12480	0.12319	DOWN
CILP	1.3552	5.7343	-2.08111	0.03431	DOWN
FGF5	1.0508	6.9476	-2.72505	0.07587	DOWN
BMPR1B	2.2124	10.4904	-2.24539	0.06503	DOWN
EGF	9.8888	95.8034	-3.27622	0.00387	DOWN
COL2A1	3.2159	28.8945	-3.16749	0.02225	DOWN
INHBE	1.2711	6.7488	-2.40859	0.10296	DOWN
TMEM132B	2.1504	12.9887	-2.59459	0.04013	DOWN
SSTR1	1.2080	5.0159	-2.05392	0.02953	DOWN
REM2	1.1855	5.3649	-2.17803	0.18441	DOWN
TSSK4	1.3100	5.6949	-2.12007	0.16215	DOWN
SLC24A4	2.0213	8.5046	-2.07296	0.05548	DOWN
DUOXA1	2.0167	14.7525	-2.87091	0.00387	DOWN
DUOX2	1.5116	6.5155	-2.10778	0.13976	DOWN
DISP2	1.6165	23.4003	-3.85556	0.04691	DOWN

Table S4 (continued)

Table S4 (continued)

Gene name	Cancer_FPKM	Non-cancer_FPKM	log2(fold change)	FDR	Trend
CYP11A1	1.6835	10.6518	-2.66160	0.01979	DOWN
ADAMTS17	3.4815	17.1040	-2.29654	0.00387	DOWN
LMAN1L	1.8280	8.1517	-2.15685	0.15479	DOWN
NTRK3	5.6003	23.1753	-2.04902	0.00387	DOWN
MYLK3	2.0101	14.2163	-2.82220	0.02756	DOWN
ADAD2	1.3984	7.5160	-2.42620	0.07941	DOWN
MYOCD	1.6679	8.6995	-2.38294	0.03737	DOWN
RASL10B	2.1628	13.3325	-2.62397	0.00387	DOWN
LRRC46	1.1009	4.5133	-2.03557	0.15139	DOWN
GNAL	2.4257	11.6784	-2.26737	0.12166	DOWN
ADCYAP1	1.2738	5.3063	-2.05862	0.16494	DOWN
SLC13A5	1.0771	7.2507	-2.75090	0.00387	DOWN
MAPK4	4.0253	16.1400	-2.00349	0.13870	DOWN
CBLN2	1.3881	14.8844	-3.42267	0.00387	DOWN
PNMT	1.0353	5.5386	-2.41941	0.13596	DOWN
ARL5C	1.1026	9.1422	-3.05161	0.03573	DOWN
KLK3	1.7818	16.8417	-3.24067	0.00655	DOWN
MMEL1	2.7267	15.5663	-2.51322	0.05784	DOWN
C1orf222	1.0937	5.8727	-2.42486	0.00880	DOWN
PRDM16	5.5053	24.0705	-2.12838	0.04758	DOWN
FHAD1	2.9305	14.8649	-2.34268	0.00387	DOWN
GPR161	3.9586	16.6552	-2.07290	0.03205	DOWN
ADCY10	1.6242	8.9589	-2.46359	0.19484	DOWN
SUSD4	5.7278	26.4717	-2.20840	0.00387	DOWN
CRNN	1.7262	12.2304	-2.82480	0.16782	DOWN
AQP10	1.0819	4.6760	-2.11165	0.17153	DOWN
FLG	1.1428	8.8859	-2.95899	0.06125	DOWN
CNIH3	5.1366	21.1800	-2.04382	0.05459	DOWN
OSR1	1.6861	13.1300	-2.96109	0.03737	DOWN
REG3G	1.9374	12.9047	-2.73572	0.07979	DOWN
ANKRD53	1.3107	12.2109	-3.21979	0.05503	DOWN
DQX1	1.8794	7.9892	-2.08779	0.17123	DOWN
ST6GAL2	1.9272	10.5922	-2.45845	0.02839	DOWN
CNGA3	1.0163	10.7642	-3.40486	0.04379	DOWN
TMEFF2	1.2330	8.8040	-2.83594	0.13576	DOWN
DLX1	1.1416	12.7442	-3.48065	0.00387	DOWN
UNC80	1.2158	8.1445	-2.74392	0.00655	DOWN
TRPM8	1.2504	11.2201	-3.16560	0.00387	DOWN
ESPNL	1.3227	9.1291	-2.78699	0.00880	DOWN
GADL1	1.6114	9.2660	-2.52367	0.06153	DOWN
ACKR2	1.7010	12.6614	-2.89600	0.00387	DOWN
FAM198A	2.5663	13.5646	-2.40210	0.02336	DOWN
SLC22A14	1.4825	8.2974	-2.48464	0.06298	DOWN
TAGLN3	1.9045	11.6918	-2.61804	0.03336	DOWN
NR1I2	1.1137	6.3257	-2.50592	0.03336	DOWN
TMEM108	1.1791	14.0857	-3.57853	0.00387	DOWN
MUC4	2.0909	13.0009	-2.63641	0.00387	DOWN
ECE2	1.7953	9.7745	-2.44478	0.10717	DOWN
VWA5B2	1.6520	11.9582	-2.85570	0.05924	DOWN
RNF175	1.3105	9.5195	-2.86083	0.01979	DOWN
CDH18	2.7142	14.8307	-2.45000	0.02839	DOWN
GABRB2	1.3512	6.1523	-2.18693	0.06727	DOWN
CPLX2	1.8329	14.6904	-3.00271	0.00387	DOWN
MLIP	1.3868	17.7006	-3.67399	0.00387	DOWN
FAXC	1.0252	4.2803	-2.06180	0.07426	DOWN
TRIM50	1.5346	10.9963	-2.84104	0.08695	DOWN
ASB10	1.0502	8.4709	-3.01190	0.08295	DOWN
PXDNL	1.2045	8.0889	-2.74749	0.00880	DOWN
ST18	2.5225	34.7950	-3.78594	0.00387	DOWN
RSPO2	1.1349	8.5042	-2.90563	0.01241	DOWN
FAM135B	2.5607	13.2629	-2.37280	0.00655	DOWN
CDKN2B	8.5338	35.8029	-2.06882	0.11588	DOWN
ACTL7B	1.1751	7.9945	-2.76620	0.01979	DOWN
RGR	1.2349	6.7846	-2.45791	0.03857	DOWN
HTR7	1.1403	6.6041	-2.53392	0.06393	DOWN
SYT8	1.9311	10.3322	-2.41962	0.01560	DOWN
KLHL35	1.1152	4.8428	-2.11849	0.14453	DOWN
DRD2	1.0163	9.6847	-3.25244	0.00387	DOWN
GRIK4	1.6957	8.6911	-2.35763	0.09163	DOWN
ADAM33	1.2617	7.6260	-2.59551	0.05784	DOWN
KIRREL3	1.4454	9.7097	-2.74791	0.00880	DOWN
FAM57B	1.3186	7.6954	-2.54496	0.14547	DOWN
HMGA2	1.9395	10.9656	-2.49921	0.00387	DOWN

