Novel pyrrolobenzodiazepine (PBD) benzofused hybrid molecules inhibit NF-κB activity and synergise with bortezomib and ibrutinib in hematological cancers. *Haematologica.*

https://doi.org/10.3324/haematol.2019.238584
Novel pyrrolobenzodiazepine benzofused hybrid molecules inhibit NF-κB activity and synergise with bortezomib and ibrutinib in hematological cancers

by Thomas Lewis, David B. Corcoran, David E. Thurston, Peter J. Giles, Kevin Ashelford, Elisabeth J. Walsby, Christopher D. Fegan, Andrea G.S. Pepper, Khondaker Miraz Rahman, and Chris Pepper

Haematologica 2020 [Epub ahead of print]

Citation: Thomas Lewis, David B. Corcoran, David E. Thurston, Peter J. Giles, Kevin Ashelford, Elisabeth J. Walsby, Christopher D. Fegan, Andrea G.S. Pepper, Khondaker Miraz Rahman, and Chris Pepper. Novel pyrrolobenzodiazepine benzofused hybrid molecules inhibit NF-κB activity and synergise with bortezomib and ibrutinib in hematological cancers.
Haematologica. 2020; 105:xxx
doi:10.3324/haematol.2019.238584

Publisher's Disclaimer.
E-publishing ahead of print is increasingly important for the rapid dissemination of science. Haematologica is, therefore, E-publishing PDF files of an early version of manuscripts that have completed a regular peer review and have been accepted for publication. E-publishing of this PDF file has been approved by the authors. After having E-published Ahead of Print, manuscripts will then undergo technical and English editing, typesetting, proof correction and be presented for the authors' final approval; the final version of the manuscript will then appear in print on a regular issue of the journal. All legal disclaimers that apply to the journal also pertain to this production process.
Novel pyrrolobenzodiazepine benzofused hybrid molecules inhibit NF-κB activity and synergise with bortezomib and ibrutinib in hematological cancers

Thomas Lewis¹, David B. Corcoran², David E. Thurston², Peter J. Giles¹,³, Kevin Ashelford¹,³, Elisabeth J. Walsby¹, Christopher D. Fegan¹, Andrea G. S. Pepper⁴, Khondaker Miraz Rahman²* and Chris Pepper¹,⁴*

¹Division of Cancer & Genetics, Cardiff University School of Medicine, Heath Park, Cardiff, CF14 4XN, ²School of Cancer and Pharmaceutical Science, King’s College London, Franklin-Wilkins Building, 150 Stamford Street, London, SE1 9NH, ³Wales Gene Park, Heath Park, Cardiff, CF14 4XN, ⁴Brighton and Sussex Medical School, University of Sussex, Brighton, East Sussex, BN1 9PX.

*These authors contributed equally to this work

Running title: Novel PBDs inhibit NF-κB in hematological cancers

Key words: pyrrolobenzodiazepine, multiple myeloma, chronic lymphocytic leukemia, NF-κB, synergy

Abstract word count: 218

Word count: 3322

Figures: 6

Corresponding author:
Professor Chris Pepper, Brighton and Sussex Medical School, University of Sussex, Brighton, East Sussex, BN1 9PX. Tel: 01273 678644 Email: c.pepper@bsms.ac.uk

Conflict of interests: All of the authors declare that they have no conflict of interests.
Abstract

Chronic lymphocytic leukemia (CLL) and multiple myeloma (MM) are incurable hematological malignancies that are pathologically linked with aberrant NF-κB activation. In this study, we identified a group of novel C8-linked benzofused Pyrrolo[2,1-c][1,4]benzdiazepines (PBD) monomeric hybrids capable of sequence-selective inhibition of NF-κB with low nanomolar LD₅₀ values in CLL (n=46) and MM cell lines (n=5). The lead compound, DC-1-192, significantly inhibited NF-κB DNA binding after just 4h exposure and demonstrating inhibitory effects on both canonical and non-canonical NF-κB subunits. In primary CLL cells, sensitivity to DC-1-192 was inversely correlated with RelA subunit expression (r²=0.2) and samples with BIRC3 or NOTCH1 mutations showed increased sensitivity (P=0.001). RNA-sequencing and gene set enrichment analysis confirmed the over-representation of NF-κB regulated genes in the down-regulated gene list. Furthermore, in vivo efficacy studies in NOD/SCID mice, using a systemic RPMI 8226 human multiple myeloma xenograft model, showed that DC-1-192 significantly prolonged survival (P=0.017). In addition, DC1-192 showed synergy with bortezomib and ibrutinib; synergy with ibrutinib was enhanced when CLL cells were co-cultured on CD40L-expressing fibroblasts in order to mimic the cytoprotective lymph node microenvironment (P = 0.01). Given that NF-κB plays a role in both bortezomib and ibrutinib resistance mechanisms, these data provide a strong rationale for the use of DC-1-192 in the treatment of NF-κB-driven cancers, particularly in the context of relapsed/refractory disease.
Introduction

Nuclear factor kappa B (NF-κB) denotes a family of homo- and heterodimeric transcription factors composed of five subunits: p65 (Rel A), p50, Rel B, p52 and c-Rel [1]. These subunits exert their effects via the canonical or non-canonical signaling pathways [2]. NF-κB is maintained in an inactive state in the cytoplasm but following IκB kinase (IKK) activation NF-κB is shuttled into the nucleus where it exerts its transcriptional effects [3]. NF-κB regulates the transcription of genes that are essential for cell survival, proliferation, inflammation and invasion/metastasis. These processes are commonly dysregulated in cancers, including CLL and MM, leading to the constitutive aberrant activation of NF-κB [2-4]. Indeed, NF-κB has been shown to play a central role in disease progression and drug resistance in these hematological cancers [5,6]. Whilst treatment with currently established therapies, such as the proteasome inhibitor bortezomib or the BTK inhibitor ibrutinib, are initially effective in a significant proportion of patients [7,8], there is evidence to suggest that treatment with both of these agents causes an increase in NF-κB activation which has been linked to drug resistance and treatment failure [9,10]. Therefore, direct inhibition of NF-κB could potentially resensitize tumor cells, thus highlighting this transcription factor as a potential therapeutic target [11-13].

Pyrrolo[2,1-c][1,4]benzodiazepines (PBDs) are naturally occurring molecules produced by Streptomyces bacteria whose family members include anthramycin (Figure 1) and tomaymycin [14,15]. PBDs are a class of sequence-specific covalent DNA minor groove binding agents that are selective for GC-rich sequences, which have recently been evaluated as potential chemotherapeutic agents in clinical trials.
More recently, members of the PBD family have been developed as cytotoxic payloads for attachment to antibodies to form Antibody-Drug Conjugates (ADCs), and a number of these are currently undergoing clinical evaluation for the treatment of leukemia and lung cancer [18].

This study identified three lead compounds (DC-1-192, DC-1-92 and DC-1-170; Figure 1) from a library screen of 87 novel synthetic C8-linked benzofused PBD monomeric hybrids based on their *in vitro* cytotoxicity. The compounds were then further evaluated for their biological properties, including differential toxicity, in malignant and age-matched normal B- and T-cells. In terms of their mechanism of action, PBD monomers can recognise and bind to specific sequences of DNA and therefore have the potential to act as competitive inhibitors of transcription factors. Previous research has shown that PBD monomers such as GWL-78 preferentially inhibit the transcription factor NF-Y [19], whilst PBD monomers such as the DC-81-indole hybrid [20] and KMR-28-39 are potent NF-κB inhibitors [21]. The aim of this study was to determine the biological properties of these novel C8-linked benzofused PBD monomers by investigating their cytotoxic profiles in multiple myeloma cell lines, primary CLL cells and age-matched normal B- and T-lymphocytes. We went on to investigate their ability to inhibit NF-κB and whether they could potentiate the effects of the targeted agents bortezomib and ibrutinib, currently used in the treatment of myeloma and CLL, respectively.
Methods

Detailed methods can be found in Supplementary information.

Cell lines, primary CLL cells and normal lymphocytes

Primary chronic lymphocytic leukemia (CLL) cells (n=46) and age-matched normal B- and T-cells were obtained with informed consent in accordance with the ethical approval granted by South East Wales Research Ethics Committee (02/4806). In addition, five multiple myeloma cell lines, JJN3, U266, OPM2, MM.1S and H929 were obtained from DSMZ. The provenance of the cell lines was verified by multiplex PCR of minisatellite markers; all were certified mycoplasma-free.

Measurement of in vitro apoptosis

Apoptosis was assessed using Annexin V and propidium iodide labeling. Samples were analyzed using an Accuri C6 flow cytometer with CFlow software (BD Biosciences).

Enzyme Linked Immuno-sorbent Assay (ELISA) for NF-κB subunits

Nuclear levels of p65, p50, p52 and RelB DNA binding were assessed in JJN3 and U266 cells treated for 4h with DC-1-92, DC-1-170 (0nM-20nM) and DC-1-192 (0nM-5nM).

Synergy with bortezomib and ibrutinib

The synergy between the PBDs and bortezomib or ibrutinib was determined in the JJN3 cells and primary CLL cells respectively. Fixed molar ratios were derived from
experimentally-determined LD_{50} values for each PBD and clinically achievable concentrations of bortezomib and ibrutinib, respectively.

**RNA Isolation and RNA-sequencing**

JJN3 cells were treated with 20nM of either DC-1-170 or DC-1-192 for 4h. RNA was extracted using an RNeasy mini-kit (Qiagen) in accordance with the manufacturer’s instructions. 100-900ng of high-quality total RNA (RNA integrity number >8) was depleted of ribosomal RNA, and the sequencing libraries were prepared using the Illumina TruSeq Stranded Total RNA with Ribo-Zero Gold™ kit (Illumina Inc.).

**In vivo systemic xenograft model of myeloma in NOD/SCID mice**

NOD/SCID mice were sub-lethally irradiated prior to tail vein inoculation with the human myeloma cell line RPMI8226 (1 x 10^7) to initiate tumor development. The date of inoculation was denoted as Day 0; intravenous treatment with vehicle only; 0.05% DMSO in saline (n=7) or 1mg/kg of DC-1-192 (n=7) was started at Day 5. Survival was evaluated from the first day of treatment until death.

**Statistical Analysis**

All statistical analysis was performed using Graphpad Prism 6.0 software (Graphpad Software). Normal distribution of the data was established using the omnibus K2 test. Univariate comparisons were made using the Student’s t-test for paired and unpaired observations. All toxicity data from drug treatment were used to produce sigmoidal dose-response curves from which LD_{50} values were calculated. Toxicity data from synergy experiments were processed using CalcuSyn software using the
median effect method to subsequently calculate the combination index (CI) for each pair of agents; CI values less than 1 were indicative of synergy [22].

**Results**

*Cytotoxic screening of PBD compounds identified three lead compounds*

Initial cytotoxicity screening (trypan blue exclusion assay) of a library of 87 novel synthetic C8-linked benzofused PBD monomeric hybrids (PBDs) was carried out using the multiple myeloma cell line, JJN3. Three lead compounds were selected for further investigation based on their cytotoxic effects at nanomolar concentrations. The chemical structures of all three compounds, together with that of Anthramycin on which they are based, are shown in Figure 1.

*In vitro and in vivo cytotoxicity of the lead PBD compounds in multiple myeloma cell lines*

The relative cytotoxicity of the three lead compounds was then assessed in five different multiple myeloma cell lines, JJN3, U266, OPM2, MM.1S and H929 using an Annexin V/propidium iodide apoptosis assay. The cells were cultured for 48h in increasing concentrations (1nM-100nM) of DC-1-92, DC-1-170 and DC-1-192 and were compared with untreated controls. Each compound showed a dose-dependent increase in apoptosis; a representative example of the data generated is shown in Figure 2A. The dose-response curves for each compound were compared in each cell line using overlaid sigmoidal plots (Figure 2B) and the mean LD$_{50}$ values were then calculated for each treatment and plotted on the bar chart shown in Figure 2C. Although each cell line showed differential sensitivity to the three compounds, in every case DC-1-192 was the most cytotoxic PBD with DC-1-170 showing the least cytotoxicity (Figure 2D). The LD$_{50}$ values for DC-1-192 were compared
with the published NF-κB index value for each cell line [23]. The NF-κB index is the average of the log2 values for 10 NF-κB regulated genes (excluding BIRC3/clAP2); the higher the index value, the more NF-κB-dependent the cell line is deemed to be. With the exception of JJN3 cells, sensitivity to DC-1-192 appeared to be inversely associated with the NF-κB index; a concept we went on to explore in subsequent experiments. In order to investigate the anti-tumor effects of DC-1-192 \textit{in vivo}, we employed a systemic model of multiple myeloma in which NOD/SCID mice (two groups of seven mice) were inoculated with the human RPMI 8226 myeloma cell line (1x10^7 cells). Treatment was initiated 5 days after inoculation with either DC-1-192 (1mg/kg) or vehicle control. DC-1-192 was administered once per day (five days/week) for three weeks by intravenous injection and animals were monitored daily for morbidity and mortality. DC-1-192 significantly prolonged the survival of the mice; median survival in the DC-1-192-treated mice was 68 days versus 56 days in untreated mice (P = 0.017, HR = 2.98; Figure 2E).

\textit{Comparative cytotoxicity in primary CLL and normal B- and T-lymphocytes}

Primary CLL cells and age-matched normal B- and T-lymphocytes obtained from healthy donors were treated with increasing concentrations of DC-1-92, DC-1-170 and DC-1-192. Apoptosis was measured using CD19/CD3/Annexin V labelling to determine the percentage of apoptosis induced by the PBDs in CD19^+ B-cells and CD3^+ T-cells as shown in Supplementary Figure 1A. Supplementary Figure 1B shows the comparative dose-responses for each of the cell types indicating that normal lymphocytes were less susceptible to the effects of the PBDs. As was the case with the three multiple myeloma cell lines, DC-1-192 was the most potent cytotoxic agent in primary CLL cells. Supplementary Figures 1C and 1D
show that CLL cells were significantly more sensitive to the effects of the PBDs when compared with age-matched normal B- and T-lymphocytes.

**DC-1-192 shows preferential cytotoxicity in CLL cells carrying a NOTCH1 or BIRC3 mutation**

All of the CLL samples treated with DC-1-192 (n= 46) showed nanomolar LD$_{50}$ values with a mean LD$_{50}$ value for the entire CLL cohort of 3.8nM (Figure 3A). We next examined whether sensitivity to DC-1-192 was associated with any of the known prognostic markers. There was no significant difference in mean LD$_{50}$ value between $IGHV$ mutated and $IGHV$ unmutated samples (Figure 3B); CD38 positive and CD38 negative samples ($\geq$/<20%) (Figure 3C) and beta2 microglobulin high and low samples ($\geq$/<3.5mg/L)(Figure 3D). However, samples derived from patients with a BIRC3 (n=3) or NOTCH1 (n=11) mutation were significantly more sensitive to the effects of DC-1-192 (Figure 3E) suggesting that elevated NF-κB signalling may be a determinant of sensitivity [24, 25]. In keeping with this concept, the nuclear expression the NF-κB subunit p65 (RelA) was inversely correlated with DC-1-192 LD$_{50}$ values (Figure 3F).

**Nuclear localisation of NF-κB subunits following treatment with PBDs**

We have previously shown that PBD monomers, such as KMR-28-39, have NF-κB inhibitory effects [21]. We, therefore, determined the NF-κB inhibitory properties of this new series of compounds in two myeloma cell lines JNJ3 and U266. JNJ3 cells overexpress both the canonical and non-canonical NF-κB subunits and possess an EFTUD2-NIK fusion gene which lacks the TRAF3 binding domain resulting in the accumulation of a cytoplasmic EFTUD2-NIK
fusion protein. U266 cells exhibit a TRAF3 mutation causing the stabilisation of wild-type NIK protein [23,24]. Both cell lines were treated for 4h with up to 20nM of each agent and the relative change in nuclear p65 (RelA), p50, p52 and RelB DNA binding was determined as a function of the untreated control. Levels of c-Rel were not evaluated in this study as JJN3 cells show very low levels of this subunit relative to the dominant canonical subunits p65 and p50. In JJN3 cells, all the PBDs showed significant inhibition of p65, p50 and RelB but no significant reduction in p52 (Figure 4A). In contrast, U266 cells showed a significant reduction in the nuclear DNA binding of all four subunits (Figure 4B).

**Transcriptional effects of DC-1-170 and DC-1-192 on JJN3 cells**

As predicted, RNA-sequencing analysis of DC-1-170 and DC-1-192 revealed a dominant inhibitory effect on gene transcription with a smaller subset of genes showing increased transcription following exposure to the drug. In unsupervised hierarchical clustering, the samples clustered according to treatment condition (Figure 5A). Strikingly, 4040/5077 (80%) of the genes altered by exposure to the drugs were common to both PBD compounds (Figure 5B) suggesting that their structural similarity resulted in the inhibition of a conserved set of genes. Furthermore, Gene set enrichment analysis, using WebGestalt (WEB-based GEne SeT AnaLysi s Toolkit)[25], confirmed that NF-κB regulated genes were significantly over-represented in the down-regulated gene list, with a normalised enrichment score of -1.7750 (Figures 5C and 5D). These data suggest that inhibition of NF-κB target genes may contribute to the cytotoxicity of these compounds.

**Synergy between DC-1-192 in combination with bortezomib or ibrutinib**
Over expression of NF-κB is associated with chemotherapeutic drug resistance in both CLL and multiple myeloma [26,27]. Having established that DC-1-192 inhibited nuclear NF-κB DNA binding and down-regulated NF-κB target genes, we set out to determine whether these inhibitory properties could enhance the killing effect of both bortezomib and ibrutinib in the JJN3 myeloma cell line and primary CLL cells, respectively. To investigate synergy, JJN3 and primary CLL cells (n = 5) were treated with increasing concentrations of DC-1-192 both alone and in combination with bortezomib in JJN3 cells and ibrutinib in CLL samples. The fixed molar ratios employed in the combination studies were determined experimentally using the LD_{50} values calculated from the previous toxicity data. The fraction affected plots and isobologram plots for the drugs and drug combinations in JJN3 cells (Figure 6A), and in primary CLL cells (Figure 6B) show that the cytotoxic effects of DC-1-192 are potentiated by the addition of bortezomib and ibrutinib, respectively. Furthermore, the combination of DC-1-192 with bortezomib and ibrutinib showed synergy (CI values <1) at the level of LD_{50}, LD_{75} and LD_{90} with an incremental increase in synergistic effect from LD_{50} to LD_{90} (Figure 6C). Furthermore, DC-1-192 showed increased synergy with ibrutinib when primary CLL cells were co-cultured on CD40L-expressing fibroblasts (Figure 6D) suggesting that these agents may be particularly effective in the treatment of tissue resident CLL cells.

Discussion

NF-κB is a master regulator of a number of cellular processes that contribute to cancer progression including cell survival and proliferation. Furthermore, it is often implicated in drug resistance, highlighting its potential as a therapeutic target [12,13]. The interest in small molecular DNA-binding agents, such as the PBD
monomers, has increased in recent years due to their ability to selectively bind to specific sequences within the minor groove of DNA; a characteristic that separates them from traditional alkylating agents. This raises the possibility that they can selectively inhibit transcription factors [16], so this study set out to determine the \textit{in vitro} and \textit{in vivo} biological effects of a series of novel C8-linked PBD-benzofused hybrids.

Initially library screening identified three lead compounds. All three PBDs showed high potency in five different multiple myeloma cell lines with LD\textsubscript{50} values in the low nanomolar range. Subsequently, the PBDs showed similar high potency in a cohort of 46 primary chronic lymphocytic leukemia samples and significantly lower toxicity in normal age-matched B- and T-lymphocytes. The most cytotoxic PBD, DC-1-192, showed a 2.4-fold and 4.6-fold differential toxicity in CLL cells suggesting that this compound has a positive therapeutic index. We went on to show that DC-1-192 was well tolerated in a systemic \textit{in vivo} xenograft model of myeloma and significantly prolonged the survival of the mice.

Subset analysis of the CLL cohort data revealed that DC-1-192 was equipotent in poor prognostic groups including \textit{IGHV} unmutated cases (P=0.96). Furthermore, samples derived from patients with BIRC3 or NOTCH1 mutations showed significantly increased sensitivity to DC-1-192. These mutations are known to cause aberrant activation of NF-\kappaB signaling and are associated with resistance to chemoimmunotherapy and inferior clinical outcome [28-32]. Although these mutations are linked with non-canonical NF-\kappaB activation, here we showed that
nuclear expression of the canonical p65 subunit was a predictor of \textit{in vitro} sensitivity to DC-1-192.

Given these findings, we plotted the previously published NF-κB index for each of the myeloma cell lines [23] against their respective LD$_{50}$ for DC-1-192. 4/5 of the cell lines showed an inverse relationship between their NF-κB index and DC-1-192 LD$_{50}$ value suggesting that response to DC-1-192 was influenced by how NF-κB-dependent the cell lines were. JJN3 cells were the exception to this rule; these cells manifest a high NF-κB index (10.8) but were relatively resistant than the other four cell lines to the cytotoxic effects of DC-1-192 (mean LD$_{50}$ = 6nM). The reasons for this are likely to be multiple and may be unrelated to NF-κB, but it is worthy of note that JJN3 cells possess a cytoplasmic EFTUD2-NIK fusion gene, which may alter p100 processing to p52. Indeed, when we assessed the impact of the PBDs on nuclear NF-κB subunit DNA binding in JJN3 cells, all three compounds showed significant inhibition of the p65 and p50 canonical subunits as well as the non-canonical subunit RelB after 4h. In contrast, no significant change in p52 was observed following treatment with the PBDs. We subsequently repeated the experiments using the U266 cell line, which has a TRAF3 mutation leading to the cytoplasmic accumulation of NF-κB inducing kinase (NIK) [23,24]. These cells showed a significant reduction in all four NF-κB subunits including p52 following short-term treatment with PBDs.

The rapid reduction in nuclear NF-κB subunit expression indicates that NF-κB inhibition precedes apoptosis in these cells and may to contribute to the efficacy of the PBDs. Given the DNA binding charcteristics of these compounds, it seems
possible that they compete for NF-κB binding motifs, thereby inhibiting the transcription of NF-κB target genes. The reduction in nuclear NF-κB subunits observed in this study may be caused by the shuttling of unbound NF-κB back to the cytoplasm and/or targeted degradation [33,34].

Activation of NF-κB has also been implicated in the development of chemotherapeutic drug resistance in myeloma and CLL [35]. Several DNA damaging agents, including melphalan and fludarabine, have been shown to induce the activity of NF-κB, thereby contributing to cellular resistance to the cytotoxic effects of these treatments [6,36]. In myeloma, bortezomib has been shown to re-sensitise malignant cells to the effects of chemotherapy [37]. However, the emergence of a bortezomib-resistant sub-clones ultimately leads to relapse in many patients [38].

One putative mechanism of bortezomib resistance is the constitutive expression of NF-κB. Although bortezomib can prevent de novo activation of the canonical pathway, it has no significant effect on constitutive NF-κB activity [27]. In this study, we showed that direct competitive inhibition of NF-κB at the site of transcription led to the re-sensitisation of multiple myeloma cells to the effects of bortezomib. This synergistic effect is likely to be multi-factorial, but indicates that bortezomib and the PBDs have different molecular targets.

Similarly, in CLL bruton’s tyrosine kinase (BTK) has been shown to be a critical downstream mediator of BCR signaling that is often constitutively activated in CLL patients. The targeting of this kinase with the BTK inhibitor, ibrutinib has shown notable effects in patients with relapsed CLL [39,40] and this is mediated, at least in
part, by the distal inhibition of NF-κB [41]. However, emerging evidence of resistance mechanisms to ibrutinib strongly implicate NF-κB [42]. Here, we show that the combination of DC-1-192 with ibrutinib produced cytotoxic synergy suggesting that the PBDs and ibrutinib target NF-κB through different mechanisms and/or that they have other, non-overlapping, molecular targets. Furthermore, synergy was enhanced when primary CLL cells were co-cultured on CD40L-expressing fibroblasts in order to mimic the lymph node microenvironment. This suggests that PBDs may be particularly useful in targeting tissue resident tumor cells.

In summary, the novel PBDs evaluated in this study showed low nanomolar toxicity in both primary CLL cells and myeloma cell lines. In addition, primary CLL cells carrying BIRC3 or NOTCH1 mutations were preferentially sensitive to the cytotoxic effects of DC-1-192 suggesting that this agent may be a potential therapeutic option for these poor risk subsets. Mechanistically, the PBDs demonstrated promising dual inhibitory properties on both the canonical and non-canonical NF-κB pathways; a characteristic that has been previously linked to significant anti-tumor effects in multiple myeloma [43]. Furthermore, the PBDs showed in vitro synergy with bortezomib and ibrutinib in MM and CLL respectively, providing a strong rationale for the use of these agents in the treatment of relapsed/refractory B-cell neoplasms.

Acknowledgements

This work was supported by a grant (No. 12-1263/JGATCBR) from Worldwide Cancer Research (formerly AICR) to DET, KMR and CP in 2012. This support included a PhD
studentship held by DBC, which enabled all of the novel medicinal chemistry. CP, CDF and AGSP are also supported by a Bloodwise Programme Continuity Grant (18005).

Author contributions

TL performed experiments, analysed data and drafted the manuscript. DBC performed experiments, analysed data and revised the manuscript. KMR and DET conceived and supervised the synthetic chemistry and revised the manuscript, PJG, KA and AGSP analysed data and revised the manuscript. EJW analysed data and revised the manuscript. CDF provided vital reagents and revised the manuscript. CP conceived and supervised the cell biology experiments, analysed data and revised the manuscript.

Conflict of interest

All of the authors declare that they have no material conflict of interests.

References

1. Zheng C, Yin Q, Wu H. Structural studies of NF-κB signaling. Cell Res. 2011;21(1):183-195.
2. Gasparini C, Celeghini C, Monasta L, Zauli G. NF-κB pathways in hematological malignancies. Cell Mol Life Sci. 2014;71(11):2083-2102.
3. Hoffmann A, Natoli G, Ghosh G. Transcriptional regulation via the NF-kappaB signaling module. Oncogene. 2006;25(51):6706-6716.
4. Braun T, Carvalho G, Fabre C, Grosjean J, Fenaux P, Kroemer G. Targeting NF-kappaB in hematologic malignancies. Cell Death Differ. 2006;13(5):748-758.
5. Abdi J, Chen G, Chang H. Drug resistance in multiple myeloma: latest findings and new concepts on molecular mechanisms. Oncotarget. 2013;4(12):2186-2207.
6. Hewamana S, Alghazal S, Lin TT, et al. The NF-kappaB subunit Rel A is associated with in vitro survival and clinical disease progression in chronic lymphocytic leukemia and represents a promising therapeutic target. Blood. 2008;111(9):4681-4689.
7. Merchionne F, Perosa F, Dammacco F. New therapies in multiple myeloma. Clin Exp Med. 2007;7(3):83-97.
8. Byrd JC, Brown JR, O'Brien S, et al. RESONATE investigators. Ibrutinib versus ofatumumab in previously treated chronic lymphoid leukemia. N Engl J Med. 2014;371(3):213-223.
9. Hideshima T, Ikeda H, Chauhan D, et al. Bortezomib induces canonical nuclear factor-kappaB activation in multiple myeloma cells. Blood. 2009;114(5):1046-1052.
10. Ahn IE, Underbayev C, Albitar A, et al. Clonal evolution leading to ibrutinib resistance in chronic lymphocytic leukemia. Blood. 2017;129(11):1469-1479.
11. Wang CY, Mayo MW, Baldwin AS. TNF- and cancer therapy-induced apoptosis: potentiation by inhibition of NF-kappaB. Science. 1996;274(5288):784-787.
12. Hideshima T, Chauhan D, Richardson P, et al. NF-kappaB as a therapeutic target in multiple myeloma. J Biol Chem. 2002;277(19):16639-16647.
13. Pepper C, Hewamana S, Brennan P, Fegan C. NF-kappaB as a prognostic marker and therapeutic target in chronic lymphocytic leukemia. Future Oncol. 2009;5(7):1027-1037.
14. Antonow D, Thurston DE. Synthesis of DNA-interactive pyrrolo[2,1-c][1,4]benzodiazepines (PBDs). Chem Rev. 2011;111(4):2815-2864.
15. Gerritana B. Biosynthesis, synthesis, and biological activities of pyrrolobenzodiazepines. Med Res Rev. 2012;32(2):254-293.
16. Rahman KM, Vassoler H, James CH, Thurston DE. DNA Sequence Preference and Adduct Orientation of Pyrrolo[2,1-c][1,4]benzodiazepine Antitumor Agents. ACS Med Chem Lett. 2010;1(8):427-432.
17. Puzanov I, Lee W, Chen AP, et al. Phase I pharmacokinetic and pharmacodynamic study of SJG-136, a novel DNA sequence selective minor groove cross-linking agent, in advanced solid tumors. Clin Cancer Res. 2011;17(11):3794-3802.
18. Mantaj J, Jackson PJ, Rahman KM, Thurston DE. From Anthracyclin to Pyrrolobenzodiazepine (PBD)-Containing Antibody-Drug Conjugates (ADCs). Angew Chem Int Ed Engl. 2017;56(2):462-488.
19. Kotecha M, Kluzar J, Wells G, et al. Inhibition of DNA binding of the NF-Y transcription factor by the pyrrolobenzodiazepine-polyamide conjugate GWL-78. Mol Cancer Ther. 2008;7(5):1319-1328.
20. Hu WP, Tsai FY, Yu HS, Sung PI, Chang LS, Wang JJ. Induction of apoptosis by DC-81-indole conjugate agent through NF-kappaB and JNK/AP-1 pathway. Chem Res Toxicol. 2008;21(7):1330-1336.
21. Rahman KM, Jackson PJ, James CH, et al. GC-targeted C8-linked pyrrolobenzodiazepine-biaryl conjugates with femtomolar in vitro cytotoxicity and in vivo antitumor activity in mouse models. J Med Chem. 2013;56(7):2911-2935.
22. Chou TC. Drug combination studies and their synergy quantification using the Chou-Talalay method. Cancer Res. 2010;70(2):440-446.
23. Demchenko YN, Glebov OK, Zingone A, Keats JJ, Bergsagel PL, Kuehl WM. Classical and/or alternative NF-kappaB pathway activation in multiple myeloma. Blood. 2010;115(17):3541-3552.
24. Keats JJ, Fonseca R, Chesi M, et al. Promiscuous mutations activate the noncanonical NF-kappaB pathway in multiple myeloma. Cancer Cell. 2007;12(2):131-144.
25. Zhang B, Kirov S, Snoddy J. WebGestalt: an integrated system for exploring gene sets in various biological contexts. Nucleic Acids Res. 2005;33(Web Server issue):W741-48.
26. Hertlein E, Byrd JC. Signalling to drug resistance in CLL. Best Pract Res Clin Haematol. 2010;23(1):121-131.
27. Markovina S, Callander NS, O’Connor SL, et al. Bortezomib-resistant nuclear factor-kappaB activity in multiple myeloma cells. Mol Cancer Res. 2008;6(8):1356-1364.
28. Diop F, Moia R, Favini C, et al. Biological and clinical implications of BIRC3 mutations in chronic lymphocytic leukemia. Haematologica. 2020;105(2):448-456.
29. Benedetti D, Tissino E, Pozzo F, et al. NOTCH1 mutations are associated with high CD49d expression in chronic lymphocytic leukemia: link between the NOTCH1 and the NF-kB pathways. Leukemia. 2018;32(3):654-662.
30. Asslaber D, Wacht N, Leisch M, Qi Y, et al. BIRC3 Expression Predicts CLL Progression and Defines Treatment Sensitivity via Enhanced NF-kB Nuclear Translocation. Clin Cancer Res. 2019;25(6):1901-1912
31. Del Poeta G, Dal Bo M, Del Principe M, et al. Clinical significance of c.7544-7545 del CT NOTCH1 mutation in chronic lymphocytic leukaemia. Br J Haematol. 2013;160(3):415-418.
32. Rossi D, Rasi S, Fabbri G, et al. Mutations of NOTCH1 are an independent predictor of survival in chronic lymphocytic leukemia. Blood. 2012; 119(2):521.
33. Hoffmann A, Levchenko A, Scott ML, Baltimore D. The I kappaB-NF-kappaB signaling module: temporal control and selective gene activation. Science. 2002;298(5596):1241-1245.
34. Natoli G, Chiocca S. Nuclear ubiquitin ligases, NF-kappaB degradation, and the control of inflammation. Sci Signal. 2008;1(1):pe1.
35. Godwin P, Baird AM, Heavey S, Barr MP, O’Byrne KJ, Gately K. Targeting nuclear factor-kappa B to overcome resistance to chemotherapy. Front Oncol. 2013;3:120.
36. Baumann P, Mandl-Weber S, Oduncu F, Schmidmaier R. Alkylating agents induce activation of NFkappaB in multiple myeloma cells. Leuk Res. 2008;32(7):1144-1147.
37. San Miguel JF, Schlag R, Khuageva NK, et al. Bortezomib plus melphalan and prednisone for initial treatment of multiple myeloma. N Engl J Med. 2008;359(9):906-917.
38. Murray MY, Auger MJ, Bowles KM. Overcoming bortezomib resistance in 548 multiple myeloma. Biochem Soc Trans. 2014;42(4):804-808.
39. Woyach JA, Bojnik E, Ruppert AS, et al. Bruton's tyrosine kinase (BTK) function is important to the development and expansion of chronic lymphocytic leukemia (CLL). Blood. 2014;123(8):1207-1213.
40. Byrd JC, Furman RR, Coutre SE, et al. Targeting BTK with ibrutinib in relapsed chronic lymphocytic leukemia. N Engl J Med. 2013;369(1):32-42.
41. Herman SE, Mustafa RZ, Gyamfi JA, et al. Ibrutinib inhibits BCR and NF-κB signaling and reduces tumor proliferation in tissue-resident cells of patients with CLL. Blood. 2014;123(21):3286-3295.

