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Publication Date	2019-11-19
Publication Information	Islam, Md Nahidul, Griffin, Tomás P., Sander, Elizabeth, Rocks, Stephanie, Qazi, Junaid, Cabral, Joana, McCaul, Jasmin, McMorrow, Tara, Griffin, Matthew D. (2019). Human mesenchymal stromal cells broadly modulate high glucose-induced inflammatory responses of renal proximal tubular cell monolayers. Stem Cell Research & Therapy, 10(1), 329. doi:10.1186/s13287-019-1424-5
Publisher	BMC
Link to publisher's version	https://doi.org/10.1186/s13287-019-1424-5
Item record	http://hdl.handle.net/10379/16413
DOI	http://dx.doi.org/10.1186/s13287-019-1424-5

Human mesenchymal stromal cells broadly modulate high glucose-induced inflammatory responses of renal proximal tubular cell monolayers

Running Head: MSCs inhibit renal epithelial cell inflammation

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Word Count, Abstract: 250

Word Count, Main Body: 5634

Abstract

Background: Renal proximal tubular epithelial cells (RPTEC) are dysfunctional in diabetic kidney disease (DKD). Mesenchymal stromal cells (MSC) may modulate DKD pathogenesis through anti-inflammatory mediators. This study aimed to investigate the pro-inflammatory effect of extended exposure to high glucose (HG) concentration on stable RPTEC monolayers and the influence of MSC on this response.

Methods: Morphologically stable human RPTEC/TERT1 cell monolayers were exposed to 5mM and 30mM (HG) *D-glucose* or to 5mM *D-glucose* + 25mM *D-mannitol* (MAN) for 5 days with sequential immunoassays of supernatants and end-point transcriptomic analysis by RNA-sequencing. Under the same conditions, MSC conditioned-media (MSC-CM) or MSC-containing transwells were added for days 4-5. Effects of CM from HG- and MAN-exposed RPTEC/MSC co-cultures on cytokine secretion by monocyte-derived macrophages were determined.

Results: After 72-80 hours, HG resulted in increased RPTEC/TERT1 release of interleukin (IL)-6, IL-8, monocyte chemoattractant protein (MCP)-1 and neutrophil gelatinase-associated lipocalin (NGAL). The HG pro-inflammatory effect was attenuated by concentrated (10X) MSC-CM and, to a greater extent, by MSC transwell co-culture. Bioinformatics analysis of RNA-sequencing data confirmed a predominant effect of HG on inflammation-related mediators and biological processes/KEGG pathways in RPTEC/TERT1 stable monolayers as well as the non-contact-dependent anti-inflammatory effect of MSC. Finally, CM from HG-exposed RPTEC/MSC transwell co-cultures was associated with attenuated secretion of inflammatory mediators by macrophages compared to CM from HG-stimulated RPTEC alone.

Conclusions: Stable RPTEC monolayers demonstrate delayed pro-inflammatory response to HG that is attenuated by close proximity to human MSC. In DKD, this MSC effect has potential to modulate hyperglycemia-associated RPTEC/macrophage cross-talk.

Keywords

Mesenchymal stem cells

Diabetes mellitus

Diabetic nephropathy

Proximal tubule

Renal epithelial cells

Glucose

Inflammation

Cytokines

Neutrophil gelatinase-associated lipocalin

Extracellular vesicles

Background

Diabetic kidney disease (DKD) is the leading cause of end stage renal disease (ESRD) worldwide [1]. The complex pro-inflammatory milieu of hyperglycaemia, reactive oxygen species (ROS), advanced glycation end products (AGE) and angiotensin-II contributes to activation of transcription factors, growth factors, inflammatory cytokines and chemokines that mediate glomerular, microvascular and tubulo-interstitial injury - eventually leading to progression to ESRD and to the increased cardiovascular mortality associated with DKD [2-4].

A substantial body of research evidence documents the links between chronic inflammation and the development and progression of DKD[5-8]. Hyperglycaemia induces cytokine production by macrophages and other immune cells which may serve both as drivers and predictive biomarkers for progressive loss of renal function[7, 9, 10]. For example, circulating concentration of monocyte chemoattractant protein-1 (MCP-1/CCL2) has been shown to correlate with the degree of interstitial macrophage infiltration in human DKD while, experimentally, inhibition of MCP-1 in models of diabetes mellitus (DM) ameliorates renal injury[11-13]. Hyperglycaemia up-regulates MCP-1 production by kidney tubular epithelial cells, leading to infiltration of monocytes into the kidneys where they may subsequently become differentiated into inflammatory macrophages[14, 15]. This is further associated with localized release of pro-inflammatory cytokines such as interleukin (IL)-1β, IL-6 and tumour necrosis factor-alpha (TNFα)[15, 16].

The renal proximal tubular epithelial cell (RPTEC) is a significant target for the adverse effects of chronic hyperglycaemia. Excessive glucose in the glomerular filtrate drives increased glucose reabsorption in the proximal tubules and activates a range of maladaptive pathways within RPTEC that contribute to the DKD pathogenesis[17-22]. As DKD progresses, secondary mediators including growth factors, angiotensin-II and AGE activate inflammatory signalling pathways to further increase ROS production, inflammation, tubular cell hypertrophy and interstitial fibrosis[17-19, 21]. These insights highlight RPTEC as a potentially important therapeutic target in DKD and *in vitro* studies involving cultured RPTEC-like cells provide a valuable test-bed for identifying and evaluating novel interventional strategies[21, 23]. Among the *in vitro* tools available, RPTEC/TERT1 is an immortalized RPTEC cell line generated by overexpression of human telomerase reverse transcriptase (hTERT)[24]. Recent studies have highlighted the potential advantages of RPTEC/TERT1 stable monolayer cultures over other cell lines for modelling renal proximal tubular function and responses[25-27].

Macrophages are key mediators of intra-renal inflammation in DM, being an important source of pro-inflammatory factors including IL-1, TNFα, IL-6 and ROS[28]. *In vivo*, macrophage infiltration and activation within the kidneys of diabetic animals as well as other models of renal injury has been shown to contribute significantly to increased production of chemokines, interstitial fibrosis and increased serum creatinine and proteinuria[29-32]. Combined with the direct effects of chronic hyperglycaemia to induce pro-inflammatory responses in RPTEC, these studies indicate that crosstalk between RPTEC and interstitial macrophages within the kidney represents a key pathological axis in the development and progression of DKD.

Currently, a limited number of therapies are available that specifically target the development and progression of DKD. Novel interventions that modulate multiple inflammatory pathways as well as promote repair of tubule-interstitial injury could well complement conventional drug classes that predominantly address maladaptive glomerular pathophysiology in DKD. Relevant to this, interventions to inhibit pro-inflammatory cross-talk between RPTEC and macrophages represent an attractive strategy. Mesenchymal stem/stromal cell (MSC) therapy is a potential therapeutic option for diverse inflammatory disease pathologies[2, 33, 34]. In their physiological, perivascular niches in the bone marrow and other tissues, MSC have critical roles in immunomodulation and self-renewal[2, 34, 35]. Recent studies in animal models of DKD indicate that systemic administration of MSC ameliorates DM-associated albuminuria and renal pathological abnormalities in a paracrine manner through immunomodulatory and anti-apoptotic effects[36-39]. The potential clinical translation of MSC therapy for progressive DKD has reached the stage of early phase clinical trials but the precise mechanisms of action of MSC remain incompletely characterized.

In this study, we aimed to determine the immunological consequences of prolonged exposure of RPTEC/TERT1 stable monolayers to high concentrations of glucose and to investigate the modulatory effects of culture-expanded human MSC and their soluble products on high glucose (HG)-induced RPTEC inflammatory response and the resulting RPTEC/macrophage cross-talk.

Methods

RPTEC/TERT1 cell culture and treatments: RPTEC/TERT1 (human renal proximal tubular epithelial cell line from the American Tissue Culture Collection) were cultured in 24-well flat-bottom plates (Sarstedt, Numbrecht, Germany) in Dulbecco's Modified Eagle's Medium (DMEM) (Gibco, Grand Island, NY, USA) and Ham's F-12 medium (Gibco) at 1:1 supplemented with ITS (Sigma Aldrich, St Louise, MO, USA) containing 10 µg/ml Insulin, 5.5 µg/ml Transferrin and 5 ng/ml sodium selenite; 10 ng/ml epidermal growth factor (Sigma); 36 ng/ml hydrocortisone (Sigma); 2mM L-glutamine (Gibco) and 100 U/ml penicillin and 100 µg/ml streptomycin (Gibco) and maintained at 37°C, 5% CO_2 in a humidified tissue culture incubator. For stabilization of the monolayer, 27,500 cells/cm^2 were plated, cultured for 6 days to 100% confluency then allowed to form stable monolayers for a further 6 days before use in individual experiments. Medium was replaced every two days. For "high glucose (HG)" and "mannitol osmotic control (MAN)" culture conditions, medium additionally supplemented with 25mM *D-glucose* (Sigma) or 25mM D-mannitol (Sigma) respectively was added at day 12 and maintained for a further 4-5 days. In some experiments, medium was also supplemented with 100 µg/ml human serum albumin (Sigma), or 1 ng/ml IL-1β (Peprotech EC Ltd, NJ, USA) and 20 ng/ml TNFα (Peprotech) for the final 5 or 2 days of culture respectively. Phase contrast microscopy and image capture of cultured cells were performed at intervals using Olympus-IX71 inverted microscope (Tokyo, Japan). Osmolality of the cell culture supernatants from CTRL, HG and MAN conditions were measured in the Clinical Biochemistry Laboratory, Galway University Hospitals.

Culture of mesenchymal stromal cells and control cells: Cryopreserved human bone marrow-derived MSCs (BM-MSCs) from two healthy donors were cultured in MEM-Alpha media (Gibco) supplemented with 10% extracellular vesicle (EV)-free heat-inactivated fetal calf serum (FCS) (Gibco), 1% penicillin/streptomycin (Gibco) and 1 ng/ml fibroblast growth factor (R&D Systems, Minneapolis, MN, USA). EV-free FCS was prepared by ultracentrifugation of FCS at 100,000 x g (Sorvall 100SE Ultra Centrifuge) for 18 hours and subsequent collection of supernatants. Culture of human corneal endothelial cells (HCEC) was carried out in DMEM supplemented with 10% FCS (Gibco) and 1% penicillin/streptomycin (Gibco). Conditioned media were prepared as described in *Supplementary Methods* (see **Additional File 1**). In the case of the MSC-derived CM, this was further divided into non-manipulated CM ("MSC-CM (Whole)") and MSC-CM from which the MSC-derived EV were depleted by ultracentrifugation for 18 hours as 100,000 x g ("MSC-CM (-EV)").

Indirect Co-culture of RPTEC/TERT1 cells and mesenchymal stromal cells: RPTEC/TERT1 cells were plated at 27,500 cells/cm^2 in 6-well tissue culture plates and were cultured for 12 days to form stable monolayers. The cells were then cultured in medium additionally supplemented with 25mM D-glucose (Sigma) or D-mannitol (Sigma) for a further 5 days as described above. Human BM-MSC, were separately seeded at 10,000 cells/cm^2 into Transwell inserts (ThinCert^{TM}, Greiner Bio-One, Kremsmünster, Austria) for 3 days in MSC culture medium. On day 15 of RPTEC/TERT1 cell culture, the BM-MSC-containing inserts were placed on top of individual RPTEC/TERT1 monolayer-containing wells and these co-cultures were maintained for a further 2 days, following which the RPTEC/TERT1 cell pellets and supernatants were collected for protein analysis and enzyme-linked immunosorbent assays (ELISA) respectively. Transwell co-cultures of RPTEC/TERT1 cells and HCEC were carried out by the same protocol.

Enzyme-linked immunosorbent assays: Assay kits for Interleukin-1β (IL-1β), IL-6, IL-8, TNFα, IL-10, MCP-1 and neutrophil gelatinase-associated lipocalin (NGAL) (R&D Systems, MN, USA) were used to perform ELISAs of culture supernatants according to the manufacturer's instructions (see **Additional File 1** (*Supplementary Methods*) for a detailed protocol).

Flow cytometry: Viability of RPTEC/TERT1 cells was determined by propidium iodide (PI) (Molecular Probes, Oregon, USA) staining. In brief, following trypsinization and centrifugation, cell pellets were re-suspended in culture media and incubated for 15 minutes at 37^0C to restore membrane integrity. The cell suspensions were then washed and re-suspended in FACS buffer containing 2% FCS (Gibco) and 0.05% NaN_2 (Sigma) in PBS (Sigma). Cells were transferred as 100 µl aliquots into 5ml polystyrene FACS tubes (Sarstedt). Finally, PI solution was added to final concentration of 1 µg/ml and the samples were analysed on an Accuri-C6 flow cytometer (Becton Dickinson, USA) using CFlow software.

Western blotting: Immunoblots of RPTEC-derived protein lysates for NF-κB p65, phospho-NF-kB p65 (pP65), p38 MAPK, phospho-p38 MAPK (pP38MAPK), p44/42 MAPK (Erk1/2), phospho-p44/42 MAPK (pErk1/2; Thr202/Tyr204), STAT1, phospho-Stat1 (pSTAT1; Tyr701), protein kinase-C alpha (PKCα), phospho-PKCα/β II (pPKCα; Thr638/641) and PPAR-γ were performed using reagents and procedures described in *Supplementary Methods* (see **Additional File 1**).

RNA isolation and quantification: Total RNA was isolated from RPTEC/TERT1 cells using TRIzol/Chloroform method and by RNEasy Midi Kit (Qiagen, Hilden, Germany). A detailed protocol for RNA isolation by TRIzol method is provided in *Supplementary Methods*. For samples prepared using RNEasy Midi Kit (Qiagen), the manufacturer's recommended protocol was followed. The quality and integrity of all RNA samples were measured by Bioanalyzer-2100 using RNA 6000 Pico kit (Agilent Technologies) according to the manufacturer's recommended protocol.

RNA sequencing and bioinformatics analysis: High-throughput RNA sequencing (RNA-seq) was performed by BGI Genomics Service (Hong Kong) using BGISEQ-500 and Bioinformatics analyses of the resulting transcriptional profiles were performed using a suite of software packages including RSEM (quantitation of gene expression level), Cluster and Java Treeview Cluster (clustering analysis of gene expressions), Medusa (protein-protein interactions), WCGNA and Cytoscape (gene co-expression network analysis). Only RNA samples with RNA integrity number (RIN) ≥7.0 were subjected to RNA-seq. In brief, following fragmentation of mRNA and subsequent reverse transcription and amplification, a sequencing library was prepared. Nucleotide sequence of the fragments was determined and high-quality reads were aligned to the reference genomic sequence. Fragments that matched the genomic sequence were assigned to a specific position of a specific chromosome in the genome, thereby the gene fragments could be linked to a specific gene. The number of reads per gene were counted and normalised. The criteria for designation of differentially expressed genes (DEG) were >1.5 absolute fold-change and statistical significance ($p < 0.05$) among experimental conditions. RNA-seq data analyses involved plotting data using principal component analysis and KEGG pathway enrichment analysis.

Quantitative, reverse transcription polymerase chain reaction (qRT-PCR): For qRT-PCR, the Luna Universal Probe One Step RT-qPCR kit (New England BioLabs, MA, USA) was used according to manufacturer's instructions. Reactions consisted of 50 ng RNA samples, mastermix, nuclease-free water, enzyme and primer/probe in a final volume of 10 μl. Individual target specific primers (both forward and reverse; for IL-6, MCP-1, IL-1β, IL-8, TNFα, NGAL and RPLP0) and TaqMan probes (for quantitation) were purchased from Integrated DNA Technologies (Coralville, Iowa, USA). The primer sequences are listed in Supplementary Table S1 [see **Additional File 2**]. The reactions were performed on Step-One Plus PCR instrument (Applied Biosystems, Waltham, MA, USA). Mean Ct values were used to calculate the fold changes in the expression of different target genes (for IL-6, MCP-1, IL-1β, IL-8, TNFα and NGAL) in treatment groups vs. control as determined relative to the housekeeping gene RPLP0 using the $2^{-\Delta\Delta Ct}$ method.

Culture of primary human macrophages and exposure to conditioned media: Human peripheral blood mononuclear cells (PBMC) were prepared and cultured overnight using a standard protocol (described in detail in *Supplementary Methods*). Plastic-adherent PBMC were cultured in 24-well plates (Sarstedt) at a density of 22,500 cells/cm^2 in macrophage medium containing 20 ng/ml granulocyte macrophage colony stimulating factor (GM-CSF, Peprotech). Medium was replaced every 3 days. After 9 days, the medium was replaced with conditioned medium (CM) from the RPTEC/TERT1 co-culture experiments with addition of GM-CSF to a final concentration of 20 ng/ml. To some wells, 100 ng/ml interferon gamma (IFNγ, Peprotech), 100 ng/ml TNFα (Peprotech) and 50 ng/ml LPS (Sigma) were added to provide a positive control for pro-inflammatory stimulation. After 24 hours, the CM was removed, the macrophages were washed with PBS and fresh macrophage medium containing GM-CSF was added. Finally, after an additional 24 hours of culture, the supernatants were collected for subsequent analysis by ELISA.

Statistical analysis: Statistical analysis was performed using GraphPad Prism version 6.0. Paired- or unpaired Student's t-test, non-parametric multiple t-test, one- or two- way ANOVA were used for analysis of individual experiments as appropriate. Details of statistical analyses performed for specific experiments are provided in individual figure legends. For all statistical analyses, the threshold for significance was < 0.05. Experiments were performed at least 3 times unless otherwise stated in the figure legends.

Results

Prolonged exposure to high glucose enhances inflammatory response of RPTEC/TERT1 monolayers: Based on previously published characterizations of the RPTEC/TERT1 cell line by us and others,[25-27] culture conditions were established under which RPTEC-TERT1 cells, seeded at an optimized initial density (Supplemental **Figure 1A** [see **Additional File 3**]), reached confluence by Day 6 and formed stable monolayers by Day 12. As shown in **Figure 1A**, seeded cells progressed from sub-confluent, spindle-shaped calls to confluent layers of tightly-packed cells of cobblestone appearance between days 0 and 6 of culture then developed frequent dome-shaped protuberances between days 8 and 12. After 12 days of culture, RPTEC/TERT1 monolayers were cultured for an additional 4 days under RM, HG or MAN conditions. As shown in **Figure 1B**, RPTEC/TERT1 monolayers continued to show a confluent, cobblestone appearance during this time period and no morphological differences were observed among the culture conditions. The osmolalities of HG and MAN culture media were confirmed to be higher than that of the basal medium (HG = 360±10 mosm/ml; MAN = 366±9 mosm/ml; CTRL = 339±3 mosm/ml).

The influence of high glucose (HG) exposure for a further 5 days (120 hours) on secretion of inflammation-related soluble factors (IL-6, IL-8 and MCP-1) and tubular injury-related marker NGAL into the culture medium was then compared to that of normal-glucose (CTRL) and mannitol osmotic control (MAN) culture conditions (**Figure 2A&B**). As shown, increased secretion of all four analytes was observed under HG but not MAN conditions relative to CTRL between 80 and 120 hours of culture. The HG-induced increases in inflammatory factors were not associated with increased cell death (**Figure 2C**). As further evidence of the relevance of the culture system to diabetic conditions, it was verified that the exposure of RPTEC/TERT1 monolayers to other relevant stimuli – human serum albumin (HSA) and IL-1β - known to exert pro-inflammatory effects on proximal tubular epithelial cells, resulted in increased secretion of IL-6, IL-8, MCP-1 and NGAL that was additive to the induction associated with HG culture (Supplementary **Figures S2 and S3** show these results in detail [see **Additional File 4** and **Additional File 5**]). Neither HSA nor IL-1β were associated with increased cell death during culture (data not shown). Western blotting of RPTEC/TERT1 monolayer-derived protein lysates collected at 24, 48 and 96 hours following exposure to CTRL, HG and MAN conditions showed evidence of activation of multiple potentially pro-inflammatory intracellular signalling pathways (NF-kB, p38 and ERK1/2 MAPK and PKCα). However, the level of activation, based on abundance of phosphorylated pathway components, was no greater for HG compared to the control conditions (**Supplementary Figure S4A and S4B** show these results in detail [see **Additional File 6** and **Additional File 7**]). It was concluded that prolonged exposure of mature RPTEC/TERT1 cell monolayers to HG results in increased release of pro-inflammatory mediators that is not driven by sustained hyperactivity of the individual signalling pathways examined and is not associated with overt loss of viability, gross morphological changes or dedifferentiation to a non-epithelial phenotype.

Conditioned medium from human mesenchymal stromal cells inhibits the high glucose-induced inflammatory response of RPTEC/TERT1 monolayers: Early-passage human BM-MSC from healthy adult donors were shown to have expected surface marker profiles and osteogenic and adipogenic differentiation potential (**Supplementary Figure S5** shows these results in detail [see **Additional File 8**]). To determine whether MSC-derived soluble products suppress RPTEC/TERT1 inflammatory responses, 10X-concentrated MSC-CM with and without depletion of extracellular vesicles (EVs) was added at 20% volume to RPTEC/TERT1 monolayers for the final 48 hours of 5-day cultures in HG and MAN conditions (**Figure 3**). Conditioned media of BM-MSC from two different donors were used. As shown, both MSC-CM preparations resulted in reduced secretion of IL-8, IL-6 and MCP-1 but not NGAL under HG and MAN conditions. Of note, the suppressive effect of MSC-CM on pro-inflammatory cytokines and chemokines was similar for CM preparations with and without EV depletion, suggesting that the effect was unlikely to be mediated by MSC-EV. In contrast, addition of CM from a non-MSC cell line (HCEC) resulted either in no reduction or in increased release of IL-6, IL-8, MCP-1 and NGAL by RPTEC/TERT1 monolayers.

Indirect co-culture of human mesenchymal stromal cells causes a more potent inhibition of high glucose-induced inflammatory response of RPTEC/TERT1: Next, it was determined, using a transwell co-culture system, whether indirect contact of BM-MSC diminishes the RPTEC/TERT1 inflammatory response to HG and control culture conditions. As shown in **Figure 4**, indirect contact with BM-MSC from two different donors (but not indirect contact with HCEC) for the final 2 days of a 5-day culture resulted in potent reductions of secretion of IL-8, IL-6 and MCP-1 by HG-exposed RPTEC/TERT1 cell monolayers as well as more modest reductions under MAN-exposed conditions. In contrast to the effect of MSC-CM addition, transwell co-culture with MSC (as well as with HCEC) resulted in potent reduction of NGAL release by the monolayers under HG and, to a lesser extent, MAN conditions.

Prolonged exposure of RPTEC/TERT1 monolayers to high glucose concentration is associated with widespread transcriptional modifications that are modulated by indirect co-culture with MSC: To more broadly characterise the effect of prolonged HG exposure, RNA-seq was performed on triplicate samples of mature RPTEC/TERT1 monolayers following 5-day culture in CTRL, HG and MAN culture conditions (**Figure 5A**). For this analysis, hierarchical clustering and principal component analyses demonstrated partial overlap between CTRL and MAN transcriptional profiles with separation of the HG profile from both controls (**Figure 5B&C**). In total, 527 and 374 genes were differentially expressed in HG-exposed compared with CTRL- and MAN-exposed RPTEC/TERT1 monolayers respectively, with 115 (26 up-regulated and 89 down-regulated) DEGs being common to both comparisons (**Figure 5D**). In contrast, only 314 DEG were identified for MAN compared to CTRL samples. Full lists of the DEGs from these comparisons are provided in Supplementary Tables S2-4 [see **Additional File 9**, **Additional File 10** and **Additional File 11**]. Biological process and pathway enrichment analysis of the DEGs from HG vs. MAN comparison indicated a predominance of processes and pathways related to inflammation and infection (**Supplementary Figure S6** shows these results in detail [see **Additional File 12**]). Prominent among the modulated pathways were TNF-signalling pathway, cytokine-cytokine receptor interaction and NOD-like receptor signalling pathway. Among 15 DEGs within the TNF signalling pathway, multiple inflammation-related transcripts were present including IL1-β, TNF, IL-6, L-selectin, colony stimulating factor 2 (CSF-2), IL-8, C-C motif chemokine ligand 2 (CCL2; also called MCP-1), lymphotoxin beta (LTB) and cellular inhibitor of apoptosis 1 and 2 (cIAP1/2) (**Supplementary Figure S5** shows these results in detail [see **Additional File 13**]).

Next, a similar RNA-seq analysis was carried out on triplicates of RPTEC/TERT1 monolayers following 5-day exposure to HG and MAN conditions in the presence or absence of indirect (transwell) MSC co-culture for the final 2 days (**Figure 6A**). As shown in **Figure 6B**, principal component analyses demonstrated distinctive transcriptional profiles for the 4 conditions – indicating broad modulatory effects of indirect MSC co-culture on RPTEC/TERT1 gene expression under both HG and osmotic control conditions. In total, 811 genes were differentially expressed in MSC-co-cultured vs. non-MSC-(control)-

cultured RPTEC/TERT1 monolayers under HG condition of which 395 were up-regulated and 416 were down-regulated. For the MAN condition, 916 genes were differentially expressed between non-MSC (control)-co-cultured vs. MSC-co-cultured cells of which 576 were up-regulated and 368 were down-regulated. A total of 281 genes (148 up-regulated and 133 down-regulated) were modulated by MSC co-culture under both HG and MAN conditions (**Figure 6C**). Among the latter, were multiple transcripts of relevance to inflammatory response including those encoding CCL2/MCP-1, Chemokine (C-X-C motif) ligand 2 (CXCL2), enolase-2, interleukin 2 receptor subunit gamma (IL2RG), IL1-β, prostaglandin-endoperoxide synthase 1 (PTGS1), lipocalin 2 (LCN2; also called NGAL), S100 calcium binding protein A14 (S100A14), L-selectin (SELL) and superoxide dismutase 2 (SOD2)(Full lists of the DEGs from these comparisons are provided in **Supplementary Tables S5 and S6** [see **Additional File 14** and **Additional File 15**].

Biological process (presented in **Supplementary Figure S8** [see **Additional File 16**]) and pathway enrichment (**Figure 6D&E**) analyses of the Control-co-cultured vs. MSC-co-cultured RNA-seq profiles under HG and MAN conditions indicated prominent modulation of a range of inflammation-related responses. Notable among the pathways that were significantly modulated by indirect MSC co-culture in the presence of HG were TNF-signalling pathway, cytokine-cytokine receptor interaction, NOD-like receptor signalling pathway and arachidonic acid metabolism. Transcripts involved in these pathways included those encoding IL1β, TNF, Interleukin-6 (IL-6), IL18R, SELL, CSF2, TNF Alpha Induced Protein 3 (TNFAIP3), IL-8, CCL2, CXCL2, LTB and cIAP1/2 (**Supplementary Figure S9** provides a representative example [see **Additional File 17**]). Quantitative RT-PCR analysis confirmed the RNA-seq results for 5 inflammation-related transcripts (**Figure 7**).

Overall, it was concluded from the transcriptional profiling analyses of RPTEC/TERT1 monolayers that prolonged exposure to HG results in enhanced expression/activity of a wide range of genes and pathways associated with immune response and inflammation and that proximity to viable human BM-MSC for 48 hours exerts a broad inhibitory effect on many of these inflammatory pathways – likely through the production of soluble mediators. Furthermore, the anti-inflammatory effect of MSC on proximal tubular epithelial monolayers is not exclusive to a HG-induced pro-inflammatory response, as it was also evident under MAN (osmotic control) conditions.

Indirect mesenchymal stromal cell contact modulates pro-inflammatory cross-talk between high glucose-exposed RPTEC/TERT1 cell monolayers and human macrophages: Finally, we sought to determine whether soluble products released during RPTEC/TERT1-MSC co-cultures under HG or MAN conditions exert anti-inflammatory effects on human macrophages. An experiment was carried out in which *in vitro*-differentiated, human monocyte-derived macrophages were cultured for 24 hours in the presence of CM from RPTEC/TERT1 monolayers that had been exposed for 5 days to HG or MAN conditions in the presence or absence of BM-MSC-containing transwells for the final 2 days (**Figure 8A**). The CM-exposed macrophages were then washed and allowed to remain in culture in macrophage medium alone for a further 24 hours, following which production of pro-inflammatory cytokines and chemokines was quantified by ELISA of the macrophage culture supernatants. Macrophages cultured for 24 hours in the absence and presence of a stimulatory cocktail of LPS, IFNγ and TNFα served as additional controls. As shown in **Figure 8B**, primary human macrophages showed significant elevation in the levels of those cytokines/chemokines when exposed for 24 hours to CM from RPTEC/TERT1 cells under HG compared to MAN condition. When macrophages were exposed to CM from the equivalent RPTEC/TERT1-MSC co-cultures, reduced secretion of IL-8, MCP-1, IL-6 and TNFα was observed – being most significant for IL-8 and TNFα. The magnitude of induction of IL-8, MCP-1 and TNFα following macrophage exposure to HG-CM from RPTEC alone was comparable to that induced by stimulation with LPS, IFNγ and TNFα. The results of qRT-PCR performed on RNA extracted from macrophages at the end of the experiment were inconclusive due to variability across technical replicates (*data not shown*). It was not possible, therefore, to confirm whether reduced macrophage secretion of inflammatory mediators was mediated specifically through suppression of transcription. A conceptual model for MSC modulation of HG-induced RPTEC/macrophage cross-talk based on the experimental results of the study is shown in **Figure 8C**.

Discussion

A growing body of evidence indicates that RPTEC play an important role in the pathogenesis of DKD[17, 21, 25, 39, 40]. *In vitro* observations using immortalised cell lines such as HK-2 provide a valuable, simplified system in which to explore specific effects of the diabetic milieu on renal epithelial cell biology but have limitations when comparing with primary RPTEC. Recent studies suggest that stable monolayers of RPTEC/TERT1 cells provide superior phenotypic and functional comparability to primary tubular epithelium[24-27]. In our hands, in keeping with previous reports [24-27], RPTEC/TERT1 cells formed stable monolayers after 12 days with an epithelial-like, cobblestone morphology which remained stable following a further 5 days exposure to HG or MAN. In this system, we observed that prolonged HG exposure induced a heightened inflammatory phenotype characterized by progressively increasing secretion of IL-6, IL-8 and MCP-1 along with greater release of the tubular injury biomarker NGAL. For IL-6 and MCP-1, our observations are comparable to those of Tang *et al*. in confluent, growth-arrested primary RPTEC, albeit only becoming evident compared to normal glucose and MAN controls following a longer exposure time[42]. Importantly, although RNA-seq analysis revealed a range of other gene expression changes, we did not observe overt toxicity or evidence of loss of epithelial-like morphology of the monolayers during the period of exposure to HG or MAN.

Consistent with the HG-induced increase in IL-6 secretion by RPTEC/TERT1 monolayers, patients with DKD have increased renal IL-6 expression which correlates with kidney hypertrophy and albuminuria[43, 44] and increases with stage of DKD[45]. Exposure to HG for 96 hours or more also resulted in increased secretion of IL-8 by RPTEC/TERT1 cells. Of vsinterest, Tashiro *et al*. reported increased levels of IL-8 in urine samples from the patients with early-stage DKD[46] while others observed increased IL-8 production by tubular epithelial cells via activation of NF-κB, ERK1/2 and STAT1 signalling in a glycated-albumin-induced diabetes model[47]. Similarly, NF-κB-dependent upregulation of MCP-1 in albumin-treated RPTEC and increased MCP-1 expressions in kidney biopsy samples from patients with DKD has been reported[48, 49]. In a hyperglycaemic environment, increased MCP-1 production by mesangial and tubular epithelial cells has also been observed *in vitro*[14, 50]. Functionally, tubular cell-derived MCP-1 triggers infiltration of the interstitium by monocytes which, along with resident macrophages, secrete additional pro-inflammatory cytokines [16]. We also describe here a progressive increase in the release of NGAL, a comparatively new biomarker of DKD, following exposure of RPTEC/TERT1 stable monolayers to HG for 80 hours or more. Of relevance, NGAL is elevated in serum and urine of DKD patients[51-53]. Furthermore, Nielsen *et al* demonstrated an association between urinary NGAL and rate of eGFR decline with the implication that renal tubular cells represent the major source of the urinary NGAL release[52]. Taken together, these observations support the relevance of our findings in the RPTEC/TERT1 culture system to renal interstitial inflammatory events related to hyperglycaemia and diabetes.

Human bone marrow-derived MSC produce immunomodulatory and cytoprotective mediators that act in a paracrine manner on a range of target cells to downregulate the production of pro-inflammatory cytokines and inhibit inflammatory signalling pathways[36, 54-56]. In animal models of diabetes, hBM-MSC infusions reduced matrix deposition in the mesangium[54] and glomerulus[56]. Nagaishi *et al*. studied the effects of BM-MSC treatment in insulin-deficient and insulin-resistant DKD models and demonstrated the benefits following systemic administration of both cells and CM[37]. Similarly, Lv *et al*. reported reduced intra-renal expression of IL1β, IL-6, TNFα and MCP-1 following intravenous injection of MSC in a streptozotocin-induced rat model of DKD[55]. The reduction in MCP-1 and other inflammatory cytokines was associated with decreased macrophage infiltration and reduced severity of renal structural injury. In keeping with these *in vivo* findings, our experiments to evaluate the effect of human BM-MSC on human RPTEC/TERT1 cells in the setting of prolonged HG exposure revealed anti-inflammatory effects both of MSC-CM and of indirect (transwell) co-culture of RPTEC-TERT1 cells with MSC – with the latter being more potent. To our knowledge, this is the first study to show the effect of MSC and their soluble products on RPTEC/TERT1 cells as an *in vitro* model of diabetic proximal tubulopathy. The results indicate that MSC have the potential to modulate RPTEC dysfunction in DKD either from a distant anatomical site or locally within the kidney. Perhaps surprisingly, MSC-CM depleted of EV had comparable anti-inflammatory effects to those of EV-containing CM, indicating that the paracrine anti-inflammatory effects were unlikely to be mediated by MSC-derived EV despite evidence that they may have reno-protective properties[57, 58]. Whether purified MSC-EV may have a distinct modulatory effect on HG-induced inflammatory responses of RPTEC/TERT1 monolayers and, if so, what mechanisms underlie such an effect, remains an interesting question that merits further investigation.

Although knowledge of the mechanism of action of MSC *in vivo* is incomplete, the paracrine effect of a range of inducible factors is well established. Transcriptomic analysis of RPTEC/TERT1 cell monolayers demonstrated that prolonged HG exposure was associated with gene expression changes that were enriched for biological processes and signalling pathways of relevance to immune response and inflammation. We also observed differential gene expression between MAN and CTRL culture conditions that likely reflect the influence of increased osmolality on RPTEC-TERT1 monolayers. However, the findings that higher numbers of DEGs were identified for HG vs CTRL than for MAN vs CTRL and that the HG condition separated fully from CTRL and MAN on a principal component analysis of the RNA-seq data are in keeping with a distinct effect of HG rather than a non-specific effect of increased osmolality. Interestingly, under both HG and MAN conditions, the modulatory effects of indirect co-culture with MSC on the RPTEC-TERT1 monolayer transcriptome were also enriched for immune/inflammatory pathways – with the TNF signalling pathway being particularly prominent. Modulation of the HG-induced TNF signalling pathway following MSC co-culture included reversion toward control levels of the increased expression of genes related to leukocyte recruitment (CCL2/MCP-1, CXCL1, CXCL2, CXCL3), leukocyte activation (CSF-2), inflammatory cytokines (IL-1β, IL-6) and cell adhesion (E-Selectin). Results for several inflammatory mediators/products (IL-6, IL-8, CCL2/MCP-1 and LCN2/NGAL) were consistent across RNA-seq, qRT-PCR and ELISA. An overall implication of these results is that human MSC, delivered directly to the kidney or transmigrating to renal interstitial spaces in the setting of diabetes/hyperglycemia are likely to initiate a paracrine interaction with RPTEC that potently down-regulates chronic inflammatory signalling. Furthermore, we provide evidence that the modulatory effect of MSC on release of inflammatory mediators by RPTEC in the setting of HG may have downstream effects on the response of monocyte-derived macrophages which are known to infiltrate the kidney and mediate renal interstitial damage during DKD[31]. Inflammatory stimuli to RPTEC have been shown to result in cross-talk with intra-renal macrophages through a number of mechanisms including cytokine/chemokine secretion, transfer of bioactive molecules in extracellular vesicles, release of danger-associated molecular patterns and triggering of specific forms of necrotic cell death[59-61].

A relatively large body of literature exists in support of the potential benefits of MSC to slow the progression of DKD through anti-inflammatory mechanisms[2]. To date, however, only one early phase clinical trial of a stromal cell therapy has been completed in human subjects with DKD. This demonstrated that, in relatively advanced DKD due to type 2 DM, intravenous injection of allogeneic bone marrow-derived Stro3$^+$ mesenchymal precursor cells was safe up to 24 weeks post-administration and was associated with preliminary evidence of efficacy including decreased serum IL-6 compared to placebo[62].

In addition to the obvious caveat that experimental work conducted in vitro using a cell line will require validation in more physiologically relevant systems, some specific limitations of the study must be acknowledged. Firstly, while our culture conditions and experimental durations are quite comparable to those used by other investigators who have extensively characterized RPTEC/TERT1 cell epithelial monolayer formation[26], they cannot be said to be identical. Thus, the influence of variability in culture conditions on the physiological relevance of our experimental findings cannot be fully determined. Nonetheless, it is clear that, in our hands, the cells consistently generated typical, mature epithelial-like monolayers and that subsequent 4-5-day exposure of the monolayers to HG and MAN did not result in overt cellular toxicity or transformation to a non-epithelial phenotype. Lack of elucidation of a clear intracellular signalling mechanism to explain HG-induced changes in the expression and secretion of inflammatory mediators by RPTEC/TERT1 cell monolayers (and its suppression by factors released by MSC) is a second limitation. While involvement of alternative signalling pathways, of post-transcriptional/post-translation modification of the gene products or of altered intracellular trafficking/secretion of inflammatory mediators may explain the observations, it is also possible that experiments carried out at earlier or later time-points could have revealed increased activity of one or more predicted signalling pathways under HG conditions. Thirdly, while our experimental focus for the study was on HG-induced inflammatory response of RPTECT/TERT1 monolayers and its modulation by MSC, other potentially important aspects of the altered transcriptomic profiles revealed by RNA-seq have not been functionally validated and explored. By sharing the full lists of DEG we have identified under different experimental conditions, we anticipate that these data can be further exploited through deeper functional investigation by others in the field. Finally, a limitation of our experiments involving the transfer of conditioned media from RPTEC/MSC co-cultures to primary macrophages is that they do not exclude the possibility that MSC- and RPTEC/TERT1-derived soluble mediators act on macrophages independently of each other rather than as a result of a distinctive MSC/RPTEC cross-talk. Thus, additional experiments beyond the scope of the current study will be needed to dissect the individual mechanistic contributions of RPTEC and MSC on downstream activity of macrophages and to investigate the potency of MSC to regulate RPTEC signalling to macrophages across a range of pathogenic conditions.

Conclusions

Our current study reveals a predominantly pro-inflammatory effect of prolonged HG exposure on stable monolayers of the RPTEC/TERT1 cell line during a 5-day time window that is substantially modulated at transcriptional level by soluble products of human MSC – particularly when the two cell types were cultured in close proximity. Experimentally, we also show that the combined secretome of RPTEC/MSC co-cultures has the capacity to dampen macrophage inflammatory response under HG conditions. These results provide a novel platform for better understanding anti-inflammatory mechanisms of action of MSC in *in vivo* studies and clinical trials of DKD. Our *in vitro* system also has the potential for identifying new targets of intervention for diabetes-associated proximal tubulopathy and pro-inflammatory epithelial cell/macrophage cross-talk. Further studies are also needed to elucidate the mechanisms whereby HG exposure induces a prolonged increased secretion of cytokines, chemokines and markers of inflammation by RPTEC in the absence of persistent over-activity of NF-κB, MAPK and other expected intracellular signalling pathways.

List of Abbreviations

DKD = diabetic kidney disease

ESRD = end-stage renal disease

ROS = reactive oxygen species

AGE = advanced glycation end-products

MCP-1 = monocyte chemoattractant protein 1

DM – diabetes mellitus

IL = interleukin

TNFα = tumor necrosis factor alpha

RPTEC = renal proximal tubular epithelial cell

hTERT = human telomerase reverse transcriptase

MSC = mesenchymal stromal cell

DMEM = Dulbecco's modified Eagle medium

HG = high glucose

MAN = mannitol

BM-MSC = bone marrow-derived mesenchymal stromal cells

FCS = fetal calf serum

HCEC = human corneal endothelial cell

NGAL = neutrophil gelatinase-associated lipocalin

PI = propidium iodide

RIN – RNA integrity number

DEG = differentially expressed gene

IFNγ = interferon gamma

GM-CSF = granulocyte macrophage colony stimulating factor

CTRL = control

EV = extracellular vesicle

CM = conditioned medium

RNA-seq = RNA sequencing

HSA = human serum albumin

Declarations

Ethics Approval and Consent to Participate

Human healthy volunteer bone marrow samples were sourced through the HRB Clinical Research Facility Galway according to a protocol approved by the Clinical Research Ethics Committee of the Galway University Hospitals. Primary culture expansion of MSC from bone marrow samples was performed at the Centre for Cell Manufacturing Ireland, National University of Ireland Galway.

Consent for Publication

Not applicable

Availability of data and material

RNA-seq data will be made publically available through GEO upon acceptance for publication[62]. All other datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing Interests

The authors have no relevant conflicts of interest to declare in relation to the work described in the manuscript.

Funding

The research was supported by a grant from the European Commission [Horizon 2020 Collaborative Health Project NEPHSTROM (grant number 634086; TPG, MNI, MDG)]. Other funding sources that contributed to the work were grants from the European Commission [FP7 Collaborative Health Project VISICORT (grant number 602470; MDG, JC)], from Science Foundation Ireland [REMEDI Strategic Research Cluster (grant number 09/SRC-B1794; MDG) and CÚRAM Research Centre (grant number

13/RC/2073; MDG)], from the Health Research board of Ireland (grant number HRA_POR/2013/341; JC, MDG) and the European Regional Development Fund. TPG is supported by a Hardiman Scholarship from the College of Medicine, Nursing and Health Science, National University of Ireland Galway and a bursary from the Irish Endocrine Society/Royal College of Physicians of Ireland. JMcC and TMcM are funded by Science Foundation Ireland (grant number 12/IP/1686) and by the School of Biomolecular and Biomedical Science, University College Dublin.

The EU Commission takes no responsibility for any use made of the information set out.

Authors' Contributions

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Matthew D. Griffin: Conception and design, Financial support, Data analysis and interpretation, Manuscript writing, Final approval of manuscript.

Acknowledgements

All flow cytometry experiments were performed in the NUI Galway Flow Cytometry Core Facility which is supported by funds from NUI Galway, Science Foundation Ireland, the Irish Government's Programme for Research in Third Level Institutions, Cycle 5 and the European Regional Development Fund. The materials presented and views expressed here are the responsibility of the author(s) only. Human corneal endothelial cells were kindly provided by Prof. Thomas Ritter, REMEDI, School of Medicine, NUI Galway. We wish to acknowledge the generous assistance of Dr. Paula O'Shea, Clinical Biochemistry Laboratory, Galway University Hospitals for facilitating the analysis of culture supernatant osmolality.

Figure Legends

Figure 1: *Morphology of RPTEC/TERT1 cell layers in culture.* **A.** Morphology at different time points before and after confluency using phase contrast microscopy at 4X magnification. **B.** Morphology of cell layers during basal medium (CTRL), HG and MAN culture conditions beginning at day 12 for four consecutive days using phase contrast microscopy at 4X magnification.

Figure 2: *High glucose exposure increases the inflammatory response of RPTEC/TERT1 cell stable monolayers:* **A.** Schematic diagram of the experimental protocol. **B.** Concentrations of inflammatory biomarkers IL-8 (top left), IL-6 (top right), MCP-1 (bottom left) and tubular injury marker NGAL (bottom right) in culture supernatants of RPTEC/TERT1 cell stable monolayers between 3 and 120 hours following exposure to medium containing Normal (5mM) Glucose (CTRL, grey line), High (30nM) Glucose (HG, red line) and 5mM Glucose + 25mM Mannitol (MAN, blue line). All results are presented as Mean ± SD. Statistical analyses were performed by one-way ANOVA and non-parametric multiple t-test. * $p < 0.05$. **C.** Representative examples of flow cytometric analysis of RPTEC/TERT1 cell viability by propidium iodide exclusion at various time-points following exposure to the three culture conditions. Percentages of dead cells (PI^{+ve}) are shown for each condition.

Figure 3: *Total and extracellular vesicle-depleted conditioned media from human MSC but not HCEC inhibit high glucose-induced secretion of inflammatory cytokines by RPTEC/TERT1 cell stable monolayers.* **A.** Schematic diagram of the experimental protocol (+/- EV = without and with extracellular vesicle depletion). **B.** Graphs depicting the concentrations of IL-8, IL-6, MCP-1 and NGAL in the supernatants from RPTEC/TERT1 cell monolayers cultured without (Control) and with various conditioned media (CM) during the final 2 days of 5-day cultures under High Glucose (HG, left graphs) and Mannitol (MAN, right graphs) conditions. All results are expressed as Mean ± SD of n=6 technical replicates for each condition. For cultures containing human (h)BM-MSC-derived CM, results are shown for MSC from two different donors [Donor 1 (blue) and Donor 2 (green)]. MSC-Control = Unconditioned

MSC medium. MSC-CM (Whole) = Non-extracellular vesicle (EV) depleted MSC-CM. MSC-CM (-EV) = Extracellular vesicle (EV) depleted MSC-CM. HCEC-Control = Unconditioned human corneal endothelial cell medium. HCEC-CM = CM from human corneal endothelial cells. Statistical analyses performed by one-way ANOVA (for hBM-MSC *versus* Control) and unpaired Student's t-test (for Endothelial Cell *versus* Control). **** p <0.0001, *** p <0.001, * p <0.05, ns = not significant.

Figure 4: *Indirect co-culture with human MSC results in potent inhibition of high glucose-induced secretion of inflammatory cytokines by RPTEC/TERT1 cell stable monolayers.* **A.** Schematic diagram of the experimental protocol. **B.** Graphs depicting the concentrations of IL-8, IL-6, MCP-1 and NGAL in the supernatants from RPTEC/TERT1 cell monolayers cultured without (Control) and with (Cells) various Transwell co-cultures during the final 2 days of 5-day cultures under High glucose (*D-glucose*, blue) and Mannitol (D-mannitol, purple) conditions. Results are shown for co-cultures carried out with human Bone Marrow MSCs from two different donors (BM-MSC-1 and BM-MSC-2) and with a non-MSC control cell line (HCEC, grey). All results are expressed as Mean ± SD of n=6 technical replicates for each condition. Statistical analyses performed by one-way ANOVA (for BM-MSC *versus* Control) and unpaired Student's t-test (for HCEC *versus* Control). **** p <0.0001, *** p <0.001, ** p <0.01, * p <0.05, ns = not significant.

