# Identification of Novel Regulators of Developmental Hematopoiesis Using *Endoglin* Regulatory Elements as Molecular Probes

Running title: *Endoglin* GREs Target Distinct Hemogenic Precursors

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Scientific category: Hematopoiesis and Stem Cells

**KEY POINTS:**

- Endoglin regulatory elements target hemogenic mesoderm and hemogenic endothelium
- Hemogenic progenitors can be enriched using these elements as molecular probes to discover novel regulators of hematopoiesis

## ABSTRACT

Enhancers are the primary determinants of cell identity and specific promoter/enhancer combinations of Endoglin (ENG) have been shown to target blood and endothelium in the embryo. Here, we generated a series of embryonic stem cell lines, each targeted with reporter constructs driven by specific promoter/enhancer combinations of ENG, to evaluate their discriminative potential and value as molecular probes of the corresponding transcriptome. The *Eng* promoter (P) in combination with the -8/+7/+9kb enhancers, targeted cells in FLK1 mesoderm that were enriched for blast colony forming potential, whereas the P/-8kb enhancer targeted TIE2+/c-KIT+/CD41- endothelial cells that were enriched for hematopoietic potential. These fractions were isolated using reporter expression and their transcriptomes profiled by RNA-seq. There was high concordance between our signatures and those from embryos with defects at corresponding stages of hematopoiesis. Of the six genes that were up-regulated in both hemogenic mesoderm and hemogenic endothelial fractions targeted by the reporters, LRP2, a multiligand receptor, was the only gene that had not previously been associated with hematopoiesis. We show that LRP2 is indeed involved in definitive hematopoiesis and by doing so validate the use of reporter gene coupled enhancers as probes to gain insights into transcriptional changes that facilitate cell fate transitions.

## INTRODUCTION

With advances in microscopy and histology, different cell types can now readily be distinguished from one another. However, the molecular characteristics that make each cell type unique and help distinguish stem cells from their more differentiated progeny in a tissue, are still obscure. Harvesting pure populations of stem cells is a pre-requisite to probing their molecular identity. Over the years, protocols combining flow cytometry with single cell serial transplantation assays have been progressively refined to purify mouse and human adult hematopoietic stem cells (HSCs)[1,2].

One of the utilitarian benefits of determining the molecular fingerprint of a HSC is that it could serve as a measurable goal when developing protocols aimed at generating HSCs from differentiated cells[3]. The failure of current protocols to generate long-term repopulating HSCs from ES/iPS cells is attributed in part to our incomplete understanding of the developmental journey that mesodermal progenitors traverse in the embryo when generating the complement of HSCs that are resident in the bone marrow of a newborn[4]. Determining the molecular identities of embryonic HSC precursors is complicated by the lack of consensus regarding the precise HSC intermediates in the embryo, functional assays that are less than ideal for assessment of these intermediates and knowledge that these intermediates are transitory cell populations that are present in very small numbers[5]. FLK1 expressing mesodermal cells in the posterior primitive streak when isolated from the embryo and cultured *in vitro* generate blast colonies that have blood, endothelial and vascular smooth muscle potential[6]. Blast colony forming cell (BL-CFC) potential in FLK1+ mesoderm has been estimated to be ~1:300[7]. Hemogenic potential in TIE2+c-KIT+ hemogenic endothelial or VE-CAD+CD45-CD41- pre-HSC cells in the dorsal aorta that transit to hematopoietic cells range from 1:100-300 [8-10]. These functional estimates are too low to probe the molecular identities of either the early hemangioblast or hemogenic endothelial cell populations in the developing embryo using currently available protocols.

Cell identity is encoded within the sequences of tissue specific gene regulatory elements that direct and coordinate gene expression in a cell[11]. A number of regulatory elements of hematopoietic transcription factors have previously been shown to direct reporter expression to developing blood cells in the mouse embryo and include enhancers of *Scl*, *Runx1*, *Gata2*, *Erg*, *Fli1*, *Lmo2* and *Lyl1*, which also form a recursive circuit in human adult HSCs[12]. The *Runx1*+23 enhancer marks a population of early hemogenic endothelial cells that transit to HSCs and has been used to isolate cells from different embryonic stages for transcriptomic analysis[13]. *Ly6a/Sca1* and Endoglin (*Eng*; CD105) serve as useful cell surface markers for isolation of murine HSC fractions[14,15]. The promoter of *Ly6a* and promoter/enhancer combinations of *Eng* also target embryonic hematopoiesis and in the case of the former have been used in conjunction with a reporter to isolate hemogenic endothelial cells and HSCs from early embryos[16-18].

ENG is an accessory receptor and modulator of TGF-β superfamily signaling[19]. ENG is expressed on FLK1+ mesoderm and is required for normal BL-CFC development and its expression facilitates the hematopoietic program in these cells[10,20]. ENG null mice die at E9.5 with vascular defects due to abnormal endothelial and pericyte development[21]. It is also a marker of adult murine HSCs that was identified using a *Scl*+19 driven fluorescent reporter coupled with transcriptomic and proteomic assessment of purified cells[15]. An emerging concept of developmental hematopoiesis posits that HSC development from the dorsal aorta at E10 reflects maturation of cells that were fated earlier during embryogenesis towards the hematopoietic lineage[13]. As such we rationalised that transcriptional regulation of ENG, which is functionally important for the development of hematopoietic intermediates could be instructive in helping elucidate the transcriptional environment of these cells. We have previously shown that sequence information within the promoter and hemato-endothelial enhancers of *Eng* determine how reporter genes are targeted to either endothelial or blood and endothelial tissues in the embryo[17,22]. Given the spectrum of cell types that are involved in the developmental journey of embryonic HSCs and the deterministic role that ENG plays in their development, we hypothesised that distinct combinations of promoter/enhancers of this gene are used by different hematopoietic intermediates to regulate *ENG* expression. We rationalised that if distinct promoter/enhancer constructs indeed targeted functionally distinct hematopoietic intermediates, they could be used as molecular probes to profile the transcriptional environment of these cells.