42. Jayappa KD, Portell CA, Gordon VL, et al. Microenvironmental agonists generate de novo phenotypic resistance to combined ibrutinib plus venetoclax in CLL and MCL. Blood Adv. 2017;1(14):933-946.

43. Fabre C, Mimura N, Bobb K, et al. Dual inhibition of canonical and noncanonical NF-κB pathways demonstrates significant antitumor activities in multiple myeloma. Clin Cancer Res. 2012;18(17):4669-4681.

Figure Legends

Figure 1. The structures of Anthramycin and three structurally-related C8-linked benzofused PBD hybrids. Anthramycin (the first PBD to be isolated from a Streptomyces species), and the three synthetic PBDs, DC-1-192, DC-1-92 and DC-1-170, identified as lead compounds in this study.

Figure 2. PBDs induce apoptosis in multiple myeloma cell lines in a dose-dependent manner. (A) An example of Annexin V and propidium iodide bivariate plots obtained from JJN3 cells treated with increasing concentrations of DC-1-92. A dose-dependent increase in the proportion of Annexin V+/PI− and Annexin V+/PI+ was observed. (B) Sigmoidal dose-response curves illustrating the comparative effects of each compound in U266, OPM2, H929, JJN3 and MM1.S multiple myeloma cell lines. (C) Comparative analysis of the three lead PBDs in the five multiple myeloma cell lines revealed significant differential sensitivity to each compound and between each cell line but DC-1-192 was the most potent PBD in all five cell lines (D) shows the relationship between the NF-κB index of each of the cell lines with their respective mean DC-1-192 LD50 value. (E) In order to investigate the in vivo anti-tumor effects of DC-1-192, NOD/SCID mice were systemically inoculated with the human RPMI 8226 myeloma cell line. DC-1-192 (1mg/kg) significantly prolonged the survival of the mice when compared to untreated control mice. All in vitro experiments were performed in triplicate and data are presented as mean ± SD. The in vivo experiment was performed in treated and untreated mice (n=7 for each group).

Figure 3. DC-1-192 was highly cytotoxic in primary CLL cells and showed preferential effects in BIRC3 and NOTCH1 mutated samples. (A) All 46 samples tested showed low nanomolar LD50 values when treated with DC-1-192. Analysis of prognostic subsets revealed that DC-1-192 was equipotent in (B) IGHV mutated and unmutated samples, (C) CD38 positive and CD38 negative samples and (D) beta2 microglobulin high and low samples. (E) In contrast, BIRC3 and NOTCH1 mutated samples showed significantly increased sensitivity to DC-1-192. (F) There was an inverse relationship between nuclear DNA binding of the canonical NF-κB subunit, p65, and DC-1-192 LD50 values.

Figure 4. PBDs show marked inhibitory effects on both canonical and non-canonical NF-κB subunits. JJN3 and U266 cells were treated with DC-1-92, DC-1-170 and DC-1-192 for 4 hours, nuclear extracts were then generated from these samples and the amount of p65,
p50, p52 and Rel B was quantified and expressed relative fold change as a function of the untreated controls. (A) JJN3 cells showed significant reductions in nuclear expression p65, p50 and Rel B NF-κB subunits but no change in p52 following exposure to DC-1-92, DC-1-170 and DC-1-192. (B) In contrast, U266 cells showed significant reductions in nuclear expression of all four NF-κB subunits. All experiments were performed in triplicate. P-values: *<0.05, **<0.01, ***<0.001 and ****<0.0001. ns denotes changes that were not statistically significant.

Figure 5. RNA sequencing and gene set enrichment analysis revealed that DC-1-170 and DC-1-192 preferentially inhibited NF-κB target genes. (A) Unsupervised hierarchical clustering revealed a strong drug-associated transcriptional signature for both DC-1-170 and DC-1-192. (B) The majority of the significantly altered transcripts were down-regulated in response to drug 4418/5077 (87%). Strikingly, 4040/5077 (80%) of the changes were common to both DC-1-170 and DC-1-192. Both (C) Gene set enrichment analysis showed over representation of NF-κB target genes in the gene list commonly down-regulated by exposure to DC-1-170 and DC-1-192. (D) Shows the top 12 over-represented pathways in the commonly down-regulated gene list following exposure to DC-1-170 and DC-1-192. The table also shows the normalized enrichment scores, p-values and false discovery rates for each canonical gene set.

Figure 6. DC-1-192 demonstrates cytotoxic synergy with bortezomib and ibrutinib. Synergy between DC-1-192 and bortezomib was experimentally determined in JJN3 cells and between DC-1-192 and ibrutinib in primary CLL cells. The fixed molar ratios for each combination were derived from the mean LD_{50} values for DC-1-192 and the clinically achievable doses of bortezomib and ibrutinib. Apoptosis was determined using the Annexin V/PI assay. (A) The fraction affected plot and the isobologram plot for DC-1-192, bortezomib and their respective combination (1:15) in JJN3 cells. (B) The fraction affected plot and isobologram plot for DC-1-192, ibrutinib and their combination (1:3000) in primary cells. (C) The combination indices for the combination DC-1-192 with bortezomib and DC-1-192 with ibrutinib at the level of LD_{50}, LD_{75} and LD_{90} in primary CLL cells (n = 5). (D) Comparison of the combination indices generated by the combination of DC-1-192 and ibrutinib in monoculture and CD40L-expressing co-culture. All JJN3 cell line experiments were performed in triplicate. All of the primary CLL experiments were performed on samples derived from 5 individual patients with data presented as the mean of duplicate experiments.
Mean $LD_{50} = 3.8 \text{nM}$

A

B

C

D

E

F

$r^2 = 0.2; p = 0.0018$
D

| GeneSet       | Description                                      | Enrichment Score | Normalized Enrichment Score | p-value  | FDR      |
|---------------|--------------------------------------------------|------------------|----------------------------|----------|----------|
| hsa04630      | JAK-STAT signaling pathway                       | -0.6824          | -1.9718                    | 0.0012   | 0.0725   |
| hsa05222      | Small cell lung cancer                           | -0.7432          | -1.7127                    | 0.0013   | 0.1986   |
| hsa04640      | Hematopoietic cell lineage                       | -0.7257          | -1.8594                    | 0.0024   | 0.0642   |
| hsa04064      | NF-kappa B signaling pathway                     | -0.7806          | -1.7750                    | 0.0026   | 0.1348   |
| hsa04080      | Neuroactive ligand-receptor interaction           | -0.5484          | -1.8622                    | 0.0053   | 0.0785   |
| hsa05323      | Rheumatoid arthritis                             | -0.6686          | -1.7070                    | 0.0062   | 0.1831   |
| hsa04727      | GABAergic synapse                                | -0.6176          | -1.6455                    | 0.0144   | 0.2779   |
| hsa05133      | Pertussis                                        | -0.6619          | -1.6262                    | 0.0280   | 0.2904   |
| hsa04150      | mTOR signaling pathway                           | 0.2546           | 1.0526                     | 0.3760   | 0.6415   |
| hsa05231      | Choline metabolism in cancer                     | 0.3838           | 1.0528                     | 0.3765   | 0.6835   |
| hsa00270      | Cysteine and methionine metabolism               | 0.3715           | 1.0227                     | 0.3816   | 0.6622   |
| hsa04662      | B cell receptor signaling pathway                | 0.2764           | 1.0024                     | 0.4237   | 0.6656   |
Methods

Culture conditions for cell lines, primary CLL cells and normal lymphocytes

Primary chronic lymphocytic leukemia (CLL) cells were obtained from patients attending outpatients’ clinics at the University Hospital of Wales with informed consent in accordance with the ethical approval granted by South East Wales Research Ethics Committee (02/4806). Age-matched normal B- and T-cells were obtained from healthy volunteers again with informed consent. Five multiple myeloma cell lines, JNJ3, U266, OPM2, MM.1S and H929, were maintained in liquid culture at densities ranging between 0.5-2x10^6 cells/ml. JNJ3 cells were maintained in DMEM media containing 20% fetal bovine serum (FBS), 1% sodium pyruvate and 1% penicillin and streptomycin. U266, OPM2, MM.1S and H929 cells were maintained in RPMI media containing 20% FBS, 1% L-glutamate and 1% penicillin and streptomycin. All cell lines were purchased from DSMZ and were used for these experiments within 6 months of purchase. In each case, the provenance of the cell lines was verified by multiplex PCR of minisatellite markers, and all were certified mycoplasma-free. In terms of NF-κB mutations, JNJ3 cells possess an EFTUD2-NIK fusion gene which lacks the TRAF3 binding domain resulting in the accumulation of a cytoplasmic EFTUD2-NIK fusion protein. MM.1S and U266 cells exhibit TRAF3 mutations resulting in the stabilisation of wild-type NIK protein. H929 and OPM2 cells do not have any NF-κB-related mutations. In terms of their reliance on NF-κB signaling, MM.1S cells exhibit the highest NF-κB index followed by JNJ3 cells (10.8), U266 cells (10.41), OPM2 cells (9.03) and H929 cells (8.37). [1]

Primary CLL and normal lymphocytes were isolated by density gradient centrifugation using Histopaque (Sigma-Aldrich) and were then maintained in RPMI media containing 10% FBS, 5ng/ml IL-4, 1% L-glutamine and 1% penicillin and streptomycin. All cells were cultured at
37°C in 5% CO₂ atmospheric conditions. Cell counts and viability (trypan blue exclusion) were determined using the Vi-Cell XR cell counter (Beckman Coulter). Primary CLL cells were also co-cultured on CD40L-expressing fibroblasts (10:1 ratio) in order to mimic the lymph node microenvironment. Subsequently, synergy between ibrutinib and DC-1-192 was determined under these cytoprotective conditions.

**Measurement of in vitro apoptosis**

Aliquots of each cell type (1x10⁶ cells) were cultured for 48h, harvested by centrifugation (300xg for 5 mins) and then resuspended in 195μL of a calcium-rich buffer. Subsequently, 5μL of Annexin V (Biolegend) was added to the cell suspension, and cells were incubated in the dark for 10 mins prior to washing. Cells were finally resuspended in 190μL of calcium-rich buffer together with 10μL of propidium iodide (PI). Apoptosis was assessed by dual-colour immunofluorescent flow cytometry using an Accuri C6 flow cytometer, and data were analysed using CFlow software (BD Biosciences).

**Measurement of apoptosis in normal B- and T-lymphocytes**

Peripheral blood mononuclear cells from age-matched healthy donors (1x10⁶ cells) were treated with concentrations of DC-1-92, DC-1-170 and DC-1-192 between 1 nM-100nM for 48h. Cells were then harvested and stained with APC-conjugated CD19, PE-conjugated CD3 and FITC-conjugated Annexin V (Biolegend). Using an Accuri C6 flow cytometer, a gating strategy (shown in Figure 2) was employed to quantify apoptosis in CD19⁺ B-cells and CD3⁺ T-cells, with appropriate compensation applied.
Enzyme Linked Immuno-sorbent Assay (ELISA) for NF-κB subunits

JJN3 and U266 cells were treated for 4h with DC-1-92, DC-1-170 (0 nM-20nM) and DC-1-192 (0nM-5nM). Pellets containing 5x10⁶ cells were then harvested, and subsequently, nuclear extracts were prepared using a nuclear extraction kit (Active Motif). Total protein was determined by DC protein assay (Biorad) in each nuclear extract using a standard curve of known concentrations of BSA. Nuclear extracts containing 1 μg of total protein from each treatment were then added to an NF-κB family kit (Active Motif) in accordance with the manufacturer’s instructions. Levels of p65, p50, p52 and Rel B DNA binding were then assessed to determine relative levels of each subunit in the nucleus. The absorbance measurements (450nm) were subsequently converted into ng/μg of nuclear extract for each sample.

Synergy with bortezomib and ibrutinib

The synergy between DC-1-192 in combination with either bortezomib or ibrutinib was determined in the JJN3 cells and primary CLL cells respectively. The molar ratios were experimentally determined using the mean LD₅₀ value for DC-1-192 and the clinically achievable concentrations of bortezomib and ibrutinib. The fixed molar ratio for DC-1-192:bortezomib was 1:15 and was 1:3000 for DC-1-192:ibrutinib. Cells were treated with each drug individually and in combination at the defined molar ratio. Treated cells were incubated alongside untreated controls for 48h, before being labelled with Annexin V-FITC/PI and then analysed on an Accuri C6 flow cytometer. CalcuSyn software (Biosoft) was used to establish whether synergy was evident between the PBD compounds and bortezomib or ibrutinib and expressed as a combination index (CI); CI values <1 were considered to demonstrate synergy.
**RNA Isolation**

JJN3 cells were treated with either DC-1-170 or DC-1-192 at 20nM in triplicate alongside untreated controls for 4h. From each sample, 5x10^6 cells were then harvested, washed in ice cold PBS and re-suspended in 1ml of Trizol reagent (Thermo Fisher). RNA was extracted following the addition of chloroform and 70% ethanol, and an RNeasy mini-kit (Qiagen) was then used in accordance with the manufacturer’s instructions to isolate RNA to be used in RNA sequencing (RNA-seq) analysis.

**RNA Sample Preparation and Sequencing**

Total RNA quality and quantity was assessed using an Agilent 2100 Bioanalyzer and an RNA Nano 6000 kit (Agilent Technologies). 100-900 ng of Total RNA with an RNA integrity number (RIN) >8 was depleted of ribosomal RNA, and the sequencing libraries were prepared using the Illumina® TruSeq® Stranded Total RNA with Ribo-Zero Gold™ kit (Illumina Inc.). The steps included rRNA depletion and cleanup, RNA fragmentation, 1st strand cDNA synthesis, 2nd strand cDNA synthesis, adenylation of 3’-ends, adapter ligation, PCR amplification (12-cycles) and validation. The manufacturer’s instructions were followed except for the cleanup after the Ribo-Zero depletion step where Ampure®XP beads (Beckman Coulter) and 80% Ethanol were used. The libraries were validated using the Agilent 2100 Bioanalyser and a high-sensitivity kit (Agilent Technologies) to ascertain the insert size, and the Qubit® (Life Technologies) was used to perform the fluorometric quantitation. Following validation, the libraries were normalized to 4nM, pooled together and clustered on the cBot™2 following the manufacturer’s recommendations. The pool was then sequenced using a 75-base paired-end (2x75bp PE) dual index read format on the Illumina® HiSeq2500 in high-output mode according to the manufacturer’s instructions. Subsequently, analysis was performed after
trimming to remove adaptor sequences and low-quality base calls. Trimmed reads were then mapped to the standard reference 'hg19' using the alignment software package 'bwa-mem' (http://bio-bwa.sourceforge.net). Downstream analysis of the data was performed using GenView2 software (in-house analysis tool developed by Peter Giles), Ingenuity Pathway Analysis (Qiagen) and WebGestalt (WEB-based GEne SeT AnaLysis Toolkit).

In vivo systemic xenograft model of myeloma in NOD/SCID mice

Female NOD/SCID mice were sourced from Beijing AK Bio-Technology Co. Ltd. (Beijing, China). The care and use of animals were conducted in accordance with the regulations of the Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC). Before commencement of treatment, all animals’ weights were measured. As body weight can influence the effectiveness of any given treatment, mice were assigned to groups using a randomized block design based on their body weight. Mice were sub-lethally irradiated with 200 cGy with a $^{60}$Co source one day before inoculation with human myeloma cells. Subsequently, each mouse was inoculated intravenously into the tail vein with RPMI8226 tumor cells ($1 \times 10^7$) in 0.1 mL of PBS to initiate tumor development. The date of tumor cell inoculation was denoted as Day 0; intravenous treatment with vehicle only; 0.05% DMSO in saline ($n = 7$) or 1mg/kg of DC-1-192 ($n = 7$) was started at Day 5 and continued once per day (five days/week) for three weeks. Survival was evaluated from the first day of treatment until death.

References

1. Demchenko YN, Glebov OK, Zingone A, Keats JJ, Bergsagel PL, Kuehl WM. Classical and/or alternative NF-kappaB pathway activation in multiple myeloma. Blood. 2010;115(17):3541-3552.
Supplementary Figure 1. PBDs showed preferential cytotoxicity in primary CLL cells compared with healthy non-malignant B- and T-lymphocytes. (A) Non-malignant B-cells and T-cells were identified using the gating strategy shown, which allowed the enumeration of the percentage of apoptotic cells in each lymphocyte subset. (B) Apoptotic dose-response graphs illustrating the comparative effects of DC-1-92, DC-1-170 and DC-1-192 on primary CLL cells and non-malignant B-cells and T-cells. (C) Comparison of the mean LD_{50} values showed that all three PBDs were significantly more potent in primary CLL cells when compared with age-matched normal B-cells and T-cells. (D) DC-1-192 showed the differential cytotoxic effects (therapeutic index), when comparing CLL cells with normal B-cells (2.4 fold) and CLL cells with normal T-cells (4.6 fold). P-values: *<0.05, **<0.01, ***<0.001 and ****<0.0001.
**Supplementary Table 1.** Summary of patient characteristics

| Parameter                  | Number |
|----------------------------|--------|
| Total number of CLL samples| 46     |
| *IGHV*-mutated             | 19     |
| *IGHV*-unmutated           | 27     |
| CD38 (<20%)                | 21     |
| CD38 (>20%)                | 25     |
| B2M (<3.5mg/L)             | 26     |
| B2M (>3.5mg/L)             | 17     |
| ND                         | 3      |
| 11q-                       | 7      |
| 17p-                       | 2      |
| Trisomy 12                 | 4      |
| Normal or 13q-             | 33     |
| NOTCH1 mutation            | 11     |
| BIRC3 Mutation             | 3      |
| ND                         | 13     |

