

Regulator of G protein Signalling 4 (RGS4) controls constitutive secretion of von Willebrand factor (VWF) to the subendothelial matrix.

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Running title: Regulation of von Willebrand Factor basolateral secretion

Summary statement

Changes in RGS4 expression alter levels of subendothelial, matrix-associated VWF, affecting platelet recruitment in a model of endothelial damage. This introduces a novel control over VWF function.

Abstract

The haemostatic protein von Willebrand Factor (VWF) exists in plasma and subendothelial pools; the former secreted from endothelial storage granules, Weibel-Palade bodies (WPBs), by basal secretion with a contribution from agonist-stimulated secretion, the latter secreted into the subendothelial matrix by a constitutive pathway, not involving WPBs. We set out to determine if the constitutive release of subendothelial VWF is actually regulated and if so, what functional consequences this might have.

Constitutive VWF secretion can be increased by a range of factors; changes in VWF expression, levels of TNF-alpha or other environmental cues. An RNAseq analysis revealed that expression of RGS4 (Regulator of G protein signalling 4) was reduced in endothelial cells (HUVECs) grown under these conditions. si-RGS4 treatment of HUVECs increased constitutive basolateral secretion of VWF, probably by affecting the anterograde secretory pathway. In a simple model of endothelial damage we show that RGS4-silenced cells increased platelet recruitment onto the subendothelial matrix under flow. These results show that changes in RGS4 expression alter levels of subendothelial VWF, affecting platelet recruitment. This introduces a novel control over VWF function.

Keywords: Weibel-Palade bodies; von Willebrand Factor; extracellular matrix; RGS4; constitutive secretion

Introduction

Endothelial Von Willebrand factor (VWF) plays several roles in haemostasis. This reflects not only its central role as a mechanosensitive binding platform for platelets, but also its presence in three secreted pools. VWF stored in Weibel-Palade bodies can be released either by localised agonist-stimulated exocytosis, to provide transient VWF strings on the endothelial surface that initiate primary haemostasis, or by general basal secretion, to provide the large pool of circulating plasma VWF (Lopes da Silva and Cutler, 2016). The third VWF pool is released by constitutive secretion into the subendothelial matrix where it presumably acts in platelet recruitment following exposure by injury.

This latter pool of VWF is the least well understood. We previously reported that it comprises very poorly multimerised VWF, not stored in Weibel-Palade bodies but secreted by a constitutive pathway targeted to the subendothelial space where it likely binds to the extracellular matrix (Lopes da Silva and Cutler, 2016). Both the regulation of this pathway and a direct analysis of the function of this VWF after delivery remain elusive. We used RNAseq to analyse cells treated with different regimes that increased constitutive VWF secretion, allowing the identification of Regulator of G protein signalling 4 (RGS4) as a commonly downregulated mRNA and as a candidate modulator of this constitutive pathway. RGS4 is known to act both as a GTPase activating (GAP) protein (Watson et al., 1996, Berman et al., 1996) and can also bind to β 'COP (also known as COPB2) (Sullivan et al., 2000), a component of the machinery underpinning the retrograde secretory pathway. Both of these functions could potentially modulate a constitutive secretory pathway. We used RGS4 siRNA to show that this protein does indeed regulate constitutive secretion of VWF to the subendothelial side, and developed an assay mimicking endothelial damage, by stripping endothelial cells from their extracellular matrix, to determine the effects on platelet recruitment under flow of changing levels of RGS4. We conclude that altering the amount of constitutively secreted VWF into the subendothelial space by decreasing RGS4 levels in endothelial cells can indeed alter platelet recruitment to an exposed subendothelial surface in a simplified model of injury.

Results

Identification of a candidate for control of VWF constitutive secretion in ECs

To identify regulators of constitutive VWF secretion we challenged human umbilical vein endothelial cells (HUVECs) with conditions known to increase unregulated (i.e. basal plus constitutive) VWF secretion. We used BFA treatment to distinguish between basal and constitutive secretion (Giblin et al., 2008, Lopes da Silva and Cutler, 2016); BFA selectively blocks constitutive secretion by disrupting endoplasmic reticulum (ER) to Golgi transport, thus preventing exit of newly synthesized material from the ER without affecting secretion from post-Golgi organelles such as WPBs (including basal secretion of VWF) (Fig. 1A). The conditions that we tested, shown in the referenced literature to increase unregulated VWF secretion, were: i) VWF knock down (KD) by siRNA (Ferraro et al., 2014); ii) nocodazole treatment (Ferraro et al., 2014); iii) TNF α treatment (Bernardo et al., 2004, van der Poll et al., 1992); iv), MyRIP KD (Bierings et al., 2012, Nightingale et al., 2009), v), GRK2 KD (Stevenson et al., 2014), vi) EBM2 medium (from our unpublished observation). We also used AP1 KD as a positive

control for the maximum possible constitutive output that could be obtained by switching all VWF secretion to constitutive: AP1 is essential for WPB formation, and once ablated, the major VWF secretory pathways (basal and agonist-stimulated) are redirected towards the constitutive pathway (Lui-Roberts et al., 2005, Lopes da Silva and Cutler, 2016). These experiments (Fig. 1B-H) showed that - besides AP1 depletion - suppressing VWF levels, treating with TNF α , or growth in EBM2 medium, all increased constitutive VWF release, while the other treatments only affected basal release.

To identify common factors among the three treatments we used an RNAseq approach (Table 1-3 in the Data Supplement). No genes were found commonly upregulated in the three conditions, but two genes - Regulator of G protein signalling 4 (RGS4) and Gap junction protein 5 (GJA5) - were downregulated in si-VWF, TNF α and EBM2 (Fig. 2A,B). Since RGS4 is a cytosolic protein, already shown to be involved in negatively regulating agonist/receptor- stimulated secretion of insulin (Ruiz de Azua et al., 2010) and catecholamines (Iankova et al., 2008) we further investigated its role in VWF constitutive secretion. We first confirmed by qPCR that RGS4 mRNA was downregulated in all three conditions (Fig. 2C), but not when constitutive secretion was not affected, i.e. in nocodazole treatment, MyRIP KD, GRK2 KD and AP1 KD (Fig. 2D). Interestingly, while AP1 KD does increase constitutive secretion of VWF, it does not decrease RGS4 expression, whereas when RGS4 expression is decreased in TNF α , EBM2, VWF KD, we did not find changes in AP1 expression (Fig. 2D and Table 1-3 in the Data Supplement), suggesting that AP1 and RGS4 act through different mechanisms. Since we were not able to measure RGS4 by immunoblot using commercial antibodies, we used an indirect approach to check whether the phenotype we observed upon decreased RGS4 mRNA expression with the different treatments was due to a consequent diminished amount of RGS4 protein. We treated the cells with a NO donor (CysNO), known to induce RGS4 proteasomal degradation (Jaba et al., 2013, Hu et al., 2005), and then measured VWF secretion compared to control Cys. We noticed an increase in unstimulated VWF secretion in cells treated with CysNO (Fig. 2E), and this prompted us to conclude that the treatments causing increased unstimulated VWF secretion also affected general RGS4 expression, not just its mRNA.

RGS4 KD increases VWF constitutive secretion from the basolateral side of ECs

To verify that the decreased expression of RGS4 was directly responsible for increasing VWF constitutive secretion we used an siRNA approach (Fig. 3A). si-RGS4 affected neither the length distribution nor the number of WPBs (Fig. 3B,C), but it increased constitutive VWF secretion about two-fold (Fig. 3D). To analyse any effect on the polarity of secretion we seeded the HUVECs in transwells and collected the medium from the top well (releasate from the apical side) and the bottom

well (releasate from the basolateral side) (Fig. 3E). This revealed that the increase in VWF secretion upon si-RGS4 was mostly from the basolateral surface of the cells and was indeed constitutive, since it was blocked by BFA (Fig. 3F). To test if this effect of RGS4 KD was specific to VWF secretion, we transfected the cells with a lumGFP construct (Blum et al., 2000, Knipe et al., 2010), a cargo known to be secreted constitutively in ECs but in a non-polarised way (Lopes da Silva and Cutler, 2016). RGS4 did not affect either the amount or polarity of lumGFP secretion, suggesting that its action is at least partly specific to VWF (Fig. 3G). These data indicate that RGS4 negatively regulates the basolateral secretion of VWF from endothelial cells.

The COPB2 binding activity of RGS4 is responsible for VWF constitutive secretion

RGS4 is known to have at least two activities: to act as a GTPase activating protein (GAP) for heterotrimeric G proteins and to bind β' -COP (COPB2), a subunit of the COPI coatamer complex essential to retrograde transport from the trans-Golgi network to the cis-Golgi network and endoplasmic reticulum (Sullivan et al., 2000). In principle, either activity could affect constitutive secretion; heterotrimeric G-proteins are active at the Golgi (Giannotta et al., 2012, Cancino et al., 2014), and we have recently shown that modulating retrograde trafficking that is dependent on COP1-coated vesicle transport can affect exit from both the ER and from the TGN (Lopes-da-Silva et al., 2019). To test if RGS4 depletion affects G-protein signalling or binding β' -COP we overexpressed (OE) a GAP-dead RGS4 mutant (“N128A”) (Fig. 4A), or an RGS4 mutant with deleted (“delta 131-205”) (Fig. 4B) or mutated (“K100E”) (Fig. 4C) binding site for β' -COP. When over-expressed in identical circumstances, the GAP-dead construct had no effect on unstimulated VWF secretion, but the constructs unable to bind β' -COP were able to replicate the phenotype observed upon RGS4 depletion. These experiments suggest that RGS4 may indeed act as an indirect brake on constitutive secretion of VWF from HUVECs by interfering with the retrograde trafficking pathway that recycles machinery for re-use by the anterograde constitutive pathway.

The functional activity of VWF delivered to the subendothelial matrix is regulated by RGS4.

Our data provide evidence that RGS4 controls constitutive basolateral secretion of VWF. Since this pool of VWF is released into the subendothelial matrix and is only in contact with circulating blood when there is an injury compromising the endothelial layer, we sought to determine the functional significance of this poorly characterised pool of VWF. We therefore designed an experiment to mimic injury that would result in exposure of the subendothelial matrix to platelets under flow. We plated

si-RGS4 or control HUVECs in flow chambers, allowed them to grow to confluence, then removed the cells under flow, and passed whole blood or platelets over the exposed subendothelial matrix. After fixation and antibody labelling of VWF, we quantified by immunofluorescence microscopy both that RGS4 KD did lead to more VWF being present within the matrix (Fig. 5A), and that there was increased platelet recruitment (shown by the marker CD41), either from whole blood (Fig. 5B,C) or isolated platelets (Fig. 5D). Taken together, this suggests that by regulating secretion of VWF into the subendothelial space, RGS4 can potentially control the ability of an endothelium-denuded surface such as an injured vessel wall to recruit platelets to the injury-exposed matrix.

Discussion

VWF is released from endothelial cells into three pools, of which that located within the subendothelial matrix has only recently been at all characterised. In this work we show that the secretion of this pool of VWF is regulated, affecting the recruitment of platelets when exposed.

We previously showed that not only is this pool of VWF targeted for release towards the subendothelial space, but is constitutively secreted i.e. not stored within WPB, and thus cannot undergo the complex biogenesis of the rest of VWF. It largely remains as dimers, not forming the ultra-large concatamers that are generated within the TGN/WPB (Lopes da Silva and Cutler, 2016). This pool is not only of much lower molecular weight but also does not form the coils that support multimerization, characteristic of lumenally secreted VWF. It is not likely to be stretched under flow to optimise its ability to recruit platelets, but rather may bind to elements such as collagen within the matrix, potentially even saturating available VWF-binding sites (although under our standard growth conditions, this seems not to be the case). Nevertheless, VWF bound to the extracellular matrix was shown to be able to bind to platelets under flow (Baruch et al., 1991, Stel et al., 1985, Sixma et al., 1987, Houdijk et al., 1986). Here we have found that the constitutive release of VWF into this pool can be controlled by RGS4, a poorly characterised protein with two previously identified functions. Our experiments showed that this protein acts to modulate the constitutive secretion of VWF, likely via its ability to bind to β' COP. β' COP is essential to forming COP1 coats that support retrograde vesicular transport from the TGN all the way back to the ER. Interfering with retrograde transport, e.g. by suppressing GBF1 that controls COP1 coat assembly by Arfs1&4, leads to modulation of VWF anterograde traffic as well (Lopes-da-Silva et al., 2019). In that study, we also reported dramatic effects on WPB formation at the TGN. Inhibiting retrograde traffic reduced recycling of components essential to anterograde trafficking, causing hold-ups at ER and TGN exit, the latter leading to the formation of giant WPB. Here, we speculate that by removing RGS4, we are promoting retrograde and

anterograde trafficking, hence also constitutive VWF trafficking, without significantly affecting WPB size.

Binding of RGS4 to β' COP was shown to prevent COPI binding to purified Golgi membranes and to impair constitutive trafficking of aquaporin in LLC-PK1 cells (Sullivan et al., 2000). Consistent with this, we show that RGS4 depletion, or overexpression of RGS4 lacking the ability to bind β' COP, caused an increase in constitutive VWF secretion to the subendothelial side of endothelial cells, arguably by removing the brake on β' COP and promoting β' COP function in retrograde/anterograde trafficking. How specific to VWF this mechanism might be remains to be elucidated. Our experiments suggest that in HUVECs, RGS4 KD specifically increases VWF constitutive secretion, but more sensitive approaches (e.g. using proteomics) could be used to fully address this question.

Is this mechanism likely to be used for physiological control? One possible mechanism would involve nitrous oxide (NO), a promoter of a healthy, anti-atherogenic endothelial phenotype, also able to trigger the proteasomal degradation of RGS4 (Jaba et al., 2013, Hu et al., 2005). We speculate that when NO is induced, it will increase the secretion of VWF towards the subendothelial space, but not towards the vessel lumen into the plasma VWF pool. In this way NO will not drive the formation of a plug that could become a thrombus, because the subendothelial VWF will only become exposed when damage has already occurred. The well-known anti-platelet actions of NO can thus act in the lumen of the vessel without jeopardising a VWF-dependent haemostatic response to actual injuries that expose VWF in the subendothelial space.

This work focusses on the neglected constitutive pool of VWF that not only has a different mode of biosynthesis from the better understood WPB-associated pools, but it is also differentially targeted for secretion to the subendothelial space, and at least in part regulated by separate machinery, depending on RGS4. Further details of all the mechanisms involved in the control of this pool, which to date was believed to have little/no control, plus the functional consequences of its regulation now clearly warrant future investigation.

Materials and Methods

Cell culture

Human umbilical vein endothelial cells (HUVECs) pooled from multiple donors are from PromoCell and used within the fifth passage. Cells were cultured in M199 (Thermo Fisher Scientific, UK) or EBM2 (Promocell, Heidelberg, Germany) with 20% foetal bovine serum (Labtech, Heathfield, UK), 30 μ g/ml endothelial cell growth supplement from bovine neural tissue (Sigma-Aldrich, UK) and 10 U/ml heparin.

Nocodazole 1 $\mu\text{g}/\text{mL}$, $\text{TNF}\alpha$ (50ng/ml) were from Sigma-Aldrich, UK. Nocodazole and $\text{TNF}\alpha$ treatment were for 16 and 24 hours respectively.

siRNA transfection

We used an AMAXA Nucleofector (Lonza, Basel, Switzerland) to nucleofect siRNAs into 1×10^6 cells using two rounds of nucleofection, two days apart. After the second nucleofection, cells were seeded into a 12 well or transwell plate at a density of 1.2×10^5 cells per well to be fully confluent at assay 48h later. The siRNAs were custom synthesised by Eurofins Genomics (Ebersberg, Germany). The target sequences are:

- si-Luciferase (ctl): CGUACGCGGAAUACUUCGA
- si-RGS4 (pool of two oligos, 250 pmol each): CCUCAAGUCUCGAUUCUAU and GAAGGAGCCAAGAGUUCA
- si-MYRIP (pool of two oligos, 250pmol each): GAUGAGAUGGGCUCCGAUA and GAUAUUGAGAGCCGGAUUU
- si-GRK2 (pool of two oligos, 150pmol each): UGUCCAGUAACUUGAUUCC and GCUCGCAUCCCUUCUCGAAUU
- si-AP1 (short for si-AP1M1, 300pmol): AAGGCAUCAAGUAUCGGAAGA
- si-VWF (200pmol): GGGCUCGAGUGUACCAAAA

Plasmids

p-MYC-HIS-RGS4 and pMYC-HIS-RGS4(131-205), pCEFL-RGS4, pCEFL-RGS4 N128A were generously gifted by Dr. Kirk Druey. pMYC-HIS-RGS4-K100E was generated from p-MYC-HIS-RGS4 by using the Q5 site directed mutagenesis kit (New England BioLabs, Herts, UK). LumGFP plasmid is described here (Blum et al., 2000). Plasmids were nucleofected (2 μg or 10 μg for lumGFP) into 1×10^6 cells and cells were seeded into 12 well plate or transwell plate at a density of 1.2×10^5 cells per well to be fully confluent and assayed 48h later. When plasmids were nucleofected with siRNAs, they were added at the second round of nucleofection.

VWF secretion assay

Confluent cells were washed in serum-free (SF) medium (M199, 0.1 mg/mL bovine serum albumin (BSA), 10 mmol l^{-1} HEPES-NaOH, pH 7.4) and then incubated in SF medium for 1 hour at 37°C. The medium was collected and the cells were then lysed to determine VWF levels in both samples (releasate and lysate). Brefeldin A (BFA, 5 $\mu\text{mol l}^{-1}$ from Sigma) was added to the cells 1 hour before the assay and then present throughout the experiment. For the NO donor experiment, CysNO or

control Cys, freshly prepared according to (Cook et al., 1996) and (Smith et al., 2018), were added to SF medium at the final concentration of 200 $\mu\text{mol l}^{-1}$ to treat confluent cells. Medium was collected and cells were lysed after 1 hour incubation at 37°C.

Relative amounts of VWF were determined by sandwich enzyme-linked immunosorbent assay (ELISA) as previously described (Ferraro et al., 2016).