Figure 5: *High-level bioinformatics analyses of* RNA-seq *transcriptional profiling of RPTEC/TERT1 monolayers following 5-day exposure to control, high glucose and mannitol culture conditions:* **A.** Table summarizing the samples subjected to RNA-seq. **B.** Unsupervised hierarchical clustering of the RNA-seq profiles of samples (nomenclature as per **4A**). **C.** Scatter plot of principal component analysis of the RNA-seq profiles. Each dot represents one sample (nomenclature as per **4A**). **D.** Figures illustrating the numbers of total, up-regulated and down-regulated DEGs for High glucose (HG) vs. Normal glucose

control (CTRL) culture conditions and High glucose vs. Mannitol control (MAN) culture conditions. Overlapping segments indicate the numbers of DEGs that were common to both comparisons.

Figure 6: *Bioinformatics analyses of* RNA-seq *transcriptional profiling of RPTEC/TERT1 monolayers following 5-day exposure to high glucose (HG) and mannitol (MAN) culture conditions in the presence or absence of MSC-containing transwells:* **A.** Table summarizing the non-MSC- (Control) and MSC-co-cultured (MSC) samples subjected to RNA-seq. **B.** Scatter plot of principal component analysis of the RNA-seq profiles. Each dot represents one sample (nomenclature as per **5A**). **C.** Figures illustrating the numbers of total, up-regulated and down-regulated DEGs for Control vs. MSC-co-cultured RPTEC/TERT1 cells under High glucose (HG) and Mannitol (MAN) culture conditions. Overlapping segments indicate the numbers of DEGs that were common to both comparisons. **D & E.** Scatter graphs indicating the enrichment factors and number of DEGs of the top 20 enriched pathways for Control vs. MSC-co-cultured RPTEC/TERT1 monolayers under HG (**D**) and MAN (**E**) conditions based on KEGG pathway enrichment analysis.

Figure 7: *Validation of the effect of BM-MSCs on RPTEC-TERT1 expression of inflammation-related transcripts.* Graphical representations of qRT-PCR analysis of the relative expression of RNA transcripts for IL-6, MCP-1 (CCL2), IL-1β, IL-8, TNFα and NGAL (LCN2) in RPTEC/TERT1 cell monolayers cultured for 5 days in high glucose (HG) (**A**) or Mannitol (MAN) (**B**) in the presence of BM-MSC-containing transwells (MSC) or no cells (Control) for the final 2 days of culture. Results are expressed as mean ± SD for n=3 samples per condition of the fold difference for MSC vs. Control as determined relative to the housekeeping gene RPLP0 using the $2^{-\Delta\Delta Ct}$ method. Statistical analysis by Student’s unpaired t-test, $^{**}p < 0.01$, $^{*}p < 0.05$, ns=not significant.

Figure 8 *Indirect mesenchymal stromal cell contact modulates pro-inflammatory cross-talk between high glucose-exposed RPTEC/TERT1 cell monolayers and human macrophages.* **A.** Schematic diagram of the experimental protocol. **B.** Graphs depicting the concentrations of IL-8, MCP-1, TNFα and IL-6 in the supernatants from monocyte-derived macrophages cultured with macrophage medium alone (Medium), macrophage medium containing a stimulatory cocktail of LPS, IFNγ and TNFα (Medium + M1 Stimuli) and conditioned media from 48 hr cultures of RPTEC/TERT1 cells alone (RPTEC) or RPTEC/TERT1 cells co-cultured with MSC-containing transwells (MSC + RPTEC) under high glucose (HG) and mannitol (MAN) conditions. Results for macrophages exposed to conditioned media from high glucose (HG) condition are represented in green and those from Mannitol (MAN) are represented in blue bars. Results are expressed as Mean ± SD of n=3 technical replicates for each condition. Statistical analyses performed unpaired Student's t-test (* for MSC *versus* Control; + for HG *versus* MAN). ****/++++ $p < 0.0001$, ***/+++ $p < 0.001$, **/++ $p < 0.01$, */+ $p < 0.05$, ns = not significant. **C**. Schematic representation of the effect of high glucose on RPTEC, the subsequent inflammatory response of macrophages (left) and the modulatory effect of indirect contact between RPTEC and MSC on the downstream macrophage response (right).

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63. GEO URL link to RNA-seq datasets (to be completed upon acceptance for publication).

Additional File Titles and Legends

Additional File 1.docx: *Supplementary methods document*.

Additional File 2.TIF: *Supplementary Table S1*: List of primer sequences used for qRT-PCR

Additional File 3.TIF: *Supplementary Figure S1*: Effect of High D-Glucose on RPTEC/TERT1 Cells. **A**. Effect of seeding density on growth of RPTEC-TERT-1 cells. Here, three different cell numbers per square centimeter (cm^2), labelled as Low (12500 cells/cm^2), Medium (12500 cells/cm^2) and High (12500 cells/cm^2), are represented as Blue, Green and Grey coloured lines respectively. Cells grown in 24 well plate for different time points and number of cells counted by haemocytometer using trypan blue and represented as cells/cm^2. **B**. Effect of high glucose on growth of RPTEC-TERT-1. Cells were seeded at 27500/cm^2. and counted at different time points using haemocytometer. **C.** Downstream experimental plan. RPTEC-TERT-1 cells cultured at 27500/cm^2, media replaced every second day. From day 12, 25 mM of D-Glucose or D-Mannitol (osmotic control to glucose) was administered for different time periods Effect of high Glucose on RPTECs for downstream comparisons of glucose versus controls: formation of stable monolayer by microscope; **D**. Similar cell size confirmed by flow cytometry

Additional File 4.TIF: *Supplementary Figure S2*: Combined effect of high glucose and albumin on RPTEC/TERT1 inflammatory responses**. A**. Schematic diagram of the experimental protocol. In brief, RPTEC-TERT-1 cells cultured at 27500/cm^2, medium was replaced every second day. From day 12, cells were grown in high-glucose or control conditions (CTRL/HG/MAN) with or without 100 μg/ml human serum albumin. Mediium was replaced at day 15 for a further two days. **B**. Mean ± SD levels of inflammatory mediators including IL-8 (top left), IL-6 (top right), MCP-1 (bottom left) and NGAL (bottom right) in the supernatants are represented in grey (CTRL), blue (HG) and green (MAN) bars. Bright colours represent the levels in samples when treated without albumin. * denoted unpaired t-tests for CTRL vs HG, HG vs MAN, MAN vs CTRL. ¥ denoted ANOVA to analyse differences between CTRL, HG and MAN.

$^{****/¥¥¥¥}$ $p < 0.0001$, $^{***/¥¥¥}$ $p < 0.001$, $^{**/¥¥}$ $p < 0.01$, $^{*/¥}$ $p < 0.05$.

Additional File 5.TIF: *Supplementary Figure S3*: Combined effect of high glucose and IL-1β as inflammatory cytokine stimuli on RPTEC/TERT1 responses. **A**. Schematic diagram of the experimental protocol. In brief, RPTEC/TERT1 cells were cultured at 27500/cm^2, medium was replaced every second day. From day 12, cells were grown in high-glucose or control conditions (CTRL/HG/MAN). Medium was replaced at day-15. In addition to CTRL/HG/MAN, cells were treated with- or without- 1 ng/ml IL-1β for the final two days; **B**. Mean ± SD levels of inflammatory mediators including IL-8 (top left), IL-6 (top right), MCP-1 (bottom left) and NGAL (bottom right) in the supernatant samples represented in grey (CTRL), blue (HG) and green (MAN) bars. Bright colours represent the levels in samples when treated without IL-1β. * denoted unpaired t-tests for CTRL vs HG, HG vs MAN, and MAN vs CTRL. ¥ denoted ANOVA to test for differences between CTRL, HG and MAN. $^{****/¥¥¥¥}$ p <0.0001, $^{***/¥¥¥}$ p <0.001, $^{**/¥¥}$ p <0.01, $^{*/¥}$ p <0.05.

Additional File 6.TIF: *Supplementary Figure S4A:* Exposure of RPTEC/TERT1 cells to high-Glucose did not alter expression in any common inflammatory signalling molecules. RPTEC-TERT-1 cells were cultured at 27500/cm^2, medium was replaced every second day. From day 12, cells were grown in high-glucose or control conditions (CTRL/HG/MAN) for 24, 48 and 96 hours. Using western blotting, cell pellets were harvested for investigating the expressions of different signalling proteins including: total and phosphorylated forms of p65 NFkB (nuclear factor kappa B – p65 sub unit), p38 MAPK (P38 mitogen-activated protein kinase), ERK-1/2 (extracellular signal–regulated kinase 1/2), STAT-1 (Signal transducer and activator of transcription 1), PKCα (Protein kinase C alpha) and total PPAR-γ (Peroxisome proliferator-activated receptor gamma) as well as housekeeping protein β-Actin (Beta Actin).

Additional File 7.TIF: *Supplementary Figure S4B: Semi-quantitative analyses of the western blots as in Supplementary Figure S4A.* ImageJ software was used to perform semi-quantitative analysis of the blots. The area and its corresponding percentage of blots were calculated. Densitometric data were then normalized for the housekeeping protein followed by further normalization relative to the control. Statistical analyses were performed using GraphPad prism. Results were expressed as the Mean$\pm$SD for three technical replicates per condition. p values ≤ 0.05 were considered significant at: *p<0.05, **p<0.01, ***p<0.001.

Additional File 8.TIF: Supplementary Figure S5: *Human bone-marrow derived MSCs showed its cell surface characteristics and were able to differentiate.* A. Immunophenotyping of cultured human BM-MSCs for different specific cell surface markers by flow cytometry. B. Osteogenic and adipogenic differentiation capacity of BM-MSCs. Unpaired t test with Welch's correction *p<0.05; **p<0.01; ***p<0.001

Additional File 9.docx: *Supplementary Table S2*: List of DEGs with significant Fold Changes in High-Glucose vs Mannitol

Additional File 10.docx: *Supplementary Table S3*: List of DEGs with significant Fold Changes in High-Glucose vs Control

Additional File 11.docx: *Supplementary Table S4*: List of DEGs with significant Fold Changes in Mannitol vs Control

Additional File 12.TIF: *Supplementary Figure S6*: Involvement of biological processes and signalling pathways associated with differentially expressed genes in high-glucose exposed RPTEC/TERT1 cells. (A) Pathway Enrichment analysis of differentially expressed genes (DEGs) performed based on KEGG database; (B) Scatter plot for the top 20 pathways of KEGG enrichment results. Here, X axis represents number of DEGs. Y axis represents second KEGG pathway terms. All second pathway terms were grouped in top pathway terms indicated in different colour.

Additional File 13.TIF: *Supplementary Figure S7:* Up-regulation of genes for inflammatory cytokines following exposure of RPTEC/TERT1 cells to high-glucose (TNF-Signalling pathway is a representative example). Up-regulated genes are marked with red borders. Unchanged genes are marked with black borders.

Additional File 14.docx: *Supplementary Table S5*: List of DEGs with significant Fold Changes in RPTEC/TERT1 cells without and with MSC co-culture in high glucose (HG) condition

Additional File 15.docx: *Supplementary Table S6*: List of DEGs with significant Fold Changes in RPTEC/TERT1 cells without and with MSC co-culture in mannitol (MAN) condition

Additional File 16.TIF: *Supplementary Figure S8*: Differential Expression of Genes in Presence of Indirect Contact of MSCs. Pathway Enrichment Analysis of Differentially Expressed Genes (DEGs) performed based on KEGG database by pairwise analysis. Here, X axis represents number of DEGs. Y axis represents second KEGG pathway terms. All second pathway terms were grouped in top pathway terms indicated in different colour.

Additional File 17.TIF: *Supplementary Figure S9*: TNF-Signalling pathway as a representative example of the signalling pathways involved in MSC mediated anti-inflammatory effects (in high-glucose environment). Here, down-regulated genes are marked with green borders and unchanged genes are marked with black borders.

Figure 1

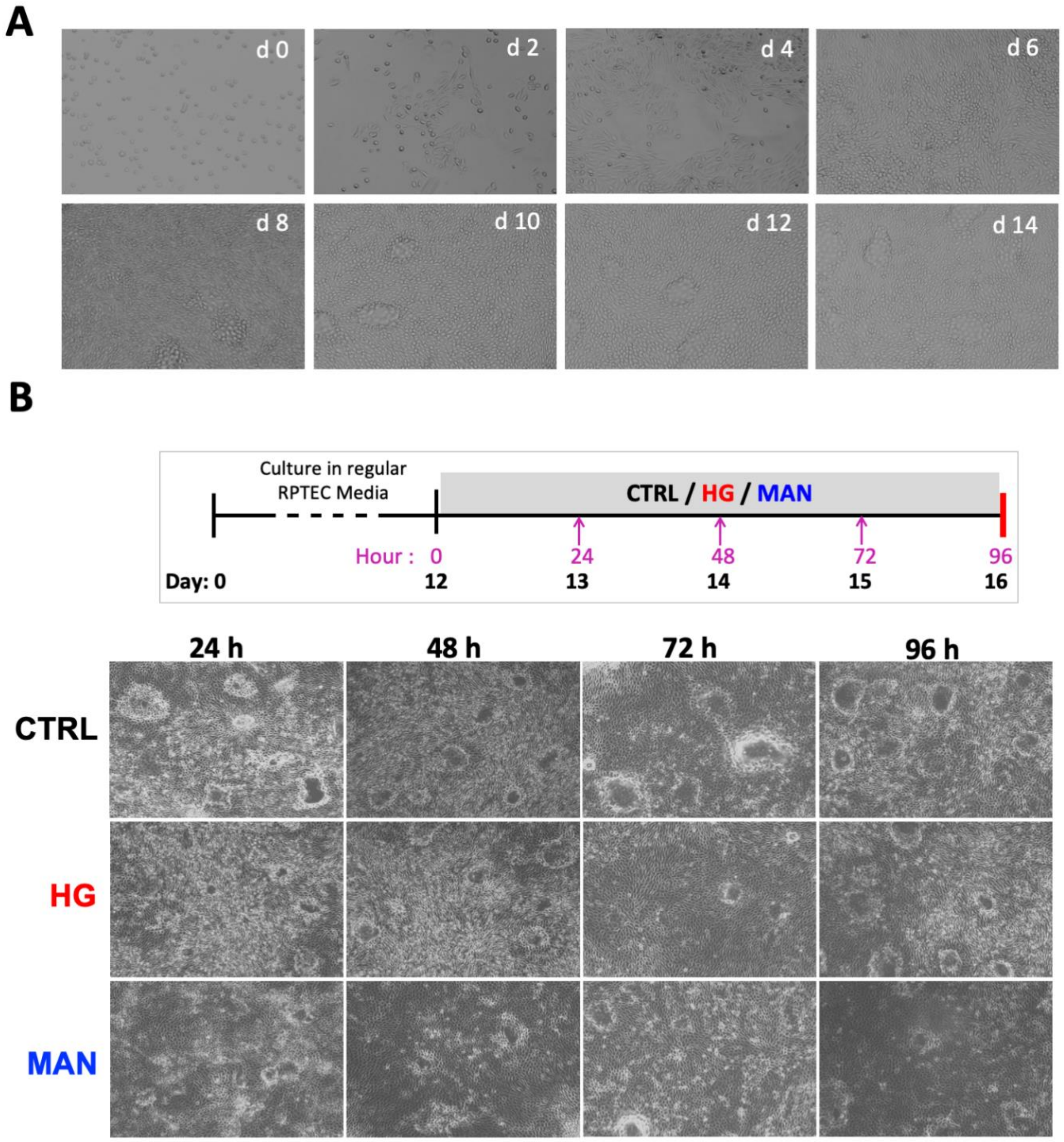

Figure 1: *Morphology of RPTEC/TERT1 cell layers in culture.* A. Morphology at different time points before and after confluency using phase contrast microscopy at 4X magnification. B. Morphology of cell layers during basal medium (CTRL), HG and MAN culture conditions beginning at day 12 for four consecutive days using phase contrast microscopy at 4X magnification.

Figure 2

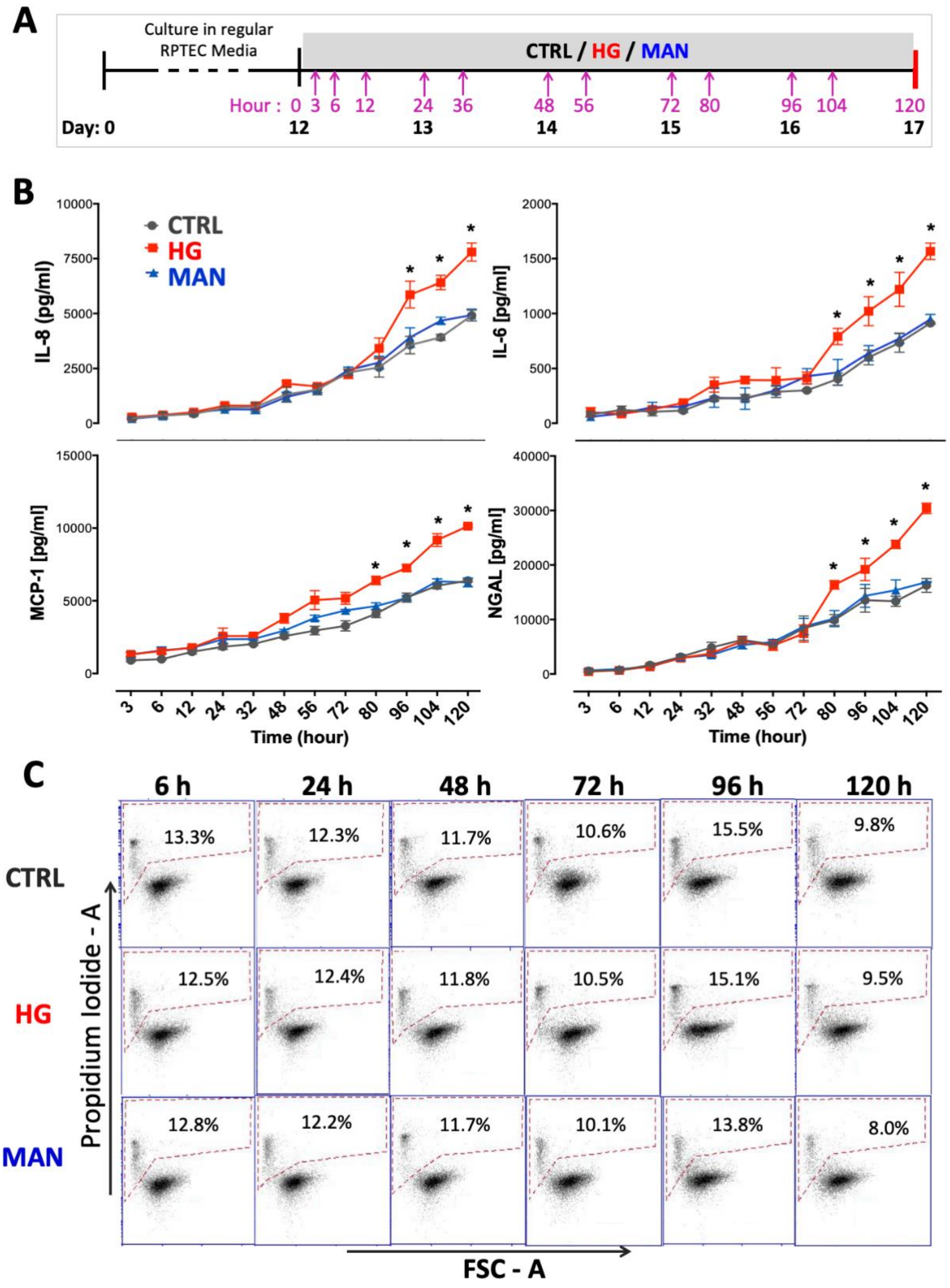

Figure 2: *High glucose exposure increases the inflammatory response of RPTEC/TERT1 cell stable monolayers:* A. Schematic diagram of the experimental protocol. B. Concentrations of inflammatory biomarkers IL-8 (top left), IL-6 (top right), MCP-1 (bottom left) and tubular injury marker NGAL (bottom right) in culture supernatants of RPTEC/TERT1 cell stable monolayers between 3 and 120 hours following exposure to medium containing Normal (5mM) Glucose (CTRL, grey line), High (30nM) Glucose (HG, red line) and 5mM Glucose + 25mM Mannitol (MAN, blue line). All results are presented as Mean ± SD. Statistical analyses were performed by one-way ANOVA and non-parametric multiple t-test. * $p < 0.05$. C. Representative examples of flow cytometric analysis of RPTEC/TERT1 cell viability by propidium iodide exclusion at various time-points following exposure to the three culture conditions. Percentages of dead cells (PI^{+ve}) are shown for each condition.

Figure 3

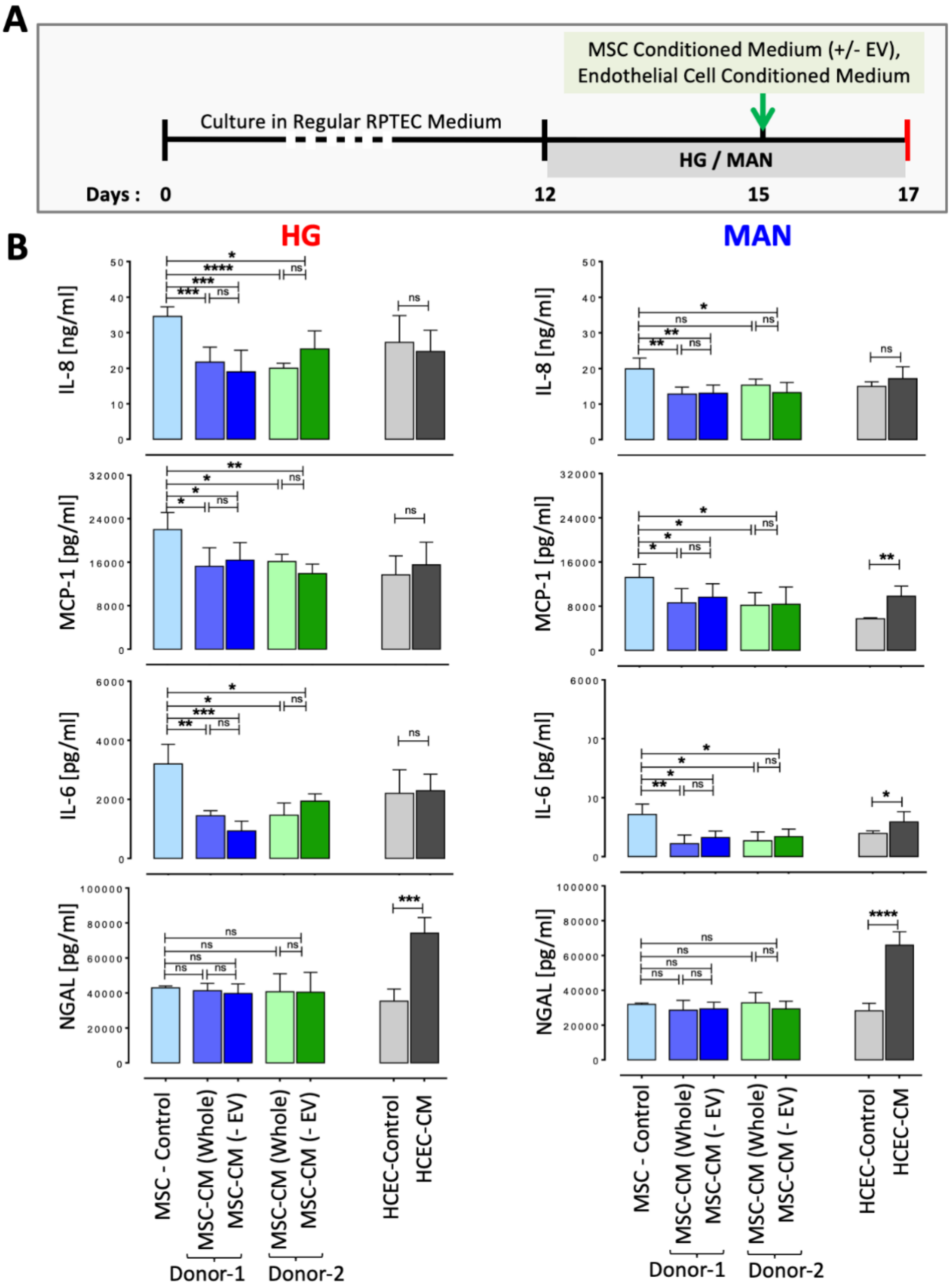

Figure 3: *Total and extracellular vesicle-depleted conditioned media from human MSC but not HCEC inhibit high glucose-induced secretion of inflammatory cytokines by RPTEC/TERT1 cell stable monolayers.* A. Schematic diagram of the experimental protocol (+/- EV = without and with extracellular vesicle depletion). B. Graphs depicting the concentrations of IL-8, IL-6, MCP-1 and NGAL in the supernatants from RPTEC/TERT1 cell monolayers cultured without (Control) and with various conditioned media (CM) during the final 2 days of 5-day cultures under High Glucose (HG, left graphs) and Mannitol (MAN, right graphs) conditions. All results are expressed as Mean ± SD of n=6 technical replicates for each condition. For cultures containing human (h)BM-MSC-derived CM, results are shown for MSC from two different donors [Donor 1 (blue) and Donor 2 (green)]. MSC-Control = Unconditioned MSC medium. MSC-CM (Whole) = Non-extracellular vesicle (EV) depleted MSC-CM. MSC-CM (-EV) = Extracellular vesicle (EV) depleted MSC-CM. HCEC-Control = Unconditioned human corneal endothelial cell medium. HCEC-CM = CM from human corneal endothelial cells. Statistical analyses performed by one-way ANOVA (for hBM-MSC *versus* Control) and unpaired Student's t-test (for Endothelial Cell *versus* Control). **** p <0.0001, *** p <0.001, * p <0.05, ns = not significant.

Figure 4

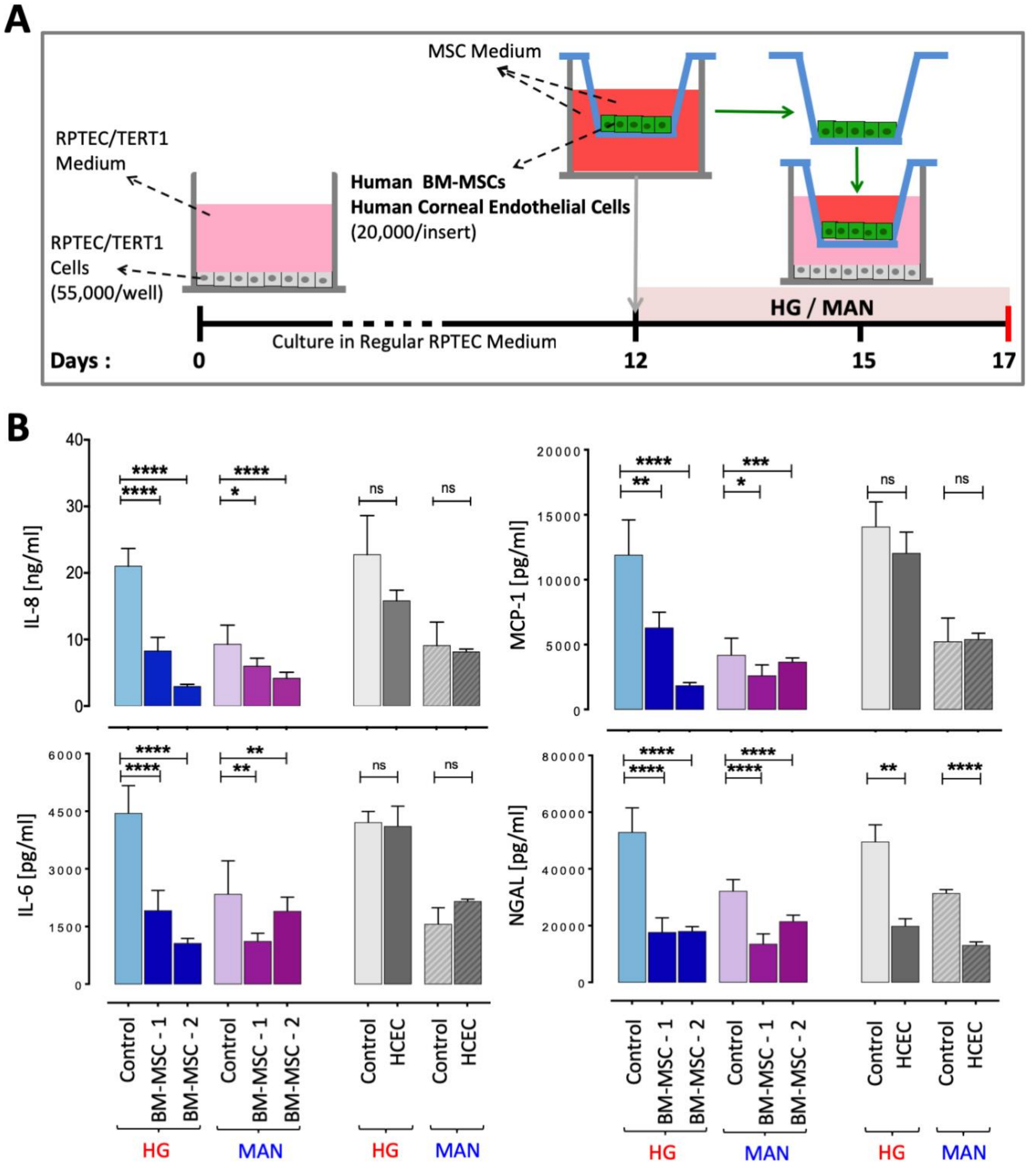

Figure 4: *Indirect co-culture with human MSC results in potent inhibition of high glucose-induced secretion of inflammatory cytokines by RPTEC/TERT1 cell stable monolayers.* A. Schematic diagram of the experimental protocol. B. Graphs depicting the concentrations of IL-8, IL-6, MCP-1 and NGAL in the supernatants from RPTEC/TERT1 cell monolayers cultured without (Control) and with (Cells) various Transwell co-cultures during the final 2 days of 5-day cultures under High glucose (*D-glucose*, blue) and Mannitol (D-mannitol, purple) conditions. Results are shown for co-cultures carried out with human Bone Marrow MSCs from two different donors (BM-MSC-1 and BM-MSC-2) and with a non-MSC control cell line (HCEC, grey). All results are expressed as Mean ± SD of n=6 technical replicates for each condition. Statistical analyses performed by one-way ANOVA (for BM-MSC *versus* Control) and unpaired Student's t-test (for HCEC *versus* Control). **** p <0.0001, *** p <0.001, ** p <0.01, * p <0.05, ns = not significant.

Figure 5

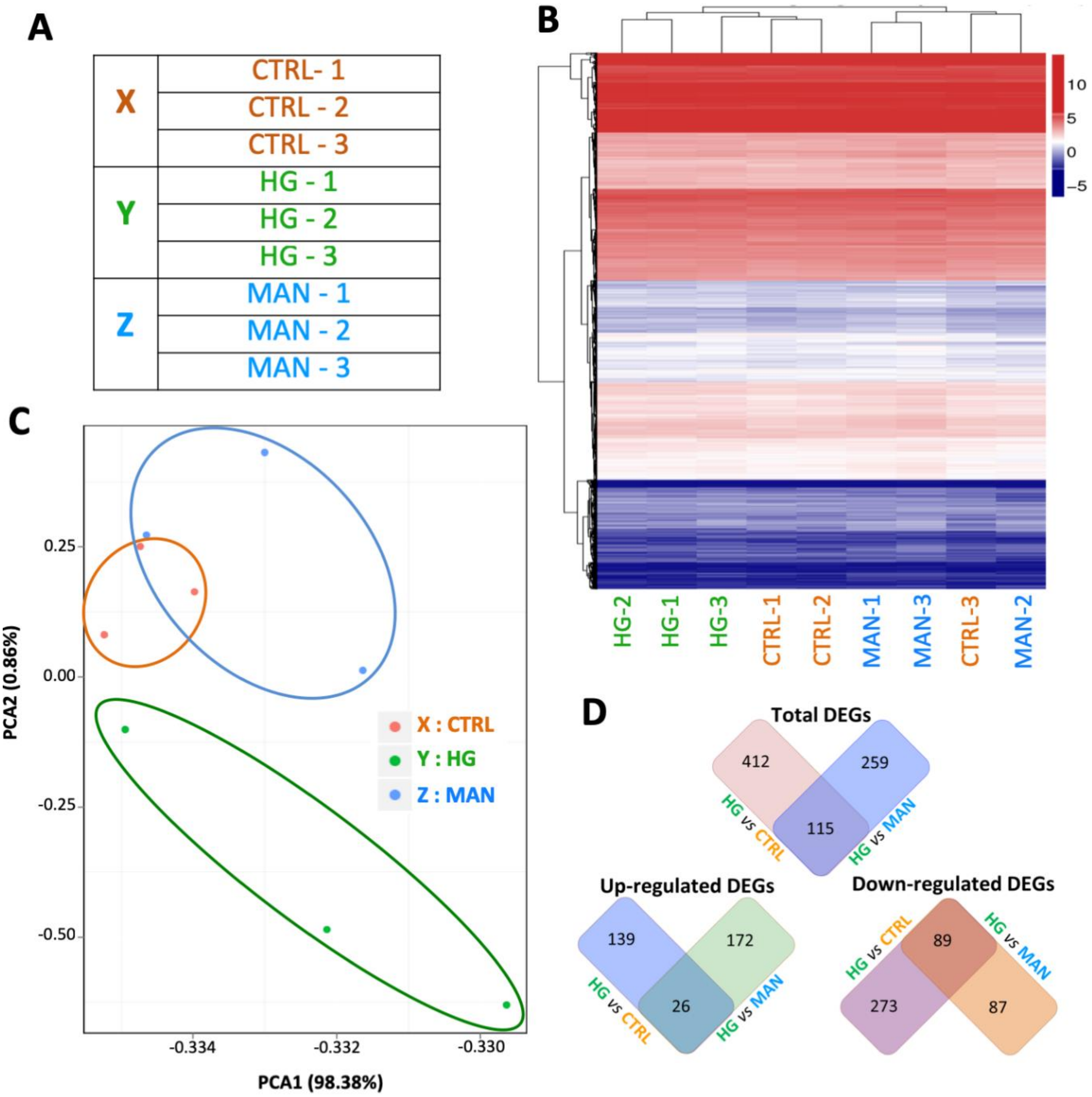

Figure 5: *High-level bioinformatics analyses of* RNA-seq *transcriptional profiling of RPTEC/TERT1 monolayers following 5-day exposure to control, high glucose and mannitol culture conditions:* A. Table summarizing the samples subjected to RNA-seq. B. Unsupervised hierarchical clustering of the RNA-seq profiles of samples (nomenclature as per 4A). C. Scatter plot of principal component analysis of the RNA-seq profiles. Each dot represents one sample (nomenclature as per 4A). D. Figures illustrating the numbers of total, up-regulated and down-regulated DEGs for High glucose (HG) vs. Normal glucose control (CTRL) culture conditions and High glucose vs. Mannitol control (MAN) culture conditions. Overlapping segments indicate the numbers of DEGs that were common to both comparisons.

Figure 6

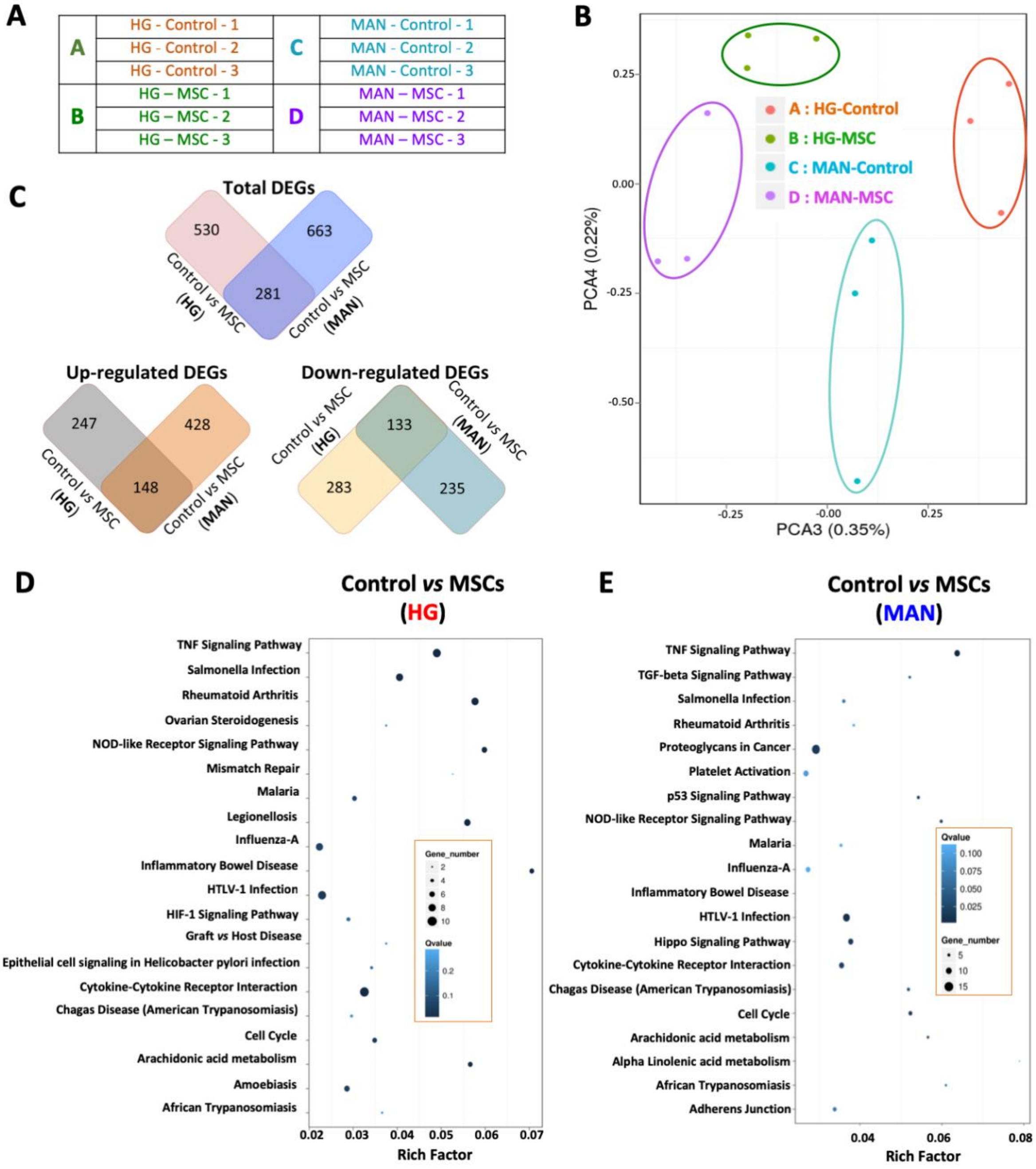

Figure 6: *Bioinformatics analyses of* RNA-seq *transcriptional profiling of RPTEC/TERT1 monolayers following 5-day exposure to high glucose (HG) and mannitol (MAN) culture conditions in the presence or absence of MSC-containing transwells:* **A.** Table summarizing the non-MSC- (Control) and MSC-co-cultured (MSC) samples subjected to RNA-seq. **B.** Scatter plot of principal component analysis of the RNA-seq profiles. Each dot represents one sample (nomenclature as per 5A). **C.** Figures illustrating the numbers of total, up-regulated and down-regulated DEGs for Control vs. MSC-co-cultured RPTEC/TERT1 cells under High glucose (HG) and Mannitol (MAN) culture conditions. Overlapping segments indicate the numbers of DEGs that were common to both comparisons. **D & E.** Scatter graphs indicating the enrichment factors and number of DEGs of the top 20 enriched pathways for Control vs. MSC-co-cultured RPTEC/TERT1 monolayers under HG (D) and MAN (E) conditions based on KEGG pathway enrichment analysis.

Figure 7

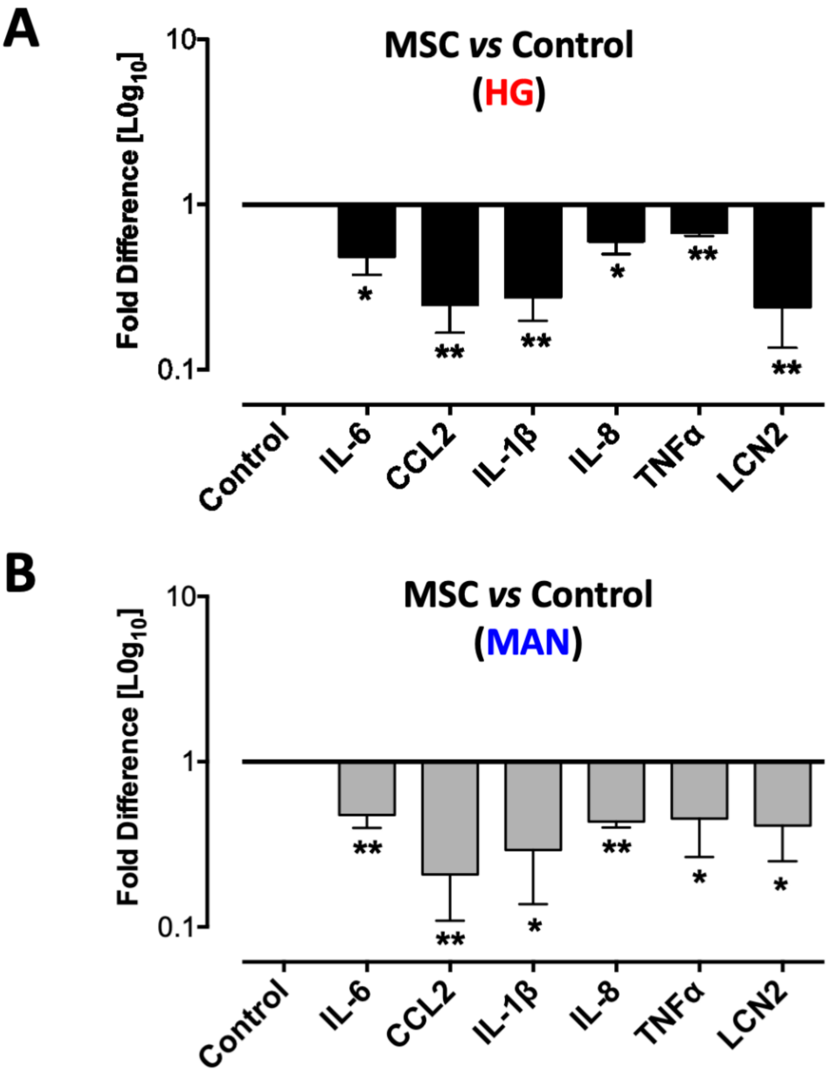

Figure 7: *Validation of the effect of BM-MSCs on RPTEC-TERT1 expression of inflammation-related transcripts.* Graphical representations of qRT-PCR analysis of the relative expression of RNA transcripts for IL-6, MCP-1 (CCL2), IL-1β, IL-8, TNFα and NGAL (LCN2) in RPTEC/TERT1 cell monolayers cultured for 5 days in high glucose (HG) (**A**) or Mannitol (MAN) (**B**) in the presence of BM-MSC-containing transwells (MSC) or no cells (Control) for the final 2 days of culture. Results are expressed as mean ± SD for n=3 samples per condition of the fold difference for MSC vs. Control as determined relative to the housekeeping gene RPLP0 using the $2^{-\Delta\Delta Ct}$ method. Statistical analysis by Student's unpaired t-test, **p <0.01, *p <0.05, ns=not significant.

Figure 8

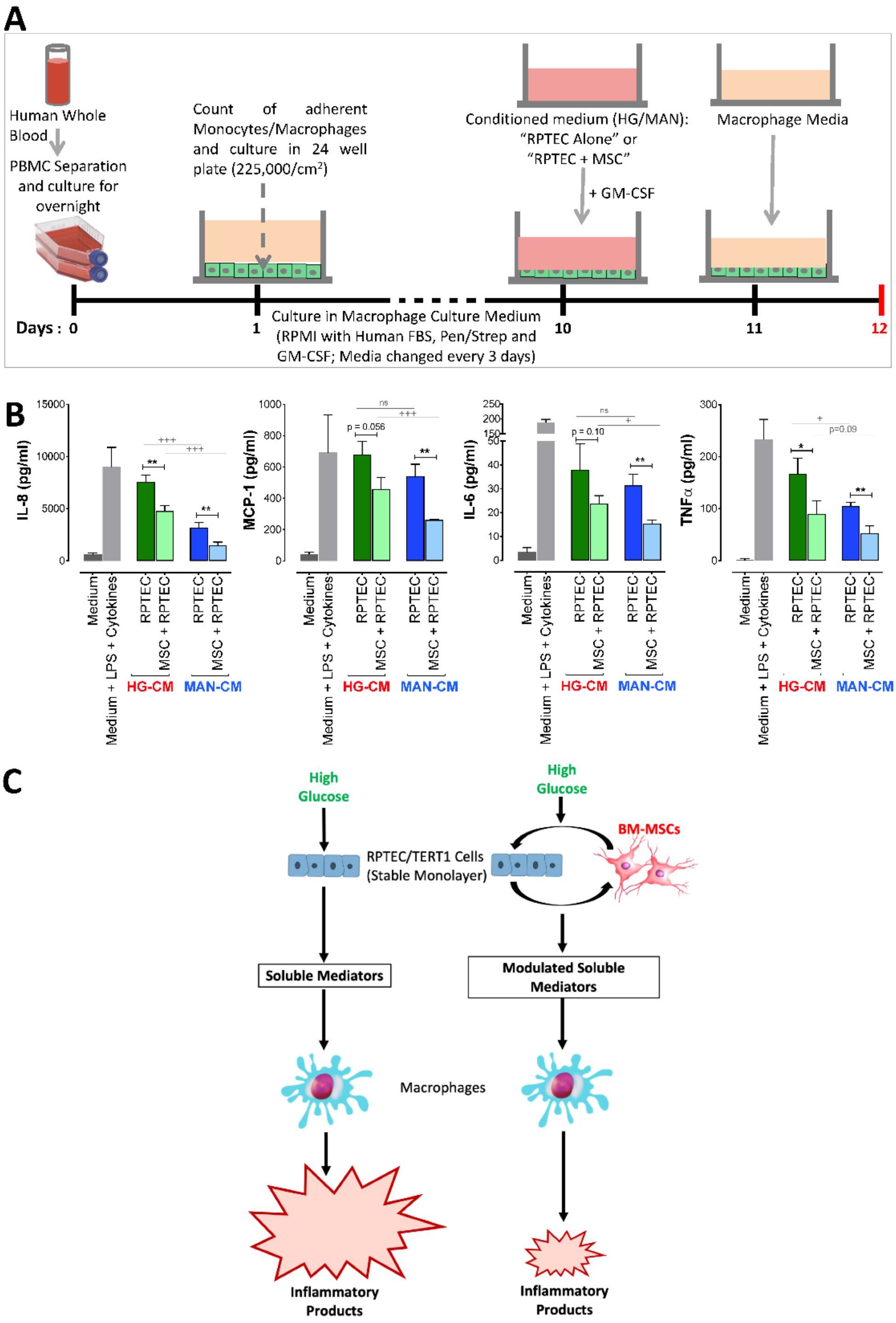

Figure 8 *Indirect mesenchymal stromal cell contact modulates pro-inflammatory cross-talk between high glucose-exposed RPTEC/TERT1 cell monolayers and human macrophages.* **A.** Schematic diagram of the experimental protocol. **B.** Graphs depicting the concentrations of IL-8, MCP-1, TNFα and IL-6 in the supernatants from monocyte-derived macrophages cultured with macrophage medium alone (Medium), macrophage medium containing a stimulatory cocktail of LPS, IFNγ and TNFα (Medium + M1 Stimuli) and conditioned media from 48 hr cultures of RPTEC/TERT1 cells alone (RPTEC) or RPTEC/TERT1 cells co-cultured with MSC-containing transwells (MSC + RPTEC) under high glucose (HG) and mannitol (MAN) conditions. Results for macrophages exposed to conditioned media from high glucose (HG) condition are represented in green and those from Mannitol (MAN)

are represented in blue bars. Results are expressed as Mean ± SD of n=3 technical replicates for each condition. Statistical analyses performed unpaired Student's t-test (* for MSC *versus* Control; + for HG *versus* MAN). ****/++++ p <0.0001, ***/+++ p <0.001, **/++ p <0.01, */+ p <0.05, ns = not significant. **C**. Schematic representation of the effect of high glucose on RPTEC, the subsequent inflammatory response of macrophages (left) and the modulatory effect of indirect contact between RPTEC and MSC on the downstream macrophage response (right).