*IGHV*-mutated: >2% deviation from the germline immunoglobulin sequence

*IGHV*-unmutated: ≤2% deviation from the germline immunoglobulin sequence

B2M – beta 2 microglobulin

ND – not determined

**Supplementary Table 2.** Down regulated genes following treatment with DC-1-192 or DC-1-170.

| NCBI gene     | Symbol | p-value      | fdr p-value | log2FC       |
|---------------|--------|--------------|-------------|--------------|
| NM_001178002  | ATP8B3 | 0.000109833  | 0.000952962 | -1.314857411 |
| NM_138813     | ATP8B3 | 0.000116051  | 0.001000195 | -1.305261044 |
| NM_053280     | ODF3   | 0.000123633  | 0.001056964 | -1.291597745 |
| NM_173502     | PRSS36 | 0.000134112  | 0.001135771 | -1.283259211 |
| NM_138277     | C6orf25| 0.000151094  | 0.001263734 | -1.28048462 |
| NR_033419     | SLC39A2| 0.000172884  | 0.001421191 | -1.27659082 |
| NM_014579     | SLC39A2| 0.000172884  | 0.001421191 | -1.27659082 |
| NM_001256588  | SLC39A2| 0.000172884  | 0.001421191 | -1.27659082 |
| NM_031948     | PRSS27 | 0.000186671  | 0.001512764 | -1.270186813 |
| NM_002773     | PRSS8  | 0.000188026  | 0.001521855 | -1.27012031 |
| NM_000835     | GRIN2C | 0.000205285  | 0.001636418 | -1.252708627 |
| NM_001198568  | ADCY4  | 0.0002614    | 0.002014009 | -1.242070041 |
| NM_001198592  | ADCY4  | 0.0002614    | 0.002014009 | -1.242070041 |
| NM_139247     | ADCY4  | 0.0002614    | 0.002014009 | -1.242070041 |
| NM_001039771  | CBLN3  | 0.000283877  | 0.002153685 | -1.223676635 |
| NM_015927     | TGFBI11| 0.000185587  | 0.001506447 | -1.22284725 |
| NM_001906     | CTRB1  | 0.00033854   | 0.002513216 | -1.218446714 |
| NM_032123     | KIRREL2| 0.000305352  | 0.002298301 | -1.217407175 |
| Gene Symbol | Description | Fold Change | P-Value | Adjusted P-Value |
|-------------|-------------|-------------|---------|-----------------|
| NM_199180   | KIRREL2     | 0.000305352 | 0.00298301 | -1.217407175   |
| NM_152784   | CATSPERD    | 0.000239338 | 0.001869228 | -1.21132651    |
| NM_016239   | MYO15A      | 0.000154472 | 0.001288362 | -1.211317261   |
| NM_145239   | PRRT2       | 0.0002754   | 0.00201225  | -1.196779346   |
| NM_024003   | L1CAM       | 0.000454228 | 0.003232351 | -1.1926505999  |
| NM_00425    | L1CAM       | 0.000454228 | 0.003232351 | -1.1926505999  |
| NM_001143963| L1CAM       | 0.000454228 | 0.003232351 | -1.1926505999  |
| NM_199179   | KIRREL2     | 0.000383961 | 0.00280004  | -1.186031884   |
| NM_018059   | RADIL       | 0.000498364 | 0.003502809 | -1.184281703   |
| NM_001098671| RASGRP2     | 0.000527608 | 0.003675322 | -1.178835719   |
| NM_004183   | BEST1       | 0.000382288 | 0.002791266 | -1.176067984   |
| NM_138275   | C6orf25     | 0.000454587 | 0.003238984 | -1.16999221    |
| NM_138273   | C6orf25     | 0.000454587 | 0.003238984 | -1.16999221    |
| NM_001256442| PRRT2       | 0.000389995 | 0.002838517 | -1.164571775   |
| NM_00139443 | BEST1       | 0.000534296 | 0.003711469 | -1.154773442   |
| NM_175931   | CBFA2T3     | 0.000154789 | 0.001290286 | -1.15435706    |
| NM_001256508| TBC1D10C    | 0.000577404 | 0.003950286 | -1.15178063    |
| NM_153819   | RASGRP2     | 0.000740038 | 0.004841853 | -1.147249819   |
| NR_046266   | TBC1D10C    | 0.000594811 | 0.004058785 | -1.14583465    |
| NM_005393   | PLXNB3      | 0.000446766 | 0.003186881 | -1.144637737   |
| NM_00163257 | PLXNB3      | 0.000446766 | 0.003186881 | -1.144637737   |
| NM_00177597 | THPO        | 0.000730469 | 0.004795087 | -1.141526079   |
| NM_00177598 | THPO        | 0.000730469 | 0.004795087 | -1.141526079   |
| NM_001506   | GPR32       | 0.000633257 | 0.004284519 | -1.154773442   |
| NM_001007533| PPP1R27     | 0.000594811 | 0.004058785 | -1.14583465    |
| NM_001098670| RASGRP2     | 0.000845102 | 0.005400835 | -1.135294123   |
| NM_030792   | GDPD5       | 0.000402889 | 0.00291968 | -1.152294082   |
| NM_001853   | COL9A3      | 0.0001981   | 0.001589349 | -1.13167239    |
| NM_198517   | TBC1D10C    | 0.000691803 | 0.004587881 | -1.133162104   |
| NM_138277   | C6orf25     | 0.000841714 | 0.005380608 | -1.129950694   |
| NM_031308   | EPPK1       | 0.00024828  | 0.001929935 | -1.127144817   |
| NM_000641   | IL11        | 0.000707282 | 0.004669694 | -1.123883233   |
| Accession | Gene Symbol | FDR | q-value | log2FoldChange | P-Value |
|-----------|-------------|-----|---------|----------------|---------|
| NR_027254| LOC388387   | 0.00078255 | 0.005070874 | -1.114064889 |
| NM_014443| IL17B       | 0.000144645 | 0.001214239 | -1.110541699 |
| NR_027004| FAM181A-S1  | 0.00073248 | 0.00480815 | -1.105933979 |
| NM_138272| C6orf25     | 0.001077966 | 0.006636403 | -1.105862299 |
| NM_025260| C6orf25     | 0.001077966 | 0.006636403 | -1.105862299 |
| NM_032512| PDZD4       | 0.000996112 | 0.00480815 | -1.102384105 |
| NM_153018| ZFP3        | 0.000935147 | 0.005892655 | -1.101579931 |
| NM_002870| RAB13       | 0.000523186 | 0.003649568 | -1.101497332 |
| NM_052874| STX1B       | 0.000830916 | 0.005327739 | -1.100476726 |
| NM_000150| FUT6        | 0.001181232 | 0.007157968 | -1.09949761 |
| NM_006149| LGALS4      | 0.001391485 | 0.008186647 | -1.08532879 |
| NR_002570| CYP2D7P1    | 0.000114372 | 0.000988025 | -1.084491767 |
| NM_001144826| RUNDC3A | 0.000170832 | 0.001407436 | -1.084313152 |
| NM_006695| RUNDC3A     | 0.000167935 | 0.00138780 | -1.084076727 |
| NM_001247994| POU2F2 | 0.000289541 | 0.00793492 | -1.076298778 |
| NM_153345| TMEM139     | 0.000972023 | 0.006082462 | -1.07496812 |
| NM_001242773| TMEM139 | 0.000972023 | 0.006082462 | -1.07496812 |
| NM_001242775| TMEM139 | 0.000972023 | 0.006082462 | -1.07496812 |
| NM_002698| POU2F2     | 0.000133678 | 0.007924045 | -1.073014597 |
| NM_001207025| POU2F2 | 0.000133678 | 0.007924045 | -1.073014597 |
| NM_006071| PKDREJ      | 0.000162376 | 0.009302771 | -1.071052625 |
| NM_033165| FGF8        | 0.000266837 | 0.002047405 | -1.06284788 |
| NM_006119| FGF8        | 0.000266837 | 0.002047405 | -1.06284788 |
| NM_138277| C6orf25     | 0.001372742 | 0.008092395 | -1.062847997 |
| NM_138272| C6orf25     | 0.001372742 | 0.008092395 | -1.062847997 |
| NM_138273| C6orf25     | 0.001372742 | 0.008092395 | -1.062847997 |
| NM_025260| C6orf25     | 0.001372742 | 0.008092395 | -1.062847997 |
| NM_001242376| GFAP   | 0.001289541 | 0.007924045 | -1.062847997 |
| NM_001080487| PABPN1L | 0.000176523 | 0.00976532 | -1.062108899 |
| NM_022124| CDH23       | 0.000121945 | 0.007349552 | -1.061403733 |
| NM_001122890| GGT6   | 0.000664366 | 0.00445832 | -1.059758779 |
| NM_001135217| LRR2C2  | 0.000101228 | 0.00088711 | -1.05841034 |
| NM_198893| STAC2       | 0.000243504 | 0.001898269 | -1.05653015 |
| NM_198847| NKP1D1      | 0.000278178 | 0.00118013 | -1.056453622 |
| NM_001143980| CCDC154 | 0.001283842 | 0.007670273 | -1.05586169 |
| NR_04090| CYP21A1P    | 0.001334671 | 0.00791507 | -1.053674168 |
| NM_001037340| PDE4B  | 0.000106826 | 0.000930133 | -1.049661921 |
| NM_021924| CDHR5       | 0.000240185 | 0.001847366 | -1.049425969 |
| NM_001171968| CDHR5  | 0.000240185 | 0.001847366 | -1.049425969 |
| NR_04003| TMEM139     | 0.001312632 | 0.007806178 | -1.044378348 |
| NM_001242776| TMEM139 | 0.001312632 | 0.007806178 | -1.044378348 |
| Gene Symbol | Description | p-Value 1 | p-Value 2 | Odds Ratio 1 | Odds Ratio 2 |
|-------------|-------------|-----------|-----------|-------------|-------------|
| NM_001242777 | TMEM139     | 0.001312632 | 0.007806178 | -1.044378348 |
| NM_153254    | TTL10       | 0.000387329 | 0.002821835 | -1.043862629 |
| NM_001130413 | SCNN1D      | 0.001850883 | 0.010373953 | -1.043125628 |
| NM_152612    | CCDC116     | 0.001907355 | 0.010614393 | -1.043060394 |
| NM_001077191 | GPBAR1      | 0.00032725  | 0.002440983 | -1.04018659 |
| NM_006142    | SFN         | 0.002226097 | 0.012049714 | -1.040074778 |
| NM_138275    | C6orf25     | 0.002052989 | 0.011285364 | -1.039853301 |
| NM_138274    | C6orf25     | 0.002052989 | 0.011285364 | -1.039853301 |
| NM_138273    | C6orf25     | 0.002052989 | 0.011285364 | -1.039853301 |
| NM_001004342 | TRIM67      | 0.00212087  | 0.011602708 | -1.038914334 |
| NM_001040701 | FUT6        | 0.002141599 | 0.011681698 | -1.038061965 |
| NM_021819    | LMAN1L      | 0.001316725 | 0.00782739  | -1.035025423 |
| NM_001018116 | MURC        | 0.001590258 | 0.009145161 | -1.033731276 |
| NM_001105669 | TTC24       | 0.00038197  | 0.002790691 | -1.031649465 |
| NM_138275    | C6orf25     | 0.001860244 | 0.010404834 | -1.030787156 |
| NM_138274    | C6orf25     | 0.001860244 | 0.010404834 | -1.030787156 |
| NM_001130045 | TTL10       | 0.000856553 | 0.005464616 | -1.029950483 |
| NM_001408    | CELSR2      | 0.00031597  | 0.002365162 | -1.025670909 |
| NM_001051    | SSTR3       | 0.002383825 | 0.012725011 | -1.024838163 |
| NM_001161440 | PTPRH       | 0.00259671  | 0.013631239 | -1.024311633 |
| NM_006841    | SLC38A3     | 0.0014923   | 0.00866146 | -1.022174013 |
| NM_153338    | GGT6        | 0.00095876  | 0.006017203 | -1.02181118 |
| NM_001077194 | GPBAR1      | 0.001080955 | 0.006650669 | -1.019459029 |
| NM_176820    | NLRP9       | 0.002641647 | 0.013815878 | -1.019252561 |
| NM_005975    | PTK6        | 0.002662642 | 0.013908731 | -1.01871768 |
| NM_001100876 | PHYHD1      | 0.002837349 | 0.014630834 | -1.014863597 |
| NM_024637    | GAL3ST4     | 0.002705608 | 0.014088411 | -1.013656315 |
| NR_037668    | SCNN1D      | 0.002571701 | 0.013529165 | -1.013185545 |
| NM_152536    | FGD5        | 0.002764637 | 0.014327996 | -1.013175585 |
| NM_001100877 | PHYHD1      | 0.002869676 | 0.014766779 | -1.011343557 |
| NM_174933    | PHYHD1      | 0.002961466 | 0.015105713 | -1.008953463 |
| NM_052819    | CARD14      | 0.001287629 | 0.007683626 | -1.008282523 |
| NM_014428    | TJP3        | 0.002946509 | 0.015068219 | -1.007851462 |
| NM_201650    | LRRC23      | 0.000262011 | 0.002017671 | -1.006671443 |
| NM_182704    | SELV        | 0.00115256 | 0.007020011 | -1.00582114 |
| NM_207348    | SLC25A34    | 0.000360877 | 0.002652532 | -1.001194349 |
| NM_002292    | LAMB2       | 0.00189131  | 0.010542871 | -1.000978473 |
| NM_001042454 | TGFBI1      | 0.002341286 | 0.012553553 | -1.00042358 |
| NM_001164719 | TGFBI1      | 0.002341286 | 0.012553553 | -1.00042358 |
| NM_138296    | PTCR4       | 0.000413202 | 0.002986892 | -0.999781656 |
| NM_001039616 | SPRED3      | 0.003413171 | 0.016958571 | -0.996005599 |
| Gene ID     | Symbol | EASE Score 1 | EASE Score 2 | q-value 1   | q-value 2   |
|-------------|--------|--------------|--------------|-------------|-------------|
| NM_005309   | GPT    | 0.000260111  | 0.002006674  | -0.99526094 |             |
| NM_004062   | CDH16  | 0.002955481  | 0.015101105  | -0.990353698|             |
| NM_006992   | LRRCC23| 0.000431963  | 0.003097647  | -0.988680871|             |
| NM_145044   | ZNF501 | 0.000474171  | 0.003350996  | -0.987824617|             |
| NM_005187   | CBFA2T3| 0.002834804  | 0.01462025   | -0.984513578|             |
| NM_0033163  | FGFR8  | 0.000977972  | 0.006114534  | -0.983191999|             |
| NM_001080395| AATK   | 0.003568841  | 0.017573363  | -0.983191999|             |
| NM_001008409| TTL9   | 0.001815318  | 0.010203481  | -0.982160005|             |
| NM_001039651| SAPC   | 0.002955481  | 0.015101105  | -0.988680871|             |
| NM_001142685| ARHGAP32| 0.000374211  | 0.002740371  | -0.97559284 |             |
| NM_001135219| PIP5KL1| 0.001815318  | 0.010203481  | -0.982160005|             |
| NM_001204285| MUC1   | 0.004426525  | 0.020873222  | -0.966281599|             |
| NR_00135219 | PIP5KL1| 0.000374211  | 0.002740371  | -0.97559284 |             |
| NM_00104285 | MUC1   | 0.004473907  | 0.021036567  | -0.960852903|             |
| NM_00102974 | LRRC73 | 0.004715676  | 0.018695909  | -0.951880318|             |
| NM_001204744| CDH16  | 0.00368224   | 0.018695909  | -0.951880318|             |
| NR_001256358| PTK6   | 0.004426525  | 0.020873222  | -0.966281599|             |
| NM_001171933| GFAP   | 0.003494719  | 0.015685098  | -0.958086639|             |
| NM_001131019| GFAP   | 0.003494719  | 0.015685098  | -0.958086639|             |
| Gene Symbol      | Gene Name | FDR   | Benjamini FDR | Z Score |
|------------------|-----------|-------|---------------|---------|
| NM_001166034     | SBSN      | 0.006462333 | 0.028212304  | -0.925594205 |
| NM_001195684     | TGFBR3    | 0.002320893 | 0.012460702  | -0.925106038 |
| NR_002930        | PTPRV     | 0.004224546 | 0.020099395  | -0.924941658 |
| NM_021569        | GRIN1     | 0.00099666  | 0.006215688  | -0.921264203 |
| NM_003049        | SLC10A1   | 0.000668709 | 0.004468635  | -0.919251556 |
| NR_002773        | AOC4      | 0.005016338 | 0.023055814  | -0.918423311 |
| NM_033025        | SYDE1     | 0.005605074 | 0.025161027  | -0.918395566 |
| NM_031264        | CDHR5     | 0.00189458  | 0.01055714   | -0.918375549 |
| NM_001203263     | IL17RC    | 0.000617937 | 0.00420019   | -0.918089274 |
| NM_003738        | PTCH2     | 0.000786021 | 0.005087824  | -0.918025904 |
| NM_032214        | SLA2      | 0.000133744 | 0.001132971  | -0.916888306 |
| NM_001042522     | SPRED3    | 0.00586107  | 0.026030997  | -0.91677008  |
| NR_026864        | PRSS30P   | 0.001846562 | 0.010353639  | -0.90693085  |
| NR_002946        | MMP23A    | 0.00115363  | 0.007025085  | -0.90498505  |
| NM_003709        | KLF7      | 0.007413631 | 0.031554119  | -0.904797639 |
| NM_0153460       | IL17RC    | 0.000565434 | 0.003886882  | -0.911117999 |
| NM_032732        | IL17RC    | 0.000565434 | 0.003886882  | -0.911117999 |
| NR_026864        | PRSS30P   | 0.001846562 | 0.010353639  | -0.90693085  |
| NR_002946        | MMP23A    | 0.006407748 | 0.028031658  | -0.905744367 |
| NM_003709        | KLF7      | 0.007413631 | 0.031554119  | -0.904797639 |
| NM_0153461       | IL17RC    | 0.000535585 | 0.003719559  | -0.90498505  |
| NM_002501        | NFIX      | 0.00115363  | 0.007025085  | -0.904243311 |
| NM_033310        | KCNK4     | 0.002070984 | 0.011369561  | -0.903498835 |
| NM_000283        | PDE6B     | 0.007754327 | 0.032690502  | -0.903132337 |
| NM_001145291     | PDE6B     | 0.007754327 | 0.032690502  | -0.903132337 |
| NM_001145292     | PDE6B     | 0.007754327 | 0.032690502  | -0.903132337 |
| NM_015237        | KIAA1107  | 0.004926227 | 0.022745911  | -0.902129408 |
| NM_015693        | INTU      | 0.002047468 | 0.011271692  | -0.899488614 |
| NM_018302        | C4orf19   | 0.00227603  | 0.012275277  | -0.89860835  |
| NM_153007        | ODF4      | 0.001531493 | 0.008864701  | -0.897872789 |
| NM_005985        | SNAI1     | 0.000575793 | 0.003943496  | -0.897535009 |
| NM_175077        | SLA2      | 0.000200285 | 0.001604281  | -0.897282221 |
| NM_018674        | ACCN4     | 0.007007998 | 0.030195395  | -0.896379141 |
| NM_182847        | ACCN4     | 0.007007998 | 0.030195395  | -0.896379141 |
| NM_001105539     | ZBTB10    | 0.000119528 | 0.001025998  | -0.895601665 |
| NM_138278        | BNIPL     | 0.000161049 | 0.001337585  | -0.894738461 |
| NM_000506        | F2        | 0.004883909 | 0.022592639  | -0.894328983 |
| NM_182920        | ADAMTS9   | 0.000753208 | 0.004907497  | -0.892686553 |
| NM_001195014     | CD4       | 0.001218496 | 0.007346327  | -0.891440203 |
| NM_001195017     | CD4       | 0.001218496 | 0.007346327  | -0.891440203 |
| NM_001195016     | CD4       | 0.001218496 | 0.007346327  | -0.891440203 |
| NM_001195015     | CD4       | 0.001218496 | 0.007346327  | -0.891440203 |
| Gene          | Probabilities | Log2 Odds | Odds Ratio |
|--------------|---------------|-----------|------------|
| NM_000616    | CD4           | 0.001218496 | 0.007346327 | -0.891444023 |
| NM_001171740 | C3orf18       | 0.008840918 | 0.036208045 | -0.890371558 |
| NM_032546    | TRIM54        | 0.07102826  | 0.030545452 | -0.889656284 |
| NM_016210    | C3orf18       | 0.008893403 | 0.036342852 | -0.889588264 |
| NM_001114100 | SEZL2         | 0.01909155  | 0.016022421 | -0.887543199 |
| NM_000633    | BCL2          | 0.02605988  | 0.013665457 | -0.887109543 |
| NM_032281    | ELAVL3        | 0.02605988  | 0.013665457 | -0.887109543 |
| NM_198479    | C19orf54      | 0.001718057 | 0.009756847 | -0.885357931 |
| NM_144698    | ANKRD35       | 0.009316253 | 0.037625863 | -0.884930440 |
| NM_01128827  | DLG4          | 0.004550814 | 0.021330684 | -0.884167677 |
| NM_032649    | CNDP1         | 0.009248071 | 0.037396236 | -0.881167677 |
| NM_014722    | FAM65B        | 0.009735321 | 0.038974071 | -0.879419576 |
| NR_033910    | LOC100130275  | 0.009876657 | 0.039428348 | -0.878014708 |
| NM_080877    | SLC34A3       | 0.00986746  | 0.039471426 | -0.877892666 |
| NM_001207026 | POU2F2        | 0.003894169 | 0.018810635 | -0.877834050 |
| NM_138277    | G6orf25       | 0.00371441  | 0.018160765 | -0.879948140 |
| NM_058164    | OLFM2         | 0.009735321 | 0.038974071 | -0.879419576 |
| NM_024719    | GRTP1         | 0.00987486  | 0.039430352 | -0.878018199 |
| NR_033910    | LOC100130275  | 0.009876657 | 0.039428348 | -0.878014708 |
| NM_00163724  | LOC388588     | 0.008234575 | 0.034224738 | -0.871638936 |
| NM_001024215 | FBLIM1        | 0.009064054 | 0.036852714 | -0.871187013 |
| NM_187841    | TRIM54        | 0.008476631 | 0.035020165 | -0.870772489 |
| NM_207627    | ABCG1         | 0.005109285 | 0.023387649 | -0.870621761 |
| NM_207628    | ABCG1         | 0.005109285 | 0.023387649 | -0.870621761 |
| NM_207629    | ABCG1         | 0.005109285 | 0.023387649 | -0.870621761 |
| NM_005373    | MPL           | 0.0098527   | 0.039353854 | -0.870512368 |
| NM_016818    | ABCG1         | 0.005094093 | 0.023386082 | -0.870423543 |
| NM_004915    | ABCG1         | 0.005094093 | 0.023386082 | -0.870423543 |
| NM_207174    | ABCG1         | 0.005094093 | 0.023386082 | -0.870423543 |
| NM_001099439 | EPHA10        | 0.00945346  | 0.038060762 | -0.869757285 |
| NM_022367    | SEMA4A        | 0.000478412 | 0.003374546 | -0.86882875 |
| NM_00119300  | SEMA4A        | 0.000478412 | 0.003374546 | -0.86882875 |
| NM_003782    | B3GALT4       | 0.003379487 | 0.016808068 | -0.867301756 |
| NM_001004323 | C7orf61       | 0.009848749 | 0.039348653 | -0.867182287 |
| NR_028048    | CRAT          | 0.02739253  | 0.014236164 | -0.866505914 |
| Gene Name    | Description | Freq1 | Freq2      | Freq3 | Freq4      | Value       |
|-------------|-------------|-------|------------|-------|------------|-------------|
| NM_001243168| PTCRA       | 0.003229311 | 0.016191235 |       | -0.866004161 |
| NM_031936   | GPR61       | 0.007771078 | 0.032747182 |       | -0.865545847 |
| NM_206961   | LTK         | 0.009079092 | 0.036898712 |       | -0.86269304 |
| NM_002344   | LTK         | 0.009079092 | 0.036898712 |       | -0.86269304 |
| NM_001525   | HCRTR1      | 0.010370774 | 0.04101521  |       | -0.864734017 |
| NM_138275   | C6orf25     | 0.007275793 | 0.03114511  |       | -0.864712138 |
| NM_138274   | C6orf25     | 0.007275793 | 0.03114511  |       | -0.864712138 |
| NM_000600   | IL6         | 0.007275793 | 0.03114511  |       | -0.864712138 |
| NM_020804   | PACSIN1     | 0.002274023 | 0.012270993 |       | -0.861679331 |
| NM_001199583| PACSIN1     | 0.002274023 | 0.012270993 |       | -0.861679331 |
| NM_001185091| GRIN1       | 0.002582327 | 0.013567718 |       | -0.853254789 |
| NM_000832   | GRIN1       | 0.002582327 | 0.013567718 |       | -0.853254789 |
| NM_001177317| SLC34A3     | 0.012237383 | 0.046814921 |       | -0.852639442 |
| NM_001177316| SLC34A3     | 0.012237383 | 0.046814921 |       | -0.852639442 |
| NM_001159554| P2RX6       | 0.0010966   | 0.006734381 |       | -0.852236548 |
| NM_005446   | P2RX6       | 0.0010966   | 0.006734381 |       | -0.852236548 |
| NM_001139515| DACH2       | 0.009881523 | 0.039437175 |       | -0.851706277 |
| NM_014276   | RBPJ        | 0.004123631 | 0.019698112 |       | -0.850028003 |
| NM_001243169| PTCRA       | 0.001545323 | 0.008931224 |       | -0.849589511 |
| NM_001193301| SEMA4A      | 0.0068495   | 0.04552597  |       | -0.849526846 |
| NM_006314   | CNKSR1      | 0.009143946 | 0.03711533  |       | -0.849496088 |
| NR_023345   | CNKSR1      | 0.009143946 | 0.03711533  |       | -0.849496088 |
| NM_178545   | TMEM52      | 0.009757996 | 0.039054324 |       | -0.84858846 |
| NM_152654   | DAND5       | 0.007650798 | 0.032359819 |       | -0.847021555 |
| NM_001159642| BNN1P       | 0.000275258 | 0.002101707 |       | -0.846635501 |
| NM_001710   | CFB         | 0.012101138 | 0.046395241 |       | -0.846298852 |
| NM_172168   | NOXO1       | 0.00665884 | 0.04452761 |       | -0.846091745 |
| NM_001185090| GRIN1       | 0.002701235 | 0.014070859 |       | -0.844676042 |
| NM_000359   | TGM1        | 0.00731877  | 0.03126321  |       | -0.844617377 |
| NM_00755    | CRAT        | 0.00379678  | 0.018427733 |       | -0.844597342 |
| NM_005608   | PTPRCAP     | 0.010619239 | 0.041758889 |       | -0.84434005 |
| NM_017857   | SSH3        | 0.001046233 | 0.006476821 |       | -0.841905474 |
| NR_038988   | LOC100287765| 0.00499089  | 0.02298021 |       | -0.841193859 |
| NM_001195520| LOC100507055| 0.011403858 | 0.044299145 |       | -0.837017585 |
| NM_001242774| TMEM139     | 0.011610621 | 0.04492232 |       | -0.836829726 |
| NM_199242   | UNC13D      | 0.010837574 | 0.042443357 |       | -0.836445361 |
| NM_053006   | TSSK2       | 0.005999274 | 0.026529826 |       | -0.836109259 |
| NM_001144825| RUNCDC3A    | 0.00209286  | 0.011474817 |       | -0.834457544 |
| NM_002386   | MC1R        | 0.000181882 | 0.001480008 |       | -0.833578026 |
| NM_025260   | C6orf25     | 0.005616122 | 0.025188789 |       | -0.831308601 |
| NM_000576   | IL1B        | 0.005616122 | 0.025188789 |       | -0.831308601 |
| Gene Symbol | Gene Name  | Fold Change Mean | Fold Change SD | Correlation |
|-------------|------------|------------------|----------------|-------------|
| NR_02726    | C15orf34   | 0.009471408      | 0.03811267     | -0.831125519|
| NM_001083606| PTCH1      | 0.003487124      | 0.017253889    | -0.830829503|
| NM_006950   | SYN1       | 0.009161102      | 0.037150719    | -0.830156924|
| NM_133499   | SYN1       | 0.009161102      | 0.037150719    | -0.830156924|
| NM_000264   | PTCH1      | 0.003806388      | 0.01847068     | -0.831125519|
| NM_001001891| ANO7       | 0.004995031      | 0.022992152    | -0.829017276|
| NM_005167   | PPMLJ      | 0.009199957      | 0.037268872    | -0.828578339|
| NM_139021   | MAPK15     | 0.004613233      | 0.020990681    | -0.827436818|
| NM_052948   | ARHGAP33   | 0.003767336      | 0.018338073    | -0.82849207 |
| NM_001083606| PTCH1      | 0.003487124      | 0.017253889    | -0.830829503|
| NM_000264   | PTCH1      | 0.003806388      | 0.01847068     | -0.831125519|
| NM_006950   | SYN1       | 0.009161102      | 0.037150719    | -0.830156924|
| NM_133499   | SYN1       | 0.009161102      | 0.037150719    | -0.830156924|
| GenBank Acc. | Gene Symbol | F | Z | p | Adj p | S1 | S2 |
|------------|-------------|---|---|---|------|----|----|
| NM_138273  | C6orf25     | 0.00778122 | 0.032762043 | -0.792954572 | | |
| NM_138274  | C6orf25     | 0.00778122 | 0.032762043 | -0.792954572 | | |
| NM_006181  | NTN3        | 0.007437195 | 0.031604622 | -0.792362325 | | |
| NM_014246  | CELSR1      | 0.000229119 | 0.001797923 | -0.792060201 | | |
| NM_001164730 | REEP1   | 0.012497385 | 0.047546381 | -0.789615161 | | |
| NM_053281  | DACH2       | 0.009548002 | 0.038348154 | -0.788522976 | | |
| NM_053284  | WFIKKN1     | 0.007133018 | 0.030618501 | -0.787719623 | | |
| NM_032580  | HES7        | 0.007213848 | 0.030907154 | -0.786807627 | | |
| NM_001165967 | HES7    | 0.007213848 | 0.030907154 | -0.786807627 | | |
| NM_016938  | EFEMP2      | 0.006715838 | 0.029147736 | -0.784302885 | | |
| NM_001163213 | FGFR3  | 0.000530996 | 0.00369459 | -0.783040493 | | |
| NM_033064  | ATCAY       | 0.004941398 | 0.022812417 | -0.779013024 | | |
| NM_002250  | KCNN4       | 0.004844033 | 0.022441182 | -0.777193954 | | |
| NM_000142  | FGFR3       | 0.006723293 | 0.0448778 | -0.77582306 | | |
| NM_015311  | OBSL1       | 0.00617628 | 0.027187157 | -0.772208417 | | |
| NM_001114171 | FOSB   | 0.0006273 | 0.004252162 | -0.771672497 | | |
| NM_172166  | MSH5        | 0.00179555 | 0.010113412 | -0.770546371 | | |