Transwell experiments

Cells were seeded at 1.2×10^5 cells per well onto transwell devices (cat#3460 Corning, Flintshire, UK), and assayed for secretion assay two days after, by measuring the amount of VWF in both the apical (top well) and basolateral chamber (bottom well).

lumGFP secretion assay

Cells nucleofected with lumGFP plasmid (Blum et al., 2000, Knipe et al., 2010) and seeded on transwells were analysed two days after nucleofection. LumGFP secretion assay was performed as VWF secretion assay, as previously described (Lopes da Silva and Cutler, 2016). Relative amounts of GFP were determined by sandwich ELISA using MaxiSorp plates (Thermo Fisher Scientific) coated with sheep anti-GFP (1:50,000 cat# 4745-1051, BioRad, Watford, UK), followed by blocking and incubation with samples. Plates were washed and incubated with rabbit anti-GFP (1:20,000, cat# A6455, Thermo Fisher Scientific) followed by washing and a final incubation with goat anti-Rabbit conjugated with horseradish peroxidase (HRP) (1:3000, cat# AB_2307391 Jackson Laboratories). Plates were developed with o-phenylenediamine dihydrochloride and hydrogen peroxide in a citrate phosphate buffer. Absorbance was analysed at 450 nm in a Thermomax microplate reader (Molecular Devices, San Jose, CA, US) using a kinetic protocol with a reading every 30 s for 30 min. A standard curve was made using a lumGFP nucleofected lysates serially diluted. Results are shown as percentage of secreted GFP from the total GFP (secreted plus lysate) measured in each sample.

RNA extraction, qPCR and RNAseq

RNA was extracted using the RNeasy kit (Qiagen, Manchester, UK), retrotranscribed into cDNAs by using the SuperScript III first-strand synthesis system (Thermo Fisher Scientific) and amplified using SYBR Green (DyNAmo SYBR Green qPCR Kit, Thermo Fisher Scientific) on a CFX Connect™ Real-Time PCR Detection System (BioRad, Watford, UK).

RNAseq was performed as described in (Lopes-da-Silva et al., 2019). The RNAseq raw and processed data were deposited on NCBI GEO under accession code GSE151854, (<https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE151854>).

Decellularisation and flow assay

We grew cells in Ibidi μ -slides VI (cat. # IB-80606, ThistleScientific, Glasgow, UK) until they were fully confluent. We then attached the slide to a pump system (Harvard Apparatus, Holliston, MA, USA) maintained at 37 °C onto a Zeiss Axiovert 100 inverted microscope (Artisan Technology Group, Champaign, IL, US). The cells were initially superfused with PBS using a constant wall shear stress of 2.5 dynes/cm² (0.25 MPa, 1.4ml/min), that was maintained throughout the experiment. After 1 minute the cells were superfused with NH₄OH 50 mmol l⁻¹ and Triton X-100 0.1% in PBS for 2 minutes (the decellularisation solution was adapted from (Sixma et al., 1987) and (Franco-Barraza et al., 2016)), during which we could observe the cells detaching in real time. We then superfused again with PBS, followed by either whole blood or platelets (1x10⁸/ml) in Tyrode buffer for 1 minute. After a final perfusion with PBS, μ -slides were fixed under reduced flow (0.7 ml/min) with 4% formaldehyde for 5 minutes. The μ -slides were fixed for a further 5 minutes under static conditions, washed with PBS and then processed for confocal immunofluorescence.

Blood and platelets

Blood (7ml) was drawn from local volunteers into citrate tubes and utilised within few hours. The relevant UK research ethics committee approved the work and the participant gave their written informed consent. Platelets were spare pooled platelets from the London transfusion service of the NHS.

Immunofluorescence and confocal microscopy

After fixation of the decellularised matrix, we incubated the slides with 5% BSA diluted in PBS for 30 minutes. Samples were subsequently incubated with primary antibodies diluted in 1% BSA in PBS for 1 hour. Antibodies used were: anti-VWF (1:1000) (cat. No A00A2, from Agilent DAKO, Stockport, UK), anti-CD41-FITC (1:200) (clone 5B12, FCMAB195F, from Millipore, Dorset, UK). Secondary antibodies: AlexaFluor 488, 564 and 647 (Thermo Fisher Scientific) at 1:500 dilution with PBS. Hoechst 33342 (Thermo Fisher Scientific) was used to counterstain nuclei (1: 10,000). Images were acquired using a spinning disc Ultraview Vox confocal microscope (PerkinElmer, Waltham, MA, US) with a 20x objective and 1.5x tube lens.

Statistical analysis

Statistical analyses were performed using GraphPad Prism software version 7. All graphs are represented as mean (horizontal bar) \pm S.D. Statistical significance was assessed using two-tailed unpaired Student's t test or one-way ANOVA.

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Competing interests. The authors declare no competing or financial interests.

Author contributions F. Patella designed, performed, analysed the experiments and wrote the manuscript; D. F. Cutler interpreted data and reviewed the manuscript.

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Legends

Figure 1. Conditions increasing VWF constitutive secretion in ECs. To measure and distinguish between basal and constitutive VWF secretion we deployed brefeldin A (BFA), a drug able to block constitutive secretion without affecting the release of pre-formed VWF-containing organelles (WPBs) via basal release (A). HUVECs were challenged with the indicated conditions known to increase unstimulated VWF secretion: VWF KD (si-VWF, B), nocodazole (C), TNF α (D), MyRIP KD (si-MyRIP, E), GRK2 KD (si-GRK2, F), EBM2 medium (G), AP1 KD (si-AP1, H). The amount of secreted VWF (in the absence of any stimulant) was measured by ELISA and plotted as a % of the total VWF in cells. Conditions A, C, F were further investigated because they induced an increase in constitutive secretion vs basal secretion, since that increase was blocked by BFA.

In A-G, a representative experiment with mean and S.D. is shown from N = 3 independent experiments. Student's t test was performed, *p \leq 0.05, **p \leq 0.01, ***p \leq 0.001, n.s. = not significant.

Figure 2. Identification of a regulator of VWF constitutive secretion in ECs. The comparison of the transcriptome (made by RNAseq) of the previously selected conditions (si-VWF, EBM2, TNF α) relative to their respective controls enabled us to identify a putative regulator of VWF constitutive secretion. The Venn diagrams show the number of down-regulated (A) and up-regulated transcripts (B). RGS4 and GJA5 were the only transcripts found significantly regulated (under-expressed) upon all three treatments (A,C), while in the other treatments where constitutive secretion was not affected (GRK2 KD and MyRIP KD) or in AP1 KD (an independent regulator of constitutive secretion), RGS4 mRNA was upregulated (D), as measured by qPCR. In C,D, a representative experiment with mean and S.D. is

shown from N = 2 independent experiments. One-way ANOVA with Dunnett's multiple comparisons test, ****p < 0.0001.

A NO donor (CysNO), which affects RGS4 at the protein level, triggering its degradation, increases unstimulated VWF secretion compared to the Cys control (E). A representative experiment with mean and S.D. is shown from N = 3 independent experiments. Student's t test was performed, *p ≤ 0.05.

Figure 3. RGS4 KD increases VWF constitutive secretion from the basolateral side of ECs. We successfully reduced RGS4mRNA in HUVEC with siRNAs (A). A representative experiment with mean and S.D. is shown from N = 4 independent experiments. Student's t test was performed, ****p < 0.0001. By doing high throughput imaging we did not observe changes in the length of WPBs (the area covered by the longer WPBs, those greater than 2µm, is used as a proxy for length) in the RGS4 KD cells (B), or in the number of WPBs per cell (C), n = 8 wells, for each well the mean of 9 fields of view were analysed. Student's t test, n.s.= not significant. We did measure, by secretion assay followed by ELISA, an increase in constitutive VWF secretion (D). The plot shows means and S.D. of a representative experiment from N = 3 independent experiments. Student's t test, ***p ≤ 0.001.

Plating cells in transwells (E-G) enabled us to better dissect the route of the increased constitutive VWF secretion upon si-RGS4 (F), which was mainly released towards the basolateral side of the ECs. Using a construct expressing a constitutively secreted protein (lumGFP) we did not measure changes in its secretion upon si-RGS4 (G). In F,G a representative experiment with mean and S.D. is shown from N = 3 independent experiments. Student's t test was performed, ***p ≤ 0.001, n.s.= not significant.

Figure 4. The COPB2 binding activity of RGS4 is responsible for VWF constitutive secretion. To understand which of the two known functions of RGS4 is responsible for controlling constitutive VWF secretion we expressed and compared the effects of mutated and wt RGS4 constructs. Expressing a GAP dead mutant (N128A) does not change the amount of unstimulated VWF secretion (A), whereas expressing a construct lacking the binding site for COPB2 (delta 131-205) or mutated in the β' COP binding activity (K100E) results in an increase in unstimulated VWF secretion (B,C). A representative experiment with mean and S.D. is shown from N = 3 independent experiments. Student's t test was performed, ***p ≤ 0.001, *p ≤ 0.05, n.s.= not significant.

Figure 5. Constitutive basolateral VWF secretion provides a functional pool of VWF in the subendothelial space. The removal of ECs exposed the subendothelial matrix and the VWF bound to

it. Upon decellularisation, more VWF is bound to the extracellular matrix in RGS4 KD cells (A,B). Scatter plots present mean and SD of a representative experiments of N=3 independent experiments. Each symbol is the VWF fluorescence intensity (integrated density) of a field of view. Student's t test was performed, ****p < 0.0001. Confocal microscopy shows VWF (magenta) and platelets (green). Scalebar is 50 µm (B). When we superfused whole blood (B,C) or isolated platelets (D) over the decellularised matrix we could see more platelets adherent in the RGS4 KD compared to control. In C,D a representative experiment with mean and S.D. is shown from N = 3 independent experiments. Each symbol represents the area covered by platelets (n=35 fields of view). Student's t test was performed, ****p < 0.0001.