Table S4 (continued)

Table S4 (continued)

Gene name	Cancer_FPKM	Non-cancer_FPKM	log2(fold change)	FDR	Trend
<i>PCDH15</i>	1.3704	7.0431	-2.36159	0.00387	DOWN
<i>CDH8</i>	2.7232	14.5363	-2.41628	0.00655	DOWN
<i>LYPD6B</i>	1.8429	7.7467	-2.07157	0.04379	DOWN
<i>CNDP1</i>	1.3604	5.8316	-2.09987	0.11443	DOWN
<i>CACNA2D4</i>	7.0745	29.6657	-2.06810	0.00387	DOWN
<i>MAT1A</i>	1.3854	6.4889	-2.22767	0.17123	DOWN
<i>AKR1C2</i>	2.0456	10.2319	-2.32245	0.01081	DOWN
<i>DPYSL4</i>	1.4058	14.7352	-3.38984	0.05233	DOWN
<i>GABRA2</i>	2.2435	10.0330	-2.16091	0.01241	DOWN
<i>TMEM163</i>	2.3896	10.7040	-2.16328	0.18784	DOWN
<i>RIT2</i>	1.5442	12.0062	-2.95886	0.15202	DOWN
<i>SH2D6</i>	2.7231	11.0224	-2.01713	0.10746	DOWN
<i>TRIM36</i>	3.2235	14.8853	-2.20719	0.02225	DOWN
<i>GRIA4</i>	1.4076	7.0618	-2.32679	0.00387	DOWN
<i>TCTEX1D1</i>	1.6870	14.2003	-3.07341	0.06247	DOWN
<i>HHEX</i>	5.0962	20.8967	-2.03579	0.09947	DOWN
<i>GRM1</i>	1.9980	20.6552	-3.36990	0.00387	DOWN
<i>ZIC1</i>	1.3839	11.7494	-3.08582	0.03336	DOWN
<i>LGI2</i>	1.5657	6.9949	-2.15953	0.02109	DOWN
<i>ACOXL</i>	1.5742	9.9141	-2.65485	0.00387	DOWN
<i>PTPRR</i>	1.1400	5.0026	-2.13360	0.08742	DOWN
<i>SCN3A</i>	1.3961	6.8391	-2.29238	0.04379	DOWN
<i>PLEKHG4B</i>	1.1928	5.8255	-2.28804	0.01560	DOWN
<i>HS3ST3A1</i>	3.6377	19.2828	-2.40622	0.02439	DOWN
<i>AK5</i>	1.9971	9.6128	-2.26708	0.00387	DOWN
<i>CABYR</i>	1.7796	7.2546	-2.02739	0.07175	DOWN
<i>JPH3</i>	1.1456	9.9048	-3.11199	0.02648	DOWN
<i>CDH12</i>	1.0736	5.4910	-2.35458	0.06906	DOWN
<i>CERS3</i>	1.5683	11.8336	-2.91563	0.02648	DOWN
<i>CHODL</i>	1.0773	4.5535	-2.07962	0.03336	DOWN
<i>PDE1C</i>	12.1834	49.7045	-2.02847	0.00655	DOWN
<i>EME1</i>	2.0895	12.2115	-2.54702	0.04141	DOWN
<i>CNTNAP5</i>	2.4244	13.2283	-2.44794	0.11729	DOWN
<i>GRIA1</i>	1.4931	10.8842	-2.86589	0.00387	DOWN
<i>FMN2</i>	2.1708	12.4225	-2.51669	0.02648	DOWN
<i>GPR61</i>	1.3359	9.5198	-2.83309	0.02336	DOWN
<i>CLDN8</i>	4.2627	23.5310	-2.46471	0.02439	DOWN
<i>PPP2R2B</i>	3.5623	14.9878	-2.07292	0.00387	DOWN
<i>UNC5D</i>	1.9130	8.1266	-2.08679	0.11052	DOWN
<i>GAREML</i>	2.1216	10.2975	-2.27909	0.12182	DOWN
<i>RADIL</i>	1.0107	8.3482	-3.04610	0.01712	DOWN
<i>EXTL1</i>	1.2214	8.5849	-2.81331	0.09896	DOWN
<i>ESYT3</i>	2.7009	13.2869	-2.29848	0.01712	DOWN
<i>C2orf62</i>	2.8931	12.4324	-2.10344	0.11111	DOWN
<i>CD1E</i>	1.3944	6.5149	-2.22412	0.00655	DOWN
<i>PLA2G2F</i>	1.4016	10.0959	-2.84863	0.09632	DOWN
<i>FGF17</i>	1.4966	8.9430	-2.57906	0.08011	DOWN
<i>ACTC1</i>	1.2520	5.0388	-2.00883	0.17903	DOWN
<i>SCUBE1</i>	2.2452	12.2665	-2.44981	0.00387	DOWN
<i>IRX6</i>	1.4938	9.6994	-2.69894	0.03205	DOWN
<i>CELF3</i>	1.0083	8.4344	-3.06436	0.03857	DOWN
<i>RGL4</i>	1.6133	11.7842	-2.86881	0.05960	DOWN
<i>FAM131B</i>	1.2662	10.1259	-2.99945	0.00387	DOWN
<i>FNDC5</i>	1.2590	16.3353	-3.69764	0.00880	DOWN
<i>TMPRSS3</i>	2.4442	11.6124	-2.24823	0.02839	DOWN
<i>FCRL3</i>	2.8201	12.9180	-2.19554	0.03281	DOWN
<i>LY6K</i>	1.6708	11.0794	-2.72923	0.04013	DOWN
<i>RECQL4</i>	3.5721	15.7277	-2.13849	0.02336	DOWN
<i>NPHS1</i>	4.7907	19.9849	-2.06060	0.18285	DOWN
<i>GRIN2C</i>	1.1117	8.5862	-2.94922	0.00880	DOWN
<i>CCDC155</i>	3.8395	26.7289	-2.79940	0.01560	DOWN
<i>CD300LG</i>	1.6037	15.1192	-3.23687	0.02109	DOWN
<i>SHANK1</i>	1.1576	14.9095	-3.68706	0.00655	DOWN
<i>TREML1</i>	1.0299	7.7564	-2.91285	0.06393	DOWN
<i>RNASEK-C17orf49</i>	1.3188	8.0372	-2.60743	0.16202	DOWN
<i>CCDC78</i>	1.5015	6.5305	-2.12078	0.02537	DOWN
<i>C16orf59</i>	1.9151	13.8582	-2.85528	0.00655	DOWN
<i>ZG16B</i>	1.6312	11.9623	-2.87446	0.03939	DOWN
<i>ITIH3</i>	4.3097	25.4460	-2.56179	0.00880	DOWN
<i>CYP4A22</i>	1.6425	8.9790	-2.45071	0.12062	DOWN
<i>SLC1A7</i>	1.5262	10.1497	-2.73341	0.15362	DOWN
<i>KNCN</i>	1.2904	10.6202	-3.04091	0.06594	DOWN
<i>PDPN</i>	2.1410	8.8707	-2.05075	0.04654	DOWN