SUPPLEMENTARY METHODS

Human mesenchymal stromal cells broadly modulate high glucose-induced inflammatory responses of renal proximal tubular cell monolayers

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Mesenchymal stromal cell differentiation assays

Differentiation of MSC to osteogenic and adipogenic phenotypes was performed using StemPro differentiation kits (Gibco) according to the manufacturer's instructions. After 21 days of incubation, differentiation of MSC into osteoblasts was confirmed by Alizarin Red S staining (Sigma) and differentiation into adipocytes was confirmed by by Oil-Red-O staining (Sigma) using well-described protocols.

Preparation of conditioned media

Mesenchymal stromal cells were plated at $1x10^6$ cells/ml into a T175 flask (Sarstedt) and incubated at 37^oC in 5% CO_2. After 3 days, MSC conditioned medium (MSC-CM) was collected and centrifuged at 400 x g for 5 minutes to remove floating cells and debris. The MSC-CM was then centrifuged at 2000 x g for 20 minutes to be cleared of apoptotic bodies and filtered through a filtropur 0.2µm vacuum filter bottle. Half of the total volume of MSC-CM was then ultra-centrifuged at 100,000 x g for 1 hour and 15 minutes to remove MSC-derived EVs. Both Total- and EV-depleted MSC-CM were then concentrated 10-times by spin concentrator (Agilent Technologies, Santa Clara, CA, USA) with cut-off of 5kDa following manufacturer's instructions.

ELISA protocol

Capture antibody was coated onto 96-well ELISA plate (Nunc Maxisorp^{TM}, Roskilde, Denmark) for 18 hours at room temperature (RT) followed by blocking with 1% BSA (Sigma) for 2 hours at RT.

Samples/standards were added and incubated overnight at 4^0C. Samples were diluted as necessary for accurate quantification. The plates were washed prior to the addition of biotin-conjugated detection antibody for 2 hours at RT. Streptavidin-HRP was added and incubated for 30 minutes at RT following which TMB-substrate (EMD Millipore Corp, Billerica, MA, USA) was added to observe blue colour. Enzyme-substrate reaction was stopped by 1M sulfuric acid (Sigma) and optical density was measured at 450nm and subtracted from the background at 630nm using microplate reader (Varioskan Flash, Thermo Scientific, UK). Concentrations of the various analytes were calculated from standard curves.

Western Blotting

The rabbit anti-human primary antibodies for NF-κB p65 (monoclonal: D14E12), Phospho-NF-kB p65 (Ser536; monoclonal: 93H1), p38 MAPK (polyclonal), Phospho-p38 MAPK (Thr180/Tyr182; monoclonal: D3F9), p44/42 MAPK (Erk1/2; polyclonal), Phospho-p44/42 MAPK (Erk1/2; Thr202/Tyr204; monoclonal: D13.14.4E), Stat1 (polyclonal), Phospho-Stat1 (Tyr701; monoclonal D4A7), , PKCα (polyclonal), Phospho-PKCα/β II (Thr638/641; polyclonal), PPAR-γ (monoclonal: 81B8), and the secondary antibody (goat anti-rabbit IgG; polyclonal) were purchased from Cell Signalling Technology, MA, USA. Anti-beta Actin antibody (HRP conjugated; mouse monoclonal AC-15) was purchased from Abcam, Cambridge, MA, USA. Cell pellets were treated with lysis buffer containing 0.5M HEPES (pH 7.5; Sigma), 1M NaCl (Sigma), 150mM MgCl2 (Sigma), 100mM EDTA (Sigma), 100mM EGTA (Sigma), 10% IGEPAL (Sigma), 10mM Sodium fluoride (Sigma), 1mM Sodium orthovanadate (Sigma) and 1% protease inhibitor cocktail (Sigma). Protein concentrations were determined by Bradford assay (Thermofisher Scientific) according to the manufacturer's protocol. 15 µg of total protein were diluted in Laemmli buffer containing 2% SDS (Sigma), 4% Glycerol (Sigma), 0.05% Bromophenol Blue (Sigma), 50 mM Tris (Sigma; pH 6.8), 1mM phenyl methyl sulfonyl fluoride (Sigma) and 5% Beta-Mercaptoethanol (Sigma). Protein samples were loaded onto 10% SDS–PAGE (Sigma) gels, separated by electrophoresis and then transferred to nitrocellulose membranes using Mini Trans-Blot® Cell (BioRad, CA, USA). Membranes were incubated in blocking buffer (5% BSA in TBS with 0.05% Tween-20; Sigma) for 1 hour at RT and then incubated overnight at 4^oC with primary antibodies. The membranes were washed 3 times with 0.05% Tween-20 in TBS (Sigma) and incubated with a horseradish peroxidase- conjugated secondary antibody at 1:2000 for 1.5 hours then washed a further 3 times. Finally, the membranes were developed by electrochemical luminescence by addition of ECL Plus Substrate (GE Healthcare Life Sciences, Pittsburgh, PA, USA). After suitable development times, bands were imaged using chemiluminescence reader (Uvitec Essential V6, Cambridge, UK).

RNA isolation by TRIzol

Cells were initially suspended in TRIzol reagent (Sigma) and stored at –80°C until use. Samples were then thawed and chloroform (Sigma) was added at 0.2 ml/1 ml TRIzol. Samples were mixed gently by inversion then allowed to stand at room temperature for 10 minutes followed by centrifugation at 12,000xg for 15 minutes at 4°C. The RNA-containing clear upper aqueous phase was transferred to 1.5ml microtubes (Sarstedt) and RNA was precipitated by adding isopropanol (Sigma) at 0.75 ml/1 ml Trizol, mixing vigorously and storing overnight at -20°C. The samples were then centrifuged at 12,000xg for 10 minutes at 4°C, the isopropanol was discarded and the RNA pellets were washed by vortexing in 75% ethanol (Sigma) followed by centrifugation at 12,000xg for 15 minutes at 4°C. Finally, the ethanol was discarded and the RNA pellets air dried for 10 minutes prior to re-suspending in the appropriate volume of RNase-free water (Qiagen) and warming up tubes for 10-15 minutes at 50^0C for complete dissolving.

Preparation and initial culture of human peripheral blood mononuclear

Samples of anticoagulated blood were collected from healthy adult volunteers by informed consent according to a protocol approved by the Research Ethics Committee of the National University of Ireland Galway (Ref:14/MAR/01). Peripheral blood mononuclear cells were separated by density gradient centrifugation using ficoll-hypaque solution (GE Healthcare) as previously described [1] and cultured in a T175 flask (Sarstedt) in macrophage medium consisting of RPMI-1640 (Gibco) containing 10% heat-inactivated human AB serum (Sigma), 1% penicillin/streptomycin (Gibco) and 1% L-Glutamine (Gibco). Floating cells were discarded the next day and adherent cells were washed with ice cold PBS (Gibco) then lifted by adding 0.25% Trypsin-EDTA (Gibco) to the flask for 3 minutes, counted using a hematocytometer.

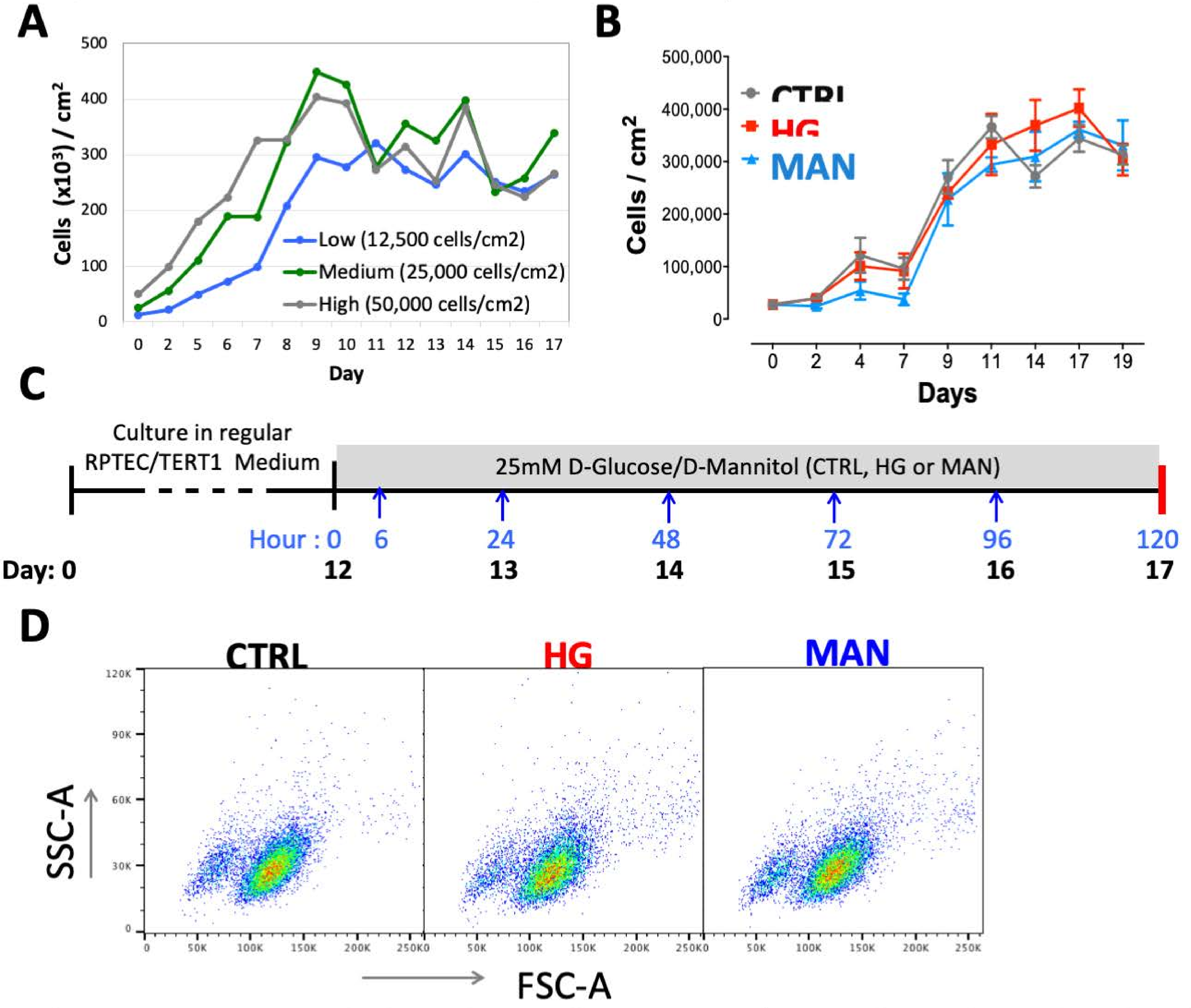
References

1. Naicker SD, Cormican S, Griffin TP, et al. Chronic kidney disease severity is associated with selective expansion of a distinctive intermediate monocyte subpopulation. Front Immunol 2018;9.

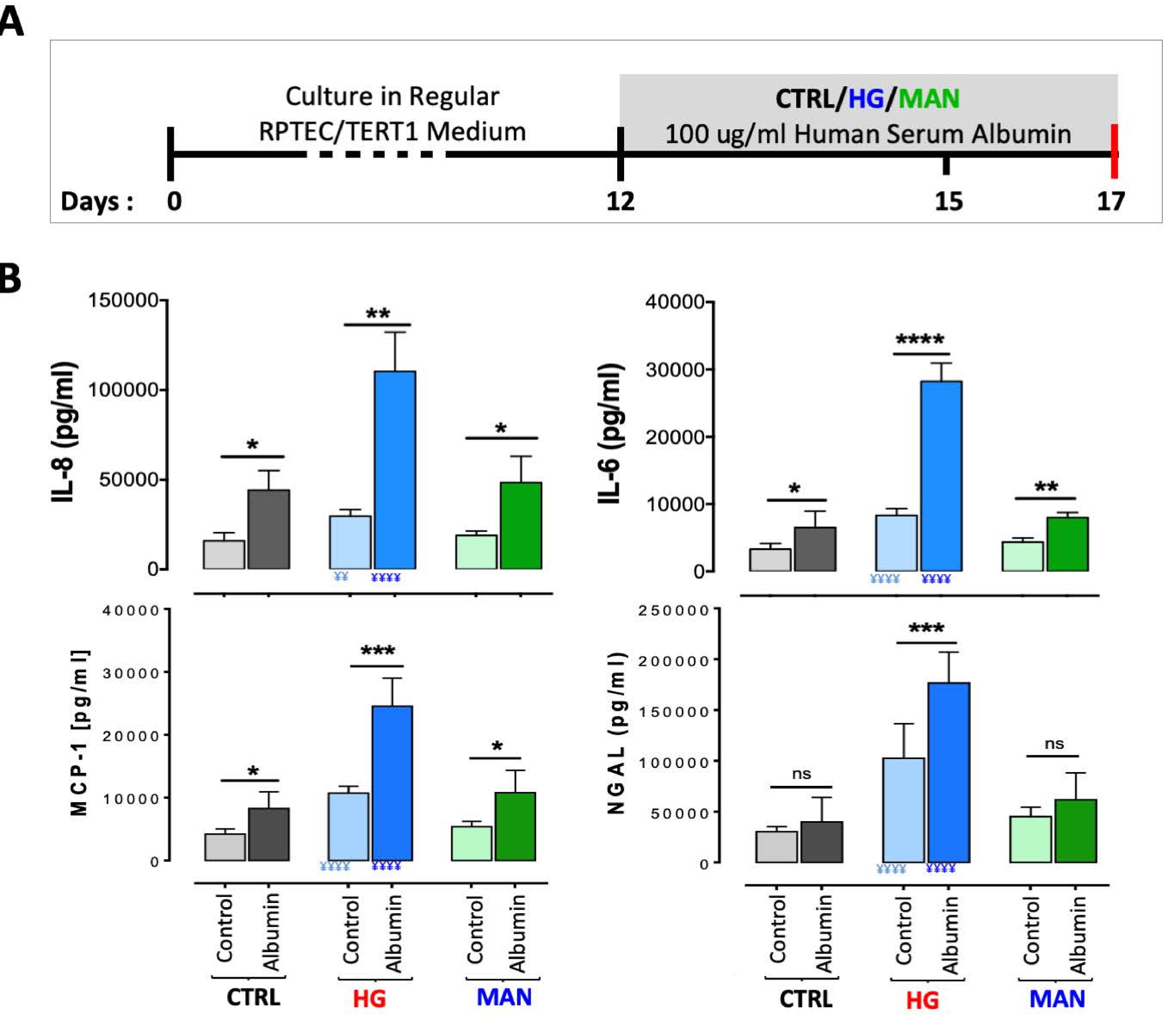
Supplementary Table S1: List of primer sequences used for qRT-PCR.

Gene Name	**Primer Sequence**
CCL2	Forward Primer : 5’-AATCCTGAACCCACTTCTGC-3’ Reverse Primer : 5’-AGTGTCCCAAAGAAGCTGTG-3’
TNF	Forward Primer : 5’-TCAGCTTGAGGGTTTGCTAC-3’ Reverse Primer : 5’-TGCACTTTGGAGTGATCGG-3’
LCN2	Forward Primer : 5’-CTGGTTGTAGTTGGTGCTCA-3’ Reverse Primer : 5’-GGAAAAAGAAGTGTGTGACTACTGG-3’
IL1B	Forward Primer : 5’-CCTGGAAGGAGCACTTCATC-3’ Reverse Primer : 5’-CCATGGCAGAAGTACCTGAG-3’
IL6	Forward Primer : 5’-TTCTGTGCCTGCAGCTTC-3’ Reverse Primer : 5’-GCAGATGAGTACAAAAGTCCTGA-3’
IL8	Forward Primer : 5’-CATCTTCACTGATTCTTGGATACC-3’ Reverse Primer : 5’-TGTCTGGACCCCAAGGAA-3’
RPLP0	Forward Primer : 5’-GGTGTAATCCGTCTCCACAG-3’ Reverse Primer : 5’-GAAACTCTGCATTCTCGCTTC-3’

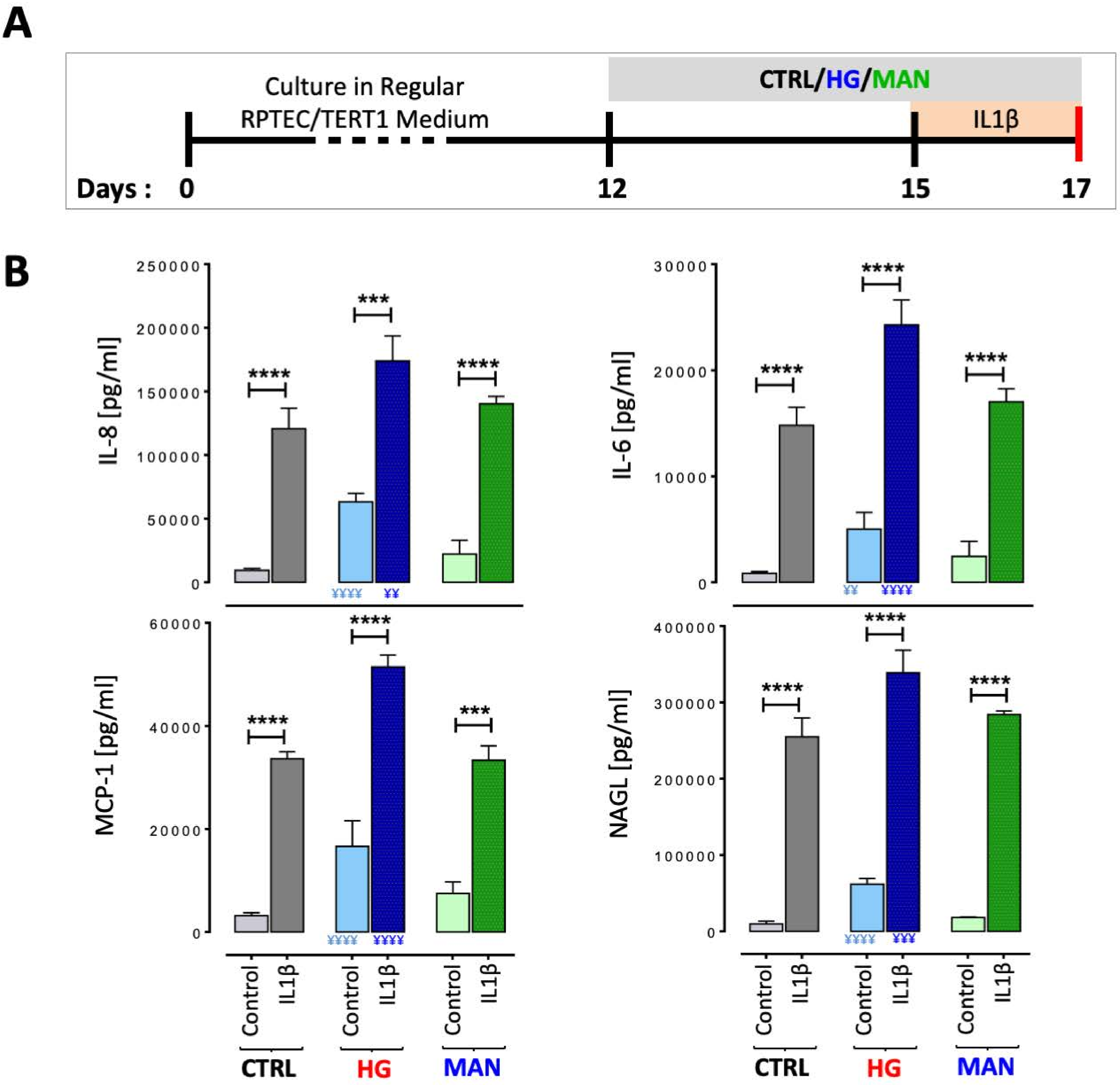
Supplementary Figure S1: Growth Analyses of RPTEC/TERT1 Cells. Formation of stable monolayer of RPTEC/TERT1 cells is important to maintain similar characteristics like the primary renal proximal tubular epithelial cells (RPTECs). Therefore, in our study, RPTEC/TERT1 cells were cultured for approximately 10 days after confluency to form stable monolayer. To determine the feasible number of RPTEC/TERT1 cells that we can culture per square centimetre in our experiments, we first cultured cells at low, medium or high density (12500, 25000 and 50000 cells/cm^2 respectively) and found that both medium and high density resulted in similar numbers from day 8 onwards till day 17 (Supplementary Figure S1). High, medium and low seeding density resulted in complete confluence after 4, 6 and 8 days of culture respectively. Newly grown cells were found to be attached on top of the monolayer and formed the dome structure (Supplementary Figure 1B). To confirm the complete confluency within first 6 days of culture, RPTEC/TERT1 cells were seeded at 27500 cells/cm^2 in all the experiments.



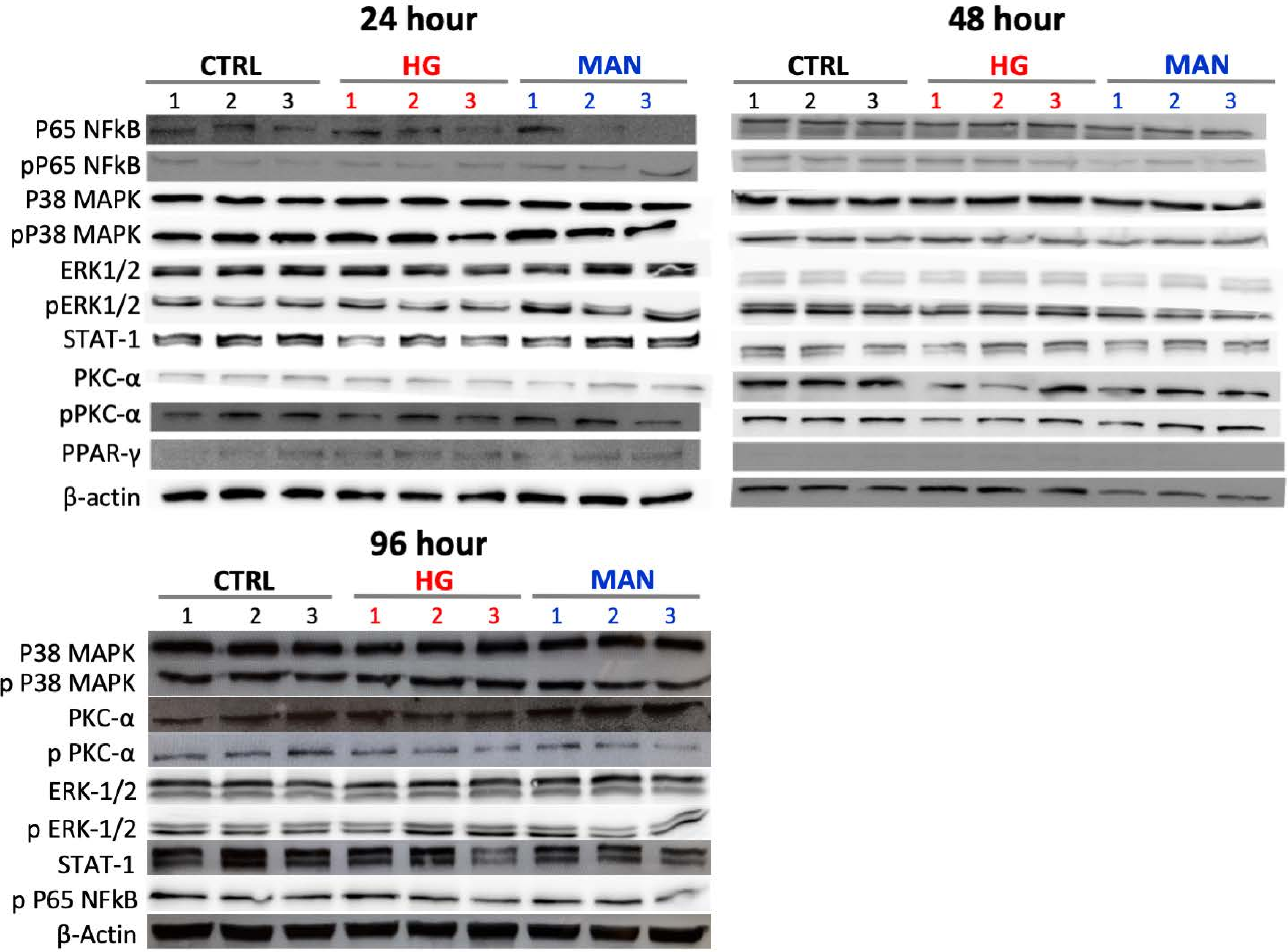
Supplementary Figure S1: ***High-Glucose has no effects on RPTEC/TERT1 Cell growth*.** **A**. Effect of seeding density on growth of RPTEC/TERT1 cells. Here, three different cell numbers per square centimetre (cm^2), labelled as Low (12500 cells/cm^2), Medium (12500 cells/cm^2) and High (12500 cells/cm^2), are represented in Blue, Green and Grey coloured lines respectively. Cells were grown in 24 well plate for different incubation periods and number of cells (cells/cm^2) were then counted by haemocytometer using trypan blue; **B.** Effect of high-glucose on growth of RPTEC/TERT1. Cells were cultured at 27500/cm^2 and counted at different time points using haemocytometer; **C.** Schematic diagram of the experimental protocol. In brief, RPTEC/TERT1 cells were cultured at 27500/cm^2, medium was replaced every second day. From day 12, cells were grown in either regular medium (CTRL), 25mM D-Glucose (high-glucose; HG) or 25 mM D-Mannitol (MAN; osmotic control to high-glucose) for different time periods; **D.** Flow cytometric confirmation of similar cell-size for RPTEC/TERT1 cells following exposure to HG or MAN compared to CTRL.



Supplementary Figure S2: ***Combined exposure to high-glucose and albumin further enhances RPTEC/TERT1 inflammatory responses.*** **A.** Schematic diagram of the experimental protocol. In brief, RPTEC/TERT1 cells were cultured at 27500/cm^2, medium was replaced every second day. From day 12, cells were grown in high-glucose or control conditions (CTRL/HG/MAN) with- or without- 100 ug/ml human serum albumin. Medium was replaced at day-15 for further two days; **B.** Mean ± SD levels of inflammatory mediators including IL-8 (top left), IL-6 (top right), MCP-1 (bottom left) and NGAL (bottom right) in the supernatant samples represented in grey (CTRL), blue (HG) and green (MAN) bars. Bright colours represent the levels in samples when treated without albumin. * denoted unpaired t-tests for CTRL vs HG, HG vs MAN and MAN vs CTRL. ¥ denoted

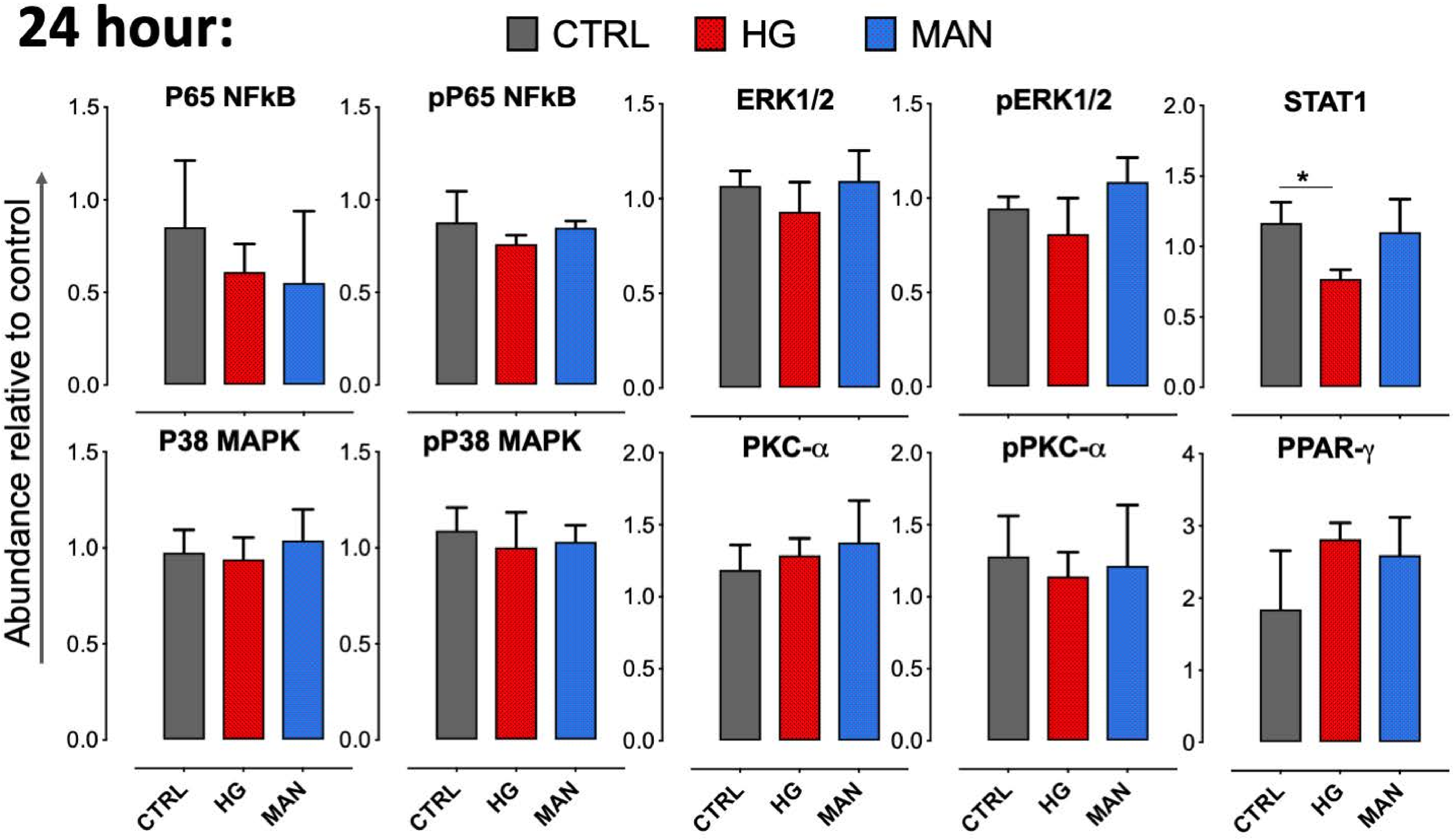


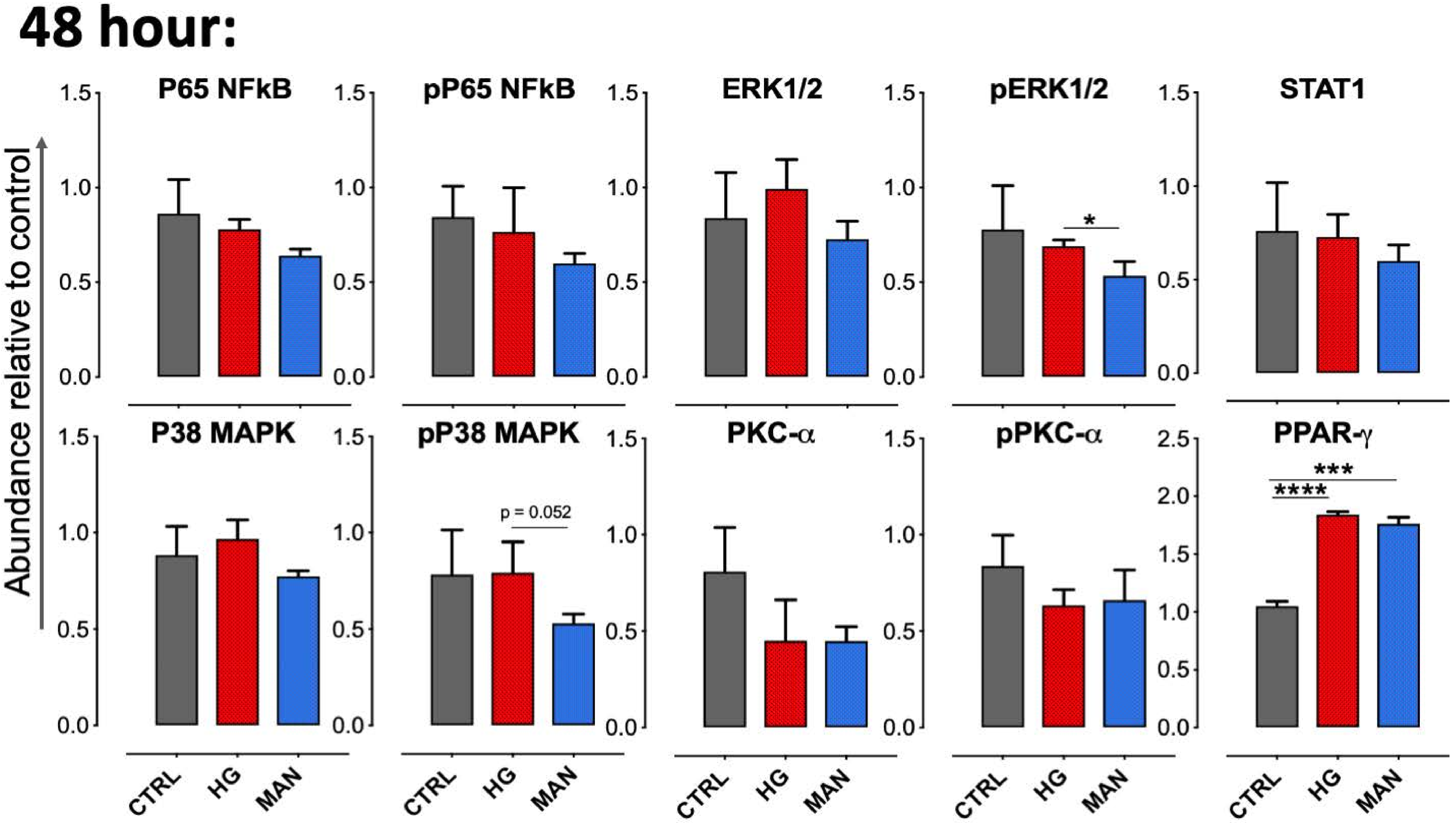
Supplementary Figure S3: Combined effect of high glucose and IL-1β as inflammatory cytokine stimuli on RPTEC/TERT1 responses. A. Schematic diagram of the experimental protocol. In brief, RPTEC/TERT1 cells were cultured at 27500/cm^2, medium was replaced every second day. From day 12, cells were grown in high-glucose or control conditions (CTRL/HG/MAN). Medium was replaced at day-15. In addition to CTRL/HG/MAN, cells were treated with- or without- 1 ng/ml IL-1β for the final two days; **B**. Mean ± SD levels of inflammatory mediators including IL-8 (top left), IL-6 (top right), MCP-1 (bottom left) and NGAL (bottom right) in the supernatant samples represented in grey (CTRL), blue (HG) and green (MAN) bars. Bright colours represent the levels in samples when treated without IL-1β. * denoted unpaired t-tests for CTRL vs HG, HG vs MAN, and MAN vs CTRL. ¥ denoted ANOVA to test for differences between



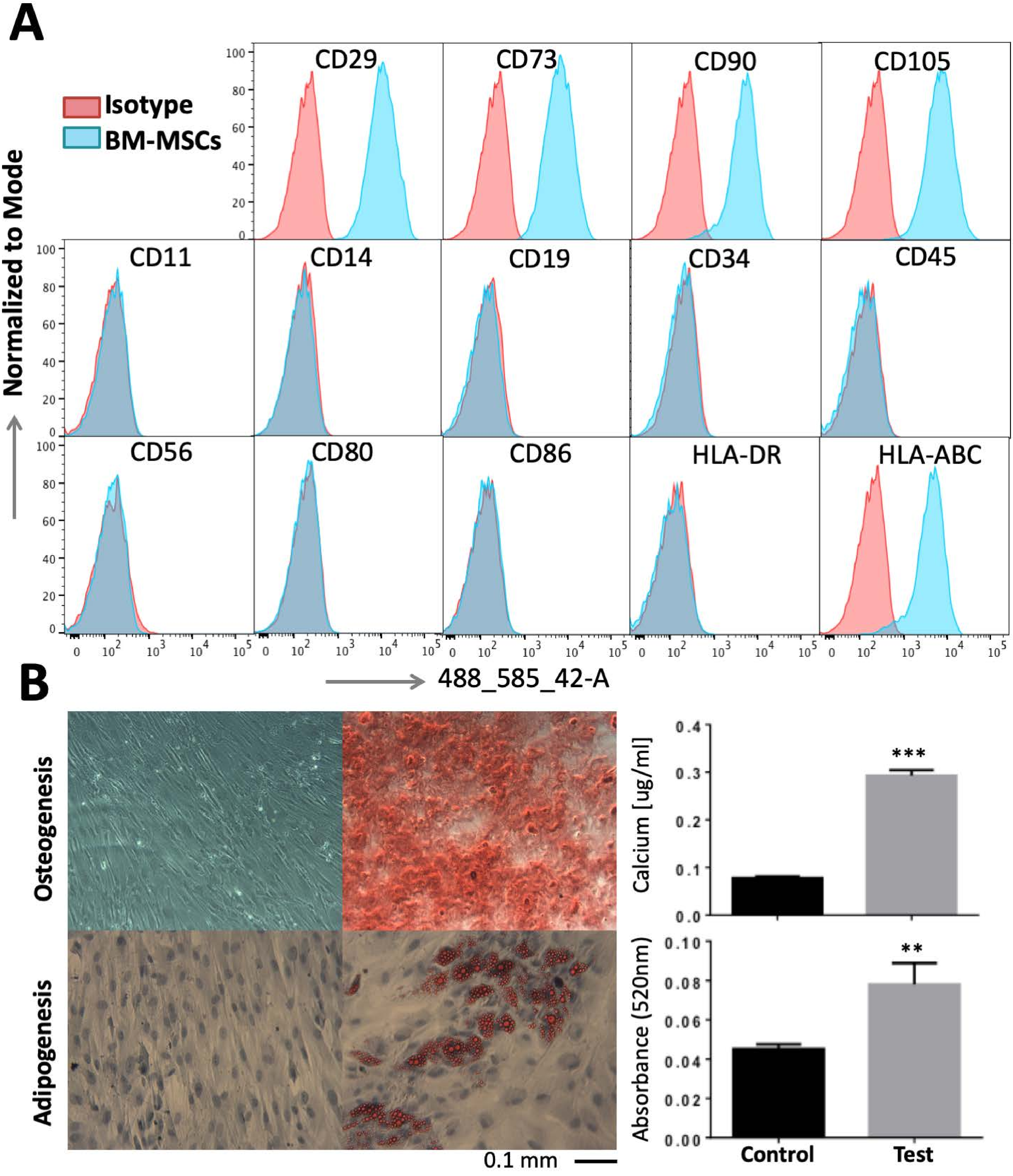
Supplementary Figure S4A: ***Exposure of RPTEC/TERT1 cells to high-Glucose did not alter expression in any common inflammatory signalling molecules .***

RPTEC-TERT-1 cells were cultured at $27500/cm^2$, medium was replaced every second day. From day 12, cells were grown in high-glucose or control conditions (CTRL/HG/MAN) for 24, 48 and 96 hours. Using western blotting, cell pellets were harvested for investigating the expressions of different signalling proteins including: total and phosphorylated forms of p65 NFkB (nuclear factor kappa B – p65 sub unit), p38 MAPK (P38 mitogen-activated protein kinase), ERK-1/2 (extracellular signal–regulated kinase 1/2), STAT-1 (Signal transducer and activator of transcription 1), PKCα (Protein kinase C alpha) and total PPAR-γ (Peroxisome proliferator-activated receptor gamma) as well as housekeeping protein β-Actin (Beta Actin).





Supplementary Figure S4B: Semi-quantitative analysis of the western blots as in Supplementary Figure S4A. ImageJ software was used to perform semi-quantitative analysis of the blots. The area and its corresponding percentage of blots were calculated. Densitometric data was then normalized for the housekeeping protein followed by further normalization relative to the control. Statistical analysis were performed using GraphPad prism. Results were expressed as the Mean±SD. The p values ≤ 0.05 were considered significant at: *p<0.05, **p<0.01, ***p<0.001.