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Figure 1

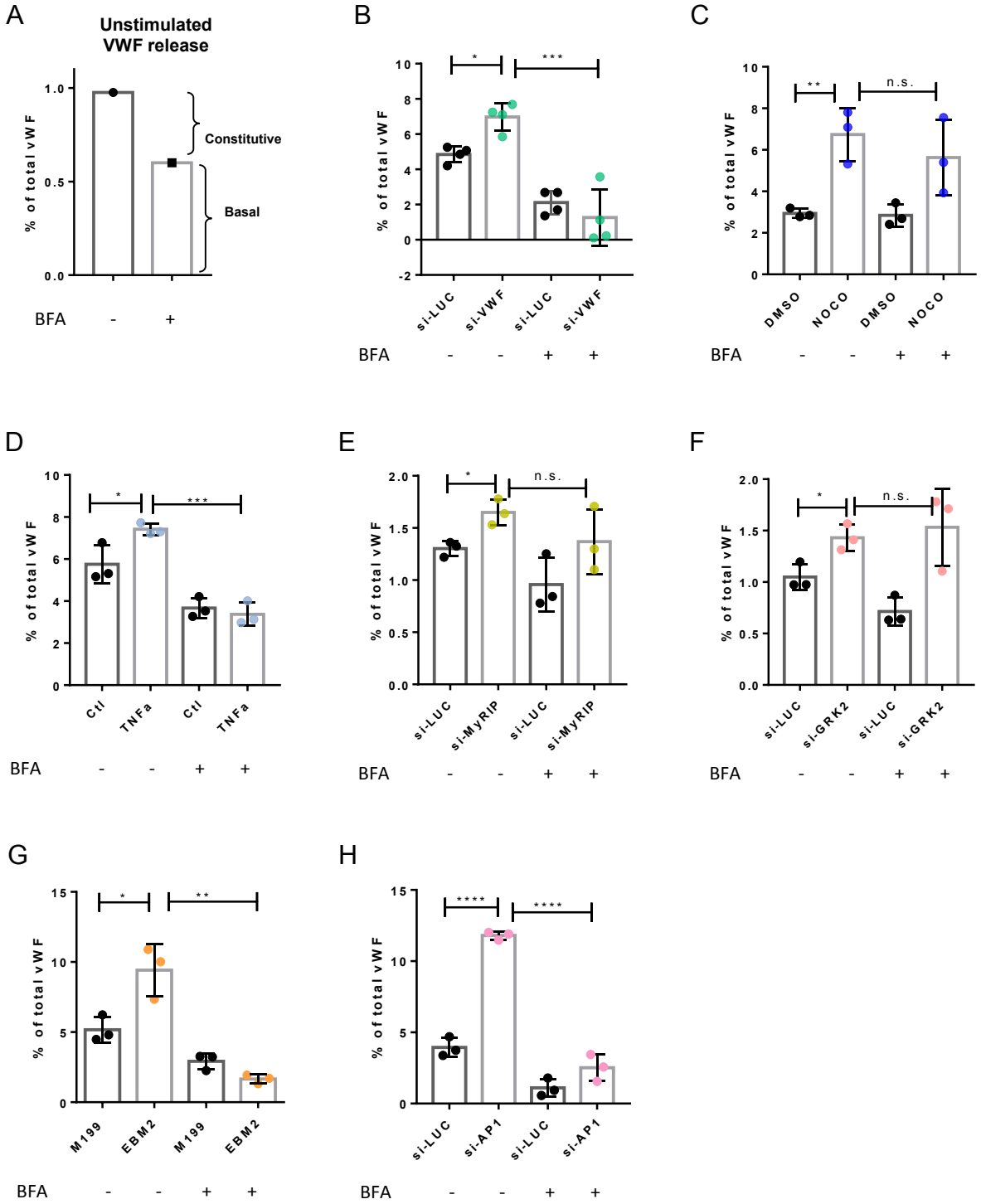


Figure 2

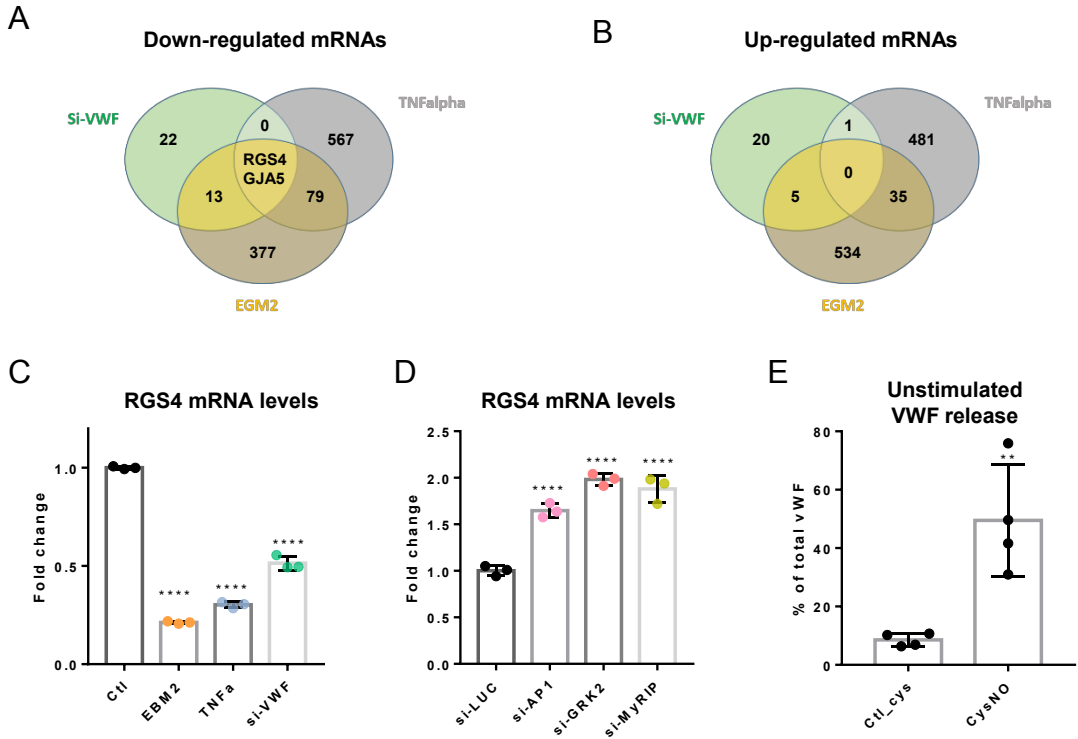


Figure 3

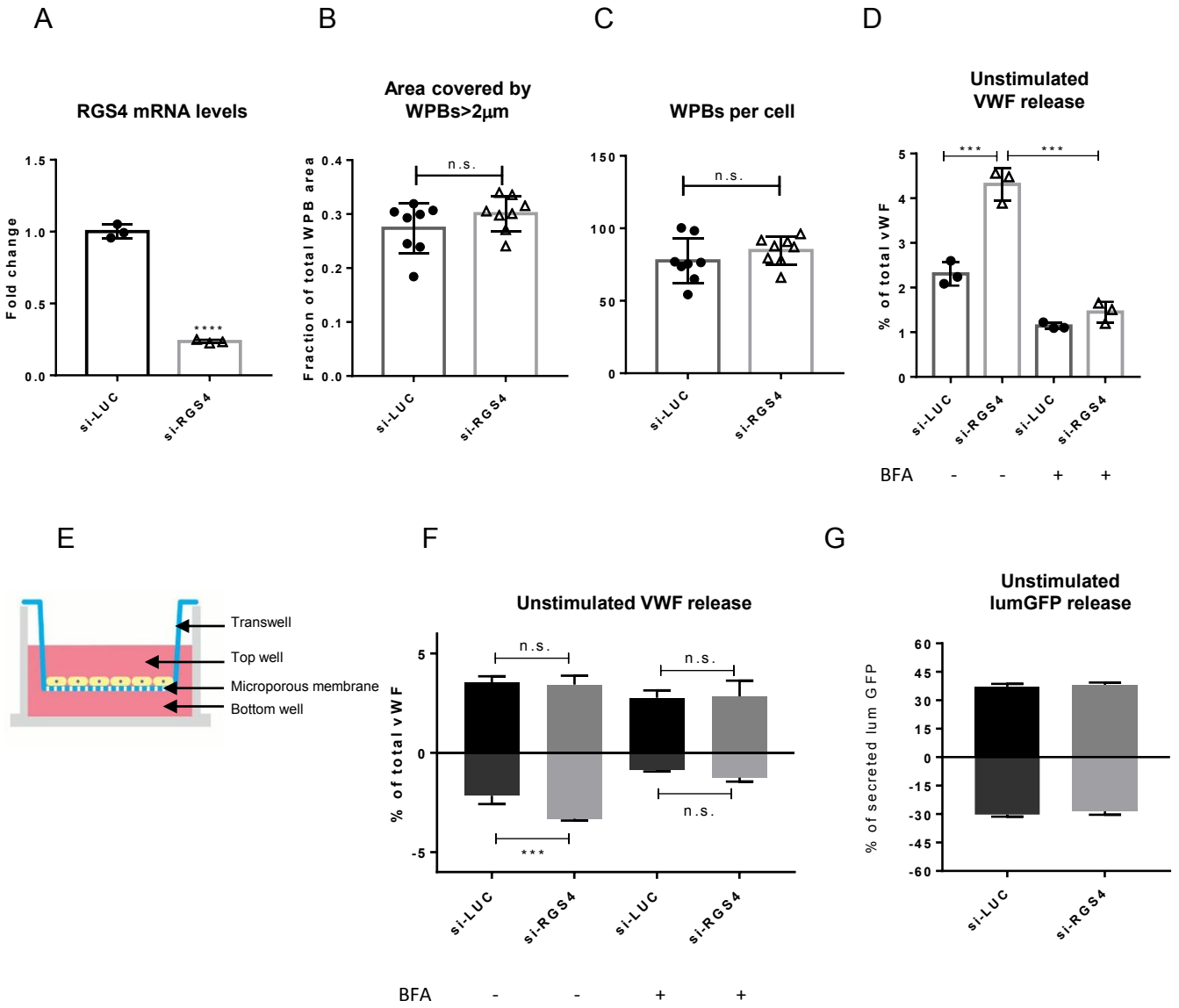


Figure 4

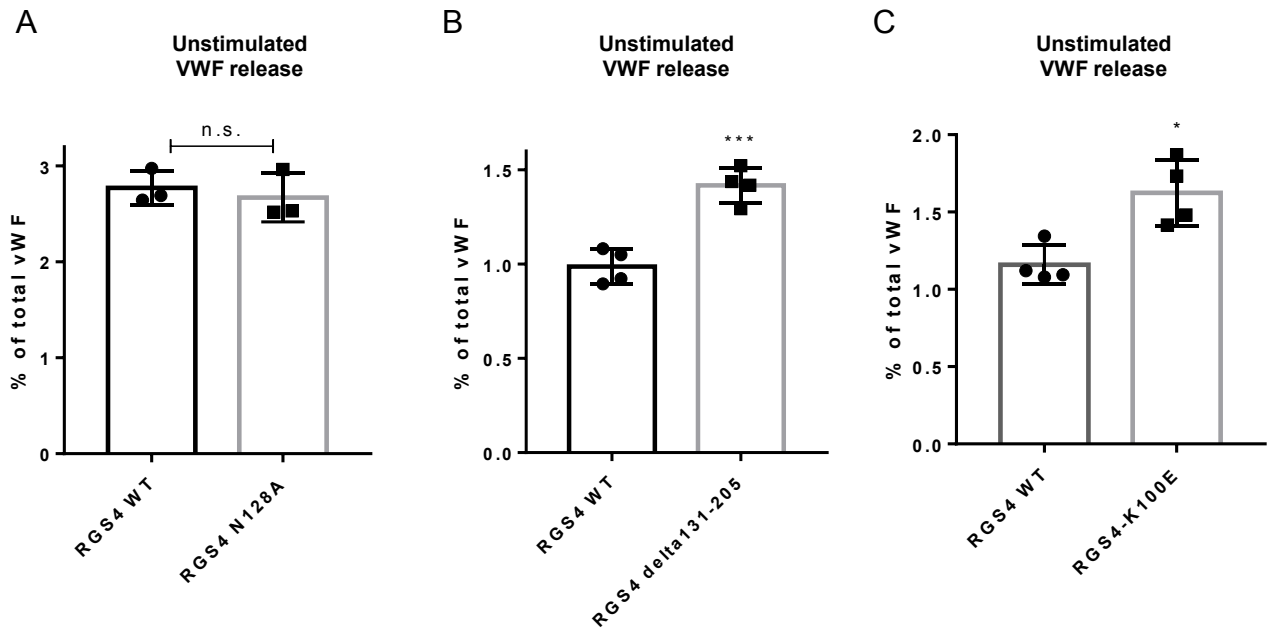
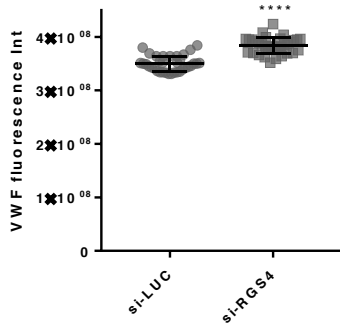
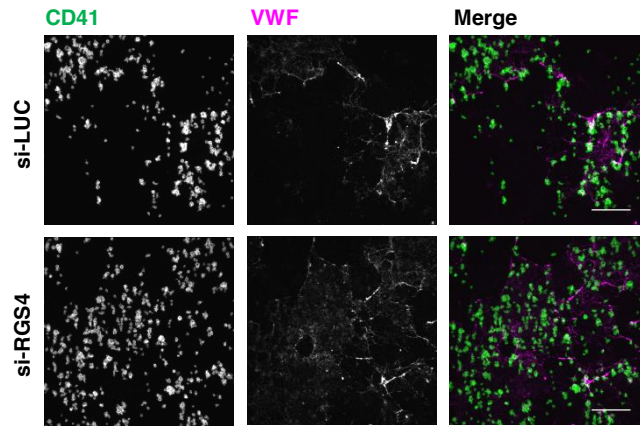


Figure 5

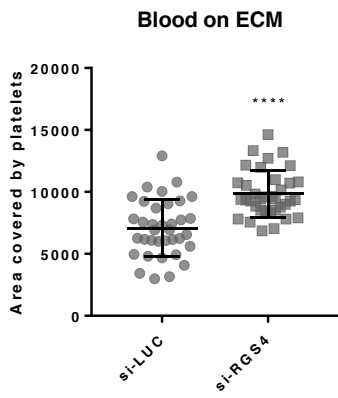
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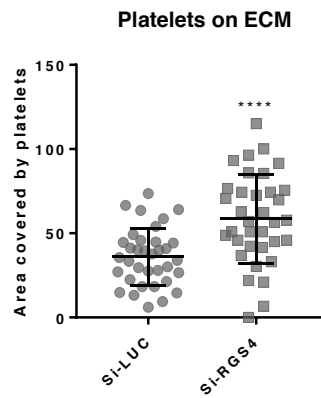
B



C



D



Supplementary tables

Legends

Table 1. List of up- and down-regulated genes in cells untreated (mock) or treated with siRNA against VWF (si-VWF), as measured by RNAseq. Statistical significance was tested by ANOVA. p-values and fold changes are shown.

Table 2. List of up- and down-regulated genes in cells untreated (ctl) or treated with TNFalpha as measured by RNAseq. Statistical significance was tested by ANOVA. p-values and fold changes are shown.

Table 3. List of up and down-regulated genes in cells grown in M199 compared to EBM2 medium as measured by RNAseq. Statistical significance was tested by ANOVA. p-values and fold changes are shown.

Table 1. List of up- and down-regulated genes in cells untreated (mock) or treated with siRNA against VWF as measured by RNAseq

Gene Symbol	p-value (Mock vs. siVWF)	Fold Change (ctl vs. siVWF)
CYP4X1	0.00128566	-32.1563
LOC643923	0.000519006	-19.4815
CNFN	0.000964625	-11.1371
ANKRD20A12P	0.00062099	-10.3165
APOL4	0.00148339	-8.58715
LOC100507291	0.000442632	-7.43832
PRSS35	0.000770663	-7.40778
IGFBPL1	0.00128278	-6.59354
APCDD1L-AS1	0.00142889	-4.99945
LINC00565	4.88E-05	-4.89898
CARD9	2.16E-05	-4.87164
C2orf88	0.000849527	-4.72221
HAP1	0.000335618	-4.51894
KLF3-AS1	0.000338168	-4.1572
PAQR6	0.000976936	-3.88911
FBXL16	3.22E-06	-3.05408
GPR160	0.000377077	-2.64192
CXCL6	0.000652395	-2.63637
LHX6	0.000528466	-2.58556
RASD1	0.000287297	-2.36891
ELMOD1	0.000121234	-2.17379
COL3A1	0.000575704	-2.17183
ANKRD36B	0.00102598	-2.16352
GCHFR	0.00014855	-2.11456
LIN7A	0.00011959	-2.10782
EBF1	0.000816184	-2.00191
ADIRF	5.06E-06	2.02722
ZFHX3	9.19E-05	2.02833
TXNIP	1.60E-05	2.03547
LAMB3	7.34E-05	2.04878
ANKRD1	0.000992435	2.04936
KLF4	0.000269786	2.08009
CTGF	0.000811784	2.08347
SCUBE1	0.000867245	2.08419
ADAMTS1	7.29E-05	2.09546
VEGFC	0.000103077	2.14703
GDF6	0.000378046	2.20022
SERPINE2	2.27E-05	2.20359
LOX	0.00016042	2.26419
SERPINE1	0.000594502	2.29084
PXDN	8.61E-07	2.3106
KRT19	0.000910754	2.40345
RGS4	6.03E-05	2.47053
ADAMTSL1	0.000220098	2.48149
EDIL3	2.29E-06	2.52136
TNFRSF6B	0.000165117	2.57799

NPTX1	0.000125057	2.70179
RECK	8.03E-05	2.77112
IL33	0.0010349	2.89954
POU2F2	0.000624745	2.91843
INHBA	0.00059908	3.2168
TGFB2	0.000369859	3.26826
KRT7	0.000112856	3.29242
PCDHB16	0.000828325	3.42038
SYT5	0.0013411	3.43382
TAGLN	0.000587612	3.76832
IGFBP3	5.63E-05	3.90883
PQLC3	0.000119829	3.99947
VCAN	0.00088607	4.43357
CPA4	0.000160024	6.77985
GJA5	0.000685553	9.08647
TMEM229B	0.000341185	9.22005
VWF	6.76E-07	13.5887

Table 2. List of up- and down-regulated genes in cells untreated (ctl) or treated with TNFalpha as measured by RNAseq

Gene Symbol	p-value vs. TNFalfa)	(ctl Fold Change (ctl vs. TNFalfa)
SELE	4.58E-13	-14391
VCAM1	6.61E-11	-4342.49
CX3CL1	1.67E-09	-1280.88
BIRC3	8.00E-11	-483.03
SLC8A3	3.89E-05	-304.933
CXCL8	4.26E-10	-257.274
TRAF1	3.50E-14	-246.029
ICAM1	2.19E-11	-241.616
RRAD	0.000188288	-225.489
C2CD4A	8.47E-10	-215.628
CD69	1.29E-08	-179.45
EBI3	3.72E-08	-174.031
CXCL3	1.99E-10	-172.838
CSF2	1.36E-07	-164.829
CCL2	1.90E-08	-152.254
NPTX1	4.81E-11	-147.952
F3	1.33E-07	-124.958
TNFRSF9	4.27E-11	-124.45
FGF18	6.03E-06	-114.36
RCSD1	0.000189104	-112.405
TFAP2A	7.97E-06	-89.1999
SLCO5A1	1.87E-07	-78.6055
TNFAIP3	5.57E-09	-72.3292
TNIP3	3.37E-05	-65.3831
C2CD4B	3.40E-10	-62.6488
BDKRB2	2.50E-08	-60.2935
CXCL10	0.000171889	-57.0595
IL18RAP	0.00137286	-56.7891
RND1	1.10E-09	-55.9531
NR4A3	1.45E-05	-49.8989
CXCL1	4.69E-09	-46.3026
FSTL3	2.05E-08	-45.914
LIF	1.29E-06	-45.2702
CXCL2	1.38E-09	-45.1224
TNFRSF11B	1.60E-10	-45.1049
CXCL5	3.41E-08	-44.8565
IL21R	5.23E-06	-42.9436
CD83	1.06E-08	-39.2605
RBM47	6.06E-05	-36.6718
CCL7	5.42E-08	-36.5141
PHOSPHO1	1.58E-05	-35.405
TNFAIP2	4.83E-12	-34.1591
IL18R1	8.81E-08	-33.1038
S100A3	1.00E-06	-31.6479
IL1A	2.31E-06	-30.1706
SLC7A2	2.92E-07	-29.7861
CXCL6	4.65E-07	-29.7164

FGF5	1.07E-05	-27.8231
LTB	2.42E-08	-25.7863
FLJ31104	0.000236579	-25.7692
CLEC2D	4.87E-10	-25.7622
NUAK2	1.92E-10	-25.1883
C8orf4	4.35E-11	-25.0895
NKD2	1.42E-07	-24.4359
SRSF12	2.49E-10	-24.2085
RELB	1.02E-09	-24.2041
LINC01215	9.21E-06	-23.4624
NOD2	8.04E-06	-22.226
MIR3142HG	2.21E-09	-21.453
PRRG4	0.000848892	-21.3132
WNT11	0.00489735	-20.4614
PTGS2	7.74E-09	-20.0075
ATP2C2-AS1	2.47E-06	-18.7725
TMEM132E	0.00480721	-18.4099
MIR155HG	3.44E-11	-17.7297
OLFM2	1.20E-07	-17.5102
SAMD11	8.63E-06	-17.4897
KCNN2	4.78E-07	-17.1038
ABTB2	2.69E-07	-17.0941
CLDN14	0.00240248	-16.9007
NFKBIA	1.32E-10	-16.1166
ENKUR	1.94E-05	-15.9888
CEBPD	1.20E-08	-14.6732
ATF3	5.46E-08	-14.117
SHH	7.15E-05	-13.8853
IDO1	6.38E-05	-13.726
HAS2	6.68E-08	-13.7155
PAPLN	0.000548653	-13.392
GREM1	0.00219646	-13.049
CLDN1	0.0106373	-13.0285
CITED4	7.09E-06	-12.7065
DUSP8	1.26E-07	-12.5073
CEMIP	4.04E-08	-12.4038
ACHE	3.74E-08	-12.3933
GLI2	1.60E-08	-11.9988
UNC5B	6.34E-10	-11.8875
RTP4	0.00722697	-11.7805
GBP5	0.000548364	-11.688
GCNT4	0.00830559	-11.4997
KYNU	2.53E-07	-11.3703
ETV7	0.000211639	-10.963
LINC01679	0.00346675	-10.7398
COL5A3	0.00161157	-10.5853
GPR68	3.65E-07	-10.561
NFKB2	5.42E-09	-10.4858
SOD2	3.90E-08	-10.1086
LOC101929319	0.000133442	-10.1001
RIPK2	1.52E-12	-10.0582
FAM46A	0.000114235	-9.84967

CSF1	9.60E-11	-9.84254
C1QTNF1	2.59E-07	-9.83086
JUNB	6.59E-09	-9.70404
ICOSLG	8.46E-10	-9.67019
KIAA1644	0.000173486	-9.60703
WWC1	2.59E-06	-9.40729
TMEM217	2.16E-07	-9.31756
BCL2A1	1.58E-07	-9.17935
LINC00598	0.000403937	-9.05212
ICAM5	7.92E-06	-8.94009
TIFA	7.25E-10	-8.76034
HIVEP2	7.38E-07	-8.52391
MSX1	2.03E-08	-8.50782
CASC10	9.66E-09	-8.41462
PRRX1	7.42E-06	-8.36487
LRRC4	2.23E-06	-8.32337
KRT81	0.00311927	-8.07335
JHDM1D-AS1	2.85E-07	-8.04097
LOC100126784	3.73E-08	-7.90815
BMPR1A	9.99E-07	-7.88982
GDF7	8.39E-06	-7.78587
LAMA1	0.00248467	-7.77198
NFKB1	1.30E-10	-7.70255
TNFRSF4	0.000162011	-7.64907
PTAFR	1.27E-05	-7.64778
RASGEF1B	0.000203754	-7.6143
SLC31A2	1.19E-09	-7.53492
DAPK2	4.34E-06	-7.46893
ATOH8	3.14E-07	-7.3788
MAP3K8	4.22E-05	-7.34232
SDC4	1.60E-09	-7.29823
ELOVL7	6.03E-05	-7.24936
TNFAIP8	2.22E-09	-7.12031
TCF7	6.76E-07	-7.10587
SMAD6	3.46E-07	-7.01084
PDE5A	1.59E-05	-7.00281
IL4I1	5.13E-07	-6.98953
NFKBIE	4.28E-09	-6.97406
DLX2	0.00308679	-6.87674
NCF4	0.00104238	-6.83695
NOCT	2.98E-09	-6.7266
NKX3-1	6.98E-09	-6.71461
ACKR3	1.24E-12	-6.70325
CHRM4	0.00702778	-6.60148
JAG1	1.81E-09	-6.53684
PCDH19	1.06E-06	-6.50047
EFNA1	2.31E-09	-6.42533
CTHRC1	2.90E-07	-6.37049
SLC6A4	0.00183283	-6.34654
PTGFR	0.0122276	-6.32527
ICAM4	0.00148247	-6.26812
RCAN1	1.02E-08	-6.23981