| NM_172165  | MSH5        | 0.00179555 | 0.010113412 | -0.770546371 | | |
| NM_002441  | MSH5        | 0.00179555 | 0.010113412 | -0.770546371 | | |
| NR_038448  | LOC440288   | 0.000555742 | 0.03830894 | -0.770391611 | | |
| NM_001083605 | PTCH1  | 0.007222075 | 0.030929301 | -0.77019033 | | |
| NM_001146175 | ZNF414  | 0.009508996 | 0.038230205 | -0.76851618 | | |
| NM_001083607 | PTCH1  | 0.007516057 | 0.031894112 | -0.767915813 | | |
| NR_026914  | MGC16275    | 0.000266221 | 0.012044264 | -0.760872636 | | |
| NM_022463  | NXN         | 0.008981935 | 0.036629086 | -0.76547845 | | |
| NM_006732  | FOSB        | 0.000522794 | 0.003647777 | -0.762049012 | | |
| NM_021641  | ADAM12      | 0.000266221 | 0.002044264 | -0.760872636 | | |
| NM_001013653 | LRR2C6  | 0.000947726 | 0.033711714 | -0.759258671 | | |
| NM_001012302 | ANO9   | 0.000220903 | 0.012032383 | -0.75958364 | | |
| NM_004099  | GUCA1A      | 0.000220903 | 0.012032383 | -0.75958364 | | |
| NM_014975  | MAST1       | 0.000220903 | 0.012032383 | -0.75958364 | | |
| NM_001083604 | PTCH1  | 0.008332486 | 0.034562975 | -0.755137781 | | |
| NM_174942  | GAS2L3      | 0.009713942 | 0.038898626 | -0.754160716 | | |
| NR_036532  | UBAC2-AS1   | 0.000220903 | 0.012032383 | -0.753359159 | | |
| NM_020870  | SH3RF1      | 0.000220903 | 0.012032383 | -0.753359159 | | |
| NM_013278  | IL17C       | 0.000220903 | 0.012032383 | -0.753359159 | | |
| NR_037846  | MSH5-SAPCD1 | 0.000220903 | 0.012032383 | -0.753359159 | | |
| NM_005418  | ST5         | 0.000220903 | 0.012032383 | -0.753359159 | | |
| NM_213618  | ST5         | 0.000220903 | 0.012032383 | -0.753359159 | | |
| NM_014298  | QPRT        | 0.000220903 | 0.012032383 | -0.753359159 | | |
| Gene               | Fold Change | p-value | q-value | Adjusted Fold Change |
|--------------------|-------------|---------|---------|----------------------|
| NM_013974 DDAH2    | 0.001134306 | 0.006930132 | -0.746680315         |
| NM_030773 TUBB1    | 0.0043947   | 0.020756088 | -0.74525736          |
| NM_003052 SLC34A1  | 0.002138    | 0.011674923 | -0.743937321         |
| NM_007000 UPK1A    | 0.003583452 | 0.017630703 | -0.742614419         |
| NR_024120 DBIL5P   | 0.006560579 | 0.028574047 | -0.742573111         |
| NM_001003794 MGLL  | 0.009052305 | 0.036839321 | -0.742400897         |
| NM_022965 FGFR3    | 0.011363051 | 0.007113087 | -0.742573111         |
| NM_003052 SLC34A1  | 0.002138    | 0.011674923 | -0.742614419         |
| NM_001136503 C19orf77 | 0.005262933 | 0.023958251 | -0.740512698         |
| NM_001003794 MGLL  | 0.009052305 | 0.036839321 | -0.740512698         |
| NM_001136503 C19orf77 | 0.005262933 | 0.023958251 | -0.740512698         |
| NM_003052 SLC34A1  | 0.002138    | 0.011674923 | -0.740512698         |
| Gene Symbol | Gene Name | Value 1 | Value 2 | Value 3 | Value 4 |
|-------------|-----------|---------|---------|---------|---------|
| NM_005567   | LGALS3BP  | 0.001517372 | 0.008793241 | -0.693730102 |
| NM_003565   | ULK1      | 0.000732482 | 0.004805995 | -0.693538394 |
| NM_020404   | CD248     | 0.003270422 | 0.016366982 | -0.692984825 |
| NM_001256313| STK3      | 0.000127942 | 0.00108879  | -0.692308685 |
| NM_001122769| LCA5      | 0.00795801  | 0.033341067 | -0.691084648 |
| NM_001253845| ADM2      | 0.011935464 | 0.045890307 | -0.687757625 |
| NM_178564   | NRB2P2    | 0.006732472 | 0.0292114   | -0.68739558 |
| NM_002334   | LRP4      | 0.00158984  | 0.009145161 | -0.684851332 |
| NM_00125008 | ADAMTSL4  | 0.001625708 | 0.009312098 | -0.684644442 |
| NM_001146316| IRS2      | 0.006314457 | 0.027709201 | -0.681696958 |
| NM_001146316| IRS2      | 0.006314457 | 0.027709201 | -0.681696958 |
| NR_034086   | LOC648987 | 0.00108081  | 0.000939684 | -0.680196631 |
| NM_001202233| NR4A1     | 0.000132301 | 0.001122351 | -0.677440194 |
| NM_025257   | SLC44A4   | 0.008796108 | 0.036064287 | -0.67416205 |
| NM_153618   | SEMA6D    | 0.001902728 | 0.010598549 | -0.676881772 |
| NM_001162499| CAND2     | 0.009237867 | 0.037362298 | -0.675013343 |
| NM_006213   | PHKG1     | 0.000897434 | 0.005682726 | -0.676128468 |
| NM_152795   | HIF3A     | 0.009237867 | 0.037362298 | -0.675013343 |
| NM_022462   | HIF3A     | 0.009237867 | 0.037362298 | -0.675013343 |
| NM_152794   | HIF3A     | 0.009237867 | 0.037362298 | -0.675013343 |
| NM_001135191| ASAP2     | 0.001873551 | 0.010469406 | -0.674594166 |
| NM_133465   | KIAA1958  | 0.000299335 | 0.002260566 | -0.67091041 |
| NM_144603   | NOXO1     | 0.002691835 | 0.014033906 | -0.6691673 |
| NM_001256105| WNT5A     | 0.00953562  | 0.030030373 | -0.668919765 |
| NM_013264   | DDX25     | 0.01057461  | 0.041633033 | -0.668296022 |
| NR_024089   | LINCO0162 | 0.004011272 | 0.019251126 | -0.668131287 |
| NM_001136021| NFATC2    | 0.006989638 | 0.030150797 | -0.667209393 |
| NM_173091   | NFATC2    | 0.007128076 | 0.030614644 | -0.66652185 |
| NM_002441   | MSH5      | 0.000531399 | 0.003695972 | -0.66561864 |
| NM_0020928  | ZSWIM6    | 0.005268433 | 0.023964988 | -0.66537749 |
| NM_001145524| YPEL3     | 0.000173096 | 0.001422536 | -0.665778035 |
| NM_001001666| ANO7      | 0.004102128 | 0.019620623 | -0.66537749 |
| NM_003887   | ASAP2     | 0.002096436 | 0.011488068 | -0.66506186 |
| NM_0019302  | ADAMTSL4  | 0.00278551  | 0.002119225 | -0.664432407 |
| NM_153619   | SEMA6D    | 0.002280698 | 0.012295989 | -0.662063195 |
| NM_032219   | MFS6D     | 0.006430953 | 0.028106948 | -0.662045026 |
| NM_001171093| FAM131A   | 0.00012867  | 0.001094046 | -0.661590781 |
| NM_153617   | SEMA6D    | 0.002381137 | 0.012713986 | -0.660450335 |
| NM_032641   | SP5B2     | 0.000643766 | 0.004341989 | -0.660323301 |
| Gene   | Symbol   | Log2FoldChange | p-Value   | Adjusted p-Value |
|--------|----------|----------------|-----------|-----------------|
| NFATC2 | NM_001174072 | 0.007912325 | 0.033182413 | -0.658855196 |
| MOGAT3 | NM_178176 | 0.004341274 | 0.020556027 | -0.658421393 |
| SGPP2  | NM_152386 | 0.001394089 | 0.008198712 | -0.658390082 |
| TMLHE  | NM_001184797 | 0.00372591 | 0.018202017 | -0.657213198 |
| MSH5   | NM_172166 | 0.00721361 | 0.004747881 | -0.656346287 |
| TRIM14 | NM_033219 | 0.001833389 | 0.010289486 | -0.655118315 |
| CAND2  | NM_012298 | 0.005519366 | 0.02485513 | -0.653943109 |
| YJEFN3 | NM_198537 | 0.005295458 | 0.024046008 | -0.653493863 |
| SEMA6D | NM_020858 | 0.002636522 | 0.013796359 | -0.652870558 |
| SNCAIP | NM_001256733 | 0.00584814 | 0.00399699 | -0.652223737 |
| GLB1L  | NM_024506 | 0.004592404 | 0.021468061 | -0.652005262 |
| WNK4   | NM_032387 | 0.009318467 | 0.03762969 | -0.651754076 |
| SNCAIP | NM_001242935 | 0.007361533 | 0.031391755 | -0.648621168 |
| TOM1L2 | NM_001033551 | 0.00967781 | 0.006062302 | -0.648162095 |
| WDFY2  | NM_052950 | 0.006355485 | 0.027835808 | -0.644314577 |
| STK3   | NM_006281 | 0.000111359 | 0.000981389 | -0.643348848 |
| DLF4   | NM_001365 | 0.003042661 | 0.015429822 | -0.642851987 |
| MSH5   | NM_025259 | 0.00941749 | 0.005926715 | -0.64129824 |
| FAM115C| NM_173678 | 0.001679933 | 0.009571046 | -0.641464635 |
| CXADR  | NM_001207065 | 0.004787508 | 0.022236696 | -0.640838767 |
| FCHO2  | NM_001146032 | 0.003665875 | 0.017945726 | -0.640597613 |
| GDF1   | NM_001492 | 0.002010878 | 0.011103169 | -0.636604408 |
| CERS1  | NM_021267 | 0.002010878 | 0.011103169 | -0.636604408 |
| ABCC3  | NM_003786 | 0.008914187 | 0.036413273 | -0.63571341 |
| THAP7-AS1| NM_027051 | 0.010390059 | 0.041065273 | -0.634692815 |
| ZBTB46 | NM_025224 | 0.004308676 | 0.020424633 | -0.63449406 |
| NCKAP5 | NM_207481 | 0.007202734 | 0.030868711 | -0.632355459 |
| DENND1B| NM_144977 | 0.00259485 | 0.00200341 | -0.630307016 |
| PHYHIP | NM_014759 | 0.012350638 | 0.047145009 | -0.629112434 |
| PHYHIP | NM_001099335 | 0.012350638 | 0.047145009 | -0.629112434 |
| FAM27C | NM_027421 | 0.012366578 | 0.047193735 | -0.627673839 |
| ANO8   | NM_020959 | 0.000212983 | 0.001688693 | -0.626047513 |
| PACSIN3| NM_016223 | 0.000104898 | 0.000916032 | -0.625547449 |
| PACSIN3| NM_001184974 | 0.000104898 | 0.000916032 | -0.625547449 |
| SSBP2  | NM_012446 | 0.00684491 | 0.004552597 | -0.625300481 |
| UBA C2-AS1| NM_036531 | 0.012496258 | 0.047546381 | -0.625276767 |
| TTN    | NM_133379 | 0.000170592 | 0.00140624 | -0.624895681 |
| RXF1   | NM_002918 | 0.011907733 | 0.045807391 | -0.624420752 |
| SERINC5| NM_001174072 | 0.000263669 | 0.002028859 | -0.623628568 |
| Gene Accession | Gene Symbol | Log2 Fold Change | p Value | q Value | Adjusted p Value |
|---------------|-------------|-----------------|---------|---------|-----------------|
| NM_000395     | CSF2RB      | 0.009377103     | 0.037825354 | -0.623207064 |
| NM_058229     | FBXO32      | 0.004972781     | 0.022925247 | -0.622945902 |
| NM_012191     | NAT6        | 0.008035589     | 0.033601352 | -0.622053628 |
| NM_001164711  | AMT         | 0.005351023     | 0.024255328 | -0.621806712 |
| NM_001012984  | C16orf86    | 0.009153011     | 0.03713311  | -0.620666454 |
| NM_003939     | BTRC        | 0.000308686     | 0.023193999 | -0.61957113  |
| NR_015454     | MAFG-AS1    | 0.000700389     | 0.004634088 | -0.617741141 |
| NM_001159643  | MCTP2       | 0.000103282     | 0.000903781 | -0.616200942 |
| NR_027422     | FAM27B      | 0.008423564     | 0.034820254 | -0.613503581 |
| NM_001143779  | IFT81       | 0.005538957     | 0.024928243 | -0.617864858 |
| NR_015454     | MAFG-AS1    | 0.000700389     | 0.004634088 | -0.617741141 |
| Gene Symbol | Description | T1 Value | P1 Value | adjustedP1 Value |
|-------------|-------------|----------|----------|-----------------|
| NM_207115   | ZNF580      | 0.00120178 | 0.007269145 | -0.594629136   |
| NR_034178   | SRGAP2P2    | 0.0019201  | 0.010675326 | -0.593372016   |
| NM_001144382| PLCL2       | 0.000384504 | 0.002803315 | -0.592188169   |
| NM_001190201| CES4A       | 0.002381332 | 0.012713986 | -0.591960908   |
| NM_015076   | CDK19       | 0.006412446 | 0.028039826 | -0.591927557   |
| NM_001184975| PACSIN3     | 0.000382021 | 0.002790691 | -0.591874756   |
| NM_172166   | MSH5        | 0.006106929 | 0.026927454 | -0.591588445   |
| NM_172165   | MSH5        | 0.006106929 | 0.026927454 | -0.591588445   |
| NM_001256312| STK3        | 0.000577682 | 0.003951885 | -0.59145188    |
| NM_001007026| ATN1        | 0.001434023 | 0.008388752 | -0.590589576   |
| NM_001201402| GALC        | 0.011576052 | 0.044821569 | -0.590379988   |
| NM_021937   | EEFSEC      | 0.000192603 | 0.001515128 | -0.589207673   |
| NM_000203   | IDUA        | 0.010369035 | 0.041013793 | -0.588795151   |
| NM_001198999| SEMA6D      | 0.003889942 | 0.018795   | -0.58873953    |
| NM_015209   | KAZN        | 0.001720209 | 0.009766805 | -0.588438006   |
| NM_024660   | IGFLR1      | 0.000851596 | 0.005435329 | -0.588048782   |
| NM_152228   | TAS1R3      | 0.010646375 | 0.041843452 | -0.587039      |
| NM_198207   | CERS1       | 0.002709221 | 0.014104753 | -0.585346059   |
| NM_001242463| FBXO32      | 0.001076722 | 0.040092373 | -0.583927749   |
| NM_021202   | TP53INP2    | 0.006865073 | 0.029695689 | -0.58139805    |
| NM_014735   | PHF16       | 0.002135596 | 0.011666084 | -0.58171345    |
| NM_001207064| CXADR       | 0.009114829 | 0.037023699 | -0.581712296   |
| NM_001199098| BAIAP3      | 0.000178801 | 0.001460136 | -0.58150743    |
| NM_001199099| BAIAP3      | 0.000178801 | 0.001460136 | -0.58150743    |
| NM_001256735| SSBP2       | 0.002218323 | 0.012022964 | -0.580550442   |
| NM_153697   | ANKRD44     | 0.001391123 | 0.008186563 | -0.58034092    |
| NM_153498   | CAMK1D      | 0.000198465 | 0.001591846 | -0.580025113   |
| NM_002441   | MSH5        | 0.007548896 | 0.032010637 | -0.579990768   |
| NM_024646   | ZYG11B      | 0.000614047 | 0.004178526 | -0.579755994   |
| NM_00135707 | ACBD4       | 0.00135146  | 0.007998672 | -0.579406027   |
| NM_001144951| GLYCTK      | 0.011091698 | 0.043295939 | -0.579152672   |
| NM_003933   | BAIAP3      | 0.000185482 | 0.001505999 | -0.578820894   |
| NM_001199097| BAIAP3      | 0.000198964 | 0.001594558 | -0.578579667   |
| NM_014055   | IFT81       | 0.006045885 | 0.026708125 | -0.577804066   |
| NM_000153   | GALC        | 0.012383256 | 0.047245246 | -0.576836882   |
| NR_045553   | THBS3       | 0.002397509 | 0.012786569 | -0.576785788   |
| NM_003793   | CTSF        | 0.000593824 | 0.004052982 | -0.576025748   |
| NM_145253   | FAM100A     | 0.011409256 | 0.044310884 | -0.573803844   |
| NM_152363   | ANKLE1      | 0.000614748 | 0.004182344 | -0.573703842   |
| NM_018349   | MCTP1       | 0.000272877 | 0.002085751 | -0.573683428   |
| NM_016368   | ISYNA1      | 0.000181381 | 0.001476736 | -0.572947126   |
| Gene Symbol   | Gene Name  | Fold Change 1 | Fold Change 2 | Log2 Fold Change |
|--------------|------------|---------------|---------------|-----------------|
| NM_001178056 | PARP8      | 0.000404446   | 0.002932873   | -0.572377443    |
| NM_182899    | CREB5      | 0.012705129   | 0.048157947   | -0.571855918    |
| NM_182898    | CREB5      | 0.012705129   | 0.048157947   | -0.571855918    |
| NM_004904    | CREB5      | 0.012705129   | 0.048157947   | -0.571855918    |
| NM_001011666 | CREB5      | 0.012705129   | 0.048157947   | -0.571855918    |
| NM_001256736 | SSBP2     | 0.002792549   | 0.014445288   | -0.571702442    |
| NM_003743    | NCOA1      | 0.001011193   | 0.000887069   | -0.570562107    |
| NM_147233    | NCOA1      | 0.001011193   | 0.000887069   | -0.570562107    |
| NM_001201427 | DAAM2     | 0.001460571   | 0.008512213   | -0.570245768    |
| NR_026702    | GLYCTK     | 0.005966176   | 0.026410971   | -0.570059155    |
| NM_001163423 | ZNF580     | 0.001484598   | 0.008624424   | -0.569752895    |
| NM_004925    | AQP3       | 0.001647432   | 0.009416570   | -0.569443221    |
| NM_001256734 | SSBP2     | 0.00261762    | 0.013721609   | -0.569145284    |
| NM_001244706 | CSAD      | 0.008096093   | 0.033781467   | -0.56893416     |
| NM_153607    | C5orf41    | 0.007884836   | 0.033099824   | -0.56863595     |
| NM_002391    | MDK        | 0.001906647   | 0.010614393   | -0.565422052    |
| NM_015345    | DAAM2      | 0.00145064    | 0.008464297   | -0.565709966    |
| NM_00191061  | SLC25A22   | 0.000115964   | 0.001000173   | -0.565422052    |
| NM_147223    | NCOA1      | 0.000117876   | 0.001014752   | -0.565145822    |
| NM_020902    | CAMSAP3    | 0.000806176   | 0.005197901   | -0.56435825     |
| NM_001080429 | CAMSAP3    | 0.000808632   | 0.005210346   | -0.563893416    |
| NM_130468    | CHST14     | 0.012167977   | 0.046609408   | -0.563846594    |
| NR_046367    | EGFL7      | 0.000497852   | 0.003500042   | -0.563652019    |
| NM_001199096 | BAIAP3     | 0.000294281   | 0.002225228   | -0.563345309    |
| NM_001014765 | FBXO44     | 0.001608583   | 0.009228234   | -0.562796458    |
| NM_024698    | SLC25A22   | 0.000162362   | 0.00347363    | -0.562682325    |
| NR_045110    | EGFL7      | 0.000508264   | 0.00355725    | -0.562050094    |
| NR_045111    | EGFL7      | 0.000508264   | 0.00355725    | -0.562050094    |
| NM_013974    | DDAH2      | 0.004079635   | 0.019535049   | -0.5618948      |
| NM_001012333 | MDK        | 0.002219414   | 0.012026683   | -0.56185275     |
| NM_012334    | MYO10      | 0.000385351   | 0.00357251    | -0.561347365    |
| NM_005528    | DNAJC4     | 0.001597016   | 0.009177822   | -0.56131709     |
| NM_001099755 | SYBU       | 0.000162586   | 0.001348468   | -0.561122718    |
| NM_016215    | EGFL7      | 0.000524581   | 0.003655091   | -0.560830523    |
| NM_001161562 | TNIK       | 0.004978117   | 0.022930664   | -0.560607529    |
| NM_001161561 | TNIK       | 0.004978117   | 0.022930664   | -0.560607529    |
| NM_001161560 | TNIK       | 0.004978117   | 0.022930664   | -0.560607529    |
| NM_015028    | TNIK       | 0.004978117   | 0.022930664   | -0.560607529    |
| NM_033401    | CNTNAP4    | 0.010058986   | 0.040037891   | -0.559399057    |
| NM_201446    | EGFL7      | 0.000588434   | 0.004018958   | -0.557138927    |
| NM_001122772 | AGAP2      | 0.000189547   | 0.001530306   | -0.557061938    |
| Gene Symbol | p-Value | FDR  | p-Value | FDR  | p-Value | FDR  | p-Value | FDR  |
|-------------|---------|------|---------|------|---------|------|---------|------|
| NM_001080475 | 0.00353711 | 0.017441706 | -0.556602294 |
| NM_001017395 | 0.001094194 | 0.006725163 | -0.556105547 |
| NM_001099746 | 0.000200634 | 0.001606208 | -0.555914945 |
| NM_001099749 | 0.000200634 | 0.001606208 | -0.555914945 |
| NR_023380 | 0.001225322 | 0.007373213 | -0.555865802 |
| NM_001161563 | 0.005710852 | 0.025516373 | -0.554525613 |
| NM_001161566 | 0.005710852 | 0.025516373 | -0.554525613 |
| NM_001161565 | 0.005710852 | 0.025516373 | -0.554525613 |
| NM_001161564 | 0.005710852 | 0.025516373 | -0.554525613 |
| NM_032042 | 0.000412373 | 0.002983806 | -0.554371952 |
| NM_020998 | 0.002175864 | 0.011829518 | -0.552704236 |
| NM_020397 | 0.000756319 | 0.004924615 | -0.552175182 |
| NM_022841 | 0.001528718 | 0.008852089 | -0.552027934 |
| NM_001135956 | 0.01254159 | 0.047684035 | -0.551428295 |
| NM_015512 | 0.000178713 | 0.001460136 | -0.549970424 |
| NM_001207063 | 0.012129193 | 0.046478819 | -0.549717123 |
| NM_001135955 | 0.010242576 | 0.040610891 | -0.549668574 |
| NM_001170938 | 0.000384708 | 0.002804114 | -0.547847225 |
| NM_138994 | 0.01188056 | 0.045727213 | -0.547701192 |
| NM_001013436 | 0.000365872 | 0.002685263 | -0.547588957 |
| NM_001077445 | 0.003771278 | 0.018354651 | -0.547301429 |
| NM_001136258 | 0.010167195 | 0.040387453 | -0.54632167 |
| NR_045573 | 0.00054161 | 0.003754381 | -0.5458604 |
| NM_001003700 | 0.00107534 | 0.00935479 | -0.545820909 |
| NM_015136 | 0.000696694 | 0.004617229 | -0.54572085 |
| NM_001164755 | 0.005847467 | 0.025978347 | -0.545608799 |
| NM_001163417 | 0.000627934 | 0.004253548 | -0.545130604 |
| NM_001256308 | 0.00419273 | 0.003021957 | -0.545046965 |
| NM_152754 | 0.004881192 | 0.022583587 | -0.544577496 |
| NM_173584 | 0.002847892 | 0.014673208 | -0.543210642 |
| NM_001161574 | 0.003525131 | 0.017395603 | -0.543043683 |
| NM_001131028 | 0.007423535 | 0.031577649 | -0.543005053 |
| NM_052893 | 0.002212502 | 0.012000167 | -0.541942961 |
| NM_001130517 | 0.000416451 | 0.003005261 | -0.541579618 |
| NM_031482 | 0.008221811 | 0.03418125 | -0.540045112 |
| NM_001018000 | 0.0032889256 | 0.016439089 | -0.539757639 |
| NM_002119 | 0.003666805 | 0.017945726 | -0.539195617 |
| NM_006642 | 0.000899009 | 0.005690279 | -0.538910574 |
| NM_018196 | 0.010103573 | 0.04017769 | -0.538538384 |
| NM_001018001 | 0.003737281 | 0.018239574 | -0.53822861 |
| NM_001080 | 0.000643367 | 0.004340283 | -0.537677686 |
| Gene ID       | Gene Symbol | Log2FoldChange1 | Log2FoldChange2 | p-value1 | p-value2 |
|--------------|-------------|----------------|----------------|----------|----------|
| NM_170740    | ALDH5A1     | 0.000643367    | 0.004340283    | -0.537677686 |
| NM_170672    | RASGRP3     | 0.001150125    | 0.007010461    | -0.537453603 |
| NM_147127    | EVC2        | 0.000682448    | 0.004540029    | -0.537188536 |
| NM_014808    | FARP2       | 0.001500241    | 0.007802451    | -0.536968516 |
| NM_183413    | FBXO44      | 0.003122766    | 0.015763417    | -0.53690242 |
| NM_021126    | MPST        | 0.000479479    | 0.003380631    | -0.536431298 |
| NM_006977    | ZBTB25      | 0.000682448    | 0.004540029    | -0.537188536 |
| NM_032824    | TMEM87B     | 0.00198885     | 0.001594354    | -0.535738435 |
| NM_001174095 | ZEB1        | 0.000841608    | 0.005380608    | -0.535369478 |
| NM_001252607 | THBS3       | 0.004510267    | 0.016288575    | -0.534382025 |
| NR_001093725 | FER1L4      | 0.000572017    | 0.003923059    | -0.53420863 |
| NM_002119    | HLA-DOA     | 0.00012857     | 0.001093504    | -0.533927749 |
| NR_037846    | MSH5-SAPCD1 | 0.005583051    | 0.025088692    | -0.533847938 |
| NM_145262    | GLYCTK      | 0.0002986752   | 0.015203374    | -0.532895626 |
| NR_026699    | GLYCTK      | 0.0002986752   | 0.015203374    | -0.532895626 |
| NM_033220    | TRIM14      | 0.001114835    | 0.043357777    | -0.532563434 |
| NM_022737    | LPPR2       | 0.005616345    | 0.025188789    | -0.531858778 |
| NM_001174093 | ZEB1        | 0.00065046     | 0.003677711    | -0.531792499 |
| NM_001099272 | BTBD9       | 0.002767329    | 0.014339446    | -0.531377008 |
| NM_006939    | SOS2        | 0.003209184    | 0.016106625    | -0.531144777 |
| NM_00114614  | MFGE8       | 0.003782345    | 0.018384026    | -0.531060084 |
| NR_024038    | MPST        | 0.000528198    | 0.003677711    | -0.530437768 |
| NM_001164754 | ASPH        | 0.008215341    | 0.034163909    | -0.530199804 |
| NM_001017999 | KAZN        | 0.004244358    | 0.02017428     | -0.52989041 |
| NM_130898    | CREB3L4     | 0.002419353    | 0.012886882    | -0.52977544 |
| NM_019600    | FAM214A     | 0.001701014    | 0.009679453    | -0.529428419 |
| NM_033182    | FBXO44      | 0.003350447    | 0.016697171    | -0.529252081 |
| NM_007112    | TMEM87B     | 0.004872739    | 0.022558527    | -0.528949041 |
| NM_001161573 | MAFF        | 0.005554225    | 0.024938365    | -0.528934465 |
| NM_001253389 | ISYNA1      | 0.000596878    | 0.004071018    | -0.528462904 |
| NM_001145963 | SLC12A4     | 0.000104693    | 0.00914779     | -0.526423434 |
| NM_000512    | GALNS       | 0.001907321    | 0.010614393    | -0.525381655 |
| NM_006257    | PRKCI       | 0.00311804     | 0.015744912    | -0.525299382 |
| NM_003306    | TRPC4       | 0.012253289    | 0.046857676    | -0.525127103 |
| NM_016179    | TRPC4       | 0.012253289    | 0.046857676    | -0.525127103 |
| NM_001256304 | DTNB        | 0.000453639    | 0.003230481    | -0.525074976 |
| NM_001145962 | SLC12A4     | 0.000113544    | 0.00981389     | -0.525024519 |
| NM_001242409 | FAM59A      | 0.000188671    | 0.001525646    | -0.524589046 |
| NM_022751    | FAM59A      | 0.000188671    | 0.001525646    | -0.524589046 |
| Gene Name | Gene_symbol | Value | Significance | LogRatio |
|-----------|-------------|-------|--------------|----------|
| NM_001255980 | CREB3L4 | 0.003077985 | 0.015579709 | -0.524446228 |
| NM_152312 | GYLT1L1B | 0.004089808 | 0.019577454 | -0.52435289 |
| NM_207363 | NCKAP5 | 0.001276694 | 0.007635677 | -0.524348024 |
| NM_001173425 | DFNB31 | 0.002781409 | 0.014402359 | -0.52286328 |
| NM_001255978 | CREB3L4 | 0.002781409 | 0.014402359 | -0.52286328 |
| NM_001242413 | PRKCQ | 0.003792708 | 0.018419335 | -0.52209187 |
| NM_001172418 | BTBD9 | 0.004570311 | 0.021388335 | -0.521930621 |
| NM_001081560 | DMPK | 0.000787356 | 0.00509424 | -0.521386273 |
| NM_001255980 | CREB3L4 | 0.002781409 | 0.014402359 | -0.52286328 |
| NM_001172418 | BTBD9 | 0.004570311 | 0.021388335 | -0.521930621 |
| NM_001081562 | DMPK | 0.000811678 | 0.005225444 | -0.519903442 |
| NM_006037 | HDAC4 | 0.000259086 | 0.002001884 | -0.519258683 |
| NM_001135706 | ACBD4 | 0.001451497 | 0.008467635 | -0.520474361 |
| NM_001135707 | ACBD4 | 0.001451497 | 0.008467635 | -0.520474361 |
| NM_006645 | STARD10 | 0.004157071 | 0.019832346 | -0.520185779 |
| NM_001081562 | DMPK | 0.000811678 | 0.005225444 | -0.519903442 |
| NM_001135705 | LPPR2 | 0.007522767 | 0.031918056 | -0.51667042 |
| NM_001170794 | BACH2 | 0.0042915 | 0.020359275 | -0.515734857 |
| NM_004409 | DMPK | 0.00964186 | 0.006042326 | -0.515605066 |
| NR_045574 | ISYNA1 | 0.000835031 | 0.005350283 | -0.515517504 |
| NM_024507 | KREMEN2 | 0.009757775 | 0.037487855 | -0.514225089 |
| NM_001145961 | SLC12A4 | 0.000206289 | 0.00164263 | -0.515350942 |
| NM_148965 | TNFRSF25 | 0.0075999 | 0.032190171 | -0.513551773 |
| NM_183360 | DTNB | 0.000412898 | 0.002985775 | -0.513550942 |
| NM_004067 | CHN2 | 0.00172334 | 0.001419024 | -0.512992669 |
| NM_003790 | TNFRSF25 | 0.00762862 | 0.032293406 | -0.512502139 |
| NM_148967 | TNFRSF25 | 0.010550326 | 0.041593888 | -0.511896948 |
| NM_014770 | AGAP2 | 0.000415813 | 0.00300284 | -0.51154081 |
| NM_001139488 | RASGRP3 | 0.001444933 | 0.008437626 | -0.511494065 |
| NM_021907 | DTNB | 0.00043976 | 0.003145964 | -0.510527475 |
| Accession   | Gene   | Fold Change | p-Value | Adjusted p-Value | q-Value |
|-------------|--------|-------------|---------|------------------|---------|
| NM_020859   | SHROOM3| 0.000252898 | 0.001960188 | -0.510383489 |
| NM_001014979| C16orf93| 0.005821261 | 0.02589677 | -0.50979944 |
| NM_001195620| C16orf93| 0.012447332 | 0.04740508 | -0.509745058 |