Table S4 (continued)

Table S4 (continued)

Gene name	Cancer_FPKM	Non-cancer_FPKM	log2(fold change)	FDR	Trend
MATN1	1.4755	8.0907	-2.45511	0.09977	DOWN
WNT4	2.0055	15.2043	-2.92245	0.07468	DOWN
FCGR3B	1.9261	9.3866	-2.28491	0.12985	DOWN
AXDND1	2.1052	10.5149	-2.32044	0.17297	DOWN
KLHDC8A	3.9796	19.1271	-2.26494	0.02839	DOWN
C1orf145	1.4398	5.8743	-2.02854	0.11921	DOWN
LRRTM1	2.3003	9.6762	-2.07262	0.19084	DOWN
KCNF1	1.5538	9.1001	-2.55008	0.00387	DOWN
MSX1	2.1096	9.2171	-2.12732	0.03797	DOWN
NIPAL1	3.5056	18.9018	-2.43081	0.14841	DOWN
SPTA1	2.1646	18.9242	-3.12804	0.02225	DOWN
EFHB	1.3828	9.6010	-2.79554	0.07401	DOWN
CADPS	2.6169	36.1534	-3.78822	0.00387	DOWN
PRRT3	1.3919	6.2608	-2.16927	0.11443	DOWN
CXCL3	2.5405	11.2573	-2.14771	0.18335	DOWN
TGM4	1.6454	13.7988	-3.06801	0.02756	DOWN
GRIK3	4.0564	17.0625	-2.07256	0.05819	DOWN
MFI2	4.9025	25.0917	-2.35563	0.00655	DOWN
CDC25A	1.6653	8.5203	-2.35516	0.02109	DOWN
BSN	1.0191	9.1517	-3.16681	0.00387	DOWN
CAMKV	1.1050	13.6353	-3.62525	0.00387	DOWN
MST1R	2.3718	10.9886	-2.21197	0.04691	DOWN
GRM2	1.0613	10.2071	-3.26563	0.00387	DOWN
PITX2	4.0647	26.7912	-2.72053	0.01847	DOWN
HAND2	1.8211	14.3861	-2.98179	0.08467	DOWN
TMEM155	1.3588	6.5494	-2.26906	0.06153	DOWN
RANBP3L	4.2740	22.3698	-2.38788	0.17549	DOWN
GPR98	3.4751	14.4260	-2.05353	0.07426	DOWN
C5orf63	4.3913	19.7241	-2.16725	0.02648	DOWN
HTR4	1.4608	14.5327	-3.31448	0.00387	DOWN
TIGD6	3.2856	13.2230	-2.00880	0.14943	DOWN
TERT	1.3342	5.5405	-2.05409	0.19590	DOWN
ACSL6	4.2795	25.2395	-2.56018	0.00387	DOWN
RAET1E	1.0594	4.9446	-2.22264	0.03737	DOWN
MYOZ3	1.9292	16.3702	-3.08501	0.00387	DOWN
KIF6	1.5083	6.9385	-2.20173	0.04889	DOWN
TMEM74	1.2513	10.6958	-3.09556	0.11138	DOWN
OSR2	2.1348	15.0057	-2.81336	0.01847	DOWN
BAALC	1.2758	10.4114	-3.02873	0.00655	DOWN
DCSTAMP	1.5551	13.6720	-3.13619	0.03573	DOWN
C9orf24	1.2131	5.2559	-2.11521	0.09505	DOWN
ZMAT4	2.0473	9.9057	-2.27455	0.05960	DOWN
C8orf34	1.6779	8.9162	-2.40978	0.00880	DOWN
TRPV6	3.5452	16.2657	-2.19788	0.01560	DOWN
C7orf34	1.4653	7.7891	-2.41032	0.18663	DOWN
WNK2	4.2902	24.2634	-2.49968	0.00387	DOWN
SLITRK5	1.6962	7.7627	-2.19427	0.08194	DOWN
FAT3	3.1207	15.3502	-2.29833	0.00655	DOWN
LRFN5	1.7496	20.2469	-3.53263	0.01241	DOWN
ZNF488	2.4674	14.3617	-2.54117	0.04187	DOWN
TSHR	2.1019	9.9055	-2.23651	0.07588	DOWN
TMEM63C	1.3230	6.4443	-2.28418	0.10588	DOWN
AMER2	1.0689	9.6523	-3.17472	0.05385	DOWN
PPP1R36	1.6052	6.9752	-2.11945	0.15171	DOWN
E2F7	1.3620	5.5400	-2.02415	0.02336	DOWN
NELL1	3.6122	17.6026	-2.28484	0.05879	DOWN
C1QL3	1.1942	5.7844	-2.27607	0.00655	DOWN
KCNC2	2.0068	12.6553	-2.65674	0.03737	DOWN
CMTM5	1.5715	12.9596	-3.04380	0.02336	DOWN
GLB1L3	1.4587	12.3495	-3.08172	0.00880	DOWN
ADAMTS15	2.9024	12.2789	-2.08088	0.00387	DOWN
LRTM2	2.0096	9.2701	-2.20567	0.08324	DOWN
TMEM100	1.0870	5.8643	-2.43165	0.06954	DOWN
NETO1	1.8968	13.7028	-2.85284	0.03857	DOWN
CYB5R2	2.8021	27.2247	-3.28034	0.00387	DOWN
SERPINB7	1.0036	4.9096	-2.29041	0.07979	DOWN
BEAN1	2.1149	15.8687	-2.90752	0.00387	DOWN
CPLX4	1.2655	5.3562	-2.08153	0.18026	DOWN
ZCCHC18	1.9948	8.1566	-2.03172	0.11371	DOWN
YPEL4	1.9571	8.0327	-2.03720	0.11225	DOWN
PLIN1	3.0015	12.9594	-2.11022	0.17451	DOWN
GREM1	1.6957	9.7799	-2.52791	0.06153	DOWN
MS4A14	1.8211	7.6889	-2.07799	0.19970	DOWN

Table S4 (continued)

Table S4 (continued)