HLA-F	0.000454645	-6.21855
IRAK2	4.37E-11	-6.20185
P2RY6	0.00181886	-6.19913
LINC02206	0.00725245	-6.12144
KCNMB1	3.79E-06	-6.00989
LOC339166	0.00615733	-5.9965
PDZRN3	6.49E-06	-5.98816
PLLP	2.93E-07	-5.97196
WNT5A	1.33E-07	-5.82118
RASL10A	0.00332827	-5.74416
LOC100130417	0.0031131	-5.70041
PDZD2	8.68E-08	-5.69449
CHSY3	7.24E-08	-5.58646
COL7A1	3.12E-05	-5.5655
GRAMD3	0.00255968	-5.54304
SLC12A7	5.44E-09	-5.53639
SARDH	0.00249661	-5.53301
IRF1	1.37E-09	-5.51371
SLC2A6	2.81E-08	-5.44636
TAP1	2.61E-09	-5.4023
IL6	2.39E-08	-5.36013
SERPINB2	6.95E-10	-5.31739
NCOA7	9.01E-09	-5.3115
DKK2	0.000277458	-5.24483
COL9A2	0.00938079	-5.2051
SSTR2	0.00107541	-5.13349
COLEC10	0.00222835	-5.12082
IFIH1	3.82E-06	-5.06464
GFPT2	5.58E-11	-4.95327
LAMC2	2.09E-09	-4.94452
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IL7R	1.03E-07	-4.90919
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HEY2	6.71E-06	-4.89532
FAM129A	1.05E-05	-4.89036
BCL3	9.12E-07	-4.86367
LOC101928123	1.48E-07	-4.83165
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LOC101926963	5.77E-05	-4.76851
CTSS	4.87E-08	-4.72141
PITPNC1	1.76E-07	-4.65607
TNIP1	9.24E-10	-4.59563
SAT1	4.07E-11	-4.5314
FOXF1	7.49E-07	-4.52207
RASGRP1	0.00668898	-4.51557
SAV1	7.87E-10	-4.5053
IL32	5.84E-08	-4.48093
BHLHE41	0.00016609	-4.46523
GBP4	1.85E-07	-4.44697
HEY1	4.18E-08	-4.38273
BIRC2	7.06E-11	-4.372
CXCL11	0.000126874	-4.33859

FGFR3	1.17E-05	-4.33647
LOC105374952	3.34E-07	-4.32635
WNT4	5.19E-06	-4.32609
GNG4	0.00268274	-4.3222
ZFP36	8.92E-07	-4.22855
SAMD4A	1.30E-07	-4.2163
YPEL2	1.18E-07	-4.20922
RHOB	1.18E-08	-4.20587
PFKFB3	2.97E-12	-4.19411
PMAIP1	1.29E-09	-4.17959
MMP10	4.97E-09	-4.10621
MMD	5.16E-10	-4.10282
DNM3OS	5.78E-10	-4.09375
TSPOAP1-AS1	0.00356049	-4.09159
CYLD	4.23E-08	-4.07922
ZSWIM4	2.17E-08	-4.04725
GAREM1	1.98E-06	-4.04214
TMIE	0.0134343	-4.03824
MYB	8.64E-05	-3.97709
CYP1B1	7.39E-06	-3.97475
IL15RA	7.25E-09	-3.9376
NEDD9	5.32E-06	-3.93689
SEMA7A	0.000704679	-3.90701
CNKSR3	1.76E-08	-3.89929
TUBB2B	2.34E-06	-3.87269
ETS1	4.34E-09	-3.87201
PLAU	1.20E-07	-3.8504
TANK	7.64E-09	-3.82414
SERPINE1	3.28E-10	-3.82222
APOL3	1.60E-08	-3.81792
DDX58	4.53E-09	-3.79768
GNAL	0.00375846	-3.79765
ISG20	2.66E-07	-3.79233
COL27A1	2.09E-06	-3.78351
LOC101929709	0.000889678	-3.77915
TNC	0.00178928	-3.77588
BMP2	2.14E-12	-3.75511
MAP3K1	5.67E-07	-3.69781
TTC39A	0.00566956	-3.6971
ABCG1	1.42E-08	-3.67598
DAAM1	3.27E-08	-3.66857
IL15	5.92E-05	-3.65754
DNAJB9	2.36E-07	-3.65235
SLC41A2	5.47E-05	-3.55662
SLC25A34	0.00461017	-3.55267
FILIP1L	3.57E-06	-3.55163
IFNGR1	7.59E-07	-3.54518
ART4	2.13E-06	-3.51847
LGI2	0.00669115	-3.51086
ZFHX2	4.03E-06	-3.50788
BAMBI	0.000124402	-3.50372
UNC13A	0.00254532	-3.48141

FGFR2	0.011097	-3.48091
ITGAV	1.00E-06	-3.47281
GADD45G	0.000197172	-3.47173
KCNQ3	0.0012451	-3.46288
IFNGR2	7.65E-11	-3.45041
KCTD16	1.07E-10	-3.44433
LYPD6	7.60E-10	-3.42542
PSMB9	0.00196667	-3.42422
BPGM	1.63E-08	-3.41685
CBR3	4.17E-06	-3.41072
HIVEP1	3.18E-05	-3.37772
KLF7	1.02E-08	-3.37656
PARP14	1.56E-05	-3.37528
APOL6	1.12E-05	-3.34803
SIK2	1.83E-06	-3.3285
OSGIN2	6.92E-10	-3.32096
SHISA2	7.17E-07	-3.3118
DUSP10	3.42E-06	-3.31053
NAV2	9.34E-06	-3.28818
ZC3H12A	1.38E-05	-3.28611
CLIP2	6.41E-08	-3.28577
NFKBIB	7.68E-09	-3.27696
SGK1	5.48E-07	-3.27149
SQSTM1	2.60E-08	-3.24483
MOB3C	2.28E-06	-3.24115
NLRP3	0.00243036	-3.23467
TNFAIP1	3.99E-12	-3.22665
STAT5A	2.32E-07	-3.22008
HRH1	1.63E-08	-3.19691
PDE9A	8.83E-06	-3.19456
ID2	5.47E-05	-3.17696
GCH1	1.78E-05	-3.1724
HTR7	0.00824472	-3.13139
EGR1	1.01E-05	-3.07874
HLA-B	1.27E-08	-3.02235
HELZ2	5.16E-06	-3.01499
CBLN3	0.00181391	-3.01373
TGFB2	2.17E-05	-2.98788
ZNF71	3.60E-07	-2.98187
A4GALT	3.34E-07	-2.97384
FAM118A	7.60E-06	-2.9721
CDC14A	1.08E-05	-2.96279
B4GALT1	7.62E-09	-2.93752
RFLNA	6.11E-08	-2.92416
HOXA4	7.16E-07	-2.91604
HSPB8	2.79E-07	-2.88963
DNAJA1	2.11E-08	-2.88765
NFKBIZ	7.23E-05	-2.88235
MT2A	1.07E-05	-2.87662
JAM2	1.88E-08	-2.86695
CCIN	0.0027305	-2.86462
ITGA8	0.00664938	-2.85246

NNMT	1.10E-07	-2.84993
GBP3	4.59E-07	-2.84891
APOL2	2.26E-09	-2.84369
NINJ1	4.44E-08	-2.84117
KIAA1147	1.50E-06	-2.82151
F2RL1	3.96E-09	-2.81835
SLC38A2	4.71E-09	-2.81791
UPP1	9.66E-07	-2.81076
KCNK1	2.32E-07	-2.80487
LRRC4B	0.000234101	-2.80058
SH3TC1	1.12E-08	-2.79907
DSEL	3.33E-08	-2.79154
LOC102724064	0.00744694	-2.77776
PRDM8	0.000461548	-2.77662
HOXB9	0.00018712	-2.77331
CSF2RB	1.28E-06	-2.76281
PSTPIP2	3.96E-06	-2.75893
VEGFA	4.71E-07	-2.75501
SLC16A9	0.00125635	-2.7521
GBP1	1.64E-05	-2.72487
MDGA1	0.000612948	-2.7239
ZDHHC23	0.00014715	-2.72345
NOV	0.0112496	-2.72095
APLF	5.79E-05	-2.71661
CSRP2	1.65E-05	-2.70966
TMCC2	1.05E-05	-2.70106
CXXC5	8.51E-08	-2.70104
VASN	0.0130709	-2.69852
FAM110A	5.11E-05	-2.69188
SLC15A3	0.00459876	-2.67305
RFX2	1.20E-06	-2.66873
GATA6	3.14E-08	-2.66583
ZXDA	2.01E-06	-2.66419
PANX1	1.05E-07	-2.66403
SLC7A11	8.71E-07	-2.63759
C3orf52	0.000136346	-2.62371
ATP13A3	4.01E-06	-2.61561
UBE2QL1	0.00315685	-2.61067
HINT3	2.41E-06	-2.5999
SGPL1	1.35E-09	-2.59894
LINC01138	0.00590041	-2.59346
F2RL3	0.000228196	-2.59321
IL3RA	2.14E-07	-2.58874
CAB39	2.06E-10	-2.58668
KLHL15	2.58E-07	-2.5639
DTX3L	1.93E-06	-2.56326
LOC101927974	0.00380678	-2.56136
HES4	1.74E-05	-2.55421
TLN2	3.66E-05	-2.55304
ZCCHC12	0.0112375	-2.54454
PTHLH	0.000320594	-2.54329
HDX	1.29E-05	-2.54317

CD58	1.14E-05	-2.53868
JAK3	0.00341533	-2.53712
MCTP1	2.53E-06	-2.53616
CLEC1A	8.52E-08	-2.53481
IPPK	1.12E-05	-2.52695
STK4	3.87E-07	-2.52694
ARHGAP31	7.73E-07	-2.52675
TBC1D10A	7.88E-05	-2.51928
ELL2	3.16E-06	-2.509
KCNK3	0.0132974	-2.49784
MAP2K3	9.10E-08	-2.49686
HTR2B	3.10E-05	-2.48994
ZBTB5	2.20E-07	-2.48023
TMEM200B	0.000910077	-2.47867
NPAS3	4.58E-05	-2.47123
RAPGEF4	1.57E-05	-2.46818
LINC00622	0.00481878	-2.46346
EXT1	9.74E-10	-2.46152
PVR	1.25E-08	-2.45599
GORAB	1.10E-06	-2.45399
LIPG	2.60E-08	-2.45106
ARNT2	0.00206207	-2.44446
OPTN	1.90E-09	-2.43726
NAB2	2.60E-05	-2.43644
CA13	1.88E-06	-2.43115
RBM38	5.35E-06	-2.42718
ZBTB10	6.21E-07	-2.42566
BTN2A2	6.21E-07	-2.42209
ID3	7.32E-06	-2.41783
TRIM47	6.20E-08	-2.41321
SPHK1	1.69E-06	-2.40786
IL1RL1	8.17E-08	-2.40247
SAMD14	4.53E-07	-2.3942
RGPD4	0.00692057	-2.39353
SERPIN8	1.56E-07	-2.39106
ADGRG1	4.62E-09	-2.39013
KLF5	5.13E-05	-2.38735
TGFBR1	2.35E-06	-2.37897
VDR	5.63E-06	-2.37071
STX11	6.94E-07	-2.36944
ZNF140	3.06E-07	-2.36879
CD200	4.42E-07	-2.36643
IRGQ	3.20E-07	-2.36372
ADAP1	0.0126901	-2.35354
PMEPA1	7.75E-08	-2.3478
TUBB2A	2.24E-06	-2.34666
WHAMMP3	0.00106757	-2.34459
DAPK3	1.73E-07	-2.33848
HLA-H	5.74E-05	-2.33658
HERPUD1	2.01E-07	-2.33583
BSDC1	1.61E-08	-2.33317
OSGIN1	3.95E-06	-2.33088

MAFF	6.04E-09	-2.32805
SLFN5	3.23E-05	-2.31916
ZC3H12C	2.84E-06	-2.313
ARID5A	4.22E-05	-2.30954
LOC100288203	9.84E-07	-2.30274
ZNF697	1.51E-06	-2.30182
NR3C1	4.21E-07	-2.29297
RHOF	9.29E-06	-2.2919
TAF4B	0.000721071	-2.28883
YIPF5	1.45E-08	-2.28592
CYP27C1	0.000740449	-2.28198
GALNT4	0.000117732	-2.28043
IKBKE	1.40E-07	-2.27836
SLC35G2	1.69E-05	-2.27584
SMURF1	8.58E-07	-2.27142
SELENOM	9.39E-05	-2.26908
P2RY1	0.000646727	-2.26661
HDAC9	0.00136608	-2.26213
TMEM86A	7.65E-05	-2.26114
IER5	2.20E-06	-2.26001
GABARAPL1	7.48E-08	-2.25258
TRAF3	8.16E-09	-2.25078
RELT	8.40E-06	-2.24968
TAB2	1.16E-07	-2.24077
TIAM2	3.77E-06	-2.23941
SHB	1.57E-06	-2.23656
HLA-L	0.00918639	-2.22938
RPS6KA6	9.90E-05	-2.22493
TNFSF15	0.000139586	-2.22224
RHEBL1	0.00568696	-2.21987
RADIL	0.00364561	-2.21844
CFLAR	4.09E-09	-2.21133
C14orf132	3.65E-08	-2.21126
RNF19B	1.11E-06	-2.21109
RNF24	5.97E-06	-2.20564
LOC284454	0.000108551	-2.20294
TRIM36	0.000323087	-2.19982
FAM110B	0.000357979	-2.19536
SPNS2	3.06E-08	-2.19378
DHX58	0.00155631	-2.178
NFATC1	1.30E-07	-2.17607
PTPRK	1.21E-05	-2.16631
RAPGEF5	1.91E-05	-2.16615
PTX3	2.61E-06	-2.16504
PRKCD	3.69E-06	-2.15944
ZC3H7B	8.15E-09	-2.15802
PNRC1	1.65E-06	-2.15572
VPS37A	5.70E-06	-2.15567
LACC1	2.05E-05	-2.15291
IRAIN	0.000119138	-2.15076
KIF13A	2.97E-06	-2.15021
SERTAD1	5.50E-06	-2.14563

SLC37A1	7.76E-05	-2.14319
PKD1L1	0.0071954	-2.12649
BAZ1A	1.65E-07	-2.12598
RIN2	2.72E-09	-2.11575
TRIP10	1.12E-07	-2.11503
ARHGEF40	2.78E-05	-2.11155
TLDC1	5.38E-08	-2.10086
THUMPD3-AS1	6.89E-05	-2.09854
IPMK	4.96E-05	-2.09607
SMOX	4.74E-05	-2.09389
SPECC1	1.29E-06	-2.09301
FZD6	1.06E-06	-2.08889
RNF145	6.59E-08	-2.08668
NUDT4P1	2.07E-05	-2.08547
FMNL3	1.80E-05	-2.08218
HHEX	2.96E-06	-2.08071
MSANTD3	1.04E-07	-2.07973
FOXL1	0.000265564	-2.07834
TAF1C	2.18E-06	-2.07826
SMAD3	3.24E-08	-2.0733
ITSN2	2.96E-07	-2.07136
STARD10	5.80E-05	-2.06766
SNAI2	0.0106922	-2.06107
NAV3	2.93E-05	-2.05793
ZHX2	4.54E-07	-2.05615
CSRNP1	1.94E-05	-2.05567
INSIG1	0.0013672	-2.05555
CDC42EP2	1.75E-05	-2.05398
EPS8L1	6.65E-05	-2.05256
BHLHE40	8.82E-05	-2.05136
INHBA	8.68E-08	-2.04917
AP5Z1	8.00E-07	-2.04862
ARHGAP21	4.97E-05	-2.04549
C21orf91	8.40E-05	-2.04461
TMEFF1	0.000173179	-2.04225
LIMD2	6.66E-06	-2.04143
SMAD9	6.10E-05	-2.02897
DUSP16	0.000153598	-2.02865
RASGRP3	2.18E-06	-2.02562
ST5	0.000174509	-2.02271
APBA3	2.67E-06	-2.02086
FNDC3B	2.47E-05	-2.01786
ANKLE2	1.02E-08	-2.01709
CHN2	1.84E-06	-2.01671
WTIP	8.36E-06	-2.01348
UHRF1BP1L	1.28E-05	-2.01178
CTSK	0.0036962	-2.00909
KLF6	1.32E-09	-2.00788
PDGFB	1.89E-05	-2.00538
EVA1C	2.87E-06	-2.00491
PLPP3	2.44E-09	-2.00466
LAMB3	1.31E-06	-2.0039

CCNG2	4.23E-06	-2.00282
FAM20C	0.000100115	-2.00053
LETM2	0.00590117	2.00059
CABLES1	6.31E-05	2.00151
TMEM223	0.00874524	2.0052
TSHZ3	0.000383885	2.00939
LINC01116	0.000137874	2.01011
B3GNT8	4.57E-05	2.01103
TFEB	0.00273953	2.0136
CYP2R1	0.0076581	2.01406
BCL2L1	9.33E-06	2.01429
LOC729603	0.0135032	2.0164
VLDLR	0.000346172	2.01669
PPP2R5A	1.96E-06	2.01919
ZBED3	0.00668349	2.01955
RANBP6	1.12E-06	2.02032
AFF1	1.66E-05	2.02099
ADAMTS9	6.64E-05	2.02101
C15orf52	4.91E-05	2.02133
KIAA1462	2.79E-05	2.02227
ZNF813	0.00150708	2.02277
LRRC20	6.40E-07	2.02395
RTKN2	0.0103579	2.0253
PATZ1	7.46E-05	2.02709
SYNGAP1	7.37E-06	2.02817
ZNF395	2.58E-05	2.03088
AFAP1L1	3.58E-06	2.03186
SCN5A	0.00102553	2.03187
TRANK1	0.00882106	2.03334
CDCA7L	5.03E-06	2.03347
FAM214A	0.000101282	2.03361
BORCS5	0.000160202	2.03476
SPRED3	7.79E-06	2.0348
LINC02407	0.00138906	2.03562
ZFYVE28	0.000245912	2.03651
ANKRD28	4.90E-07	2.0366
RPRD2	6.75E-06	2.03824
PIM2	0.00207029	2.04036
LIMD1	3.49E-07	2.04183
LYN	4.81E-05	2.04223
TIGD2	0.00141619	2.04348
NEU3	0.00998184	2.04357
MARS2	0.0027541	2.04802
ZNF252P	8.20E-05	2.04971
SAMD10	0.00919362	2.05043
NAIP	0.00385707	2.05056
FDXACB1	0.00354034	2.05058
C22orf34	0.00272028	2.05229
PRKAB1	8.40E-05	2.05256
ANGPTL4	3.45E-06	2.05305
TM4SF18	2.99E-06	2.05341
NIPAL1	0.000665263	2.05468