| NM_001159770| SLC39A11| 0.00783904 | 0.05077437 | -0.50466866 |
| NM_021916   | ZNF70  | 0.009765714 | 0.039079952 | -0.50269766 |
| NM_016202   | ZNF580 | 0.004049373 | 0.019403155 | -0.50922244 |
| NM_001174101| PRR7   | 0.005806649 | 0.0258395 | -0.508573978 |
| NM_015833   | ADARB1 | 0.00174267 | 0.009871698 | -0.508549586 |
| NM_172389   | NFATC1 | 0.000189146 | 0.001528655 | -0.508020129 |
| NM_001256303| DTNB   | 0.00477025 | 0.003367961 | -0.507922858 |
| NM_015188   | TBC1D12| 0.003041297 | 0.015425536 | -0.507841102 |
| NM_001174096| ZEB1   | 0.000949258 | 0.005966391 | -0.506764397 |
| NM_015376   | RASGRP3| 0.002740052 | 0.014237827 | -0.50571429 |
| NM_001166136| EVC2   | 0.001530225 | 0.00885909 | -0.505624221 |
| NM_001128128| ZEB1   | 0.001093166 | 0.006720235 | -0.505443792 |
| NM_030567   | PRR7   | 0.004589069 | 0.021455845 | -0.505035318 |
| NM_021140   | KDM6A  | 0.001171972 | 0.007113457 | -0.50502102 |
| NM_012338   | SLC17A1| 0.000260303 | 0.002007633 | -0.50655595 |
| NM_001174094| ZEB1   | 0.001089279 | 0.006697728 | -0.50589316 |
| NM_015376   | RASGRP3| 0.002740052 | 0.014237827 | -0.50571429 |
| NM_001166136| EVC2   | 0.001530225 | 0.00885909 | -0.505624221 |
| NM_001128128| ZEB1   | 0.001093166 | 0.006720235 | -0.505443792 |
| NM_030567   | PRR7   | 0.004589069 | 0.021455845 | -0.505035318 |
| NM_021140   | KDM6A  | 0.001171972 | 0.007113457 | -0.50502102 |
| NM_012338   | SLC17A1| 0.000260303 | 0.002007633 | -0.50655595 |
| NM_001174094| ZEB1   | 0.001089279 | 0.006697728 | -0.50589316 |
| Gene Symbol | Gene Name | Fold Change | q Value | P Value |
|-------------|-----------|-------------|---------|---------|
| NM_001243733 | VEGFB | 0.001888079 | 0.01053046 | -0.499068807 |
| NM_001112 | ADARB1 | 0.002291819 | 0.012351468 | -0.498673797 |
| NM_172387 | NFATC1 | 0.000223596 | 0.001760625 | -0.498601076 |
| NM_000080 | CHRNA5 | 0.005874624 | 0.026075611 | -0.498015122 |
| NM_001163152 | ETV1 | 0.000766566 | 0.004979245 | -0.497439931 |
| NM_005704 | PTPRU | 0.001471195 | 0.008555677 | -0.496659989 |
| NM_133177 | PTPRU | 0.001471195 | 0.008555677 | -0.496659989 |
| NM_133178 | PTPRU | 0.001471195 | 0.008555677 | -0.496659989 |
| NM_145007 | NLRP11 | 0.000766566 | 0.004979245 | -0.497439931 |
| NR_027140 | TNFRSF10B | 0.007988967 | 0.033451898 | -0.496198907 |
| NM_001002266 | Mar-08 | 0.005726458 | 0.025574564 | -0.496113882 |
| NM_022478 | CDH24 | 0.00196753 | 0.010896213 | -0.496034795 |
| NM_001128613 | NUDB22 | 0.002524264 | 0.013331004 | -0.495901456 |
| NM_003377 | VEGFB | 0.001805417 | 0.010161284 | -0.495310379 |
| NM_001184906 | FBXL20 | 0.007302114 | 0.031204619 | -0.493915133 |
| NM_183412 | FBXO44 | 0.006532511 | 0.028464316 | -0.495181772 |
| NM_001002265 | Mar-08 | 0.002507482 | 0.013258871 | -0.494842938 |
| NM_198584 | CA13 | 0.000795407 | 0.005140735 | -0.493768308 |
| NM_001193524 | FAM65A | 0.000795407 | 0.005140735 | -0.493768308 |
| NM_012477 | WBP1 | 0.000795407 | 0.005140735 | -0.493768308 |
| NM_016573 | GMIP | 0.002415615 | 0.012533849 | -0.493768308 |
| NM_001039569 | AP1S3 | 0.002415615 | 0.012533849 | -0.493768308 |
| NM_001105529 | ATP8A1 | 0.002415615 | 0.012533849 | -0.493768308 |
| NM_207351 | PRRT3 | 0.002415615 | 0.012533849 | -0.493768308 |
| NM_014048 | MKL2 | 0.002415615 | 0.012533849 | -0.493768308 |
| NM_033148 | DTNB | 0.002415615 | 0.012533849 | -0.493768308 |
| NM_015016 | MAST3 | 0.002415615 | 0.012533849 | -0.493768308 |
| NM_152243 | CDC42EP1 | 0.002415615 | 0.012533849 | -0.493768308 |
| NM_001142641 | FBRS1 | 0.002415615 | 0.012533849 | -0.493768308 |
| NM_172114 | CAMK2D | 0.002415615 | 0.012533849 | -0.493768308 |
| NM_172115 | CAMK2D | 0.002415615 | 0.012533849 | -0.493768308 |
| NM_172129 | CAMK2D | 0.002415615 | 0.012533849 | -0.493768308 |
| NM_00135704 | ACBD4 | 0.002415615 | 0.012533849 | -0.493768308 |
| NM_014831 | TRAK1 | 0.002415615 | 0.012533849 | -0.493768308 |
| NM_00199621 | NCOA7 | 0.002415615 | 0.012533849 | -0.493768308 |
| NM_001012957 | DISC1 | 0.002415615 | 0.012533849 | -0.493768308 |
| NM_183361 | DTNB | 0.002415615 | 0.012533849 | -0.493768308 |
| NM_021813 | BACH2 | 0.002415615 | 0.012533849 | -0.493768308 |
| NM_145021 | Mar-08 | 0.002415615 | 0.012533849 | -0.493768308 |
| NM_001160230 | ADARB1 | 0.002415615 | 0.012533849 | -0.493768308 |
| Gene Symbol | Gene Name | Expression Value | Gene Expression Value | Log2 Fold Change |
|-------------|-----------|------------------|-----------------------|-----------------|
| NM_144641   | PPM1M     | 0.002523581      | 0.013331004           | -0.48879979     |
| NM_032875   | FBXL20    | 0.001444011      | 0.008433899           | -0.48817769     |
| NM_001163418| FAM172A   | 0.003905575      | 0.018856533           | -0.488679031    |
| NM_173511   | FAM117B   | 0.010712531      | 0.042064521           | -0.48837353     |
| NM_032344   | NUDT22    | 0.00170117       | 0.009679453           | -0.488140397    |
| NM_001198535| OXR1      | 0.000177689      | 0.001454176           | -0.487626343    |
| NM_001120   | MFS5D10   | 0.000189241      | 0.001529002           | -0.487423949    |
| NM_005533   | IFI35     | 0.000329718      | 0.002456928           | -0.487307069    |
| NR_026845   | C21orf119 | 0.008338834      | 0.03457585            | -0.486759023    |
| NM_001253726| KREMen2   | 0.012396163      | 0.047270212           | -0.485641308    |
| NM_194291   | TMEM65    | 0.000884818      | 0.005616003           | -0.48546322     |
| NM_001145923| SCAPEr    | 0.006367831      | 0.02792024            | -0.485276922    |
| NM_005781   | TNK2      | 0.000570785      | 0.003917323           | -0.485038047    |
| NM_152730   | C6orf170  | 0.011781341      | 0.045429949           | -0.485017032    |
| NM_000052   | ATP7A     | 0.000426052      | 0.003062651           | -0.484970184    |
| NM_001159601| RAB28     | 0.000204955      | 0.001634631           | -0.481527744    |
| NM_006095   | ATP8A1    | 0.005136664      | 0.023491267           | -0.481470314    |
| NM_024770   | METTL8    | 0.000348331      | 0.002568982           | -0.481331671    |
| NM_001146069| MFS5D10   | 0.000205507      | 0.001637282           | -0.480845182    |
| NM_005786   | TSHZ1     | 0.000194808      | 0.001565467           | -0.48059998     |
| NM_001010938| TNK2      | 0.000735018      | 0.004818561           | -0.480236273    |
| NM_014869   | IQSEC1    | 0.002359144      | 0.012622736           | -0.480184484    |
| NM_021224   | ZNF462    | 0.007024535      | 0.030270899           | -0.480028723    |
| NM_021994   | ZNF277    | 0.010078672      | 0.040094764           | -0.479903999    |
| NM_003890   | FCGBP     | 0.001992355      | 0.011021372           | -0.47983759     |
| NM_015073   | SIPA1L3   | 0.00049934       | 0.003508844           | -0.479561902    |
| NM_001017979| RAB28     | 0.000223949      | 0.001762942           | -0.479456996    |
| NM_020800   | IFT80     | 0.000142458      | 0.001192849           | -0.47926214     |
| NM_001164540| DISC1     | 0.0038903        | 0.018795              | -0.47910211     |
| NM_004943   | DMWD      | 0.000190253      | 0.001534673           | -0.479047946    |
| NM_006346   | PIBF1     | 0.000952017      | 0.005978674           | -0.478377529    |
| NM_006162   | NFATC1    | 0.000403212      | 0.002925355           | -0.478062014    |
| NM_020376   | PNPLA2    | 0.001009306      | 0.006287955           | -0.477663271    |
| NM_001142782| MAGI3     | 0.00069931       | 0.004630435           | -0.477479864    |
| NM_001199620| NCOA7     | 0.000657646      | 0.004412568           | -0.476078098    |
| NR_036467   | IFFO1     | 0.002312151      | 0.012431542           | -0.475660504    |
| NR_016815   | GYPC      | 0.000584374      | 0.003994905           | -0.475304289    |
| NR_024408   | LOC253039 | 0.006130555      | 0.0270179             | -0.475092144    |
| NM_001255981| CREB3L4   | 0.00846058       | 0.034973298           | -0.475023439    |
| NR_027674   | ADARB1    | 0.004277413      | 0.020307029           | -0.474887555    |
| NM_001255979| CREB3L4   | 0.007625195      | 0.032283506           | -0.474679744    |
| Gene Symbol | Gene Symbol | Value 1 | Value 2 | Value 3 |
|-------------|-------------|--------|--------|--------|
| NM_080730   | IF001       | 0.002798961 | 0.014461479 | -0.474459227 |
| NM_001039670| IF001       | 0.002798961 | 0.014461479 | -0.474459227 |
| NM_001199619| NCOA7       | 0.000676747 | 0.004512203 | -0.473984974 |
| NM_173078   | SLITRK4     | 0.001279259 | 0.007649043 | -0.473921323 |
| NM_024113   | C11orf49    | 0.009997029 | 0.039844648 | -0.473753204 |
| NM_001003677| C11orf49    | 0.009997029 | 0.039844648 | -0.473753204 |
| NM_001164537| DISC1       | 0.002897538 | 0.014874095 | -0.473205198 |
| NM_018662   | DISC1       | 0.002897538 | 0.014874095 | -0.473205198 |
| NM_152900   | MAGI3       | 0.000768593 | 0.004990227 | -0.473196567 |
| NM_001003676| C11orf49    | 0.007657208 | 0.032377524 | -0.472873113 |
| NM_152686   | DNAJC18     | 0.012670751 | 0.0480767 | -0.471321904 |
| NM_006295   | VAR         | 0.000518763 | 0.003623054 | -0.470685549 |
| NM_032591   | SLC9A7      | 0.009890523 | 0.039452444 | -0.470620398 |
| NM_001193457| IF001       | 0.003022228 | 0.015356253 | -0.469808585 |
| NM_001242607| NCAM1       | 0.007502628 | 0.0318508 | -0.469529206 |
| NM_181351   | NCAM1       | 0.007502628 | 0.0318508 | -0.469529206 |
| NM_181782   | NCOA7       | 0.001049549 | 0.006489689 | -0.469453147 |
| NM_003842   | TNFRSF10B   | 0.010310375 | 0.040825239 | -0.469188097 |
| NM_001024382| HMBS        | 0.002050029 | 0.011281611 | -0.468894685 |
| NM_052916   | RNF157      | 0.00019228  | 0.001549405 | -0.468244445 |
| NM_145738   | SYNGR1      | 0.010918669 | 0.042710291 | -0.468206457 |
| NM_007255   | B4GALT7     | 0.000414244 | 0.002993702 | -0.467916457 |
| NM_001164750| ASPH        | 0.003199717 | 0.016069964 | -0.467722696 |
| NM_001190241| IFT80       | 0.000217286 | 0.001719598 | -0.467314499 |
| NM_001206484| ATF3        | 0.002309548 | 0.012423824 | -0.466739524 |
| NM_001122842| NCOA7       | 0.001136028 | 0.006939228 | -0.466657234 |
| NR_026777   | ZNF37BP     | 0.00011048  | 0.0009583 | -0.466543992 |
| NM_001149   | ANK3        | 0.002425446 | 0.012912393 | -0.466042882 |
| NM_139076   | FAM175A     | 0.003476702 | 0.017208053 | -0.465979121 |
| NM_024776   | PEAK1       | 0.002716154 | 0.014128467 | -0.46591644 |
| NM_000615   | NCAM1       | 0.007908988 | 0.033173566 | -0.465641333 |
| NM_015556   | SIPA1L1     | 0.001133494 | 0.006926597 | -0.465226565 |
| NM_004249   | RAB28       | 0.000319629 | 0.002388935 | -0.46504104 |
| NM_147187   | TNFRSF10B   | 0.01111177  | 0.043357203 | -0.464954375 |
| NM_032499   | C15orf41    | 0.008399056 | 0.034762498 | -0.464796153 |
| NM_031413   | CECR2       | 0.00074814  | 0.004883038 | -0.464694557 |
| NM_001166271| SPATA13     | 0.000689655 | 0.004577725 | -0.463567538 |
| NM_002101   | GYPC        | 0.000575221 | 0.003940489 | -0.463137712 |
| NM_001256584| GYPC        | 0.000575221 | 0.003940489 | -0.463137712 |
| NM_002917   | RFNG        | 0.001363663 | 0.008053252 | -0.462240732 |
| NR_028080   | FAM172A     | 0.006497223 | 0.028341422 | -0.462003448 |
| Gene Symbol | Description | p-value 1 | p-value 2 | p-value 3 |
|-------------|-------------|-----------|-----------|-----------|
| NM_001206488 | ATF3        | 0.002489457 | 0.013172936 | -0.46174321 |
| NM_001184883 | PLCB3       | 0.000142371 | 0.001197861 | -0.460820873 |
| NM_014934    | DZIP1       | 0.00028542  | 0.002164284 | -0.459565251 |
| NM_016154    | RAB4B       | 0.010318153 | 0.040850592 | -0.458774916 |
| NM_145886    | PIDD        | 0.000466643 | 0.00330487  | -0.45867863  |
| NM_001168724 | TMEM135     | 0.000112027 | 0.000969741 | -0.457765423 |
| NM_001184749 | SLITRK4     | 0.001163023 | 0.007070692 | -0.457632326 |
| NM_001171133 | FAM3A       | 0.004793115 | 0.022252306 | -0.457001503 |
| NM_001184750 | SLITRK4     | 0.001957269 | 0.010853549 | -0.456530992 |
| NM_032306    | ALKBH7      | 0.00393962  | 0.018983898 | -0.455740096 |
| NM_022918    | TMEM135     | 0.000117973 | 0.001014998 | -0.455151581 |
| NM_144973    | DENNDSB     | 0.001385779 | 0.008161157 | -0.455094689 |
| NM_001080448 | EPHA6       | 0.000714726 | 0.00471256  | -0.454748174 |
| NM_001161662 | WWC1        | 0.001053168 | 0.00650257  | -0.454491712 |
| NM_001161661 | WWC1        | 0.001053168 | 0.00650257  | -0.454491712 |
| NM_015238    | WWC1        | 0.001053168 | 0.00650257  | -0.454491712 |
| NM_001082579 | RBFOX2      | 0.000188049 | 0.001521855 | -0.454454809 |
| NM_001082578 | RBFOX2      | 0.000188049 | 0.001521855 | -0.454454809 |
| NM_020843    | SCAPER      | 0.008054628 | 0.033665172 | -0.454363811 |
| NM_018438    | FBXO6       | 0.011313404 | 0.044022578 | -0.454063078 |
| NM_001024647 | RAB3IP      | 0.000728209 | 0.004783419 | -0.454023357 |
| NM_030962    | SFB2        | 0.002666435 | 0.013925912 | -0.454023236 |
| NM_203474    | PORCN       | 0.00549483  | 0.024767158 | -0.453958858 |
| NM_203475    | PORCN       | 0.00549483  | 0.024767158 | -0.453958858 |
| NM_002839    | PTPRD       | 0.003313127 | 0.016538922 | -0.452965992 |
| NM_001005739 | VPS54       | 0.004051562 | 0.019410006 | -0.452772525 |
| NM_001025239 | TSPAN4      | 0.002883095 | 0.014820437 | -0.452726628 |
| NM_001082577 | RBFOX2      | 0.000264826 | 0.002035813 | -0.452566298 |
| NM_014309    | RBFOX2      | 0.000268503 | 0.002057534 | -0.452540996 |
| NM_018226    | RNPEPL1     | 0.000813879 | 0.005237339 | -0.452460554 |
| NM_199334    | THRA        | 0.010481785 | 0.041366162 | -0.452205105 |
| NM_130393    | PTPRD       | 0.004567474 | 0.021381794 | -0.451825346 |
| NM_130392    | PTPRD       | 0.004567474 | 0.021381794 | -0.451825346 |
| NM_130391    | PTPRD       | 0.004567474 | 0.021381794 | -0.451825346 |
| NM_001171025 | PTPRD       | 0.004567474 | 0.021381794 | -0.451825346 |
| NM_001040712 | PTPRD       | 0.004567474 | 0.021381794 | -0.451825346 |
| NM_052924    | RHPN1       | 0.002017365 | 0.011130714 | -0.45181514 |
| NM_001190242 | IFT80       | 0.000673312 | 0.004493332 | -0.451653333 |
| NM_001122870 | PPM1M       | 0.006827261 | 0.029557942 | -0.451341677 |
| NM_001134368 | SLC6A6      | 0.000532379 | 0.003699887 | -0.450604921 |
| NM_021120    | DLG3        | 0.002035183 | 0.011210293 | -0.449166186 |
| Accession     | Description | Expression Level 1 | Expression Level 2 | Adjusted p-Value |
|--------------|-------------|--------------------|--------------------|------------------|
| NM_003271    | TSPAN4      | 0.003639036        | 0.017853927        | -0.448967721     |
| NM_144571    | CNOT6L      | 0.001020063        | 0.006343005        | -0.448791449     |
| NM_002119    | HLA-DOA     | 0.001484758        | 0.008624424        | -0.448538732     |
| NM_016516    | VPS54       | 0.004372734        | 0.02065891         | -0.448465474     |
| NM_001987    | ETV6        | 0.000441909        | 0.0031583          | -0.448462978     |
| NM_145887    | PIDD        | 0.000595682        | 0.004063793        | -0.448224204     |
| NM_198968    | DZIP1       | 0.000396481        | 0.002882626        | -0.448140039     |
| NM_021021    | SNTPB1      | 0.000681105        | 0.004532664        | -0.447874173     |
| NM_001134382 | IQSEC1      | 0.001668023        | 0.009515959        | -0.446908379     |
| NM_024949    | WWC2        | 0.000867765        | 0.005524288        | -0.44686701      |
| NM_001136127 | DNM3        | 0.001718127        | 0.009756847        | -0.446846633     |
| NM_015569    | DNM3        | 0.001718127        | 0.009756847        | -0.446846633     |
| NM_022825    | PORCN       | 0.006154206        | 0.027106051        | -0.44762179      |
| NM_203473    | PORCN       | 0.006154206        | 0.027106051        | -0.44762179      |
| NM_014887    | N4BP2L2     | 0.001330409        | 0.007897677        | -0.44651145      |
| NM_001243960 | NEDD4L      | 0.001378464        | 0.01165395         | -0.446544898     |
| NR_037687    | PLXNC1      | 0.000212839        | 0.001688002        | -0.446425059     |
| NM_014957    | DENND3      | 0.000221257        | 0.001744522        | -0.445727455     |
| NM_00932     | PLCB3       | 0.000247376        | 0.001923915        | -0.444944392     |
| NM_024527    | ABHD8       | 0.003477928        | 0.017211257        | -0.444924706     |
| NM_022092    | CHTF18      | 0.001463094        | 0.008521904        | -0.444289931     |
| NM_001243750 | NUDT8       | 0.005827866        | 0.02591496         | -0.444206499     |
| NM_001204505 | DGKH        | 0.000160856        | 0.00133636         | -0.443846542     |
| NR_033237    | FAM3A       | 0.003281444        | 0.016408323        | -0.443798313     |
| NM_015185    | ARHGEF9     | 0.003840427        | 0.018608508        | -0.443484246     |
| NM_021806    | FAM3A       | 0.003225149        | 0.016173092        | -0.443348561     |
| NM_001031695 | RBFOX2      | 0.000354716        | 0.002613064        | -0.443156621     |
| NM_001082576 | RBFOX2      | 0.000359528        | 0.00264458         | -0.443127662     |
| NM_020461    | TUBGCP6     | 0.000477696        | 0.003371095        | -0.442892724     |
| NR_037945    | STX16-NPEPL1 | 0.000531598   | 0.003695972         | -0.442774904     |
| NM_001204506 | DGKH        | 0.000170473        | 0.001406053        | -0.442434412     |
| NR_027783    | SAT1        | 0.000653334        | 0.004390577        | -0.442260239     |
| NR_033422    | SLC11A2     | 0.0001979632       | 0.010957190        | -0.442250601     |
| NR_033948    | P2RX7       | 0.0011465087       | 0.044507901        | -0.442104007     |
| NM_003422    | MZF1        | 0.005295032        | 0.024046008        | -0.441777577     |
| NM_177401    | MIDN        | 0.005138844        | 0.023497619         | -0.441730301     |
| NM_032918    | RERG        | 0.000108767        | 0.000944269        | -0.441650961     |
| NR_045786    | LOC100861402| 0.00014537         | 0.001219638        | -0.441149181     |
| NR_045787    | LOC100861402| 0.00014537         | 0.001219638        | -0.441149181     |
| NM_147128    | ZNRF2       | 0.001965072        | 0.010890721        | -0.440779302     |
| NM_023078    | PYCRL       | 0.000561752        | 0.003866944        | -0.440750335     |
| Gene Symbol | Description | Log2 Fold Change | Log10 (p-value) |
|-------------|-------------|-----------------|----------------|
| NM_001253884 | ALPK1        | 0.007390533     | 0.031482865    |
| NM_001164213 | LRCH1        | 0.007347713     | 0.031358897    |
| NM_181843    | NUDT8        | 0.007131615     | 0.030616904    |
| NM_016340    | RAPGEF6      | 0.000735412     | 0.004819973    |
| NM_033951    | P2RX7        | 0.01273032      | 0.048228827    |
| NM_014925    | R3HDM2       | 0.002458536     | 0.013041552    |
| NM_001715    | BLK          | 0.009890659     | 0.039452444    |
| NM_024734    | CLMN         | 0.000404983     | 0.002936055    |
| NM_001030287 | ATF3         | 0.008609399     | 0.035450671    |
| NM_001099281 | HEATR7A      | 0.001015699     | 0.006320172    |
| NM_001012758 | NUDT17       | 0.010995555     | 0.042960152    |
| NM_001674    | ATF3         | 0.004116292     | 0.019672539    |
| NM_001025237 | TSPAN4       | 0.00470738      | 0.02193052     |
| NM_001244871 | DAB2         | 0.011306378     | 0.044006763    |
| NM_130849    | SLC39A4      | 0.005614821     | 0.025188789    |
| NM_001171132 | FAM3A        | 0.004107173     | 0.019638434    |
| NM_001025234 | TSPAN4       | 0.004709563     | 0.021936378    |
| NR_003003    | SCARNA17     | 0.001215721     | 0.007338527    |
| NM_001040619 | ATF3         | 0.004785303     | 0.022229926    |
| NM_001039936 | CHN2         | 0.008472987     | 0.035009976    |
| NM_001164386 | RAPGEF6      | 0.000837575     | 0.005358494    |
| NR_027673    | ADARB1       | 0.008948597     | 0.03653324     |
| NM_017667    | CCDC132      | 0.00324647      | 0.016266286    |
| NM_198055    | MZF1         | 0.005043011     | 0.023152444    |
| NM_014790    | JAKMIP2      | 0.010740027     | 0.042144464    |
| NM_001244888 | AGAP1        | 0.005124568     | 0.023450385    |
| NM_001079803 | GAA          | 0.001998244     | 0.011045725    |
| NM_001204873 | NPEPL1       | 0.012842054     | 0.04855927     |
| NM_001113299 | HIPK2        | 0.000103814     | 0.000907636    |
| NM_032852    | ATG4C        | 0.010069871     | 0.040075849    |
| NM_001025236 | TSPAN4       | 0.00494377      | 0.022816279    |
| NM_001025235 | TSPAN4       | 0.00494377      | 0.022816279    |
| NM_000152    | GAA          | 0.002145341     | 0.011693527    |
| NM_175080    | P2RX5        | 0.009053884     | 0.036839321    |
| NM_001204520 | P2RX5        | 0.009053884     | 0.036839321    |
| NM_198904    | GABRG2       | 0.009048197     | 0.036833599    |
| NM_000816    | GABRG2       | 0.009048197     | 0.036833599    |
| NM_012181    | FKBP8        | 0.000368438     | 0.002702088    |
| NM_198903    | GABRG2       | 0.009200458     | 0.037268872    |
| Gene Symbol | Description | P1 | P2 | P3 |
|-------------|-------------|----|----|----|
| EYA1        |             | 0.011964637 | 0.045972733 | -0.430558309 |
| P2RX5       |             | 0.010001272 | 0.039848881 | -0.430257537 |
| P2RX5       |             | 0.010001272 | 0.039848881 | -0.430257537 |
| PDE4B       |             | 0.0002615 | 0.002014253 | -0.430136561 |
| POM121L10P  |             | 0.012709787 | 0.048163153 | -0.430031123 |
| LSR         |             | 0.00339981 | 0.016898752 | -0.429961455 |
| GAA         |             | 0.001994414 | 0.011026606 | -0.429721886 |
| RYK         |             | 0.000664399 | 0.004445832 | -0.429696337 |
| RYK         |             | 0.000664399 | 0.004445832 | -0.429696337 |
| PIK3R5      |             | 0.011530425 | 0.044685661 | -0.429678062 |
| ALPK1       |             | 0.006747805 | 0.02925657 | -0.429345718 |
| RGS13       |             | 0.00795883 | 0.005141708 | -0.429106432 |
| VPS13A      |             | 0.000417221 | 0.003009885 | -0.429101448 |
| ATG4C       |             | 0.012765444 | 0.048331088 | -0.429066477 |
| RAPGEF6     |             | 0.001200038 | 0.007260086 | -0.42900883 |
| RAPGEF6     |             | 0.001200038 | 0.007260086 | -0.42900883 |
| SLC39A4     |             | 0.006191836 | 0.027239496 | -0.428996053 |
| PIK3R5      |             | 0.012229318 | 0.046802142 | -0.42735066 |
| RGS13       |             | 0.00891044 | 0.005650697 | -0.428481024 |
| CASK        |             | 0.003465724 | 0.017165154 | -0.427884131 |
| CHCHD6      |             | 0.002630584 | 0.01377499 | -0.42785444 |
| DENND1A     |             | 0.002694805 | 0.014044462 | -0.427726183 |
| CASK        |             | 0.003426187 | 0.017009021 | -0.427443249 |
| PIK3R5      |             | 0.012341301 | 0.047121476 | -0.427405485 |
| VPS13A      |             | 0.000448746 | 0.003198699 | -0.426872724 |
| FAM3A       |             | 0.004375699 | 0.020669631 | -0.426841053 |
| TRMT11      |             | 0.004363694 | 0.020630491 | -0.426692408 |
| UBAC2       |             | 0.000151801 | 0.001268937 | -0.426386399 |
| HEATR7A     |             | 0.001029095 | 0.006388471 | -0.426265434 |
| ATG4C       |             | 0.011870099 | 0.045700953 | -0.426072832 |
| PDE4B       |             | 0.000312556 | 0.002343735 | -0.42574692 |
| APBA2       |             | 0.000231715 | 0.001816852 | -0.425594117 |
| APBA2       |             | 0.000231715 | 0.001816852 | -0.425594117 |
| ZNF711      |             | 0.012933863 | 0.04882566 | -0.42508517 |
| SLC11A2     |             | 0.003909236 | 0.018871144 | -0.42503532 |
| MZT2B       |             | 0.00154539 | 0.008931224 | -0.424991764 |
| UAP1L1      |             | 0.001578692 | 0.009092728 | -0.424714873 |
| SLC25A10    |             | 0.00143597 | 0.008396838 | -0.424590193 |
| RAB3IP      |             | 0.000254258 | 0.001968861 | -0.424588012 |
| LETMD1      |             | 0.000766247 | 0.004979245 | -0.424468583 |
| LOC100287042|             | 0.001034948 | 0.006422122 | -0.424168816 |
| Gene ID       | Gene Symbol | Value1  | Value2  | Value3  |
|--------------|-------------|---------|---------|---------|
| NM_003730    | RNASET2     | 0.001593487 | 0.009159313 | -0.424013068 |