Gene name	Cancer_FPKM	Non-cancer_FPKM	log2(fold change)	FDR	Trend
EPB42	1.1762	7.9643	-2.75947	0.16802	DOWN
TCP10L2	1.2342	8.7963	-2.83338	0.01979	DOWN
TMEM92	1.6376	7.4292	-2.18165	0.01712	DOWN
ISLR2	2.2529	10.4272	-2.21051	0.01979	DOWN
LOXHD1	1.8385	13.5908	-2.88605	0.00387	DOWN
IGF2	1.5055	8.7953	-2.54646	0.14461	DOWN
RBFOX3	2.6353	30.4001	-3.52803	0.00387	DOWN
PROCA1	3.6641	15.1827	-2.05090	0.00387	DOWN
CORO6	2.2124	9.6548	-2.12564	0.05960	DOWN
AQP2	34.4014	314.3140	-3.19167	0.19405	DOWN
ANKRD33	1.1989	7.8403	-2.70916	0.02953	DOWN
TTYH1	1.7639	7.8649	-2.15665	0.00387	DOWN
PSCA	2.3018	15.3477	-2.73719	0.07047	DOWN
TRPV3	1.2606	8.7779	-2.79975	0.05960	DOWN
KLK1	1.1769	10.1195	-3.10409	0.05924	DOWN
KLK2	2.8110	25.1975	-3.16415	0.00387	DOWN
KLK11	1.1479	8.1591	-2.82935	0.03939	DOWN
MGAT5B	1.6848	10.5701	-2.64930	0.01081	DOWN
SCARA3	3.6710	14.6887	-2.00045	0.02439	DOWN
SCARA5	1.7970	7.4509	-2.05186	0.17751	DOWN
PNOC	1.7439	8.0888	-2.21361	0.10990	DOWN
HR	3.0898	15.6785	-2.34323	0.03336	DOWN
SFTPC	1.0818	8.4815	-2.97083	0.01847	DOWN
PHYHIP	1.9280	15.4350	-3.00107	0.00387	DOWN
CHRM1	1.2075	7.3837	-2.61230	0.11820	DOWN
GDNF	1.0794	22.1578	-4.35951	0.00387	DOWN
VWA3B	1.2658	8.2473	-2.70392	0.00387	DOWN
KCTD19	1.4027	6.3071	-2.16879	0.08504	DOWN
LRP1B	1.4032	5.9362	-2.08086	0.08467	DOWN
CXXC4	1.7086	7.1277	-2.06067	0.09137	DOWN
SHOX2	1.4123	9.4855	-2.74767	0.08742	DOWN
ATOH8	4.3953	19.5524	-2.15331	0.01560	DOWN
STXBP6	4.0774	20.0143	-2.29530	0.03042	DOWN
GRM5	1.7480	11.2137	-2.68147	0.03135	DOWN
IL13	1.7191	12.2524	-2.83332	0.12143	DOWN
SH3TC2	2.6061	15.0426	-2.52911	0.00387	DOWN
C22orf15	1.0505	10.0300	-3.25512	0.10971	DOWN
UMOD	322.0180	1,581.1700	-2.29578	0.10074	DOWN
GP2	6.2821	27.1751	-2.11296	0.12404	DOWN
CTNND2	1.1562	6.9836	-2.59464	0.00387	DOWN
KCNAB3	2.0300	9.9246	-2.28955	0.06125	DOWN
NSG2	1.1870	7.2905	-2.61865	0.00655	DOWN
SERPINA6	3.2618	17.6907	-2.43926	0.05233	DOWN
FOXD4	1.4778	9.3829	-2.66657	0.00655	DOWN
MRGPRX1	1.4045	10.0331	-2.83665	0.17521	DOWN
SEMA3E	2.0254	9.9708	-2.29952	0.16392	DOWN
VSTM2A	1.4024	20.0056	-3.83439	0.02336	DOWN
SGCD	1.4361	5.8962	-2.03765	0.01560	DOWN
GPR37	1.8776	9.0453	-2.26829	0.01399	DOWN
PSG6	3.3034	20.6101	-2.64133	0.00387	DOWN
CEACAM3	2.3413	16.0010	-2.77277	0.02953	DOWN
FPR2	1.7499	7.2168	-2.04408	0.18356	DOWN
C8orf74	1.0361	11.7999	-3.50950	0.00655	DOWN
ALK	1.9375	13.7053	-2.82250	0.04090	DOWN
PROL1	1.0237	8.7535	-3.09603	0.08828	DOWN
NPTX1	2.0137	8.7358	-2.11706	0.08194	DOWN
KRT15	1.4240	10.9587	-2.94411	0.00387	DOWN
KRT13	3.3453	24.1010	-2.84888	0.03737	DOWN
KSR2	1.4306	10.6844	-2.90081	0.00387	DOWN
COL24A1	1.3502	8.8503	-2.71255	0.03281	DOWN
PCDHB1	1.0385	7.9833	-2.94250	0.01847	DOWN
NINJ2	2.3774	11.1801	-2.23346	0.08595	DOWN
LGALS9C	1.3688	8.0950	-2.56410	0.05879	DOWN
FOXB1	1.8784	15.5277	-3.04729	0.12859	DOWN
REG3A	1.2930	19.2338	-3.89483	0.01241	DOWN
REG1B	1.2173	6.4894	-2.41443	0.05548	DOWN
ABCG4	2.4646	17.9363	-2.86349	0.05710	DOWN
PRSS27	2.0389	9.4991	-2.22001	0.07175	DOWN
C2orf54	2.1172	10.9529	-2.37105	0.13576	DOWN
AGXT	2.2997	16.4344	-2.83720	0.02648	DOWN
CARNS1	1.0983	6.3471	-2.53084	0.08790	DOWN
SNX32	1.7688	13.2596	-2.90619	0.02756	DOWN
OVOL1	1.9558	11.6182	-2.57058	0.04437	DOWN

Table S4 (continued)

Table S4 (continued)