RRN3P2	0.0129486	2.05667
HOXA11	0.000447851	2.05699
GPR155	0.00492357	2.05753
DPF1	3.09E-05	2.05801
PPP1R3E	0.00665331	2.0598
ZNF561-AS1	0.0037384	2.06017
ARHGEF39	0.000343482	2.06045
KIAA1161	0.000125337	2.06118
SLC25A25-AS1	0.00668295	2.06308
LINC00476	4.43E-05	2.06326
ZNF467	6.02E-05	2.0642
ZNF215	0.00432189	2.06518
ARHGAP23	1.91E-05	2.06866
SLC43A1	1.34E-05	2.07121
ELK3	1.12E-07	2.07207
PAXIP1-AS1	0.00670334	2.07348
ZKSCAN4	0.00422341	2.0762
LYVE1	0.00194093	2.07662
TMCC1-AS1	0.00581506	2.07808
BARD1	0.00291646	2.07897
TRIM46	0.00120944	2.0797
TRIB3	8.80E-06	2.08182
WDFY4	5.58E-05	2.08189
ZNF577	0.014027	2.08257
ZNF354C	0.000217158	2.08269
TSC22D3	0.0054488	2.08494
ADAT2	0.000156445	2.08606
STARD9	0.00262019	2.08644
LPAR1	0.0107829	2.08758
NSD1	0.00155466	2.08831
PDP2	0.000275535	2.09033
LOC100133091	0.00280858	2.09192
ELMOD2	8.65E-06	2.09211
ORC1	0.00884455	2.09362
XKR8	1.70E-05	2.09424
TSNARE1	0.0021819	2.09432
MAGEF1	0.000342153	2.09509
LOC100129034	3.54E-06	2.09946
EFNA5	2.53E-05	2.09999
SCAMP5	0.000851707	2.10107
TRPS1	0.00588904	2.10327
KIAA0754	0.00991632	2.106
TSC22D4	3.42E-05	2.1068
LRRC8D	1.35E-06	2.1071
PFKFB4	0.00535566	2.1072
LOC105376575	0.00619287	2.10971
ZNF518A	0.000461366	2.11011
AFG1L	0.000185291	2.11036
NLRC3	0.000877432	2.11156
APH1B	2.93E-05	2.11161
KBTBD6	0.000321329	2.11378
XYLT2	0.000119403	2.11466

PLS1	6.59E-05	2.11548
PTGIR	8.43E-05	2.11822
PRX	0.00249398	2.12301
ZNF391	0.000799507	2.12419
ZNF782	0.00681096	2.12574
ZNF438	4.31E-05	2.12715
LOC730102	0.000409575	2.12786
KCNMB4	0.00616833	2.12802
SLC16A7	0.000308004	2.13037
CHAMP1	9.51E-05	2.13198
MAP1A	0.000110896	2.13301
CDCA7	9.71E-05	2.13448
PNMA8A	0.0044357	2.13556
EGFL7	1.37E-06	2.13689
PAR6A	0.00366984	2.14185
ZFP14	0.000997334	2.14242
DDR2	0.000701051	2.1445
SLC44A3	0.00223183	2.14498
PAIP2B	0.00559481	2.14695
ZNF700	0.00264281	2.14901
CACFD1	0.00107679	2.14928
UBL4A	9.10E-05	2.15373
PTCD2	0.00141323	2.15502
EPHA4	9.32E-05	2.15512
GPAM	0.000157851	2.15548
FAM227A	0.0025458	2.15604
HSPA12B	3.24E-06	2.16153
ZNF619	0.00129364	2.16281
IQSEC1	3.41E-06	2.16282
LDLRAP1	1.14E-05	2.16572
HOXD4	0.00076564	2.16607
MID2	1.29E-05	2.16782
MMACHC	0.00504868	2.16887
ZNF521	1.23E-06	2.16904
SWSAP1	2.89E-05	2.17116
NFIA	5.16E-07	2.17133
CROT	0.00565561	2.17284
PTPRH	0.000496326	2.1748
LOC101928120	0.00354606	2.1775
PDZD7	0.00124161	2.18227
ELL3	0.00930885	2.18619
MYLIP	1.38E-05	2.18682
RASSF9	0.00206381	2.18913
ACBD4	0.00883112	2.19157
PDIK1L	0.000148467	2.19227
ALKBH2	0.00220971	2.19527
RREB1	9.85E-07	2.19583
NT5DC3	0.00251743	2.19594
PRTG	0.000424638	2.19928
IFFO1	2.39E-05	2.20123
SOCS1	0.0058145	2.20229
CASP8	0.000268581	2.20715

LRR75A	7.21E-05	2.20746
HOXD8	4.59E-05	2.20868
PHACTR1	0.00135125	2.21073
ZNF846	0.000790585	2.21219
OAS1	0.00352019	2.2148
DHFR2	0.0019645	2.21613
TEAD4	1.76E-05	2.21728
EIF3J-AS1	0.0137438	2.21831
PRR19	0.00280469	2.22112
MID1	0.000382067	2.22263
SASH1	3.36E-07	2.22275
TBC1D31	0.000811956	2.22388
SKP2	8.71E-05	2.22429
EME1	0.00259915	2.22951
PELI2	4.84E-05	2.23083
PLEKHA5	1.02E-05	2.23086
LOC100132077	0.0125888	2.23157
ZCCHC24	0.000682932	2.23435
FAM185A	0.00961933	2.23453
ZNF503	3.13E-05	2.23612
STX3	3.02E-06	2.23826
MYZAP	3.62E-05	2.24054
KIAA1958	0.000110266	2.2422
SNHG20	0.00686966	2.2434
FUT1	0.000160002	2.24918
EHD3	0.00144849	2.24936
SLC2A10	1.23E-05	2.24945
FBXL4	0.000610903	2.25435
S1PR3	8.51E-06	2.25475
PRMT9	0.00105463	2.25675
JADE1	7.50E-05	2.25707
RAB36	0.000246971	2.25839
ARL4C	1.73E-05	2.26615
ABCG2	9.76E-06	2.26701
MIR503HG	0.00253191	2.26873
SLC16A13	0.00842743	2.26897
PET117	0.0014318	2.27156
PTPN22	0.00159317	2.27614
KIAA0040	6.31E-05	2.27802
BRCA2	0.00114199	2.28005
MRPS31P5	0.000712881	2.28052
SETD6	0.000637924	2.28246
LMCD1	0.00444156	2.28497
ZHX3	5.40E-05	2.28575
VMAC	0.00724281	2.28581
PEAR1	1.28E-07	2.29842
ULBP1	0.0059318	2.2995
LYRM9	0.00173299	2.30037
IRAK3	0.000933185	2.30328
NFIB	2.22E-06	2.30362
MKNK2	2.56E-06	2.30734
EEF2K	1.09E-05	2.30908

SDAD1P1	0.00341942	2.31111
DISC1	4.81E-05	2.31166
INPP5D	3.79E-08	2.31875
HIC1	4.89E-05	2.31923
LFNG	0.000141077	2.32338
TMEM121	0.00742241	2.3248
CFAP44	0.00192789	2.33056
LINC02035	0.000651937	2.34206
MET	3.25E-06	2.34293
SYNC	1.09E-05	2.34385
PLEKHG1	4.04E-08	2.34571
HOXD3	0.00906429	2.34802
KAT14	0.000343374	2.34908
AQP3	0.00963457	2.35051
SLC1A1	4.23E-08	2.35061
CFAP97	4.96E-07	2.35158
STON1	9.40E-06	2.35572
NLRX1	0.00826029	2.35854
FZD8	1.33E-05	2.35931
SNX18	5.41E-07	2.3632
SPAAR	1.32E-05	2.36429
ZBTB18	5.30E-05	2.36886
CNNM2	0.00172511	2.37012
LOC105376114	0.00782078	2.37266
PRAG1	3.25E-06	2.37814
ZNF589	0.000241579	2.37871
LIPE	0.00333159	2.38488
TSPAN5	4.21E-07	2.38525
TRIM2	0.000160876	2.3853
KANK2	6.03E-07	2.38545
PQLC2	0.000283526	2.38791
ST8SIA4	0.000141644	2.39092
ZBTB42	0.00291368	2.39676
ANKS1A	0.00018322	2.40163
INPP1	5.77E-06	2.40174
SLC7A5	6.40E-10	2.40466
HOXA1	0.00496467	2.4048
EHHADH	0.0109575	2.40704
BCORL1	7.40E-06	2.40791
OSBPL7	0.000398109	2.41041
SLC45A3	3.09E-06	2.41196
CTTNBP2	0.00144345	2.41308
TGFBR3	0.000100206	2.41363
DCLRE1A	0.000475856	2.41452
DISP1	0.00249931	2.4206
ARHGEF15	6.28E-07	2.42142
WFS1	6.62E-07	2.43131
RAB3D	8.94E-08	2.4332
FLJ20021	0.00756647	2.43325
SLC25A42	0.00458925	2.43636
THAP10	0.00547901	2.44317
ERG	3.10E-08	2.44367

RHOBTB2	1.49E-05	2.44384
SLC26A6	0.000155089	2.44462
SCN8A	9.28E-05	2.44701
PLCXD1	5.37E-05	2.44993
AJUBA	2.59E-05	2.45159
FANCE	0.000350962	2.45432
ZNF57	0.00379272	2.45804
CARD8	3.27E-09	2.47363
ASB13	8.45E-05	2.47496
NOTCH1	1.98E-07	2.47715
PAQR7	1.23E-06	2.47885
FAM124B	9.65E-08	2.47942
SNPH	5.80E-06	2.4812
FAT4	2.48E-05	2.48633
HEXIM2	0.000424712	2.48661
B3GALT4	0.00417007	2.48778
RNF144A	1.84E-06	2.49054
RNF152	0.00480449	2.49071
LOC100506022	0.0088335	2.49433
DLG3	0.00194261	2.49958
PTCH1	5.31E-06	2.50143
TMEM170B	0.0013454	2.50604
TBKBP1	3.49E-05	2.51043
DHRS13	0.00911919	2.51082
CREB3L1	0.00345101	2.51243
FAM50B	0.00335894	2.51414
CCND2	1.70E-05	2.51742
MEDAG	1.59E-06	2.52128
NYNRIN	0.000452727	2.52151
ZNF367	5.78E-05	2.52575
MPZL2	0.000217783	2.52972
RFXAP	0.000274	2.53442
TSHZ1	1.42E-06	2.53957
POLG2	9.53E-05	2.54342
RASSF7	3.53E-05	2.54648
PXMP4	0.00190499	2.54693
TNRC6C	5.68E-06	2.55153
GPB1	2.00E-05	2.55297
ABHD15	1.37E-05	2.5534
F8A1	0.000482445	2.55441
MEF2C	6.55E-05	2.556
KCNK6	5.07E-05	2.56066
MAP3K12	0.000232065	2.56191
THEMIS2	0.00406105	2.56304
FAM13A	0.000655377	2.5782
CCDC125	0.00333579	2.58031
PPM1J	0.00981286	2.5824
HTATSF1P2	0.0038168	2.58483
GDF3	0.000349838	2.58761
WDR81	3.28E-07	2.588
CHST15	9.15E-05	2.59488
IER5L	0.000447859	2.59684

METTL7A	0.00613379	2.599
JDP2	2.66E-05	2.59905
FAM217B	2.13E-05	2.60094
UBXN2B	1.27E-05	2.60206
MYO5C	0.00287252	2.61205
LINC00639	0.0050766	2.61367
DNM1	0.00496611	2.61845
ZNF608	2.71E-05	2.61936
GNAI1	2.58E-05	2.62449
PPARGC1B	0.0017977	2.6247
ZBTB25	0.00870573	2.62596
HAGLROS	0.00678222	2.62725
TMEM171	2.16E-06	2.62908
CTDSPL	6.18E-06	2.63437
RUNX1T1	1.94E-07	2.6398
PARP16	0.000278291	2.6443
CCDC96	0.000328231	2.64549
PRKAA2	0.000303921	2.64696
PCDH12	0.00743079	2.6481
KLF8	0.000172298	2.65139
SHROOM3	9.98E-05	2.65282
ISL1	0.00139803	2.65949
E2F2	0.000508352	2.66615
TGFBRAP1	5.09E-07	2.66732
GCNT2	9.03E-05	2.6723
PNMA2	1.73E-06	2.67615
OCLN	0.000322729	2.67642
C3orf70	0.000887741	2.67857
NR1D1	1.77E-06	2.68621
CAVIN2	1.09E-05	2.69235
FBXO41	0.000368004	2.69285
LMTK3	0.00306598	2.69502
TNFRSF1B	7.77E-05	2.69977
PGPEP1	4.04E-05	2.70256
OSGEPL1	0.0007152	2.70298
MAGEE1	0.00257414	2.71352
SPIN4	0.00013074	2.72052
HS3ST1	0.00349639	2.7207
SETBP1	3.53E-06	2.73031
KIAA0895	0.00712226	2.73135
TMEFF2	0.0107209	2.73862
RGCC	0.00819785	2.74194
ZFP36L2	5.39E-07	2.74747
SORBS1	0.00195218	2.74847
ZBTB12	0.000435353	2.75104
SSR4P1	0.0126268	2.761
ZMYM3	1.55E-06	2.76641
FILIP1	0.000498447	2.76765
BDNF	1.26E-05	2.77019
C3orf58	4.62E-06	2.77324
ZNF280B	0.00116555	2.77586
KIAA0922	2.99E-05	2.7849

TTC30A	0.000267213	2.78652
CYP2S1	4.50E-05	2.79546
FAM117B	3.03E-05	2.80239
LINC00265	0.00490599	2.80563
KBTBD3	0.00102704	2.80624
TNS2	5.92E-07	2.80647
EMILIN2	0.00749556	2.80978
MARVELD2	0.00146853	2.81624
LOC105376554	0.0117626	2.81638
LINC00346	4.39E-05	2.82006
FRY	1.33E-06	2.82013
DUSP19	0.000251732	2.82571
ACKR4	0.00113856	2.82577
PLPP7	0.00158109	2.82653
POU4F1	0.00129523	2.82953
THAP8	0.00611659	2.83164
ATP6V0E2-AS1	0.0079083	2.83419
VIPR1	5.48E-05	2.83933
SSFA2	6.33E-08	2.84561
FOXO6	0.00115041	2.84975
ST3GAL5	6.76E-06	2.85933
TRAF3IP2	6.46E-06	2.8609
PALD1	0.000711368	2.86962
ARHGAP28	5.11E-07	2.87098
STYK1	2.00E-05	2.87959
CGN	0.0121316	2.88466
SYNE3	8.52E-05	2.88476
DLL3	0.013478	2.88499
NRSN2-AS1	0.000279624	2.90205
JARID2	3.44E-06	2.91237
MTUS1	1.95E-07	2.91376
SAMD13	0.00210908	2.92502
RARA	7.47E-07	2.92888
SHE	1.57E-07	2.93131
ALX1	0.00475367	2.93248
PTPN4	0.000239822	2.93338
SLC37A2	8.76E-05	2.94215
MLYCD	3.46E-05	2.94231
MBLAC2	0.000101162	2.94578
HTR7P1	8.47E-06	2.94623
LRP5L	0.00258912	2.95283
MPZ	0.00972471	2.95496
RNASEL	0.00370146	2.9559
TIRAP	0.00125462	2.96132
HOXB8	1.98E-05	2.97481
SOX12	4.10E-07	2.98398
KBTBD7	0.00944094	2.98574
KIAA1107	0.0056958	2.99529
ZNF30	0.00146867	3.00557
FBXO36	0.00119709	3.00669
DNAJB4	8.97E-09	3.0104
FIGN	0.0010808	3.02189

TRIM6	0.00996705	3.02447
CAMKK1	0.000126001	3.02665
PDE3A	1.05E-06	3.03873
MEIS1	0.000214188	3.03908
MRVI1	0.0015561	3.04359
IKZF2	0.00108035	3.04788
PARGP1	0.00724024	3.05007
SPEG	0.000288598	3.05307
SPTB	0.00938578	3.05381
ZC3HAV1L	0.000771793	3.05901
TRAM2	1.87E-07	3.06091
APOLD1	8.53E-06	3.0784
FZD5	0.000715147	3.07941
PROB1	0.000509802	3.08247
LOC101927759	0.000939306	3.09585
HOXD9	0.00826584	3.09972
EVI2B	0.00273938	3.10243
LINC00847	0.00174781	3.12252
CBX7	0.00141122	3.15441
DNMT3B	6.12E-06	3.17507
MTHFR	4.01E-05	3.17647
LOC100506178	1.85E-05	3.19033
ETV1	6.34E-06	3.20317
RIN1	4.60E-05	3.20925
FGF16	0.000904978	3.20996
GDPGP1	5.53E-05	3.2104
LGR4	2.94E-05	3.22741
SALL2	0.00359268	3.23623
RGS4	1.52E-08	3.25209
CARD10	7.18E-07	3.26049
ZNF703	1.36E-05	3.26092
DDIT4L	0.00272903	3.265
CBX3P2	0.000542705	3.26788
FAM221A	0.00487793	3.27412
LRRC37A4P	0.00483998	3.28348
MPZL3	5.52E-06	3.28477
ZNF792	0.000166352	3.287
USP51	0.0034578	3.31915
THSD1	9.69E-11	3.34352
ARHGEF28	2.14E-08	3.34534
ORAI3	5.04E-06	3.3486
TTC30B	0.00898626	3.35064
C20orf204	0.000243207	3.35088
MAP2K6	1.02E-05	3.35209
LOC155060	0.00549289	3.35991
SLC2A12	0.000706338	3.36509
TTYH2	1.50E-05	3.37242
PAX9	0.000208274	3.39876
GBA2	1.18E-06	3.41119
MYCL	1.68E-06	3.41237
TFAP4	2.34E-05	3.41631
SNRK	6.38E-09	3.4253