Here we show using ES cells with single copy reporter coupled transgenes targeted to the constitutively active HPRT locus that distinct promoter/enhancer combinations of ENG are used by FLK1+ mesoderm and hemogenic endothelium that are enriched for BL-CFC and hematopoietic potential respectively. Using these reporter coupled transgenes as probes to harvest cell populations from ESC differentiation assays, we performed RNA-seq to identify gene sets that were associated with functional enrichment of hematopoietic potential and show their complementarity with primary mouse tissues at matching stages of development.
Of the six genes that were up-regulated in both hemogenic mesoderm and hemogenic endothelial fractions targeted by the reporters, LRP2, a multiligand receptor, was the only gene that had not previously been associated with hematopoiesis. Here, we show that LRP2 is indeed involved in AGM hematopoiesis and by doing so validate the use of reporter gene coupled enhancers as a discovery tool.

## MATERIALS AND METHODS

### Murine ES cell culture and Hprt targeting

The Bry/GFP[7] and HM1 ES cells[23] were cultured as previously described. See *Supplemental data*

### ES cell differentiation into EBs and lacZ staining

To generate EBs, ES cells were collected and cultured as detailed in *Supplemental data*.

### Flow cytometry and cell sorting

Cells were collected from EBs and liquid blast cultures and dissociated into a single cell suspension. Details of procedure and antibodies are listed in *Supplemental data*

### Methylcellulose blast colony forming (BL-CFC) assay and liquid cultures

*See Supplemental data*

### Hematopoietic methylcellulose colony-forming assay

Cells isolated from day 2 or 4 of liquid blast cultures and seeded for CFU-C assays as detailed in *Supplemental data*.

### RT-PCR

List of primers and methods are in *Supplemental data*.

### Chromatin immunoprecipitation (ChIP) assay

ChIP assays were performed as detailed previously[22]. See *Supplemental data* for a list of primers and experimental details.

## Mouse embryo immunostaining and imaging

Details of procedure and antibodies are listed in *Supplemental data*.

## Generating zebrafish morpholinos and analysis

Details are listed in *Supplemental data*.

## Statistical analysis

RT-PCR data, BL-CFCs and hematopoietic colony counts were statistically analysed using Student's T-test or Paired Student's T-test.

## RNA sequencing and analysis

The data has been deposited in GEO under the accession number GSE77390. The Ingenuity IPA Core Analysis Tool (version 17199142) and the GSEA Java Desktop tool (v 2.0.13) were used for analysis. See *Supplemental data* for details.

**RESULTS**

**Mesoderm to hemangioblast transition is accompanied by increased *Eng* expression and chromatin accessibility at hemato-endothelial regulatory elements.** The promoter of *ENG* when coupled with -8kb, +7kb and +9kb enhancers have previously been shown to direct reporter expression to either endothelial or blood and endothelial tissues in the embryo (Figure 1A; [17,22]). The Bry-GFP ESC line has been used extensively to investigate the developmental progression of pre-mesoderm (GFP-/FLK1-) to pre-hemangioblast mesoderm (GFP+/FLK1-; G+/F-) to the hemangioblast (GFP+/FLK1+; G+F+)[7] (Figure 1B). We used this cell line to first evaluate expression of *Eng* and chromatin accessibility at hemato-endothelial regulatory elements of *Eng*[17,22] as cells progressed from pre-hemangioblast mesoderm to hemangioblast mesoderm. *Eng* expression increased by ~ 3-fold (Figure 1C) and enrichments of H3K9 acetylation (an active chromatin mark) increased ~ 10-20 fold at the *Eng* promoter and -8kb, +7kb and +9kb *Eng* enhancers (Figure 1D). There was no change in H3K9Ac at -4kb, a region that is highly conserved across species but shows no enhancer activity[22].

**The *Eng* promoter when combined with the -8, +7 and +9 hemato-endothelial enhancers, targets FLK1+ mesodermal cells enriched for BL-CFC potential.** HM1 ESCs have a disrupted *Hprt* locus that can be reconstituted by homologous recombination of a targeting vector[23]. They serve as a useful tool to evaluate reporter activity of single copies of gene regulatory elements at a constitutively active locus at different stages of ESC differentiation. We took advantage of this system to introduce combinations of *Eng* regulatory elements with blood and endothelial activity in *in vivo* transgenic assays (Figure S1). Successful recombination and generation of ESC lines with -8/P/lacZ, -8/P/lacZ/+7, -8/P/lacZ/+9, -8/P/lacZ/+7/+9, -8/P/lacZ/+7Δ (GATA)/+9 and -8/P/lacZ/+7Δ (GATA)/+9 Δ

(ETS), was confirmed by RT-PCR and southern blotting (Figure S2). We used these ESC lines as a tool-kit with which to track, evaluate and compare the activity of each of these gene regulatory elements (GREs) during different stages of hematopoietic development and to fractionate cells for functional validation and transcriptomic analysis.