Supplementary Figure S5: ***Human bone-marrow derived MSCs showed its cell surface characteristics and were able to differentiate.*** **A.** Immunophenotyping of cultured human BM-MSCs for different specific cell surface markers by flow cytometry. **B.** Osteogenic and adipogenic differentiation capacity of BM-MSCs. Unpaired t test with Welch's correction $*p<0.05$; $**p<0.01$; $***p<0.001$

Supplementary Table S2: List of DEGs with significant Fold Changes in High-Glucose vs Mannitol

🟨	Upregulated by HG		
🟦	Downregulated by HG		

Gene Symbol	Gene Description	Fold Changes in HG	P Value
PRAMEF17	PRAME family member 17	20.33	0.047
TEKT4	tektin 4	16.00	0.013
CECR7	cat eye syndrome chromosome region, candidate 7 (non-protein coding)	12.00	0.008
IL18RAP	interleukin 18 receptor accessory protein	12.00	0.008
CACNA1S	calcium channel, voltage-dependent, L type, alpha 1S subunit	11.00	0.010
SCN1B	sodium channel, voltage-gated, type I, beta subunit	9.14	0.045
FNDC8	fibronectin type III domain containing 8	9.13	0.05
SNORD76	small nucleolar RNA, C/D box 76	8.55	0.049
IGSF9B	immunoglobulin superfamily, member 9B	8.00	0.020
SH3GL1P1	SH3-domain GRB2-like 1 pseudogene 1	7.91	0.040
FGF1	fibroblast growth factor 1 (acidic)	6.78	0.018
CEP128	centrosomal protein 128kDa	6.55	0.011
PIK3CG	phosphatidylinositol-4,5-bisphosphate 3-kinase, catalytic subunit gamma	6.17	0.047
TGM1	transglutaminase 1 (K polypeptide epidermal type I, protein-glutamine-gamma-glutamyltransferase)	6.08	0.002
LHFPL3	lipoma HMGIC fusion partner-like 3	5.83	0.041
KRT25	keratin 25	5.67	0.002
AOC3	amine oxidase, copper containing 3 (vascular adhesion protein 1)	5.20	0.020
RUNDC3A	RUN domain containing 3A	5.17	0.025
FAM179A	family with sequence similarity 179, member A	4.80	0.049
NPFF	neuropeptide FF-amide peptide precursor	4.50	0.049
CRYGS	crystallin, gamma S	4.33	0.008
ACSBG1	acyl-CoA synthetase bubblegum family member 1	4.25	0.023
COL16A1	collagen, type XVI, alpha 1	3.41	0.028
NR2E1	nuclear receptor subfamily 2, group E, member 1	3.33	0.020
SELL	selectin L	3.31	0.037
NUTM2G	NUT family member 2G	3.25	0.035
NEK10	NIMA-related kinase 10	3.25	0.035
PDE2A	phosphodiesterase 2A, cGMP-stimulated	3.24	0.019
C7orf63	chromosome 7 open reading frame 63	3.13	0.008
SNORD10	small nucleolar RNA, C/D box 10	3.11	0.031
CD160	CD160 molecule	3.11	0.019
TNNC1	troponin C type 1 (slow)	3.11	0.003
LINC00310	long intergenic non-protein coding RNA 310	3.05	0.035

GJB5	gap junction protein, beta 5, 31.1kDa	3.04	0.002
CYP1B1	cytochrome P450, family 1, subfamily B, polypeptide 1	2.96	0.018
LOC283856	uncharacterized LOC283856	2.88	0.034
SLC25A18	solute carrier family 25 (glutamate carrier), member 18	2.87	0.013
LINC00634	long intergenic non-protein coding RNA 634	2.84	0.015
LOC100506071	uncharacterized LOC100506071	2.76	0.026
POF1B	premature ovarian failure, 1B	2.71	0.020
FGF11	fibroblast growth factor 11	2.69	0.035
SNORA40	small nucleolar RNA, H/ACA box 40	2.68	0.016
FAM198B	family with sequence similarity 198, member B	2.67	0.038
ESPL1	extra spindle pole bodies homolog 1 (S. cerevisiae)	2.65	0.004
FLJ37035	uncharacterized LOC399821	2.63	0.017
CENPE	centromere protein E, 312kDa	2.61	0.034
ALDH1A3	aldehyde dehydrogenase 1 family, member A3	2.60	0.002
POLE2	polymerase (DNA directed), epsilon 2, accessory subunit	2.57	0.033
IQCD	IQ motif containing D	2.48	0.039
TTC14	tetratricopeptide repeat domain 14	2.39	0.044
DNER	delta/notch-like EGF repeat containing	2.37	0.038
DAPK2	death-associated protein kinase 2	2.33	0.015
LY6G5B	lymphocyte antigen 6 complex, locus G5B	2.33	0.006
SLC9C1	solute carrier family 9, subfamily C (Na+-transporting carboxylic acid decarboxylase), member 1	2.31	0.042
ZNF432	zinc finger protein 432	2.31	0.049
TREML2	triggering receptor expressed on myeloid cells-like 2	2.29	0.035
ANKS1B	ankyrin repeat and sterile alpha motif domain containing 1B	2.28	0.026
ASB2	ankyrin repeat and SOCS box containing 2	2.26	0.037
USP2	ubiquitin specific peptidase 2	2.23	0.043
FBLN5	fibulin 5	2.21	0.003
TPTE2	transmembrane phosphoinositide 3-phosphatase and tensin homolog 2	2.21	0.008
GJB2	gap junction protein, beta 2, 26kDa	2.18	0.047
TNFRSF11B	tumor necrosis factor receptor superfamily, member 11b	2.17	0.006
RFC3	replication factor C (activator 1) 3, 38kDa	2.17	0.013
GCSAM	germinal center-associated, signaling and motility	2.16	0.025
KCND1	potassium voltage-gated channel, Shal-related subfamily, member 1	2.15	0.049
ALPK2	alpha-kinase 2	2.15	0.011
EFCAB10	EF-hand calcium binding domain 10	2.14	0.003
FLJ45079	FLJ45079 protein	2.14	0.015
FBXW10	F-box and WD repeat domain containing 10	2.13	0.035
PRRT1	proline-rich transmembrane protein 1	2.13	0.035
AHRR	aryl-hydrocarbon receptor repressor	2.10	0.041
AGER	advanced glycosylation end product-specific receptor	2.09	0.020

ALX3	ALX homeobox 3	2.08	0.044
IL1B	interleukin 1, beta	2.07	0.05
GPC2	glypican 2	2.06	0.042
CENPQ	centromere protein Q	2.04	0.040
GALNT9	UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 9 (GalNAc-T9)	2.03	0.018
LINC00909	uncharacterized LOC400657	2.01	0.037
TRIM34	tripartite motif containing 34	2.01	0.043
ZNF239	zinc finger protein 239	2.00	0.030
SNORD22	small nucleolar RNA, C/D box 22	2.00	0.031
EMX2	empty spiracles homeobox 2	1.96	0.016
SLC43A2	solute carrier family 43, member 2	1.96	0.034
LINC01239	uncharacterized LOC441389	1.95	0.049
CXCL5	chemokine (C-X-C motif) ligand 5	1.95	0.029
MTBP	Mdm2, transformed 3T3 cell double minute 2, p53 binding protein (mouse) binding protein, 104kDa	1.94	0.016
PAX6	paired box 6	1.93	0.014
DISP2	dispatched homolog 2 (Drosophila)	1.91	0.004
NOL8	nucleolar protein 8	1.91	0.048
LOC284865	uncharacterized LOC284865	1.89	0.021
DCLRE1A	DNA cross-link repair 1A	1.89	0.012
SCRN3	secernin 3	1.86	0.045
MBTD1	mbt domain containing 1	1.86	0.008
MATN2	matrilin 2	1.86	0.033
NEURL3	neuralized homolog 3 (Drosophila) pseudogene	1.85	0.011
WDR4	WD repeat domain 4	1.83	0.010
ULK4	unc-51-like kinase 4 (C. elegans)	1.83	0.011
BTN2A3P	butyrophilin, subfamily 2, member A3, pseudogene	1.83	0.035
CDCA2	cell division cycle associated 2	1.83	0.025
SLCO2B1	solute carrier organic anion transporter family, member 2B1	1.81	0.004
CDC14A	cell division cycle 14A	1.80	0.027
EHHADH-AS1	EHHADH antisense RNA 1	1.80	0.047
ASF1A	ASF1 anti-silencing function 1 homolog A (S. cerevisiae)	1.80	0.009
MBLAC2	metallo-beta-lactamase domain containing 2	1.78	0.012
ZNF30	zinc finger protein 30	1.78	0.001
DPF3	D4, zinc and double PHD fingers, family 3	1.77	0.013
LNP1	leukemia NUP98 fusion partner 1	1.74	0.003
ZNF300	zinc finger protein 300	1.74	0.044
ZPLD1	zona pellucida-like domain containing 1	1.73	0.012
MALT1	mucosa associated lymphoid tissue lymphoma translocation gene 1	1.71	0.006
HIST2H2BC	histone cluster 2, H2bc (pseudogene)	1.71	0.004

SLC6A6	solute carrier family 6 (neurotransmitter transporter, taurine), member 6	1.70	0.003
ZNF75A	zinc finger protein 75a	1.70	0.010
RECK	reversion-inducing-cysteine-rich protein with kazal motifs	1.69	0.022
KCTD12	potassium channel tetramerisation domain containing 12	1.68	0.043
ADAMTSL4	ADAMTS-like 4	1.68	0.05
SLC7A5	solute carrier family 7 (amino acid transporter light chain, L system), member 5	1.68	0.017
TMEM169	transmembrane protein 169	1.68	0.008
DEPDC5	DEP domain containing 5	1.67	0.048
TLR6	toll-like receptor 6	1.66	0.028
CCZ1B	CCZ1 vacuolar protein trafficking and biogenesis associated homolog B (S. cerevisiae)	1.66	0.048
IZUMO4	IZUMO family member 4	1.65	0.05
NALCN-AS1	NALCN antisense RNA 1	1.65	0.030
LINC00888	uncharacterized LOC100505687	1.65	0.026
TGFBI	transforming growth factor, beta-induced, 68kDa	1.65	0.049
MTFR2	mitochondrial fission regulator 2	1.65	0.038
LOC100288637	OTU domain containing 7A pseudogene	1.65	0.044
CCDC146	coiled-coil domain containing 146	1.64	0.015
NOL11	nucleolar protein 11	1.64	0.021
RABL2B	RAB, member of RAS oncogene family-like 2B	1.64	0.019
C9orf84	chromosome 9 open reading frame 84	1.64	0.020
ENOX2	ecto-NOX disulfide-thiol exchanger 2	1.64	0.015
SH3BP5-AS1	SH3BP5 antisense RNA 1	1.63	0.0008
FBXO9	F-box protein 9	1.63	0.021
ODC1	ornithine decarboxylase 1	1.63	0.045
FUT8	fucosyltransferase 8 (alpha (1,6) fucosyltransferase)	1.63	0.021
ACR	acrosin	1.63	0.038
LAMA3	laminin, alpha 3	1.62	0.042
KLHL20	kelch-like family member 20	1.62	0.046
DNA2	DNA replication helicase 2 homolog (yeast)	1.62	0.017
LTB	lymphotoxin beta (TNF superfamily, member 3)	1.62	0.027
CNIH3	cornichon homolog 3 (Drosophila)	1.61	0.035
FERMT1	fermitin family member 1	1.61	0.037
ARHGEF10	Rho guanine nucleotide exchange factor (GEF) 10	1.61	0.022
RNF219-AS1	RNF219 antisense RNA 1	1.61	0.023
AZI2	5-azacytidine induced 2	1.60	0.015
CEP162	KIAA1009	1.60	0.049
DOCK4	dedicator of cytokinesis 4	1.59	0.007
NUP37	nucleoporin 37kDa	1.59	0.023
LOC100132352	FSHD region gene 1 pseudogene	1.59	0.046
RBM4B	RNA binding motif protein 4B	1.59	0.026

KCTD4	potassium channel tetramerisation domain containing 4	1.59	0.0004
DYSF	dysferlin, limb girdle muscular dystrophy 2B (autosomal recessive)	1.59	0.024
HMGA2	high mobility group AT-hook 2	1.59	0.038
FAM135A	family with sequence similarity 135, member A	1.59	0.008
ZNF34	zinc finger protein 34	1.58	0.05
LOH12CR1	loss of heterozygosity, 12, chromosomal region 1	1.58	0.003
SYP	synaptophysin	1.58	0.032
EFCAB7	EF-hand calcium binding domain 7	1.57	0.038
ADCK3	aarF domain containing kinase 3	1.57	0.036
GOLGA7B	golgin A7 family, member B	1.56	0.028
RCOR3	REST corepressor 3	1.56	0.017
AP4B1	adaptor-related protein complex 4, beta 1 subunit	1.56	0.009
ITGAE	integrin, alpha E (antigen CD103, human mucosal lymphocyte antigen 1; alpha polypeptide)	1.55	0.036
ZNF18	zinc finger protein 18	1.55	0.015
KCNJ15	potassium inwardly-rectifying channel, subfamily J, member 15	1.55	0.006
MPP3	membrane protein, palmitoylated 3 (MAGUK p55 subfamily member 3)	1.55	0.033
LOC613037	nuclear pore complex interacting protein pseudogene	1.55	0.049
ANKRD26	ankyrin repeat domain 26	1.54	0.011
ZNHIT6	zinc finger, HIT-type containing 6	1.54	0.023
GPAT2	glycerol-3-phosphate acyltransferase 2, mitochondrial	1.54	0.017
FREM2	FRAS1 related extracellular matrix protein 2	1.53	0.002
ENC1	ectodermal-neural cortex 1 (with BTB domain)	1.53	0.018
PPAP2B	phosphatidic acid phosphatase type 2B	1.53	0.044
RFK	riboflavin kinase	1.53	0.041
BATF3	basic leucine zipper transcription factor, ATF-like 3	1.53	0.027
ALG1L	ALG1, chitobiosyldiphosphodolichol beta-mannosyltransferase-like	1.53	0.004
ALKBH1	alkB, alkylation repair homolog 1 (E. coli)	1.53	0.013
FAM86C2P	family with sequence similarity 86, member A pseudogene	1.53	0.037
SLCO4C1	solute carrier organic anion transporter family, member 4C1	1.53	0.001
PPM1M	protein phosphatase, Mg2+/Mn2+ dependent, 1M	1.52	0.030
LSM5	LSM5 homolog, U6 small nuclear RNA associated (S. cerevisiae)	1.52	0.005
DHX57	DEAH (Asp-Glu-Ala-Asp/His) box polypeptide 57	1.52	0.026
PDGFB	platelet-derived growth factor beta polypeptide	1.52	0.002
CDH6	cadherin 6, type 2, K-cadherin (fetal kidney)	1.52	0.020
WDR12	WD repeat domain 12	1.52	0.031
CD58	CD58 molecule	1.52	0.002
C9orf41	chromosome 9 open reading frame 41	1.52	0.045
TRAM2	translocation associated membrane protein 2	1.52	0.008
PIK3R1	phosphoinositide-3-kinase, regulatory subunit 1 (alpha)	1.51	0.024

HHAT	hedgehog acyltransferase	1.51	0.023
CCDC175	coiled-coil domain containing 175	1.51	0.042
PDCD2L	programmed cell death 2-like	1.51	0.007
KANSL1-AS1	KANSL1 antisense RNA 1	1.51	0.048
ARHGAP22	Rho GTPase activating protein 22	1.50	0.042
APC2	adenomatosis polyposis coli 2	1.50	0.023
LOC728743	zinc finger protein pseudogene	1.50	0.035
PRR15L	proline rich 15-like	0.05	0.012
FSCN2	fascin homolog 2, actin-bundling protein, retinal (Strongylocentrotus purpuratus)	0.09	0.038
OR7E91P	olfactory receptor, family 7, subfamily E, member 91 pseudogene	0.10	0.009
PLA2G4F	phospholipase A2, group IVF	0.11	0.035
RENBP	renin binding protein	0.11	0.028
BBOX1	butyrobetaine (gamma), 2-oxoglutarate dioxygenase (gamma-butyrobetaine hydroxylase) 1	0.12	0.0009
LOC90246	uncharacterized LOC90246	0.15	0.008
NAPSA	napsin A aspartic peptidase	0.16	0.004
UBE2Q2P2	ubiquitin-conjugating enzyme E2Q family member 2 pseudogene 2	0.16	0.046
MYO7B	myosin VIIB	0.16	0.002
PLA1A	phospholipase A1 member A	0.20	0.020
NME9	NME/NM23 family member 9	0.21	0.049
GPNMB	glycoprotein (transmembrane) nmb	0.21	0.010
ADH4	alcohol dehydrogenase 4 (class II), pi polypeptide	0.22	0.029
SPX	chromosome 12 open reading frame 39	0.24	0.032
ACP5	acid phosphatase 5, tartrate resistant	0.24	0.009
LINC00323	long intergenic non-protein coding RNA 323	0.26	0.046
C4orf47	chromosome 4 open reading frame 47	0.28	0.013
GPM6B	glycoprotein M6B	0.28	0.039
RORC	RAR-related orphan receptor C	0.28	0.001
SMARCD3	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily d, member 3	0.28	0.009
SCARNA2	small Cajal body-specific RNA 2	0.28	0.012
ABI3BP	ABI family, member 3 (NESH) binding protein	0.28	0.012
MLXIPL	MLX interacting protein-like	0.29	0.003
HRASLS5	HRAS-like suppressor family, member 5	0.29	0.034
FXYD6	FXYD domain containing ion transport regulator 6	0.29	0.007
PCDHGA9	protocadherin gamma subfamily A, 9	0.30	0.020
HSD17B14	hydroxysteroid (17-beta) dehydrogenase 14	0.30	0.002
ADH6	alcohol dehydrogenase 6 (class V)	0.31	0.0002
CLCA3P	chloride channel accessory 3, pseudogene	0.31	0.034
GPX3	glutathione peroxidase 3 (plasma)	0.32	0.018

ATP6V1B1	ATPase, H+ transporting, lysosomal 56/58kDa, V1 subunit B1	0.33	0.008
NR1H4	nuclear receptor subfamily 1, group H, member 4	0.34	0.032
FAM131C	family with sequence similarity 131, member C	0.34	0.002
PANX2	pannexin 2	0.34	0.028
CCDC81	coiled-coil domain containing 81	0.34	0.046
PBX1	pre-B-cell leukemia homeobox 1	0.35	0.039
IFIT3	interferon-induced protein with tetratricopeptide repeats 3	0.35	0.016
BDKRB2	bradykinin receptor B2	0.36	0.048
STC1	stanniocalcin 1	0.36	0.022
RN7SL1	RNA, 7SL, cytoplasmic 1	0.36	0.041
LTF	lactotransferrin	0.37	0.014
NRAP	nebulin-related anchoring protein	0.37	0.013
TNNI3	troponin I type 3 (cardiac)	0.38	0.049
IFIT1	interferon-induced protein with tetratricopeptide repeats 1	0.38	0.009
HABP2	hyaluronan binding protein 2	0.38	0.008
MAP2	microtubule-associated protein 2	0.38	0.010
SECTM1	secreted and transmembrane 1	0.39	0.020
PSCA	prostate stem cell antigen	0.39	0.016
KCNIP4	Kv channel interacting protein 4	0.40	0.047
CAPN14	calpain 14	0.40	0.002
NPR1	natriuretic peptide receptor A/guanylate cyclase A (atrionatriuretic peptide receptor A)	0.40	0.012
NTRK2	neurotrophic tyrosine kinase, receptor, type 2	0.40	0.029
TTYH2	tweety homolog 2 (Drosophila)	0.41	0.014
LOC100130705	uncharacterized LOC100130705	0.41	0.035
DEFB1	defensin, beta 1	0.41	0.049
HILPDA	hypoxia inducible lipid droplet-associated	0.42	0.004
RTBDN	retbindin	0.42	0.014
IL12A	interleukin 12A (natural killer cell stimulatory factor 1, cytotoxic lymphocyte maturation factor 1, p35)	0.43	0.023
CASP1	caspase 1, apoptosis-related cysteine peptidase	0.44	0.05
HPSE	heparanase	0.44	0.018
CRYAB	crystallin, alpha B	0.44	0.031
TMEM91	transmembrane protein 91	0.44	0.045
FKBP9P1	FK506 binding protein 9-like	0.44	0.042
KRTAP5-1	keratin associated protein 5-1	0.44	0.0005
CLDN14	claudin 14	0.44	0.020
ENO2	enolase 2 (gamma, neuronal)	0.44	0.001
LOC100133669	uncharacterized LOC100133669	0.44	0.006
LAMA2	laminin, alpha 2	0.45	0.004
PRSS22	protease, serine, 22	0.45	0.004
CTSF	cathepsin F	0.45	0.026
FRAT1	frequently rearranged in advanced T-cell lymphomas	0.46	0.008

ANKRD37	ankyrin repeat domain 37	0.47	0.019
NRN1L	neuritin 1-like	0.47	0.028
VTRNA2-1	vault RNA 2-1	0.47	0.038
WFDC2	WAP four-disulfide core domain 2	0.47	0.013
FOXJ1	forkhead box J1	0.48	0.002
PFKFB4	6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 4	0.48	0.045
EHD3	EH-domain containing 3	0.48	0.025
MIR210HG	MIR210 host gene (non-protein coding)	0.48	0.022
BIK	BCL2-interacting killer (apoptosis-inducing)	0.49	0.037
SEPP1	selenoprotein P, plasma, 1	0.49	0.013
PALM2-AKAP2	PALM2-AKAP2 readthrough	0.49	0.040
ENDOD1	endonuclease domain containing 1	0.49	0.018
METAP1D	methionyl aminopeptidase type 1D (mitochondrial)	0.49	0.011
SLC3A1	solute carrier family 3 (cystine, dibasic and neutral amino acid transporters, activator of cystine, dibasic and neutral amino acid transport), member 1	0.49	0.029
SH3D21	SH3 domain containing 21	0.50	0.010
ANKRD22	ankyrin repeat domain 22	0.50	0.038
CFB	complement factor B	0.51	0.020
NDRG1	N-myc downstream regulated 1	0.51	0.005
CDIP1	cell death-inducing p53 target 1	0.51	0.031
CLU	clusterin	0.52	0.001
TMC4	transmembrane channel-like 4	0.52	0.017
SHC4	SHC (Src homology 2 domain containing) family, member 4	0.52	0.036
SCGB2A1	secretoglobin, family 2A, member 1	0.53	0.006
PTH1R	parathyroid hormone 1 receptor	0.53	0.022
MIR3064	microRNA 3064	0.53	0.048
ACSS1	acyl-CoA synthetase short-chain family member 1	0.53	0.016
CNTNAP1	contactin associated protein 1	0.53	0.036
CARD16	caspase recruitment domain family, member 16	0.53	0.018
LRAT	lecithin retinol acyltransferase (phosphatidylcholine--retinol O-acyltransferase)	0.54	0.043
BNIP3	BCL2/adenovirus E1B 19kDa interacting protein 3	0.55	0.014
RAP1GAP	RAP1 GTPase activating protein	0.55	0.031
IFITM1	interferon induced transmembrane protein 1	0.55	0.003
S100A1	S100 calcium binding protein A1	0.55	0.019
BCAM	basal cell adhesion molecule (Lutheran blood group)	0.56	0.005
NCKIPSD	NCK interacting protein with SH3 domain	0.56	0.011
CDH16	cadherin 16, KSP-cadherin	0.57	0.018
ADAMTS9-AS2	ADAMTS9 antisense RNA 2	0.57	0.011
HGD	homogentisate 1,2-dioxygenase	0.57	0.029
MEGF11	multiple EGF-like-domains 11	0.57	0.012
IFITM10	interferon induced transmembrane protein 10	0.57	0.035

SLC2A12	solute carrier family 2 (facilitated glucose transporter), member 12	0.57	0.031
SLC6A13	solute carrier family 6 (neurotransmitter transporter, GABA), member 13	0.58	0.041
SEMA4A	sema domain, immunoglobulin domain (Ig), transmembrane domain (TM) and short cytoplasmic domain, (semaphorin) 4A	0.58	0.023
C4orf3	chromosome 4 open reading frame 3	0.58	0.007
CDK18	cyclin-dependent kinase 18	0.58	0.012
HK2	hexokinase 2	0.58	0.006
GBP2	guanylate binding protein 2, interferon-inducible	0.59	0.015
MUC16	mucin 16, cell surface associated	0.59	0.009
APOL1	apolipoprotein L, 1	0.59	0.001
GBE1	glucan (1,4-alpha-), branching enzyme 1	0.59	0.009
AGR2	anterior gradient 2 homolog (Xenopus laevis)	0.59	0.010
OGDHL	oxoglutarate dehydrogenase-like	0.59	0.028
LINC00478	long intergenic non-protein coding RNA 478	0.60	0.013
RAP2B	RAP2B, member of RAS oncogene family	0.60	0.024
PBLD	phenazine biosynthesis-like protein domain containing	0.60	0.026
CFI	complement factor I	0.60	0.032
IRS1	insulin receptor substrate 1	0.60	0.008
ZIM3	zinc finger, imprinted 3	0.61	0.037
TGM5	transglutaminase 5	0.61	0.016
COL11A1	collagen, type XI, alpha 1	0.61	0.049
ST3GAL4	ST3 beta-galactoside alpha-2,3-sialyltransferase 4	0.61	0.040
GPLD1	glycosylphosphatidylinositol specific phospholipase D1	0.61	0.041
ZNF559	zinc finger protein 559	0.61	0.027
NEURL1	neuralized homolog (Drosophila)	0.61	0.029
IFITM2	interferon induced transmembrane protein 2	0.61	0.012
HRASLS	HRAS-like suppressor	0.62	0.017
SIAE	sialic acid acetylesterase	0.62	0.022
MPI	mannose phosphate isomerase	0.62	0.026
ACSM3	acyl-CoA synthetase medium-chain family member 3	0.62	0.029
CKB	creatine kinase, brain	0.62	0.005
LINC00663	long intergenic non-protein coding RNA 663	0.62	0.024
MIR17HG	miR-17-92 cluster host gene (non-protein coding)	0.63	0.041
LINC00327	long intergenic non-protein coding RNA 327	0.63	0.001
FXYD2	FXYD domain containing ion transport regulator 2	0.63	0.012
MAP1LC3B2	microtubule-associated protein 1 light chain 3 beta 2	0.63	0.031
PFKL	phosphofructokinase, liver	0.63	0.008
CLDN4	claudin 4	0.63	0.011
P4HA1	prolyl 4-hydroxylase, alpha polypeptide I	0.64	0.002
MIOX	myo-inositol oxygenase	0.64	0.012
CTSD	cathepsin D	0.64	<0.0001

CECR5	cat eye syndrome chromosome region, candidate 5	0.64	0.041
CA11	carbonic anhydrase XI	0.64	0.011
DNAJB7	DnaJ (Hsp40) homolog, subfamily B, member 7	0.64	0.025
GAS2L3	growth arrest-specific 2 like 3	0.64	0.036
SHC2	SHC (Src homology 2 domain containing) transforming protein 2	0.65	0.043
ONECUT3	one cut homeobox 3	0.65	0.021
LOC100130872	uncharacterized LOC100130872	0.65	0.008
BCKDK	branched chain ketoacid dehydrogenase kinase	0.65	0.037
MACC1	metastasis associated in colon cancer 1	0.66	0.007
SNX33	sorting nexin 33	0.66	0.010
ERO1LB	ERO1-like beta (S. cerevisiae)	0.66	0.047
TSPAN33	tetraspanin 33	0.66	0.017
FLT4	fms-related tyrosine kinase 4	0.66	0.014
IFITM3	interferon induced transmembrane protein 3	0.66	0.002
FAM162A	family with sequence similarity 162, member A	0.66	0.015
KLHDC9	kelch domain containing 9	0.66	0.003
FLOT1	flotillin 1	0.66	0.001
PREPL	prolyl endopeptidase-like	0.66	0.008
PGK1	phosphoglycerate kinase 1	0.66	0.027
STBD1	starch binding domain 1	0.66	0.039
SLC16A3	solute carrier family 16, member 3 (monocarboxylic acid transporter 4)	0.66	0.05
ITM2C	integral membrane protein 2C	0.67	0.012
TTC39A	tetratricopeptide repeat domain 39A	0.67	0.025
CELF2	CUGBP, Elav-like family member 2	0.67	0.038

Supplementary Table S3: List of DEGs with significant Fold Changes in High-Glucose vs Control

🟨	Upregulated by HG		
🟦	Downregulated by HG		

Gene Symbol	**Gene Description**	**Fold Changes in HG**	**P Value**
SEMA3E	sema domain, immunoglobulin domain (Ig), short basic domain, secreted, (semaphorin) 3E	16.00	0.038
PHOSPHO2-KLHL23	PHOSPHO2-KLHL23 readthrough	15.65	0.0002
IL18RAP	interleukin 18 receptor accessory protein	12.00	0.032
LINC00293	long intergenic non-protein coding RNA 293	9.50	0.023
AOC3	amine oxidase, copper containing 3 (vascular adhesion protein 1)	8.67	0.034
BAGE	B melanoma antigen	7.67	0.039
SNORD76	small nucleolar RNA, C/D box 76	6.49	0.013
HCG22	HLA complex group 22 (non-protein coding)	6.05	0.034
OSR1	odd-skipped related 1 (Drosophila)	6.00	0.038
ZP3	zona pellucida glycoprotein 3 (sperm receptor)	5.76	0.017
GLYATL1	glycine-N-acyltransferase-like 1	5.50	0.035
KIF7	kinesin family member 7	5.00	0.015
FAM179A	family with sequence similarity 179, member A	4.80	0.003
LHFPL3	lipoma HMGIC fusion partner-like 3	4.38	0.016
HCN2	hyperpolarization activated cyclic nucleotide-gated potassium channel 2	4.00	<0.0001
SNORD47	small nucleolar RNA, C/D box 47	3.93	0.003
IQCD	IQ motif containing D	3.79	0.041
AQP5	aquaporin 5	3.71	0.034
PKD1L3	polycystic kidney disease 1-like 3	3.70	0.046
CYP1B1	cytochrome P450, family 1, subfamily B, polypeptide 1	3.46	0.039
LOC654342	lymphocyte-specific protein 1 pseudogene	3.41	0.0004
SCN1B	sodium channel, voltage-gated, type I, beta subunit	3.37	0.027
KNG1	kininogen 1	3.24	0.011
SLC12A3	solute carrier family 12 (sodium/chloride transporters), member 3	3.17	0.006
IAPP	islet amyloid polypeptide	3.11	0.039
SNCG	synuclein, gamma (breast cancer-specific protein 1)	3.09	0.048
RSU1P2	Ras suppressor protein 1 pseudogene 2	3.07	0.008
POLE2	polymerase (DNA directed), epsilon 2, accessory subunit	3.01	0.049
RRS1-AS1	uncharacterized LOC100505676	2.87	0.034
FAM151B	family with sequence similarity 151, member B	2.71	0.029
GDAP1	ganglioside induced differentiation associated protein 1	2.58	0.019
C3orf35	chromosome 3 open reading frame 35	2.52	0.013

AGER	advanced glycosylation end product-specific receptor	2.51	0.035
EMCN	endomucin	2.50	0.038
RNU2-1	RNA, U2 small nuclear 1	2.48	0.028
KRT42P	keratin 42 pseudogene	2.46	0.011
ASB2	ankyrin repeat and SOCS box containing 2	2.46	0.002
TUBB1	tubulin, beta 1 class VI	2.43	0.038
BAI2	brain-specific angiogenesis inhibitor 2	2.42	0.030
SLC35G1	solute carrier family 35, member G1	2.38	0.037
PAX9	paired box 9	2.35	0.010
SFMBT2	Scm-like with four mbt domains 2	2.33	0.045
PROB1	proline-rich basic protein 1	2.29	0.008
ALDH1A3	aldehyde dehydrogenase 1 family, member A3	2.26	0.049
AKAP3	A kinase (PRKA) anchor protein 3	2.25	0.013
SH3GL1P1	SH3-domain GRB2-like 1 pseudogene 1	2.23	0.017
GRIP2	glutamate receptor interacting protein 2	2.22	0.014
C17orf53	chromosome 17 open reading frame 53	2.21	0.007
TSACC	TSSK6 activating co-chaperone	2.20	0.025
SSTR2	somatostatin receptor 2	2.19	0.037
LINC00921	uncharacterized protein FLJ39639	2.17	0.034
LOC100131347	RAD52 motif 1 pseudogene	2.16	0.002
OR7D2	olfactory receptor, family 7, subfamily D, member 2	2.16	0.050
LOC100506469	uncharacterized LOC100506469	2.15	0.035
IPCEF1	interaction protein for cytohesin exchange factors 1	2.14	0.028
C19orf40	chromosome 19 open reading frame 40	2.14	0.041
NLRP8	NLR family, pyrin domain containing 8	2.13	0.040
NCRUPAR	non-protein coding RNA, upstream of F2R/PAR1	2.13	0.025
RLTPR	RGD motif, leucine rich repeats, tropomodulin domain and proline-rich containing	2.12	0.041
FBXL13	F-box and leucine-rich repeat protein 13	2.11	0.019
USP2	ubiquitin specific peptidase 2	2.10	0.035
C9orf66	chromosome 9 open reading frame 66	2.09	0.021
MS4A2	membrane-spanning 4-domains, subfamily A, member 2	2.09	0.021
STXBP5-AS1	STXBP5 antisense RNA 1	2.08	0.012
ZNF551	zinc finger protein 551	2.07	0.022
KRT15	keratin 15	2.06	0.039
ZRANB2-AS2	ZRANB2 antisense RNA 2 (head to head)	2.05	0.044
RAB33A	RAB33A, member RAS oncogene family	2.05	0.024
PPP1R1A	protein phosphatase 1, regulatory (inhibitor) subunit 1A	2.03	0.011
MCF2L-AS1	MCF2L antisense RNA 1	2.00	0.025
FIRRE	family with sequence similarity 195, member A pseudogene	1.93	0.010
BMF	Bcl2 modifying factor	1.92	0.003
DBF4B	DBF4 homolog B (S. cerevisiae)	1.91	0.028
ZNF716	zinc finger protein 716	1.86	0.039

CCDC28B	coiled-coil domain containing 28B	1.84	0.039
LOC283693	actin, alpha 2, smooth muscle, aorta pseudogene	1.84	0.036
INGX	inhibitor of growth family, X-linked, pseudogene	1.83	0.004
KLHL14	kelch-like family member 14	1.83	0.013
COCH	coagulation factor C homolog, cochlin (Limulus polyphemus)	1.82	0.015
LINC01140	uncharacterized LOC339524	1.82	0.012
LHFPL3-AS2	LHFPL3 antisense RNA 2	1.81	0.036
GABRE	gamma-aminobutyric acid (GABA) A receptor, epsilon	1.81	0.044
GGT6	gamma-glutamyltransferase 6	1.81	0.022
LAIR1	leukocyte-associated immunoglobulin-like receptor 1	1.80	0.044
MT1E	metallothionein 1E	1.80	0.012
EMR2	egf-like module containing, mucin-like, hormone receptor-like 2	1.80	0.041
RGPD4-AS1	uncharacterized LOC729121	1.79	0.041
SLC7A5	solute carrier family 7 (amino acid transporter light chain, L system), member 5	1.78	0.022
LINC00574	long intergenic non-protein coding RNA 574	1.77	0.043
PKN3	protein kinase N3	1.77	0.047
TRIM59	tripartite motif containing 59	1.75	0.031
ODC1	ornithine decarboxylase 1	1.74	0.0004
KCNQ4	potassium voltage-gated channel, KQT-like subfamily, member 4	1.74	0.009
PROSER2-AS1	PROSER2 antisense RNA 1	1.74	0.034
ATAT1	alpha tubulin acetyltransferase 1	1.74	0.042
TPCN1	two pore segment channel 1	1.73	0.039
HMGA2	high mobility group AT-hook 2	1.73	0.030
ZNF341	zinc finger protein 341	1.72	0.002
H1FX-AS1	H1FX antisense RNA 1	1.71	0.007
DNM1P46	DNM1 pseudogene 46	1.71	0.014
SMTN	smoothelin	1.71	0.014
KCND1	potassium voltage-gated channel, Shal-related subfamily, member 1	1.69	0.035
TEKT4P2	tektin 4 pseudogene 2	1.68	0.003
BIN3-IT1	uncharacterized LOC80094	1.67	0.029
LTB	lymphotoxin beta (TNF superfamily, member 3)	1.67	0.014
GATSL3	GATS protein-like 3	1.67	0.006
TDGF1	teratocarcinoma-derived growth factor 1	1.67	0.050
AFG3L1P	AFG3 ATPase family member 3-like 1 (S. cerevisiae), pseudogene	1.66	0.009
KCNH3	potassium voltage-gated channel, subfamily H (eag-related), member 3	1.66	0.004
PLSCR3	phospholipid scramblase 3	1.65	0.038
PDGFB	platelet-derived growth factor beta polypeptide	1.65	0.003

GRB14	growth factor receptor-bound protein 14	1.63	0.008
TPRA1	transmembrane protein, adipocyte asscociated 1	1.63	0.005
MLLT4-AS1	MLLT4 antisense RNA 1 (head to head)	1.63	0.031
SLCO2B1	solute carrier organic anion transporter family, member 2B1	1.62	<0.0001
SLC4A11	solute carrier family 4, sodium borate transporter, member 11	1.62	0.004
VARS2	valyl-tRNA synthetase 2, mitochondrial	1.61	0.007
LDLRAD2	low density lipoprotein receptor class A domain containing 2	1.61	0.032
SSH1	slingshot protein phosphatase 1	1.61	0.030
BMP8A	bone morphogenetic protein 8a	1.61	0.040
PRR23C	proline rich 23C	1.61	0.003
TXNRD1	thioredoxin reductase 1	1.60	0.045
RDH10	retinol dehydrogenase 10 (all-trans)	1.60	0.010
FBXL22	F-box and leucine-rich repeat protein 22	1.60	0.003
GOLGA7B	golgin A7 family, member B	1.59	0.008
SIX5	SIX homeobox 5	1.58	0.029
SLC6A6	solute carrier family 6 (neurotransmitter transporter, taurine), member 6	1.58	0.006
STC2	stanniocalcin 2	1.58	0.013
PIN4P1	protein (peptidylprolyl cis/trans isomerase) NIMA-interacting, 4 pseudogene 1	1.58	0.034
MAL	mal, T-cell differentiation protein	1.58	0.034
CITED4	Cbp/p300-interacting transactivator, with Glu/Asp-rich carboxy-terminal domain, 4	1.58	0.012
KCNJ5	potassium inwardly-rectifying channel, subfamily J, member 5	1.58	0.035
ULK4	unc-51-like kinase 4 (C. elegans)	1.57	0.025
PABPC1P2	poly(A) binding protein, cytoplasmic 1 pseudogene 2	1.57	0.029
SCIMP	SLP adaptor and CSK interacting membrane protein	1.57	0.041
AP4B1	adaptor-related protein complex 4, beta 1 subunit	1.56	0.049
DPH7	WD repeat domain 85	1.55	0.048
EXOC3L2	exocyst complex component 3-like 2	1.55	0.011
TNFAIP8L3	tumor necrosis factor, alpha-induced protein 8-like 3	1.55	0.039
NANOG	Nanog homeobox	1.55	0.011
SLC43A1	solute carrier family 43, member 1	1.55	0.015
SNORA10	small nucleolar RNA, H/ACA box 10	1.55	0.0014
BYSL	bystin-like	1.55	0.034
MPL	myeloproliferative leukemia virus oncogene	1.55	0.028
NRGN	neurogranin (protein kinase C substrate, RC3)	1.54	0.045
TBXAS1	thromboxane A synthase 1 (platelet)	1.54	0.040
KCNIP3	Kv channel interacting protein 3, calsenilin	1.54	0.010
DSCAML1	Down syndrome cell adhesion molecule like 1	1.54	0.038
RRP1	ribosomal RNA processing 1 homolog (S. cerevisiae)	1.54	0.033
FAM167A	family with sequence similarity 167, member A	1.54	0.038
FASN	fatty acid synthase	1.54	0.039

NME1-NME2	NME1-NME2 readthrough	1.53	0.002
IL1RN	interleukin 1 receptor antagonist	1.53	0.040
ST8SIA1	ST8 alpha-N-acetyl-neuraminide alpha-2,8-sialyltransferase 1	1.52	0.044
SOX7	SRY (sex determining region Y)-box 7	1.52	0.017
HOXB5	homeobox B5	1.52	0.026
CTU2	cytosolic thiouridylase subunit 2 homolog (S. pombe)	1.52	0.043
MT2A	metallothionein 2A	1.52	0.025
ARMC9	armadillo repeat containing 9	1.51	0.016
DGKA	diacylglycerol kinase, alpha 80kDa	1.51	0.017
ASMTL-AS1	ASMTL antisense RNA 1	1.51	0.034
TCEANC2	transcription elongation factor A (SII) N-terminal and central domain containing 2	1.51	0.050
CRYM	crystallin, mu	1.51	0.004
ADRA1B	adrenoceptor alpha 1B	1.50	0.005
SP6	Sp6 transcription factor	1.50	0.034
PRR15L	proline rich 15-like	0.04	0.001
ADAM7	ADAM metallopeptidase domain 7	0.07	0.0002
PLA2G4F	phospholipase A2, group IVF	0.07	0.025
PPFIA4	protein tyrosine phosphatase, receptor type, f polypeptide (PTPRF), interacting protein (liprin), alpha 4	0.07	0.043
LOC90246	uncharacterized LOC90246	0.07	0.029
PLA1A	phospholipase A1 member A	0.07	0.026
WAS	Wiskott-Aldrich syndrome	0.08	0.039
LIMS3	LIM and senescent cell antigen-like domains 3	0.09	0.007
PRR22	proline rich 22	0.09	0.046
HIST1H4E	histone cluster 1, H4e	0.11	0.030
BBOX1	butyrobetaine (gamma), 2-oxoglutarate dioxygenase (gamma-butyrobetaine hydroxylase) 1	0.11	0.006
SPX	chromosome 12 open reading frame 39	0.14	0.043
LOC100133920	uncharacterized LOC100133920	0.14	0.049
LOC154761	family with sequence similarity 115, member C pseudogene	0.14	0.004
MYO7B	myosin VIIB	0.16	0.015
C1QTNF4	C1q and tumor necrosis factor related protein 4	0.16	0.005
C4BPA	complement component 4 binding protein, alpha	0.16	0.005
PLCH2	phospholipase C, eta 2	0.17	0.025
GPNMB	glycoprotein (transmembrane) nmb	0.17	0.0009
TMEM45A	transmembrane protein 45A	0.17	0.032
DNAJC12	DnaJ (Hsp40) homolog, subfamily C, member 12	0.18	0.031
ANKRD37	ankyrin repeat domain 37	0.18	0.008
LAMA1	laminin, alpha 1	0.19	0.014
ATP6V1B1	ATPase, H+ transporting, lysosomal 56/58kDa, V1 subunit B1	0.19	0.018
GPR146	G protein-coupled receptor 146	0.19	0.0008
HILPDA	hypoxia inducible lipid droplet-associated	0.20	0.006

C4orf47	chromosome 4 open reading frame 47	0.20	0.05
DHRS2	dehydrogenase/reductase (SDR family) member 2	0.20	0.015
C21orf49	chromosome 21 open reading frame 49	0.20	0.030
SCGB1D2	secretoglobin, family 1D, member 2	0.20	0.022
STC1	stanniocalcin 1	0.20	0.002
GRK4	G protein-coupled receptor kinase 4	0.21	0.028
USP51	ubiquitin specific peptidase 51	0.21	0.034
ESPN	espin	0.21	0.017
DLL1	delta-like 1 (Drosophila)	0.21	0.030
ADH6	alcohol dehydrogenase 6 (class V)	0.22	0.023
PGF	placental growth factor	0.22	0.023
ANGPTL4	angiopoietin-like 4	0.23	0.038
PCDHB11	protocadherin beta 11	0.24	0.004
CDH17	cadherin 17, LI cadherin (liver-intestine)	0.25	0.018
FLJ44635	TPT1-like protein	0.25	0.040
NAPSA	napsin A aspartic peptidase	0.25	0.011
SLC8A1	solute carrier family 8 (sodium/calcium exchanger), member 1	0.26	0.025
BLNK	B-cell linker	0.26	0.006
DMGDH	dimethylglycine dehydrogenase	0.27	0.019
AMZ2P1	archaelysin family metallopeptidase 2 pseudogene 1	0.27	0.013
RTDR1	rhabdoid tumor deletion region gene 1	0.28	0.026
ASTN1	astrotactin 1	0.28	0.034
VEPH1	ventricular zone expressed PH domain-containing 1	0.28	0.014
LOC286359	uncharacterized LOC286359	0.29	0.019
IFIT1	interferon-induced protein with tetratricopeptide repeats 1	0.29	0.0007
ABI3BP	ABI family, member 3 (NESH) binding protein	0.29	0.015
SCGB2A2	secretoglobin, family 2A, member 2	0.29	0.033
FAM13A-AS1	FAM13A antisense RNA 1	0.29	0.0005
GNN	Grp94 neighboring nucleotidase pseudogene	0.29	0.014
MAP7D2	MAP7 domain containing 2	0.29	0.015
ADM	adrenomedullin	0.30	0.032
SCGB2A1	secretoglobin, family 2A, member 1	0.30	0.008
NDRG1	N-myc downstream regulated 1	0.31	0.005
LRRIQ3	leucine-rich repeats and IQ motif containing 3	0.31	0.022
ENO2	enolase 2 (gamma, neuronal)	0.32	0.002
FXYD6	FXYD domain containing ion transport regulator 6	0.32	0.05
PFKFB4	6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 4	0.32	0.005
PBX1	pre-B-cell leukemia homeobox 1	0.32	0.038
TLR4	toll-like receptor 4	0.32	0.049
CLEC2B	C-type lectin domain family 2, member B	0.32	0.008
NTRK2	neurotrophic tyrosine kinase, receptor, type 2	0.33	0.002
WBSCR28	Williams-Beuren syndrome chromosome region 28	0.34	0.05

TMEM91	transmembrane protein 91	0.34	0.007
BEST3	bestrophin 3	0.34	0.008
IFIT3	interferon-induced protein with tetratricopeptide repeats 3	0.35	0.029
TBC1D3P5	TBC1 domain family, member 3 pseudogene 5	0.35	0.032
IGFBP3	insulin-like growth factor binding protein 3	0.36	0.001
TSLP	thymic stromal lymphopoietin	0.36	0.040
HLA-DQA1	major histocompatibility complex, class II, DQ alpha 1	0.36	0.035
TMEM37	transmembrane protein 37	0.36	0.0004
TUBA8	tubulin, alpha 8	0.36	0.009
GPX3	glutathione peroxidase 3 (plasma)	0.36	0.013
NR1H4	nuclear receptor subfamily 1, group H, member 4	0.36	0.030
TMED10P1	transmembrane emp24-like trafficking protein 10 (yeast) pseudogene 1	0.37	0.028
ENDOD1	endonuclease domain containing 1	0.37	0.007
DEFB1	defensin, beta 1	0.37	0.004
GBE1	glucan (1,4-alpha-), branching enzyme 1	0.37	0.002
SH3D21	SH3 domain containing 21	0.37	0.018
HABP2	hyaluronan binding protein 2	0.37	0.002
MAP2	microtubule-associated protein 2	0.37	0.008
RRN3P2	RNA polymerase I transcription factor homolog (S. cerevisiae) pseudogene 2	0.37	0.042
ZBTB37	zinc finger and BTB domain containing 37	0.37	0.035
RHOU	ras homolog family member U	0.37	0.022
SMARCD3	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily d, member 3	0.37	0.017
FCGR2C	Fc fragment of IgG, low affinity IIc, receptor for (CD32) (gene/pseudogene)	0.38	0.038
PODNL1	podocan-like 1	0.38	0.036
NNAT	neuronatin	0.38	0.007
GPR113	G protein-coupled receptor 113	0.38	0.026
RABL2A	RAB, member of RAS oncogene family-like 2A	0.38	0.018
SYNGR4	synaptogyrin 4	0.38	0.044
NEBL	nebulette	0.39	0.023
KHDC1	KH homology domain containing 1	0.39	0.014
IFI44L	interferon-induced protein 44-like	0.39	0.013
GPBAR1	G protein-coupled bile acid receptor 1	0.39	0.024
LTF	lactotransferrin	0.40	0.032
WDR66	WD repeat domain 66	0.40	0.034
GOLGA8S	golgin A8 family, member S	0.41	0.013
SEL1L	sel-1 suppressor of lin-12-like (C. elegans)	0.41	0.005
HPSE	heparanase	0.41	0.003
SMIM24	chromosome 19 open reading frame 77	0.41	0.045

IL12A	interleukin 12A (natural killer cell stimulatory factor 1, cytotoxic lymphocyte maturation factor 1, p35)	0.41	0.015
MSH5	mutS homolog 5 (E. coli)	0.41	0.042
NRAP	nebulin-related anchoring protein	0.42	0.024
C6orf222	chromosome 6 open reading frame 222	0.42	0.025
HK2	hexokinase 2	0.42	0.001
ERO1LB	ERO1-like beta (S. cerevisiae)	0.42	0.004
GIMAP2	GTPase, IMAP family member 2	0.42	0.041
SYNM	synemin, intermediate filament protein	0.42	0.045
CRELD2	cysteine-rich with EGF-like domains 2	0.42	0.019
ERO1L	ERO1-like (S. cerevisiae)	0.43	0.008
DHDH	dihydrodiol dehydrogenase (dimeric)	0.43	0.022
CP	ceruloplasmin (ferroxidase)	0.43	0.012
LUM	lumican	0.43	0.020
RNASE4	ribonuclease, RNase A family, 4	0.43	0.013
BIK	BCL2-interacting killer (apoptosis-inducing)	0.43	0.048
C2CD4C	C2 calcium-dependent domain containing 4C	0.43	0.012
HLA-DPA1	major histocompatibility complex, class II, DP alpha 1	0.43	0.027
RASAL2-AS1	RASAL2 antisense RNA 1	0.43	0.023
RGMA	RGM domain family, member A	0.44	0.035
HSPA5	heat shock 70kDa protein 5 (glucose-regulated protein, 78kDa)	0.44	0.022
PTGS1	prostaglandin-endoperoxide synthase 1 (prostaglandin G/H synthase and cyclooxygenase)	0.44	0.002
CASP1	caspase 1, apoptosis-related cysteine peptidase	0.44	0.002
TTC18	tetratricopeptide repeat domain 18	0.44	0.035
ZNF502	zinc finger protein 502	0.44	0.028
CNTNAP1	contactin associated protein 1	0.45	0.016
CKB	creatine kinase, brain	0.45	0.007
ESRRG	estrogen-related receptor gamma	0.45	0.030
MIR210HG	MIR210 host gene (non-protein coding)	0.45	0.013
RASD1	RAS, dexamethasone-induced 1	0.45	0.002
BNIP3	BCL2/adenovirus E1B 19kDa interacting protein 3	0.45	0.002
CFB	complement factor B	0.45	0.002
TDRG1	testis development related 1 (non-protein coding)	0.45	0.0008
SAPCD1	suppressor APC domain containing 1	0.45	0.033
RSG1	REM2 and RAB-like small GTPase 1	0.45	0.003
PDK1	pyruvate dehydrogenase kinase, isozyme 1	0.45	0.008
PDIA4	protein disulfide isomerase family A, member 4	0.46	0.011
TMC4	transmembrane channel-like 4	0.46	0.018
ACSS1	acyl-CoA synthetase short-chain family member 1	0.46	0.010
NUPR1	nuclear protein, transcriptional regulator, 1	0.46	0.020
PTH1R	parathyroid hormone 1 receptor	0.46	0.010