Gene name	Cancer_FPKM	Non-cancer_FPKM	log2(fold change)	FDR	Trend
AQPEP	1.3292	8.4646	-2.67093	0.04691	DOWN
MRGPRF	2.9806	18.5720	-2.63948	0.02537	DOWN
ARPP21	1.8205	18.7284	-3.36279	0.00387	DOWN
RP11-683L23.1	1.2271	15.0884	-3.62014	0.03737	DOWN
SLC2A14	1.8558	10.1889	-2.45688	0.00655	DOWN
DAB1	1.1783	9.7049	-3.04196	0.00387	DOWN
CCDC36	4.0788	18.7375	-2.19971	0.14532	DOWN
C2orf70	1.3119	7.4850	-2.51234	0.11750	DOWN
GPR113	1.1564	6.9420	-2.58577	0.11389	DOWN
XCR1	1.7973	7.9867	-2.15179	0.10867	DOWN
HSPB7	2.2056	12.5944	-2.51354	0.09797	DOWN
PHOSPHO1	1.3907	5.6388	-2.01958	0.09551	DOWN
TUBB8	1.2534	8.4242	-2.74868	0.07047	DOWN
CBX2	3.4815	16.4630	-2.24143	0.00655	DOWN
C9orf131	1.7134	11.1189	-2.69807	0.03205	DOWN
SLC16A11	1.8512	9.1467	-2.30481	0.11778	DOWN
GALNTL6	2.1232	14.7362	-2.79506	0.03042	DOWN
IGDCC3	1.1649	5.0227	-2.10824	0.14787	DOWN
SLC26A9	2.2187	9.2199	-2.05506	0.03939	DOWN
MFSD4	11.0637	57.6549	-2.38161	0.04585	DOWN
TMEM81	2.2897	9.3406	-2.02837	0.02336	DOWN
BRSK2	1.1687	7.0507	-2.59289	0.00387	DOWN
AMZ1	1.4375	6.8645	-2.25557	0.16933	DOWN
ZIC4	1.5568	24.3535	-3.96748	0.00387	DOWN
DES	5.5612	61.8504	-3.47530	0.16766	DOWN
SPSB4	2.2703	21.7403	-3.25942	0.01081	DOWN
RAG2	1.6527	17.8718	-3.43481	0.00387	DOWN
CADM2	1.2702	7.5653	-2.57436	0.12166	DOWN
FAM182B	3.4270	22.6674	-2.72561	0.09524	DOWN
GAL3ST3	2.2305	10.7924	-2.27461	0.19405	DOWN
GRAMD2	2.6725	11.0085	-2.04235	0.00387	DOWN
CHRNA7	1.2036	6.6043	-2.45604	0.14581	DOWN
SCUBE2	1.8694	9.3307	-2.31938	0.00387	DOWN
UBQLNL	1.7561	9.8823	-2.49247	0.15231	DOWN
UBQLN3	2.1374	14.3828	-2.75044	0.09505	DOWN
P2RY2	1.9212	8.6559	-2.17169	0.07662	DOWN
GPR156	1.2504	9.7542	-2.96360	0.00387	DOWN
EIF4E1B	1.0420	7.6232	-2.87105	0.03281	DOWN
DOK7	3.6909	22.3180	-2.59616	0.02225	DOWN
PLEKHD1	1.2216	6.0927	-2.31826	0.07047	DOWN
AMIGO3	1.3284	6.0563	-2.18879	0.18898	DOWN
AIM1L	1.8656	15.0620	-3.01317	0.00387	DOWN
LRRTM4	1.2171	7.6152	-2.64539	0.02336	DOWN
OR51B6	1.2648	12.1611	-3.26532	0.13406	DOWN
OR4K13	1.0587	11.5990	-3.45365	0.17521	DOWN
OR4N2	3.9325	28.6419	-2.86460	0.18898	DOWN
AC110781.3	1.0994	8.1111	-2.88322	0.13175	DOWN
DIRAS1	1.6990	7.9708	-2.23002	0.16538	DOWN
GRIN1	1.0131	12.2730	-3.59859	0.00387	DOWN
SOX11	1.1683	5.0523	-2.11256	0.05710	DOWN
FUT2	1.2230	6.4629	-2.40177	0.11528	DOWN
LY6H	1.1356	6.2145	-2.45223	0.11417	DOWN
CLVS1	2.3005	22.7880	-3.30824	0.02839	DOWN
FBXO39	1.0596	4.9721	-2.23030	0.15494	DOWN
C10orf71	1.5094	11.3935	-2.91613	0.00387	DOWN
NIM1K	1.6495	8.9009	-2.43188	0.08718	DOWN
OR2G2	1.1885	7.9495	-2.74175	0.19116	DOWN
NHLH2	1.0085	6.1672	-2.61241	0.02336	DOWN
C12orf68	1.4851	7.1343	-2.26420	0.00880	DOWN
PRSS42	2.2940	11.7986	-2.36267	0.04966	DOWN
CA8	1.4914	14.1672	-3.24781	0.00655	DOWN
FAM132B	3.1436	13.4003	-2.09177	0.03737	DOWN
CD300LB	1.4374	7.6091	-2.40425	0.05819	DOWN
TRIML2	1.2696	10.1401	-2.99761	0.00387	DOWN
C12orf42	2.2124	9.1356	-2.04586	0.01712	DOWN
GGN	2.0205	12.9871	-2.68433	0.04829	DOWN
C17orf96	1.1737	6.1578	-2.39132	0.02439	DOWN
GATA2	6.4189	33.2709	-2.37388	0.03493	DOWN
MKRN3	1.5590	11.1192	-2.83434	0.00387	DOWN
LBX2	1.6758	7.1746	-2.09805	0.11820	DOWN
TPPP2	1.1848	6.7381	-2.50772	0.04141	DOWN
LRRC3B	1.6815	13.1190	-2.96383	0.04141	DOWN
MRGPRX3	1.0861	9.9607	-3.19713	0.12207	DOWN

Table S4 (continued)

Table S4 (continued)