To identify which, if any of the *Eng* GREs, targeted FLK1+ mesoderm enriched for hemangioblast potential, we generated embryoid bodies (EBs) from each ESC line and fractionated FLK1+lacZ- (F+L-) and FLK1+lacZ+ (F+L+) cells and performed blast colony forming cell (BL-CFC) assays (Figure 2A). The *Eng* -8/P/lacZ/+7/+9 construct, which showed robust blood and endothelial staining *in vivo*[17] targeted a fraction of the FLK1+ mesoderm that showed increased (~ 4 fold) BL-CFC potential (Figure 2B and Figure S3A). We have previously shown that mutating the GATA binding motifs in +7 and ETS binding motifs in +9 diminished endothelial activity and extinguished hematopoietic activity of the *Eng* -8/P/lacZ/+7/+9 construct in transgenic assays[17]. There was a corresponding reduction or failure of the mutant constructs to preferentially target cells with BL-CFC potential (Figure 2C (i)-(ii) and Figure S3B). The -8P/lacZ construct showed strong endothelial but no hematopoietic activity in transgenic assays[17]. FLK1+ cells targeted by this construct (F+L+) showed significantly lower BL-CFC potential than F+L- cells (Figure 2D (i) and Figure S3A). For the -8P/lacZ/+7 and -8P/lacZ/+9 constructs, which showed strong endothelial and low- to moderate hematopoietic activity in *in vivo* transgenic assays[17], FLK1+ mesoderm (F+L+) had either lower or equivalent BL-CFC activity than FLK1+ (F+L-) cells (Figure 2D (ii)-(iii) and Figure S3A). It is important to note that the total number of BL-CFCs generated by FLK1+ mesoderm will vary from clone to clone but that comparisons are of BL-CFC potential of L+ and L- sorted FLK1+ cells from each clone.

Taken together, these data show that the GREs of ENG that showed increased chromatin accessibility as pre-hemangioblast mesoderm progressed to hemangioblast mesoderm (i.e. -8/P/+7/+9; Figure 1D) act collectively to target reporter gene expression to BL-CFCs in FLK1+ mesoderm. It is noteworthy that in *in vivo* transgenic assays, it was also this construct (-8/P/lacZ/+7/+9) that had the strongest and most specific activity in blood and endothelium in the developing embryo[17].

**Global transcriptomic analysis of FLK1 mesoderm targeted by *Eng* -8/P/LacZ/+7/+9 identifies genes associated with hemangioblast activity.** To discover genes associated with the activation of these GREs and increased activity of the reporters, we performed RNA-sequencing on sorted *lacZ*+ and *lacZ*- cell fractions from three independent experiments. As expected *Kdr* (*Flk1*) expression was comparable in both fractions and *Eng* transcripts were increased in the *lacZ*+ fraction consistent with *Eng* GRE driven reporter activity (Figure 3A). There was also a shared set of genes that was consistently differentially expressed between the *lacZ*+ and *lacZ*- cell fractions (Figure 3B (i)) and included 107 up-regulated and 101 down-regulated genes. These included cell surface receptors and transcription factors known to be associated with blood and endothelium (fold change ≥ 2 and p-value <0.5; Table S1 and Figure S4A) and genes that have been associated with hemangioblast development in the LifeMap Sciences embryonic development compendium (Figure 3B (ii)). Individually the expression of many genes known to be associated with early mesoderm (e.g. *Bry*/*T* and *Bmp4*), blood (e.g. *Gata1* and *Tal1*) and endothelial (e.g. *Foxc2* and *Etv2*) development did not vary significantly between these cell fractions (Figure 3B (ii)). Indeed, as hemangioblasts are a sub-population of FLK1+ mesoderm with multi-lineage differentiation potential, it would have been unusual to see significant differences in expression of individual genes that are strongly associated with commitment to a specific lineage. However, ingenuity pathway analysis (IPA) revealed that when differentially expressed genes were considered as a collective, there were strong associations with blood and blood vessel development for genes in the FLK1+/*lacZ*+ set (Figure S4B). Consistent with these biological functions, this gene set also showed significant associations with signaling pathways that govern endothelial development and eNOS signaling (Figure S4C-F).

To investigate the *in vivo* relevance of our gene set, we used GSEA analysis to compare expression overlaps with gene expression data from FLK1+ cells in ETV2 [24,25] and LDB1[26] KO embryos, both of which are defective in hemangioblasts (Figure 3C). There were strong overlaps between genes expressed in FLK1+ mesoderm targeted by *ENG* -8/P/lacZ/+7/+9 and genes expressed in hemangioblast competent WT ETV2 and LDB1 embryos compared to ETV2+/- or LDB1-/- embryos respectively. Therefore the molecular signature of BL-CFC enriched FLK1+ mesoderm that was identified using differential reporter activity of *ENG* GREs is consistent with *in vivo* functional capacity.

**The *Eng* promoter in combination with the -8 endothelial enhancer targets hemogenic endothelial cells enriched for hematopoietic potential.** Definitive hematopoiesis in the embryo progresses through a TIE2+/c-KIT+/CD41- hemogenic endothelial (HE) intermediate [9]. We used a cell culture system that mirrors this *in vivo* transition to investigate whether any of the reporter ESC lines preferentially targeted HE cells and whether they could be used to isolate cell fractions that were enriched for hematopoietic potential[9]. To this end, FLK1+ cells were sorted from day 3EBs and seeded into liquid blast culture media (Figure 4A). At day 2 of culture, *lacZ*+ and *lacZ*- HE cells were isolated by FACS and re-seeded into liquid blast media (LBM) for two further days followed by flowcytometry and CFU-C assays to evaluate the hematopoietic potential of each fraction. Of the reporter ESC lines, *Eng* -

8/P/*lac*Z was unique in that it was active in a fraction of HE cells that generated more TIE2-/CD41+ and CD45+ cells after 48 hours in culture (Figure 4B (i)- (ii)) and contained almost all CFU-C potential (Figure 4B (iii)). Whereas *Eng* -8/P/lacZ/+7/+9 targeted FLK1+ mesoderm with increased BL-CFC potential (Figure 2), it did not target HE cells with increased hematopoietic potential (Figure 4C (i) - (iii)). Indeed this and each of the other constructs, targeted HE cells that had lower hematopoietic potential (Figure 4D-E; Figure S5). Taken together, these data showed that not only was there a specific combination of ENG GREs that targeted HE cells but that the combination was distinct from that which targeted BL-CFCs in FLK1+ mesoderm.