C4orf3	chromosome 4 open reading frame 3	0.46	0.006
SEPP1	selenoprotein P, plasma, 1	0.46	0.043
NEU3	sialidase 3 (membrane sialidase)	0.46	0.021
CTSF	cathepsin F	0.46	0.007
RAB27B	RAB27B, member RAS oncogene family	0.46	0.016
RNF217	ring finger protein 217	0.46	0.026
SPEF1	sperm flagellar 1	0.46	0.039
SLC3A1	solute carrier family 3 (cystine, dibasic and neutral amino acid transporters, activator of cystine, dibasic and neutral amino acid transport), member 1	0.47	0.006
BTC	betacellulin	0.47	0.035
NCKIPSD	NCK interacting protein with SH3 domain	0.47	0.010
P4HA1	prolyl 4-hydroxylase, alpha polypeptide I	0.47	0.032
SLMO1	slowmo homolog 1 (Drosophila)	0.47	0.044
PHYHIP	phytanoyl-CoA 2-hydroxylase interacting protein	0.48	0.032
RAP2B	RAP2B, member of RAS oncogene family	0.48	0.012
ZNF808	zinc finger protein 808	0.48	0.05
PGK1	phosphoglycerate kinase 1	0.48	0.008
KLHDC7A	kelch domain containing 7A	0.48	0.049
C2	complement component 2	0.48	0.027
FUT11	fucosyltransferase 11 (alpha (1,3) fucosyltransferase)	0.48	0.040
NXNL2	nucleoredoxin-like 2	0.48	0.002
PLOD2	procollagen-lysine, 2-oxoglutarate 5-dioxygenase 2	0.48	0.030
LIX1	Lix1 homolog (chicken)	0.49	0.032
NBEAL1	neurobeachin-like 1	0.49	0.05
LINC-PINT	uncharacterized LOC378805	0.49	0.020
STBD1	starch binding domain 1	0.49	0.017
CCL28	chemokine (C-C motif) ligand 28	0.49	0.006
MACROD2	MACRO domain containing 2	0.49	0.021
MORN3	MORN repeat containing 3	0.50	0.028
SOX8	SRY (sex determining region Y)-box 8	0.50	0.005
DYNAP	dynactin associated protein	0.50	0.022
CRYAB	crystallin, alpha B	0.50	0.028
PRSS22	protease, serine, 22	0.50	0.028
RNF150	ring finger protein 150	0.50	0.019
ZEB2	zinc finger E-box binding homeobox 2	0.50	0.006
AATK	apoptosis-associated tyrosine kinase	0.50	0.023
NFATC2	nuclear factor of activated T-cells, cytoplasmic, calcineurin-dependent 2	0.50	0.034
ITGA4	integrin, alpha 4 (antigen CD49D, alpha 4 subunit of VLA-4 receptor)	0.50	0.035
C5	complement component 5	0.50	0.044
BEX2	brain expressed X-linked 2	0.50	0.042

CCDC153	coiled-coil domain containing 153	0.50	0.042
HSP90B1	heat shock protein 90kDa beta (Grp94), member 1	0.50	0.009
AGR2	anterior gradient 2 homolog (Xenopus laevis)	0.50	0.004
PRKAR2A	protein kinase, cAMP-dependent, regulatory, type II, alpha	0.50	0.046
SNX33	sorting nexin 33	0.51	0.008
IL1RL1	interleukin 1 receptor-like 1	0.51	0.044
SLC2A1	solute carrier family 2 (facilitated glucose transporter), member 1	0.51	0.026
CGREF1	cell growth regulator with EF-hand domain 1	0.51	0.009
EHD3	EH-domain containing 3	0.51	0.017
THAP8	THAP domain containing 8	0.51	0.039
IFIT2	interferon-induced protein with tetratricopeptide repeats 2	0.52	0.005
C16orf74	chromosome 16 open reading frame 74	0.52	0.002
LOX	lysyl oxidase	0.52	0.005
TMEM182	transmembrane protein 182	0.52	0.003
SNHG12	small nucleolar RNA host gene 12 (non-protein coding)	0.52	0.022
ULBP1	UL16 binding protein 1	0.53	0.017
RRAGB	Ras-related GTP binding B	0.53	0.035
INTU	inturned planar cell polarity protein	0.53	0.0008
ZNF12	zinc finger protein 12	0.53	0.027
TVP23C-CDRT4	TVP23C-CDRT4 readthrough	0.53	0.046
SLC6A13	solute carrier family 6 (neurotransmitter transporter, GABA), member 13	0.53	0.023
SEC11C	SEC11 homolog C (S. cerevisiae)	0.54	0.026
GMDS-AS1	uncharacterized LOC100508120	0.54	0.034
GAS2L3	growth arrest-specific 2 like 3	0.54	0.020
APOL1	apolipoprotein L, 1	0.54	0.018
FABP3	fatty acid binding protein 3, muscle and heart (mammary-derived growth inhibitor)	0.54	0.031
NUCB2	nucleobindin 2	0.54	0.023
MFSD2A	major facilitator superfamily domain containing 2A	0.54	0.040
RAP1GAP	RAP1 GTPase activating protein	0.54	0.012
ANG	angiogenin, ribonuclease, RNase A family, 5	0.54	0.038
HLA-DRB5	major histocompatibility complex, class II, DR beta 5	0.54	0.030
TRIB2	tribbles homolog 2 (Drosophila)	0.54	0.023
FAM162A	family with sequence similarity 162, member A	0.54	0.001
IFITM10	interferon induced transmembrane protein 10	0.54	0.033
ZNF165	zinc finger protein 165	0.55	0.014
MALL	mal, T-cell differentiation protein-like	0.55	0.001
FAM110C	family with sequence similarity 110, member C	0.55	0.028
ZNF860	zinc finger protein 860	0.55	0.012
DENND5B-AS1	DENND5B antisense RNA 1	0.55	0.010
PPFIBP2	PTPRF interacting protein, binding protein 2 (liprin beta 2)	0.55	0.023

CFI	complement factor I	0.55	0.022
CDK18	cyclin-dependent kinase 18	0.55	0.015
CACNA1H	calcium channel, voltage-dependent, T type, alpha 1H subunit	0.55	0.028
ARRDC3	arrestin domain containing 3	0.56	0.017
HIST2H2BE	histone cluster 2, H2be	0.56	0.024
SIAE	sialic acid acetylesterase	0.56	0.022
BBS1	Bardet-Biedl syndrome 1	0.56	0.010
HLA-DRA	major histocompatibility complex, class II, DR alpha	0.56	0.016
HGD	homogentisate 1,2-dioxygenase	0.56	0.006
SERPINI1	serpin peptidase inhibitor, clade I (neuroserpin), member 1	0.56	0.022
LOC728323	uncharacterized LOC728323	0.56	0.040
LGI2	leucine-rich repeat LGI family, member 2	0.56	0.038
ZNF23	zinc finger protein 23	0.56	0.009
PDXP	pyridoxal (pyridoxine, vitamin B6) phosphatase	0.56	0.009
PIGR	polymeric immunoglobulin receptor	0.56	0.012
FAM84A	family with sequence similarity 84, member A	0.57	0.002
HYOU1	hypoxia up-regulated 1	0.57	0.017
DNM1	dynamin 1	0.57	0.031
SHC4	SHC (Src homology 2 domain containing) family, member 4	0.57	0.009
GALNT1	UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 1 (GalNAc-T1)	0.57	0.026
NME7	NME/NM23 family member 7	0.58	0.010
LTC4S	leukotriene C4 synthase	0.58	0.029
NPR1	natriuretic peptide receptor A/guanylate cyclase A (atrionatriuretic peptide receptor A)	0.58	0.007
C14orf132	chromosome 14 open reading frame 132	0.58	0.008
AK4	adenylate kinase 4	0.58	0.015
HMGN3-AS1	uncharacterized LOC100288198	0.58	0.008
SCN9A	sodium channel, voltage-gated, type IX, alpha subunit	0.58	0.039
SLC25A36	solute carrier family 25 (pyrimidine nucleotide carrier), member 36	0.58	0.002
INSIG2	insulin induced gene 2	0.58	0.044
DKK1	dickkopf 1 homolog (Xenopus laevis)	0.58	0.035
IFITM1	interferon induced transmembrane protein 1	0.59	0.044
ATP1B1	ATPase, Na+/K+ transporting, beta 1 polypeptide	0.59	0.020
CRELD1	cysteine-rich with EGF-like domains 1	0.59	0.008
CCT6P1	chaperonin containing TCP1, subunit 6 (zeta) pseudogene 1	0.59	0.047
VWA7	von Willebrand factor A domain containing 7	0.59	0.046
DNAJB7	DnaJ (Hsp40) homolog, subfamily B, member 7	0.59	0.003
CHIC2	cysteine-rich hydrophobic domain 2	0.59	0.041
MXI1	MAX interactor 1, dimerization protein	0.59	0.010
NUP62CL	nucleoporin 62kDa C-terminal like	0.59	0.040
ZEB1-AS1	ZEB1 antisense RNA 1	0.60	0.048

CFH	complement factor H	0.60	0.011
SECTM1	secreted and transmembrane 1	0.60	0.010
FAM222A	family with sequence similarity 222, member A	0.60	0.018
LGMN	legumain	0.60	0.007
PREX2	phosphatidylinositol-3,4,5-trisphosphate-dependent Rac exchange factor 2	0.60	0.024
BCKDK	branched chain ketoacid dehydrogenase kinase	0.60	0.029
NAMPT	nicotinamide phosphoribosyltransferase	0.60	0.017
MYH7B	myosin, heavy chain 7B, cardiac muscle, beta	0.60	0.015
PROS1	protein S (alpha)	0.60	0.027
PBLD	phenazine biosynthesis-like protein domain containing	0.60	0.034
CLU	clusterin	0.60	0.038
ATP8B3	ATPase, aminophospholipid transporter, class I, type 8B, member 3	0.60	0.032
FRK	fyn-related kinase	0.60	0.028
TTC39A	tetratricopeptide repeat domain 39A	0.61	0.023
TMTC2	transmembrane and tetratricopeptide repeat containing 2	0.61	0.047
DNAJB11	DnaJ (Hsp40) homolog, subfamily B, member 11	0.61	0.025
TMEM213	transmembrane protein 213	0.61	0.004
C2orf88	chromosome 2 open reading frame 88	0.61	0.013
TCN2	transcobalamin II	0.61	0.026
EGLN1	egl nine homolog 1 (C. elegans)	0.61	0.011
RHOQ	ras homolog family member Q	0.61	0.002
FAM210A	family with sequence similarity 210, member A	0.61	0.019
MME	membrane metallo-endopeptidase	0.61	0.019
TPI1	triosephosphate isomerase 1	0.61	0.025
ABHD16B	abhydrolase domain containing 16B	0.61	0.025
ZFAND2A	zinc finger, AN1-type domain 2A	0.62	0.032
PREPL	prolyl endopeptidase-like	0.62	0.047
ZNF559	zinc finger protein 559	0.62	0.019
CSRNP1	cysteine-serine-rich nuclear protein 1	0.62	0.039
ENPP5	ectonucleotide pyrophosphatase/phosphodiesterase 5 (putative)	0.62	0.018
TIGD2	tigger transposable element derived 2	0.62	0.004
TRABD2B	TraB domain containing 2B	0.62	0.035
MAN2B2	mannosidase, alpha, class 2B, member 2	0.62	0.020
GPRC5A	G protein-coupled receptor, family C, group 5, member A	0.62	0.004
IPMK	inositol polyphosphate multikinase	0.62	0.044
HPS3	Hermansky-Pudlak syndrome 3	0.62	0.040
PTPN20B	protein tyrosine phosphatase, non-receptor type 20B	0.62	0.008
EEPD1	endonuclease/exonuclease/phosphatase family domain containing 1	0.62	0.039
ETV3	ets variant 3	0.62	0.019

CDH16	cadherin 16, KSP-cadherin	0.62	0.004
MTFP1	mitochondrial fission process 1	0.63	0.018
GAB1	GRB2-associated binding protein 1	0.63	0.031
GBP2	guanylate binding protein 2, interferon-inducible	0.63	0.018
FLJ23867	uncharacterized protein FLJ23867	0.63	0.032
FOLR2	folate receptor 2 (fetal)	0.63	0.002
PFKFB3	6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 3	0.63	0.016
SH3RF1	SH3 domain containing ring finger 1	0.63	0.0003
IRS2	insulin receptor substrate 2	0.63	0.006
EPB41L4B	erythrocyte membrane protein band 4.1 like 4B	0.63	0.014
BNIP3L	BCL2/adenovirus E1B 19kDa interacting protein 3-like	0.64	0.003
MILR1	mast cell immunoglobulin-like receptor 1	0.64	0.019
RGS17	regulator of G-protein signaling 17	0.64	0.022
METTL10	methyltransferase like 10	0.64	0.012
HLA-DQB1	major histocompatibility complex, class II, DQ beta 1	0.64	0.009
ARHGEF19	Rho guanine nucleotide exchange factor (GEF) 19	0.64	0.041
PLEKHA8P1	pleckstrin homology domain containing, family A member 8 pseudogene 1	0.64	0.031
HSF2BP	heat shock transcription factor 2 binding protein	0.64	0.014
ZNF543	zinc finger protein 543	0.64	0.0007
NOV	nephroblastoma overexpressed	0.64	0.019
ERMARD	chromosome 6 open reading frame 70	0.64	0.008
NEK6	NIMA-related kinase 6	0.64	0.011
ALDH6A1	aldehyde dehydrogenase 6 family, member A1	0.64	0.042
SYTL2	synaptotagmin-like 2	0.64	0.028
HERC3	HECT and RLD domain containing E3 ubiquitin protein ligase 3	0.64	0.021
ITGB2-AS1	ITGB2 antisense RNA 1	0.64	0.035
PKIB	protein kinase (cAMP-dependent, catalytic) inhibitor beta	0.64	0.010
RC3H2	ring finger and CCCH-type domains 2	0.64	0.013
MALAT1	metastasis associated lung adenocarcinoma transcript 1 (non-protein coding)	0.65	0.006
SPIRE1	spire homolog 1 (Drosophila)	0.65	0.0006
ZNF33B	zinc finger protein 33B	0.65	0.030
MANF	mesencephalic astrocyte-derived neurotrophic factor	0.65	0.030
PGBD5	piggyBac transposable element derived 5	0.65	0.002
OR7E37P	olfactory receptor, family 7, subfamily E, member 37 pseudogene	0.65	0.003
TMEM47	transmembrane protein 47	0.65	0.004
PDIA3	protein disulfide isomerase family A, member 3	0.65	0.003
CD74	CD74 molecule, major histocompatibility complex, class II invariant chain	0.65	0.041
IL7	interleukin 7	0.65	0.041
FEM1C	fem-1 homolog c (C. elegans)	0.65	0.018

BACE1	beta-site APP-cleaving enzyme 1	0.65	0.017
MAOA	monoamine oxidase A	0.65	0.036
LOC399715	uncharacterized LOC399715	0.66	0.020
SLC35A3	solute carrier family 35 (UDP-N-acetylglucosamine (UDP-GlcNAc) transporter), member A3	0.66	0.031
GNGT1	guanine nucleotide binding protein (G protein), gamma transducing activity polypeptide 1	0.66	0.014
USP27X	ubiquitin specific peptidase 27, X-linked	0.66	0.008
KLHDC10	kelch domain containing 10	0.66	0.027
CTSA	cathepsin A	0.66	0.002
ASAH1	N-acylsphingosine amidohydrolase (acid ceramidase) 1	0.66	0.005
LYRM9	LYR motif containing 9	0.66	0.002
PFKL	phosphofructokinase, liver	0.66	0.003
BATF2	basic leucine zipper transcription factor, ATF-like 2	0.66	0.009
LINC01158	uncharacterized LOC100506421	0.66	0.021
CAMSAP1	calmodulin regulated spectrin-associated protein 1	0.66	0.0002
SYNE1	spectrin repeat containing, nuclear envelope 1	0.66	0.020
RNF24	ring finger protein 24	0.66	0.036
BRAF	v-raf murine sarcoma viral oncogene homolog B1	0.66	0.025
PPIP5K1	diphosphoinositol pentakisphosphate kinase 1	0.66	0.029
RHBDL1	rhomboid, veinlet-like 1 (Drosophila)	0.67	0.021

Supplementary Table S4: List of DEGs with significant Fold Changes in Mannitol vs Control

🟨	Upregulated by MAN		
🟦	Downregulated by MAN		

Gene Symbol	Gene Description	Fold Changes in MAN	P Value
CECR7	cat eye syndrome chromosome region, candidate 7 (non-protein coding)	17.00	0.015
NELL2	NEL-like 2 (chicken)	12.00	0.032
S1PR1	sphingosine-1-phosphate receptor 1	11.50	0.044
CCDC110	coiled-coil domain containing 110	11.33	0.05
RTN4RL2	reticulon 4 receptor-like 2	9.33	0.028
GRIA3	glutamate receptor, ionotropic, AMPA 3	9.00	0.015
LOC100287072	ribosomal protein S6 kinase, 70kDa, polypeptide 1 pseudogene	8.00	0.049
TOP1P1	topoisomerase (DNA) I pseudogene 1	7.75	0.05
LOC440461	Rho GTPase activating protein 27 pseudogene	7.75	0.05
PIK3CG	phosphatidylinositol-4,5-bisphosphate 3-kinase, catalytic subunit gamma	7.00	0.016
MST1P2	macrophage stimulating 1 (hepatocyte growth factor-like) pseudogene 2	6.86	0.025
PCDHB11	protocadherin beta 11	6.83	0.033
ZNF625-ZNF20	ZNF625-ZNF20 readthrough	6.32	0.037
DCAF8L2	DDB1 and CUL4 associated factor 8-like 2	6.00	0.013
LIMS3	LIM and senescent cell antigen-like domains 3	5.69	0.036
FAM178B	family with sequence similarity 178, member B	5.63	0.005
OR7E12P	olfactory receptor, family 7, subfamily E, member 12 pseudogene	5.47	0.045
TGM1	transglutaminase 1 (K polypeptide epidermal type I, protein-glutamine-gamma-glutamyltransferase)	5.31	0.0003
KCNK4	potassium channel, subfamily K, member 4	5.25	0.003
USP27X-AS1	uncharacterized LOC158572	5.20	0.031
LINC00488	long intergenic non-protein coding RNA 488	5.18	0.037
ANXA2R	annexin A2 receptor	4.91	0.046
TIGD4	tigger transposable element derived 4	4.77	0.011
DGCR9	DiGeorge syndrome critical region gene 9	4.63	0.018
PGAM4	phosphoglycerate mutase family member 4	4.50	0.044
MGARP	mitochondria-localized glutamic acid-rich protein	4.43	0.015
MCIDAS	multiciliate differentiation and DNA synthesis associated cell cycle protein	4.33	0.035
KHDC1	KH homology domain containing 1	3.81	0.018
AANAT	aralkylamine N-acetyltransferase	3.78	0.002
TMEM45A	transmembrane protein 45A	3.61	0.045

SNORA45A	small nucleolar RNA, H/ACA box 3	3.59	0.008
CCDC171	coiled-coil domain containing 171	3.50	0.038
FGF14-AS2	FGF14 antisense RNA 2	3.34	0.025
ZFPM2	zinc finger protein, FOG family member 2	3.25	0.05
FAM13A	family with sequence similarity 13, member A	3.24	0.033
LOC100506071	uncharacterized LOC100506071	3.16	0.019
LOC100288123	uncharacterized LOC100288123	3.16	0.048
LINC01144	uncharacterized LOC400752	3.08	0.038
ARC	activity-regulated cytoskeleton-associated protein	3.00	0.012
CIB2	calcium and integrin binding family member 2	3.00	0.047
TTC25	tetratricopeptide repeat domain 25	2.95	0.008
CLEC2B	C-type lectin domain family 2, member B	2.85	0.047
RAX2	retina and anterior neural fold homeobox 2	2.82	0.010
LEP	leptin	2.77	0.024
PGBD4	piggyBac transposable element derived 4	2.75	0.015
BASP1P1	brain abundant, membrane attached signal protein 1 pseudogene 1	2.71	0.014
GMDS-AS1	uncharacterized LOC100508120	2.69	0.020
PLA1A	phospholipase A1 member A	2.67	0.033
DNAH7	dynein, axonemal, heavy chain 7	2.65	0.019
ACER2	alkaline ceramidase 2	2.57	0.0006
ANKRD37	ankyrin repeat domain 37	2.56	0.026
SNORD99	small nucleolar RNA, C/D box 99	2.55	0.012
DMGDH	dimethylglycine dehydrogenase	2.53	0.031
CUZD1	CUB and zona pellucida-like domains 1	2.52	0.012
IGFBP3	insulin-like growth factor binding protein 3	2.48	0.004
TMEM232	transmembrane protein 232	2.47	0.046
GEMIN8P4	gem (nuclear organelle) associated protein 8 pseudogene 4	2.47	0.044
CNTNAP2	contactin associated protein-like 2	2.46	0.034
CRMP1	collapsin response mediator protein 1	2.43	0.021
PGF	placental growth factor	2.39	0.028
LINC01003	uncharacterized LOC100128822	2.39	0.009
CCL26	chemokine (C-C motif) ligand 26	2.36	0.026
LOC441461	uncharacterized LOC441461	2.36	0.039
ZCWPW1	zinc finger, CW type with PWWP domain 1	2.33	0.018
CACHD1	cache domain containing 1	2.32	0.020
ACADL	acyl-CoA dehydrogenase, long chain	2.31	0.016
COL7A1	collagen, type VII, alpha 1	2.30	0.033
ATL1	atlastin GTPase 1	2.30	0.006
ADM	adrenomedullin	2.29	0.036
AGAP5	ArfGAP with GTPase domain, ankyrin repeat and PH domain 5	2.28	0.014
TMEM182	transmembrane protein 182	2.27	0.002
MYH7B	myosin, heavy chain 7B, cardiac muscle, beta	2.22	0.008

ACTRT3	actin-related protein T3	2.22	0.020
CBWD6	COBW domain containing 6	2.21	0.023
LOC440311	glioma tumor suppressor candidate region gene 2 pseudogene	2.20	0.020
TPPP3	tubulin polymerization-promoting protein family member 3	2.20	0.029
NHLRC1	NHL repeat containing 1	2.18	0.023
LRRC34	leucine rich repeat containing 34	2.18	0.023
LINC00410	long intergenic non-protein coding RNA 410	2.18	0.033
NAALADL2	N-acetylated alpha-linked acidic dipeptidase-like 2	2.17	0.028
HILPDA	hypoxia inducible lipid droplet-associated	2.16	0.021
C10orf99	chromosome 10 open reading frame 99	2.15	0.034
CEP83	coiled-coil domain containing 41	2.15	0.013
APBB3	amyloid beta (A4) precursor protein-binding, family B, member 3	2.12	0.009
ZNF334	zinc finger protein 334	2.11	0.010
FOXN3-AS1	FOXN3 antisense RNA 1	2.11	0.034
LAMA1	laminin, alpha 1	2.10	0.008
DNAH12	dynein, axonemal, heavy chain 12	2.10	0.032
C7orf63	chromosome 7 open reading frame 63	2.10	0.026
SNORA25	small nucleolar RNA, H/ACA box 25	2.07	0.028
DENND5B-AS1	DENND5B antisense RNA 1	2.06	0.008
MADCAM1	mucosal vascular addressin cell adhesion molecule 1	2.06	0.019
ZBTB37	zinc finger and BTB domain containing 37	2.02	0.007
TTC14	tetratricopeptide repeat domain 14	2.02	0.007
SOX8	SRY (sex determining region Y)-box 8	2.01	0.049
ABCC6	ATP-binding cassette, sub-family C (CFTR/MRP), member 6	2.01	0.019
ERO1L	ERO1-like (S. cerevisiae)	1.98	0.031
RAD51AP1	RAD51 associated protein 1	1.97	0.026
XIRP1	xin actin-binding repeat containing 1	1.96	0.027
LOC643770	uncharacterized LOC643770	1.96	0.003
ARSF	arylsulfatase F	1.95	0.027
IL1RL1	interleukin 1 receptor-like 1	1.94	0.032
C20orf203	chromosome 20 open reading frame 203	1.93	0.001
LINC-PINT	uncharacterized LOC378805	1.92	0.005
ABCA5	ATP-binding cassette, sub-family A (ABC1), member 5	1.92	0.041
SEL1L	sel-1 suppressor of lin-12-like (C. elegans)	1.92	0.028
SOX6	SRY (sex determining region Y)-box 6	1.91	0.038
N4BP2L2-IT2	N4BPL2 intronic transcript 2 (non-protein coding)	1.91	0.044
UBA6-AS1	uncharacterized LOC550112	1.91	0.014
HIST1H2BG	histone cluster 1, H2bg	1.90	0.049
ADAM11	ADAM metallopeptidase domain 11	1.89	0.042
SEC11C	SEC11 homolog C (S. cerevisiae)	1.89	0.018
ARRDC4	arrestin domain containing 4	1.88	0.024
LRRC49	leucine rich repeat containing 49	1.88	0.027

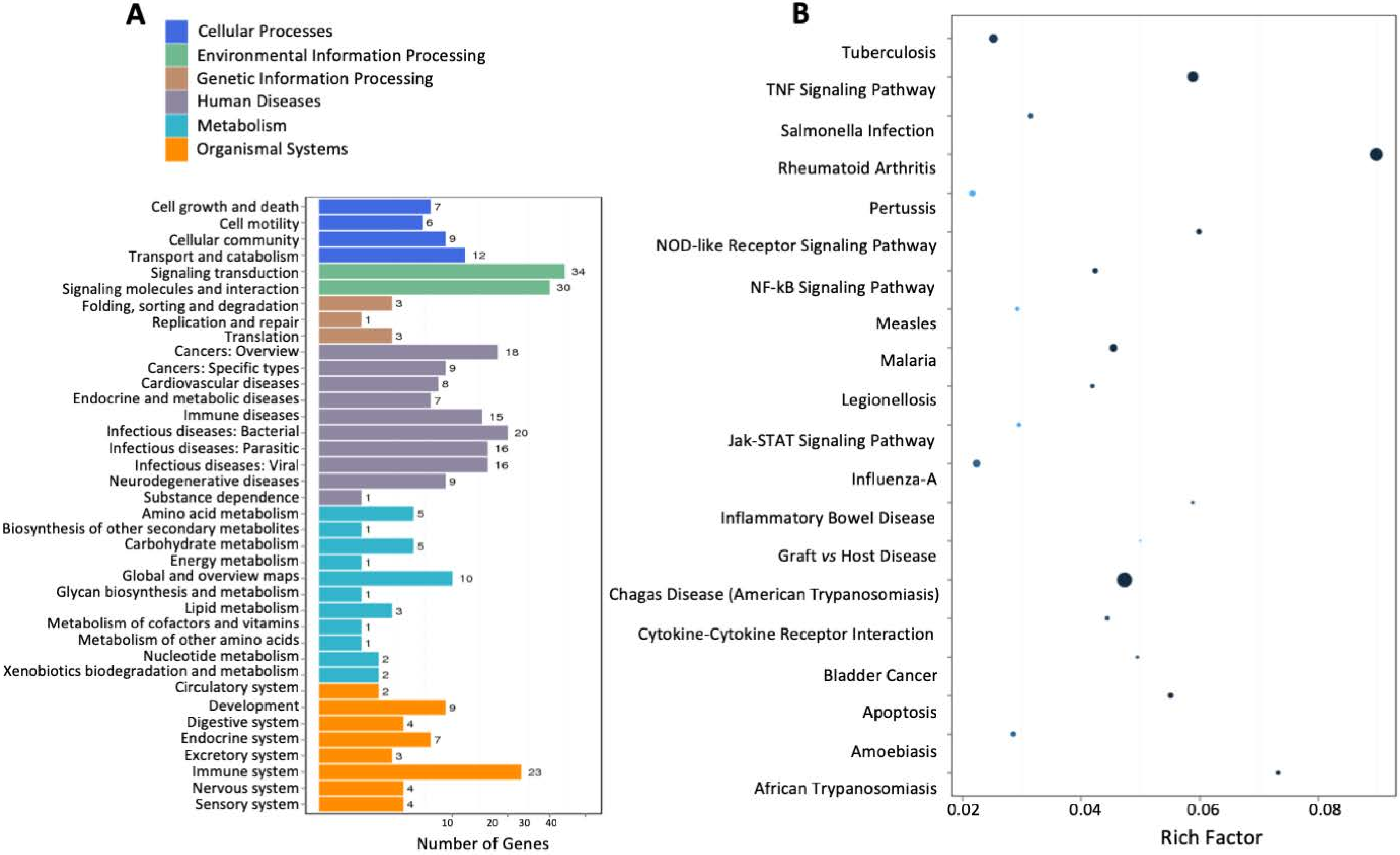
PDE5A	phosphodiesterase 5A, cGMP-specific	1.87	0.007
GEN1	Gen endonuclease homolog 1 (Drosophila)	1.86	0.016
PP2D1	protein phosphatase 2C-like domain containing 1	1.84	0.013
RNF217	ring finger protein 217	1.83	0.014
CGREF1	cell growth regulator with EF-hand domain 1	1.83	0.015
FBXO5	F-box protein 5	1.82	0.0009
TIGD2	tigger transposable element derived 2	1.82	0.047
PIK3IP1	phosphoinositide-3-kinase interacting protein 1	1.82	0.028
DCAF17	DDB1 and CUL4 associated factor 17	1.81	0.009
ZNF284	zinc finger protein 284	1.80	0.049
PARD6G-AS1	PARD6G antisense RNA 1	1.79	0.048
HIST1H2BD	histone cluster 1, H2bd	1.79	0.035
LINC01011	uncharacterized LOC401232	1.78	0.018
PCGF6	polycomb group ring finger 6	1.78	0.016
EFCAB12	EF-hand calcium binding domain 12	1.77	0.038
COL2A1	collagen, type II, alpha 1	1.76	0.006
HIST2H2BE	histone cluster 2, H2be	1.76	0.040
STC1	stanniocalcin 1	1.76	0.035
SMG1P5	smg-1 homolog, phosphatidylinositol 3-kinase-related kinase (C. elegans) pseudogene	1.75	0.017
ASB14	ankyrin repeat and SOCS box containing 14	1.75	0.034
SCGB2A1	secretoglobin, family 2A, member 1	1.75	0.014
PDK1	pyruvate dehydrogenase kinase, isozyme 1	1.74	0.0003
ATP6V1B1	ATPase, H+ transporting, lysosomal 56/58kDa, V1 subunit B1	1.73	0.035
HSPA5	heat shock 70kDa protein 5 (glucose-regulated protein, 78kDa)	1.72	0.037
APITD1	apoptosis-inducing, TAF9-like domain 1	1.72	0.001
CCDC150	coiled-coil domain containing 150	1.72	0.009
CDH17	cadherin 17, LI cadherin (liver-intestine)	1.72	0.035
FAM171B	family with sequence similarity 171, member B	1.71	0.004
TRPC1	transient receptor potential cation channel, subfamily C, member 1	1.70	0.030
SDCBP2-AS1	SDCBP2 antisense RNA 1	1.70	0.028
MPP6	membrane protein, palmitoylated 6 (MAGUK p55 subfamily member 6)	1.70	0.038
NCOA2	nuclear receptor coactivator 2	1.70	0.003
PLOD2	procollagen-lysine, 2-oxoglutarate 5-dioxygenase 2	1.70	0.007
LINC00472	long intergenic non-protein coding RNA 472	1.69	0.030
UBR1	ubiquitin protein ligase E3 component n-recognin 1	1.69	0.049
SPTBN4	spectrin, beta, non-erythrocytic 4	1.68	0.006
USP27X	ubiquitin specific peptidase 27, X-linked	1.68	0.046
ZNF81	zinc finger protein 81	1.68	0.028
C15orf38	chromosome 15 open reading frame 38	1.67	0.012
KIAA1715	KIAA1715	1.66	0.002

PIH1D2	PIH1 domain containing 2	1.66	0.019
CEP78	centrosomal protein 78kDa	1.66	0.038
RAP2A	RAP2A, member of RAS oncogene family	1.65	0.016
ZNF585A	zinc finger protein 585A	1.65	0.021
WLS	wntless homolog (Drosophila)	1.65	0.014
PTGS1	prostaglandin-endoperoxide synthase 1 (prostaglandin G/H synthase and cyclooxygenase)	1.65	0.010
LOX	lysyl oxidase	1.65	0.006
NDRG1	N-myc downstream regulated 1	1.65	0.022
C2orf88	chromosome 2 open reading frame 88	1.64	0.001
SHPRH	SNF2 histone linker PHD RING helicase, E3 ubiquitin protein ligase	1.64	0.037
LINC00888	uncharacterized LOC100505687	1.64	0.045
ARL5B	ADP-ribosylation factor-like 5B	1.64	0.043
RNASE4	ribonuclease, RNase A family, 4	1.64	0.007
DOCK10	dedicator of cytokinesis 10	1.63	0.038
LINC00847	long intergenic non-protein coding RNA 847	1.62	0.046
FLJ12825	uncharacterized LOC440101	1.62	0.026
C15orf41	chromosome 15 open reading frame 41	1.62	0.028
RAD50	RAD50 homolog (S. cerevisiae)	1.61	0.044
STAC	SH3 and cysteine rich domain	1.60	0.034
GBE1	glucan (1,4-alpha-), branching enzyme 1	1.60	0.0005
SH3TC2	SH3 domain and tetratricopeptide repeats 2	1.60	0.020
CDCA2	cell division cycle associated 2	1.60	0.040
HSD17B12	hydroxysteroid (17-beta) dehydrogenase 12	1.59	0.017
ZNF77	zinc finger protein 77	1.59	0.030
TRIM23	tripartite motif containing 23	1.59	0.045
GOLGA1	golgin A1	1.58	0.014
CCDC69	coiled-coil domain containing 69	1.58	0.042
PMS2P5	postmeiotic segregation increased 2 pseudogene 5	1.58	0.027
DNAJC18	DnaJ (Hsp40) homolog, subfamily C, member 18	1.58	0.025
HERC2P7	hect domain and RLD 2 pseudogene 7	1.58	0.048
CHML	choroideremia-like (Rab escort protein 2)	1.58	0.031
SLC14A1	solute carrier family 14 (urea transporter), member 1 (Kidd blood group)	1.58	0.049
HOMER1	homer homolog 1 (Drosophila)	1.57	0.014
C4orf46	chromosome 4 open reading frame 46	1.57	0.007
ZNF32-AS2	ZNF32 antisense RNA 2	1.57	0.023
ERO1LB	ERO1-like beta (S. cerevisiae)	1.57	0.002
TMEM64	transmembrane protein 64	1.56	0.048
MOB3B	MOB kinase activator 3B	1.56	0.016
SLC22A15	solute carrier family 22, member 15	1.56	0.023
ORC5	origin recognition complex, subunit 5	1.55	0.033

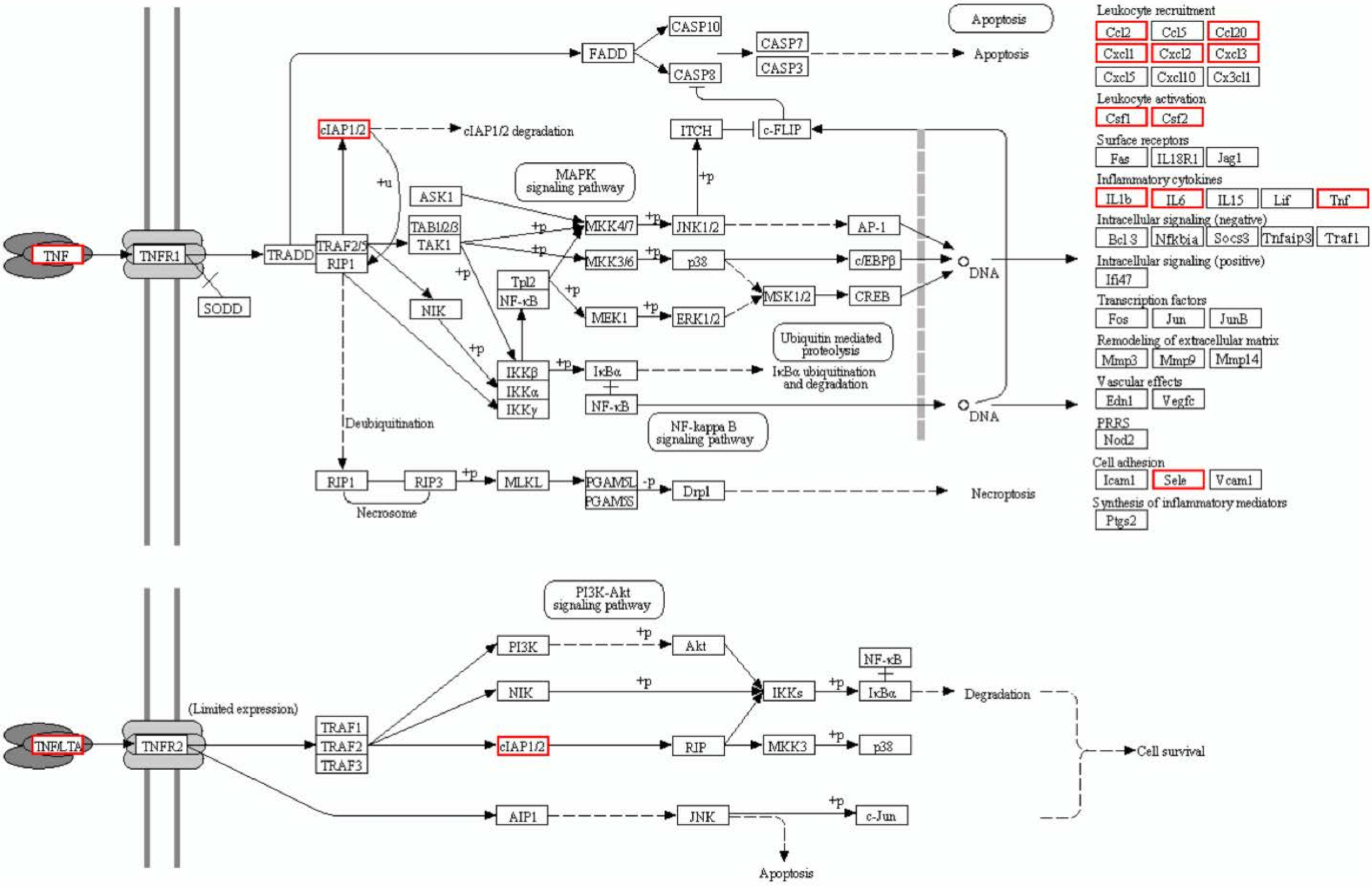
WDR5B	WD repeat domain 5B	1.55	0.042
LOC100133985	uncharacterized LOC100133985	1.55	0.020
UPRT	uracil phosphoribosyltransferase (FUR1) homolog (S. cerevisiae)	1.54	0.042
PEX3	peroxisomal biogenesis factor 3	1.54	0.049
ZBTB24	zinc finger and BTB domain containing 24	1.54	0.025
BHLHB9	basic helix-loop-helix domain containing, class B, 9	1.54	0.027
CAMK4	calcium/calmodulin-dependent protein kinase IV	1.54	0.031
C1orf109	chromosome 1 open reading frame 109	1.53	0.045
NUCB2	nucleobindin 2	1.53	0.043
ZBTB25	zinc finger and BTB domain containing 25	1.53	0.019
DNAJB9	DnaJ (Hsp40) homolog, subfamily B, member 9	1.51	0.027
DCK	deoxycytidine kinase	1.51	0.039
PPP2R5E	protein phosphatase 2, regulatory subunit B', epsilon isoform	1.51	0.041
TROAP	trophinin associated protein	1.51	0.046
RBM44	RNA binding motif protein 44	1.51	0.049
SNAPC5	small nuclear RNA activating complex, polypeptide 5, 19kDa	1.51	0.005
PFKFB4	6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 4	1.50	0.022
ULBP1	UL16 binding protein 1	1.50	0.043
ULBP2	UL16 binding protein 2	1.50	0.005
CPA6	carboxypeptidase A6	1.50	0.032
MSL2	male-specific lethal 2 homolog (Drosophila)	1.50	0.022
RNA5SP244	RNA, 5S ribosomal pseudogene 244	0.05	0.037
LOC100507351	uncharacterized LOC100507351	0.11	0.015
CCDC81	coiled-coil domain containing 81	0.12	0.009
STKLD1	chromosome 9 open reading frame 96	0.13	0.006
DKFZp686K1684	uncharacterized LOC440034	0.16	0.001
XCL1	chemokine (C motif) ligand 1	0.18	0.017
STMN4	stathmin-like 4	0.20	0.020
SRGAP2D	SLIT-ROBO Rho GTPase activating protein 2D	0.20	0.039
SLC47A1	solute carrier family 47, member 1	0.28	0.038
LINC00578	long intergenic non-protein coding RNA 578	0.29	0.031
TEDDM1	transmembrane epididymal protein 1	0.30	0.041
HYMAI	hydatidiform mole associated and imprinted (non-protein coding)	0.30	0.034
AKR7L	aldo-keto reductase family 7-like	0.32	0.049
FAM151B	family with sequence similarity 151, member B	0.32	0.043
GNGT2	guanine nucleotide binding protein (G protein), gamma transducing activity polypeptide 2	0.32	0.035
NLRP8	NLR family, pyrin domain containing 8	0.34	0.012
EMCN	endomucin	0.34	0.019
SIX2	SIX homeobox 2	0.35	0.003
SIGLEC14	sialic acid binding Ig-like lectin 14	0.35	0.036

SCML2	sex comb on midleg-like 2 (Drosophila)	0.39	0.013
GPR157	G protein-coupled receptor 157	0.39	0.003
LINC00852	long intergenic non-protein coding RNA 852	0.40	0.043
MCF2L2	MCF.2 cell line derived transforming sequence-like 2	0.40	0.027
LOC100506469	uncharacterized LOC100506469	0.41	0.033
IL11	interleukin 11	0.42	0.042
LOC286177	uncharacterized LOC286177	0.43	0.014
ACSL6	acyl-CoA synthetase long-chain family member 6	0.44	0.043
NPAP1	nuclear pore associated protein 1	0.44	0.021
SCARF2	scavenger receptor class F, member 2	0.45	0.026
LOC646999	akirin 1 pseudogene	0.45	0.038
PROB1	proline-rich basic protein 1	0.45	0.005
TSC22D1-AS1	TSC22D1 antisense RNA 1	0.46	0.036
FKBP1AP1	FK506 binding protein 1A, 12kDa pseudogene 1	0.47	0.05
LOC283683	uncharacterized LOC283683	0.48	0.015
IRAK3	interleukin-1 receptor-associated kinase 3	0.48	0.003
VTRNA1-3	vault RNA 1-3	0.48	0.041
KANK4	KN motif and ankyrin repeat domains 4	0.49	0.038
PART1	prostate androgen-regulated transcript 1 (non-protein coding)	0.49	0.048
KCNH6	potassium voltage-gated channel, subfamily H (eag-related), member 6	0.50	0.026
LIMS2	LIM and senescent cell antigen-like domains 2	0.50	0.031
LINC00907	uncharacterized LOC284260	0.50	0.028
ADCY1	adenylate cyclase 1 (brain)	0.51	0.019
SOX7	SRY (sex determining region Y)-box 7	0.52	0.045
CELF2	CUGBP, Elav-like family member 2	0.53	0.020
PBOV1	prostate and breast cancer overexpressed 1	0.54	0.035
RFPL1S	RFPL1 antisense RNA 1	0.54	0.045
ZNF850	zinc finger protein 850	0.54	0.05
SLC25A53	solute carrier family 25, member 53	0.55	0.035
ZNF665	zinc finger protein 665	0.56	0.008
SP6	Sp6 transcription factor	0.56	0.037
NME1-NME2	NME1-NME2 readthrough	0.56	0.003
LOC100288181	uncharacterized LOC100288181	0.57	0.017
KIAA0087	KIAA0087	0.57	0.0011
GVINP1	GTPase, very large interferon inducible pseudogene 1	0.57	<0.0001
NWD1	NACHT and WD repeat domain containing 1	0.57	0.019
BREA2	breast cancer estrogen-induced apoptosis 2	0.57	0.026
LINC01089	uncharacterized LOC338799	0.58	0.019
C1orf229	chromosome 1 open reading frame 229	0.58	0.036
MYOZ3	myozenin 3	0.58	0.043
PPP1R1A	protein phosphatase 1, regulatory (inhibitor) subunit 1A	0.59	0.031
A1BG-AS1	A1BG antisense RNA 1	0.59	0.049

NRN1L	neuritin 1-like	0.59	0.031
FAM153C	family with sequence similarity 153, member C, pseudogene	0.59	0.035
OTUD6A	OTU domain containing 6A	0.59	0.034
GPR63	G protein-coupled receptor 63	0.59	0.014
LOC100287225	uncharacterized LOC100287225	0.59	0.021
AUNIP	aurora kinase A and ninein interacting protein	0.60	0.0002
VWCE	von Willebrand factor C and EGF domains	0.60	0.020
ZBTB20	zinc finger and BTB domain containing 20	0.60	0.017
BIN3-IT1	uncharacterized LOC80094	0.60	0.026
LOC100289019	uncharacterized LOC100289019	0.60	0.010
GPLD1	glycosylphosphatidylinositol specific phospholipase D1	0.60	0.014
SLC35F1	solute carrier family 35, member F1	0.61	0.030
NAPSA	napsin A aspartic peptidase	0.61	<0.0001
PCYT1B	phosphate cytidylyltransferase 1, choline, beta	0.62	0.025
POU2F2	POU class 2 homeobox 2	0.62	0.022
PRDM7	PR domain containing 7	0.63	0.007
C9orf172	chromosome 9 open reading frame 172	0.63	0.025
POM121L10P	POM121 transmembrane nucleoporin-like 10, pseudogene	0.64	0.021
LOC284950	uncharacterized LOC284950	0.64	0.006
PRG2	proteoglycan 2, bone marrow (natural killer cell activator, eosinophil granule major basic protein)	0.64	0.046
TRIM66	tripartite motif containing 66	0.64	0.023
KCNH3	potassium voltage-gated channel, subfamily H (eag-related), member 3	0.64	0.048
TRIM58	tripartite motif containing 58	0.64	0.038
NEK5	NIMA-related kinase 5	0.65	0.008
ZNF341	zinc finger protein 341	0.65	0.005
PPM1K	protein phosphatase, Mg2+/Mn2+ dependent, 1K	0.65	0.039
TVP23C	trans-golgi network vesicle protein 23 homolog C (S. cerevisiae)	0.65	0.018
RPGR	retinitis pigmentosa GTPase regulator	0.65	0.023
LOC440600	uncharacterized LOC440600	0.65	0.048
ADORA2A	adenosine A2a receptor	0.65	0.003
LINC00598	long intergenic non-protein coding RNA 598	0.65	0.049
CXorf36	chromosome X open reading frame 36	0.65	0.039
IQCD	IQ motif containing D	0.65	0.048
COLCA1	chromosome 11 open reading frame 92	0.65	0.014
EFNB3	ephrin-B3	0.66	0.046
PPM1J	protein phosphatase, Mg2+/Mn2+ dependent, 1J	0.66	0.025
IGF1	insulin-like growth factor 1 (somatomedin C)	0.67	0.013
C8orf86	chromosome 8 open reading frame 86	0.67	0.030



Supplementary Figure S6: ***Involvement of biological processes and signalling pathways associated with differentially expressed genes in high-glucose exposed RPTEC/TERT1 cells.*** (A) Pathway Enrichment analysis of differentially expressed genes (DEGs) performed based on KEGG database; (B) Scatter plot for the top 20 pathways of KEGG enrichment results. Here, X axis represents number of DEGs. Y axis represents second KEGG pathway terms. All second pathway terms were grouped in top pathway terms indicated in different colour.