TRIM45	0.00147369	3.43059
PKP2	0.00424143	3.43227
AQP1	0.00287447	3.45185
ZCCHC2	9.06E-07	3.47727
APLN	4.68E-08	3.48733
IL6R	0.00128778	3.49428
LOC105370941	0.00660736	3.4956
B3GALNT1	8.33E-08	3.49782
HRCT1	0.00264008	3.50752
OTOGL	0.000442664	3.51269
CAND2	0.000691477	3.52853
RBM43	0.000111325	3.5301
FAM86JP	0.00469951	3.53423
NCALD	0.00935106	3.55491
FAM117A	0.000119009	3.56532
SH3RF2	0.00025319	3.56867
TRPV1	0.00807802	3.57811
C1orf226	3.42E-05	3.60226
BMS1P5	0.00073832	3.62392
FRMD3	3.55E-07	3.63336
DMRTA1	0.000228627	3.63359
SLAIN1	0.000118552	3.63554
KIF19	0.000438808	3.64338
PALMD	1.39E-06	3.65373
ZNF382	0.00367723	3.6653
ZMYND8	4.67E-10	3.6752
TMEM246	0.00287027	3.68421
KSR2	0.000131318	3.69561
ITPKB	1.05E-06	3.69651
LINC01123	0.000155774	3.70373
ADGRE5	6.08E-05	3.70503
MN1	1.72E-05	3.7062
SH3TC2	0.000155143	3.73497
CCDC113	0.00413986	3.73645
VSIG2	0.00790698	3.74351
RGS14	0.00019156	3.75367
FAM174B	1.89E-08	3.76133
ATP8B1	5.43E-09	3.79826
LOC101928489	0.00109956	3.80704
LENG8-AS1	0.0136864	3.85305
C22orf46	3.22E-05	3.85474
E2F8	3.26E-06	3.87131
CROCCP3	0.000329922	3.90275
PLEKHF1	0.000133017	3.90636
KCNJ12	0.00333369	3.91827
ABHD6	8.76E-05	3.93032
TRIB2	1.02E-05	3.93097
EPHX4	9.96E-05	3.95867
MAST3	0.000229093	3.9751
KCNN3	0.00599546	3.97551
ZNF710-AS1	0.00196811	3.97597
PLEKHH3	1.70E-05	3.9796

KCND2	0.0140845	3.98343
C22orf29	1.84E-08	4.00331
STEAP2	0.000310913	4.00749
FAM212B	1.70E-07	4.04255
PRRT1	0.00852572	4.07337
NHSL2	0.00180018	4.07528
CCDC88C	1.28E-07	4.07933
USP2	0.00392016	4.08602
FIRRE	0.000938436	4.10976
FUT8-AS1	7.99E-06	4.18807
KIAA1211L	5.60E-05	4.19269
GNA14	0.000757672	4.19701
USP44	0.00386245	4.22816
PRICKLE1	5.10E-08	4.27582
CTH	0.00563092	4.29684
RRN3P1	0.00417485	4.29847
MERTK	1.00E-06	4.3066
CALCRL	2.42E-08	4.3624
MAMSTR	0.000532123	4.36534
C10orf10	0.000313323	4.36796
LOC143666	0.00999315	4.36996
CLEC4GP1	4.48E-06	4.3759
LINC02273	0.0135637	4.38396
GSTT2	0.0128767	4.42593
JPH3	0.00417361	4.42812
AVPI1	0.00229632	4.46876
GCNT1	4.77E-06	4.50003
ZNF488	0.00114503	4.54185
GFOD1	0.000602589	4.54649
AGFG2	5.52E-07	4.56065
NR3C2	1.30E-07	4.57898
LOC100506127	0.00458011	4.59186
TMEM37	0.000322764	4.65427
ABCG4	0.00751912	4.70232
PIK3CG	1.34E-05	4.72197
RTN4R	0.00841972	4.83353
ADAMTS9-AS2	0.0142419	4.88171
SLC46A3	1.34E-06	4.96694
SH2D3C	5.57E-08	4.96752
FLRT3	0.000117829	5.01421
FAXDC2	0.000184078	5.02022
LOC100132249	0.0010369	5.02665
LRFN1	0.0016798	5.08426
LOC284023	0.00452159	5.11797
BRSK1	0.00679354	5.12374
ADRB2	7.86E-05	5.13779
SMIM3	0.00220441	5.18098
SERTAD4	4.79E-05	5.18558
TBX1	1.91E-06	5.19311
PCDH9	1.09E-05	5.26409
RCOR2	0.00213346	5.26737
ACER2	8.37E-05	5.29801

HTR1B	5.74E-07	5.29864
RAB11FIP1	5.17E-05	5.33887
LNX1	0.000322915	5.34508
ANKRD35	0.00463554	5.3983
PCDHAC2	0.000101059	5.40626
PSG4	0.0132282	5.46701
RASSF10	0.000320023	5.47207
NYAP1	1.46E-05	5.49222
JPH1	0.00217882	5.54919
FBXO43	0.00280468	5.65954
RGS7BP	9.49E-05	5.69083
SEMA4D	3.91E-06	5.69564
GDF5	0.011783	5.75995
STC1	4.90E-08	5.7648
ARHGEF3	3.70E-08	5.79621
KLHL3	5.62E-06	5.864
SESN3	2.97E-06	5.8965
CXADR	4.11E-06	5.90466
CLSTN2	0.000616117	5.9133
DBP	0.00736122	5.92836
FAM110D	0.000341145	5.93917
SLC46A1	6.14E-05	5.95428
SSTR1	0.00094043	5.96264
LONRF3	0.00301229	6.04832
DLL4	2.23E-06	6.05219
GJA5	3.06E-05	6.08154
FAM184A	0.00967676	6.1073
GPAT3	1.72E-08	6.24767
AATBC	1.39E-06	6.2557
APCDD1	2.68E-05	6.37208
TMCC3	1.01E-07	6.50763
LINC00857	0.006252	6.64204
DLL1	1.27E-05	6.64802
NOS1AP	1.58E-05	6.68498
PPFIBP2	6.49E-06	6.73395
ZNF366	1.69E-05	6.87464
PDE7B	5.95E-07	6.89125
TRERF1	2.07E-06	6.95618
WNT9A	0.00710578	7.06401
THBD	2.14E-07	7.1497
KLLN	0.00448072	7.1787
ARRDC3-AS1	0.0116609	7.18471
SRL	0.00674943	7.19612
KCNJ15	0.00765122	7.21462
FAM212A	2.33E-06	7.37395
KLF2	4.64E-07	7.48237
GRAMD1B	0.000103145	7.84381
PCAT1	0.00516156	7.86476
RNF125	6.92E-06	7.92817
PDK4	0.00017983	7.9827
DUSP4	6.80E-11	8.09577
GPR146	0.00583363	8.17964

SSTR5	0.00363461	8.23733
CMKLR1	0.00394958	8.2921
KIT	0.00361002	8.56246
POF1B	0.00861839	9.04084
NHLRC4	0.00294529	9.32285
KCNS1	0.00210461	9.36025
LHX6	0.00618233	9.37001
KCNIP3	0.00414348	9.85933
XIRP2	0.000835066	10.3495
NRROS	0.000443131	10.4932
CYP26B1	4.90E-05	10.5168
FAM78A	1.87E-08	10.6464
LINC00957	0.0136721	11.535
CREG2	0.00476448	11.5755
SOX18	1.02E-08	12.7883
RHPN1-AS1	0.000205548	13.3406
DTX4	0.00536555	13.406
LINC00211	0.00898361	13.586
GUCY1A2	0.00826862	13.7048
ADAMTS15	0.000104458	14.0614
ADM	4.50E-06	14.2314
PPP1R3C	0.00164453	14.3336
SYT16	0.000881004	15.0809
GPR19	0.000175273	15.7581
ANKRD34A	0.00293405	20.193
NLRP12	0.0117896	23.2097

Table 3. List of up and down-regulated genes in cells grown in M199 compared to EBM2 medium as measured by RNAseq

Gene Symbol	p-value vs. EBM2)	(M199 vs. EBM2)	Fold Change (M199 vs. EBM2)
A2M	5.72E-09		-67.7171
SPARCL1	0.00223966		-47.4361
NUDT16P1	0.00273107		-42.6537
PON3	0.00087549		-26.7554
COL1A2	1.50E-05		-26.4502
PKHD1L1	0.00278496		-26.4258
CC2D2B	0.000315182		-24.3566
C6orf141	0.00065719		-21.7413
CD34	4.58E-09		-20.2779
PCDHB3	0.0103131		-19.0987
KIF17	2.05E-05		-18.9269
KCNE3	5.81E-07		-18.2862
ABCB1	4.10E-06		-18.1147
TEC	0.000278508		-16.854
GALNT15	2.34E-07		-16.8057
BCO1	0.00238153		-15.7692
LOC100506083	0.00294184		-15.6257
NPR1	3.76E-08		-15.2405
RNF138P1	0.000893278		-15.0951
IGFBP1	0.00454524		-13.759
GPC5	6.49E-06		-13.5971
NUPR1	1.81E-05		-12.9176
AFAP1L2	7.54E-07		-12.8802
FAM228A	0.00726467		-12.5557
KCNQ1	0.00776196		-11.8786
PCDHB7	6.31E-06		-11.1712
SBK3	1.21E-06		-10.7541
KCTD21-AS1	0.00158533		-10.392
CLEC10A	1.22E-05		-10.2318
FBXO32	4.58E-08		-10.1138
GPIHBP1	0.00140883		-10.1069
FADS2	2.57E-07		-9.65557
BCL2L10	0.0106481		-9.63271
PCYT1B	1.33E-05		-9.17076
KCNJ16	0.00322863		-9.01545
MEOX2	1.37E-07		-8.98077
SIM1	0.00330886		-8.91848
SCD	2.64E-08		-8.80634
SLCO2A1	9.18E-10		-8.65295
PIPOX	0.00135824		-8.58611
APOC1	0.00255458		-8.48204
PAPLN	0.00859005		-8.47665
HMGCS1	1.75E-11		-8.30596
N4BP2L1	0.000408995		-8.29395
	Sep-04	0.00129341	-8.25904
CELSR3	0.000329934		-8.13494

PNPLA3	2.74E-06	-8.10779
MAP2	7.86E-07	-7.95943
ITGA10	1.76E-09	-7.9119
GIMAP5	0.00857795	-7.81853
LOC101928126	0.00028642	-7.76013
NAT8B	0.0084505	-7.59335
MMP28	7.91E-05	-7.49516
SPRY1	1.62E-07	-7.43441
KIAA1614	2.12E-05	-7.22671
H19	4.67E-05	-7.17545
INHBB	0.00030327	-6.94201
HIF3A	9.84E-05	-6.80685
SMPDL3B	0.00069805	-6.64482
GDF7	3.00E-05	-6.5994
AREG	0.0108608	-6.55972
ACSS1	1.26E-08	-6.46168
APOL4	3.60E-05	-6.44682
LINC00865	0.00538743	-6.36078
CLDN3	1.42E-05	-6.33405
EMBP1	0.000129404	-6.29304
ENPP2	0.00142128	-6.2451
ANKRD2	0.00109856	-6.21565
PCDHB9	0.00520255	-6.07615
MYO15A	0.00977615	-6.06089
SULT1E1	0.00294219	-6.05913
RGN	0.00454712	-6.04783
REC8	1.04E-06	-6.03127
AQP5	0.000324417	-6.02808
SLC16A6	6.88E-05	-5.96414
C11orf45	2.16E-05	-5.90187
C1QTNF4	0.000165057	-5.83008
EPDR1	6.60E-06	-5.81445
LRRC43	0.0041128	-5.75855
CIDEA	0.00104201	-5.62724
INSIG1	8.98E-08	-5.61396
LMOD1	0.00479578	-5.51828
ZNF506	1.35E-05	-5.43741
Mar-01	2.69E-05	-5.4266
PTGIS	3.71E-07	-5.42225
TIMP3	6.18E-07	-5.411
RNF144A-AS1	1.45E-05	-5.40125
BMF	6.41E-10	-5.39941
FABP4	4.60E-07	-5.38037
SARDH	0.00312641	-5.34778
CYP4X1	0.00213595	-5.31948
SRD5A3-AS1	0.000270964	-5.27887
LOC100129203	0.00535117	-5.27484
EPHX2	0.000328702	-5.21962
CEBPD	3.74E-05	-5.19515
GIMAP1-GIMAP5	4.80E-08	-5.17777
ST6GALNAC2	2.45E-05	-5.16286
NPPA-AS1	0.00285768	-5.13951

LDLR	8.89E-09	-5.11724
C9orf64	5.11E-05	-5.01011
ACAT2	4.24E-09	-4.97754
LINC01869	0.00595443	-4.97257
RUNDC3B	0.0117028	-4.92755
APBA1	1.48E-06	-4.9098
HIST1H2BH	0.00026003	-4.90597
ITGA9	0.0107847	-4.89
GPR146	5.50E-07	-4.86346
GJA4	1.24E-05	-4.85498
IL12A	0.0106264	-4.84741
USP32P1	0.000969021	-4.84287
TCN2	3.05E-10	-4.79959
MSMO1	4.84E-10	-4.77931
MAOA	1.89E-08	-4.77715
LOC729970	0.00435361	-4.76865
C8orf4	1.66E-05	-4.73803
MYCN	6.83E-06	-4.71922
RAB42	0.000990281	-4.70619
SV2A	3.42E-06	-4.68775
ACSS3	0.00181529	-4.64428
TTC39A	0.00119108	-4.59966
DAPK2	0.00021341	-4.56064
MYOZ3	0.00620311	-4.52869
EFCC1	9.37E-05	-4.50856
MGP	2.32E-07	-4.50792
FDFT1	3.00E-09	-4.49466
SOCS2	0.000319992	-4.47221
TM4SF18	5.35E-12	-4.45499
LINC00886	0.00957176	-4.45412
MVK	3.94E-08	-4.44797
GRAMD3	0.0104763	-4.441
FAM129A	2.38E-05	-4.43919
SQLI	2.25E-08	-4.401
CYP27A1	4.26E-06	-4.40016
RFTN2	3.11E-05	-4.39788
PALD1	1.23E-08	-4.38986
DDX43	0.000893732	-4.3572
AGBL3	0.0067125	-4.3566
LINC01006	0.00190324	-4.32389
MAST4-AS1	0.0113432	-4.31627
GAS6-AS2	0.00199909	-4.27764
SPINT2	2.29E-07	-4.25676
GABRR2	0.0031709	-4.25581
INS-IGF2	0.00899218	-4.25039
PRKN	0.00011729	-4.24305
ADPRH	4.61E-08	-4.21847
PLLPL	5.77E-06	-4.20895
CRYBG1	1.22E-08	-4.18757
NUP210	6.69E-06	-4.18325
RAMP2	1.42E-06	-4.14472
FRRS1	0.00427017	-4.1122

NXPH3	3.27E-05	-4.10276
SGSM1	8.81E-05	-4.1003
LOC730098	0.000825334	-4.06559
METTL7A	2.78E-07	-4.02105
C1R	0.00131839	-4.01345
LPIN3	0.00578895	-4.00773
TMTC1	1.28E-05	-3.97776
CHRNA1	0.00166575	-3.93196
OLMALINC	5.86E-05	-3.9271
UNC5C	0.000902908	-3.92686
IFI44L	0.00267486	-3.91876
TMC8	6.32E-05	-3.91252
IPCEF1	0.00386293	-3.91252
SLC29A2	0.00210769	-3.90199
ARHGAP25	0.00587504	-3.8883
FKBP5	1.49E-09	-3.88734
FAM185BP	0.000183321	-3.88173
LSS	1.80E-07	-3.87914
OPLAH	0.000101177	-3.85731
P2RX7	5.40E-05	-3.85579
LDLRAD4-AS1	0.00359131	-3.85083
MPZL2	6.28E-09	-3.8504
SLC30A3	9.21E-08	-3.73916
IFIT2	0.000258122	-3.7298
CYP51A1	2.51E-07	-3.72555
LY75-CD302	0.00946269	-3.72463
LHX6	7.43E-06	-3.71093
LINC00654	0.000650485	-3.70582
DHCR24	7.82E-08	-3.65263
SLC22A23	2.76E-08	-3.63991
RASGRP3	3.26E-09	-3.63203
MMAB	2.89E-07	-3.62716
UACA	2.66E-09	-3.62114
AQP1	7.40E-07	-3.61399
OAS3	8.15E-07	-3.6051
PCDHB10	0.00115879	-3.59818
PPM1H	2.51E-05	-3.5732
FBXO4	4.82E-06	-3.54472
NAGS	0.000103989	-3.54214
HMGCR	5.33E-08	-3.52211
GPX7	1.28E-05	-3.51183
IDI1	1.57E-07	-3.50067
CXCL11	0.000744664	-3.50045
GABRP	0.00181787	-3.49217
B4GALT1-AS1	0.00995124	-3.49077
MVD	1.26E-06	-3.48124
SNAP91	0.00281882	-3.4686
RNLS	0.00217336	-3.45561
LY75	1.84E-06	-3.44901
ANKRD53	0.00216062	-3.43022
CTHRC1	6.34E-05	-3.40736
OLFML3	0.000250903	-3.39664