**Hematopoietic potential is highest in *Eng* -8/P/*lacZ* targeted HE cells that do not as yet express surface ENG.** Cell fate transitions are dynamic and our purpose was to use these reporter constructs to capture HE cells that were intrinsically fated towards the hematopoietic lineage at the earliest possible time point in culture. Based on the assumption that there would be a delay between transactivating the *Eng* GRE reporter and surface expression of ENG, we repeated the experiments described in Figure 4 using the *Eng* -8/P/lacZ ES cell line but here also incorporating surface ENG expression to isolate TIE2+/C-KIT+/CD41- HE fractions that were ENG+/*lacZ*-, ENG+/*lacZ*+ or ENG-/*lacZ*+ (Figure 5A). Interestingly, CFU-C potential within the *lacZ*+ fraction was highest in ENG-/*lacZ*+ HE cells (Figure 5B (i) – (ii)). ENG+/*lacZ*-, ENG+/*lacZ*+ and ENG-/*lacZ*+ HE cells were re-seeded in LBM and analysed by flow cytometry and CFU-C assays after two further days of culture. The proportions of TIE2-/CD41+ (Figure 5C (i)) and CD45+ (Figure 5C (ii)) cells and CFU-C potential (Figure 5C (iii)) were highest for cultured ENG-/*lacZ*+ HE cells. Taken together, these data show that the hematopoietic potential within HE cells can be targeted by *Eng* -

8/P/*lacZ* and that these ESCs could be used to interrogate the earliest transcriptional changes associated with this cell fate decision.

**Transcriptomic analysis of HE fractions identifies genes associated with hemogenic endothelial to hematopoietic transition.** To discover genes, that act on *Eng* -8/P/*lacZ* and drive reporter gene activity and by extension are associated with hemogenic potential in TIE2+/C-KIT+/CD41- HE cells, we performed RNA-sequencing on sorted ENG+/*lacZ*-, ENG+/*lacZ*+ and ENG-/*lacZ*+ HE cell fractions from three independent experiments. As expected the fractions, which expressed surface ENG had abundant *Eng* transcripts, which were still comparatively low in ENG-/*lacZ*+ HE cells (Figure 6A). Consistent with its role as a major determinant of endothelial to hematopoietic transition (EHT)[9,27,28], *Runx1* transcripts were abundant in HE cells that were enriched with functional hemogenic cells (ENG-/*lacZ*+ HE) and relatively low in those (ENG+/*lacZ*- and ENG+/*lacZ*+ HE) that were not. In total, there were 707 up-regulated and 981 down-regulated genes in ENG-/*lacZ*+ HE cells compared with ENG+/*lacZ*- and ENG+/*lacZ*+ HE cells (Figure 6B (i); Table S2). It was interesting to note that only a subset of genes that have previously been attributed to mark HE cells based on cell surface protein expression were[16] differentially expressed between these functionally distinct HE sub-populations (Figure 6B (ii)). This does not imply that these genes are not important but that their higher or lower expression is not associated with these early subtle transitions.

To investigate the *in vivo* relevance of our gene set, we used GSEA analysis to compare expression overlaps between ENG-/*lacZ*+ HE vs. ENG+/*lacZ*- HE and gene sets generated from primary embryonic endothelial cell (EC), hemogenic endothelial cells (HECs) and HSCs[16]. Consistent with our functional data, the gene sets associated with EC to HE transition (Figure 6C (i) and HE to HSC transition (Figure 6C (ii)) showed strong overlaps with genes expressed in ENG-/*lacZ*+ HE. Gene sets associated with HIF1a and DNA replication also showed strong overlaps with genes expressed in ENG-/*lacZ*+ HE cells (Figure S6A). Genes that were UP in ENG-/*lacZ*+ HE compared with ENG+/*lacZ*- HE cells feature prominently in IPA reconstructions of gene networks governing hematopoietic development (Figure S6B). Whereas genes that were UP in ENG-/*lacZ*+ HE cells compared with either ENG+/*lacZ*- HE or ENG+/lacZ+ HE cells were associated with biological processes relating to blood development, genes that were DOWN in ENG-/*lacZ*+ HE cells relative to the other two fractions were associated more with angiogenesis or vasculogenesis (Figure S6C-E). Interrogation of differentially expressed transcription factors (TFs) and cell surface receptors (CSRs) in the more functionally hemogenic ENG-/*lacZ*+ HE fraction relative to the ENG+/*lacZ*- HE fraction showed up-regulation of a number of TFs (e.g. *Runx1*[29], *Myb*[30], *Gfi1b*[31] *etc.*) and CSRs (*Lgr5*[32]) that are known to play a role in HSC development and down regulation of others (e.g. *Sox17*[33]), which are important for HE to HSC transition (Figure 6D).