| NM_000190    | HMBS        | 0.002097508 | 0.011491823 | -0.423899983 |
| NM_001134773 | STX16       | 0.000148229 | 0.001242046 | -0.423651909 |
| NM_000252    | MTM1        | 0.005033338 | 0.023118346 | -0.423641352 |
| NM_003763    | STX16       | 0.000155179 | 0.001293175 | -0.423580084 |
| NM_080702    | EVI2A       | 0.000564388 | 0.003881488 | -0.422967309 |
| NM_001130026 | FAM115C     | 0.005088756 | 0.023329613 | -0.422469516 |
| NM_001001433 | STX16       | 0.000149527 | 0.001251692 | -0.421065817 |
| NM_001134772 | STX16       | 0.00015643  | 0.001302865 | -0.420997172 |
| NM_001698    | AUH         | 0.006431579 | 0.035522381 | -0.41996923 |
| NM_001113528 | METTL15     | 0.008248409 | 0.034277438 | -0.42037325 |
| NM_025144    | ALPK1       | 0.007990315 | 0.033452828 | -0.420436185 |
| NM_015925    | LSR         | 0.004395626 | 0.020757162 | -0.42021955 |
| NR_037941    | STX16       | 0.000190113 | 0.001533963 | -0.419970771 |
| NM_017771    | PXK         | 0.000159689 | 0.028106947 | -0.420865021 |
| NM_177454    | FAM171B     | 0.00934937  | 0.036805447 | -0.422711724 |
| NM_004639    | BAG6        | 0.000254961 | 0.001973093 | -0.422469516 |
| NM_080703    | BAG6        | 0.000251795 | 0.001953172 | -0.419656973 |
| NM_002890    | RASA1       | 0.001311848 | 0.007806178 | -0.418386306 |
| NM_000503    | EYA1        | 0.011113627 | 0.043357777 | -0.419705841 |
| NM_180989    | GPR180      | 0.004556873 | 0.021355715 | -0.417873511 |
| NM_177967    | UBAC2       | 0.000388343 | 0.002827834 | -0.418094564 |
| NM_00118037  | VPS13A      | 0.00544853  | 0.003773339 | -0.417604642 |
| NM_205834    | LSR         | 0.004046563 | 0.019401696 | -0.417487511 |
| NM_033305    | VPS13A      | 0.0055043  | 0.003799567 | -0.416432193 |
| NM_006747    | SIPA1       | 0.009416576 | 0.037945841 | -0.416425954 |
| NM_024430    | PSTPIP2     | 0.011690365 | 0.0451524 | -0.415973613 |
| NM_003688    | CASK        | 0.004436136 | 0.020890383 | -0.415512225 |
| NM_130847    | AMOTL1      | 0.000824941 | 0.005300493 | -0.415490517 |
| NR_045018    | LETMD1      | 0.001152377 | 0.007020011 | -0.4152706 |
| NM_001003927 | EVI2A       | 0.000656206 | 0.00440485 | -0.41526096 |
| NM_001174116 | DMXL2       | 0.006966173 | 0.03006736 | -0.415184723 |
| NM_015263    | DMXL2       | 0.006966173 | 0.03006736 | -0.415184723 |
| NM_001174129 | SLC11A2     | 0.003535407 | 0.01744052 | -0.415169749 |
| NM_033396    | TNKS1BP1    | 0.000273857 | 0.002092621 | -0.415151378 |
| NM_001001795 | C8orf82     | 0.002797269 | 0.01445929 | -0.415089149 |
| Gene Symbol | Name   | FDR  | Adjusted FDR | p Value |
|-------------|--------|------|--------------|---------|
| NM_002039   | GAB1   | 0.007354753 | 0.03137542 | -0.414992003 |
| NM_001243689| LETMD1 | 0.001060757 | 0.006541461 | -0.414937041 |
| NM_152586   | USP54  | 0.010539231 | 0.041526695 | -0.414472867 |
| NM_153690   | FAM43A | 0.001599078 | 0.009184348 | -0.414372734 |
| NM_172208   | TAPBP  | 0.001382724 | 0.008148007 | -0.414285623 |
| NM_003172   | SURF1  | 0.002694999 | 0.0020641   | -0.413666863 |
| NM_175625   | RAB3IP | 0.000330559 | 0.002461943 | -0.413593967 |
| NM_002335   | LRP5   | 0.002093852 | 0.011478138 | -0.41324951  |
| NM_001174128| SLC11A2| 0.00369917  | 0.018089228 | -0.412933588 |
| NM_000617   | SLC11A2| 0.00369917  | 0.018089228 | -0.412933588 |
| NM_014737   | RASSF2 | 0.000167738 | 0.001386558 | -0.412909966 |
| NM_001174125| SLC11A2| 0.003816498 | 0.018507646 | -0.412889276 |
| NM_172208   | TAPBP  | 0.002954946 | 0.015100968 | -0.41286018  |
| NM_015023   | WDTC1  | 0.00103213  | 0.000903442 | -0.412259091 |
| NM_001173480| ARHgef9| 0.007907094 | 0.033173566 | -0.411745135 |
| NM_005077   | TLE1   | 0.008314551 | 0.034513402 | -0.410822575 |
| NM_015328   | AHCYL2 | 0.001859236 | 0.01040311  | -0.410635342 |
| NM_001130720| AHCYL2 | 0.001859236 | 0.01040311  | -0.410635342 |
| NM_001540   | HSPB1  | 0.004549659 | 0.021328635 | -0.410616021 |
| NM_001025238| TSPAN4 | 0.008695588 | 0.035735968 | -0.410536488 |
| NM_001694   | ATP6V0C| 0.00575171  | 0.025676998 | -0.409786225 |
| NM_025204   | TRABD  | 0.004043666 | 0.019390935 | -0.409247434 |
| NM_003061   | SLIT1  | 0.006861874 | 0.029686173 | -0.409242953 |
| NM_207123   | GAB1   | 0.008179096 | 0.034063277 | -0.409038998 |
| NM_001204   | BMPR2  | 0.012049554 | 0.046245203 | -0.408998798 |
| NR_026644   | UBAC2  | 0.00352466  | 0.002597773 | -0.408811095 |
| NM_001142885| TMOD2  | 0.010538286 | 0.041526695 | -0.408593455 |
| NM_020761   | RPTOR  | 0.000667707 | 0.004463506 | -0.40854243  |
| NM_001009998| SSBP4  | 0.001687065 | 0.009607995 | -0.408148731 |
| NR_037719   | PLSCR3 | 0.011177894 | 0.043575164 | -0.407868999 |
| NM_002314   | LIMK1  | 0.001012   | 0.006302094 | -0.407457796 |
| NM_152636   | METTL15| 0.010527388 | 0.041502043 | -0.407433521 |
| NM_170774   | RASSF2 | 0.000197231 | 0.00158323  | -0.407272846 |
| NM_172208   | TAPBP  | 0.001385454 | 0.00816086  | -0.406669394 |
| NM_032627   | SSBP4  | 0.001776928 | 0.0100327   | -0.406525144 |
| NM_020319   | ANKY2  | 0.00042498  | 0.003057902 | -0.40609063  |
| NM_012478   | WBP2   | 0.000780766 | 0.005060421 | -0.405904263 |
| NR_037943   | STX16  | 0.000771426 | 0.00507529  | -0.405818706 |
| NM_134262   | RORA   | 0.001942494 | 0.010787722 | -0.405692302 |
| NM_001105251| ZFYVE16| 0.004253518 | 0.020214584 | -0.405465639 |
| NM_001174130| SLC11A2| 0.005655691 | 0.025334667 | -0.404337602 |
| Gene Name  | Symbol | Log2 Fold Change | Adj. P Value | q Value |
|------------|--------|-----------------|-------------|---------|
| GNG4       | NM_001098721 | 0.009828284 | 0.039277448 | -0.403991112 |
| POLG2      | NM_007215 | 0.000832094 | 0.005333764 | -0.403694631 |
| TMOD2      | NM_014548 | 0.011729707 | 0.04525142 | -0.403686751 |
| SIDT1      | NM_017699 | 0.005690546 | 0.025463931 | -0.403441037 |
| BRD3       | NM_007371 | 0.012633199 | 0.04794646 | -0.403421527 |
| LIMK1      | NM_01204426 | 0.001447193 | 0.008449164 | -0.403277832 |
| POLG2      | NM_139245 | 0.000832094 | 0.005333764 | -0.403277832 |
| TMOD2      | NM_01174126 | 0.011729707 | 0.04525142 | -0.403686751 |
| SLC11A2    | NM_01134398 | 0.00321792 | 0.016145014 | -0.402201403 |
| BRD3       | NM_017699 | 0.005690546 | 0.025463931 | -0.403441037 |
| LIMK1      | NM_001098721 | 0.009828284 | 0.039277448 | -0.403991112 |
| POLG2      | NM_007215 | 0.000832094 | 0.005333764 | -0.403694631 |
| TMOD2      | NM_014548 | 0.011729707 | 0.04525142 | -0.403686751 |
| SIDT1      | NM_017699 | 0.005690546 | 0.025463931 | -0.403441037 |
| BRD3       | NM_007371 | 0.012633199 | 0.04794646 | -0.403421527 |
| LIMK1      | NM_01204426 | 0.001447193 | 0.008449164 | -0.403277832 |
| POLG2      | NM_139245 | 0.000832094 | 0.005333764 | -0.403277832 |
| TMOD2      | NM_01174126 | 0.011729707 | 0.04525142 | -0.403686751 |
| SLC11A2    | NM_01134398 | 0.00321792 | 0.016145014 | -0.402201403 |
| BRD3       | NM_017699 | 0.005690546 | 0.025463931 | -0.403441037 |
| LIMK1      | NM_001098721 | 0.009828284 | 0.039277448 | -0.403991112 |
| POLG2      | NM_007215 | 0.000832094 | 0.005333764 | -0.403694631 |
| TMOD2      | NM_014548 | 0.011729707 | 0.04525142 | -0.403686751 |
| SIDT1      | NM_017699 | 0.005690546 | 0.025463931 | -0.403441037 |
| BRD3       | NM_007371 | 0.012633199 | 0.04794646 | -0.403421527 |
| LIMK1      | NM_01204426 | 0.001447193 | 0.008449164 | -0.403277832 |
| POLG2      | NM_139245 | 0.000832094 | 0.005333764 | -0.403277832 |
| TMOD2      | NM_01174126 | 0.011729707 | 0.04525142 | -0.403686751 |
| SLC11A2    | NM_01134398 | 0.00321792 | 0.016145014 | -0.402201403 |
| Gene Accession | Gene Symbol | Fold Change | p-value | q-value | Benjamini-Hochberg corrected p-value |
|---------------|-------------|-------------|---------|---------|-------------------------------------|
| NM_033544     | RCCD1       | 0.005291946 | 0.024038636 | -0.392789177 |
| NM_001244193  | KIAA0586    | 0.002884135 | 0.014823217 | -0.392786735 |
| NR_037942     | STX16       | 0.001252243 | 0.007513204 | -0.39273222 |
| NM_005668     | ST8SIA4     | 0.000225786 | 0.001775991 | -0.392500518 |
| NM_001025160  | CD97        | 0.001490796 | 0.008656112 | -0.391317372 |
| NM_133494     | NEK7        | 0.000116888 | 0.001006828 | -0.391306745 |
| NM_201266     | NRP2        | 0.000645796 | 0.004350739 | -0.391258604 |
| NM_003872     | NRP2        | 0.000645796 | 0.004350739 | -0.391258604 |
| NM_001098722  | GNG4        | 0.009784386 | 0.039133981 | -0.391025322 |
| NM_198569     | GPR126      | 0.011282421 | 0.043945757 | -0.390970196 |
| NR_045019     | LETMD1      | 0.002634384 | 0.013787601 | -0.390861404 |
| NM_144718     | MICAL3      | 0.002682421 | 0.013992191 | -0.390828117 |
| NM_001032395  | GPR126      | 0.011870133 | 0.045700953 | -0.390465672 |
| NM_001166693  | AFF1        | 0.001014599 | 0.000914224 | -0.38872587 |
| NM_001077238  | SPPL2B      | 0.000656347 | 0.00440485 | -0.387946146 |
| NR_029427     | WDR13       | 0.008719275 | 0.035803339 | -0.38738069 |
| NM_015241     | MICAL3      | 0.002131315 | 0.011646981 | -0.387505754 |
| NM_001079669  | TMTC4       | 0.004433027 | 0.020889775 | -0.387188483 |
| NM_004785     | SLC9A3R2    | 0.004707568 | 0.02193052 | -0.387141414 |
| NM_006729     | DIAPH2      | 0.005223678 | 0.023801296 | -0.38695642 |
| NM_004639     | BAG6        | 0.001602241 | 0.009198954 | -0.386883969 |
| NM_080703     | BAG6        | 0.001602241 | 0.009198954 | -0.386883969 |
| NM_080702     | BAG6        | 0.001610895 | 0.00923793 | -0.386703144 |
| NM_153047     | FYN         | 0.000272888 | 0.002085751 | -0.386688443 |
| NM_024112     | C9orf16     | 0.012954148 | 0.048877402 | -0.386604463 |
| NM_005935     | AFF1        | 0.00113523 | 0.00981839 | -0.38621572 |
| NM_001244191  | KIAA0586    | 0.002981753 | 0.015185733 | -0.386107652 |
| NM_201279     | NRP2        | 0.000743352 | 0.004860325 | -0.385623951 |
| NM_001166163  | PPP1R9A     | 0.000234598 | 0.001835586 | -0.385446852 |
| NM_181312     | TAZ         | 0.001453347 | 0.008475101 | -0.385120647 |
| NM_001171796  | C8orf83     | 0.009650854 | 0.038708924 | -0.385112646 |
| NM_006901     | MYO9A       | 0.001610895 | 0.00923793 | -0.384968858 |
| NM_015170     | SULF1       | 0.003547038 | 0.017483383 | -0.384818134 |
| NM_001244189  | KIAA0586    | 0.002787653 | 0.014427146 | -0.383984675 |
| NM_001244192  | KIAA0586    | 0.003005724 | 0.015279013 | -0.383625873 |
| Gene     | Symbol | p-value | q-value | p-value | q-value | p-value |
|----------|--------|---------|---------|---------|---------|---------|
| NM_002093 | GSK3B  | 0.000617039 | 0.004196939 | -0.383489427 |
| NM_001146156 | GSK3B | 0.000619616 | 0.004210637 | -0.383478035 |
| NM_198082 | CCDC57 | 0.00302247 | 0.015356253 | -0.383474352 |
| NM_017650 | PPP1R9A | 0.0002531 | 0.001961242 | -0.383303013 |
| NM_014738 | KIAA0195 | 0.000351808 | 0.002593571 | -0.38311618 |
| NM_004480 | FUT8 | 0.00866145 | 0.035605521 | -0.38297355 |
| NM_001159547 | BEND4 | 0.000517064 | 0.003613732 | -0.382965427 |
| NM_001080453 | INTS1 | 0.000317184 | 0.002371411 | -0.382926012 |
| NM_001636 | SLC25A6 | 0.000760642 | 0.00498057 | -0.382846177 |
| NM_178167 | ZNF598 | 0.000750154 | 0.004891888 | -0.382557107 |
| NM_001166426 | WDR13 | 0.008274301 | 0.034365813 | -0.382474208 |
| NM_001244190 | KIAA0586 | 0.002949898 | 0.015082951 | -0.382423043 |
| NM_012197 | RABGAP1 | 0.002573651 | 0.013534097 | -0.382376777 |
| NM_002943 | RORA | 0.004412942 | 0.020815775 | -0.382295223 |
| NM_134261 | RORA | 0.004412942 | 0.020815775 | -0.382295223 |
| NM_024050 | DDA1 | 0.001427026 | 0.008350879 | -0.382271349 |
| NM_004104 | FASN | 0.000415227 | 0.002999346 | -0.382259798 |
| NM_181313 | TAZ | 0.001587542 | 0.009137512 | -0.382219936 |
| NM_152988 | SPPL2B | 0.000872208 | 0.005546628 | -0.381884698 |
| NM_178155 | FUT8 | 0.005287058 | 0.02402745 | -0.381680577 |
| NM_001163034 | RPTOR | 0.001611539 | 0.009239845 | -0.381563138 |
| NM_134260 | RORA | 0.004399915 | 0.020770815 | -0.381507926 |
| NM_017883 | WDR13 | 0.009887981 | 0.039452356 | -0.381102806 |
| NM_017694 | MFSDE6 | 0.004522174 | 0.021220343 | -0.381009504 |
| NM_001018073 | PCK2 | 0.000167036 | 0.001382288 | -0.380965262 |
| NM_001160392 | TRPT1 | 0.007732533 | 0.032631027 | -0.380912481 |
| NM_018999 | FAM190B | 0.010938781 | 0.042772074 | -0.380693262 |
| NM_138385 | TMEM129 | 0.00305522 | 0.015483 | -0.38032409 |
| NM_001142594 | ITPK1 | 0.007668611 | 0.032411905 | -0.380280475 |
| NM_001166161 | PPP1R9A | 0.000212165 | 0.001683221 | -0.379701239 |
| NM_005160 | ADRBK2 | 0.000745107 | 0.00486859 | -0.379655937 |
| NM_058237 | PPP4R4 | 0.008963643 | 0.036584615 | -0.379468869 |
| NM_004560 | ROR2 | 0.008589278 | 0.035387157 | -0.379408911 |
| NM_001128204 | SULF1 | 0.004289825 | 0.02035458 | -0.379329238 |
| NM_017514 | PLXNA3 | 0.009793295 | 0.03915028 | -0.379210014 |
| NM_152542 | PPM1K | 0.004506589 | 0.021163447 | -0.379129191 |
| NM_032023 | RASSF4 | 0.000416261 | 0.003004623 | -0.37907417 |
| NM_000116 | TAZ | 0.001574575 | 0.009073422 | -0.37867431 |
| NM_000156 | GAMT | 0.003808246 | 0.018476678 | -0.378389898 |
| NM_000218 | KCNQ1 | 0.001630888 | 0.009337147 | -0.378007953 |
| NM_152992 | POMZP3 | 0.0111398 | 0.04344376 | -0.377563482 |
| NM_001080477 | ODZ3 | 0.004196912 | 0.019990325 | -0.377555432 |
| NM_194071 | CREB3L2 | 0.012245771 | 0.046840979 | -0.376218854 |
| NM_153048 | FYN | 0.000474334 | 0.003351354 | -0.37976566 |
| NM_002065 | GLUL | 0.00054682 | 0.003780795 | -0.37582366 |
| NM_006339 | HMG20B | 0.000122622 | 0.001049527 | -0.37584065 |
| NM_032813 | TMTC4 | 0.004100361 | 0.01961533 | -0.375718193 |
| NM_181311 | TAZ | 0.001737014 | 0.009843412 | -0.375713627 |
| NM_052905 | FMNL2 | 0.000809747 | 0.005216399 | -0.374946378 |
| NM_004095 | EIF4EBP1 | 0.000367699 | 0.002698 | -0.374276532 |
| NM_153265 | EML3 | 0.000512431 | 0.003584726 | -0.374128726 |
| NM_207578 | PRKACB | 0.000677092 | 0.004512482 | -0.374042973 |
| NM_004639 | BAG6 | 0.001880477 | 0.010500212 | -0.37355379 |
| NM_080703 | BAG6 | 0.001880477 | 0.010500212 | -0.37355379 |
| NM_024704 | KIF16B | 0.003891456 | 0.018772872 | -0.373442302 |
| NM_001127266 | TMEM129 | 0.002860549 | 0.014724916 | -0.373408293 |
| NM_001033044 | GLUL | 0.000625961 | 0.004247258 | -0.373308661 |
| NM_001128221 | VGLL4 | 0.000202417 | 0.001618737 | -0.373040737 |
| NM_007309 | DIAPH2 | 0.007156509 | 0.030698483 | -0.372549803 |
| NM_001142649 | ANOS | 0.005842655 | 0.025960854 | -0.372542405 |
| NM_213599 | ANOS | 0.005842655 | 0.025960854 | -0.372542405 |
| NM_025009 | CEP135 | 0.007767614 | 0.032737228 | -0.372132569 |
| NM_018474 | PLK1S1 | 0.006779886 | 0.029369954 | -0.371623527 |
| NM_015312 | KIAA1109 | 0.000139057 | 0.001174631 | -0.371612714 |
| NM_139265 | EHD4 | 0.000338849 | 0.002514429 | -0.371401107 |
| NM_001127395 | METTL21A | 0.010727643 | 0.042107169 | -0.371716488 |
| NM_207406 | BEND4 | 0.000727344 | 0.004778791 | -0.371169795 |
| NM_013301 | CDC106 | 0.007320566 | 0.031265485 | -0.37110472 |
| NM_032167 | SNX29 | 0.000213483 | 0.001691754 | -0.370921666 |
| NM_001128220 | VGLL4 | 0.000238652 | 0.00186485 | -0.370889859 |
| NM_005052 | RAC3 | 0.000685133 | 0.004552796 | -0.370498137 |
| NM_001164840 | LYRM4 | 0.007350868 | 0.031367854 | -0.370366183 |
| NM_001166162 | PPP1R9A | 0.000346071 | 0.002555082 | -0.37027786 |
| NM_080702 | BAG6 | 0.00206408 | 0.011342135 | -0.370236514 |
| NM_001163022 | PLK1S1 | 0.009682255 | 0.038804964 | -0.370040142 |
| NM_003801 | GPAA1 | 0.001046594 | 0.006479509 | -0.369867033 |
| NM_001142864 | PIEZO1 | 0.000316759 | 0.002370414 | -0.369795717 |
| NM_001166160 | PPP1R9A | 0.000288585 | 0.002184941 | -0.369651858 |
| NM_001165417 | SLC25A11 | 0.000290806 | 0.00220007 | -0.369614324 |
| NM_001252076 | SLC9A3R2 | 0.010677975 | 0.041939913 | -0.369578072 |
| NM_001164165 | ASB3 | 0.005046046 | 0.023162396 | -0.36949146 |
| NM_001163023 | PLK1S1 | 0.011861666 | 0.045689323 | -0.369360556 |
| Entrez Gene ID | Symbol | Log2 Fold Change | p-value         |
|----------------|--------|-----------------|-----------------|
| NM_016436      | PHF20  | 0.000275623     | -0.368952419    |
| NM_182734      | PLCB1  | 0.001785698     | -0.3688515      |
| NM_001174157   | ZFAT   | 0.006134113     | -0.368849708    |
| NM_006295      | VARS   | 0.000180336     | -0.368510681    |
| NM_001198569   | ATP6V0C| 0.012819241     | -0.36843678     |
| NM_031472      | TRPT1  | 0.003347063     | -0.368296138    |
| NM_001130012   | SLC9A3R2| 0.007650843    | -0.36794335     |
| NM_013265      | C11orf2| 0.002028927     | -0.367885775    |
| NM_001033056   | GLUL   | 0.000640952     | -0.36763666     |
| NM_006521      | TFE3   | 0.004277754     | -0.36736846     |
| NM_003864      | SAP30  | 0.0083976       | -0.367170867    |
| NM_001197026   | PLEKHA8| 0.003130104     | -0.365904869    |
| NM_001080497   | MEGF9  | 0.011549224     | -0.365716058    |
| NM_015055      | SWAP70 | 0.00322211      | -0.36581778     |
| NM_014427      | CPNE7  | 0.00569545      | -0.36535496     |
| NM_020410      | ATP13A1| 0.000172766     | -0.365238791    |
| NM_001013841   | STAP2  | 0.001606111     | -0.365084067    |
| NM_001105204   | RUSC1  | 0.004223699     | -0.36499309     |
| NM_001243403   | CLEC16A| 0.00275442      | -0.364821116    |
| NM_033407      | DOCK7  | 0.002623418     | -0.364559501    |
| NM_000944      | PPP3CA | 0.000678278     | -0.364308576    |
| NM_001130691   | PPP3CA | 0.000684666     | -0.364288454    |
| NM_199051      | FAM5C  | 0.001936249     | -0.363923418    |
| NM_001160389   | TRPT1  | 0.003759611     | -0.363707057    |
| NM_001199865   | KIF16B | 0.005792066     | -0.363500745    |
| NM_001160393   | TRPT1  | 0.004761685     | -0.363264921    |
| NM_178156      | FUT8   | 0.009191347     | -0.363192936    |
| NM_015175      | NBEAL2 | 0.00278315      | -0.362992926    |
| NM_001135751   | DERL3  | 0.000204007     | -0.36269397     |
| NM_000254      | MTR    | 0.00126039      | -0.362502506    |
| NM_006309      | LRRFIP2| 0.000745613     | -0.362500079    |
| NM_001201965   | ASB3   | 0.005458574     | -0.362435877    |
| NM_014667      | VGLL4  | 0.000163654     | -0.361908325    |
| NM_001033678   | TRPT1  | 0.003968428     | -0.361891914    |
| NR_037648      | FOXRED1| 0.001778084     | -0.361869306    |
| NM_178507      | OAF    | 0.002135215     | -0.361707305    |
| NM_001165418   | SLC25A11| 0.000417502    | -0.361643233    |
| NM_001040118   | ARAP1  | 0.00113293      | -0.361586379    |
| NM_014875      | KIF14  | 0.000162517     | -0.361274817    |
| NM_153636      | CPNE7  | 0.006700325     | -0.360866828    |
| NM_005600      | NIT1   | 0.004354248     | -0.360509965    |
| Gene ID     | Gene Name | log2 Ratio | log2 Fold Change | p-Value  |
|-------------|-----------|------------|------------------|----------|
| NM_001204088| NBL1      | 0.002186309| 0.011877614      | -0.360374197 |
| NM_017724   | LRRFIP2   | 0.000962352| 0.006033382      | -0.360276349 |
| NM_181671   | PITPNC1   | 0.000284967| 0.002161396      | -0.36015866 |
| NM_138924   | GAMT      | 0.00709236 | 0.030532184      | -0.359797565 |
| NM_005380   | NBL1      | 0.005824744| 0.025908385      | -0.359482633 |
| NM_182744   | NBL1      | 0.005019473| 0.023065361      | -0.359042879 |
| NM_001204089| NBL1      | 0.002919451| 0.014950425      | -0.358423119 |
| NM_001204086| NBL1      | 0.005554922| 0.024983658      | -0.358422933 |
| NM_033100   | CDHR1     | 0.001233408| 0.007415169      | -0.357974467 |
| NM_175052   | ST8SIA4   | 0.002577625| 0.01354803       | -0.357325682 |
| NM_012102   | RERE      | 0.011870837| 0.045700953      | -0.357323616 |
| NM_003562   | SLC25A11  | 0.000427819| 0.003073865      | -0.357026251 |
| NM_145182   | LRPRF5    | 0.003788825| 0.018403483      | -0.356905606 |
| NM_014045   | LRP10     | 0.000320467| 0.002393998      | -0.356541545 |
| NM_01128205 | SULF1     | 0.007814477| 0.03286947       | -0.356880833 |
| NM_006453   | TBL3      | 0.005976531| 0.026444991      | -0.356541545 |
| NM_01171690 | GCAT      | 0.007691566| 0.03248121       | -0.356266933 |
| NM_018645   | HES6      | 0.008069644| 0.033708969      | -0.356218123 |
| NM_001142853| HES6      | 0.008134137| 0.033916395      | -0.356179171 |
| NM_001204084| NBL1      | 0.005421692| 0.24523046       | -0.356178093 |
| NM_001164773| BCAT2     | 0.000414674| 0.002995957      | -0.356171885 |
| NM_001013703| EIF2AK4   | 0.000277457| 0.00114153       | -0.356098784 |
| NM_005188   | CBL       | 0.000182843| 0.0014862        | -0.355907288 |
| NM_006295   | VARS      | 0.000499476| 0.00350897       | -0.355791574 |
| NM_152641   | ARID2     | 0.000267547| 0.002051265      | -0.35556932 |
| NM_153828   | RTN4      | 0.000675193| 0.004504175      | -0.355526757 |
| NM_001135190| ARAP1     | 0.000892927| 0.005659012      | -0.355460994 |
| NM_000837   | GRINA     | 0.001248315| 0.007492665      | -0.355333625 |
| NR_024333   | LOC147727 | 0.001854061| 0.010385884      | -0.355238105 |
| NM_016208   | VPS28     | 0.000835256| 0.00535057       | -0.354719888 |
| NM_183057   | VPS28     | 0.000878502| 0.005794956      | -0.354456181 |
| NM_001160390| TRPT1     | 0.004923442| 0.022736584      | -0.354309159 |
| NM_001164389| RAPGEF6   | 0.012141427| 0.046519699      | -0.35415974 |
| NM_006799   | PRSS21    | 0.001047823| 0.006484414      | -0.35411038 |
| NM_144956   | PRSS21    | 0.001047823| 0.006484414      | -0.35411038 |
| NR_040711   | KCNQ1     | 0.003464556| 0.017165092      | -0.353840502 |
| NM_001260   | CDK8      | 0.011669529| 0.045093866      | -0.353624439 |
| NM_001135924| VWDE      | 0.005659799| 0.025349245      | -0.353619277 |
| NM_017918   | CCDC109B  | 0.007386417| 0.031469843      | -0.353588316 |
| NM_015407   | ABHD14A   | 0.005305041| 0.024079714      | -0.353134121 |
| Gene   | Description | Fold Change | p-Value  |
|--------|-------------|-------------|----------|
| NM_001042681 | RERE        | 0.012784003 | 0.048389023 |
| NM_207520   | RTN4        | 0.000745604 | 0.004869752 |
| NM_001201482 | OSBPL6     | 0.005526263 | 0.024882416 |
| NM_001134369 | LRRFIP2    | 0.001060163 | 0.006540347 |
| NM_004563   | PCK2        | 0.002488855 | 0.001933394 |
| NM_001478   | B4GALNT1    | 0.011485294 | 0.044568879 |
| NM_144767   | AKAP13      | 0.000340389 | 0.002521272 |
| NM_015192   | PLCB1       | 0.0028863   | 0.014831777 |
| NM_001185094 | NIT1       | 0.00544491  | 0.024600787 |
| NM_015559   | SETBP1      | 0.006698947 | 0.029091423 |
| NR_038120   | ELMO1       | 0.000553614 | 0.003819766 |
| NM_017547   | FOXRED1     | 0.002920017 | 0.014950751 |
| NM_012292   | HMHA1       | 0.003650957 | 0.017900593 |
| NM_001128206 | SULF1      | 0.009411849 | 0.037940511 |
| NM_001042517 | DIAPH3     | 0.007665958 | 0.032405301 |
| NM_005419   | STAT2       | 0.000528523 | 0.003679106 |
| NM_001127396 | STXB2      | 0.001432556 | 0.00838182 |
| NM_001009184 | GRINA      | 0.001396626 | 0.008212017 |
| NM_198332   | STAT2       | 0.00055689  | 0.003837026 |
| NM_015035   | ZHX3        | 0.00029854  | 0.002255709 |
| NM_005009   | NME4        | 0.008106627 | 0.03382067 |
| NM_201263   | WARS2       | 0.003733854 | 0.018227987 |
| NM_001122837 | SLC5OA1    | 0.000180194 | 0.001470244 |
| NM_032523   | OSBPL6      | 0.005274303 | 0.02397682 |
| NM_145159   | JAG2        | 0.005197404 | 0.023717945 |
| NM_152663   | RALGPS2     | 0.001166975 | 0.00709182 |
| NM_014431   | KIAA1274    | 0.002212906 | 0.012000167 |
| NM_001197126 | IRF3       | 0.002685668 | 0.014004591 |
| NM_144957   | PRSS21      | 0.00179109  | 0.010097861 |
| NM_015836   | WARS2       | 0.003754158 | 0.0182979 |
| NM_001220767 | IKZF1      | 0.000780376 | 0.005060096 |
| NM_001201480 | OSBPL6     | 0.005587496 | 0.025104872 |
| NM_020145   | SH3GLB2     | 0.000760766 | 0.00498057 |
| NM_001001132 | ITSN1      | 0.005440077 | 0.024593264 |
| NM_181472   | CMTM7       | 0.001102871 | 0.006767296 |
| NM_001018076 | NR3C1      | 0.001855781 | 0.010389648 |
| NM_145207   | SPATA5      | 0.00033902  | 0.002514891 |
| NR_037849   | WBPI        | 0.00337171  | 0.016639381 |
| NM_001220770 | IKZF1      | 0.001053289 | 0.00650257 |
| NM_006184   | NUCB1       | 0.000186887 | 0.00151403 |
| NR_038121   | ELMO1       | 0.000503538 | 0.003529161 |