Gene name	Cancer_FPKM	Non-cancer_FPKM	log2(fold change)	FDR	Trend
<i>ITLN1</i>	1.1105	5.9767	-2.42809	0.14270	DOWN
<i>NRXN1</i>	3.4001	22.3314	-2.71544	0.00387	DOWN
<i>GPBAR1</i>	1.2928	10.7516	-3.05595	0.06153	DOWN
<i>TH</i>	2.2495	15.3266	-2.76836	0.02537	DOWN
<i>SLC9A4</i>	2.6837	13.3339	-2.31284	0.03281	DOWN
<i>PLD5</i>	1.6598	11.8960	-2.84143	0.02336	DOWN
<i>KCNE1</i>	2.8083	14.1199	-2.32998	0.02336	DOWN
<i>PRR26</i>	2.1317	8.8073	-2.04672	0.16260	DOWN
<i>RNF182</i>	2.2348	11.4437	-2.35632	0.07886	DOWN
<i>GSX2</i>	1.7144	9.0542	-2.40087	0.14668	DOWN
<i>CXCR2</i>	1.0059	9.5426	-3.24586	0.01081	DOWN
<i>CHRM2</i>	1.7820	18.8644	-3.40407	0.00387	DOWN
<i>PENK</i>	2.0170	20.6810	-3.35801	0.00387	DOWN
<i>TMEM132C</i>	1.1870	5.7916	-2.28667	0.08790	DOWN
<i>CCDC108</i>	2.1087	11.1786	-2.40633	0.04236	DOWN
<i>SOX2</i>	1.4039	9.5569	-2.76708	0.17049	DOWN
<i>OR6T1</i>	1.1590	14.6323	-3.65819	0.14980	DOWN
<i>OR52H1</i>	1.1320	6.8029	-2.58732	0.12319	DOWN
<i>ATG9B</i>	3.0314	14.8863	-2.29595	0.03573	DOWN
<i>OR8H2</i>	1.0857	5.9950	-2.46516	0.19857	DOWN
<i>BAI1</i>	1.8399	7.8108	-2.08581	0.12143	DOWN
<i>FTMT</i>	1.0155	6.4860	-2.67514	0.19213	DOWN
<i>RGMA</i>	2.5927	18.6495	-2.84660	0.00387	DOWN
<i>HHIPL1</i>	1.0056	5.3393	-2.40866	0.01081	DOWN
<i>GABRG3</i>	1.2511	7.3951	-2.56339	0.03939	DOWN
<i>KCNK4</i>	1.0932	10.1171	-3.21013	0.02109	DOWN
<i>NXPH3</i>	1.3061	8.5497	-2.71061	0.09929	DOWN
<i>OR10G7</i>	1.1384	11.0636	-3.28075	0.19484	DOWN
<i>OR4Q3</i>	1.2128	11.7693	-3.27861	0.16782	DOWN
<i>KCNB2</i>	1.0361	8.5278	-3.04100	0.02839	DOWN
<i>BRICD5</i>	6.0436	27.7794	-2.20055	0.08904	DOWN
<i>RGS6</i>	2.5201	17.0502	-2.75824	0.00387	DOWN
<i>GRID1</i>	1.0636	6.7717	-2.67063	0.14906	DOWN
<i>GPR97</i>	1.1178	6.4381	-2.52602	0.03797	DOWN
<i>SLC25A18</i>	1.5111	6.2176	-2.04079	0.08862	DOWN
<i>C21orf90</i>	1.1019	6.0760	-2.46318	0.09481	DOWN
<i>C19orf59</i>	1.1668	7.7963	-2.74022	0.11138	DOWN
<i>BEGAIN</i>	2.0072	11.3704	-2.50201	0.01241	DOWN
<i>CSMD1</i>	2.3762	12.5067	-2.39600	0.00387	DOWN
<i>C2CD4C</i>	1.3300	6.0671	-2.18958	0.01241	DOWN
<i>OR52L1</i>	1.0449	8.5290	-3.02896	0.16399	DOWN
<i>SSTR3</i>	1.2874	7.6012	-2.56181	0.01979	DOWN
<i>MEX3B</i>	1.8757	8.3602	-2.15608	0.04654	DOWN
<i>PCBP3</i>	6.9221	34.0061	-2.29651	0.00387	DOWN
<i>CCR3</i>	1.0621	14.4286	-3.76389	0.00387	DOWN
<i>MARCH11</i>	2.5567	14.4958	-2.50326	0.16228	DOWN
<i>ASCL2</i>	1.6185	7.0308	-2.11907	0.04236	DOWN
<i>TRAIP</i>	1.7204	9.3775	-2.44648	0.01399	DOWN
<i>AIFM3</i>	3.3657	16.4446	-2.28862	0.08230	DOWN
<i>SCN5A</i>	1.0490	9.7146	-3.21111	0.01081	DOWN
<i>ARSI</i>	1.4029	8.4650	-2.59305	0.03042	DOWN
<i>NPB</i>	1.3047	6.4250	-2.30000	0.18129	DOWN
<i>TMPRSS2</i>	12.0821	49.1996	-2.02577	0.06594	DOWN
<i>TBX1</i>	2.9917	13.1834	-2.13970	0.16585	DOWN
<i>CNTN2</i>	1.5366	8.1021	-2.39859	0.05767	DOWN
<i>KCNJ12</i>	1.7432	12.4800	-2.83983	0.00880	DOWN
<i>GOLGA6L4</i>	1.3134	6.7130	-2.35370	0.04585	DOWN
<i>OLIG1</i>	1.2981	5.4216	-2.06231	0.13203	DOWN
<i>TACSTD2</i>	13.3267	57.1704	-2.10095	0.01712	DOWN
<i>KRTAP19-1</i>	1.3714	11.3690	-3.05142	0.18980	DOWN
<i>PKP3</i>	2.9119	15.8907	-2.44814	0.04437	DOWN
<i>C21orf88</i>	1.4727	5.9452	-2.01331	0.15192	DOWN
<i>ROBO2</i>	2.7206	13.8227	-2.34505	0.06153	DOWN
<i>NT5C1B</i>	1.3720	10.4913	-2.93485	0.03042	DOWN
<i>SLC24A3</i>	1.4530	5.8704	-2.01439	0.04013	DOWN
<i>INPP5J</i>	4.4583	19.3608	-2.11856	0.03939	DOWN
<i>MFSD6L</i>	1.2327	6.8051	-2.46485	0.00387	DOWN
<i>SFTPA2</i>	1.0339	8.7939	-3.08846	0.05784	DOWN
<i>SHC4</i>	1.1732	8.3681	-2.83450	0.03135	DOWN
<i>NTF3</i>	1.9387	11.8294	-2.60926	0.04236	DOWN
<i>SYN3</i>	1.8961	17.9251	-3.24089	0.11729	DOWN
<i>ADARB2</i>	2.5824	23.3592	-3.17719	0.00387	DOWN
<i>KCNQ5</i>	1.6685	21.0549	-3.65751	0.00880	DOWN

Table S4 (continued)

Table S4 (continued)