Supplementary Figure S7: ***Up-regulation of genes for inflammatory cytokines following exposure of RPTEC/TERT1 cells to high-glucose (TNF-Signalling pathway is a representative example).*** Up-regulated genes are marked with red borders. Unchanged genes are marked with black borders.

Supplementary Table S5: List of DEGs with significant Fold Changes in RPTEC/TERT1 cells without and with MSC co-culture in high glucose (HG) condition

🟨	Higher expression in No-MSC versus MSC co-culture (HG)		
🟦	Lower expression in No-MSC versus MSC co-culture (HG)		

Gene Symbol	**Gene Description**	**Fold change No-MSC vs MSC**	**P Value**
DLX1	distal-less homeobox 1	14.00	0.0015
TEX11	testis expressed 11	9.67	0.035
GRK7	G protein-coupled receptor kinase 7	8.67	0.0019
FCAMR	Fc receptor, IgA, IgM, high affinity	7.67	0.05
GATM	glycine amidinotransferase (L-arginine:glycine amidinotransferase)	6.75	0.007
ALS2CR12	amyotrophic lateral sclerosis 2 (juvenile) chromosome region, candidate 12	6.60	0.023
SCARNA27	small Cajal body-specific RNA 27	6.34	0.040
SMAD5-AS1	SMAD5 antisense RNA 1	6.33	0.026
AOX1	aldehyde oxidase 1	6.17	0.028
HIST1H2AG	histone cluster 1, H2ag	6.10	0.012
DGAT2	diacylglycerol O-acyltransferase 2	5.93	0.05
LINC00525	long intergenic non-protein coding RNA 525	5.80	0.026
MAMDC2-AS1	uncharacterized LOC100507244	5.67	0.020
PHGDH	phosphoglycerate dehydrogenase	5.46	0.005
NPPA	natriuretic peptide A	5.18	0.003
DYX1C1-CCPG1	DYX1C1-CCPG1 readthrough (non-protein coding)	4.98	0.002
SYT1	synaptotagmin I	4.83	0.009
SNORD18C	small nucleolar RNA, C/D box 18C	4.79	0.006
FGF1	fibroblast growth factor 1 (acidic)	4.50	0.020
BAALC	brain and acute leukemia, cytoplasmic	4.50	0.020
CCDC169	coiled-coil domain containing 169	4.44	0.013
MIR4767	microRNA 4767	4.25	0.05
ISM1	isthmin 1 homolog (zebrafish)	4.13	0.049
TAS2R3	taste receptor, type 2, member 3	4.08	0.036
IL19	interleukin 19	4.05	0.022
PHEX	phosphate regulating endopeptidase homolog, X-linked	4.00	0.020
REP15	RAB15 effector protein	4.00	0.027
LOC646938	TBC1 domain family, member 2B pseudogene	3.91	0.047
RAPSN	receptor-associated protein of the synapse	3.75	0.032
LOC100506655	uncharacterized LOC100506655	3.75	0.05
KRTAP5-9	keratin associated protein 5-9	3.75	0.05
SELL	selectin L	3.75	0.008
TRPM3	transient receptor potential cation channel, subfamily M, member 3	3.74	0.026

CST2	cystatin SA	3.69	0.033
KRTDAP	keratinocyte differentiation-associated protein	3.63	0.043
RRN3P2	RNA polymerase I transcription factor homolog (S. cerevisiae) pseudogene 2	3.63	0.044
ABCA12	ATP-binding cassette, sub-family A (ABC1), member 12	3.62	0.018
C11orf82	chromosome 11 open reading frame 82	3.25	0.008
HEY1	hairy/enhancer-of-split related with YRPW motif 1	3.17	0.021
IGDCC4	immunoglobulin superfamily, DCC subclass, member 4	3.17	0.019
TSACC	TSSK6 activating co-chaperone	3.05	0.037
CHAC1	ChaC, cation transport regulator homolog 1 (E. coli)	3.05	0.009
FLJ22447	uncharacterized LOC400221	3.03	0.012
IL1B	interleukin 1, beta	2.93	0.005
LCN2	lipocalin 2	2.91	0.016
PLEKHS1	pleckstrin homology domain containing, family S member 1	2.88	0.05
Mar-03	membrane-associated ring finger (C3HC4) 3, E3 ubiquitin protein ligase	2.83	0.032
EXO1	exonuclease 1	2.81	0.015
ZBED3-AS1	ZBED3 antisense RNA 1	2.80	0.005
HIST1H2BG	histone cluster 1, H2bg	2.79	0.05
C17orf51	chromosome 17 open reading frame 51	2.73	0.019
PCDHB3	protocadherin beta 3	2.67	0.038
MMP10	matrix metallopeptidase 10 (stromelysin 2)	2.67	0.009
CCL2	chemokine (C-C motif) ligand 2	2.64	0.039
SPTBN5	spectrin, beta, non-erythrocytic 5	2.63	0.040
BLM	Bloom syndrome, RecQ helicase-like	2.63	0.020
FAM111B	family with sequence similarity 111, member B	2.61	0.0019
CECR7	cat eye syndrome chromosome region, candidate 7 (non-protein coding)	2.58	0.041
FST	follistatin	2.57	0.024
PTCD1	pentatricopeptide repeat domain 1	2.56	0.011
ESCO2	establishment of cohesion 1 homolog 2 (S. cerevisiae)	2.54	0.009
CXCL2	chemokine (C-X-C motif) ligand 2	2.53	0.042
SKA3	spindle and kinetochore associated complex subunit 3	2.51	0.023
THSD7B	thrombospondin, type I, domain containing 7B	2.50	0.012
SCUBE3	signal peptide, CUB domain, EGF-like 3	2.50	0.035
CENPI	centromere protein I	2.49	0.020
CDC45	cell division cycle 45	2.44	0.013
LINC00634	long intergenic non-protein coding RNA 634	2.43	0.032
RFTN1	raftlin, lipid raft linker 1	2.43	0.05
MIR181A1HG	familial acute myelogenous leukemia related factor	2.42	0.0010
ZNF367	zinc finger protein 367	2.41	0.031
SNORD76	small nucleolar RNA, C/D box 76	2.40	0.039
NUDT9P1	nudix (nucleoside diphosphate linked moiety X)-type motif 9 pseudogene 1	2.38	0.009

HRK	harakiri, BCL2 interacting protein (contains only BH3 domain)	2.38	0.041
TREX2	three prime repair exonuclease 2	2.38	0.05
FAIM3	Fas apoptotic inhibitory molecule 3	2.36	0.031
MCM10	minichromosome maintenance complex component 10	2.35	0.0005
GINS2	GINS complex subunit 2 (Psf2 homolog)	2.33	0.004
IL18R1	interleukin 18 receptor 1	2.33	0.022
LINC00626	long intergenic non-protein coding RNA 626	2.30	0.0011
NOP56	NOP56 ribonucleoprotein	2.29	0.045
SP5	Sp5 transcription factor	2.28	0.020
HIST2H3D	histone cluster 2, H3d	2.27	0.036
E2F1	E2F transcription factor 1	2.23	0.007
ZWINT	ZW10 interactor, kinetochore protein	2.23	0.040
CDC6	cell division cycle 6	2.22	0.013
MKI67	antigen identified by monoclonal antibody Ki-67	2.22	0.007
BUB1B	BUB1 mitotic checkpoint serine/threonine kinase B	2.22	0.008
FAM71F2	family with sequence similarity 71, member F2	2.21	0.031
MYBL2	v-myb myeloblastosis viral oncogene homolog (avian)-like 2	2.21	0.010
CENPF	centromere protein F, 350/400kDa	2.18	0.019
ASF1B	ASF1 anti-silencing function 1 homolog B (S. cerevisiae)	2.16	0.007
ACTBL2	actin, beta-like 2	2.13	0.0016
ASPM	asp (abnormal spindle) homolog, microcephaly associated (Drosophila)	2.11	0.013
KIF26B	kinesin family member 26B	2.11	0.022
CDCA2	cell division cycle associated 2	2.11	0.012
CDH5	cadherin 5, type 2 (vascular endothelium)	2.10	0.032
RAPGEFL1	Rap guanine nucleotide exchange factor (GEF)-like 1	2.09	0.049
CDCA5	cell division cycle associated 5	2.09	0.010
ASNS	asparagine synthetase (glutamine-hydrolyzing)	2.09	0.023
C16orf59	chromosome 16 open reading frame 59	2.09	0.014
PBK	PDZ binding kinase	2.08	0.021
SLC1A4	solute carrier family 1 (glutamate/neutral amino acid transporter), member 4	2.06	0.028
KIF15	kinesin family member 15	2.06	0.007
DNER	delta/notch-like EGF repeat containing	2.05	0.038
PINX1	PIN2/TERF1 interacting, telomerase inhibitor 1	2.04	0.028
DTL	denticleless E3 ubiquitin protein ligase homolog (Drosophila)	2.04	0.013
CENPM	centromere protein M	2.02	0.020
NUF2	NUF2, NDC80 kinetochore complex component, homolog (S. cerevisiae)	2.00	0.018
SERPINB7	serpin peptidase inhibitor, clade B (ovalbumin), member 7	2.00	0.004
NOP2	NOP2 nucleolar protein	2.00	0.037
CCNE2	cyclin E2	1.99	0.0006
CHAC2	ChaC, cation transport regulator homolog 2 (E. coli)	1.98	0.012
CXCL5	chemokine (C-X-C motif) ligand 5	1.97	0.012

GTSE1	G-2 and S-phase expressed 1	1.96	0.0014
CENPW	centromere protein W	1.96	0.029
HMMR	hyaluronan-mediated motility receptor (RHAMM)	1.95	0.041
VNN1	vanin 1	1.95	0.0012
PSAT1	phosphoserine aminotransferase 1	1.94	0.038
RFC3	replication factor C (activator 1) 3, 38kDa	1.94	0.021
LOC152225	uncharacterized LOC152225	1.94	0.026
CDCA3	cell division cycle associated 3	1.93	0.005
CENPA	centromere protein A	1.93	0.006
CKAP2L	cytoskeleton associated protein 2-like	1.93	0.007
SLC6A9	solute carrier family 6 (neurotransmitter transporter, glycine), member 9	1.92	0.017
FEN1	flap structure-specific endonuclease 1	1.92	0.012
FNTB	farnesyltransferase, CAAX box, beta	1.91	0.023
KYNU	kynureninase	1.91	0.049
NKX3-1	NK3 homeobox 1	1.91	0.004
LOC554206	leucine carboxyl methyltransferase 1 pseudogene	1.91	0.044
IL23A	interleukin 23, alpha subunit p19	1.91	0.036
HBQ1	hemoglobin, theta 1	1.91	0.05
KIF2C	kinesin family member 2C	1.90	0.007
SP140	SP140 nuclear body protein	1.89	0.05
AURKB	aurora kinase B	1.88	0.0013
DSCC1	defective in sister chromatid cohesion 1 homolog (S. cerevisiae)	1.88	0.013
NCAPH	non-SMC condensin I complex, subunit H	1.88	0.002
MYBL1	v-myb myeloblastosis viral oncogene homolog (avian)-like 1	1.88	0.017
CEP55	centrosomal protein 55kDa	1.88	0.006
DIAPH3	diaphanous homolog 3 (Drosophila)	1.87	0.0004
FAM83D	family with sequence similarity 83, member D	1.87	0.002
CDC25C	cell division cycle 25C	1.87	0.039
TOP2A	topoisomerase (DNA) II alpha 170kDa	1.87	0.020
PLK1	polo-like kinase 1	1.86	0.0004
IFI16	interferon, gamma-inducible protein 16	1.86	0.019
MTHFD2	methylenetetrahydrofolate dehydrogenase (NADP+ dependent) 2, methenyltetrahydrofolate cyclohydrolase	1.86	0.033
NEIL3	nei endonuclease VIII-like 3 (E. coli)	1.85	0.05
MCM4	minichromosome maintenance complex component 4	1.85	0.022
CCM2L	cerebral cavernous malformation 2-like	1.85	0.014
BIRC5	baculoviral IAP repeat containing 5	1.84	0.004
KIF23	kinesin family member 23	1.84	0.0018
KIFC1	kinesin family member C1	1.84	0.006
URB2	URB2 ribosome biogenesis 2 homolog (S. cerevisiae)	1.84	0.044
STX11	syntaxin 11	1.84	0.011
TPX2	TPX2, microtubule-associated, homolog (Xenopus laevis)	1.83	0.003

ZFP69B	ZFP69 zinc finger protein B	1.83	0.035
XDH	xanthine dehydrogenase	1.83	0.025
RRM2	ribonucleotide reductase M2	1.83	0.020
SNPH	syntaphilin	1.82	0.047
CCNA2	cyclin A2	1.82	0.009
SPAG5	sperm associated antigen 5	1.82	0.012
OAS3	2'-5'-oligoadenylate synthetase 3, 100kDa	1.81	0.0008
ANLN	anillin, actin binding protein	1.81	0.025
KIF20A	kinesin family member 20A	1.81	0.012
ZIC5	Zic family member 5	1.81	0.023
CSPG5	chondroitin sulfate proteoglycan 5 (neuroglycan C)	1.81	0.003
SFMBT1	Scm-like with four mbt domains 1	1.81	0.015
PIGR	polymeric immunoglobulin receptor	1.80	0.002
DLGAP5	discs, large (Drosophila) homolog-associated protein 5	1.80	0.042
TNIP3	TNFAIP3 interacting protein 3	1.80	0.005
DEPDC1	DEP domain containing 1	1.80	0.032
CENPE	centromere protein E, 312kDa	1.80	0.041
NUSAP1	nucleolar and spindle associated protein 1	1.80	0.010
SHCBP1	SHC SH2-domain binding protein 1	1.79	0.029
GPATCH4	G patch domain containing 4	1.79	0.044
KIAA1524	KIAA1524	1.79	0.008
TRIM31	tripartite motif containing 31	1.79	0.024
AURKA	aurora kinase A	1.79	0.0016
SLC36A1	solute carrier family 36 (proton/amino acid symporter), member 1	1.79	0.042
PTGDR2	prostaglandin D2 receptor 2	1.78	0.041
HBB	hemoglobin, beta	1.78	0.0012
DHRS3	dehydrogenase/reductase (SDR family) member 3	1.77	0.003
CLEC4E	C-type lectin domain family 4, member E	1.77	0.029
CTH	cystathionase (cystathionine gamma-lyase)	1.77	0.045
KIF4A	kinesin family member 4A	1.77	0.0009
SH3RF3-AS1	SH3RF3 antisense RNA 1	1.77	0.008
E2F8	E2F transcription factor 8	1.77	0.005
FOXM1	forkhead box M1	1.77	0.002
PCNA	proliferating cell nuclear antigen	1.76	0.014
WDR62	WD repeat domain 62	1.76	0.016
C1orf112	chromosome 1 open reading frame 112	1.76	0.023
CDK1	cyclin-dependent kinase 1	1.76	0.028
STAB1	stabilin 1	1.76	0.010
CCDC15	coiled-coil domain containing 15	1.75	0.046
ALPK2	alpha-kinase 2	1.75	0.014
C10orf2	chromosome 10 open reading frame 2	1.75	0.030
PNO1	partner of NOB1 homolog (S. cerevisiae)	1.75	0.023

MARS	methionyl-tRNA synthetase	1.75	0.008
CENPU	MLF1 interacting protein	1.74	0.027
TICRR	TOPBP1-interacting checkpoint and replication regulator	1.74	0.005
LY6G5C	lymphocyte antigen 6 complex, locus G5C	1.74	0.015
NCF2	neutrophil cytosolic factor 2	1.73	0.005
FAM169A	family with sequence similarity 169, member A	1.72	0.049
SYT16	synaptotagmin XVI	1.72	0.011
KPNA2	karyopherin alpha 2 (RAG cohort 1, importin alpha 1)	1.72	0.011
HAUS8	HAUS augmin-like complex, subunit 8	1.72	0.011
PODXL2	podocalyxin-like 2	1.72	0.05
CMSS1	cms1 ribosomal small subunit homolog (yeast)	1.72	0.007
XPOT	exportin, tRNA	1.72	0.035
BYSL	bystin-like	1.72	0.021
LYAR	Ly1 antibody reactive	1.72	0.0003
TRIB3	tribbles homolog 3 (Drosophila)	1.71	0.05
CNNM1	cyclin M1	1.71	0.0013
CIITA	class II, major histocompatibility complex, transactivator	1.71	0.033
HAUS7	HAUS augmin-like complex, subunit 7	1.71	0.045
FAM169B	family with sequence similarity 169, member B	1.71	0.0009
DDX21	DEAD (Asp-Glu-Ala-Asp) box helicase 21	1.70	0.045
KIF20B	kinesin family member 20B	1.70	0.05
CDCA8	cell division cycle associated 8	1.70	0.009
PTCHD3	patched domain containing 3	1.69	0.042
SLFN5	schlafen family member 5	1.69	0.033
ADAMTS3	ADAM metallopeptidase with thrombospondin type 1 motif, 3	1.69	0.016
TCF19	transcription factor 19	1.69	0.016
CEBPG	CCAAT/enhancer binding protein (C/EBP), gamma	1.69	0.035
FAM64A	family with sequence similarity 64, member A	1.69	0.008
NOLC1	nucleolar and coiled-body phosphoprotein 1	1.68	0.028
ZNF239	zinc finger protein 239	1.68	0.018
UTP14A	UTP14, U3 small nucleolar ribonucleoprotein, homolog A (yeast)	1.68	0.027
OGFRL1	opioid growth factor receptor-like 1	1.68	0.016
PAK1IP1	PAK1 interacting protein 1	1.68	0.014
PKMYT1	protein kinase, membrane associated tyrosine/threonine 1	1.68	0.006
ANTXR1	anthrax toxin receptor 1	1.68	0.011
CHRNA10	cholinergic receptor, nicotinic, alpha 10 (neuronal)	1.68	0.05
FBXO5	F-box protein 5	1.68	0.05
RRS1	RRS1 ribosome biogenesis regulator homolog (S. cerevisiae)	1.67	0.021
NR1D2	nuclear receptor subfamily 1, group D, member 2	1.67	0.021
SOD2	superoxide dismutase 2, mitochondrial	1.67	0.018
IQCD	IQ motif containing D	1.67	0.048
COL12A1	collagen, type XII, alpha 1	1.67	0.003

NCAPG2	non-SMC condensin II complex, subunit G2	1.67	0.025
CDT1	chromatin licensing and DNA replication factor 1	1.67	0.0016
UBE2C	ubiquitin-conjugating enzyme E2C	1.66	0.022
MCM3	minichromosome maintenance complex component 3	1.66	0.006
TUBA1B	tubulin, alpha 1b	1.66	0.012
FUT8-AS1	FUT8 antisense RNA 1	1.66	0.05
MARS2	methionyl-tRNA synthetase 2, mitochondrial	1.66	0.037
PTPRB	protein tyrosine phosphatase, receptor type, B	1.66	0.0018
PRKCH	protein kinase C, eta	1.66	0.014
DNAJC6	DnaJ (Hsp40) homolog, subfamily C, member 6	1.66	0.030
PRC1	protein regulator of cytokinesis 1	1.66	0.0008
MTFR2	mitochondrial fission regulator 2	1.66	0.008
ELOVL3	ELOVL fatty acid elongase 3	1.66	0.007
GTPBP4	GTP binding protein 4	1.66	0.031
TACC3	transforming, acidic coiled-coil containing protein 3	1.66	0.0004
TNFRSF11B	tumor necrosis factor receptor superfamily, member 11b	1.66	0.0008
TRIM6	tripartite motif containing 6	1.65	0.011
ATF5	activating transcription factor 5	1.65	0.038
CENPJ	centromere protein J	1.65	0.023
VTI1A	vesicle transport through interaction with t-SNAREs 1A	1.65	0.016
CDC20	cell division cycle 20	1.64	0.003
WDR3	WD repeat domain 3	1.64	0.046
C3	complement component 3	1.64	0.025
FANCI	Fanconi anemia, complementation group I	1.64	0.017
IARS	isoleucyl-tRNA synthetase	1.64	0.036
AIMP2	aminoacyl tRNA synthetase complex-interacting multifunctional protein 2	1.64	0.032
FICD	FIC domain containing	1.63	0.035
PIF1	PIF1 5'-to-3' DNA helicase homolog (S. cerevisiae)	1.63	0.033
CCNB1	cyclin B1	1.63	0.034
HJURP	Holliday junction recognition protein	1.63	0.011
ARHGDIB	Rho GDP dissociation inhibitor (GDI) beta	1.63	0.008
NLRC4	NLR family, CARD domain containing 4	1.63	0.05
CDH4	cadherin 4, type 1, R-cadherin (retinal)	1.62	0.012
SPAG1	sperm associated antigen 1	1.62	0.008
TERT	telomerase reverse transcriptase	1.62	0.002
H2AFX	H2A histone family, member X	1.62	0.022
NEXN	nexilin (F actin binding protein)	1.62	0.042
PRKAR1B	protein kinase, cAMP-dependent, regulatory, type I, beta	1.62	0.047
ORC5	origin recognition complex, subunit 5	1.62	0.042
RAD51	RAD51 homolog (S. cerevisiae)	1.62	0.047
ZNF678	zinc finger protein 678	1.61	0.008
LTV1	LTV1 homolog (S. cerevisiae)	1.61	0.003

KNSTRN	kinetochore-localized astrin/SPAG5 binding protein	1.61	0.003
KIF18A	kinesin family member 18A	1.61	0.026
ZWILCH	zwilch kinetochore protein	1.61	0.010
LARS	leucyl-tRNA synthetase	1.61	0.034
SLC22A18AS	solute carrier family 22 (organic cation transporter), member 18 antisense	1.61	0.037
CHORDC1	cysteine and histidine-rich domain (CHORD) containing 1	1.61	0.038
MON1A	MON1 homolog A (yeast)	1.61	0.042
NUP35	nucleoporin 35kDa	1.60	0.012
ZNF319	zinc finger protein 319	1.60	0.013
MAK16	MAK16 homolog (S. cerevisiae)	1.60	0.018
DHFR	dihydrofolate reductase	1.60	0.036
RPP25	ribonuclease P/MRP 25kDa subunit	1.60	0.026
IDI2-AS1	IDI2 antisense RNA 1	1.60	0.035
UTP20	UTP20, small subunit (SSU) processome component, homolog (yeast)	1.60	0.007
TARS	threonyl-tRNA synthetase	1.59	0.011
HLA-DRA	major histocompatibility complex, class II, DR alpha	1.59	0.011
UHRF1	ubiquitin-like with PHD and ring finger domains 1	1.59	0.0012
FAM208B	family with sequence similarity 208, member B	1.59	0.036
TRIP13	thyroid hormone receptor interactor 13	1.58	0.007
TEX10	testis expressed 10	1.58	0.026
KLHDC7A	kelch domain containing 7A	1.58	0.007
POLA2	polymerase (DNA directed), alpha 2, accessory subunit	1.58	0.023
BICC1	bicaudal C homolog 1 (Drosophila)	1.58	0.009
POLR3B	polymerase (RNA) III (DNA directed) polypeptide B	1.58	0.002
SPRTN	SprT-like N-terminal domain	1.58	0.036
LYPD6B	LY6/PLAUR domain containing 6B	1.58	0.017
LRRIQ1	leucine-rich repeats and IQ motif containing 1	1.58	0.005
SLC12A2	solute carrier family 12 (sodium/potassium/chloride transporters), member 2	1.58	0.015
PRIM2	primase, DNA, polypeptide 2 (58kDa)	1.58	0.030
SUV39H1	suppressor of variegation 3-9 homolog 1 (Drosophila)	1.58	0.013
CA2	carbonic anhydrase II	1.57	0.013
CIRH1A	cirrhosis, autosomal recessive 1A (cirhin)	1.57	0.032
HLA-DRB1	major histocompatibility complex, class II, DR beta 1	1.57	0.013
PRKAR2B	protein kinase, cAMP-dependent, regulatory, type II, beta	1.57	0.019
CAPN13	calpain 13	1.56	0.028
CCDC18	coiled-coil domain containing 18	1.56	0.028
IQGAP3	IQ motif containing GTPase activating protein 3	1.56	0.007
COA7	Sel1 repeat containing 1	1.56	0.039
TUBA1C	tubulin, alpha 1c	1.56	0.032
SLC1A5	solute carrier family 1 (neutral amino acid transporter), member 5	1.56	0.021

POLR1A	polymerase (RNA) I polypeptide A, 194kDa	1.56	0.014
HEATR3	HEAT repeat containing 3	1.56	0.040
TNFSF15	tumor necrosis factor (ligand) superfamily, member 15	1.56	0.031
SPRN	shadow of prion protein homolog (zebrafish)	1.56	0.005
EXOSC8	exosome component 8	1.56	0.010
NCOA5	nuclear receptor coactivator 5	1.56	0.032
TYMS	thymidylate synthetase	1.55	0.003
AMER1	APC membrane recruitment protein 1	1.55	0.003
MCM2	minichromosome maintenance complex component 2	1.55	0.044
POLR1B	polymerase (RNA) I polypeptide B, 128kDa	1.55	0.039
PRKDC	protein kinase, DNA-activated, catalytic polypeptide	1.55	0.039
C4orf19	chromosome 4 open reading frame 19	1.55	0.040
WARS	tryptophanyl-tRNA synthetase	1.55	0.027
ESF1	ESF1, nucleolar pre-rRNA processing protein, homolog (S. cerevisiae)	1.55	0.007
TNC	tenascin C	1.55	0.0010
RECQL4	RecQ protein-like 4	1.55	0.016
POLR3K	polymerase (RNA) III (DNA directed) polypeptide K, 12.3 kDa	1.54	0.025
NOP14	NOP14 nucleolar protein	1.54	0.010
NCAPG	non-SMC condensin I complex, subunit G	1.54	0.05
GEMIN5	gem (nuclear organelle) associated protein 5	1.54	0.016
PLK2	polo-like kinase 2	1.54	0.039
PCK2	phosphoenolpyruvate carboxykinase 2 (mitochondrial)	1.54	0.017
BRCC3	BRCA1/BRCA2-containing complex, subunit 3	1.54	0.042
RHCE	Rh blood group, CcEe antigens	1.54	0.019
PYCR1	pyrroline-5-carboxylate reductase 1	1.54	0.035
TOMM40	translocase of outer mitochondrial membrane 40 homolog (yeast)	1.54	0.021
CCT5	chaperonin containing TCP1, subunit 5 (epsilon)	1.54	0.019
ARHGAP31	Rho GTPase activating protein 31	1.54	0.029
UBIAD1	UbiA prenyltransferase domain containing 1	1.54	0.011
DNAJC9	DnaJ (Hsp40) homolog, subfamily C, member 9	1.54	0.009
SH2D4A	SH2 domain containing 4A	1.54	0.006
CLN6	ceroid-lipofuscinosis, neuronal 6, late infantile, variant	1.54	0.024
LRR1	leucine rich repeat protein 1	1.54	0.039
NOP58	NOP58 ribonucleoprotein	1.53	0.018
EBNA1BP2	EBNA1 binding protein 2	1.53	0.0008
GRHL1	grainyhead-like 1 (Drosophila)	1.53	0.038
KIAA0020	KIAA0020	1.53	0.007
PMAIP1	phorbol-12-myristate-13-acetate-induced protein 1	1.53	0.012
ETV3	ets variant 3	1.53	0.004
NUFIP1	nuclear fragile X mental retardation protein interacting protein 1	1.53	0.026
ORC1	origin recognition complex, subunit 1	1.53	0.036

ZNF407	zinc finger protein 407	1.53	0.014
TK1	thymidine kinase 1, soluble	1.53	0.0013
SLC7A5	solute carrier family 7 (amino acid transporter light chain, L system), member 5	1.53	0.025
TOMM34	translocase of outer mitochondrial membrane 34	1.53	0.037
ST5	suppression of tumorigenicity 5	1.53	0.019
PPIL1	peptidylprolyl isomerase (cyclophilin)-like 1	1.53	<0.0001
FAM129A	family with sequence similarity 129, member A	1.53	0.007
ZFAND4	zinc finger, AN1-type domain 4	1.53	0.009
C6orf99	chromosome 6 open reading frame 99	1.52	0.006
FANCM	Fanconi anemia, complementation group M	1.52	0.024
GBP5	guanylate binding protein 5	1.52	0.009
USP2-AS1	uncharacterized LOC100499227	1.52	0.027
SPC24	SPC24, NDC80 kinetochore complex component, homolog (S. cerevisiae)	1.52	0.033
SYNCRIP	synaptotagmin binding, cytoplasmic RNA interacting protein	1.52	0.018
AMD1	adenosylmethionine decarboxylase 1	1.52	0.025
SLC3A2	solute carrier family 3 (activators of dibasic and neutral amino acid transport), member 2	1.52	0.032
CCDC150	coiled-coil domain containing 150	1.52	0.013
FABP5	fatty acid binding protein 5 (psoriasis-associated)	1.51	0.013
NCAPD2	non-SMC condensin I complex, subunit D2	1.51	0.0003
BUB1	BUB1 mitotic checkpoint serine/threonine kinase	1.51	0.041
PANK3	pantothenate kinase 3	1.51	0.042
TROAP	trophinin associated protein	1.51	0.023
SHMT2	serine hydroxymethyltransferase 2 (mitochondrial)	1.51	0.013
ACER3	alkaline ceramidase 3	1.51	0.013
FADS1	fatty acid desaturase 1	1.51	0.004
FAM86A	family with sequence similarity 86, member A	1.51	0.05
UTP15	UTP15, U3 small nucleolar ribonucleoprotein, homolog (S. cerevisiae)	1.51	0.025
SIGMAR1	sigma non-opioid intracellular receptor 1	1.50	0.027
TP53	tumor protein p53	1.50	0.034
BRIX1	BRX1, biogenesis of ribosomes, homolog (S. cerevisiae)	1.50	0.028
CDIP1	cell death-inducing p53 target 1	1.50	0.023
MCM7	minichromosome maintenance complex component 7	1.50	0.003
ALPK3	alpha-kinase 3	1.50	0.05
PRTN3	proteinase 3	0.04	0.005
CLEC2B	C-type lectin domain family 2, member B	0.06	0.015
KISS1R	KISS1 receptor	0.07	0.05
ISM2	isthmin 2 homolog (zebrafish)	0.08	0.017
LINC00535	long intergenic non-protein coding RNA 535	0.09	0.002
PMP2	peripheral myelin protein 2	0.10	0.035
PDPN	podoplanin	0.11	0.05

CYP26A1	cytochrome P450, family 26, subfamily A, polypeptide 1	0.11	0.008
HLA-G	major histocompatibility complex, class I, G	0.11	0.012
TRIL	TLR4 interactor with leucine-rich repeats	0.13	0.020
DEFB109P1B	defensin, beta 109, pseudogene 1B	0.13	0.018
MIR2861	microRNA 2861	0.14	0.026
DTNA	dystrobrevin, alpha	0.15	0.003
LMO1	LIM domain only 1 (rhombotin 1)	0.15	0.022
DCAF12L2	DDB1 and CUL4 associated factor 12-like 2	0.15	0.008
LGI4	leucine-rich repeat LGI family, member 4	0.15	0.008
OLFM2	olfactomedin 2	0.16	0.047
TTLL9	tubulin tyrosine ligase-like family, member 9	0.17	0.013
DRP2	dystrophin related protein 2	0.17	0.038
ALK	anaplastic lymphoma receptor tyrosine kinase	0.17	0.038
LOC145837	uncharacterized LOC145837	0.17	0.008
SNORD116-4	small nucleolar RNA, C/D box 116-4	0.18	0.020
PTGS1	prostaglandin-endoperoxide synthase 1 (prostaglandin G/H synthase and cyclooxygenase)	0.19	0.0002
NACAP1	nascent-polypeptide-associated complex alpha polypeptide pseudogene 1	0.19	0.038
LOC100129617	uncharacterized LOC100129617	0.19	0.021
RASIP1	Ras interacting protein 1	0.19	0.026
AMZ1	archaelysin family metallopeptidase 1	0.21	0.019
SLC2A5	solute carrier family 2 (facilitated glucose/fructose transporter), member 5	0.23	0.025
ORM2	orosomucoid 2	0.23	0.016
CPXM2	carboxypeptidase X (M14 family), member 2	0.23	0.010
EEF1A2	eukaryotic translation elongation factor 1 alpha 2	0.24	0.020
VILL	villin-like	0.24	0.003
NKAIN1	Na+/K+ transporting ATPase interacting 1	0.24	0.030
S1PR4	sphingosine-1-phosphate receptor 4	0.25	0.050
HCG27	HLA complex group 27 (non-protein coding)	0.25	0.020
MRPL23-AS1	MRPL23 antisense RNA 1	0.25	0.023
ANGPTL4	angiopoietin-like 4	0.26	0.003
FLJ43315	asparagine synthetase pseudogene	0.26	0.042
DHDH	dihydrodiol dehydrogenase (dimeric)	0.26	0.044
AQP2	aquaporin 2 (collecting duct)	0.26	0.020
RGS11	regulator of G-protein signaling 11	0.27	0.05
G0S2	G0/G1switch 2	0.27	0.008
H2BFM	H2B histone family, member M	0.27	0.007
FAM83A	family with sequence similarity 83, member A	0.28	0.044
GIPR	gastric inhibitory polypeptide receptor	0.28	0.003
SERPINE1	serpin peptidase inhibitor, clade E (nexin, plasminogen activator inhibitor type 1), member 1	0.28	0.020
LINC00312	long intergenic non-protein coding RNA 312	0.29	0.038

AKR1C2	aldo-keto reductase family 1, member C2	0.29	0.042
CSPG4	chondroitin sulfate proteoglycan 4	0.29	0.036
LGALS4	lectin, galactoside-binding, soluble, 4	0.29	0.008
HCG4B	HLA complex group 4B (non-protein coding)	0.29	0.041
SUSD3	sushi domain containing 3	0.30	0.0015
KCNK15	potassium channel, subfamily K, member 15	0.30	0.004
CRYAB	crystallin, alpha B	0.30	0.05
SNORD69	small nucleolar RNA, C/D box 69	0.30	0.002
TCTE3	t-complex-associated-testis-expressed 3	0.31	0.004
EFEMP2	EGF containing fibulin-like extracellular matrix protein 2	0.31	0.019
TMEM191C	transmembrane protein 191C	0.31	0.028
RNASE4	ribonuclease, RNase A family, 4	0.31	0.003
DSCR9	Down syndrome critical region gene 9 (non-protein coding)	0.31	0.037
RASA4B	RAS p21 protein activator 4B	0.32	0.020
TFF3	trefoil factor 3 (intestinal)	0.32	0.029
CNDP1	carnosine dipeptidase 1 (metallopeptidase M20 family)	0.32	0.034
NDRG1	N-myc downstream regulated 1	0.32	0.005
TEX19	testis expressed 19	0.33	0.050
PLCH2	phospholipase C, eta 2	0.33	0.012
NDUFAF4P1	NADH dehydrogenase (ubiquinone) complex I, assembly factor 4 pseudogene 1	0.33	0.020
ENPEP	glutamyl aminopeptidase (aminopeptidase A)	0.33	0.038
SPTBN4	spectrin, beta, non-erythrocytic 4	0.33	0.020
DPEP1	dipeptidase 1 (renal)	0.34	0.034
ANG	angiogenin, ribonuclease, RNase A family, 5	0.34	0.0013
PPP1R3C	protein phosphatase 1, regulatory subunit 3C	0.34	0.0009
ASGR1	asialoglycoprotein receptor 1	0.35	0.029
ADM	adrenomedullin	0.35	0.020
CLCNKB	chloride channel, voltage-sensitive Kb	0.35	0.010
CDK18	cyclin-dependent kinase 18	0.36	0.014
FAM25A	family with sequence similarity 25, member A	0.36	0.039
GPER1	G protein-coupled estrogen receptor 1	0.36	0.038
PCOLCE2	procollagen C-endopeptidase enhancer 2	0.36	0.023
TREH	trehalase (brush-border membrane glycoprotein)	0.37	0.025
INSC	inscuteable homolog (Drosophila)	0.38	0.038
MAPT	microtubule-associated protein tau	0.38	0.023
LINC00202-1	long intergenic non-protein coding RNA 202-1	0.38	0.023
NRN1L	neuritin 1-like	0.38	0.042
WFDC3	WAP four-disulfide core domain 3	0.38	0.007
TRIM29	tripartite motif containing 29	0.38	0.012
ADAM11	ADAM metallopeptidase domain 11	0.38	0.005
C1orf213	chromosome 1 open reading frame 213	0.38	0.005
LEMD1	LEM domain containing 1	0.38	0.019

TMEM74B	transmembrane protein 74B	0.38	0.017
USP6	ubiquitin specific peptidase 6 (Tre-2 oncogene)	0.39	0.007
SEMA5B	sema domain, seven thrombospondin repeats (type 1 and type 1-like), transmembrane domain (TM) and short cytoplasmic domain, (semaphorin) 5B	0.39	0.032
CGB7	chorionic gonadotropin, beta polypeptide 7	0.39	0.013
IL2RG	interleukin 2 receptor, gamma	0.39	0.007
RAET1G	retinoic acid early transcript 1G	0.39	0.030
HILPDA	hypoxia inducible lipid droplet-associated	0.39	0.009
ANKRD37	ankyrin repeat domain 37	0.39	0.017
FLJ44511	uncharacterized LOC441307	0.39	0.022
SNORD89	small nucleolar RNA, C/D box 89	0.40	0.012
SLC38A11	solute carrier family 38, member 11	0.40	0.010
NAPSA	napsin A aspartic peptidase	0.40	0.010
S100A14	S100 calcium binding protein A14	0.40	0.013
NR4A1	nuclear receptor subfamily 4, group A, member 1	0.40	0.0015
LINC00482	long intergenic non-protein coding RNA 482	0.40	0.044
ODF3L1	outer dense fiber of sperm tails 3-like 1	0.40	0.022
LINC00466	long intergenic non-protein coding RNA 466	0.40	0.035
AKAP12	A kinase (PRKA) anchor protein 12	0.41	0.0008
ADAMTS16	ADAM metallopeptidase with thrombospondin type 1 motif, 16	0.41	0.011
FGF9	fibroblast growth factor 9 (glia-activating factor)	0.41	0.011
ENO2	enolase 2 (gamma, neuronal)	0.41	0.006
POM121L1P	POM121 transmembrane nucleoporin-like 1, pseudogene	0.41	0.05
CD40LG	CD40 ligand	0.41	0.038
BEND5	BEN domain containing 5	0.41	0.028
TMEM178A	transmembrane protein 178A	0.41	0.035
CES4A	carboxylesterase 4A	0.42	0.020
CASR	calcium-sensing receptor	0.42	0.0006
NANOGNB	NANOG neighbor homeobox	0.43	0.026
LINC00887	uncharacterized LOC100131551	0.43	0.008
MMP28	matrix metallopeptidase 28	0.43	0.018
AQP7P3	aquaporin 7 pseudogene 3	0.43	0.019
AOC1	amiloride binding protein 1 (amine oxidase (copper-containing))	0.43	0.006
AQP3	aquaporin 3 (Gill blood group)	0.43	0.025
AIM1L	absent in melanoma 1-like	0.43	0.018
MIR614	microRNA 614	0.43	0.012
SNORA44	small nucleolar RNA, H/ACA box 44	0.43	0.049
LINC00035	long intergenic non-protein coding RNA 35	0.43	0.025
ENOX1	ecto-NOX disulfide-thiol exchanger 1	0.43	0.033
ESPN	espin	0.43	0.005
TGM5	transglutaminase 5	0.44	0.005

SLC9A3	solute carrier family 9, subfamily A (NHE3, cation proton antiporter 3), member 3	0.44	0.019
C19orf71	chromosome 19 open reading frame 71	0.44	0.020
TRIM60	tripartite motif containing 60	0.44	0.036
SNHG12	small nucleolar RNA host gene 12 (non-protein coding)	0.44	0.014
ICAM5	intercellular adhesion molecule 5, telencephalin	0.44	0.015
MEF2C	myocyte enhancer factor 2C	0.44	0.037
OPRL1	opiate receptor-like 1	0.44	0.038
MYO7B	myosin VIIB	0.45	0.007
TEKT3	tektin 3	0.45	0.05
ZNF571-AS1	uncharacterized LOC100507433	0.45	0.027
RORC	RAR-related orphan receptor C	0.45	0.021
LINC-PINT	uncharacterized LOC378805	0.46	0.019
TNXB	tenascin XB	0.46	0.048
NKAIN4	Na+/K+ transporting ATPase interacting 4	0.46	0.012
PLXNB3	plexin B3	0.46	0.005
C9orf173	chromosome 9 open reading frame 173	0.46	0.010
DCDC5	doublecortin domain containing 5	0.46	0.047
LOC100270804	uncharacterized LOC100270804	0.46	0.025
VTN	vitronectin	0.47	0.015
C4orf47	chromosome 4 open reading frame 47	0.47	0.021
C2CD4C	C2 calcium-dependent domain containing 4C	0.47	0.002
UPP2	uridine phosphorylase 2	0.47	0.019
CD68	CD68 molecule	0.47	0.014
CTAGE7P	CTAGE family, member 7, pseudogene	0.47	0.011
SCN4B	sodium channel, voltage-gated, type IV, beta subunit	0.47	0.010
SIGLEC1	sialic acid binding Ig-like lectin 1, sialoadhesin	0.47	0.038
IGFBP3	insulin-like growth factor binding protein 3	0.47	0.0008
WAS	Wiskott-Aldrich syndrome	0.48	0.022
SMIM24	chromosome 19 open reading frame 77	0.48	0.038
FAM110C	family with sequence similarity 110, member C	0.48	0.005
LINC00996	uncharacterized LOC285972	0.48	0.015
SNORA16A	small nucleolar RNA, H/ACA box 16A	0.49	0.006
SPAG8	sperm associated antigen 8	0.49	0.043
PPFIA4	protein tyrosine phosphatase, receptor type, f polypeptide (PTPRF), interacting protein (liprin), alpha 4	0.49	0.012
SEMA3B	sema domain, immunoglobulin domain (Ig), short basic domain, secreted, (semaphorin) 3B	0.49	0.010
FGL2	fibrinogen-like 2	0.49	0.014
NPR1	natriuretic peptide receptor A/guanylate cyclase A (atrionatriuretic peptide receptor A)	0.49	0.019
RRAGD	Ras-related GTP binding D	0.50	0.005
SUGT1P1	suppressor of G2 allele of SKP1 (S. cerevisiae) pseudogene 1	0.50	0.003
NKAPP1	NFKB activating protein pseudogene 1	0.50	0.019

ACSL6	acyl-CoA synthetase long-chain family member 6	0.50	0.021
ISLR2	immunoglobulin superfamily containing leucine-rich repeat 2	0.50	0.022
MDK	midkine (neurite growth-promoting factor 2)	0.50	0.034
OSCAR	osteoclast associated, immunoglobulin-like receptor	0.50	0.041
BBOX1	butyrobetaine (gamma), 2-oxoglutarate dioxygenase (gamma-butyrobetaine hydroxylase) 1	0.50	0.013
TMEM110-MUSTN1	TMEM110-MUSTN1 readthrough	0.50	0.009
SCART1	scavenger receptor protein family member	0.50	0.013
PRSS53	protease, serine, 53	0.50	0.029
DUSP1	dual specificity phosphatase 1	0.50	0.013
LTC4S	leukotriene C4 synthase	0.50	0.016
ANK1	ankyrin 1, erythrocytic	0.50	0.007
AKR1C1	aldo-keto reductase family 1, member C1	0.50	0.029
LINC00939	uncharacterized LOC400084	0.50	0.009
CKB	creatine kinase, brain	0.51	0.012
DCN	decorin	0.51	0.019
SNORD104	small nucleolar RNA, C/D box 104	0.51	0.016
SERPINF2	serpin peptidase inhibitor, clade F (alpha-2 antiplasmin, pigment epithelium derived factor), member 2	0.51	0.05
ENTPD8	ectonucleoside triphosphate diphosphohydrolase 8	0.51	0.029
LMCD1-AS1	LMCD1 antisense RNA 1 (head to head)	0.51	0.028
KIAA1549L	KIAA1549-like	0.51	0.010
LINC01018	uncharacterized LOC255167	0.51	0.002
SH3D21	SH3 domain containing 21	0.51	0.017
LINC01021	uncharacterized LOC643401	0.51	0.049
ADAMTSL4	ADAMTS-like 4	0.51	0.003
SUSD2	sushi domain containing 2	0.52	0.033
BTBD16	BTB (POZ) domain containing 16	0.52	0.026
CA9	carbonic anhydrase IX	0.52	0.030
PRRT1	proline-rich transmembrane protein 1	0.52	0.009
ZNF404	zinc finger protein 404	0.52	0.0005
FZD10	frizzled family receptor 10	0.52	0.003
MIR155HG	MIR155 host gene (non-protein coding)	0.52	0.009
M1AP	meiosis 1 associated protein	0.52	0.037
FRZB	frizzled-related protein	0.52	0.05
JAG2	jagged 2	0.52	0.002
MXRA8	matrix-remodelling associated 8	0.52	0.020
C2	complement component 2	0.53	0.05
LOC154761	family with sequence similarity 115, member C pseudogene	0.53	0.006
P4HA1	prolyl 4-hydroxylase, alpha polypeptide I	0.53	0.0015
ZNF208	zinc finger protein 208	0.53	0.015
PADI1	peptidyl arginine deiminase, type I	0.53	0.021
MLXIPL	MLX interacting protein-like	0.53	0.034