**Lrp2 is required for normal blood emergence in the zebrafish aorta.** We then overlapped our gene sets to visualise associations between genes that were UP or DOWN in haemogenic mesoderm (HB) and/or hemogenic endothelium (HE) (Figure S7 and S8; Table S1-S2) to interrogate their function. Six genes were shared between the up-regulated groups (Figure 7A; Figure S7C) and eight genes between the down-regulated groups (Figure S8A). Genes that were DOWN in both HB and HE cells included several with no known association with haematopoiesis (Figure S8B). However, we focused on genes that were UP in both HB and HE cells (Figure 7A and S7C) for practical considerations given that their expression and functional role would be easier to validate. This group included hematopoietic transcription factors (*Gfi1* [31] and *Lyl1*[34]), a platelet protein kinase C substrate (*Plek*[35]) and granulocyte lysosomal and lysosomal membrane proteins (*Mpo*[36] and *Laptm5*[37]), all of which have known functions in the hematopoietic system. It also included a multifunctional ligand (*Lrp2*) with no previously described role in blood or blood development. Lrp2/Megalin is a member of an endocytic receptor complex that is involved in maternal-fetal transport of folate and other nutrients, lipids and morphogens such as sonic hedgehog (Shh) and retinoids[38]. Given these associations we postulated that *Lrp2* up-regulation in blood precursors was likely to be of functional significance.

The *Ly6aGFP* (Sca1) mouse model, in which all HSCs throughout development are GFP+[14,39] has facilitated the study of EHT. There mice were used to show in real-time, the transition of morphologically flat endothelial GFP+ cells in the E10.5 aorta to round GFP+ cells that co-express other HSC markers[40]. Given that LRP2 was up-regulated in HE cells, we evaluated LRP2 expression in *Ly6aGFP* E10.5 AGM. LRP2 shows specific expression in endothelial cells with strong expression in Ly6aGFP+ endothelial cells and hematopoietic clusters (Figure 7B).

EHT is an evolutionarily conserved process in vertebrates and real-time imaging of transgenic zebrafish embryos has also shown the transition of aortic endothelial cells to hematopoietic cells[41,42]. *Lrp2* is highly conserved across different vertebrate species (Figure 7C; average sequence identity across all species shown = 70 %). The zebrafish genome has two closely related protein- coding genes, *lrp2a* on chr. 9 and *lrp2b* on chr. 12, both of which are expressed at 24-72hpf [43]. To validate the involvement of LRP2 in HSC generation, we used a zebrafish morpholino oligo (MO) knockdown approach targeting both *lrp2a* and *2b* together and each alone. At 36h post fertilization (hpf), morphants were assayed by ISH for *cmyb* and *runx1*, markers for emerging blood progenitors in the aorta[44]. WT embryos showed robust *cmyb* and *runx1* expressing cells along the dorsal aorta in contrast to *lrp2a/b* morphants that showed severe reductions (Figure 7D (i); Figure S9A). There was partial rescue of AGM blood progenitors when *lrp2a/b* morphants were co-injected with *hLRP2* mRNA. The partial rescue was probably due to only partial homology of protein sequences between humans and fish (~ 65%) and quality of *in vitro* transcribed mRNA given the large size of *LRP2* cDNA (~14kb). To exclude non-specific toxicity related loss of *cmyb* and *runx1* expressing cells, we co-injected *lrp*2*a/b* MO with *tp53* MO and saw no restitution of *cmyb* expressing cells in the morphants (Figure S9B). Injection of *lrp2b*MO but not *lrp2a*MO, reduced the numbers of cmyb expressing AGM blood progenitors (*lrp2b*MO; Figure 7D (ii); *lrp2a*; data not shown). To establish that this defect in blood cell production was not a secondary to loss of vascular integrity, we injected *lrp2a/b* MO into flk:zsgreen transgenic embryos and saw no difference between morphants and controls at 32 hpf (Figure 7E). In addition to vascular integrity we also assessed blood flow in morphants. Both heart function as well as blood flow was indistinguishable from control embryos (data not shown). Taken together these data support a role for LRP2 during AGM hematopoiesis.

**DISCUSSION**

Regulatory elements of genes that demonstrate tissue specific expression have previously been used to target and characterise various cell populations in ESC systems[45-48]. When initiating these experiments, we did not envisage that distinct combinations of ENG promoter/enhancers would target haemangioblast potential in FLK1 mesoderm and hemogenic potential in TIE2+/C-KIT+/CD41- hemogenic endothelium. In retrospect, given the distinct transcriptomes and functional properties of haemangioblasts and hemogenic endothelium, this should not have come as a surprise. Nor did we predict that hemogenic potential would be enriched in ENG- HE1 cells targeted by the ENG *-8PlacZ* transgene. Given that F+L+ cells expressed higher levels of ENG (Figure 3A), these data raise the question whether HE1 cells emerge from F+L- ENG low cells which are less able than their F+L+ counterparts to generate BL-CFCs or whether F+L+ ENG high cells subsequently shutdown ENG expression to facilitate their haemogenic potential in HE1 cells. As these populations were targeted by different transgenes (F+L+; *Eng-8/P/lacZ/+7/+9* and ENG-L+ HE; *Eng-8/P/lacZ*), this could not be directly tested. However, ES cells targeted with dual reporters each driven by either *Eng-8/P/+7/+9 or Eng-8/P* may assist in addressing this specific question.

*Lrp2,* a gene that encodes megalin, a multiligand uptake receptor that regulates circulating levels of diverse compounds[49] emerged as a novel regulator of hematopoiesis. Mutations in LRP2 result in impaired neuro-epithelial development and are causative of Donnai-Barrow and facio-oculo-acoustico-renal syndromes[50]. It has been implicated in balancing BMP4 and SHH signaling in neuro-epithelium by acting as a clearance receptor for BMP4 and by concentrating or depleting SHH by ligand recycling or clearance respectively in a cell type and context dependent manner[51]. This is of mechanistic interest as the BMP4-