Gene name	Cancer_FPKM	Non-cancer_FPKM	log2(fold change)	FDR	Trend
ADAMTSL5	2.1026	10.2644	-2.28742	0.02109	DOWN
NAT8L	2.4407	13.8808	-2.50773	0.02225	DOWN
TAS2R60	1.4757	10.3619	-2.81186	0.18511	DOWN
KLHL34	1.0456	6.6467	-2.66838	0.00387	DOWN
KRT5	3.7927	22.1922	-2.54876	0.00655	DOWN
TEX38	1.1905	10.3122	-3.11469	0.13394	DOWN
KDM4D	1.1826	5.7779	-2.28856	0.02953	DOWN
GABRA5	1.2402	9.4133	-2.92418	0.02109	DOWN
GLDN	3.0892	18.0341	-2.54541	0.00387	DOWN
MYT1L	3.0669	31.2526	-3.34913	0.00387	DOWN
C5orf38	2.6566	18.4211	-2.79371	0.07543	DOWN
CLCNKA	6.7145	55.5415	-3.04822	0.02109	DOWN
OR9Q2	1.0552	10.8214	-3.35832	0.19590	DOWN
FAM86B1	1.0040	5.3156	-2.40441	0.11805	DOWN
MPPED1	1.8774	14.7388	-2.97284	0.01081	DOWN
KRT16	1.5228	11.7834	-2.95196	0.14980	DOWN
ZACN	3.1807	12.8009	-2.00883	0.16251	DOWN
PNLIPRP1	1.3514	8.0312	-2.57120	0.00387	DOWN
LCE2A	1.4268	18.8615	-3.72461	0.12512	DOWN
RP11-195F19.5	4.8957	22.6202	-2.20802	0.12045	DOWN
MAGI2	4.0559	19.8056	-2.28781	0.06557	DOWN
KCNJ11	1.7359	9.3888	-2.43526	0.03042	DOWN
C1orf170	1.1533	5.6068	-2.28137	0.18164	DOWN
DNAH17	1.2105	7.0580	-2.54361	0.02537	DOWN
TTC24	1.6328	7.1148	-2.12349	0.11443	DOWN
LCN10	2.2743	15.3972	-2.75920	0.03797	DOWN
COL25A1	3.4429	23.8886	-2.79464	0.05077	DOWN
SKOR1	1.1642	5.3976	-2.21295	0.11956	DOWN
SHISA6	1.5443	14.2848	-3.20949	0.00387	DOWN
KLRG2	1.7199	16.6187	-3.27243	0.14604	DOWN
GPR179	1.3001	6.4091	-2.30149	0.05077	DOWN
MSANTD1	2.2561	12.8789	-2.51311	0.04187	DOWN
KRT77	1.2158	7.7884	-2.67936	0.13208	DOWN
FAM180A	1.1002	9.1746	-3.05985	0.05193	DOWN
S100A14	2.4532	11.2759	-2.20053	0.17163	DOWN
FAM179A	1.7811	8.2454	-2.21079	0.09527	DOWN
TBC1D28	1.6264	8.9268	-2.45649	0.03336	DOWN
PAX5	1.2856	7.6305	-2.56936	0.00387	DOWN
KIF19	1.5426	7.9070	-2.35780	0.10529	DOWN
CTSE	1.3829	6.2008	-2.16481	0.15824	DOWN
GREB1	3.0744	13.3222	-2.11545	0.01560	DOWN
NOXO1	1.5005	6.3186	-2.07415	0.16241	DOWN
FAM72A	1.9547	15.8243	-3.01716	0.00387	DOWN
SLC30A10	1.5309	10.6327	-2.79605	0.03857	DOWN
SLC6A17	1.2404	7.5932	-2.61391	0.00655	DOWN
RP11-366L20.2	2.0139	12.1623	-2.59438	0.05329	DOWN
FBXL22	1.6416	8.2167	-2.32348	0.10466	DOWN
OR8S1	1.4798	11.7795	-2.99279	0.09411	DOWN
GYPE	1.0226	7.8264	-2.93610	0.10971	DOWN
FAM177B	1.5329	12.3834	-3.01411	0.09855	DOWN
COL4A6	2.3819	14.0278	-2.55814	0.03042	DOWN
DLGAP2	2.0235	9.6370	-2.25172	0.15529	DOWN
OR2T6	1.1627	20.0800	-4.11027	0.13952	DOWN
MB	1.2400	7.5334	-2.60293	0.04013	DOWN
ANTXRL	1.1390	7.5966	-2.73766	0.05924	DOWN
PEG3	3.4848	14.6126	-2.06809	0.00387	DOWN
TMEM239	1.3876	6.3350	-2.19078	0.18010	DOWN
DCAF12L2	1.0234	8.4256	-3.04146	0.16976	DOWN
NTRK1	2.1268	9.1867	-2.11083	0.16258	DOWN
ARC	1.2319	8.0989	-2.71682	0.02756	DOWN
ZNF536	2.4901	16.3905	-2.71859	0.03205	DOWN
RYR2	1.5535	8.3104	-2.41936	0.03042	DOWN
TAT	1.0287	8.5594	-3.05666	0.04187	DOWN
ABCA4	1.2329	15.5451	-3.65632	0.00387	DOWN
MT-ND6	530.3260	22,334.5000	-5.39625	0.00387	DOWN
MT-CO2	636.0730	5,042.6300	-2.98691	0.03205	DOWN
MT-CYB	1,043.8400	14,942.2000	-3.83942	0.00387	DOWN
SMOC1	1.8984	8.9622	-2.23910	0.08130	DOWN
COLGALT2	1.5137	7.7851	-2.36260	0.04236	DOWN
EPS8L3	4.8180	32.7555	-2.76524	0.07378	DOWN
MT-ND2	1,025.0800	11,556.8000	-3.49493	0.01081	DOWN
APCDD1L	1.8150	7.2664	-2.00129	0.12116	DOWN
GRIN3A	1.0027	9.1362	-3.18776	0.00387	DOWN

Table S4 (continued)

Table S4 (continued)