FZD10-AS1	uncharacterized LOC440119	0.53	0.015
ENG	endoglin	0.53	0.049
IGFBP1	insulin-like growth factor binding protein 1	0.54	0.020
PTH1R	parathyroid hormone 1 receptor	0.54	0.009
LINC00271	long intergenic non-protein coding RNA 271	0.54	0.048
PIM1	pim-1 oncogene	0.54	0.017
CLIP3	CAP-GLY domain containing linker protein 3	0.54	0.037
TENM1	teneurin transmembrane protein 1	0.54	0.041
GAPDHS	glyceraldehyde-3-phosphate dehydrogenase, spermatogenic	0.54	0.008
PROCA1	protein interacting with cyclin A1	0.54	0.039
C10orf10	chromosome 10 open reading frame 10	0.54	0.014
BDKRB2	bradykinin receptor B2	0.54	0.037
LRP1	low density lipoprotein receptor-related protein 1	0.54	0.0003
LOC284454	uncharacterized LOC284454	0.54	0.029
VAMP5	vesicle-associated membrane protein 5	0.54	0.009
S100A1	S100 calcium binding protein A1	0.54	0.020
LOC100129722	uncharacterized LOC100129722	0.54	0.017
FAM26F	family with sequence similarity 26, member F	0.54	0.044
IHH	indian hedgehog	0.54	0.026
MFNG	MFNG O-fucosylpeptide 3-beta-N-acetylglucosaminyltransferase	0.55	0.05
DGKK	diacylglycerol kinase, kappa	0.55	0.038
PMS2L2	postmeiotic segregation increased 2-like 2 pseudogene	0.55	0.020
C7orf65	chromosome 7 open reading frame 65	0.55	0.035
B3GNT6	UDP-GlcNAc:betaGal beta-1,3-N-acetylglucosaminyltransferase 6 (core 3 synthase)	0.55	0.05
INGX	inhibitor of growth family, X-linked, pseudogene	0.55	0.050
C10orf99	chromosome 10 open reading frame 99	0.55	0.017
CAPN14	calpain 14	0.55	0.031
PRODH	proline dehydrogenase (oxidase) 1	0.56	0.022
TRIM17	tripartite motif containing 17	0.56	0.026
ATP6V1G2	ATPase, H+ transporting, lysosomal 13kDa, V1 subunit G2	0.56	0.05
SSTR5-AS1	SSTR5 antisense RNA 1	0.56	0.006
ACKR4	chemokine (C-C motif) receptor-like 1	0.56	0.049
MSLN	mesothelin	0.56	0.020
TMEM229B	transmembrane protein 229B	0.56	0.006
MT1X	metallothionein 1X	0.56	0.017
SLC26A4	solute carrier family 26, member 4	0.56	0.046
LOC100132062	uncharacterized LOC100132062	0.56	0.014
FAM83E	family with sequence similarity 83, member E	0.56	0.013
LINC00473	long intergenic non-protein coding RNA 473	0.56	0.019
THEMIS2	thymocyte selection associated family member 2	0.57	0.007
UNC13A	unc-13 homolog A (C. elegans)	0.57	0.038
ATG16L2	autophagy related 16-like 2 (S. cerevisiae)	0.57	0.0011

COX6B2	cytochrome c oxidase subunit VIb polypeptide 2 (testis)	0.57	0.039
ARL11	ADP-ribosylation factor-like 11	0.57	0.030
N4BP2L2-IT2	N4BPL2 intronic transcript 2 (non-protein coding)	0.57	0.008
NEAT1	nuclear paraspeckle assembly transcript 1 (non-protein coding)	0.57	0.013
WSB1	WD repeat and SOCS box containing 1	0.57	0.0011
THBS4	thrombospondin 4	0.57	0.037
C20orf203	chromosome 20 open reading frame 203	0.57	0.027
FAM115C	family with sequence similarity 115, member C	0.57	0.043
SSPO	SCO-spondin homolog (Bos taurus)	0.57	0.027
LINC00950	uncharacterized LOC92973	0.57	0.036
TSSK3	testis-specific serine kinase 3	0.57	0.014
GS1-259H13.2	transmembrane protein 225-like	0.57	0.036
UCN	urocortin	0.57	0.004
KRT42P	keratin 42 pseudogene	0.57	0.034
SLC6A10P	solute carrier family 6 (neurotransmitter transporter, creatine), member 10, pseudogene	0.57	0.031
Sep-01	septin 1	0.58	0.029
LOC729683	uncharacterized LOC729683	0.58	0.046
LOC155060	AI894139 pseudogene	0.58	0.021
RND2	Rho family GTPase 2	0.58	0.037
SSX5	synovial sarcoma, X breakpoint 5	0.58	0.020
KCNIP2-AS1	uncharacterized LOC100289509	0.58	0.031
RTBDN	retbindin	0.59	0.010
LINC00936	uncharacterized LOC338758	0.59	0.022
SLPI	secretory leukocyte peptidase inhibitor	0.59	0.006
N4BP2L1	NEDD4 binding protein 2-like 1	0.59	0.014
DIRAS2	DIRAS family, GTP-binding RAS-like 2	0.59	0.010
KIAA0087	KIAA0087	0.59	0.029
CFD	complement factor D (adipsin)	0.59	0.004
MST1	macrophage stimulating 1 (hepatocyte growth factor-like)	0.59	0.007
SFMBT2	Scm-like with four mbt domains 2	0.59	0.006
LOX	lysyl oxidase	0.59	0.006
ST7-OT4	ST7 overlapping transcript 4	0.59	0.008
C1QL4	complement component 1, q subcomponent-like 4	0.59	0.05
PRSS8	protease, serine, 8	0.59	0.033
GSDMC	gasdermin C	0.60	0.05
ITM2C	integral membrane protein 2C	0.60	0.006
GABRE	gamma-aminobutyric acid (GABA) A receptor, epsilon	0.60	0.004
SLC2A1	solute carrier family 2 (facilitated glucose transporter), member 1	0.60	0.014
CYP4F3	cytochrome P450, family 4, subfamily F, polypeptide 3	0.60	0.005
KRT15	keratin 15	0.60	0.014
TNNI3	troponin I type 3 (cardiac)	0.60	0.007

PRSS22	protease, serine, 22	0.60	0.05
C6orf141	chromosome 6 open reading frame 141	0.60	0.032
FBXL16	F-box and leucine-rich repeat protein 16	0.60	0.028
SNORA8	small nucleolar RNA, H/ACA box 8	0.60	0.041
F3	coagulation factor III (thromboplastin, tissue factor)	0.60	0.010
HHLA2	HERV-H LTR-associating 2	0.60	0.009
CEL	carboxyl ester lipase	0.60	0.046
VKORC1	vitamin K epoxide reductase complex, subunit 1	0.60	0.005
VSIG10L	V-set and immunoglobulin domain containing 10 like	0.60	0.05
LOC286297	uncharacterized LOC286297	0.60	0.048
SAPCD1	suppressor APC domain containing 1	0.60	0.009
TINAG	tubulointerstitial nephritis antigen	0.60	0.008
PCAT6	KDM5B antisense RNA 1 (head to head)	0.60	0.034
SYT13	synaptotagmin XIII	0.60	0.012
LMNTD2	chromosome 11 open reading frame 35	0.61	0.011
C1R	complement component 1, r subcomponent	0.61	0.020
PDE6B	phosphodiesterase 6B, cGMP-specific, rod, beta	0.61	0.048
MYO15B	myosin XVB pseudogene	0.61	0.0001
PSCA	prostate stem cell antigen	0.61	0.031
MTMR11	myotubularin related protein 11	0.61	0.002
FTLP10	ferritin, light polypeptide pseudogene 10	0.61	0.0014
RASA4	RAS p21 protein activator 4	0.61	0.05
FOS	FBJ murine osteosarcoma viral oncogene homolog	0.61	0.021
GSDMA	gasdermin A	0.61	0.003
HLA-F-AS1	HLA-F antisense RNA 1	0.61	0.016
FGFR3	fibroblast growth factor receptor 3	0.61	0.011
KCTD7	potassium channel tetramerisation domain containing 7	0.61	0.042
PNPLA7	patatin-like phospholipase domain containing 7	0.61	0.042
RHBDL1	rhomboid, veinlet-like 1 (Drosophila)	0.61	0.022
SNHG18	uncharacterized LOC100505806	0.61	0.025
PAK6	p21 protein (Cdc42/Rac)-activated kinase 6	0.61	0.020
LOC100131564	uncharacterized LOC100131564	0.61	0.034
BMP7	bone morphogenetic protein 7	0.61	0.029
SNX33	sorting nexin 33	0.61	0.009
HTR2A	5-hydroxytryptamine (serotonin) receptor 2A, G protein-coupled	0.62	0.010
CLU	clusterin	0.62	0.009
TMEM70	transmembrane protein 70	0.62	0.005
C4A	complement component 4A (Rodgers blood group)	0.62	0.017
PTPRS	protein tyrosine phosphatase, receptor type, S	0.62	0.015
CDKN1C	cyclin-dependent kinase inhibitor 1C (p57, Kip2)	0.62	0.026
CEACAM5	carcinoembryonic antigen-related cell adhesion molecule 5	0.62	0.0006
LINC00515	long intergenic non-protein coding RNA 515	0.62	0.030

TMC4	transmembrane channel-like 4	0.62	0.002
PLAUR	plasminogen activator, urokinase receptor	0.62	0.025
APOE	apolipoprotein E	0.62	0.011
TSLP	thymic stromal lymphopoietin	0.62	0.006
EPOR	erythropoietin receptor	0.62	0.016
LMBR1L	limb region 1 homolog (mouse)-like	0.62	0.005
LDLRAD1	low density lipoprotein receptor class A domain containing 1	0.63	0.033
CTSF	cathepsin F	0.63	0.039
KRTCAP3	keratinocyte associated protein 3	0.63	0.05
LINC01004	uncharacterized LOC100216546	0.63	0.021
GNRH1	gonadotropin-releasing hormone 1 (luteinizing-releasing hormone)	0.63	0.024
IRF8	interferon regulatory factor 8	0.63	0.003
ZNF674-AS1	ZNF674 antisense RNA 1 (head to head)	0.63	0.05
SLC3A1	solute carrier family 3 (cystine, dibasic and neutral amino acid transporters, activator of cystine, dibasic and neutral amino acid transport), member 1	0.63	0.011
C10orf95	chromosome 10 open reading frame 95	0.63	0.032
TBC1D3F	TBC1 domain family, member 3F	0.63	0.020
SH3YL1	SH3 domain containing, Ysc84-like 1 (S. cerevisiae)	0.63	0.017
BIN3-IT1	uncharacterized LOC80094	0.63	0.032
CYP2B7P	cytochrome P450, family 2, subfamily B, polypeptide 7 pseudogene 1	0.63	0.031
LOC440434	aminopeptidase puromycin sensitive pseudogene	0.63	0.039
INSR	insulin receptor	0.63	0.05
ZNF540	zinc finger protein 540	0.63	0.042
F2RL2	coagulation factor II (thrombin) receptor-like 2	0.63	0.048
CACNB4	calcium channel, voltage-dependent, beta 4 subunit	0.63	0.009
SEC14L6	SEC14-like 6 (S. cerevisiae)	0.63	0.006
PDK4	pyruvate dehydrogenase kinase, isozyme 4	0.63	0.039
SLC25A29	solute carrier family 25 (mitochondrial carnitine/acylcarnitine carrier), member 29	0.64	0.011
YPEL4	yippee-like 4 (Drosophila)	0.64	0.015
DICER1-AS1	DICER1 antisense RNA 1	0.64	0.023
TMEM61	transmembrane protein 61	0.64	0.022
VAC14-AS1	uncharacterized LOC100130894	0.64	0.018
DGCR5	DiGeorge syndrome critical region gene 5 (non-protein coding)	0.64	0.003
ASS1	argininosuccinate synthase 1	0.64	0.005
RSRP1	chromosome 1 open reading frame 63	0.64	0.002
LINC00937	uncharacterized LOC389634	0.64	0.018
CYP21A1P	cytochrome P450, family 21, subfamily A, polypeptide 1 pseudogene	0.64	0.031
MAPK8IP3	mitogen-activated protein kinase 8 interacting protein 3	0.64	0.037

RNASET2	ribonuclease T2	0.64	0.004
AMT	aminomethyltransferase	0.64	0.009
UGT1A6	UDP glucuronosyltransferase 1 family, polypeptide A6	0.64	0.003
GPRC5A	G protein-coupled receptor, family C, group 5, member A	0.64	0.002
KLHL6	kelch-like family member 6	0.64	0.003
THBS3	thrombospondin 3	0.64	0.004
SNORA6	small nucleolar RNA, H/ACA box 6	0.64	0.014
PLXNA3	plexin A3	0.64	0.024
CLDN14	claudin 14	0.64	0.034
LETMD1	LETM1 domain containing 1	0.64	0.009
PAQR6	progestin and adipoQ receptor family member VI	0.65	0.003
TCN2	transcobalamin II	0.65	0.019
SEC14L5	SEC14-like 5 (S. cerevisiae)	0.65	0.025
CD55	CD55 molecule, decay accelerating factor for complement (Cromer blood group)	0.65	0.012
CLEC19A	C-type lectin domain family 19, member A	0.65	0.028
SYTL3	synaptotagmin-like 3	0.65	0.0005
SCARF1	scavenger receptor class F, member 1	0.65	0.005
PPP1R3E	protein phosphatase 1, regulatory subunit 3E	0.65	0.044
LGALS1	lectin, galactoside-binding, soluble, 1	0.65	0.013
LRAT	lecithin retinol acyltransferase (phosphatidylcholine--retinol O-acyltransferase)	0.65	0.025
CCDC114	coiled-coil domain containing 114	0.65	0.026
ADAMTS14	ADAM metallopeptidase with thrombospondin type 1 motif, 14	0.65	0.041
SLC25A27	solute carrier family 25, member 27	0.65	0.038
PAXIP1-AS1	uncharacterized LOC202781	0.65	0.043
ARNT2	aryl-hydrocarbon receptor nuclear translocator 2	0.65	0.026
LOC728743	zinc finger protein pseudogene	0.65	0.015
PAG1	phosphoprotein associated with glycosphingolipid microdomains 1	0.65	0.034
GPR146	G protein-coupled receptor 146	0.65	0.035
FANK1	fibronectin type III and ankyrin repeat domains 1	0.65	0.014
MC1R	melanocortin 1 receptor (alpha melanocyte stimulating hormone receptor)	0.66	0.008
VWA7	von Willebrand factor A domain containing 7	0.66	0.025
EMILIN3	elastin microfibril interfacer 3	0.66	0.006
CCDC88B	coiled-coil domain containing 88B	0.66	0.011
LOC100506469	uncharacterized LOC100506469	0.66	0.015
CD36	CD36 molecule (thrombospondin receptor)	0.66	0.025
LENG8	leukocyte receptor cluster (LRC) member 8	0.66	0.011
ATP6V1B1	ATPase, H+ transporting, lysosomal 56/58kDa, V1 subunit B1	0.66	0.032
KIZ	polo-like kinase 1 substrate 1	0.66	0.023
ADHFE1	alcohol dehydrogenase, iron containing, 1	0.66	0.018

LOC400655	uncharacterized LOC400655	0.66	0.007
PEX6	peroxisomal biogenesis factor 6	0.66	0.003
IFNE	interferon, epsilon	0.67	0.024
CYP2E1	cytochrome P450, family 2, subfamily E, polypeptide 1	0.67	<0.0001
KCND1	potassium voltage-gated channel, Shal-related subfamily, member 1	0.67	0.045

Supplementary Table S6: List of DEGs with significant Fold Changes in RPTEC/TERT1 cells without and with MSC co-culture in mannitol (MAN) condition

🟨	Higher expression in No-MSC versus MSC co-culture (MAN)		
🟦	Lower expression in No-MSC versus MSC co-culture (MAN)		
Gene Symbol	**Gene Description**	**Fold change No-MSC vs MSC**	**P Value**
KBTBD8	kelch repeat and BTB (POZ) domain containing 8	26.00	0.045
GAL	galanin/GMAP prepropeptide	12.40	0.042
BEGAIN	brain-enriched guanylate kinase-associated	11.00	0.044
MYRIP	myosin VIIA and Rab interacting protein	10.00	0.035
ZFP91-CNTF	ZFP91-CNTF readthrough (non-protein coding)	8.63	0.002
IL1RL1	interleukin 1 receptor-like 1	8.14	0.045
ATOH8	atonal homolog 8 (Drosophila)	8.00	0.020
AOX1	aldehyde oxidase 1	7.75	0.004
CABYR	calcium binding tyrosine-(Y)-phosphorylation regulated	6.67	0.011
TMEFF1	transmembrane protein with EGF-like and two follistatin-like domains 1	6.36	0.025
THRSP	thyroid hormone responsive	6.33	0.022
EPN2-IT1	EPN2 intronic transcript 1 (non-protein coding)	6.00	0.031
B3GALT1	UDP-Gal:betaGlcNAc beta 1,3-galactosyltransferase, polypeptide 1	5.45	0.003
RAB40AL	RAB40A, member RAS oncogene family-like	5.44	0.044
PCDHA11	protocadherin alpha 11	5.00	0.015
UBD	ubiquitin D	4.66	0.033
-	BMS1 pseudogene 2	4.63	0.018
HIST1H4H	histone cluster 1, H4h	4.55	0.019
MIR4683	microRNA 4683	4.48	0.021
AVPR1B	arginine vasopressin receptor 1B	4.47	0.018
ASIC5	acid-sensing (proton-gated) ion channel family member 5	4.33	0.038
LOC339240	keratin 17 pseudogene	4.20	0.047
NAV3	neuron navigator 3	4.05	0.017
PLEKHS1	pleckstrin homology domain containing, family S member 1	4.04	0.033
SYT1	synaptotagmin I	4.00	0.020
BEND6	BEN domain containing 6	4.00	0.027
ALKBH3-AS1	uncharacterized LOC100507300	4.00	0.035
SNORA76C	small nucleolar RNA, H/ACA box 76	3.71	0.023
C6orf7	chromosome 6 open reading frame 7	3.65	0.05
FLJ22447	uncharacterized LOC400221	3.55	0.003
UNC45B	unc-45 homolog B (C. elegans)	3.50	0.038
TMEM72	transmembrane protein 72	3.25	0.006
OR12D2	olfactory receptor, family 12, subfamily D, member 2	3.20	0.017
LINC00518	long intergenic non-protein coding RNA 518	3.20	0.032

MIR3960	microRNA 3960	3.12	0.013
BMPR1B	bone morphogenetic protein receptor, type IB	3.11	0.011
CCL2	chemokine (C-C motif) ligand 2	3.11	0.019
PPM1L	protein phosphatase, Mg2+/Mn2+ dependent, 1L	3.02	0.001
APOL3	apolipoprotein L, 3	3.00	0.010
NLRP9	NLR family, pyrin domain containing 9	3.00	0.010
EPPK1	epiplakin 1	3.00	0.038
LINC00313	long intergenic non-protein coding RNA 313	3.00	0.040
STEAP1B	STEAP family member 1B	3.00	0.026
FAM66B	family with sequence similarity 66, member B	2.95	0.021
CXCL2	chemokine (C-X-C motif) ligand 2	2.94	0.027
PLAC8L1	PLAC8-like 1	2.93	0.008
MIR200A	microRNA 200a	2.92	0.042
PHGDH	phosphoglycerate dehydrogenase	2.91	0.021
BEST3	bestrophin 3	2.89	0.042
ERCC6L	excision repair cross-complementing rodent repair deficiency, complementation group 6-like	2.86	0.006
MCM10	minichromosome maintenance complex component 10	2.86	0.004
ABCA12	ATP-binding cassette, sub-family A (ABC1), member 12	2.84	0.037
EXO1	exonuclease 1	2.82	0.005
SKA3	spindle and kinetochore associated complex subunit 3	2.82	0.008
CASC5	cancer susceptibility candidate 5	2.78	0.022
SCUBE3	signal peptide, CUB domain, EGF-like 3	2.78	0.004
HIST1H2AG	histone cluster 1, H2ag	2.77	0.045
ASPM	asp (abnormal spindle) homolog, microcephaly associated (Drosophila)	2.77	0.005
EGFR-AS1	EGFR antisense RNA 1	2.76	0.028
ESCO2	establishment of cohesion 1 homolog 2 (S. cerevisiae)	2.76	0.014
C17orf51	chromosome 17 open reading frame 51	2.74	0.033
SYT16	synaptotagmin XVI	2.74	0.049
POLQ	polymerase (DNA directed), theta	2.73	0.0006
HIST1H2BC	histone cluster 1, H2bc	2.72	0.038
GREM1	gremlin 1, DAN family BMP antagonist	2.71	0.045
KIF14	kinesin family member 14	2.70	0.007
SSR4P1	signal sequence receptor, delta pseudogene 1	2.69	0.048
SERTAD4	SERTA domain containing 4	2.68	0.012
LNPEP	leucyl/cystinyl aminopeptidase	2.68	0.040
DEPDC1	DEP domain containing 1	2.61	0.004
NCR3LG1	natural killer cell cytotoxicity receptor 3 ligand 1	2.61	0.039
LINC00701	long intergenic non-protein coding RNA 701	2.60	0.015
TP53AIP1	tumor protein p53 regulated apoptosis inducing protein 1	2.60	0.048
CKAP2L	cytoskeleton associated protein 2-like	2.59	0.0009
FAM111B	family with sequence similarity 111, member B	2.58	0.010

GDAP1	ganglioside induced differentiation associated protein 1	2.57	<0.0001
SELL	selectin L	2.57	0.011
MLLT10P1	myeloid/lymphoid or mixed-lineage leukemia (trithorax homolog, Drosophila); translocated to, 10 pseudogene 1	2.57	0.041
ZIC5	Zic family member 5	2.56	0.011
BRCA2	breast cancer 2, early onset	2.54	0.0009
ANLN	anillin, actin binding protein	2.53	0.007
TGFB2	transforming growth factor, beta 2	2.52	0.004
SLFN11	schlafen family member 11	2.50	0.026
SNORD26	small nucleolar RNA, C/D box 26	2.50	0.047
ACTL10	actin-like 10	2.49	0.003
DDO	D-aspartate oxidase	2.49	0.001
SOD2	superoxide dismutase 2, mitochondrial	2.49	0.038
KIF26B	kinesin family member 26B	2.48	0.05
PIGR	polymeric immunoglobulin receptor	2.45	0.013
RFX3	regulatory factor X, 3 (influences HLA class II expression)	2.45	0.030
NR1D2	nuclear receptor subfamily 1, group D, member 2	2.44	0.05
CEP97	centrosomal protein 97kDa	2.44	0.049
HMCN1	hemicentin 1	2.43	0.019
GTSE1	G-2 and S-phase expressed 1	2.42	0.007
THSD7B	thrombospondin, type I, domain containing 7B	2.41	0.047
PTGS2	prostaglandin-endoperoxide synthase 2 (prostaglandin G/H synthase and cyclooxygenase)	2.40	0.034
CDC45	cell division cycle 45	2.39	0.004
LRGUK	leucine-rich repeats and guanylate kinase domain containing	2.38	0.029
IL1B	interleukin 1, beta	2.37	<0.0001
IL6	interleukin 6 (interferon, beta 2)	2.37	0.050
C11orf82	chromosome 11 open reading frame 82	2.37	0.015
TERT	telomerase reverse transcriptase	2.37	0.038
HPD	4-hydroxyphenylpyruvate dioxygenase	2.36	0.038
CENPA	centromere protein A	2.36	0.001
GNAZ	guanine nucleotide binding protein (G protein), alpha z polypeptide	2.36	0.024
CENPF	centromere protein F, 350/400kDa	2.36	0.003
PBK	PDZ binding kinase	2.35	0.022
ACTBL2	actin, beta-like 2	2.34	0.032
BUB1B	BUB1 mitotic checkpoint serine/threonine kinase B	2.33	0.006
DTL	denticleless E3 ubiquitin protein ligase homolog (Drosophila)	2.33	0.020
TOP2A	topoisomerase (DNA) II alpha 170kDa	2.33	0.003
DLL3	delta-like 3 (Drosophila)	2.32	0.019
BLM	Bloom syndrome, RecQ helicase-like	2.32	0.037
SLFN5	schlafen family member 5	2.32	0.049
CDKL5	cyclin-dependent kinase-like 5	2.30	0.05

DYNC1I1	dynein, cytoplasmic 1, intermediate chain 1	2.30	0.033
ALPK2	alpha-kinase 2	2.28	0.013
ERCC6L2	excision repair cross-complementing rodent repair deficiency, complementation group 6-like 2	2.26	0.008
CDCA5	cell division cycle associated 5	2.26	0.004
EDN2	endothelin 2	2.26	0.023
FAM71F1	family with sequence similarity 71, member F1	2.25	0.038
KIF15	kinesin family member 15	2.25	0.005
PTPLB	protein tyrosine phosphatase-like (proline instead of catalytic arginine), member b	2.24	0.032
NDC80	NDC80 kinetochore complex component	2.23	0.013
ITIH2	inter-alpha-trypsin inhibitor heavy chain 2	2.23	0.0007
TMPO-AS1	TMPO antisense RNA 1	2.23	0.012
SHCBP1	SHC SH2-domain binding protein 1	2.22	0.016
TRIM6	tripartite motif containing 6	2.22	0.006
PCNA-AS1	PCNA antisense RNA 1	2.20	0.001
COL21A1	collagen, type XXI, alpha 1	2.19	0.046
RC3H2	ring finger and CCCH-type domains 2	2.18	0.039
DLGAP5	discs, large (Drosophila) homolog-associated protein 5	2.18	0.009
MIR4321	microRNA 4321	2.18	0.044
TLL1	tolloid-like 1	2.18	0.017
NUF2	NUF2, NDC80 kinetochore complex component, homolog (S. cerevisiae)	2.17	0.025
PMFBP1	polyamine modulated factor 1 binding protein 1	2.17	0.005
ZGRF1	chromosome 4 open reading frame 21	2.16	0.012
RRAD	Ras-related associated with diabetes	2.16	0.010
MKI67	antigen identified by monoclonal antibody Ki-67	2.16	0.007
HELLS	helicase, lymphoid-specific	2.14	<0.0001
KIF4A	kinesin family member 4A	2.14	0.001
PTPRB	protein tyrosine phosphatase, receptor type, B	2.14	0.0004
BARD1	BRCA1 associated RING domain 1	2.12	0.05
SPC24	SPC24, NDC80 kinetochore complex component, homolog (S. cerevisiae)	2.12	0.009
CEP55	centrosomal protein 55kDa	2.12	0.031
LDHAL6B	lactate dehydrogenase A-like 6B	2.11	0.041
KCNAB3	potassium voltage-gated channel, shaker-related subfamily, beta member 3	2.11	0.041
SNORD16	small nucleolar RNA, C/D box 16	2.11	0.007
RAD51AP1	RAD51 associated protein 1	2.11	0.007
NIPAL1	NIPA-like domain containing 1	2.10	0.024
SYNE1	spectrin repeat containing, nuclear envelope 1	2.10	0.037
TNF	tumor necrosis factor	2.09	0.017
C3orf36	chromosome 3 open reading frame 36	2.09	0.0007

RFC3	replication factor C (activator 1) 3, 38kDa	2.08	0.016
ANTXR1	anthrax toxin receptor 1	2.07	0.0009
ULBP3	UL16 binding protein 3	2.07	0.016
XYLB	xylulokinase homolog (H. influenzae)	2.07	0.040
FRK	fyn-related kinase	2.07	0.037
BIRC5	baculoviral IAP repeat containing 5	2.06	0.012
CLIC5	chloride intracellular channel 5	2.06	0.024
ZNF891	zinc finger protein 891	2.04	0.05
GPR89B	G protein-coupled receptor 89B	2.03	0.042
PCLO	piccolo presynaptic cytomatrix protein	2.03	0.016
WDR43	WD repeat domain 43	2.03	0.037
PSAT1	phosphoserine aminotransferase 1	2.03	0.031
LRRC31	leucine rich repeat containing 31	2.03	0.035
LCN2	lipocalin 2	2.02	0.044
ENC1	ectodermal-neural cortex 1 (with BTB domain)	2.01	0.014
IKZF2	IKAROS family zinc finger 2 (Helios)	2.01	0.028
TGM4	transglutaminase 4 (prostate)	2.00	0.035
NUSAP1	nucleolar and spindle associated protein 1	2.00	0.033
IL6ST	interleukin 6 signal transducer (gp130, oncostatin M receptor)	2.00	0.042
NEBL	nebulette	1.99	0.041
BDNF	brain-derived neurotrophic factor	1.99	0.024
CIITA	class II, major histocompatibility complex, transactivator	1.99	0.023
CDC6	cell division cycle 6	1.98	0.016
ALKBH8	alkB, alkylation repair homolog 8 (E. coli)	1.98	0.014
LARP4	La ribonucleoprotein domain family, member 4	1.98	0.049
VTI1A	vesicle transport through interaction with t-SNAREs 1A	1.98	0.012
CAPN13	calpain 13	1.98	0.0007
DHRS3	dehydrogenase/reductase (SDR family) member 3	1.98	0.047
TICRR	TOPBP1-interacting checkpoint and replication regulator	1.97	0.018
GPATCH11	G patch domain containing 11	1.97	0.049
TTK	TTK protein kinase	1.97	0.007
CENPE	centromere protein E, 312kDa	1.97	0.010
NTM	neurotrimin	1.97	0.015
ASAH2	N-acylsphingosine amidohydrolase (non-lysosomal ceramidase) 2	1.97	0.033
NCAPG2	non-SMC condensin II complex, subunit G2	1.97	0.008
CXCL1	chemokine (C-X-C motif) ligand 1 (melanoma growth stimulating activity, alpha)	1.95	0.025
PCDHB13	protocadherin beta 13	1.95	0.016
SOSTDC1	sclerostin domain containing 1	1.95	0.003
CDK1	cyclin-dependent kinase 1	1.95	0.019
HEG1	heart development protein with EGF-like domains 1	1.94	0.005
ZWINT	ZW10 interactor, kinetochore protein	1.94	0.005

MIR1260B	microRNA 1260b		1.94	0.018
NCAPH	non-SMC condensin I complex, subunit H		1.94	0.036
SERPINB8	serpin peptidase inhibitor, clade B (ovalbumin), member 8		1.94	0.003
DNAJC6	DnaJ (Hsp40) homolog, subfamily C, member 6		1.93	0.023
FBXO5	F-box protein 5		1.93	0.013
MYBL1	v-myb myeloblastosis viral oncogene homolog (avian)-like 1		1.93	0.017
DDX11-AS1	DDX11 antisense RNA 1		1.93	0.013
CHAC2	ChaC, cation transport regulator homolog 2 (E. coli)		1.92	0.039
TAS1R3	taste receptor, type 1, member 3		1.92	0.029
KIFC1	kinesin family member C1		1.92	0.015
SLFN12	schlafen family member 12		1.92	0.026
EBLN2	endogenous Bornavirus-like nucleoprotein 2		1.91	0.001
BICC1	bicaudal C homolog 1 (Drosophila)		1.91	0.034
LATS1	LATS, large tumor suppressor, homolog 1 (Drosophila)		1.91	0.019
SPAG5	sperm associated antigen 5		1.91	0.009
KIF20B	kinesin family member 20B		1.90	0.002
MCM4	minichromosome maintenance complex component 4		1.90	0.004
C1orf101	chromosome 1 open reading frame 101		1.89	0.020
IL9R	interleukin 9 receptor		1.89	0.020
POLR3B	polymerase (RNA) III (DNA directed) polypeptide B		1.89	0.012
COL12A1	collagen, type XII, alpha 1		1.89	0.042
AMD1	adenosylmethionine decarboxylase 1		1.89	0.036
SOX6	SRY (sex determining region Y)-box 6		1.88	0.049
HMMR	hyaluronan-mediated motility receptor (RHAMM)		1.88	0.009
GINS4	GINS complex subunit 4 (Sld5 homolog)		1.88	0.009
KRTAP5-4	keratin associated protein 5-4		1.88	0.020
CHAC1	ChaC, cation transport regulator homolog 1 (E. coli)		1.88	0.05
ATAD2	ATPase family, AAA domain containing 2		1.87	0.033
TWISTNB	TWIST neighbor		1.86	0.049
ZFAND4	zinc finger, AN1-type domain 4		1.86	0.015
GAN	gigaxonin		1.86	0.024
CXCL3	chemokine (C-X-C motif) ligand 3		1.86	0.037
MAFB	v-maf musculoaponeurotic fibrosarcoma oncogene homolog B (avian)		1.86	0.005
GRHL1	grainyhead-like 1 (Drosophila)		1.86	0.012
RRM2	ribonucleotide reductase M2		1.86	0.021
RAPGEF6	Rap guanine nucleotide exchange factor (GEF) 6		1.86	0.040
MARS2	methionyl-tRNA synthetase 2, mitochondrial		1.86	0.041
SFMBT1	Scm-like with four mbt domains 1		1.86	0.011
FBXO43	F-box protein 43		1.86	0.023
FITM2	fat storage-inducing transmembrane protein 2		1.86	0.047
LTB	lymphotoxin beta (TNF superfamily, member 3)		1.86	0.033
NRP1	neuropilin 1		1.86	0.0001

NRIP1	nuclear receptor interacting protein 1	1.85	0.042
SMG1P5	smg-1 homolog, phosphatidylinositol 3-kinase-related kinase (C. elegans) pseudogene	1.85	0.028
PCNA	proliferating cell nuclear antigen	1.85	0.023
CMTR2	FtsJ methyltransferase domain containing 1	1.85	0.05
SMC4	structural maintenance of chromosomes 4	1.85	0.022
ZWILCH	zwilch kinetochore protein	1.85	0.006
ZNF407	zinc finger protein 407	1.84	0.033
KIF11	kinesin family member 11	1.84	0.003
TCF19	transcription factor 19	1.84	0.010
RCAN2	regulator of calcineurin 2	1.84	0.029
KIF23	kinesin family member 23	1.83	0.022
PIK3AP1	phosphoinositide-3-kinase adaptor protein 1	1.83	0.020
C21orf67	chromosome 21 open reading frame 67	1.83	0.0004
CCNA2	cyclin A2	1.82	0.020
ORC1	origin recognition complex, subunit 1	1.82	0.007
ZNF300	zinc finger protein 300	1.82	0.020
FAM83D	family with sequence similarity 83, member D	1.82	0.026
DHFR	dihydrofolate reductase	1.81	0.008
CDCA8	cell division cycle associated 8	1.81	0.016
TBC1D30	TBC1 domain family, member 30	1.80	0.003
LCTL	lactase-like	1.80	0.009
ENOX2	ecto-NOX disulfide-thiol exchanger 2	1.80	0.044
PHLPP2	PH domain and leucine rich repeat protein phosphatase 2	1.80	0.037
ZNF827	zinc finger protein 827	1.80	0.018
KIF20A	kinesin family member 20A	1.80	0.018
ASCC3	activating signal cointegrator 1 complex subunit 3	1.80	0.046
MEGF11	multiple EGF-like-domains 11	1.80	0.0007
PTPRN2	protein tyrosine phosphatase, receptor type, N polypeptide 2	1.80	0.031
FAM126A	family with sequence similarity 126, member A	1.80	0.027
PLK2	polo-like kinase 2	1.79	0.042
PCDH20	protocadherin 20	1.79	0.044
BMP2K	BMP2 inducible kinase	1.79	0.043
KLHL23	kelch-like family member 23	1.79	0.005
ZNF365	zinc finger protein 365	1.79	0.006
ITGA4	integrin, alpha 4 (antigen CD49D, alpha 4 subunit of VLA-4 receptor)	1.79	0.032
ACER3	alkaline ceramidase 3	1.79	0.003
PLK4	polo-like kinase 4	1.78	0.004
DPY19L2P1	dpy-19-like 2 pseudogene 1 (C. elegans)	1.78	0.048
MFAP3L	microfibrillar-associated protein 3-like	1.78	0.001
DSCC1	defective in sister chromatid cohesion 1 homolog (S. cerevisiae)	1.78	0.012

MAD2L1	MAD2 mitotic arrest deficient-like 1 (yeast)	1.77	0.006
DIAPH3	diaphanous homolog 3 (Drosophila)	1.77	0.034
CTGF	connective tissue growth factor	1.77	0.013
LIMCH1	LIM and calponin homology domains 1	1.77	0.009
INCENP	inner centromere protein antigens 135/155kDa	1.77	0.016
SETD9	SET domain containing 9	1.77	0.015
UHRF1	ubiquitin-like with PHD and ring finger domains 1	1.76	0.028
GRIP1	glutamate receptor interacting protein 1	1.76	0.0007
PVRL4	poliovirus receptor-related 4	1.76	0.011
DHX9	DEAH (Asp-Glu-Ala-His) box polypeptide 9	1.76	0.021
FAM64A	family with sequence similarity 64, member A	1.76	0.033
MBNL2	muscleblind-like splicing regulator 2	1.75	0.048
KIF18A	kinesin family member 18A	1.75	0.012
HJURP	Holliday junction recognition protein	1.75	0.002
EFNB2	ephrin-B2	1.74	0.014
LMNB1	lamin B1	1.74	0.013
LHFP	lipoma HMGIC fusion partner	1.74	0.040
PKHD1	polycystic kidney and hepatic disease 1 (autosomal recessive)	1.74	0.038
MYCBP2	MYC binding protein 2, E3 ubiquitin protein ligase	1.74	0.044
MYO5A	myosin VA (heavy chain 12, myoxin)	1.74	0.034
TMPO	thymopoietin	1.74	0.041
RSC1A1	regulatory solute carrier protein, family 1, member 1	1.74	0.012
BHLHE40-AS1	BHLHE40 antisense RNA 1	1.74	0.049
NTRK2	neurotrophic tyrosine kinase, receptor, type 2	1.73	0.006
TLR3	toll-like receptor 3	1.73	0.007
DCBLD1	discoidin, CUB and LCCL domain containing 1	1.73	0.039
RAB11FIP2	RAB11 family interacting protein 2 (class I)	1.73	0.026
PELI1	pellino E3 ubiquitin protein ligase 1	1.73	0.043
ESRRG	estrogen-related receptor gamma	1.73	0.013
SLMO2-ATP5E	SLMO2-ATP5E readthrough	1.72	0.047
SGOL2	shugoshin-like 2 (S. pombe)	1.72	0.007
VNN1	vanin 1	1.72	0.049
NTN4	netrin 4	1.72	0.033
HIST1H2AC	histone cluster 1, H2ac	1.72	0.018
EPC2	enhancer of polycomb homolog 2 (Drosophila)	1.72	0.022
CHORDC1	cysteine and histidine-rich domain (CHORD) containing 1	1.72	0.048
CCAR1	cell division cycle and apoptosis regulator 1	1.72	0.05
HIPK2	homeodomain interacting protein kinase 2	1.72	0.046
FNDC3B	fibronectin type III domain containing 3B	1.72	0.040
CEP76	centrosomal protein 76kDa	1.72	0.009
CYR61	cysteine-rich, angiogenic inducer, 61	1.72	0.003
FOXM1	forkhead box M1	1.71	0.018

EFCAB5	EF-hand calcium binding domain 5	1.71	0.024
CRIM1	cysteine rich transmembrane BMP regulator 1 (chordin-like)	1.71	0.05
STAG1	stromal antigen 1	1.71	0.016
ERO1LB	ERO1-like beta (S. cerevisiae)	1.71	0.005
CENPK	centromere protein K	1.71	0.041
KIAA1024	KIAA1024	1.71	0.042
ECE2	endothelin converting enzyme 2	1.70	0.027
PIGW	phosphatidylinositol glycan anchor biosynthesis, class W	1.70	0.021
CTTNBP2	cortactin binding protein 2	1.70	0.010
GPC2	glypican 2	1.70	0.016
SLC26A2	solute carrier family 26 (sulfate transporter), member 2	1.70	0.049
KPNA2	karyopherin alpha 2 (RAG cohort 1, importin alpha 1)	1.70	0.041
UHRF1BP1L	UHRF1 binding protein 1-like	1.70	0.031
CCNB1	cyclin B1	1.70	0.007
SEMA3A	sema domain, immunoglobulin domain (Ig), short basic domain, secreted, (semaphorin) 3A	1.70	0.011
ACVR1C	activin A receptor, type IC	1.70	0.004
F11-AS1	uncharacterized LOC285441	1.70	0.001
NIPAL2	NIPA-like domain containing 2	1.69	0.048
LCA5	Leber congenital amaurosis 5	1.69	0.045
SPPL2A	signal peptide peptidase like 2A	1.69	0.048
FAM102B	family with sequence similarity 102, member B	1.69	0.047
DCUN1D1	DCN1, defective in cullin neddylation 1, domain containing 1 (S. cerevisiae)	1.69	0.049
ALMS1	Alstrom syndrome 1	1.69	0.006
FBXL4	F-box and leucine-rich repeat protein 4	1.69	0.045
INPP4B	inositol polyphosphate-4-phosphatase, type II, 105kDa	1.69	0.021
PHACTR2	phosphatase and actin regulator 2	1.69	0.028
LZTS1	leucine zipper, putative tumor suppressor 1	1.68	0.019
TRIP13	thyroid hormone receptor interactor 13	1.68	0.033
CKAP2	cytoskeleton associated protein 2	1.68	0.034
MID1	midline 1 (Opitz/BBB syndrome)	1.68	0.002
CHUK	conserved helix-loop-helix ubiquitous kinase	1.68	0.028
TENM4	teneurin transmembrane protein 4	1.68	0.026
IQGAP3	IQ motif containing GTPase activating protein 3	1.68	0.011
ZBTB6	zinc finger and BTB domain containing 6	1.68	0.042
HIF1A	hypoxia inducible factor 1, alpha subunit (basic helix-loop-helix transcription factor)	1.68	0.019
TROAP	trophinin associated protein	1.68	0.034
NCAPG	non-SMC condensin I complex, subunit G	1.68	0.012
KLHDC7A	kelch domain containing 7A	1.68	0.002
UBTD2	ubiquitin domain containing 2	1.68	0.013
CDC25A	cell division cycle 25A	1.68	0.004

G3BP1	GTPase activating protein (SH3 domain) binding protein 1	1.67	0.023
ARHGAP11A	Rho GTPase activating protein 11A	1.67	0.001
PDF	peptide deformylase (mitochondrial)	1.67	0.003
SLC31A2	solute carrier family 31 (copper transporters), member 2	1.67	0.011
CDC73	cell division cycle 73	1.67	0.05
CDCA2	cell division cycle associated 2	1.67	0.005
PINX1	PIN2/TERF1 interacting, telomerase inhibitor 1	1.67	0.032
VANGL1	VANGL planar cell polarity protein 1	1.67	0.014
DNAH5	dynein, axonemal, heavy chain 5	1.66	0.044
TNC	tenascin C	1.66	0.006
TMEM38B	transmembrane protein 38B	1.66	0.049
TEX10	testis expressed 10	1.66	0.017
LTV1	LTV1 homolog (S. cerevisiae)	1.66	0.028
SETBP1	SET binding protein 1	1.66	0.040
HCFC2	host cell factor C2	1.66	0.016
HHEX	hematopoietically expressed homeobox	1.65	0.015
EPHA4	EPH receptor A4	1.65	0.010
PARPBP	PARP1 binding protein	1.65	0.036
GPD2	glycerol-3-phosphate dehydrogenase 2 (mitochondrial)	1.65	0.026
ENTPD7	ectonucleoside triphosphate diphosphohydrolase 7	1.65	0.035
APC	adenomatous polyposis coli	1.65	0.011
WDR3	WD repeat domain 3	1.65	0.05
FEN1	flap structure-specific endonuclease 1	1.65	0.022
STS	steroid sulfatase (microsomal), isozyme S	1.65	0.026
QSER1	glutamine and serine rich 1	1.64	0.030
B3GALT5	UDP-Gal:betaGlcNAc beta 1,3-galactosyltransferase, polypeptide 5	1.64	0.025
MELK	maternal embryonic leucine zipper kinase	1.64	0.004
LRCH3	leucine-rich repeats and calponin homology (CH) domain containing 3	1.64	0.031
GPAM	glycerol-3-phosphate acyltransferase, mitochondrial	1.64	0.032
NOP56	NOP56 ribonucleoprotein	1.64	0.010
ZNF778	zinc finger protein 778	1.64	0.015
ZC2HC1C	zinc finger, C2HC-type containing 1C	1.64	0.021
DCAF13	DDB1 and CUL4 associated factor 13	1.64	0.024
MAP3K1	mitogen-activated protein kinase kinase kinase 1, E3 ubiquitin protein ligase	1.64	0.029
ZDHHC20	zinc finger, DHHC-type containing 20	1.64	0.027
CALCRL	calcitonin receptor-like	1.63	0.008
DCK	deoxycytidine kinase	1.63	0.046
SYNCRIP	synaptotagmin binding, cytoplasmic RNA interacting protein	1.63	0.043
EFR3A	EFR3 homolog A (S. cerevisiae)	1.63	0.038
CDC20	cell division cycle 20	1.63	0.040