SHH gradient between the neural tube and dorsal aorta has also been implicated in the induction of the HSC developmental program in the ventral wall of the dorsal aorta[52]. On a C57Bl/6N background the LRP2 mutation causes lethality in mice around the time of birth and there are no mutant pups although embryo collections at all embryonic stages to E18.5 show expected Mendellian ratios. LRP2 mutations on 129 or CD1 backgrounds also do not yield survivors (Hammes et al, unpublished data). On a FVB/N background however, LRP2 null mice are viable with neural tube defects and this receptor has previously been implicated in folate endocytosis in the developing neural tube[53]. However, peripheral blood and bone marrow hematopoietic stem and progenitor cell numbers were comparable in FVB/N wild type and mutant adult mice at 6-9 months of age (Figure S10). A more detailed analysis of embryonic hematopoiesis in mutant mice on both C57Bl/6N and FVB/N backgrounds will be required to establish whether the numbers of emergent HSCs differ at various time points and the identity of any modifier genes in FVB/N that compensate for the loss of LRP2 and these investigations are ongoing. However, taken together with the zebrafish data, which shows reduction rather than loss of HSCs, LRP2 is likely to facilitate rather than be absolutely required for EHT. Indeed, it is important to keep in mind that *Lrp2* transcripts were higher in HB cells with greater BL-CFC potential and HE cells with greater CFU-C potential but cells with lower numbers of transcripts were also able to generate BL-CFCs and CFU-Cs.

Deficiency of dietary folate also results in impaired neural tube development and megaloblastic anemia[54]. Targeted inactivation of the reduced folate carrier (RFC1), which facilitates folate delivery into cells results in embryonic lethality at E10.5 due to neural and hematopoietic defects[55] and components of the Megalin complex are amongst the most significantly disrupted genes in null embryos[38]. Coordinated up-regulation of a receptor that facilitates folate uptake in hemogenic endothelial cells would be consistent with demand for an essential hematinic in cells that are on the threshold of a replicative phase.

Although we focused our attention on *Lrp2*, as a gene without a described role in hematopoiesis, from a list of six that were up-regulated in both hemangioblasts and HE cells, there were other genes that were UP in only one or the other cell fraction. Given the overlap of these gene sets with those generated from gene knockout embryos with specific developmental defects they will serve as a rich resource to explore and manipulate the emergence of hemangioblasts from FLK1+ mesoderm or hematopoiesis in HE cells. Insights gained from these manipulations will in turn inform tissue regeneration protocols that aim to generate functional HSCs.

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## AUTHOR CONTRIBUTIONS

R.N, E.F, P.S, K.K, R.T., M.S., J.K., A.U, J.T, D.B, A.E and R.P performed research and analysed data. A.S, J.W, A.H, D.K., R.R., T.W., B.G, E.D, and L.Z contributed essential reagents and advice with data analysis and interpretation. R.N, G.L, V.K and J.E.P contributed to study design, data interpretation and manuscript preparation. All authors have read and approve the manuscript.

## DISCLOSURES

No conflicts of interest to declare.

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## FIGURE LEGENDS

**FIGURE 1. Mesoderm to hemangioblast transition is accompanied by increased Eng expression and chromatin accessibility at hemato-endothelial regulatory elements. (A)** Schematic representation of the *ENG* locus. The transcription start site is marked with an arrow. The -8kb, +7kb and +9kb enhancers and the promoter (P) are marked in orange, exons are marked in brown and the 5'UTR in cyan. **(B)** Schematic representation of *Bry*-GFP ES cell differentiation. At day 3 of EB differentiation, *Bry*-GFP+/FLK1- (G+F-) and Bry-GFP+/FLK1+ (G+F+) cells were sorted and analysed by RT-PCR and ChIP. **(C)** Bar graph showing *Eng* mRNA expression levels in sorted FLK1+ve and –ve mesodermal cell populations in day 3 EBs generated from *Bry*-GFP ES cells. **(D)** A bar graph showing levels of enrichment of the active chromatin mark, H3K9Ac at *Eng -8, P, +7 and +9* hemato-endothelial enhancers relative to IgG in pre-hemangioblast mesoderm (G+F-; black) and in hemangioblast mesoderm (G+F+; gray). *Eng -4* was included as a negative control region. **; $P < 0.01$, ***; $p < 0.001$

**FIGURE 2. The *Eng* promoter when combined with the -8, +7 and +9 haemato-endothelial enhancers targets FLK1+ mesodermal cells enriched for BL-CFC potential. (A)** Schematic representation of the experimental procedure. The Eng -8/P/LacZ, Eng -8/P/LacZ/+7, Eng -8/P/LacZ/+9, Eng -8/P/LacZ/+7/+9, Eng -8/P/LacZ/+7Δ/+9, and Eng -8/P/LacZ/+7Δ/+9Δ reporter constructs were introduced by homologous recombination into the HPRT locus of HM1 ES cells. Recombinant clones were differentiated into day 3 EBs and stained for FLK1 expression and β-galactosidase activity. FLK1+/LacZ- (F+/L-; gray) and FLK1+/LacZ+ (F+/L+; blue) cells were sorted and seeded into BL-CFC assays. Fractions sorted from the *Eng* -8/P/LacZ/+7/+9 were further analysed by RNA-sequencing. **(B)** Flow cytometry profiles of *Eng* -8/P/LacZ/+7/+9 day 3 EBs (left). BL-CFCs from sorted F+/L-

(gray) and F+/L+ (blue) fractions. **(C)** (i) Flow cytometry profile of day 3 EBs derived from ES cells targeted with *Eng* -8/P/LacZ/+7Δ /+9 (mutated GATA motifs in the +7 enhancer) is shown to the left with corresponding BL-CFCs from sorted F+/L- (gray) and F+/L+ (blue) fractions shown to the right. (ii) Flow cytometry profile of day 3 EBs derived from ES cells targeted with *Eng* -8/P/LacZ/+7Δ /+9Δ (mutated GATA motifs in the +7 enhancer and mutated ETS motifs in the +9 enhancer) and corresponding BL-CFCs from sorted F+/L- (gray) and F+/L+ (blue) fractions. **(D)** Flow cytometry profiles of day 3 EBs and BL-CFCs from sorted F+/L- (gray) and F+/L+ (blue) fractions are shown for ES cells targeted with (i) *Eng* -8/P/LacZ (ii) *Eng* -8/P/LacZ/+9 and (iii) *Eng* -8/P/LacZ/+7. BL-CFC counts are the total number of blast colonies generated from $2x10^4$ seeded cells. Statistical analysis was using students T-test, $*p<0.05$, $**p< 0.01$.