Gene name	Cancer_FPKM	Non-cancer_FPKM	log2(fold change)	FDR	Trend
MT-ND5	730.9050	10,246.7000	-3.80933	0.00387	DOWN
BRINP2	1.1426	8.0815	-2.82227	0.09527	DOWN
PAX9	2.7461	18.3078	-2.73700	0.02439	DOWN
DUSP27	1.4671	8.7790	-2.58109	0.02109	DOWN
CES1	1.9708	9.1446	-2.21417	0.05077	DOWN
MT-ND4	39.4311	4,131.4700	-6.71118	0.12022	DOWN
MT-ND1	799.0490	6,561.9900	-3.03778	0.04187	DOWN
MT-ATP6	677.6510	7,392.9900	-3.44754	0.00880	DOWN
C1orf95	1.9609	8.4744	-2.11159	0.00387	DOWN
TCP10	1.3872	12.9789	-3.22596	0.00387	DOWN
CAPN8	2.3052	10.3725	-2.16982	0.04437	DOWN
CENPW	1.0746	5.7700	-2.42478	0.19064	DOWN
HSD3B1	1.2478	14.4836	-3.53701	0.02839	DOWN
HSD3B2	1.5398	6.4124	-2.05816	0.10677	DOWN
SAMD13	1.0206	5.9732	-2.54906	0.05329	DOWN
NEU4	2.6974	12.5380	-2.21666	0.05609	DOWN
NPY4R	1.3809	13.3205	-3.26999	0.17219	DOWN
COL11A2	1.9754	9.7104	-2.29740	0.05077	DOWN
PRRT1	2.1848	15.7600	-2.85073	0.00387	DOWN
SP5	1.5658	8.3764	-2.41948	0.17049	DOWN
CSHL1	1.4613	9.1288	-2.64318	0.02839	DOWN
KRTAP5-10	1.3248	9.4194	-2.82982	0.19671	DOWN
TRIM31	1.2338	14.0165	-3.50599	0.00387	DOWN
C5orf60	1.4031	8.3857	-2.57932	0.01847	DOWN
PSG5	1.2016	10.6864	-3.15273	0.00387	DOWN
LRRC10B	1.1943	5.1378	-2.10497	0.04585	DOWN
PCDHGA1	2.3688	9.5591	-2.01270	0.18429	DOWN
PCDHA5	2.3824	10.1467	-2.09054	0.14461	DOWN
PCDHA2	1.4505	9.3862	-2.69404	0.08011	DOWN
PRSS1	1.5583	14.9059	-3.25788	0.08666	DOWN
CCNI2	3.1212	17.4700	-2.48472	0.15362	DOWN
MUC12	1.0936	7.3007	-2.73891	0.01081	DOWN
KRT6A	2.1158	16.2543	-2.94154	0.05024	DOWN
SERPINB5	1.1846	6.8852	-2.53913	0.04829	DOWN
ZDHHC11B	1.7757	8.0244	-2.17598	0.19291	DOWN
C3orf72	1.1782	9.5382	-3.01717	0.06906	DOWN
TMEM200C	1.8587	9.5679	-2.36389	0.05077	DOWN
VGLL3	1.9752	12.0393	-2.60767	0.02537	DOWN
PRSS50	1.3241	7.1207	-2.42702	0.17431	DOWN
DIO2	3.0417	13.2519	-2.12323	0.01399	DOWN
C17orf51	2.9122	17.4716	-2.58485	0.00387	DOWN
KRTAP3-1	2.0845	19.4546	-3.22237	0.13853	DOWN
CCDC19	2.2564	12.8781	-2.51282	0.13040	DOWN
ASIC3	2.6110	11.3970	-2.12596	0.05924	DOWN
OR2F1	1.2892	16.6556	-3.69150	0.18441	DOWN
ATP6V1G2	1.5561	11.6176	-2.90027	0.16106	DOWN
PPM1N	1.3000	5.8772	-2.17663	0.08535	DOWN
PRCD	3.0234	16.0721	-2.41032	0.01241	DOWN
IQCJ	1.4319	14.8175	-3.37128	0.03573	DOWN
NUTM2D	1.4907	9.4296	-2.66124	0.05144	DOWN
TBC1D26	1.9726	8.9793	-2.18653	0.12927	DOWN
AP000974.1	1.7410	7.0348	-2.01463	0.06125	DOWN
HMX1	1.0239	7.6265	-2.89695	0.13796	DOWN
GCGR	4.7686	26.2124	-2.45861	0.15536	DOWN
TTC34	1.8101	8.8655	-2.29216	0.08263	DOWN
HTR5A-AS1	1.3346	7.7682	-2.54117	0.19689	DOWN
TAS2R41	1.4647	7.8757	-2.42677	0.19687	DOWN
C1orf229	1.2856	5.8539	-2.18702	0.03573	DOWN
ADRA2B	1.9165	7.9237	-2.04774	0.04013	DOWN
REXO1L11P	9.6644	84.6481	-3.13073	0.00387	DOWN
CKMT1A	1.0104	8.6133	-3.09166	0.10296	DOWN
C5orf66	2.3976	17.2659	-2.84825	0.01560	DOWN
PRRT4	1.2766	8.6891	-2.76688	0.03797	DOWN
ZNF469	1.2850	8.1171	-2.65915	0.00387	DOWN
AC104809.3	1.9570	13.4865	-2.78483	0.02439	DOWN
OR2T7	3.5054	20.6900	-2.56129	0.01847	DOWN
CTB-58E17.5	1.1962	9.1993	-2.94303	0.15873	DOWN
C14orf144	1.6183	8.4079	-2.37729	0.19041	DOWN
CASP16	1.1202	6.2886	-2.48896	0.11921	DOWN
C1orf233	1.1972	5.6246	-2.23214	0.03797	DOWN
PROB1	1.7245	7.5133	-2.12330	0.02336	DOWN
SFTA3	1.4605	14.1962	-3.28101	0.00387	DOWN
IQCF3	2.7249	17.7870	-2.70653	0.05144	DOWN

Table S4 (continued)

Table S4 (continued)

Gene name	Cancer_FPKM	Non-cancer_FPKM	log2(fold change)	FDR	Trend
CYP21A2	3.0739	14.3148	-2.21935	0.14817	DOWN
PSG1	1.9864	13.4196	-2.75609	0.00880	DOWN
TMEM253	1.2096	9.3437	-2.94946	0.09524	DOWN
TMEM229A	1.0733	6.8050	-2.66450	0.18519	DOWN
C5orf58	1.8844	12.7191	-2.75481	0.12011	DOWN
WASH4P	2.9614	12.5209	-2.08000	0.01399	DOWN
FAM203A	1.5045	8.3537	-2.47317	0.12960	DOWN
C8orf56	2.1215	11.9896	-2.49862	0.16441	DOWN
PATE4	2.1381	21.3311	-3.31856	0.05385	DOWN
OR2W3	2.5016	13.9134	-2.47553	0.16472	DOWN
GATSL3	6.0146	35.4995	-2.56127	0.01560	DOWN
C2orf61	1.1734	8.0924	-2.78585	0.09193	DOWN
LCE1F	1.1307	11.8595	-3.39080	0.08718	DOWN
TNFRSF13B	2.4431	18.2838	-2.90380	0.02439	DOWN
TDGF1	2.1974	15.1549	-2.78591	0.01081	DOWN
CDRT1	1.8032	9.7092	-2.42882	0.09506	DOWN
ARHGDIG	1.5602	8.1089	-2.37775	0.14885	DOWN
ERVW-1	1.2929	12.4272	-3.26487	0.02756	DOWN
PSG11	1.3175	18.9324	-3.84499	0.00387	DOWN
PSG4	1.9314	24.3538	-3.65642	0.00387	DOWN
PTCHD4	2.1240	8.5641	-2.01151	0.03336	DOWN
RP11-766F14.2	1.0138	5.9778	-2.55987	0.01712	DOWN
ATP6V1E2	2.7996	11.2994	-2.01296	0.12859	DOWN
LINC00923	3.0587	14.9941	-2.29340	0.18381	DOWN
RP11-1102P16.1	1.1963	5.1457	-2.10474	0.16026	DOWN
EIF5AL1	1.1979	5.4828	-2.19446	0.02439	DOWN
NOX5	1.1329	7.2134	-2.67067	0.03135	DOWN
PCDHA3	1.9929	11.4911	-2.52756	0.15642	DOWN
C21orf119	3.3372	14.7841	-2.14733	0.03431	DOWN
SALL3	2.2937	9.7002	-2.08031	0.04187	DOWN
OVCH1-AS1	1.4554	8.8108	-2.59784	0.13358	DOWN
RP11-347C12.3	1.2235	5.3860	-2.13824	0.14086	DOWN
CLEC5A	2.0959	15.3091	-2.86873	0.08324	DOWN
RP11-204N11.1	1.9637	16.8874	-3.10433	0.14998	DOWN
C16orf95	2.8051	14.2367	-2.34350	0.07203	DOWN
RP11-77K12.1	1.0649	8.2597	-2.95544	0.19643	DOWN
UBBP4	1.3371	7.1485	-2.41857	0.09193	DOWN
PTGES3L	1.0802	4.4050	-2.02789	0.12960	DOWN
AC004466.1	2.4625	13.5172	-2.45659	0.18831	DOWN
AC093677.1	1.3382	21.4097	-3.99991	0.12182	DOWN
AC010327.2	1.0732	8.6130	-3.00460	0.14266	DOWN
KRBOX1	1.8851	9.3947	-2.31723	0.12317	DOWN