**Fold Change and p-Value**
| Gene Name   | Symbol | Fold Change | p-Value | q-Value | Beta Value |
|------------|--------|-------------|---------|---------|------------|
| PPP3CA     | NM_001130692 | 0.001331621 | 0.007901411 | -0.345168777 |
| STXBP2     | NM_006949 | 0.001590947 | 0.009146481 | -0.345145395 |
| ELMO1      | NM_001039459 | 0.000518443 | 0.003621668 | -0.345121385 |
| ZNF395     | NM_018660 | 0.000383358 | 0.002796898 | -0.344794187 |
| IKZF1      | NM_001220772 | 0.001587199 | 0.009137312 | -0.344128986 |
| STXBP2     | NM_006949 | 0.001590947 | 0.009146481 | -0.345145395 |
| ELMO1      | NM_001039459 | 0.000518443 | 0.003621668 | -0.345121385 |
| ZNF395     | NM_018660 | 0.000383358 | 0.002796898 | -0.344794187 |
| IKZF1      | NM_001220772 | 0.001587199 | 0.009137312 | -0.344128986 |
| STXBP2     | NM_006949 | 0.001590947 | 0.009146481 | -0.345145395 |
| ELMO1      | NM_001039459 | 0.000518443 | 0.003621668 | -0.345121385 |
| ZNF395     | NM_018660 | 0.000383358 | 0.002796898 | -0.344794187 |
| IKZF1      | NM_001220772 | 0.001587199 | 0.009137312 | -0.344128986 |
| STXBP2     | NM_006949 | 0.001590947 | 0.009146481 | -0.345145395 |
| ELMO1      | NM_001039459 | 0.000518443 | 0.003621668 | -0.345121385 |
| ZNF395     | NM_018660 | 0.000383358 | 0.002796898 | -0.344794187 |
| IKZF1      | NM_001220772 | 0.001587199 | 0.009137312 | -0.344128986 |
| STXBP2     | NM_006949 | 0.001590947 | 0.009146481 | -0.345145395 |
| ELMO1      | NM_001039459 | 0.000518443 | 0.003621668 | -0.345121385 |
| ZNF395     | NM_018660 | 0.000383358 | 0.002796898 | -0.344794187 |
| Gene ID               | Gene Name | Log2 Fold Change | | | |
|----------------------|-----------|-----------------|---|---|---|
| NM_001139467         | TBL1X     | 0.00206599      | 0.011344239 | -0.340017924 |
| NM_002226            | JAG2      | 0.005489748     | 0.024755515  | -0.339936931  |
| NM_001139466         | TBL1X     | 0.002064616     | 0.011342984  | -0.339793013  |
| NM_001122839         | SLC50A1   | 0.000234375     | 0.001834323  | -0.339535592  |
| NM_001114752         | CD55      | 0.002178678     | 0.01184265   | -0.339425372  |
| NM_001139466         | TBL1X     | 0.002064616     | 0.011342984  | -0.339793013  |
| NM_001122839         | SLC50A1   | 0.000234375     | 0.001834323  | -0.339535592  |
| NM_001114752         | CD55      | 0.002178678     | 0.01184265   | -0.339425372  |
| NM_001139466         | TBL1X     | 0.002064616     | 0.011342984  | -0.339793013  |
| NM_001122839         | SLC50A1   | 0.000234375     | 0.001834323  | -0.339535592  |
| NM_001114752         | CD55      | 0.002178678     | 0.01184265   | -0.339425372  |
| Gene ID           | Gene Symbol | FPKM (Mean) | FPKM (Standard Deviation) | Fold Change |
|------------------|-------------|-------------|---------------------------|-------------|
| NM_001080121     | PRNP        | 0.002960616 | 0.015103968               | -0.33414264|
| NM_183079        | PRNP        | 0.002960616 | 0.015103968               | -0.33414264|
| NM_000311        | PRNP        | 0.002960616 | 0.015103968               | -0.33414264|
| NM_019001        | XRN1        | 0.000154605 | 0.001289112               | -0.333607942|
| NM_006286        | TFDP2       | 0.000937616 | 0.00590571                | -0.33406395|
| NM_001127715     | STXB5       | 0.008834984 | 0.036193717               | -0.333894634|
| NM_000574        | CD55        | 0.002417176 | 0.012877594               | -0.333064859|
| NM_001723        | DST         | 0.000399688 | 0.002157961               | -0.333182194|
| NM_001042604     | XRN1        | 0.000168868 | 0.001395125               | -0.333064859|
| NM_001202502     | NIPSNAP1    | 0.000270546 | 0.002070517               | -0.332797767|
| NM_015401        | HDAC7       | 0.000731336 | 0.004799719               | -0.33220073|
| NM_054012        | ASS1        | 0.001287238 | 0.010464833               | -0.332367026|
| NM_001100423     | SPATS2L     | 0.003742436 | 0.018249749               | -0.332350515|
| NM_001008485     | SLC41A3     | 0.000125101 | 0.001067993               | -0.331949762|
| NM_001098416     | HDAC7       | 0.000731336 | 0.004799719               | -0.33187955|
| NM_015384        | NIPBL       | 0.002460365 | 0.013046873               | -0.331852906|
| NM_015535        | SPATS2L     | 0.00187238  | 0.010464833               | -0.331739394|
| NR_024188        | PPP1R21     | 0.00813259  | 0.033914704               | -0.331638478|
| NM_197974        | HOMER1      | 0.010470071 | 0.041330911               | -0.33198643|
| NM_173630        | RTTN        | 0.000125101 | 0.001067993               | -0.331949762|
| NM_017693        | BIVM        | 0.005365863 | 0.024307523               | -0.33198643|
| NM_001098416     | HDAC7       | 0.000731336 | 0.004799719               | -0.33187955|
| NM_015384        | NIPBL       | 0.002460365 | 0.013046873               | -0.331852906|
| NM_015535        | SPATS2L     | 0.00187238  | 0.010464833               | -0.331739394|
| NR_024188        | PPP1R21     | 0.00813259  | 0.033914704               | -0.331638478|
| NM_014982        | PCNX        | 0.000754193 | 0.004912836               | -0.33159633|
| NM_006876        | B3GNT1      | 0.011173414 | 0.043543414               | -0.331459996|
| NM_058195        | CDKN2A      | 0.00674273  | 0.029243097               | -0.33103267|
| NM_139029        | CD151       | 0.002406134 | 0.012825664               | -0.330971372|
| NM_004357        | CD151       | 0.002406134 | 0.012825664               | -0.330971372|
| NM_006295        | VARS        | 0.00121613  | 0.00733951                | -0.3304861|
| NM_138822        | PAM         | 0.000310631 | 0.002331657               | -0.330699863|
| NM_002603        | PDE7A       | 0.000227412 | 0.001787357               | -0.33052965|
| NM_006060        | IKZF1       | 0.001008019 | 0.006648765               | -0.330377389|
| NM_014835        | OSBPL2      | 0.002143532 | 0.011687953               | -0.33030843|
| NM_001178141     | TFDP2       | 0.001285309 | 0.007676042               | -0.33006316|
| NM_133433        | NIPBL       | 0.002733074 | 0.014206537               | -0.329859068|
| NM_001167583     | ZFAT        | 0.014109863 | 0.044310884               | -0.329853161|
| NM_014911        | AAK1        | 0.011881786 | 0.045727213               | -0.32983212|
| NM_001220775     | IKZF1       | 0.003443542 | 0.017072362               | -0.329742949|
| NM_177974        | CASC4       | 0.002111943 | 0.011562385               | -0.329309931|
| NM_002121        | HLA-DPB1    | 0.002845702 | 0.014666271               | -0.329203931|
| NM_032520        | GNPTG       | 0.006249581 | 0.027456948               | -0.328986152|
| NM_173471        | SLC25A26    | 0.007102957 | 0.030545452               | -0.328953146|
| accession  | gene   | log2 fold change | p-value 1 | p-value 2 | fold change |
|------------|--------|-----------------|-----------|-----------|-------------|
| NM_001220765 | IKZF1  | 0.001428632     | 0.008362153 | -0.328692074 |
| NM_001080394 | KIAA0146 | 0.000896346     | 0.005677051 | -0.328594915 |
| NM_001202546 | CUX1   | 0.007986467     | 0.033446144 | -0.328449119 |
| NM_001098534 | BAG6   | 0.010513486     | 0.04145712  | -0.328447425 |
| NM_001178140 | TFDP2  | 0.001723702     | 0.009775751 | -0.328444208 |
| NM_001080394 | KIAA0146 | 0.000896346     | 0.005677051 | -0.328594915 |
| NM_001202546 | CUX1   | 0.007986467     | 0.033446144 | -0.328449119 |
| NM_001098534 | BAG6   | 0.010513486     | 0.04145712  | -0.328447425 |
| NM_001178140 | TFDP2  | 0.001723702     | 0.009775751 | -0.328444208 |
| NM_001080394 | KIAA0146 | 0.000896346     | 0.005677051 | -0.328594915 |
| NM_001202546 | CUX1   | 0.007986467     | 0.033446144 | -0.328449119 |
| NM_001098534 | BAG6   | 0.010513486     | 0.04145712  | -0.328447425 |
| NM_001178140 | TFDP2  | 0.001723702     | 0.009775751 | -0.328444208 |
| NM_001080394 | KIAA0146 | 0.000896346     | 0.005677051 | -0.328594915 |
| NM_001202546 | CUX1   | 0.007986467     | 0.033446144 | -0.328449119 |
| NM_001098534 | BAG6   | 0.010513486     | 0.04145712  | -0.328447425 |
| NM_001178140 | TFDP2  | 0.001723702     | 0.009775751 | -0.328444208 |
| NM_001080394 | KIAA0146 | 0.000896346     | 0.005677051 | -0.328594915 |
| NM_001202546 | CUX1   | 0.007986467     | 0.033446144 | -0.328449119 |
| NM_001098534 | BAG6   | 0.010513486     | 0.04145712  | -0.328447425 |
| NM_001178140 | TFDP2  | 0.001723702     | 0.009775751 | -0.328444208 |
| NM_001080394 | KIAA0146 | 0.000896346     | 0.005677051 | -0.328594915 |
| NM_001202546 | CUX1   | 0.007986467     | 0.033446144 | -0.328449119 |
| NM_001098534 | BAG6   | 0.010513486     | 0.04145712  | -0.328447425 |
| NM_001178140 | TFDP2  | 0.001723702     | 0.009775751 | -0.328444208 |
| NM_001080394 | KIAA0146 | 0.000896346     | 0.005677051 | -0.328594915 |
| NM_001202546 | CUX1   | 0.007986467     | 0.033446144 | -0.328449119 |
| NM_001098534 | BAG6   | 0.010513486     | 0.04145712  | -0.328447425 |
| NM_001178140 | TFDP2  | 0.001723702     | 0.009775751 | -0.328444208 |
| NM_001080394 | KIAA0146 | 0.000896346     | 0.005677051 | -0.328594915 |
| NM_001202546 | CUX1   | 0.007986467     | 0.033446144 | -0.328449119 |
| NM_001098534 | BAG6   | 0.010513486     | 0.04145712  | -0.328447425 |
| NM_001178140 | TFDP2  | 0.001723702     | 0.009775751 | -0.328444208 |
| NM_001080394 | KIAA0146 | 0.000896346     | 0.005677051 | -0.328594915 |
| NM_001202546 | CUX1   | 0.007986467     | 0.033446144 | -0.328449119 |
| NM_001098534 | BAG6   | 0.010513486     | 0.04145712  | -0.328447425 |
| NM_001178140 | TFDP2  | 0.001723702     | 0.009775751 | -0.328444208 |
| Gene          | Description | Log2 Fold Change | P-Value  |
|--------------|-------------|-----------------|----------|
| BCAT2        |             | 0.000721659     | 0.004748789 | -0.324176431 |
| SLC41A3      |             | 0.005744633     | 0.025631203 | -0.324170868 |
| STK39        |             | 0.0003689       | 0.002704812 | -0.32361608 |
| RASA3        |             | 0.002457864     | 0.013041552 | -0.323506516 |
| CMTM7        |             | 0.001903932     | 0.010603291 | -0.323274334 |
| SPATS2L      |             | 0.002677423     | 0.013975932 | -0.322476915 |
| GCAT         |             | 0.0090556       | 0.036839321 | -0.322461671 |
| SLC41A3      |             | 0.003273295     | 0.016373089 | -0.32205856 |
| ZAK          |             | 0.002302928     | 0.012397849 | -0.321800847 |
| ELOVL6       |             | 0.00775375      | 0.025738873 | -0.321695949 |
| ARID3A       |             | 0.002009732     | 0.011100969 | -0.32168691 |
| LLGL1        |             | 0.007342818     | 0.031346305 | -0.321502954 |
| IFR3         |             | 0.004770773     | 0.022176294 | -0.321502954 |
| RPS6KA3      |             | 0.005626895     | 0.0252323   | -0.321611398 |
| MIF4GD       |             | 0.001750059     | 0.009907885 | -0.321558494 |
| IRF3         |             | 0.002163073     | 0.011772898 | -0.32103107 |
| GRN          |             | 0.003363959     | 0.016736441 | -0.320888487 |
| PDK1         |             | 0.00363959      | 0.016736441 | -0.320888487 |
| LW6E         |             | 0.003363959     | 0.016736441 | -0.320888487 |
| C19orf6      |             | 0.008389017     | 0.034735464 | -0.320872745 |
| ICAM3        |             | 0.002457864     | 0.013041552 | -0.323506516 |
| ATXN3        |             | 0.012581065     | 0.047803543 | -0.321239654 |
| IRF3         |             | 0.005209318     | 0.023103453 | -0.32103107 |
| GRN          |             | 0.002163073     | 0.011772898 | -0.32103107 |
| PDK1         |             | 0.00104819      | 0.006485334 | -0.320006061 |
| LY6E         |             | 0.003363959     | 0.016736441 | -0.320888487 |
| C19orf6      |             | 0.008389017     | 0.034735464 | -0.320872745 |
| WDR18        |             | 0.007841059     | 0.032962618 | -0.320802097 |
| CUX1         |             | 0.010016455     | 0.039884632 | -0.320628292 |
| SKIV2L       |             | 0.00386773      | 0.018716386 | -0.32050481 |
| TCN2         |             | 0.006655104     | 0.028934852 | -0.320264671 |
| GGT1         |             | 0.004182423     | 0.019937288 | -0.320248784 |
| C1orf85      |             | 0.001964717     | 0.010890721 | -0.320210074 |
| PCYT2        |             | 0.005737719     | 0.025615384 | -0.320140172 |
| CNTNA1       |             | 0.00062766      | 0.004253548 | -0.320071073 |
| PAM          |             | 0.000505126     | 0.003538622 | -0.31969875 |
| DCBLD2       |             | 0.00773512      | 0.032751095 | -0.319636732 |
| BCAT2        |             | 0.000705447     | 0.004661066 | -0.319627037 |
| PCYT2        |             | 0.006104542     | 0.026927221 | -0.319206348 |
| PCYT2        |             | 0.006104542     | 0.026927221 | -0.319206348 |
| PCYT2        |             | 0.005705683     | 0.025508617 | -0.319016762 |
| TDP2         |             | 0.00219492      | 0.01191568  | -0.318859775 |
| Wnt5B        |             | 0.000628541     | 0.004256687 | -0.318786028 |
| Gene   | Description | P-value_1 | P-value_2 | P-value_3 |
|--------|-------------|-----------|-----------|-----------|
| NM_032642 | WNT5B | 0.000645947 | 0.004350774 | -0.318687043 |
| NM_000321 | RB1   | 0.000555886 | 0.003830998 | -0.318263695 |
| NM_015173 | TBC1D1 | 0.006282195 | 0.027587997 | -0.318177691 |
| NM_198440 | DERL3  | 0.00272796  | 0.002085751 | -0.318168861 |
| NM_000876 | IGF2R | 0.00175162  | 0.001437925 | -0.318151587 |
| NM_000876 | FLNA   | 0.01303587  | 0.007764822 | -0.317954909 |
| NM_00110556 | FLNA | 0.01303587  | 0.007774017 | -0.317954909 |
| NM_000321 | RB1   | 0.000555886 | 0.003830998 | -0.318263695 |
| NM_015173 | TBC1D1 | 0.006282195 | 0.027587997 | -0.318177691 |
| NM_198440 | DERL3  | 0.00272796  | 0.002085751 | -0.318168861 |
| NM_000876 | IGF2R | 0.00175162  | 0.001437925 | -0.318151587 |
| NM_000876 | FLNA   | 0.01303587  | 0.007764822 | -0.317954909 |
| NM_00110556 | FLNA | 0.01303587  | 0.007774017 | -0.317954909 |
| Gene ID      | Gene Name | FDR   | q-value | Log10_p_value | Log10_fdr   |
|-------------|-----------|-------|---------|---------------|-------------|
| NM_001184787 | PARD3     | 0.000259188 | 0.002002016 | -0.313573532 |
| NM_002843    | PTPRJ     | 0.002845477  | 0.014666271 | -0.313394304 |
| NM_005265    | GGT1      | 0.004458176  | 0.020979193 | -0.313211653 |
| NM_018036    | ATG2B     | 0.001008139  | 0.006283922 | -0.313015894 |
| NM_003113    | SP100     | 0.009403806  | 0.037917628 | -0.312824135 |
| NM_176096    | CDK5RAP3  | 0.00663008   | 0.044440525 | -0.312712861 |
| NM_030802    | FAM117A   | 0.003435564  | 0.017035649 | -0.31238444  |
| NM_001008395 | C7orf59   | 0.008715369  | 0.03579746  | -0.312315754 |
| NR_033289    | GK5       | 0.00337987   | 0.02510365  | -0.312315754 |
| NM_148416    | ATXN2L    | 0.001631338  | 0.009337147 | -0.312130145 |
| NM_001033028 | CYFIP1    | 0.00154162   | 0.01286139  | -0.311863584 |
| NM_001032365 | GGT1      | 0.005050286  | 0.023171935 | -0.311694023 |
| NM_001145008 | BTN3A1    | 0.001404237  | 0.008249395 | -0.311623127 |
| NM_001166112 | PNPLA6    | 0.009431562  | 0.037993457 | -0.311623127 |
| NM_001033026 | C19orf6   | 0.008755028  | 0.035930559 | -0.311505492 |
| NR_002569    | SCARNA9   | 0.008212686  | 0.034157646 | -0.310976531 |
| NM_002431    | MNAT1     | 0.011260355  | 0.043867851 | -0.31048999  |
| NM_145714    | ATXN2L    | 0.001706852  | 0.009337147 | -0.31048999  |
| NM_001134649 | EIF4E3    | 0.003605708  | 0.017710882 | -0.31048999  |
| NM_001184726 | TCN2      | 0.009057041  | 0.036839321 | -0.310638057 |
| NM_025256    | EHMT2     | 0.005668398  | 0.025383932 | -0.30956347  |
| NM_032378    | EEF1D     | 0.006685448  | 0.029044265 | -0.309072568 |
| NM_001166345 | MDFIC     | 0.007398768  | 0.031499885 | -0.309072568 |
| NM_199072    | MDFIC     | 0.007398768  | 0.031499885 | -0.309072568 |
| NM_001164605 | FXD5      | 0.005373889  | 0.003732191 | -0.308989582 |
| NM_001242501 | MIF4GD    | 0.009478111  | 0.019014116 | -0.308213622 |
| NM_002336    | LRPR6     | 0.00935349   | 0.037740348 | -0.308213622 |
| NM_030587    | B4GALT2   | 0.004521408  | 0.021220343 | -0.308059042 |
| NM_013976    | GCDH      | 0.001491719  | 0.008659781 | -0.307984904 |
| NM_003780    | B4GALT2   | 0.00590003   | 0.02331732  | -0.307318186 |
| NM_001253912 | TBC1D1    | 0.010390342  | 0.041065273 | -0.3070728  |
| NM_033071    | SYNE1     | 0.005040874  | 0.023149383 | -0.306775683 |
| NM_031229    | RBCK1     | 0.01254888   | 0.047699548 | -0.306762972 |
| NM_001020    | RPS16     | 0.006178271  | 0.027191896 | -0.306566544 |
| NM_006702    | PNPLA6    | 0.010761212  | 0.042205483 | -0.306519248 |
| NM_001130053 | EIF1D     | 0.00735248   | 0.03170231  | -0.306340025 |
| NM_001184970 | PACSIN2   | 0.011865609  | 0.045698857 | -0.306106187 |
| NM_007245    | ATXN2L    | 0.001883252  | 0.01051176  | -0.305861234 |
| NM_005962    | MXI1      | 0.00961298   | 0.006029313 | -0.305693657 |
| NM_001199629 | MYL6B     | 0.008921482  | 0.036432554 | -0.305663453 |
| NM_002311 | LIG3   | 0.000872054 | 0.005546628 | -0.305617601 |
| NM_002116 | HLA-A  | 0.002957543 | 0.015103968 | -0.30550874  |
| NM_182961 | SYNE1  | 0.005223436 | 0.023801296 | -0.30362337  |
| NM_018200 | HMG20A | 0.007938586 | 0.033287845 | -0.30523709  |
| NM_016434 | RTEL1  | 0.011557627 | 0.044767729 | -0.30490567  |
| NM_001823 | CKB    | 0.007680032 | 0.032446334 | -0.30479034  |
| NM_001163484 | DCAF11 | 0.001122315 | 0.006868172 | -0.30470933  |
| NM_001146191 | MPZL1 | 0.000376828 | 0.002756819 | -0.30158833  |
| Gene      | Description | Expression 1 | Expression 2 | Expression 3 | Expression 4 |
|-----------|-------------|--------------|--------------|--------------|--------------|
| NM_003959 | HIP1R       | 0.003506163  | 0.017330778  | -0.301300841 |
| NR_001298 | HLA-DRB6    | 0.009060237  | 0.036842236  | -0.30126095  |
| NM_006623 | PHGDH       | 0.000286274  | 0.002169649  | -0.301232512 |
| NM_024751 | GSTCD       | 0.003875047  | 0.018739701  | -0.300977517 |
| NM_001134650 | EIF4E3   | 0.005890501  | 0.036842236  | -0.300977517 |
| NR_001298 | HLA-DRB6    | 0.009060237  | 0.036842236  | -0.30126095  |
| NM_001100166 | PHACTR2 | 0.007424472  | 0.031577649  | -0.300468582 |
| NM_006623 | PHGDH       | 0.000286274  | 0.002169649  | -0.301232512 |
| NM_024751 | GSTCD       | 0.003875047  | 0.018739701  | -0.300977517 |
| NM_001134650 | EIF4E3   | 0.005890501  | 0.036842236  | -0.300977517 |
| NM_001100166 | PHACTR2 | 0.007424472  | 0.031577649  | -0.300468582 |
NM_001008487 SLC41A3 0.006961138 0.030054355 -0.297834785
NM_001242868 SLAIN1 0.003450735 0.017099463 -0.297785728
NM_006569 CGREF1 0.000328699 0.002449947 -0.297670445
NM_00135555 EPB41L2 0.002519249 0.013313982 -0.297657756
NM_001184793 PARD3 0.00148208 0.008612236 -0.297597653
NM_199073 NDUFAF3 0.002321551 0.012460835 -0.297496623
NM_021978 ST14 0.001427745 0.008360253 -0.297486867
NM_001100164 PHACTR2 0.007425607 0.031577957 -0.297084277
NM_022748 TNS3 0.00026422 0.00203257 -0.29706736
NM_001256265 EPB41L2 0.002566504 0.013520438 -0.296563412
NM_002617 PEX10 0.008153978 0.033985958 -0.296421453
NM_00528 MAN2B1 0.011645311 0.045042785 -0.296395999
NM_00173498 MAN2B1 0.011645311 0.045042785 -0.296395999
NR_028406 FYXD5 0.00100845 0.006283939 -0.296295487
NM_001040153 SLAIN1 0.007368238 0.031402715 -0.295952186
NM_153827 MINK1 0.001164167 0.007076204 -0.295805937
NM_015340 LARS2 0.001402967 0.008246041 -0.295680373
NM_00134367 SLC6A6 0.000157765 0.001312513 -0.295192014
NM_003043 SLC6A6 0.000157765 0.001312513 -0.295192014
NM_002401 MAP3K3 0.004757781 0.022126286 -0.295121306
NR_003190 USP32P1 0.012295373 0.046988374 -0.294951435
NM_001256265 FLII 0.000197297 0.001583328 -0.294942805
NM_134445 CD99L2 0.005131604 0.023478965 -0.294908999
NM_007326 CYB5R3 0.01086184 0.045042785 -0.294821935
NM_001171661 CYB5R3 0.010966442 0.042857675 -0.294778615
NM_018227 UBA6 0.008283654 0.034399852 -0.294724762
NM_007181 MAP4K1 0.01039763 0.041088612 -0.294386066
NM_001184790 PARD3 0.000663181 0.004440685 -0.294026146
NM_024874 KIAA0319L 0.002494153 0.013195431 -0.293993365
NM_006117 ECI2 0.007800219 0.032824893 -0.29399007
NR_028588 ECI2 0.007800219 0.032824893 -0.29399007
NM_022977 ACSL4 0.003271053 0.016367381 -0.293789963
NM_005514 HLA-B 0.006344151 0.027818475 -0.293747535
NM_00134364 MAP4 0.000141083 0.001188705 -0.293626865
NM_198321 GALNT10 0.004547911 0.021323803 -0.293275444
NM_001166239 CGREF1 0.000482953 0.003402542 -0.293242446
NM_001431 EPB41L2 0.002391149 0.01275723 -0.29299255
NM_199002 ARHGEF1 0.003754852 0.018298284 -0.292992311
NM_022457 RFWD2 0.001086802 0.00668388 -0.292978009
NM_001184788 PARD3 0.000622995 0.004229732 -0.292904975
NM_004458 ACSL4 0.003565153 0.017558654 -0.292846038
| gene          | symbol | p-value   | q-value   | adj.p.value |
|--------------|--------|-----------|-----------|-------------|
| NM_001252660 | EPB41L2| 0.003156294 | 0.015897557 | -0.292758589 |
| NM_016086    | STYXL1 | 0.004073432 | 0.019508488 | -0.292698518 |
| NM_198970    | AES    | 0.000700641 | 0.004634088 | -0.292662013 |
| NM_001130    | AES    | 0.000700641 | 0.004634088 | -0.292662013 |
| NM_001024937 | MINK1  | 0.00134174  | 0.007945891 | -0.292643144 |
| NM_016824    | ADD3   | 0.002611663 | 0.013692802 | -0.292539239 |
| NM_015716    | MINK1  | 0.00425023  | 0.008354216 | -0.29252408  |
| NM_170663    | MINK1  | 0.00426447  | 0.008358079 | -0.29251581  |
| NM_001042600 | MAP4K1 | 0.010812229 | 0.042355263 | -0.292311965 |
| NM_001039547 | GK5    | 0.00112805  | 0.006899006 | -0.292218456 |
| NM_001166010 | ECI2   | 0.007808403 | 0.032853225 | -0.292073012 |
| NM_001253826 | GALNT14| 0.00966601  | 0.038754022 | -0.291514518 |
| NM_018842    | BAIAP2L1| 0.001123531 | 0.007422344 | -0.291457469 |
| NR_038103    | TECR   | 0.003057205 | 0.015487722 | -0.29144122  |
| NR_038104    | TECR   | 0.00308872  | 0.015626062 | -0.291418904 |
| NM_145802    | Sep-06 | 0.005363497 | 0.024304214 | -0.291373814 |
| NM_001500    | GMDS   | 0.008335367 | 0.034650396 | -0.291322164 |
| NM_001184786 | PARD3  | 0.000566559 | 0.003893715 | -0.291157523 |
| NM_006035    | CDC42BPB| 0.011535566 | 0.044699756 | -0.291028252 |
| NM_021723    | ADAM22 | 0.00399888  | 0.002897462 | -0.291023059 |
| NM_203390    | RBM12B | 0.012754056 | 0.04830457  | -0.290773006 |
| NM_206836    | ECI2   | 0.00914082  | 0.037111533 | -0.290769949 |
| NM_031462    | CD99L2 | 0.003126936 | 0.015781786 | -0.290768593 |
| NM_001242614 | CD99L2| 0.003133532 | 0.015804339 | -0.290764267 |
| NM_001184785 | PARD3  | 0.000626148 | 0.004247258 | -0.290416993 |
| NM_006373    | VAT1   | 0.007254278 | 0.004247258 | -0.290416993 |
| NM_00138501  | TECR   | 0.003081747 | 0.015596098 | -0.290341074 |
| NM_004240    | TRIP10 | 0.003893715 | 0.002897462 | -0.29023059  |
| NM_001129819 | CY5R3  | 0.012754056 | 0.04830457  | -0.290773006 |
| NM_006373    | VAPI   | 0.003081747 | 0.015596098 | -0.290341074 |
| NM_007056    | CLASRP | 0.008019896 | 0.03355304  | -0.289881444 |
| NM_00142650  | HNRPLP | 0.00914082  | 0.037111533 | -0.290769949 |
| NM_001121    | ADD3   | 0.003519981 | 0.017387512 | -0.289458637 |
| NM_005312    | RAPGEF1| 0.00895736  | 0.005674394 | -0.289156178 |
| NM_014868    | RNF10  | 0.000626148 | 0.004247258 | -0.290416993 |
| Gene Symbol | Gene Name | CRP (Old) | CRP (New) | CRP (New) |
|-------------|-----------|-----------|-----------|-----------|
| NM_021722   | ADAM22    | 0.000430966 | 0.003092552 | -0.289016443 |
| NM_016351   | ADAM22    | 0.0004376 | 0.003132024 | -0.289000057 |
| NM_139048   | HLTF      | 0.000722916 | 0.004754958 | -0.288476959 |
| NM_203351   | MAP3K3    | 0.0058305 | 0.025922347 | -0.288467895 |
| NM_001243777| CEP57     | 0.0020526 | 0.011285364 | -0.288457513 |
| NM_001206609| SELPLG    | 0.000698472 | 0.004626947 | -0.287334771 |
| NM_01135589 | GDAP2     | 0.000910068 | 0.005746808 | -0.287179358 |
| NM_001206609| SELPLG    | 0.008815516 | 0.036138875 | -0.285059732 |
| NM_01136135 | RPL28     | 0.006224103 | 0.027357148 | -0.28591988 |
| NM_001003828| PARVB     | 0.009640427 | 0.038672322 | -0.28457219 |
| NM_025230   | DCAF11    | 0.000496009 | 0.022877387 | -0.28457219 |
| NM_003884   | KAT2B     | 0.008815516 | 0.036138875 | -0.285059732 |
| NM_173359   | EIF4E3    | 0.00039099 | 0.003141931 | -0.284689767 |
| NM_001199388| EPB41L2   | 0.009535929 | 0.038320378 | -0.28457219 |
| NM_001256430| STON2     | 0.005973969 | 0.02468547 | -0.285513732 |
| NM_198969   | AES       | 0.00039099 | 0.003141931 | -0.284689767 |
| Gene Symbol | Description | Log2 Fold Change | Degree | Enrichment Score |
|-------------|-------------|-----------------|--------|-----------------|
| NM_001077198 | ATG9A       | 0.006442116     | 0.028140579 | -0.283665754    |
| NM_001077198 | MBNL1       | 0.000121869     | 0.001044584 | -0.283568377    |
| NM_001077198 | KIAA0664    | 0.003406384     | 0.016927678 | -0.283373227    |
| NM_001077198 | SELPLG      | 0.008554291     | 0.035267462 | -0.283011996    |
| NM_001077198 | RNF31       | 0.005833371     | 0.025931231 | -0.283261632    |
| NM_001077198 | EPG5        | 0.002421651     | 0.012896809 | -0.283259777    |
| NM_001077198 | MBP         | 0.000546291     | 0.003779566 | -0.283128664    |
| NM_001077198 | GALK2       | 0.004354871     | 0.02060383  | -0.282998614    |
| NM_001077198 | SCMH1       | 0.008709958     | 0.03578279  | -0.282703767    |
| NM_001077198 | HLA-DP1     | 0.002702612     | 0.014075275 | -0.28267096     |
| NM_001077198 | MAGED1      | 0.003942269     | 0.018990501 | -0.282528065    |
| NM_001077198 | MAGED1      | 0.003942269     | 0.018990501 | -0.282528065    |
| NM_001077198 | MBNL1       | 0.000140284     | 0.00118307  | -0.282515515    |
| NM_001077198 | ATG9A       | 0.007090114     | 0.030528657 | -0.282244098    |
| NM_001077198 | UNC13B      | 0.000246842     | 0.001920267 | -0.282067789    |
| NM_001077198 | CAPN1       | 0.004288017     | 0.020349249 | -0.282065161    |
| NM_001077198 | TPDS2       | 0.001420896     | 0.008334931 | -0.281948884    |
| NM_001077198 | GTPBP1      | 0.00168514      | 0.009598873 | -0.281767228    |
| NM_001077198 | VPS13B      | 0.000567966     | 0.003901584 | -0.2815708      |
| NM_001077198 | KIAA1979    | 0.000210657     | 0.001673378 | -0.281559494    |
| NM_001077198 | MAPKAP1     | 0.000289607     | 0.00219212  | -0.280908856    |
| NM_001077198 | RALY        | 0.000515517     | 0.003605467 | -0.2808717      |
| NM_001077198 | HLA-B       | 0.002476298     | 0.013112641 | -0.280492332    |
| NM_001077198 | NBR1        | 0.000554835     | 0.003826944 | -0.280337756    |
| NM_001077198 | MXI1        | 0.002852393     | 0.014688018 | -0.280218957    |
| NM_001077198 | CBS         | 0.000839799     | 0.005371571 | -0.279989014    |
| NM_001077198 | ACTN1       | 0.000203359     | 0.001624961 | -0.279863479    |
| NM_001077198 | ACTN1       | 0.000205344     | 0.001636418 | -0.279859525    |
| NM_001077198 | MBNL1       | 0.000185949     | 0.001508558 | -0.279788022    |
| NM_001077198 | SVIL        | 0.006686133     | 0.029044265 | -0.279736482    |
| NM_001077198 | DPYD        | 0.000549406     | 0.003794261 | -0.279657909    |
| NM_001077198 | BTN3A2      | 0.001353235     | 0.008053252 | -0.279629477    |
| NM_001077198 | BSL2        | 0.001411229     | 0.008283131 | -0.27962757     |
| NM_001077198 | IGFBP7      | 0.001161047     | 0.006832624 | -0.279568363    |
| NM_001077198 | BTN3A1      | 0.003027965     | 0.015378914 | -0.27942483     |
| NM_001077198 | MAPKAP1     | 0.000227259     | 0.001786631 | -0.279402679    |
| NM_001077198 | ADD3        | 0.005439903     | 0.024593264 | -0.279238354    |
| NM_001077198 | NDUF11      | 0.012376612     | 0.047225962 | -0.279005587    |
| NM_001077198 | NDUFV1      | 0.004799148     | 0.022276834 | -0.278995196    |
| NM_001077198 | TARS2       | 0.000301557     | 0.002275036 | -0.278936697    |
| NM_001077198 | CD99L2      | 0.006726703     | 0.029194535 | -0.278805385    |
| Gene Symbol | Description | Fold Change | p-Value | Log2FoldChange |
|-------------|-------------|-------------|---------|----------------|
| NM_002746   |             |             |         |                |
| NM_012154   |             |             |         |                |
| NM_017684   |             |             |         |                |
| NM_020821   |             |             |         |                |
| NM_031862   |             |             |         |                |
| NM_00198868 |             |             |         |                |
| NM_003162   |             |             |         |                |
| NM_024757   |             |             |         |                |
| NM_00119939 |             |             |         |                |
| NM_00116833 |             |             |         |                |
| NM_020921   |             |             |         |                |
| NM_00103733 |             |             |         |                |
| NM_005186   |             |             |         |                |
| NM_018303   |             |             |         |                |
| NM_0011553  |             |             |         |                |
| NM_021738   |             |             |         |                |
| NM_00103733 |             |             |         |                |
| NM_00117220 |             |             |         |                |
| NM_016479   |             |             |         |                |
| NM_017890   |             |             |         |                |
| NM_00112862 |             |             |         |                |
| NM_031858   |             |             |         |                |
| NM_152221   |             |             |         |                |
| NR_045602   |             |             |         |                |
| NM_024572   |             |             |         |                |
| NM_207295   |             |             |         |                |
| NM_017432   |             |             |         |                |
| NR_024388   |             |             |         |                |
| NM_00116610 |             |             |         |                |
| NM_020148   |             |             |         |                |
| NM_00101588 |             |             |         |                |
| NM_003119   |             |             |         |                |
| NR_040008   |             |             |         |                |
| NM_012120   |             |             |         |                |
| NM_018080   |             |             |         |                |
| NM_00118088 |             |             |         |                |
| NM_00114516 |             |             |         |                |