B3GALT4	6.76E-07	-3.39211
DHCR7	4.70E-07	-3.38153
POU6F1	0.000271105	-3.38031
NR5A2	0.000126232	-3.37802
PKD1L1	0.000100803	-3.36736
HIST1H4J	0.00264884	-3.36013
FKBP9P1	0.0106908	-3.35858
MEGF10	0.000874897	-3.35482
KLF9	1.16E-06	-3.34812
RAMP2-AS1	0.00026698	-3.34574
C10orf10	1.97E-07	-3.34572
CYP39A1	0.000196401	-3.34257
PPP1R14A	6.15E-05	-3.34203
CDH4	0.00191902	-3.33869
FLJ27354	0.0040224	-3.32837
MX1	9.97E-05	-3.32314
RGCC	3.23E-06	-3.31046
AIF1L	1.97E-08	-3.29334
BCL2L11	1.27E-05	-3.28708
TXNIP	1.14E-06	-3.27508
ZNF366	2.17E-08	-3.26544
PRR15	9.36E-05	-3.25377
GUCY1A3	0.00016441	-3.24291
JAK3	0.000398601	-3.2388
MYO5C	8.19E-07	-3.2372
GK3P	0.00938615	-3.23716
ELN	0.000317082	-3.21773
RN7SL3	0.000236865	-3.2098
SREBF2	6.32E-08	-3.19899
TRIM16L	6.73E-06	-3.19534
ACOT1	0.000506052	-3.19456
LAMP3	0.000349517	-3.19324
ARHGAP45	1.68E-05	-3.19246
FBP1	0.00930376	-3.17823
SORT1	5.48E-08	-3.16997
SLC27A3	1.39E-07	-3.15766
MAP10	0.000500072	-3.15624
PSMB9	0.00396759	-3.12818
SULT1C4	6.46E-06	-3.11372
RRAGD	0.00161969	-3.10896
NPR3	4.03E-05	-3.10687
IL33	0.000125474	-3.08607
TET1	0.000137526	-3.08224
HSBP1L1	0.00141841	-3.07147
FAM167B	0.00030964	-3.06649
C10orf107	0.00136565	-3.06312
IL3RA	3.53E-08	-3.06234
RIBC2	0.000280831	-3.05343
CAP2	9.61E-07	-3.05216
GLIDR	2.70E-05	-3.05177
SYNE2	2.85E-07	-3.0454
APOL6	2.85E-05	-3.03923

LOC102724580	0.00202446	-3.03833
LRRTM2	0.00218433	-3.02244
C1QTNF1	0.00333921	-3.00242
ZNF726	0.00285682	-2.999
CEACAM1	0.000284306	-2.99303
CCDC74A	5.26E-05	-2.98476
MAPK13	4.91E-06	-2.97906
CH25H	0.00840091	-2.97078
FAM189A2	5.71E-07	-2.97044
CFB	0.00679975	-2.96906
LOC101927811	0.000649906	-2.96569
KLF15	0.0018705	-2.96244
PDGFRB	0.00273998	-2.96195
CPXM1	0.00010629	-2.95936
ACE	1.06E-07	-2.95858
SRL	5.76E-05	-2.94879
ABCA4	0.000256602	-2.9343
LIFR	8.11E-09	-2.93151
LRRC4	0.00769036	-2.93096
SETDB2-PHF11	0.00184505	-2.92166
CALCRL	4.29E-11	-2.91282
TCEA3	6.68E-05	-2.90414
NLRX1	6.26E-06	-2.90186
NIPSNAP3B	0.00541751	-2.90125
SEMA3G	7.67E-08	-2.89996
WNT3	0.000158883	-2.89933
LOC642366	0.00339615	-2.88668
TSPY26P	7.56E-05	-2.88431
MAPK8IP2	0.000665458	-2.8758
C1GALT1C1L	0.00664457	-2.87207
FAXC	0.000819613	-2.85419
FAT4	1.11E-08	-2.8494
MAN1C1	1.67E-05	-2.84679
SSPN	0.00342477	-2.83032
FASN	3.83E-06	-2.82565
FILIP1	5.12E-07	-2.82476
LRRC37A3	6.74E-05	-2.82424
IQCA1	0.000911285	-2.82237
FBLN5	3.18E-06	-2.8149
DLEU2	0.00480062	-2.78918
C2orf27A	9.65E-05	-2.78716
NR1H3	2.53E-05	-2.76275
EHD3	8.80E-07	-2.76034
MATN3	0.000449032	-2.75947
PLEKHA7	1.26E-05	-2.74841
LOC101926963	0.00528863	-2.7484
ENTPD1	4.14E-06	-2.73738
GSN	2.45E-08	-2.73625
GYPC	0.0105426	-2.73045
FAM117A	3.42E-07	-2.72933
MEIS3P1	0.00269259	-2.71712
FAM84B	8.24E-06	-2.71526

FAM81A	0.00755544	-2.71524
PATJ	1.95E-05	-2.7099
FADS1	8.95E-08	-2.69919
SCN9A	2.99E-05	-2.69567
B3GNT7	0.00133345	-2.69094
GOLGA8K	0.00130584	-2.68699
EPAS1	2.23E-10	-2.6866
ZNF253	0.000872096	-2.68106
SYNM	7.99E-09	-2.68046
HDDC2	0.000809792	-2.66802
LEPR	4.75E-07	-2.66009
FAXDC2	1.52E-06	-2.65931
PDE1A	0.000898675	-2.64612
LINC02021	0.00910021	-2.64549
ACACA	8.65E-08	-2.64017
ADHFE1	0.00481393	-2.63925
NUAK1	1.91E-09	-2.63725
MYL9	3.71E-08	-2.63516
RARRES1	0.0041327	-2.62499
BDH1	8.33E-06	-2.61444
EFNA1	9.64E-06	-2.61342
TMEM154	4.55E-07	-2.61321
LOXL4	0.00213389	-2.60845
HDAC9	0.000330608	-2.60454
PCDHGA2	0.0056598	-2.59588
LPAR6	5.63E-07	-2.59577
KLHL24	5.70E-07	-2.5915
TSC22D3	6.07E-06	-2.58697
GAL	0.0126808	-2.58541
PEX11A	1.32E-06	-2.58265
PCYT2	3.29E-05	-2.58176
GALM	2.00E-05	-2.58138
TNFRSF1B	1.59E-07	-2.58114
KLHDC8B	1.99E-06	-2.58087
NEDD9	0.000297549	-2.57889
ME1	6.07E-07	-2.57531
SELPLG	0.000280237	-2.57134
STAP2	0.000190585	-2.56626
PCDHGA4	5.31E-05	-2.56571
C14orf1	1.05E-07	-2.56169
GAB1	6.48E-06	-2.5612
PTCH2	0.00581686	-2.55717
STARD9	2.73E-06	-2.55507
RPGR	9.31E-07	-2.55116
EBF3	0.000293626	-2.54657
LAYN	0.00202157	-2.54626
HTATIP2	3.09E-06	-2.54159
GIPC2	6.79E-06	-2.54105
SLFN13	7.23E-06	-2.53573
PLA2G4C	0.000335507	-2.53273
STARD5	0.00282256	-2.52798
RTL5	0.00015651	-2.5262

DNHD1	0.00657739	-2.52501
VASH1	5.80E-09	-2.52236
TMEM220	0.0074005	-2.52153
UCP2	3.83E-05	-2.51703
MT1F	0.00220776	-2.51651
MYO7A	6.55E-05	-2.51629
MDK	8.34E-07	-2.51445
SEMA6D	4.67E-05	-2.50434
APOE	0.00531989	-2.49455
LRRC37A4P	5.27E-05	-2.49397
CHST15	2.43E-07	-2.48939
KANSL1-AS1	0.000575611	-2.48928
GPRC5B	8.58E-08	-2.48879
ARID5B	1.98E-06	-2.48877
LIPA	7.96E-06	-2.48059
HNMT	6.18E-05	-2.47734
HERC2P3	8.24E-05	-2.47586
NCALD	0.000165055	-2.47484
IRAK3	2.00E-06	-2.47281
TSPAN13	1.44E-05	-2.46993
SNAP25	0.00463705	-2.46697
NUDT8	0.000114282	-2.4656
CABP4	0.00522453	-2.46135
SEL1L3	6.32E-09	-2.45716
ZFP69	0.00042609	-2.45493
C5orf56	0.00695397	-2.45224
CD40	1.32E-07	-2.44974
LOC101928123	0.000102234	-2.44644
EFNB2	9.96E-07	-2.44199
COL21A1	0.00200442	-2.42882
PPP1R3C	0.000125026	-2.42869
P4HA3	3.55E-08	-2.42392
P2RX4	1.52E-05	-2.42081
GNG7	0.00371477	-2.41686
ELOVL6	1.56E-05	-2.41565
COL4A6	0.00329165	-2.41168
HDAC5	6.09E-07	-2.41094
PRTFDC1	1.08E-05	-2.4042
NIPAL2	0.000213111	-2.40364
DLL4	6.32E-08	-2.40313
IFIT3	2.96E-05	-2.39992
CCDC85A	1.02E-06	-2.39945
LOC643733	0.000750254	-2.39823
NYNRIN	1.98E-06	-2.39212
DCAF12L1	0.000336022	-2.38928
NID1	6.60E-07	-2.38516
BACE2	2.06E-08	-2.37667
SHROOM1	1.62E-05	-2.3759
LOC441204	0.0112643	-2.3745
TM7SF2	1.54E-05	-2.37108
EMILIN1	1.63E-05	-2.36767
TCP11L2	2.09E-06	-2.36479

TSPAN2	0.00753426	-2.35859
LINC00607	3.97E-05	-2.35521
DTX3	0.000998196	-2.35091
KIAA1671	1.35E-07	-2.34976
VSIR	5.39E-05	-2.34551
FBXL5	2.40E-08	-2.33684
LOC728673	0.000274506	-2.3353
EMILIN2	0.000117432	-2.33253
DYNC2H1	6.97E-05	-2.32405
HSD17B14	6.57E-05	-2.32211
SREBF1	1.03E-06	-2.32132
KIAA1211L	1.44E-06	-2.31889
SCARB1	1.47E-06	-2.31239
FTX	0.0103815	-2.30079
HSD17B7	0.000245971	-2.29523
ATP10D	4.28E-06	-2.28828
SORBS2	5.22E-06	-2.28642
ENDOD1	1.12E-07	-2.28594
SLC26A4	0.00504598	-2.28408
HIST1H1C	0.00314021	-2.27326
HERC2P2	0.000340017	-2.27322
PCDH12	0.000124821	-2.27297
LOC101927765	0.00856467	-2.27079
HSD17B2	0.00169624	-2.26873
HERC2P9	8.86E-05	-2.26546
GSAP	0.0113912	-2.26367
TMEM170B	1.29E-05	-2.26362
PPARA	1.26E-05	-2.26334
PABPC4L	0.00431126	-2.26079
VAV3	0.00482761	-2.26067
ARHGEF17	2.85E-07	-2.25756
AFAP1L1	6.99E-09	-2.25679
AKR1E2	0.0124607	-2.25502
FAIM	0.000678866	-2.25412
CASZ1	0.000185157	-2.25004
COMTD1	0.00035758	-2.2498
ABCA1	0.000429555	-2.24855
CD36	0.000298962	-2.24509
AKAP7	0.000917598	-2.24508
OSMR	1.10E-07	-2.24432
TMEFF1	5.79E-05	-2.23809
RFLNB	4.34E-07	-2.23253
DNAJC28	0.00856788	-2.23251
MPP7	0.00646797	-2.2297
KLF11	1.56E-05	-2.22933
CDKL1	0.005507	-2.22769
KIAA1551	5.60E-10	-2.22332
SERPINB9P1	0.0033635	-2.21846
GCHFR	0.0106357	-2.21844
P2RY2	0.000218664	-2.21769
ZNF43	9.27E-05	-2.21578
CSF1	7.78E-05	-2.21257

IDH1	9.07E-10	-2.20915
N4BP3	2.24E-05	-2.20801
PODN	0.00197558	-2.1996
DOCK9	2.73E-07	-2.19912
FIGNL2	9.48E-06	-2.19785
HLA-L	0.0104868	-2.19542
GADD45G	0.0111503	-2.1937
LOC100419583	0.000323438	-2.19249
OAS2	0.000186575	-2.19225
CLCN6	9.42E-06	-2.1901
TMEM53	0.00596251	-2.18113
FAM89A	0.000968266	-2.1805
SIK2	0.000162198	-2.17879
HERC1	3.05E-05	-2.17246
KIAA1161	5.33E-07	-2.16959
ZBTB20	1.59E-05	-2.1694
APOBEC3G	0.00146388	-2.16819
HOXD1	5.14E-05	-2.16683
C19orf33	0.00112799	-2.16677
FAM107A	7.44E-05	-2.16481
LOC100132111	0.00832661	-2.161
DDIT4	1.20E-07	-2.15979
LIMS2	3.59E-06	-2.15569
GIPC3	5.66E-05	-2.15444
FBN1	4.92E-05	-2.15303
RSPH3	0.000937439	-2.15117
STARD4	4.40E-06	-2.15086
Sep-05	7.39E-06	-2.14946
LOC100129434	5.27E-07	-2.1471
STEAP2	2.09E-05	-2.14534
TRIM6	0.000556662	-2.14183
RASSF4	2.86E-05	-2.1407
ALDH5A1	0.00104761	-2.13784
TNFSF10	0.000322718	-2.13409
LOC100129940	0.00893381	-2.13333
OCLN	7.02E-06	-2.13308
LOC100190986	0.000430662	-2.13202
MKL2	3.28E-05	-2.1311
FN3K	0.00045984	-2.12989
PTGR1	1.70E-07	-2.12915
PDE2A	3.23E-06	-2.12641
NAAA	0.000403365	-2.12483
PDGFD	4.50E-05	-2.12046
RDX	2.68E-07	-2.11849
KCNN3	0.000662877	-2.11689
USP51	0.000230499	-2.11529
URB1-AS1	0.00349491	-2.11464
MATN2	0.000108192	-2.11274
FBLN7	0.0028694	-2.10715
FAM212A	4.34E-07	-2.10521
MET	3.67E-08	-2.10138
LOC105376805	0.00597203	-2.09594

SPINT1	0.000212816	-2.09444
LRRC37A2	0.00314294	-2.09426
FDPS	3.76E-08	-2.09355
PXMP4	5.42E-05	-2.0912
DHRS3	1.47E-05	-2.09055
DACH1	3.01E-07	-2.08894
HIST2H2AA3	2.77E-05	-2.08799
HIST2H2AA4	2.77E-05	-2.08799
FAM69B	7.91E-09	-2.08461
PLEKHO1	2.97E-05	-2.08373
FST	0.00567001	-2.08209
GMFG	6.54E-06	-2.08194
SLC16A4	0.000119719	-2.08116
ZNF532	6.69E-06	-2.0792
REL	0.00417625	-2.07852
SH2D4A	0.00852014	-2.07795
EPB41	5.03E-07	-2.07659
AMPD3	3.96E-05	-2.07509
MBNL1-AS1	0.00340436	-2.07474
MAP9	0.00781637	-2.07448
CREB5	0.0012948	-2.0711
HVCN1	0.0029273	-2.0698
PIK3C2A	9.19E-08	-2.0671
KANSL1L	0.00336754	-2.06548
HSPB1	2.76E-06	-2.06386
ZNF138	0.000195345	-2.06039
TMEM135	5.22E-05	-2.06027
ACOT2	0.000179984	-2.05964
RENBP	0.00225237	-2.05791
TMEM204	5.41E-05	-2.05696
MTHFR	2.26E-06	-2.055
CTDSPL	1.66E-07	-2.05389
KIAA1462	1.95E-07	-2.05307
DHX58	0.0029051	-2.05177
RHOB	2.43E-05	-2.04877
RNF144A	3.90E-08	-2.04788
PDZD2	0.00155205	-2.04502
NT5E	4.60E-08	-2.04469
GPR160	0.00162002	-2.04139
TACSTD2	0.000304521	-2.03774
NOL3	7.50E-06	-2.03756
HTR1B	1.07E-07	-2.03535
RNF213	1.07E-06	-2.03474
THSD7A	0.000163211	-2.03078
JAM3	1.50E-08	-2.03029
EBP	1.42E-06	-2.03018
GLB1L	1.97E-05	-2.02918
FGFR4	0.00111779	-2.02798
LAP3	1.90E-06	-2.02638
LTBP1	3.07E-05	-2.0247
ARRDC3	1.33E-05	-2.02201
RASSF2	2.49E-06	-2.02182

FRY	5.65E-08	-2.02098
WARS	1.04E-09	-2.01904
MIR503HG	7.09E-05	-2.01499
MSX1	0.00721829	-2.01375
CREBRF	1.10E-05	-2.01342
ARMC4	0.000104942	-2.01155
SYBU	0.00355315	-2.00599
C8orf88	0.0065186	-2.00299
LINC02407	0.00152324	2.00211
ETV1	5.14E-05	2.0038
TNFSF4	1.10E-05	2.0048
TNFRSF10D	8.91E-08	2.00893
ENC1	4.38E-06	2.01673
AUTS2	5.34E-05	2.01781
VPS9D1-AS1	0.000388602	2.03327
ARSJ	9.73E-06	2.03618
JDP2	9.01E-05	2.03959
CA8	0.0117492	2.04202
KIFC2	0.00012403	2.04719
F2RL1	2.32E-05	2.04901
FAM107B	5.60E-08	2.04955
DACT3	0.00936125	2.05055
PMEPA1	5.27E-05	2.05515
KIAA0513	7.52E-05	2.05951
PIK3CG	0.000204559	2.06955
SFMBT2	0.000317594	2.07041
CBWD3	0.00642921	2.07272
SLC25A37	0.000397069	2.07569
NRG3	0.000241141	2.07615
CCND2	4.51E-05	2.08119
NFE2L3	1.81E-06	2.08717
SNAPC1	1.47E-05	2.08816
CLDN11	5.84E-08	2.08875
LGR4	0.000173942	2.09706
PALM	9.76E-06	2.10205
SH3RF2	0.00164673	2.10302
CD99P1	0.00107684	2.10688
TNFRSF25	0.00317025	2.107
RELT	0.00185458	2.11226
APCDD1	0.000518546	2.11632
ELOF1	7.40E-06	2.11722
PLAC9	8.14E-05	2.11774
LOC730101	9.49E-05	2.11825
ZNF175	5.80E-06	2.12007
DNM3	0.00732931	2.12169
VLDLR	0.000256866	2.12422
CACNG6	0.000382675	2.12604
CD68	0.000148721	2.13067
LOC284454	0.0109198	2.13121
TNFRSF12A	5.08E-06	2.13325
SPEG	0.00117299	2.13381
LPAR1	0.00981195	2.13469