**FIGURE 3**. **RNA-sequencing of FLK1 mesoderm targeted by *Eng* -8/P/LacZ/+7/+9 identifies genes associated with hemangioblast activity. (A)** RNA-sequencing profiles showing *Kdr* (*Flk1*) transcripts (top panel) and *Eng* transcripts (bottom panel) in the F+/L- and F+/L+ fractions. FPKM expression values are shown to the right. **(B)** (i) Heat map representation of up- and down-regulated genes in FLK1+/LacZ- (F+/L-) and FLK1+/LacZ+ (F+/L+) fractions in three independent experiments. (ii) Expression (FPKM values) levels of genes that have previously been associated with hemangioblast function. The left panel shows a subset of genes that are differentially expressed between F+/L- and F+/L+ fractions and the right panel shows a subset of genes that are not. **(C)** GSEA profiles showing the correspondence of genes that are differentially expressed between F+/L- and F+/L+ fractions and those that are differentially expressed in ETV2+/- vs. ETV2-/- (top panel) and LDB wt vs. LDB -/- gene sets. DEG; differentially expressed genes.

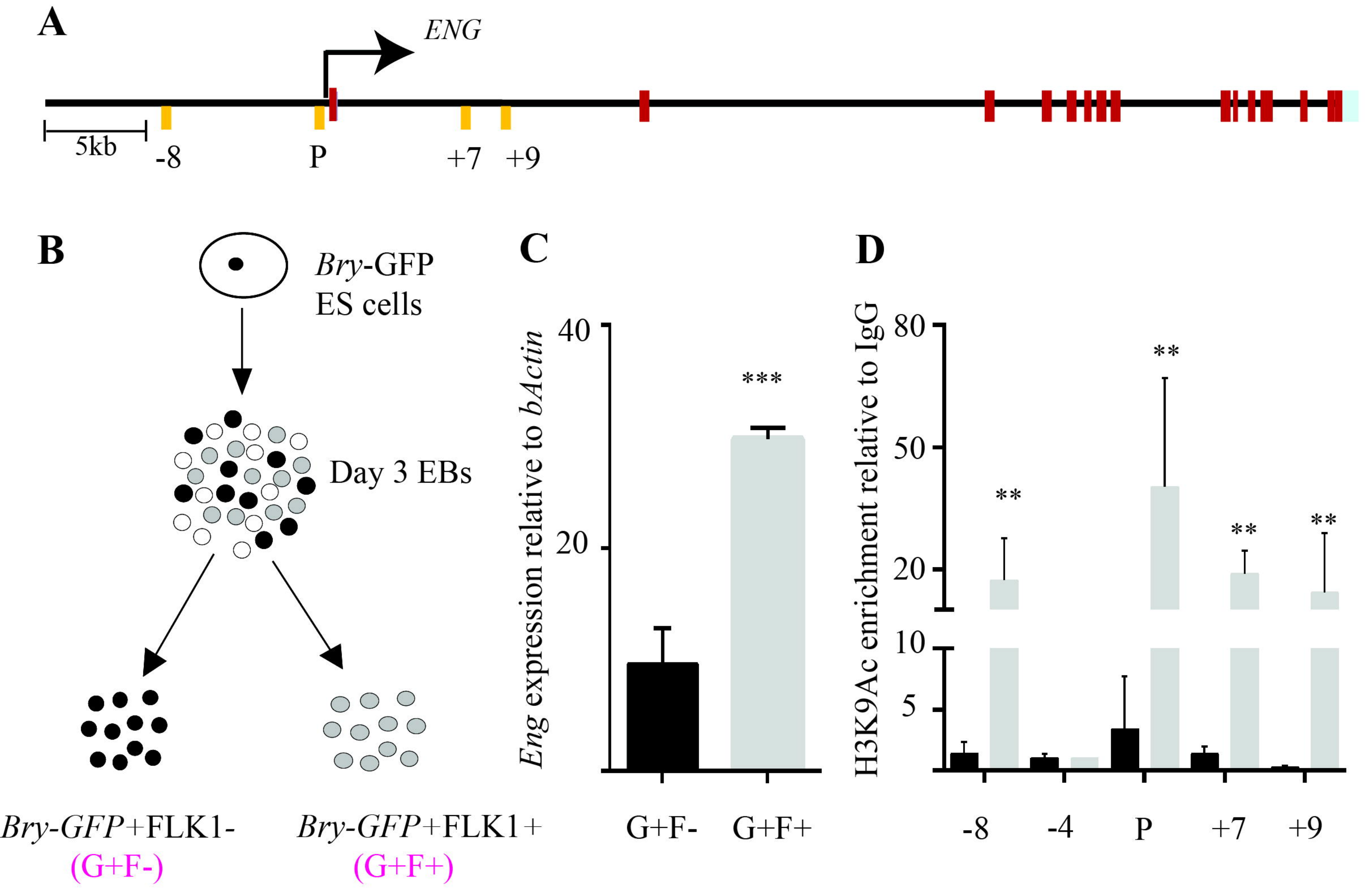
**FIGURE 4. The Eng promoter in combination with the -8 endothelial enhancer targets hemogenic endothelial cells enriched for hematopoietic potential. (A)** Schematic diagram outlining the experimental procedure. Recombinant ES cells generated using the *Eng* reporter constructs were differentiated into day 3 EBs. FLK1+ mesodermal cells were sorted from representative clones for each recombinant ES cell line and cultured in liquid blast media. At 48 hours, CD41-/TIE2+/c-KIT+ (HE) cells were sorted into *lacZ*+ and *lacZ*– fractions. The sorted fractions were re-cultured in liquid blast media for a further 48 hours followed by flow cytometry and CFU-C assays. **(B)** (i) CD41 and TIE2 expression in sorted c-KIT+ HE LacZ- (white) and LacZ+ (blue) fractions (after 2 days of re-culture) derived from *Eng -8/P/LacZ* ES cells. (ii) Percentage of CD45+ cells generated from LacZ- and LacZ+ HE fractions. (iii) Bar chart showing the number and type of hematopoietic colonies generated by each fraction. **(C)** (i)-(iii) Corresponding data to (B) generated from *Eng -8/P/LacZ/+7/+9* ES cells. **(D)** (i)-(iii) Corresponding data to (B) generated from *Eng -8/P/LacZ/+7* ES cells. **(E)** (i)-(iii) Corresponding data to (B) generated from *Eng -8/P/LacZ/+9* ES cells. Primitive and definitive colonies were scored after four and nine days respectively. Statistical analysis was using students T-test, *; $p<0.05$, **; $p< 0.01$.