| NM_012448   |             |             |         |                |
| NM_022373   |             |             |         |                |
| NM_014608   |             |             |         |                |
| NM_002746   |             |             |         |                |
| MAPK3       |             | 0.011384843 | 0.044245014 | -0.278745458 |
| CYFIP1      |             | 0.003266068 | 0.016350698 | -0.277942464 |
| VPS13C      |             | 0.003272206 | 0.016370396 | -0.277939437 |
| NBR1        |             | 0.000681189 | 0.004532664 | -0.277614759 |
| CAPN1       |             | 0.004844371 | 0.022441182 | -0.277573537 |
| STRN        |             | 0.007612372 | 0.032233807 | -0.27746089 |
| EHM1        |             | 0.004535474 | 0.021275563 | -0.277135781 |
| EPB41L2     |             | 0.005479401 | 0.024716357 | -0.277079197 |
| ME2         |             | 0.00018977  | 0.001531611 | -0.277074558 |
| NIN         |             | 0.008398599 | 0.034762498 | -0.27701657 |
| CYFIP2      |             | 0.005270354 | 0.023964988 | -0.27684393 |
| EXOC2       |             | 0.004587292 | 0.021450916 | -0.276774165 |
| IGFBP7      |             | 0.000990738 | 0.006185244 | -0.276569552 |
| SVIL        |             | 0.006438483 | 0.028128844 | -0.276490583 |
| CYFIP2      |             | 0.003283469 | 0.016415686 | -0.276470409 |
| SCMH1       |             | 0.012154379 | 0.046563321 | -0.276358957 |
| SHISA5      |             | 0.004129256 | 0.019713582 | -0.276252815 |
| VPS13B      |             | 0.000710026 | 0.004684689 | -0.276195526 |
| SPIRE1      |             | 0.003857916 | 0.018684106 | -0.276124927 |
| NBR1        |             | 0.00079444  | 0.005136721 | -0.276070776 |
| CSNK1E      |             | 0.006885024 | 0.029768989 | -0.275959566 |
| GALNT14     |             | 0.009030403 | 0.036781318 | -0.275805125 |
| GALNT14     |             | 0.009100176 | 0.036969234 | -0.275800612 |
| MBNL1       |             | 0.000220457 | 0.001739875 | -0.275764179 |
| PT0V1       |             | 0.010137439 | 0.040296186 | -0.275598242 |
| LOC152217   |             | 0.010002113 | 0.039848881 | -0.275359824 |
| NDUFV1      |             | 0.005296136 | 0.024046008 | -0.2753356 |
| SPIRE1      |             | 0.00396871  | 0.019093113 | -0.275293085 |
| TSC22D3     |             | 0.008496511 | 0.035082788 | -0.275210042 |
| SPG7        |             | 0.00198698  | 0.010995735 | -0.275146134 |
| CAPN1       |             | 0.005203718 | 0.023743112 | -0.27504606 |
| CD2AP       |             | 0.007453375 | 0.031668853 | -0.275007203 |
| VPS13C      |             | 0.005269656 | 0.023964988 | -0.274920467 |
| VPS13C      |             | 0.005270894 | 0.023964988 | -0.274919873 |
| PRMT3       |             | 0.010742232 | 0.042147732 | -0.274772777 |
| STAT5B      |             | 0.001157438 | 0.007042505 | -0.274479134 |
| HERPUD2     |             | 0.009319874 | 0.037630257 | -0.274369397 |
| CYFIP1      |             | 0.000677078 | 0.004512482 | -0.274256527 |
| MAPK3       |             | 0.007738185 | 0.03264097 | -0.274181349 |
| Accession | Gene Name | Expression | Fold Change | Adj P Value |
|-----------|-----------|------------|-------------|-------------|
| NM_001040056 | MAPK3 | 0.007738185 | 0.03264097 | -0.274181349 |
| NM_198057 | TSC2D3 | 0.008848214 | 0.036222948 | -0.27411209 |
| NM_001172219 | SCMH1 | 0.011937083 | 0.045890595 | -0.274073225 |
| NM_207294 | MBNL1 | 0.00244134 | 0.01901683 | -0.273444125 |
| NR_034166 | NDUFA11 | 0.008114513 | 0.033848817 | -0.273275884 |
| NM_181719 | TMCO4 | 0.004094979 | 0.019403155 | -0.272847992 |
| NM_024605 | ARHGAP10 | 0.005243631 | 0.023884885 | -0.27278491 |
| NM_00730 | CTDSP2 | 0.00163373 | 0.001353861 | -0.272671884 |
| NM_005862 | STAG1 | 0.002037986 | 0.011223655 | -0.272283382 |
| NM_172209 | TAPBP | 0.007061467 | 0.030408002 | -0.271880428 |
| NM_006828 | ASCC3 | 0.000445023 | 0.003178261 | -0.27183337 |
| NM_03644 | FBXW11 | 0.001914299 | 0.010649048 | -0.27173272 |
| NM_139045 | SMARCC2 | 0.000928007 | 0.005850144 | -0.270698315 |
| NM_001719 | BMP7 | 0.002322052 | 0.012460835 | -0.270593939 |
| NM_13905 | SMARCA2 | 0.001640503 | 0.009328279 | -0.27023524 |
| NM_0013070 | BSCL2 | 0.001914299 | 0.010649048 | -0.270053154 |
| NM_001493 | GDI1 | 0.006798685 | 0.02942806 | -0.27005938 |
| NM_001130420 | BCL2L1 | 0.000928007 | 0.005850144 | -0.270698315 |
| NM_001130702 | MANBA | 0.008064942 | 0.033694066 | -0.270053154 |
| NM_001145166 | PRMT3 | 0.000928007 | 0.005850144 | -0.270698315 |
| NM_002044 | GALK2 | 0.005704152 | 0.02550561 | -0.26889928 |
| NM_002116 | HLA-A | 0.007126879 | 0.030614259 | -0.268547459 |
| NM_003310 | TSSC1 | 0.004668533 | 0.021775983 | -0.268445408 |
| Gene Name     | Gene ID     | Gene Feature | F-test   | p-value  | Log2 Fold Change | q-value  |
|--------------|-------------|--------------|----------|----------|------------------|----------|
| RNF167       | NM_015528   |             | 0.003967858 | 0.019093113 | -0.268386994    |          |
| EIF2C2       | NM_01164623 |             | 0.003628824 | 0.017815589 | -0.268317693    |          |
| CYP1P2       | NM_014376   |             | 0.003894916 | 0.018811184 | -0.268288616    |          |
| SH3BP1       | NM_018957   |             | 0.005872432 | 0.026073666 | -0.26654351     |          |
| RPL8         | NM_033301   |             | 0.008030739 | 0.033588948 | -0.266224514    |          |
| SLC37A4      | NM_001164623|             | 0.005110979 | 0.023391802 | -0.263574178    |          |
| HLA-C        | NM_001164279|             | 0.005872432 | 0.026073666 | -0.26654351     |          |
| HLA-C        | NM_001164280|             | 0.005872432 | 0.026073666 | -0.26654351     |          |
| ZDHHC16      | NM_001164278|             | 0.005872432 | 0.026073666 | -0.26654351     |          |
| EIF2C2       | NM_001164623|             | 0.005110979 | 0.023391802 | -0.263574178    |          |
| HLA-C        | NM_001164280|             | 0.005872432 | 0.026073666 | -0.26654351     |          |
| HLA-C        | NM_001164280|             | 0.005872432 | 0.026073666 | -0.26654351     |          |
| ZDHHC16      | NM_001164278|             | 0.005872432 | 0.026073666 | -0.26654351     |          |
| EIF2C2       | NM_001164623|             | 0.005110979 | 0.023391802 | -0.263574178    |          |
| HLA-C        | NM_001164280|             | 0.005872432 | 0.026073666 | -0.26654351     |          |
| HLA-C        | NM_001164280|             | 0.005872432 | 0.026073666 | -0.26654351     |          |
| ZDHHC16      | NM_001164278|             | 0.005872432 | 0.026073666 | -0.26654351     |          |
|     |     |     |     |
|-----|-----|-----|-----|
| NM_033688 | PEF1 | 0.007800565 | 0.032824893 | -0.262916248 |
| NM_001042679 | RHOC | 0.00146789 | 0.008543907 | -0.262790213 |
| NM_147175 | HS6ST2 | 0.004779317 | 0.02220559 | -0.262459812 |
| NM_198046 | ZDHHC16 | 0.00917987 | 0.037211594 | -0.261774189 |
| NM_001128627 | SPIRE1 | 0.007774211 | 0.032751095 | -0.261766012 |
| NM_003190 | TAPBP | 0.007751577 | 0.032690502 | -0.261742645 |
| NM_198043 | ZDHHC16 | 0.012339358 | 0.047120112 | -0.261562938 |
| NM_001031804 | MAF | 0.00030939 | 0.002324103 | -0.261452422 |
| NM_052966 | FAM129A | 0.002139953 | 0.011681025 | -0.26144455 |
| NM_000289 | PFKM | 0.000125184 | 0.001068165 | -0.261241782 |
| NM_006364 | SEC23A | 0.00628501 | 0.027592204 | -0.261031828 |
| NM_001077188 | HS6ST2 | 0.005077555 | 0.023281585 | -0.261020459 |
| NM_002116 | HLA-A | 0.002260959 | 0.012220609 | -0.261018116 |
| NM_033020 | TRIM33 | 0.001234957 | 0.00742148 | -0.260645861 |
| NM_021154 | PSAT1 | 0.001119103 | 0.006849923 | -0.260429078 |
| NM_001164277 | SLC37A4 | 0.006036659 | 0.026679266 | -0.259883719 |
| NM_003818 | CDS2 | 0.003465344 | 0.017165154 | -0.259762614 |
| NM_015906 | TRIM33 | 0.001224264 | 0.007370633 | -0.259689941 |
| NM_207122 | EXT2 | 0.000941696 | 0.005926715 | -0.259331143 |
| NM_198044 | ZDHHC16 | 0.012623506 | 0.047921913 | -0.259107785 |
| NM_005505 | SCARB1 | 0.003307367 | 0.016515176 | -0.25893414 |
| NM_001001329 | PRKCSH | 0.001411177 | 0.008283131 | -0.258855059 |
| NM_145012 | CCNY | 0.010198472 | 0.040471223 | -0.258817026 |
| NM_001082533 | CA10 | 0.007273831 | 0.031114511 | -0.258567885 |
| NM_002743 | PRKCSH | 0.001372218 | 0.008093295 | -0.258351755 |
| NM_012414 | RAB3GAP2 | 0.004363942 | 0.020630491 | -0.258298092 |
| NM_001398 | ECH1 | 0.002864008 | 0.014740168 | -0.258211011 |
| NM_000184 | HBG2 | 0.012902591 | 0.048726179 | -0.258129615 |
| NM_015057 | MYCBP2 | 0.000344971 | 0.002550122 | -0.257684151 |
| NM_022307 | ICA1 | 0.009472698 | 0.03811267 | -0.25750051 |
| NM_001006617 | MAPKAP1 | 0.000354358 | 0.00261107 | -0.257405018 |
| NM_002496 | NDUFS8 | 0.011300776 | 0.043996486 | -0.257083324 |
| NM_014857 | RABGAP1L | 0.002525136 | 0.013333237 | -0.256830599 |
| NM_015965 | NDUFA13 | 0.006288642 | 0.027604704 | -0.256236809 |
| NM_001013253 | LSP1 | 0.003962133 | 0.019080003 | -0.256099581 |
| NM_145799 | Sep-06 | 0.002912552 | 0.014925384 | -0.256049152 |
| NM_001013255 | LSP1 | 0.004094135 | 0.019595007 | -0.255671352 |
| NM_001082534 | CA10 | 0.008009131 | 0.03351744 | -0.255624543 |
| NR_003010 | SCARNA12 | 0.008062004 | 0.033691263 | -0.255415033 |
| NM_012392 | PEF1 | 0.011523045 | 0.044674539 | -0.255299948 |
| NM_001166269 | HAUS4 | 0.009159959 | 0.037150719 | -0.255291973 |
| Gene ID     | Gene Name   | p-value  | Adjusted p-value | Fold Change |
|------------|-------------|----------|------------------|-------------|
| NM_017815  | HAUS4       | 0.009140798 | 0.037111533 | -0.255260346 |
| NM_001242932 | LSP1       | 0.004143784 | 0.019775306 | -0.25514982  |
| NM_012233  | RAB3GAP1    | 0.008086541 | 0.033746348 | -0.255097711 |
| NM_001172435 | RAB3GAP1   | 0.008086541 | 0.033746348 | -0.255097711 |
| NM_001013254 | LSP1       | 0.004186048 | 0.01994642  | -0.255092045 |
| NM_006726  | LRBA        | 0.003631758 | 0.017824105 | -0.254972523 |
| NM_199141  | CARM1       | 0.003753224 | 0.018296353 | -0.254667587 |
| NM_001256030 | CD48       | 0.012874145 | 0.048641218 | -0.254350913 |
| NM_001199282 | LRBA       | 0.003588371 | 0.017649062 | -0.254121057 |
| NM_001038702 | CDC42SE2  | 0.002724879 | 0.014168893 | -0.253896714 |
| NM_001197248 | BTN3A2    | 0.002065178 | 0.011343976 | -0.253669354 |
| NM_024044  | SLX1B       | 0.009442456 | 0.038021879 | -0.2535072  |
| NM_001014999 | SLX1A     | 0.009442456 | 0.038021879 | -0.2535072  |
| NM_020178  | CA10        | 0.008401977 | 0.034768701 | -0.253488342 |
| NM_018959  | DAZAP1      | 0.001114838 | 0.006827957 | -0.253458549 |
| NM_001197247 | BTN3A2    | 0.002001361 | 0.011060896 | -0.253299123 |
| NM_170711  | DAZAP1      | 0.001137751 | 0.006945472 | -0.253209578 |
| NM_007047  | BTN3A2      | 0.002118552 | 0.011592159 | -0.253201126 |
| NM_133631  | ROBO1       | 0.000980927 | 0.006131723 | -0.253086936 |
| NM_015937  | PIGT        | 0.000390001 | 0.002838517 | -0.25300642  |
| NM_001668  | ARNT        | 0.000635859 | 0.004297435 | -0.252982531 |
| NM_020135  | WRNIP1      | 0.009834488 | 0.039296957 | -0.252940178 |
| NM_058179  | PSAT1       | 0.000959251 | 0.006019019 | -0.252926735 |
| NM_014203  | AP2A1       | 0.012948892 | 0.04863776  | -0.252844043 |
| NM_130787  | AP2A1       | 0.012948892 | 0.04863776  | -0.252844043 |
| NM_181672  | OGT         | 0.00105222  | 0.006502149 | -0.252702473 |
| NM_014865  | NCAPD2      | 0.000152884 | 0.001276552 | -0.252679673 |
| NR_037672  | SERF2       | 0.00010267  | 0.00089895  | -0.252506567 |
| NM_004599  | SREBF2      | 0.000676555 | 0.004511937 | -0.252472403 |
| NM_001178083 | EXT2       | 0.001315357 | 0.007820824 | -0.252468048 |
| NM_000262  | NAGA        | 0.012125745 | 0.046474259 | -0.252277295 |
| NM_052875  | VPS26B      | 0.001951787 | 0.010828081 | -0.252132175 |
| NM_178427  | ARNT        | 0.000645662 | 0.004350739 | -0.251680609 |
| NM_001197325 | ARNT      | 0.000645662 | 0.004350739 | -0.251680609 |
| NM_002121  | HLA-DPB1    | 0.005713852 | 0.0255221  | -0.251647782 |
| NM_001033853 | RPL3      | 0.000259942 | 0.002006418 | -0.251263533 |
| NM_181673  | OGT         | 0.001012813 | 0.006305838 | -0.251083009 |
| NM_030796  | VOPP1       | 0.000227877 | 0.001790537 | -0.250809563 |
| NM_004194  | ADAM22      | 0.004620004 | 0.021573328 | -0.25052069  |
| NM_004356  | CDB1        | 0.010495616 | 0.041409747 | -0.250443962 |
| NM_001197249 | BTN3A2    | 0.002504968 | 0.013247934 | -0.250413842 |
| Gene Symbol | Description | Score | p Value | q Value |
|-------------|-------------|-------|---------|---------|
| NM_001143830 | PIGT | 0.000926631 | 0.00584395 | -0.25029671 |
| NM_001200001 | NOTCH2 | 0.000130872 | 0.001112131 | -0.250136165 |
| NM_006875 | PIM2 | 0.000249175 | 0.001935371 | -0.249943331 |
| NM_005095 | ZMYM4 | 0.003448527 | 0.017091375 | -0.249205135 |
| NM_001166270 | HAUS4 | 0.012308264 | 0.047031591 | -0.249177402 |
| NR_037949 | BSCL2 | 0.003521923 | 0.017388436 | -0.249049041 |
| NR_037948 | BSCL2 | 0.003521923 | 0.017388436 | -0.249049041 |
| NM_005852 | CHD3 | 0.000543285 | 0.003764238 | -0.248965077 |
| NM_002223 | ITPR2 | 0.004891641 | 0.022624888 | -0.248787094 |
| NM_001145845 | ROBO1 | 0.001262503 | 0.007567126 | -0.248782983 |
| NM_001122955 | BSCL2 | 0.003523616 | 0.017391012 | -0.248649258 |
| NM_001206974 | DHP5 | 0.007896564 | 0.033139697 | -0.248002425 |
| NM_021721 | ADAM22 | 0.000504701 | 0.023163245 | -0.247855082 |
| NM_133443 | GPT2 | 0.003206846 | 0.01609761 | -0.247799174 |
| NM_001184729 | PIGT | 0.000407241 | 0.002949538 | -0.247755517 |
| NM_002941 | ROBO1 | 0.00227441 | 0.012270993 | -0.247755455 |
| NM_138392 | SHKB1 | 0.008221297 | 0.03418125 | -0.247620805 |
| NR_038370 | NDRG3 | 0.010328255 | 0.040879695 | -0.246858192 |
| NM_023018 | NADK | 0.008195871 | 0.034113857 | -0.246763695 |
| NM_032750 | ABHD14B | 0.010357708 | 0.040979899 | -0.246545889 |
| NM_013406 | DHP5 | 0.006456538 | 0.028191145 | -0.244649625 |
| NM_001006619 | MAPKAP1 | 0.000628724 | 0.004256958 | -0.246308162 |
| NM_198196 | CD96 | 0.010637942 | 0.041815836 | -0.246277954 |
| NM_001005273 | CHD3 | 0.000669689 | 0.004473171 | -0.24621156 |
| NM_013335 | GMPPA | 0.010324957 | 0.040872086 | -0.245940971 |
| NM_003367 | USF2 | 0.006742551 | 0.029243097 | -0.245766364 |
| NM_001080432 | FTO | 0.005447157 | 0.024600787 | -0.24560586 |
| NM_002123 | HLA-DQ81 | 0.001232329 | 0.007410183 | -0.245121175 |
| NM_024117 | MAPKAP1 | 0.000784752 | 0.005080712 | -0.244622046 |
| NM_017653 | DYM | 0.00998655 | 0.039813565 | -0.244585468 |
| NM_001243961 | HLA-DQ81 | 0.001271717 | 0.00760987 | -0.244356979 |
| NM_001005271 | CHD3 | 0.000660697 | 0.00442803 | -0.244346285 |
| NM_001012516 | ITM2C | 0.001425027 | 0.008354216 | -0.244077424 |
| NM_009967 | RPL3 | 0.00305569 | 0.002298301 | -0.243724052 |
| NM_014891 | PDAP1 | 0.003880281 | 0.018761479 | -0.243627462 |
| NM_001146314 | ABHD14B | 0.011906467 | 0.045807391 | -0.243553319 |
| NM_001144995 | CCDC85C | 0.011267954 | 0.043891703 | -0.243251342 |
| NM_031407 | HUWE1 | 0.000358296 | 0.002636171 | -0.24311189 |
| NM_001085471 | FOXN3 | 0.001221263 | 0.007358386 | -0.242960791 |
| NM_005816 | CD96 | 0.01171892 | 0.04522742 | -0.242833906 |
| NM_001143830 | GAS2 | 0.010647848 | 0.041843706 | -0.242791261 |
| Gene   | Description | MaxFoldChange | AdjPVal | FDR   |
|--------|-------------|---------------|---------|-------|
| NM_000992 | RPL29       | 0.00470884    | 0.0033014 | 0.242589104 |
| NM_021629 | GNB4        | 0.0107963     | 0.042304016 | 0.242097923 |
| NM_020240 | CDC42SE2    | 0.03764861    | 0.018329028 | 0.242044885 |
| NM_015902 | UBR5        | 0.00276019    | 0.002104811 | 0.241560145 |
| NM_001199877 | SERF2  | 0.00182123    | 0.001480755 | 0.241198521 |
| NM_005443 | PAPSS1      | 0.009793828   | 0.03915028  | 0.24111362 |
| NM_001184730 | PIGT  | 0.001542496   | 0.008917966 | 0.241033698 |
| NM_005617 | RPS14       | 0.00059955    | 0.004086426 | -0.240868197 |
| NM_022733 | SMAP2       | 0.005946615   | 0.026340145 | -0.240778118 |
| NM_000991 | RPL28       | 0.004088893   | 0.019576225 | -0.240231476 |
| NM_001198995 | NADK  | 0.01046063    | 0.041304614 | -0.240193504 |
| NR_038192 | DHPS        | 0.007434684   | 0.03159901  | -0.23988494 |
| NM_001146333 | SUMF2 | 0.00780733    | 0.005060421 | -0.23978931 |
| NM_020165 | RAD18       | 0.010757574   | 0.042196781 | -0.239753911 |
| NM_001166241 | CGREF1  | 0.006384058   | 0.027944477 | -0.239705047 |
| NM_006633 | IQGAP2      | 0.003059343   | 0.015493687 | -0.23958174 |
| NM_001190965 | ZMYM2 | 0.005641613   | 0.02528685  | -0.239437192 |
| NM_001018108 | SERF2  | 0.00203558    | 0.001625676 | -0.239383073 |
| NM_001198994 | NADK  | 0.008317477   | 0.034513402 | -0.239130638 |
| NM_001083613 | TMEM219  | 0.011882274   | 0.045727213 | -0.239110071 |
| NM_001199876 | SERF2  | 0.00208256    | 0.001656517 | -0.239109942 |
| NM_001198993 | NADK  | 0.00909209    | 0.036941432 | -0.239095462 |
| NM_004824 | CDYL        | 0.007323568   | 0.031273813 | -0.239024078 |
| NM_005514 | HLA-B       | 0.002232432   | 0.012081804 | -0.238924598 |
| NM_005197 | FOXN3       | 0.001742059   | 0.009870119 | -0.238866041 |
| NM_015302 | HAUS5       | 0.005946631   | 0.026340145 | -0.238537397 |
| NM_003331 | TYK2        | 0.009563661   | 0.038405854 | -0.23844441 |
| NM_194280 | TMEM219     | 0.012111535   | 0.046429112 | -0.238382484 |
| NM_172020 | POM121      | 0.008467996   | 0.034990088 | -0.238370414 |
| NM_001605 | AARS        | 0.00654112    | 0.00439481  | -0.238279947 |
| NM_006675 | TSPAN9      | 0.005140872   | 0.023503278 | -0.238082397 |
| NM_001168320 | TSPAN9 | 0.005148219   | 0.023526008 | -0.238080815 |
| NM_198837 | ACACA       | 0.003656804   | 0.017923346 | -0.237986745 |
| NM_002372 | MAN2A1      | 0.002140392   | 0.011681025 | -0.237975983 |
| NM_001930 | DHPS        | 0.008007588   | 0.033515702 | -0.237947763 |
| NM_005907 | MAN1A1      | 0.002821636   | 0.014559917 | -0.237929158 |
| NM_000401 | EXT2        | 0.003002016   | 0.015265386 | -0.237916891 |
| NM_198838 | ACACA       | 0.003515192   | 0.017366743 | -0.237835271 |
| NM_001136134 | RPL28  | 0.00456542    | 0.021381794 | -0.237581618 |
| NM_001242992 | PARN  | 0.00848333    | 0.034937244 | -0.23749891 |
| NM_005028 | PIP4K2A     | 0.002030011   | 0.011185951 | -0.237080153 |
| Gene Identifier | Gene Symbol | log2Ratio | P-value | Fold Change |
|----------------|-------------|-----------|---------|-------------|
| NM_016145      | WDR83OS     | 0.002116886 | 0.011585173 | -0.23700554 |
| NM_145341      | PDCD4       | 0.000817723 | 0.005258658 | -0.236816838 |
| NM_005993      | TBCD        | 0.011384518 | 0.044245014 | -0.236754536 |
| NM_014456      | PDCD4       | 0.000830337 | 0.005259947 | -0.23621633  |
| NM_001199875   | SERF2       | 0.000251659 | 0.001953133 | -0.235806713 |
| NM_145341      | PDCD4       | 0.000817723 | 0.005258658 | -0.236816838 |
| NM_005993      | TBCD        | 0.011384518 | 0.044245014 | -0.236754536 |
| NM_014456      | PDCD4       | 0.000830337 | 0.005259947 | -0.23621633  |
| NM_001199875   | SERF2       | 0.000251659 | 0.001953133 | -0.235806713 |
| NM_145341      | PDCD4       | 0.000817723 | 0.005258658 | -0.236816838 |
| NM_005993      | TBCD        | 0.011384518 | 0.044245014 | -0.236754536 |
| NM_014456      | PDCD4       | 0.000830337 | 0.005259947 | -0.23621633  |
| NM_001199875   | SERF2       | 0.000251659 | 0.001953133 | -0.235806713 |
| NM_145341      | PDCD4       | 0.000817723 | 0.005258658 | -0.236816838 |
| NM_005993      | TBCD        | 0.011384518 | 0.044245014 | -0.236754536 |
| NM_014456      | PDCD4       | 0.000830337 | 0.005259947 | -0.23621633  |
| NM_001199875   | SERF2       | 0.000251659 | 0.001953133 | -0.235806713 |
| NM_145341      | PDCD4       | 0.000817723 | 0.005258658 | -0.236816838 |
| NM_005993      | TBCD        | 0.011384518 | 0.044245014 | -0.236754536 |
| NM_014456      | PDCD4       | 0.000830337 | 0.005259947 | -0.23621633  |
| NM_001199875   | SERF2       | 0.000251659 | 0.001953133 | -0.235806713 |
| NM_145341      | PDCD4       | 0.000817723 | 0.005258658 | -0.236816838 |
| NM_005993      | TBCD        | 0.011384518 | 0.044245014 | -0.236754536 |
| NM_014456      | PDCD4       | 0.000830337 | 0.005259947 | -0.23621633  |
| Gene ID     | Symbol | FPKM 1 | FPKM 2 | log2 Fold Change |
|------------|--------|--------|--------|----------------|
| NR_026590  | CDYL   | 0.009046484 | 0.036833599 | -0.230056456   |
| NM_002582  | PARN   | 0.010004943 | 0.039854812 | -0.229506058   |
| NM_015411  | SUMF2  | 0.001310131 | 0.007800676 | -0.229429473   |
| NM_018387  | STRBP  | 0.001385444 | 0.00816086  | -0.229356986   |
| NM_001012514 | ITM2C | 0.002482701 | 0.013141864 | -0.2288134     |
| NM_001042469 | SUMF2 | 0.001428169 | 0.00836109  | -0.2285318     |
| NM_016604  | KDM3B  | 0.001310131 | 0.007800676 | -0.2285318     |
| NM_001242828 | ELOVL5 | 0.004047742 | 0.019401796 | -0.228122477   |
| NM_001136131 | APP  | 0.000207422 | 0.001651211 | -0.228327279   |
| NM_020365  | EIF2B3 | 0.012416242 | 0.047322489 | -0.228122477   |
| NM_001143970 | CDYL | 0.009522163 | 0.038280589 | -0.228122477   |
| NM_001136136 | RPL28 | 0.00185209 | 0.010378758 | -0.229285318   |
| NM_001244580 | TRRAP | 0.001080602 | 0.006649877 | -0.229285318   |
| NM_001130069 | SUMF2 | 0.002096216 | 0.011488068 | -0.229285318   |
| NM_001031835 | PHKB | 0.01063315  | 0.041802531 | -0.22978725    |
| NM_032361  | THOC3  | 0.007708043 | 0.032537862 | -0.2293075     |
| NM_0198591 | BSG    | 0.00117916  | 0.0010148  | -0.2293075     |
| NM_004635  | MAPKAPK3 | 0.009873694 | 0.039428348 | -0.225643461   |
| NM_006196  | PCBP1  | 0.012435848 | 0.04736684  | -0.225643461   |
| NM_003496  | TRRAP  | 0.002753546 | 0.014285463 | -0.227371673   |
| NM_01166588 | ELOVL5 | 0.001460493 | 0.00812213  | -0.226674297   |
| NM_001145933 | TKTL1 | 0.000117916 | 0.0010148  | -0.225930539   |
| NM_198591  | BSG    | 0.004161919 | 0.019852285 | -0.22527492    |
| NM_001031835 | PHKB | 0.009873694 | 0.039428348 | -0.225643461   |
| NM_001136136 | RPL28 | 0.001460493 | 0.00812213  | -0.226674297   |
| NM_001031835 | PHKB | 0.009873694 | 0.039428348 | -0.225643461   |
| NM_001136136 | RPL28 | 0.001460493 | 0.00812213  | -0.226674297   |
| Gene Accession | Gene Symbol | FPKM | Adj FPKM | Volcano Score |
|----------------|-------------|------|----------|---------------|
| NM_022156      | DUS1L       | 0.010541445 | 0.041529912 | -0.220783906 |
| NM_003003      | SEC14L1     | 0.008840032  | 0.036208045  | -0.219921196 |
| NM_001386      | DPYSL2      | 0.006611122  | 0.028756948  | -0.219215082 |
| NM_001640      | APEH        | 0.005995811  | 0.026518456  | -0.219044497 |
| NR_037673      | SERF2       | 0.004355232  | 0.02060383   | -0.218899732 |
| NM_145869      | ANXA11      | 0.00877591   | 0.036308197  | -0.218134708 |
| NM_145868      | ANXA11      | 0.008877591  | 0.036308197  | -0.218134708 |
| NM_016480      | PAIP2       | 0.010383748  | 0.041050132  | -0.218020297 |
| NM_001145934   | TKTL1       | 0.002428123  | 0.001929915  | -0.217670234 |
| NM_001157      | ANXA11      | 0.009007577  | 0.036698629  | -0.21709097  |
| NM_0032360     | ACBD6       | 0.011385457  | 0.044245014  | -0.216697802 |
| NM_018979      | WNK1        | 0.012583274  | 0.047805825  | -0.215773051 |
| NM_003486      | SLC7A5      | 0.011326806  | 0.044063189  | -0.215901109 |
| NM_001135243   | TCOF1       | 0.003509653  | 0.017342259  | -0.215773051 |
| NM_001143999   | SEC14L1     | 0.009590909  | 0.038233205  | -0.215214644 |
| NM_001143998   | SEC14L1     | 0.009590909  | 0.038233205  | -0.215214644 |
| NM_006289      | TLN1        | 0.001069192  | 0.00658921   | -0.21518568  |
| NM_001144001   | SEC14L1     | 0.012083281  | 0.046334692  | -0.214541091 |
| NM_003760      | EIF4G3      | 0.012737779  | 0.048250936  | -0.214383888 |
| NM_024665      | TBL1XR1     | 0.010881502  | 0.04259294   | -0.213893206 |
| NM_198834      | ACACA       | 0.008122233  | 0.033876266  | -0.213811654 |
| NM_182762      | MACC1       | 0.001618146  | 0.009272357  | -0.212780743 |
| NM_080546      | SLC44A1     | 0.004916735  | 0.022712673  | -0.21256207  |
| NR_003249      | HNRNPD1     | 0.002312534  | 0.012431542  | -0.211821533 |
| NM_001207000   | HNRNPD1     | 0.004529452  | 0.021250667  | -0.211795469 |
| NM_001042470   | SUMF2       | 0.002473237  | 0.013098767  | -0.21171588  |
| NM_015909      | NBAS        | 0.003428611  | 0.017012531  | -0.211354274 |
| NM_006353      | HMGN4       | 0.002745566  | 0.014258996  | -0.211145716 |
| NM_032217      | ANKRD17     | 0.008915688  | 0.036413893  | -0.211004016 |
| NM_198839      | ACACA       | 0.009148356  | 0.037119291  | -0.21058078  |
| NM_014313      | TMEM50A     | 0.010359093  | 0.04097992   | -0.21054623  |
| NM_001135244   | TCOF1       | 0.004129523  | 0.019713582  | -0.210263077 |
| NM_001195141   | TCOF1       | 0.004129523  | 0.019713582  | -0.210263077 |
| NM_001135245   | TCOF1       | 0.004370813  | 0.020653118  | -0.210153113 |
| NM_000356      | TCOF1       | 0.004370813  | 0.020653118  | -0.210153113 |
| NM_001008657   | TCOF1       | 0.012074908  | 0.046318581  | -0.209912232 |
| NM_198889      | ANKRD17     | 0.009200958  | 0.037268872  | -0.209748318 |
| NM_018238      | AGK         | 0.010469965  | 0.041330911  | -0.209725477 |
| NM_032635      | TMEM147     | 0.011048681  | 0.043139359  | -0.209204956 |
| NM_033554      | HLA-DPA1    | 0.004524259  | 0.021301602  | -0.209098412 |
| NM_002227      | JAK1        | 0.01723391   | 0.009775751  | -0.208947565 |
| Gene ID       | Gene Name | Log2 Fold Change | p-Value | q-Value | Adjusted Fold Change |
|--------------|-----------|------------------|---------|---------|---------------------|
| NM_001242597 | TMEM147   | 0.011291416      | 0.043965803 | -0.208473552 |
| NM_001009    | RPS5      | 0.005275628      | 0.023979171 | -0.208322036 |
| NM_001202414 | AKR1A1    | 0.005176062      | 0.023635069 | -0.207128024 |
| NM_002070    | GNAI2     | 0.010010011      | 0.039869655 | -0.206930111 |
| NM_001198801 | EIF4G3    | 0.012080876      | 0.046334692 | -0.206766392 |
| NR_003001    | SCARNA7   | 0.00317131       | 0.015951561 | -0.206605910 |
| NM_000516    | GNAS      | 0.005275628      | 0.023979171 | -0.206513535 |
| NM_001022    | RPS19     | 0.007896464      | 0.033139697 | -0.204781922 |
| NM_001202413 | AKR1A1    | 0.00541254       | 0.024489108 | -0.204742090 |
| NM_007051    | FAF1      | 0.008911768      | 0.0364129  | -0.204694822 |
| NM_006809    | TOMM34    | 0.008643098      | 0.035544832 | -0.204573666 |
| NM_006066    | AKR1A1    | 0.006136513      | 0.027036137 | -0.203767466 |
| NM_001981    | EPS15     | 0.011337205      | 0.04409787 | -0.203203771 |
| NM_080426    | GNAS      | 0.001878088      | 0.010492788 | -0.202766167 |
| NM_001077489 | GNAS      | 0.001893074      | 0.010550729 | -0.202707015 |
| NM_00135242  | NDRG1     | 0.0012527        | 0.008837464 | -0.202448466 |
| NM_006311    | NCOR1     | 0.011934377      | 0.045890307 | -0.201994437 |
| NM_153326    | AKR1A1    | 0.006417607      | 0.028058266 | -0.20133756 |
| NM_005892    | FMNL1     | 0.008872892      | 0.036298972 | -0.200220071 |
| NM_00130065  | MYO9B     | 0.006543379      | 0.028507491 | -0.198639518 |
| NM_000997    | RP1L37    | 0.00662397       | 0.04437436 | -0.198480453 |
| NM_015236    | LPHN3     | 0.009467441      | 0.038106996 | -0.198047945 |
| NM_001110    | ADAM10    | 0.011390762      | 0.044259844 | -0.197998526 |
| NM_004145    | MYO9B     | 0.006687911      | 0.029047744 | -0.19795049 |
| NM_001042466 | PSAP      | 0.000887105      | 0.00562932 | -0.195668901 |
| NM_002778    | PSAP      | 0.000887546      | 0.005630918 | -0.195668801 |
| NM_057161    | KLHDC3    | 0.011603541      | 0.044910447 | -0.195607825 |
| NM_001042465 | PSAP      | 0.000897936      | 0.005684695 | -0.195513744 |
| NM_181077    | GOLGA8A   | 0.009353489      | 0.037740348 | -0.194788952 |
| NM_001039590 | USP9X     | 0.008829094      | 0.036174574 | -0.194679665 |
| NM_001039591 | USP9X     | 0.008970144      | 0.036591045 | -0.19428313 |
| NM_174908    | CCDC50    | 0.00740282       | 0.031512622 | -0.19410848 |
| NM_006332    | IFI30     | 0.00236105       | 0.012629588 | -0.193342841 |
| NM_001166425 | GNAI2     | 0.012477014      | 0.047493203 | -0.192378996 |
| NM_016592    | GNAS      | 0.003192489      | 0.016047226 | -0.191393815 |
| NR_003259    | GNAS      | 0.002922255      | 0.014959631 | -0.191213963 |
| NM_080425    | GNAS      | 0.003328687      | 0.016602651 | -0.190946989 |
| Gene Symbol | Gene Name | Fold Change | t-value | q-value |
|-------------|-----------|-------------|---------|---------|
| NM_001077490 | GNAS     | 0.003328687 | 0.016602651 | -0.190946989 |
| NM_004152    | OAZ1      | 0.010456656 | 0.041297231 | -0.190033283 |
| NR_037946    | HNRNPUL2-BSCL2 | 0.01052969 | 0.041505611 | -0.18993567 |
| NM_00334     | UBA1      | 0.006998789 | 0.031109042 | -0.18970904 |
| NM_153280    | UBA1      | 0.00726928  | 0.031109042 | -0.18953153 |
| NM_001199184 | ATP2C1    | 0.012435526 | 0.04736684  | -0.18776274 |
| NM_002568    | PABPC1    | 0.002631681 | 0.013778305 | -0.18293938 |
| NM_001862    | COX5B     | 0.008636783 | 0.035533611 | -0.18163318 |
| NM_001242524 | HLA-DPA1  | 0.012060288 | 0.046274446 | -0.18123488 |
| NM_006460    | HEXIM1    | 0.003537381 | 0.017441706 | -0.18014658 |
| NM_001749    | CAPNS1    | 0.0107265   | 0.042107169 | -0.17950936 |
| NM_003554    | HLA-DPA1  | 0.012886261 | 0.048676881 | -0.17946298 |
| NM_001003962 | CAPNS1    | 0.010805213 | 0.042333356 | -0.17934321 |
| NM_005216    | DDOST     | 0.007532265 | 0.031949232 | -0.17804501 |
| NM_005165    | ALDOC     | 0.012847881 | 0.048575123 | -0.17561723 |
| NM_019111    | HLA-DRA   | 0.00238923  | 0.01274928  | -0.17364567 |
| NM_001155    | ANXA6     | 0.003399995 | 0.016898752 | -0.17191251 |
| NM_052862    | RCSD1     | 0.003665682 | 0.017945726 | -0.17140560 |
| NM_001009999 | KDM1A     | 0.010348359 | 0.04094836  | -0.16822977 |
| NM_005051    | QARS      | 0.01086094  | 0.042521577 | -0.16836148 |
| NM_015013    | KDM1A     | 0.010238814 | 0.040606812 | -0.16780205 |
| NM_002124    | HLA-DRB1  | 0.010676885 | 0.041939913 | -0.16611429 |
| NM_001243965 | HLA-DRB1  | 0.010569452 | 0.041623694 | -0.16600693 |
| NM_030810    | TXNDC5    | 0.00224222  | 0.012041758 | -0.16533845 |
| NM_001193544 | ANXA6     | 0.005959876 | 0.026387015 | -0.16209334 |
| NM_006098    | GN2B1L    | 0.011824719 | 0.045576545 | -0.16099044 |
| NR_037616    | TXNDC5    | 0.004467484 | 0.021013015 | -0.15882978 |
| NM_001145549 | TXNDC5    | 0.004497718 | 0.021135151 | -0.15844295 |
| NM_019111    | HLA-DRA   | 0.008381413 | 0.03471365  | -0.15330944 |
| NR_003662    | RPSAP58   | 0.006115955 | 0.026961553 | -0.15289890 |