NPAS2		4.25E-07	2.13559
SPHK1		0.000882624	2.14075
	Mar-03	3.18E-06	2.14309
CYTL1		0.00571502	2.14526
ROBO3		8.40E-05	2.14849
SETBP1		1.10E-05	2.14946
BNC1		9.65E-05	2.15033
GATA6		6.83E-05	2.15047
KSR2		0.000860249	2.15485
CSF2RB		0.0024029	2.15731
ZMAT3		2.72E-06	2.16565
FAM216A		0.000318	2.16831
STX11		0.00031967	2.16948
PDE10A		3.84E-05	2.17634
LETM2		0.00392291	2.18144
AQP3		0.0126177	2.18433
IGSF3		0.00311575	2.18793
MAFF		2.84E-06	2.19236
SMURF2		1.15E-05	2.19243
CTTNBP2		0.00217293	2.19404
CST3		7.27E-06	2.19688
LRP1		0.000130574	2.21011
DUSP6		2.80E-07	2.2192
CLEC4GP1		4.24E-05	2.22131
RHPN2		7.42E-05	2.22667
AXL		4.56E-06	2.2268
CDKN1A		1.89E-06	2.23027
ANK3		0.000547683	2.2314
MIR100HG		9.17E-06	2.23345
SMAD3		3.06E-06	2.24033
CORO1A		0.000230211	2.24196
ADAMTSL1		3.56E-05	2.24882
FBXO41		0.000769305	2.25118
NOS3		7.10E-08	2.25392
INHBA		6.58E-06	2.25632
GPR4		4.62E-06	2.26043
VSIG10L		0.000749111	2.26138
ADRB2		0.000734319	2.27712
CHAC1		0.000188513	2.28412
SPRED3		3.95E-06	2.28648
ST3GAL5		1.75E-05	2.29248
CARD11		6.28E-07	2.29539
FAM227A		0.00191324	2.29781
PLK2		4.47E-08	2.30028
ETV4		3.26E-05	2.30117
SLC39A4		0.00853341	2.3024
DAW1		0.0077165	2.30748
CD3EAP		7.64E-08	2.31146
NRCAM		1.18E-05	2.31215
EPS8		1.56E-07	2.31273
CHN2		8.60E-05	2.32109
ZIK1		0.000787992	2.322

RGS2	0.000193982	2.32539
METTL12	2.82E-06	2.33015
CDC42EP2	0.000819118	2.33715
SIPA1L2	0.000105648	2.34498
AP1S3	0.000958164	2.35092
KRT80	0.000141273	2.35208
PLAU	0.00341421	2.35534
LMTK3	0.00484865	2.36001
SULT1A1	0.00156049	2.36569
TIAM1	0.000739836	2.36745
ASTN2	0.00625309	2.36956
MIR31HG	0.000663139	2.37159
APOLD1	2.34E-05	2.38152
TRIB1	3.29E-06	2.38411
FZD8	1.26E-05	2.38426
HES7	0.0113412	2.38643
LTBP4	1.44E-07	2.38703
RUNX1	9.85E-06	2.39095
FUT8	1.19E-06	2.39391
ADAMTS1	5.18E-05	2.39405
GALNT16	0.0126092	2.39409
PAX9	0.00065333	2.40874
ABHD17C	5.87E-06	2.41198
PHEX	0.00721794	2.41651
ADCY1	0.00733976	2.41875
NYAP1	0.000126228	2.42044
PLAC8	1.52E-05	2.42635
TTYH2	4.79E-05	2.43452
CCND1	2.52E-09	2.43549
PDE1C	1.37E-06	2.4446
NRXN3	0.0102005	2.44735
ARHGEF3	3.76E-07	2.44856
PTPRD	4.45E-05	2.45104
ZNF814	9.84E-06	2.45615
SLC4A11	5.17E-06	2.45697
PHLDA3	3.89E-05	2.45875
CPXM2	0.000143287	2.4643
DOCK10	0.000319751	2.46479
TMEM200A	0.000392299	2.46574
RASSF10	0.00204977	2.46781
PLCB2	0.000365706	2.46832
SLC7A5	5.48E-10	2.4827
SFRP1	1.66E-06	2.48762
SLC8A1	0.00737803	2.48961
MEG9	0.00343454	2.49842
PSAT1	2.32E-07	2.50171
EFNB3	0.00195272	2.50228
FGF16	0.00196699	2.50394
MIR34AHG	0.00653994	2.51356
ZNF503	1.78E-05	2.51404
ADAMTSL4	0.00178673	2.52432
MYCL	4.85E-06	2.52699

PRSS23	1.97E-09	2.53062
CYFIP2	1.48E-07	2.53382
CYP2S1	6.52E-05	2.54108
EFR3B	0.000485596	2.55744
FRMD5	5.33E-06	2.56068
MAP3K21	0.00647815	2.56431
SLC25A25-AS1	0.00278815	2.56434
CACNG8	0.000925692	2.56937
SERPINE2	1.27E-06	2.57642
SH3RF3-AS1	0.000483215	2.58467
CA13	0.000461681	2.59005
CTXN1	2.67E-06	2.59139
APLN	1.32E-07	2.59146
MAFB	3.42E-07	2.60222
DRAXIN	0.00744507	2.61218
PRRT2	0.00075172	2.61425
LIPG	8.82E-06	2.62798
NR2F1	4.08E-05	2.62894
PLEKHH2	0.00183831	2.63666
NPL	0.0103961	2.64393
MFSD2A	0.000577785	2.6476
COL13A1	1.79E-06	2.65228
EVA1C	6.61E-05	2.67417
NCEH1	2.42E-07	2.67818
CAMK1D	0.00249201	2.68609
SLIT2	9.86E-05	2.68719
NRIP3	1.96E-06	2.68907
FAM27E3	0.0118034	2.69569
ETV5	2.05E-08	2.71258
EDA2R	0.0102549	2.71501
RGS5	5.87E-07	2.74512
TFEC	6.93E-06	2.74712
GBP4	0.00741292	2.75237
CCDC184	0.00673093	2.76025
SPTB	0.0117219	2.78843
JUN	3.42E-08	2.80513
MMD	2.49E-05	2.8193
RARB	7.56E-08	2.82361
C8orf48	0.0107587	2.82571
RAB3B	1.98E-08	2.8476
NPTXR	0.00500089	2.86336
PTPRH	0.000154013	2.88449
DPYSL4	8.31E-08	2.89722
IL6	0.00464658	2.91988
ATP2A3	4.39E-05	2.93916
TMEM156	0.0110613	2.94255
GPR3	1.92E-05	2.9446
FRMD3	6.58E-07	2.96141
PTGS1	1.05E-07	2.96397
PLAUR	5.60E-07	2.96711
HMCN1	1.45E-05	2.98058
VDR	0.000583709	2.9832

C15orf54	1.61E-05	2.98567
LY6K	0.0114539	2.98929
SUGCT	0.000101564	3.01173
DKK1	3.88E-07	3.02285
PRKG1	0.00143891	3.03884
LOC101928464	0.00979586	3.046
MEG3	0.000167017	3.04875
FBLN2	1.79E-05	3.05231
GDF15	7.33E-07	3.05407
AHRR	3.59E-06	3.07168
ADAMTS9	9.92E-06	3.07515
NEGR1	3.19E-07	3.11207
LMO7	3.01E-06	3.11609
SLC37A2	7.22E-05	3.12898
PTGER4	4.13E-06	3.13011
GATA6-AS1	0.00030567	3.13457
SDC1	2.37E-06	3.14016
ZNF185	1.61E-07	3.14723
FAT1	1.73E-05	3.1618
SLC1A1	1.26E-08	3.16428
TMEM171	1.09E-06	3.17283
GRIN3B	0.0118332	3.17925
SPOCK1	2.43E-07	3.19834
ZNF703	1.42E-05	3.21273
DUSP1	2.28E-05	3.21692
FAM196B	4.20E-06	3.23423
GFPT2	9.55E-06	3.23439
PCDH9	3.12E-05	3.23616
LOC100506178	1.76E-05	3.23839
IL1RL1	1.00E-05	3.25749
PSTPIP2	0.0014371	3.26279
FOXO6	0.000767275	3.28874
TFRC	2.79E-07	3.31822
TBC1D2	6.35E-05	3.3468
EXOC3L2	0.00452611	3.35097
VIT	0.000615799	3.35555
TMEM163	0.00667767	3.35765
CPE	1.49E-06	3.3605
CREB3L1	0.00145481	3.38643
DLGAP1	0.0117631	3.40475
SEZ6L2	3.01E-06	3.41285
CD163L1	2.98E-07	3.42394
CFAP44	0.000551584	3.4375
PLPP3	2.73E-08	3.44578
LOC101927759	0.000710823	3.44793
PPFIBP2	2.17E-05	3.4494
DMRTA1	0.000259106	3.45162
SEMA3D	9.63E-05	3.46852
PLCL1	4.68E-07	3.51297
DPF3	8.65E-06	3.51592
PNMA2	6.90E-07	3.52804
ITGB3	1.57E-07	3.53976

CEP126	3.96E-06	3.54108
ITGB4	1.18E-06	3.57202
COL6A2	3.33E-06	3.5744
ULBP1	0.00162612	3.57679
C7	0.000488685	3.57962
CHST2	2.46E-06	3.58824
ASPHD1	0.00134164	3.60729
SLCO3A1	0.00177282	3.62004
PLS1	8.16E-06	3.62972
PLXNA4	1.49E-07	3.63133
MAL2	2.49E-05	3.64828
TMEM200C	0.00677009	3.64913
DCN	0.000592958	3.66365
ANGPT1	8.45E-07	3.68734
PDZD7	0.000210097	3.68921
LAMC2	0.000191813	3.69485
B4GALNT4	5.64E-05	3.71269
BMP2	2.14E-08	3.79033
FAM46C	0.00130581	3.82461
KLF4	0.00406321	3.84914
TMEFF2	0.00502022	3.86566
GOS2	0.00262555	3.86677
C21orf59-TCP10L	0.00570081	3.87371
HAPLN1	0.00893193	3.90578
HEPH	0.00087006	3.9098
MSMP	3.81E-06	3.91548
ADAMTS15	0.000412634	3.9178
SHISA2	0.00107663	3.93094
DGAT2	0.00249622	3.93404
AMIGO2	9.24E-07	3.93596
UNC13D	1.70E-06	3.94315
GABRE	0.000570829	3.96372
RGS4	8.82E-09	3.98143
VIPR1	2.11E-05	3.99651
SPOCD1	6.94E-07	3.99879
MEST	1.67E-06	4.0195
GJA5	6.04E-05	4.03982
DNAH8	0.000185775	4.05528
CD44	6.12E-07	4.06374
CDKN2B	6.35E-05	4.07823
ACKR3	1.58E-06	4.09274
EGFR	0.0040251	4.11718
PTGIR	7.89E-06	4.12378
EPHA5	0.000376901	4.1313
NOTCH3	0.000298096	4.17639
CDCP1	0.0019529	4.177
HR	0.00859045	4.21572
NTM	0.00132906	4.21907
NRG1	1.48E-07	4.22907
LAMB3	8.12E-06	4.27924
CCDC68	5.64E-05	4.28672
ADAMTS4	6.40E-07	4.31123

CMKLR1	0.00778234	4.32746
RIMS1	0.00474146	4.34118
TSPAN11	4.02E-05	4.3414
KCNC4-AS1	0.00329941	4.34901
SHANK1	4.69E-06	4.4014
ASNS	2.06E-08	4.4091
ADGRB2	7.76E-07	4.46618
KCNJ12	0.00267211	4.46734
COL17A1	3.74E-05	4.47641
PRSS3	2.92E-05	4.49216
TRNP1	8.10E-05	4.51691
PTCHD4	5.55E-06	4.55384
BDNF	3.26E-06	4.57422
C10orf111	0.00313766	4.6242
KCNA6	0.0122902	4.63651
STX1A	1.50E-05	4.64847
TMEM158	4.47E-05	4.64996
DLG5-AS1	0.00138152	4.69621
VEGFA	9.90E-05	4.70419
ZNF488	0.00107786	4.71826
ST8SIA6	1.32E-06	4.72618
XIRP2	0.00181458	4.73268
ADAMTS18	4.82E-07	4.74626
RPSAP52	0.00247935	4.7906
CCNA1	1.72E-05	4.81692
CLMP	0.00890739	4.82889
TCF15	1.17E-05	4.8347
NIPAL1	4.39E-05	4.83603
ESPN	0.00743025	4.93718
ENO3	0.00124286	4.94626
KCNN1	0.00487853	4.97905
KRT7	8.92E-07	5.023
CCDC78	0.0124654	5.02657
GRB14	4.55E-10	5.0435
FOSL1	1.13E-06	5.10875
TFF3	0.000664666	5.11879
KIF19	0.000231688	5.136
LTA	0.00151706	5.13684
HCN2	0.000888717	5.18449
LOC102467226	0.00614302	5.23981
MYEOV	0.000293463	5.24761
STC2	3.61E-07	5.35889
AFF2	0.000619012	5.40006
CCDC3	6.83E-05	5.41418
AMPH	2.19E-07	5.50911
SHC3	1.73E-05	5.53705
MMP10	4.37E-05	5.55421
LUM	0.00059124	5.59714
ZNF804A	0.000107601	5.63254
HES2	2.32E-07	5.65329
HS6ST3	0.00065402	5.73057
APLP1	8.52E-05	5.76875

SYCP2	0.00821727	5.77705
CD24	0.00850575	5.84183
MMP1	6.21E-09	5.86225
ADIRF	1.17E-05	6.00247
KCNG1	0.000180133	6.03248
MYH15	0.00271389	6.04001
LPXN	1.79E-05	6.06758
DUSP4	9.35E-11	6.15126
GSDMC	4.44E-06	6.22204
LYPD1	1.51E-07	6.22434
TGFBI	1.38E-07	6.23663
HSPC324	9.91E-06	6.26377
RFLNA	1.69E-05	6.3394
EPHB6	1.48E-06	6.36864
GLI1	0.00594935	6.393
KTN1-AS1	0.00674634	6.45676
BICC1	0.000539455	6.4639
ELMOD1	6.49E-08	6.49541
PIEZO2	4.99E-07	6.58163
ALDH1A3	1.80E-07	6.58738
NSG1	0.00555356	6.81194
TNFSF15	0.00121728	6.84664
NGEF	0.00251741	6.88612
KCNMA1	0.00010708	6.93453
LOC101926941	0.000812576	6.96131
CLIC3	0.00375264	6.9999
CACNG7	9.40E-06	7.07729
TMEM108	0.000577333	7.1191
STC1	3.71E-08	7.1678
MGARP	8.90E-07	7.17211
FBXL16	0.00283575	7.283
LOC105376554	0.00270445	7.3608
CCDC181	0.00277445	7.41458
DGKI	0.0081275	7.43022
C3orf70	0.000123723	7.44203
STAB2	0.00464418	7.48971
SPOCK3	4.81E-05	7.51623
ADAM12	0.00595916	7.58185
ADM2	1.25E-05	7.63146
DIO2	0.0125392	7.65472
EEF1A2	3.10E-06	7.69312
CHPF	8.80E-07	7.70784
NTSR1	6.09E-06	7.71023
SERPINB2	4.03E-05	7.71483
RAI2	5.11E-09	7.80904
CRLF1	0.00203133	8.01967
CEND1	9.88E-09	8.13024
TMEM59L	2.45E-06	8.13922
PLPPR3	0.00109913	8.1741
PLPPR1	0.00129466	8.17812
CDH11	3.91E-09	8.23645
ANGPTL4	8.65E-08	8.23769

TNFRSF6B	9.73E-07	8.59146
PDE11A	0.00033885	8.78819
IL7R	0.00160346	8.801
FUT8-AS1	2.85E-06	8.85691
PLVAP	1.00E-07	8.98145
C21orf62-AS1	0.00821443	9.06958
VCAN	2.90E-05	9.10494
TFPI2	9.15E-09	9.13632
TRIM58	0.000994263	9.33163
GCKR	0.000322859	9.46916
TTC25	0.00405109	9.58138
GEM	0.00107474	9.6131
APCDD1L	0.000349977	9.70583
CSMD2	0.00625165	9.75071
TENM4	0.00222602	9.84298
SLIT3	1.70E-07	9.93788
SELP	4.49E-08	10.2476
ACTN2	0.0016786	10.445
PTPN22	8.82E-05	10.4736
BMPER	9.72E-05	10.9937
PAPPA	3.18E-07	11.123
CPM	0.00914808	11.414
ANGPTL5	0.000349195	11.4955
ABCA8	1.24E-07	11.6721
NLRP14	1.15E-06	11.7138
SERPIND1	1.58E-06	11.8223
ADTRP	1.87E-06	11.8957
FLRT3	4.91E-05	12.1245
BTBD11	0.00706069	12.5599
ANKS1B	0.01111114	12.8224
LINC00520	0.000926989	13.297
CYP27C1	0.00451492	13.4223
LINC01605	0.00139045	13.528
NHS	0.00195034	13.613
GP6	0.000688331	13.8491
LINC01358	0.00429142	14.1001
TSPAN8	7.68E-06	14.6272
TMEM100	0.00328684	14.9514
KCTD16	8.70E-08	15.0057
KCNAB1	1.90E-07	15.903
ST6GALNAC1	0.000630752	16.9885
DRP2	3.49E-06	17.8865
PTHLH	0.00515059	18.091
CSF3	0.00273508	18.1189
CYP26B1	3.56E-05	20.1278
FLJ41200	5.04E-07	20.3564
ANOS1	1.01E-06	21.1492
GDF6	3.71E-08	21.4677
TNNT1	0.000462861	23.0326
ACP5	9.15E-07	23.4159
SCUBE1	2.13E-05	23.934
PAQR5	0.00569464	24.7539

SOCS1	0.000235715	25.1217
BRSK1	0.00269594	26.2844
PCDH15	0.00089006	34.3985
RBMXL2	0.000467757	35.3142
LRRC4B	0.00749027	35.3441
CYP1B1	0.0063181	40.2478
SEMA5A	0.0038664	45.9376
PAPPA2	0.000115147	51.0541
CPA4	2.91E-05	69.2121
BTK	5.63E-07	85.9733
CST1	5.88E-06	318.461