PRIM2	primase, DNA, polypeptide 2 (58kDa)	1.63	0.048
MGA	MGA, MAX dimerization protein	1.63	0.045
HS2ST1	heparan sulfate 2-O-sulfotransferase 1	1.63	0.028
SGMS1	sphingomyelin synthase 1	1.62	0.010
CCNF	cyclin F	1.62	0.039
ERAP2	endoplasmic reticulum aminopeptidase 2	1.62	0.027
BCLAF1	BCL2-associated transcription factor 1	1.62	0.029
MCM2	minichromosome maintenance complex component 2	1.62	0.025
MKL2	MKL/myocardin-like 2	1.62	0.028
ZNF326	zinc finger protein 326	1.62	0.032
EXOC6	exocyst complex component 6	1.62	0.044
POP1	processing of precursor 1, ribonuclease P/MRP subunit (S. cerevisiae)	1.62	0.029
NDST1	N-deacetylase/N-sulfotransferase (heparan glucosaminyl) 1	1.62	0.025
KIAA1462	KIAA1462	1.61	0.005
NOP2	NOP2 nucleolar protein	1.61	0.022
KGFLP1	fibroblast growth factor 7 pseudogene	1.61	0.026
NSUN3	NOP2/Sun domain family, member 3	1.61	0.017
AP5M1	adaptor-related protein complex 5, mu 1 subunit	1.61	0.020
DHX36	DEAH (Asp-Glu-Ala-His) box polypeptide 36	1.61	0.033
OAS3	2'-5'-oligoadenylate synthetase 3, 100kDa	1.61	0.043
NRG1	neuregulin 1	1.61	0.026
TGFBR2	transforming growth factor, beta receptor II (70/80kDa)	1.61	0.012
ITPR2	inositol 1,4,5-trisphosphate receptor, type 2	1.61	0.020
TRANK1	tetratricopeptide repeat and ankyrin repeat containing 1	1.61	0.0004
PEG10	paternally expressed 10	1.61	0.025
ZNF530	zinc finger protein 530	1.61	0.012
CEP57L1	centrosomal protein 57kDa-like 1	1.61	0.023
NIN	ninein (GSK3B interacting protein)	1.61	0.046
DOCK3	dedicator of cytokinesis 3	1.61	0.010
MBNL3	muscleblind-like splicing regulator 3	1.61	0.029
CSRNP3	cysteine-serine-rich nuclear protein 3	1.60	0.044
KLHL14	kelch-like family member 14	1.60	0.010
RECQL4	RecQ protein-like 4	1.60	0.028
KIAA1468	KIAA1468	1.60	0.031
SMC1A	structural maintenance of chromosomes 1A	1.60	0.042
BIRC3	baculoviral IAP repeat containing 3	1.60	0.040
BAZ1A	bromodomain adjacent to zinc finger domain, 1A	1.60	0.040
ERVMER34-1	endogenous retrovirus group MER34, member 1	1.60	0.020
RNF144B	ring finger protein 144B	1.60	0.005
CBX2	chromobox homolog 2	1.60	0.024
ZNF485	zinc finger protein 485	1.60	0.032
ABCB1	ATP-binding cassette, sub-family B (MDR/TAP), member 1	1.60	0.020

THBS1	thrombospondin 1	1.60	0.045
IFI16	interferon, gamma-inducible protein 16	1.60	0.008
GINS3	GINS complex subunit 3 (Psf3 homolog)	1.60	0.004
TMEM2	transmembrane protein 2	1.60	0.038
INHBB	inhibin, beta B	1.60	0.030
MBNL1	muscleblind-like splicing regulator 1	1.60	0.048
USP31	ubiquitin specific peptidase 31	1.59	0.038
ECT2	epithelial cell transforming sequence 2 oncogene	1.59	0.031
SCYL2	SCY1-like 2 (S. cerevisiae)	1.59	0.044
TRIM33	tripartite motif containing 33	1.59	0.05
TRIP11	thyroid hormone receptor interactor 11	1.59	0.039
ATL3	atlastin GTPase 3	1.59	0.039
TNFAIP2	tumor necrosis factor, alpha-induced protein 2	1.58	0.006
PLEK	pleckstrin	1.58	0.021
BUB1	BUB1 mitotic checkpoint serine/threonine kinase	1.58	0.003
ITGA1	integrin, alpha 1	1.58	0.003
TMEM178B	transmembrane protein 178B	1.58	0.037
SAMHD1	SAM domain and HD domain 1	1.58	0.040
ZNF319	zinc finger protein 319	1.58	0.007
LIN54	lin-54 homolog (C. elegans)	1.58	0.023
SLC38A1	solute carrier family 38, member 1	1.58	0.034
RAPGEF2	Rap guanine nucleotide exchange factor (GEF) 2	1.58	0.044
TCF12	transcription factor 12	1.58	0.036
TNS3	tensin 3	1.58	0.030
PLXNC1	plexin C1	1.58	0.007
SFTA1P	surfactant associated 1, pseudogene	1.58	0.028
SLC25A46	solute carrier family 25, member 46	1.57	0.022
LIN9	lin-9 homolog (C. elegans)	1.57	0.018
ANKRD44	ankyrin repeat domain 44	1.57	0.010
ABHD5	abhydrolase domain containing 5	1.57	0.003
NRDE2	NRDE-2, necessary for RNA interference, domain containing	1.57	0.041
TTC30A	tetratricopeptide repeat domain 30A	1.57	0.034
ING3	inhibitor of growth family, member 3	1.57	0.028
PKMYT1	protein kinase, membrane associated tyrosine/threonine 1	1.57	0.018
KCTD12	potassium channel tetramerisation domain containing 12	1.57	0.003
LYPD6	LY6/PLAUR domain containing 6	1.57	0.014
ATP9B	ATPase, class II, type 9B	1.57	0.009
MED1	mediator complex subunit 1	1.57	0.026
MCM3	minichromosome maintenance complex component 3	1.57	0.007
GLIS3	GLIS family zinc finger 3	1.57	0.026
IARS	isoleucyl-tRNA synthetase	1.57	0.021
TRIM31	tripartite motif containing 31	1.56	0.038

TP53RK	TP53 regulating kinase	1.56	0.035
CYP2U1	cytochrome P450, family 2, subfamily U, polypeptide 1	1.56	0.038
TYMS	thymidylate synthetase	1.56	0.005
SPRY3	sprouty homolog 3 (Drosophila)	1.56	0.042
USP16	ubiquitin specific peptidase 16	1.56	0.012
MAP1B	microtubule-associated protein 1B	1.56	0.036
GORAB	golgin, RAB6-interacting	1.56	0.020
LRIG1	leucine-rich repeats and immunoglobulin-like domains 1	1.56	0.039
ADAM28	ADAM metallopeptidase domain 28	1.55	0.006
NCBP1	nuclear cap binding protein subunit 1, 80kDa	1.55	0.033
CP	ceruloplasmin (ferroxidase)	1.55	0.008
KDM8	lysine (K)-specific demethylase 8	1.55	0.008
ZDHHC13	zinc finger, DHHC-type containing 13	1.55	0.043
ZNF345	zinc finger protein 345	1.55	0.036
TRAK2	trafficking protein, kinesin binding 2	1.55	0.022
SYNE3	spectrin repeat containing, nuclear envelope family member 3	1.55	0.032
RACGAP1	Rac GTPase activating protein 1	1.55	0.017
RFK	riboflavin kinase	1.55	0.021
PCYT1A	phosphate cytidylyltransferase 1, choline, alpha	1.55	0.028
SPDL1	spindle apparatus coiled-coil protein 1	1.55	0.040
CIT	citron (rho-interacting, serine/threonine kinase 21)	1.55	0.019
SDPR	serum deprivation response	1.55	0.005
GALNT10	UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 10 (GalNAc-T10)	1.55	0.002
EPHB2	EPH receptor B2	1.55	0.005
GMFB	glia maturation factor, beta	1.54	0.032
ARID2	AT rich interactive domain 2 (ARID, RFX-like)	1.54	0.006
SNHG15	small nucleolar RNA host gene 15 (non-protein coding)	1.54	0.010
LYAR	Ly1 antibody reactive	1.54	0.027
MALT1	mucosa associated lymphoid tissue lymphoma translocation gene 1	1.54	0.012
CROT	carnitine O-octanoyltransferase	1.54	0.023
NOLC1	nucleolar and coiled-body phosphoprotein 1	1.54	0.049
LRRCC1	leucine rich repeat and coiled-coil centrosomal protein 1	1.54	0.032
ZNF624	zinc finger protein 624	1.54	0.022
TMEM199	transmembrane protein 199	1.54	0.011
PPP6R3	protein phosphatase 6, regulatory subunit 3	1.54	0.015
NOL11	nucleolar protein 11	1.54	0.036
RNF219	ring finger protein 219	1.54	0.042
SPAG1	sperm associated antigen 1	1.54	0.0002
PHF20L1	PHD finger protein 20-like 1	1.54	0.046
MTOR	mechanistic target of rapamycin (serine/threonine kinase)	1.54	0.031
RNF219-AS1	RNF219 antisense RNA 1	1.54	0.027

MIPEPP3	mitochondrial intermediate peptidase pseudogene 3	1.54	0.008
PPIP5K2	diphosphoinositol pentakisphosphate kinase 2	1.54	0.021
NLGN1	neuroligin 1	1.53	0.028
C3	complement component 3	1.53	0.027
THAP1	THAP domain containing, apoptosis associated protein 1	1.53	0.004
CYTH3	cytohesin 3	1.53	0.025
ZNF625	zinc finger protein 625	1.53	0.037
LBH	limb bud and heart development	1.53	0.009
ARL15	ADP-ribosylation factor-like 15	1.53	0.047
SLX4IP	SLX4 interacting protein	1.53	0.002
PDS5B	PDS5, regulator of cohesion maintenance, homolog B (S. cerevisiae)	1.53	0.023
PPP2R1B	protein phosphatase 2, regulatory subunit A, beta	1.53	0.046
SRSF3	serine/arginine-rich splicing factor 3	1.53	0.017
NCEH1	neutral cholesterol ester hydrolase 1	1.53	0.029
CGGBP1	CGG triplet repeat binding protein 1	1.53	0.036
H2AFX	H2A histone family, member X	1.52	0.030
RAET1K	retinoic acid early transcript 1K pseudogene	1.52	0.002
G2E3	G2/M-phase specific E3 ubiquitin protein ligase	1.52	0.049
FSTL1	follistatin-like 1	1.52	0.007
ST5	suppression of tumorigenicity 5	1.52	0.023
OSBPL11	oxysterol binding protein-like 11	1.52	0.037
ZCCHC10	zinc finger, CCHC domain containing 10	1.52	0.002
TTN-AS1	TTN antisense RNA 1	1.52	0.024
LOC100132356	uncharacterized LOC100132356	1.52	0.004
EIF4G2	eukaryotic translation initiation factor 4 gamma, 2	1.52	0.025
ATF2	activating transcription factor 2	1.52	0.014
FAM212B	family with sequence similarity 212, member B	1.52	0.017
TIMELESS	timeless circadian clock	1.51	0.001
TRAM1	translocation associated membrane protein 1	1.51	0.004
PPARGC1A	peroxisome proliferator-activated receptor gamma, coactivator 1 alpha	1.51	0.009
ZNF420	zinc finger protein 420	1.51	0.016
CDC27	cell division cycle 27	1.51	0.046
SNX13	sorting nexin 13	1.51	0.028
TWSG1	twisted gastrulation homolog 1 (Drosophila)	1.51	0.008
MFAP3	microfibrillar-associated protein 3	1.51	0.014
NUDT6	nudix (nucleoside diphosphate linked moiety X)-type motif 6	1.51	0.05
TAF5	TAF5 RNA polymerase II, TATA box binding protein (TBP)-associated factor, 100kDa	1.51	0.010
PTCHD3P1	patched domain containing 3 pseudogene 1	1.51	0.044
TMEM168	transmembrane protein 168	1.51	0.038

ERCC4	excision repair cross-complementing rodent repair deficiency, complementation group 4	1.51	0.045
FAM81A	family with sequence similarity 81, member A	1.51	0.028
NETO2	neuropilin (NRP) and tolloid (TLL)-like 2	1.51	0.032
TMEM217	transmembrane protein 217	1.51	0.043
ZC3H12A	zinc finger CCCH-type containing 12A	1.51	0.006
SORT1	sortilin 1	1.51	0.0006
KLHL5	kelch-like family member 5	1.51	0.041
PRC1	protein regulator of cytokinesis 1	1.51	0.014
TACC3	transforming, acidic coiled-coil containing protein 3	1.51	0.020
SLC33A1	solute carrier family 33 (acetyl-CoA transporter), member 1	1.51	0.049
RPGRIP1L	RPGRIP1-like	1.51	0.042
ZNFX1	zinc finger, NFX1-type containing 1	1.51	0.022
FKRP	fukutin related protein	1.50	0.004
FEZ1	fasciculation and elongation protein zeta 1 (zygin I)	1.50	0.015
PRTN3	proteinase 3	0.06	0.041
DEGS2	delta(4)-desaturase, sphingolipid 2	0.06	0.010
LMO1	LIM domain only 1 (rhombotin 1)	0.07	0.008
NXF3	nuclear RNA export factor 3	0.09	0.010
PSD2	pleckstrin and Sec7 domain containing 2	0.10	0.035
FCER1G	Fc fragment of IgE, high affinity I, receptor for; gamma polypeptide	0.11	0.044
NXNL1	nucleoredoxin-like 1	0.11	0.042
TEX29	testis expressed 29	0.12	0.026
TRIM63	tripartite motif containing 63, E3 ubiquitin protein ligase	0.12	0.038
TXNDC2	thioredoxin domain containing 2 (spermatozoa)	0.13	0.006
PTGS1	prostaglandin-endoperoxide synthase 1 (prostaglandin G/H synthase and cyclooxygenase)	0.14	0.025
C11orf86	chromosome 11 open reading frame 86	0.15	0.040
ISM2	isthmin 2 homolog (zebrafish)	0.15	0.003
MRPL23-AS1	MRPL23 antisense RNA 1	0.16	0.05
CYP26A1	cytochrome P450, family 26, subfamily A, polypeptide 1	0.17	0.012
DUOX2	dual oxidase 2	0.17	0.038
MOGAT3	monoacylglycerol O-acyltransferase 3	0.17	0.042
GNAT1	guanine nucleotide binding protein (G protein), alpha transducing activity polypeptide 1	0.20	0.020
FAM83A	family with sequence similarity 83, member A	0.20	0.040
ARMC12	armadillo repeat containing 12	0.20	0.018
ANGPTL4	angiopoietin-like 4	0.20	0.019
RNU6-35P	RNA, U6 small nuclear 35	0.21	0.040
CSPG4	chondroitin sulfate proteoglycan 4	0.21	0.028
PSORS1C2	psoriasis susceptibility 1 candidate 2	0.21	0.009
ACP5	acid phosphatase 5, tartrate resistant	0.21	0.0004

DDX11L9	DEAD/H (Asp-Glu-Ala-Asp/His) box helicase 11 like 9	0.21	0.037
SLC2A5	solute carrier family 2 (facilitated glucose/fructose transporter), member 5	0.22	0.016
EEF1A2	eukaryotic translation elongation factor 1 alpha 2	0.22	0.013
CIB4	calcium and integrin binding family member 4	0.22	0.006
MIR205	microRNA 205	0.22	0.027
IL2RG	interleukin 2 receptor, gamma	0.22	0.015
CHIA	chitinase, acidic	0.23	0.049
DHDH	dihydrodiol dehydrogenase (dimeric)	0.23	0.042
EPX	eosinophil peroxidase	0.24	0.008
PLA2G4B	phospholipase A2, group IVB (cytosolic)	0.25	0.026
NUDT16P1	nudix (nucleoside diphosphate linked moiety X)-type motif 16 pseudogene 1	0.26	0.044
TNXB	tenascin XB	0.26	0.047
RNA28S5	RNA, 28S ribosomal 5	0.27	0.002
MLPH	melanophilin	0.28	0.042
G0S2	G0/G1switch 2	0.28	0.007
CATIP	chromosome 2 open reading frame 62	0.28	0.039
STRA8	stimulated by retinoic acid 8	0.28	0.034
HSPA6	heat shock 70kDa protein 6 (HSP70B')	0.29	0.038
TMEM74B	transmembrane protein 74B	0.29	0.0002
SNORA44	small nucleolar RNA, H/ACA box 44	0.29	0.021
ZPBP2	zona pellucida binding protein 2	0.30	0.020
SHANK1	SH3 and multiple ankyrin repeat domains 1	0.30	0.020
TRPC7	transient receptor potential cation channel, subfamily C, member 7	0.30	0.034
AQP7P3	aquaporin 7 pseudogene 3	0.30	0.039
KRTAP5-1	keratin associated protein 5-1	0.31	0.0001
WFDC3	WAP four-disulfide core domain 3	0.31	0.013
RAB41	RAB41, member RAS oncogene family	0.31	0.011
LEMD1	LEM domain containing 1	0.31	0.017
LINC00158	long intergenic non-protein coding RNA 158	0.32	0.009
EFEMP2	EGF containing fibulin-like extracellular matrix protein 2	0.32	0.013
NDRG1	N-myc downstream regulated 1	0.32	0.023
CACNA2D2	calcium channel, voltage-dependent, alpha 2/delta subunit 2	0.32	0.013
ANG	angiogenin, ribonuclease, RNase A family, 5	0.33	0.015
S100A14	S100 calcium binding protein A14	0.33	0.004
S100P	S100 calcium binding protein P	0.33	0.026
TTBK1	tau tubulin kinase 1	0.33	0.035
MMP28	matrix metallopeptidase 28	0.34	0.035
CDK18	cyclin-dependent kinase 18	0.34	0.009
SPOCD1	SPOC domain containing 1	0.34	0.004

CYP4F30P	cytochrome P450, family 4, subfamily F, polypeptide 30, pseudogene	0.34	0.029
SYT7	synaptotagmin VII	0.35	0.013
CFP	complement factor properdin	0.35	0.035
CLDND2	claudin domain containing 2	0.35	0.028
SAPCD1	suppressor APC domain containing 1	0.36	0.045
PROCA1	protein interacting with cyclin A1	0.36	0.041
ENO2	enolase 2 (gamma, neuronal)	0.36	0.024
HILPDA	hypoxia inducible lipid droplet-associated	0.37	0.005
HCG27	HLA complex group 27 (non-protein coding)	0.37	0.027
SCGB2A2	secretoglobin, family 2A, member 2	0.38	0.047
CAPN14	calpain 14	0.38	0.004
TDRD6	tudor domain containing 6	0.38	0.023
CD68	CD68 molecule	0.39	0.003
VILL	villin-like	0.39	0.005
LOC101241902	chromosome 4 open reading frame 46 pseudogene	0.39	0.039
SLC38A5	solute carrier family 38, member 5	0.39	0.005
PRSS53	protease, serine, 53	0.39	0.008
FTH1P18	ferritin, heavy polypeptide 1 pseudogene 18	0.39	0.040
PLXNB3	plexin B3	0.39	0.006
NDRG4	NDRG family member 4	0.39	0.035
ANKRD37	ankyrin repeat domain 37	0.39	0.008
TRIM29	tripartite motif containing 29	0.40	0.005
IQSEC3	IQ motif and Sec7 domain 3	0.40	0.049
GIPR	gastric inhibitory polypeptide receptor	0.40	0.044
SPDYE1	speedy homolog E1 (Xenopus laevis)	0.41	0.036
NR4A1	nuclear receptor subfamily 4, group A, member 1	0.41	0.008
LINGO2	leucine rich repeat and Ig domain containing 2	0.41	0.010
TMEM178A	transmembrane protein 178A	0.41	0.012
GABRE	gamma-aminobutyric acid (GABA) A receptor, epsilon	0.41	0.009
PRODH	proline dehydrogenase (oxidase) 1	0.42	0.007
IGFBP3	insulin-like growth factor binding protein 3	0.42	0.013
C12orf79	uncharacterized LOC256021	0.42	0.019
PLCH2	phospholipase C, eta 2	0.42	0.029
SUSD2	sushi domain containing 2	0.42	0.022
TREH	trehalase (brush-border membrane glycoprotein)	0.42	0.010
SIDT1	SID1 transmembrane family, member 1	0.43	0.035
FAM229A	family with sequence similarity 229, member A	0.43	0.007
PCOLCE2	procollagen C-endopeptidase enhancer 2	0.43	0.027
LENG9	leukocyte receptor cluster (LRC) member 9	0.43	0.028
CRABP2	cellular retinoic acid binding protein 2	0.43	0.011
AIM1L	absent in melanoma 1-like	0.43	0.020

GDPD3	glycerophosphodiester phosphodiesterase domain containing 3	0.43	0.044
LINC00202-1	long intergenic non-protein coding RNA 202-1	0.43	0.047
LAPTM5	lysosomal protein transmembrane 5	0.44	0.001
LOC154761	family with sequence similarity 115, member C pseudogene	0.44	0.029
HLA-F-AS1	HLA-F antisense RNA 1	0.44	0.033
HES7	hairy and enhancer of split 7 (Drosophila)	0.44	0.006
MYO7B	myosin VIIB	0.44	0.019
GNAS-AS1	GNAS antisense RNA 1	0.44	0.0005
FAM132A	family with sequence similarity 132, member A	0.44	0.048
C1S	complement component 1, s subcomponent	0.44	0.008
PKLR	pyruvate kinase, liver and RBC	0.44	0.041
RNASE4	ribonuclease, RNase A family, 4	0.44	0.0001
SLPI	secretory leukocyte peptidase inhibitor	0.44	0.046
C16orf74	chromosome 16 open reading frame 74	0.45	0.039
C9orf173	chromosome 9 open reading frame 173	0.45	0.007
MYH16	myosin, heavy chain 16 pseudogene	0.45	0.022
SERPINE1	serpin peptidase inhibitor, clade E (nexin, plasminogen activator inhibitor type 1), member 1	0.45	0.0005
NANOGNB	NANOG neighbor homeobox	0.46	0.002
NOG	noggin	0.46	0.048
FA2H	fatty acid 2-hydroxylase	0.46	0.015
CRYAB	crystallin, alpha B	0.46	0.008
KIF17	kinesin family member 17	0.46	0.015
CNIH2	cornichon homolog 2 (Drosophila)	0.46	0.043
C1QL4	complement component 1, q subcomponent-like 4	0.47	0.004
PLAUR	plasminogen activator, urokinase receptor	0.47	0.002
RBAK-RBAKDN	RBAK-LOC389458 readthrough	0.47	0.021
ZNF404	zinc finger protein 404	0.47	0.016
HLA-J	major histocompatibility complex, class I, J (pseudogene)	0.47	0.027
TMEM207	transmembrane protein 207	0.48	0.044
PADI1	peptidyl arginine deiminase, type I	0.48	0.010
AQP7P1	aquaporin 7 pseudogene 1	0.48	0.044
RTBDN	retbindin	0.48	0.015
FZD10	frizzled family receptor 10	0.48	0.023
ANXA2P2	annexin A2 pseudogene 2	0.49	0.021
TMEM255B	transmembrane protein 255B	0.49	0.011
LOC100506469	uncharacterized LOC100506469	0.49	0.008
TMEM91	transmembrane protein 91	0.49	0.047
PRSS8	protease, serine, 8	0.49	0.002
MT1L	metallothionein 1L (gene/pseudogene)	0.49	0.039
SEMA3B	sema domain, immunoglobulin domain (Ig), short basic domain, secreted, (semaphorin) 3B	0.49	0.015

SSTR5	somatostatin receptor 5	0.49	0.005
FAM74A1	family with sequence similarity 74, member A1	0.49	0.038
MT1X	metallothionein 1X	0.49	0.038
DPEP1	dipeptidase 1 (renal)	0.49	0.042
TBX6	T-box 6	0.49	0.018
LDHD	lactate dehydrogenase D	0.49	0.011
SNORD103A	small nucleolar RNA, C/D box 103A	0.49	0.038
SNORD103B	small nucleolar RNA, C/D box 103B	0.49	0.038
THEMIS2	thymocyte selection associated family member 2	0.50	0.006
ADAMTSL4	ADAMTS-like 4	0.50	0.005
KCND1	potassium voltage-gated channel, Shal-related subfamily, member 1	0.50	0.022
FZD10-AS1	uncharacterized LOC440119	0.50	0.022
LINC00607	long intergenic non-protein coding RNA 607	0.50	0.006
CYGB	cytoglobin	0.50	0.032
TBC1D3P5	TBC1 domain family, member 3 pseudogene 5	0.50	0.034
ZNF385C	zinc finger protein 385C	0.50	0.049
TP53TG5	TP53 target 5	0.50	0.002
F3	coagulation factor III (thromboplastin, tissue factor)	0.51	0.013
DICER1-AS1	DICER1 antisense RNA 1	0.51	0.019
MIR155HG	MIR155 host gene (non-protein coding)	0.51	0.018
LOC100129722	uncharacterized LOC100129722	0.51	0.024
CKB	creatine kinase, brain	0.51	0.005
JAM2	junctional adhesion molecule 2	0.51	0.006
AKR1C1	aldo-keto reductase family 1, member C1	0.51	0.017
TGM5	transglutaminase 5	0.51	0.0008
C10orf10	chromosome 10 open reading frame 10	0.51	0.027
KRT24	keratin 24	0.51	0.021
FAM95C	family with sequence similarity 95, member C	0.51	0.036
NAPSA	napsin A aspartic peptidase	0.51	0.035
PLA2G4F	phospholipase A2, group IVF	0.51	0.023
SLCO4A1	solute carrier organic anion transporter family, member 4A1	0.51	0.033
OXCT2	3-oxoacid CoA transferase 2	0.52	0.047
DCN	decorin	0.52	0.045
LOC286297	uncharacterized LOC286297	0.52	0.035
ESPN	espin	0.52	0.024
HSD17B2	hydroxysteroid (17-beta) dehydrogenase 2	0.52	0.029
PPIAP30	peptidylprolyl isomerase A (cyclophilin A) pseudogene 30	0.52	0.031
LINC00899	uncharacterized LOC100271722	0.52	0.037
DUSP1	dual specificity phosphatase 1	0.52	0.021
DUSP5P1	dual specificity phosphatase 5 pseudogene 1	0.52	0.012
LGALS1	lectin, galactoside-binding, soluble, 1	0.52	0.037
ZNF540	zinc finger protein 540	0.52	0.044

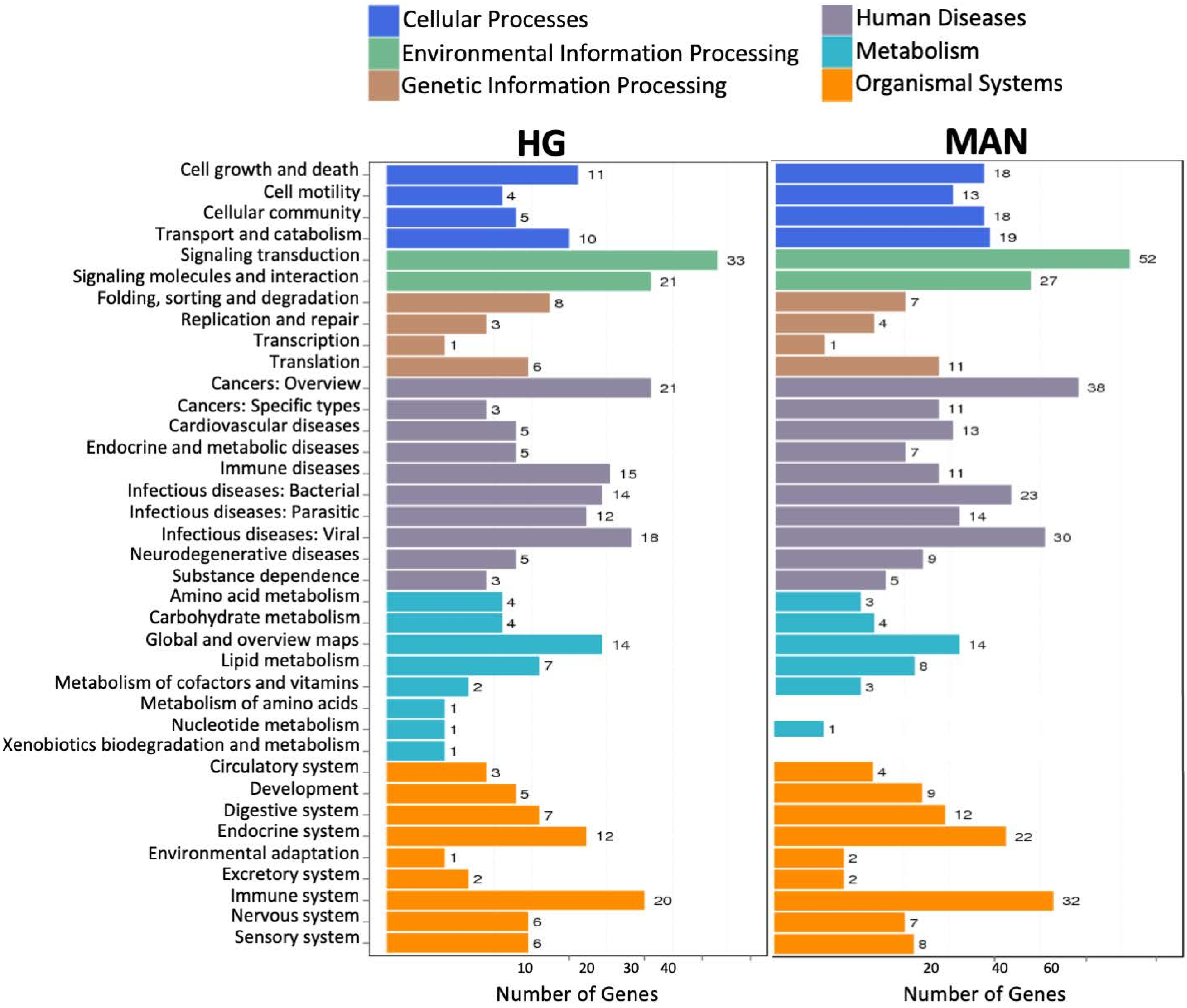
NAT6	N-acetyltransferase 6 (GCN5-related)	0.52	0.017
LINC00282	long intergenic non-protein coding RNA 282	0.53	0.049
SAP25	Sin3A-associated protein, 25kDa	0.53	0.036
INHA	inhibin, alpha	0.53	0.032
SERPINE2	serpin peptidase inhibitor, clade E (nexin, plasminogen activator inhibitor type 1), member 2	0.53	0.006
RASA4	RAS p21 protein activator 4	0.53	0.041
KIAA1549L	KIAA1549-like	0.53	0.032
KCNK3	potassium channel, subfamily K, member 3	0.53	0.036
KCNK7	potassium channel, subfamily K, member 7	0.53	0.049
GRIN3B	glutamate receptor, ionotropic, N-methyl-D-aspartate 3B	0.53	0.039
FIBCD1	fibrinogen C domain containing 1	0.53	0.002
ROCK1P1	Rho-associated, coiled-coil containing protein kinase 1 pseudogene 1	0.53	0.048
ATG16L2	autophagy related 16-like 2 (S. cerevisiae)	0.53	0.005
NEAT1	nuclear paraspeckle assembly transcript 1 (non-protein coding)	0.54	0.043
TBC1D3F	TBC1 domain family, member 3F	0.54	0.027
HYPK	huntingtin interacting protein K	0.54	0.021
SLC30A2	solute carrier family 30 (zinc transporter), member 2	0.54	0.008
SYP	synaptophysin	0.54	0.024
CLDN10-AS1	CLDN10 antisense RNA 1	0.54	0.037
HYKK	aminoglycoside phosphotransferase domain containing 1	0.54	0.029
PNMAL1	paraneoplastic Ma antigen family-like 1	0.54	0.026
SCXB	scleraxis homolog B (mouse)	0.55	0.011
-	scleraxis homolog A (mouse)	0.55	0.011
LINC00685	long intergenic non-protein coding RNA 685	0.55	0.009
OLFML3	olfactomedin-like 3	0.55	0.038
IZUMO4	IZUMO family member 4	0.55	0.002
PPP1R3C	protein phosphatase 1, regulatory subunit 3C	0.55	0.018
HMGN2P46	high mobility group nucleosomal binding domain 2 pseudogene 46	0.55	0.025
GSTM2	glutathione S-transferase mu 2 (muscle)	0.55	0.05
CD55	CD55 molecule, decay accelerating factor for complement (Cromer blood group)	0.55	0.003
TSLP	thymic stromal lymphopoietin	0.55	0.013
VKORC1	vitamin K epoxide reductase complex, subunit 1	0.55	0.025
ADM5	adrenomedullin 5 (putative)	0.55	0.002
CORO6	coronin 6	0.56	0.008
TPM2	tropomyosin 2 (beta)	0.56	0.008
TSSK3	testis-specific serine kinase 3	0.56	0.016
SPATA12	spermatogenesis associated 12	0.56	0.044
RNASET2	ribonuclease T2	0.56	0.002
LPCAT4	lysophosphatidylcholine acyltransferase 4	0.56	0.036

SGSM1	small G protein signaling modulator 1	0.57	0.002
MAPK8IP2	mitogen-activated protein kinase 8 interacting protein 2	0.57	0.022
CLDN14	claudin 14	0.57	0.028
WSB1	WD repeat and SOCS box containing 1	0.57	0.017
M1AP	meiosis 1 associated protein	0.57	0.05
SULT1C2P1	sulfotransferase family, cytosolic, 1C, member 2 pseudogene 1	0.57	0.025
PEX5L	peroxisomal biogenesis factor 5-like	0.57	0.049
LOC100128076	protein tyrosine phosphatase pseudogene	0.58	0.044
C8orf31	chromosome 8 open reading frame 31	0.58	0.030
RAC2	ras-related C3 botulinum toxin substrate 2 (rho family, small GTP binding protein Rac2)	0.58	0.048
CCDC88B	coiled-coil domain containing 88B	0.58	0.040
COX6B2	cytochrome c oxidase subunit VIb polypeptide 2 (testis)	0.58	0.019
PPFIA4	protein tyrosine phosphatase, receptor type, f polypeptide (PTPRF), interacting protein (liprin), alpha 4	0.58	0.008
ZNF582-AS1	ZNF582 antisense RNA 1 (head to head)	0.58	0.032
LINC00624	long intergenic non-protein coding RNA 624	0.58	0.038
ZNF83	zinc finger protein 83	0.58	0.005
LOC143666	uncharacterized LOC143666	0.58	0.021
ZFPM2	zinc finger protein, FOG family member 2	0.58	0.033
HOXA4	homeobox A4	0.58	0.032
BAIAP2L2	BAI1-associated protein 2-like 2	0.58	0.004
C20orf195	chromosome 20 open reading frame 195	0.59	0.042
LOC284454	uncharacterized LOC284454	0.59	0.010
NYAP2	neuronal tyrosine-phosphorylated phosphoinositide-3-kinase adaptor 2	0.59	0.011
P4HA1	prolyl 4-hydroxylase, alpha polypeptide I	0.59	0.016
FTL	ferritin, light polypeptide	0.59	0.011
CDH17	cadherin 17, LI cadherin (liver-intestine)	0.59	0.015
PDXDC2P	pyridoxal-dependent decarboxylase domain containing 2, pseudogene	0.59	0.012
KCNQ4	potassium voltage-gated channel, KQT-like subfamily, member 4	0.59	0.005
AGER	advanced glycosylation end product-specific receptor	0.59	0.022
PPM1E	protein phosphatase, Mg2+/Mn2+ dependent, 1E	0.59	0.035
LOX	lysyl oxidase	0.59	0.033
DNAAF1	dynein, axonemal, assembly factor 1	0.59	0.009
ITM2C	integral membrane protein 2C	0.59	0.009
-	ArfGAP with GTPase domain, ankyrin repeat and PH domain 8	0.59	0.024
NTF4	neurotrophin 4	0.60	0.009
CPLX1	complexin 1	0.60	0.044
UNC5A	unc-5 homolog A (C. elegans)	0.60	0.026
MIOX	myo-inositol oxygenase	0.60	0.003

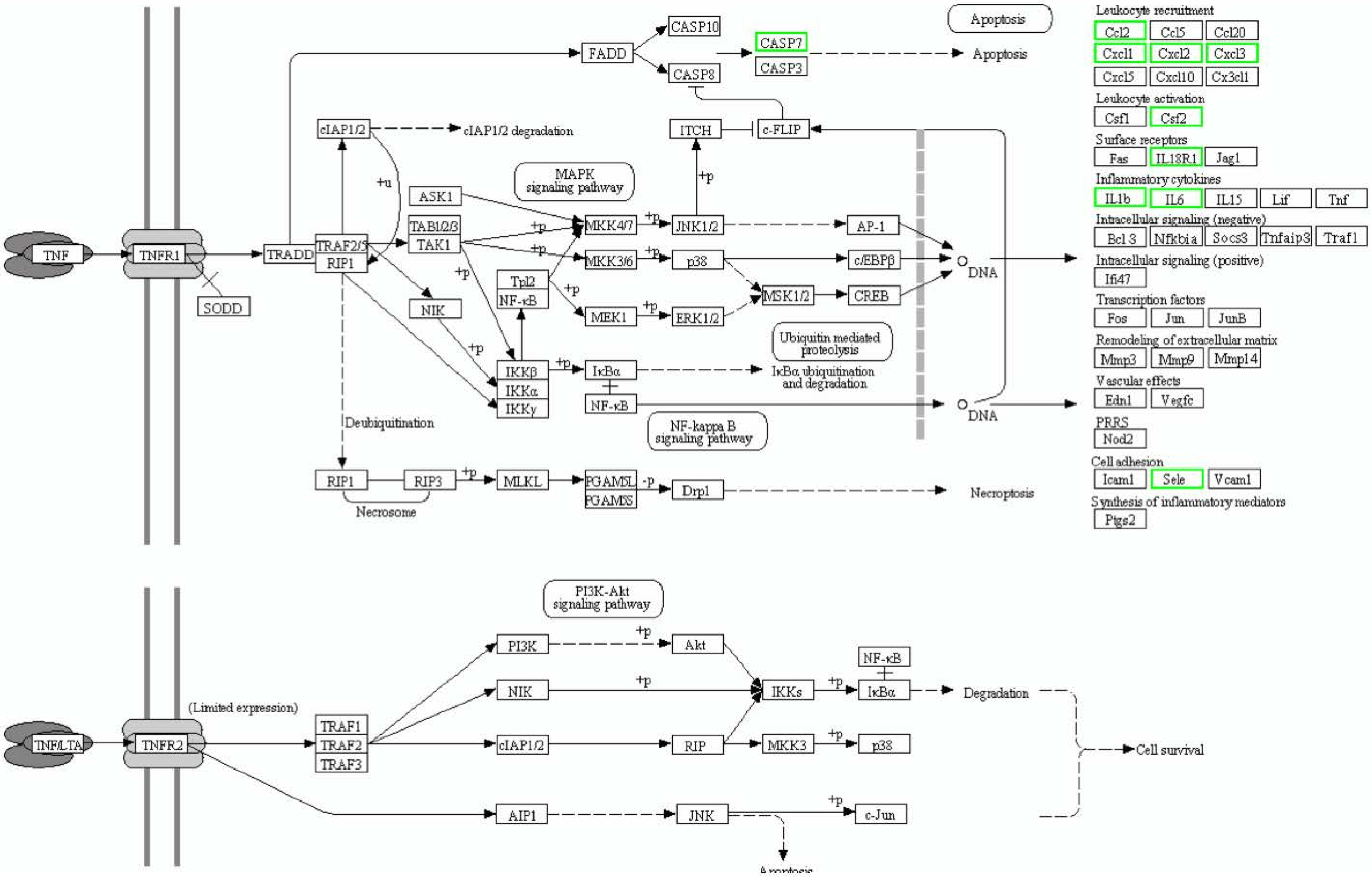
NCRNA00185	non-protein coding RNA 185	0.60	0.027
ATP2C2	ATPase, Ca++ transporting, type 2C, member 2	0.60	0.027
PTPRH	protein tyrosine phosphatase, receptor type, H	0.60	0.013
ROM1	retinal outer segment membrane protein 1	0.60	0.0006
GFAP	glial fibrillary acidic protein	0.60	0.035
RORC	RAR-related orphan receptor C	0.60	0.044
MIR614	microRNA 614	0.60	0.042
LOC442028	uncharacterized LOC442028	0.60	0.0005
LOC283683	uncharacterized LOC283683	0.60	0.034
MC1R	melanocortin 1 receptor (alpha melanocyte stimulating hormone receptor)	0.60	0.020
LINC00663	long intergenic non-protein coding RNA 663	0.60	0.010
DCST2	DC-STAMP domain containing 2	0.61	0.016
LINC00887	uncharacterized LOC100131551	0.61	0.006
MMP19	matrix metallopeptidase 19	0.61	0.036
EXD3	exonuclease 3'-5' domain containing 3	0.61	0.021
SLC2A1	solute carrier family 2 (facilitated glucose transporter), member 1	0.61	0.012
REC8	REC8 homolog (yeast)	0.61	0.044
HLA-A	major histocompatibility complex, class I, A	0.61	0.004
TRABD2B	TraB domain containing 2B	0.61	0.022
FBXL16	F-box and leucine-rich repeat protein 16	0.61	0.002
WBSCR27	Williams Beuren syndrome chromosome region 27	0.61	0.0007
TCN2	transcobalamin II	0.61	0.005
CD72	CD72 molecule	0.61	0.019
KRT15	keratin 15	0.61	0.011
HCFC1R1	host cell factor C1 regulator 1 (XPO1 dependent)	0.61	0.044
RASA4CP	RAS p21 protein activator 4C, pseudogene	0.61	0.048
SMPD3	sphingomyelin phosphodiesterase 3, neutral membrane (neutral sphingomyelinase II)	0.61	0.009
VAMP1	vesicle-associated membrane protein 1 (synaptobrevin 1)	0.62	0.043
PER1	period circadian clock 1	0.62	0.040
MFI2-AS1	MFI2 antisense RNA 1	0.62	0.0007
LOC115110	uncharacterized LOC115110	0.62	0.012
B3GAT2	beta-1,3-glucuronyltransferase 2 (glucuronosyltransferase S)	0.62	0.046
KCNN4	potassium intermediate/small conductance calcium-activated channel, subfamily N, member 4	0.62	0.034
FAM86HP	family with sequence similarity 86, member A pseudogene	0.62	0.047
LOC100506472	uncharacterized LOC100506472	0.62	0.045
PRR15L	proline rich 15-like	0.62	0.018
PRKCG	protein kinase C, gamma	0.62	0.05
PHF1	PHD finger protein 1	0.62	0.010
ALS2CL	ALS2 C-terminal like	0.62	0.013

TCP10L	t-complex 10-like	0.62	0.002
CD96	CD96 molecule	0.63	0.046
ARHGAP22	Rho GTPase activating protein 22	0.63	0.025
EGFLAM-AS4	EGFLAM antisense RNA 4	0.63	0.043
FLJ44511	uncharacterized LOC441307	0.63	0.021
PRRT2	proline-rich transmembrane protein 2	0.63	0.044
PAXIP1-AS1	uncharacterized LOC202781	0.63	0.001
MRPS6	mitochondrial ribosomal protein S6	0.63	0.013
PPM1J	protein phosphatase, Mg2+/Mn2+ dependent, 1J	0.63	0.017
CYLC2	cylicin, basic protein of sperm head cytoskeleton 2	0.63	0.006
SNORA61	small nucleolar RNA, H/ACA box 61	0.63	0.015
HES2	hairy and enhancer of split 2 (Drosophila)	0.63	0.038
MAPK8IP3	mitogen-activated protein kinase 8 interacting protein 3	0.63	0.046
CLEC7A	C-type lectin domain family 7, member A	0.63	0.016
CCBL1	cysteine conjugate-beta lyase, cytoplasmic	0.63	0.027
IRF8	interferon regulatory factor 8	0.63	0.029
PAQR6	progestin and adipoQ receptor family member VI	0.63	<0.0001
MGC16275	uncharacterized protein MGC16275	0.63	0.018
GJB3	gap junction protein, beta 3, 31kDa	0.64	0.017
LENG8	leukocyte receptor cluster (LRC) member 8	0.64	0.025
EEPD1	endonuclease/exonuclease/phosphatase family domain containing 1	0.64	0.021
PI4KAP1	phosphatidylinositol 4-kinase, catalytic, alpha pseudogene 1	0.64	0.023
AMT	aminomethyltransferase	0.64	0.019
LOC100133445	uncharacterized LOC100133445	0.64	0.047
DBP	D site of albumin promoter (albumin D-box) binding protein	0.64	0.022
HERC2P7	hect domain and RLD 2 pseudogene 7	0.64	0.022
UPK1B	uroplakin 1B	0.64	0.019
SNHG18	uncharacterized LOC100505806	0.64	0.042
HMOX1	heme oxygenase (decycling) 1	0.64	0.016
SFTPB	surfactant protein B	0.64	0.007
LINC01289	uncharacterized LOC286184	0.64	0.049
EPOR	erythropoietin receptor	0.64	0.040
LOXL2	lysyl oxidase-like 2	0.64	0.003
BAIAP3	BAI1-associated protein 3	0.64	0.016
FAM86JP	family with sequence similarity 86, member A pseudogene	0.64	0.045
GLRX	glutaredoxin (thioltransferase)	0.65	0.019
LY6E	lymphocyte antigen 6 complex, locus E	0.65	0.05
MIR4458HG	uncharacterized LOC100505738	0.65	0.027
INPP5D	inositol polyphosphate-5-phosphatase, 145kDa	0.65	0.006
LOC100133331	uncharacterized LOC100133331	0.65	0.042
NAB2	NGFI-A binding protein 2 (EGR1 binding protein 2)	0.65	0.010
CALCR	calcitonin receptor	0.65	0.035

MST1	macrophage stimulating 1 (hepatocyte growth factor-like)	0.65	0.007
C1orf54	chromosome 1 open reading frame 54	0.65	0.041
WNK4	WNK lysine deficient protein kinase 4	0.65	0.044
C3orf67	chromosome 3 open reading frame 67	0.65	0.033
FGFBP1	fibroblast growth factor binding protein 1	0.65	0.021
RHCE	Rh blood group, CcEe antigens	0.65	0.035
MTMR11	myotubularin related protein 11	0.65	0.008
MOG	myelin oligodendrocyte glycoprotein	0.65	0.029
CPNE7	copine VII	0.66	0.010
FOXD2-AS1	FOXD2 antisense RNA 1 (head to head)	0.66	0.035
PRR27	chromosome 4 open reading frame 40	0.66	0.006
TNFRSF6B	tumor necrosis factor receptor superfamily, member 6b, decoy	0.66	0.049
SNX33	sorting nexin 33	0.66	0.020
LOC729970	hCG2028352-like	0.66	0.044
37135	septin 1	0.66	0.014
FN3K	fructosamine 3 kinase	0.66	0.014
ARSF	arylsulfatase F	0.66	0.026
ZEB1-AS1	ZEB1 antisense RNA 1	0.66	0.030
PDZD7	PDZ domain containing 7	0.66	0.043
SUV420H2	suppressor of variegation 4-20 homolog 2 (Drosophila)	0.66	0.016
MAMDC4	MAM domain containing 4	0.66	0.001
LTBP4	latent transforming growth factor beta binding protein 4	0.66	0.019
SYTL3	synaptotagmin-like 3	0.67	0.006



Supplementary Figure S8***: Differential Expression of Genes in Presence of Indirect Contact of MSCs.*** Pathway Enrichment Analysis of Differentially Expressed Genes (DEGs) performed based on KEGG database by pairwise analysis. Here, X axis represents number of DEGs. Y axis represents second KEGG pathway terms. All second pathway terms were grouped in top pathway terms indicated in different color.



Supplementary Figure S9***: TNF-Signalling pathway as a representative example of the signalling pathways involved in MSC mediated anti-inflammatory effects (in high-glucose environment)*****.** Here, down-regulated genes are marked with green borders and unchanged genes are marked with black borders.