**FIGURE 5. Hematopoietic potential is highest in *Eng* -8/P/lacZ targeted HE cells that do not express surface ENG. (A)** Schematic diagram outlining the experimental procedure. FLK1+ mesodermal cells were sorted from day 3 EBs generated from the *Eng -8/P/LacZ* recombinant ES cell line and cultured in liquid blast culture media. At 48 hours, CD41-/TIE2+/c-KIT+ (HE) cells were sorted into ENG+/LacZ-, ENG+/LacZ+, and ENG-/LacZ+ fractions. These fractions were either directly seeded into CFU-C assays (B) or re-cultured in liquid blast media for a further 48 hours and analysed by flow cytometry and CFU-C assays (C). **(B)** (i)- (ii) Flow cytometry to show the frequencies of CD41-/TIE2+/c-KIT+ (HE) cells

in ENG+/*lacZ*+, ENG+/*lacZ*- and ENG-*lacZ*+ fractions. (iii) CFU-C potential of each sorted fractions in (i). **(C)** (i) Flow cytometry analysis of CD41 and TIE2 expression in sorted HE cell fractions after two days of re-culture in liquid blast media. (ii) Bar chart showing the percentage of CD45 positive cells in sorted fraction. (iii) Bar chart showing hematopoietic colony numbers from each fraction. Primitive and definitive colonies were scored after four and nine days respectively. Statistical analysis was using student T-test, *; $p < 0.05$, **; $p < 0.01$ and ***; $p < 0.001$.

**FIGURE 6. Transcriptomic analysis of HE fractions identifies genes associated with hemogenic endothelial to hematopoietic transition.** **(A)** RNA-sequencing profiles showing *Eng* transcripts (top panel) and *Runx1* transcripts (bottom panel) in the E+/L-, E+/L+ and E-/L+ fractions. FPKM expression values are shown to the right. **(B)** (i) Heat map representation of up- and down-regulated genes in ENG+/LacZ- (E+/L-) HE, ENG+/LacZ+ (E+/L+) HE and ENG-/LacZ+ (E-/L+) HE fractions in three independent experiments. (ii) Expression (FPKM values) levels of genes that have previously been associated with hemogenic endothelium. The top panel shows a subset of genes that are differentially expressed between E+/L-, E+/L+ and E-/L+ fractions and the bottom panel shows a subset of genes that are not. **(C)** GSEA profiles showing the correspondence of genes that are differentially expressed between the E+/L-, E+/L+ and E-/L+ fractions and those that are differentially expressed in endothelial cells (EC) vs. hemogenic endothelial cells (HEC) (top panel) and HECs vs. hematopoietic stem cells (HSC) gene sets. **(D)** Transcription factors and cell surface receptors that are up- and down regulated in the *Eng* -8/P E-/L+ HE fraction. The log fold changes (logFC) and log false discovery rates (logFDR) are listed for each gene. DEG; differentially expressed genes.

**FIGURE 7. Lrp2 is required for normal definitive hematopoiesis. (A)** Venn diagram showing the overlap of genes that are UP in FLK1 mesoderm enriched for BL-CFCs and/or HE cells enriched for hemogenic potential. **(B)** Immunohistochemistry of E10.5 *Ly6aGFP* AGM shows co-expression of GFP and LRP2 in endothelial cells and hematopoietic clusters. The insets show the same sections at low magnification. **(C)** Homology relationships of zebrafish *lrp2a* and *lrp2b* coding sequences with that of *Lrp2* in different vertebrate species. **(D)** ISH for the HSC marker cmyb in zebrafish at 36 hpf. (i) Low (left-side panels) and high (right-side panels) magnification images of control zebrafish (top row), lrp2 a/b morpholinos (middle row) and lrp2a/b morpholinos co-injected with *hLRP2* mRNA (bottom row) zebrafish. (ii) Low (left-side panels) and high (right-side panels) magnification images of control zebrafish (top row) and lrp2b morpholinos. **(E)** Confocal images of flk:zsgreen reporter embryos show an intact vasculature in both control (upper panel) and *lrp*2a/b morphant (lower panel) embryos. DA; dorsal aorta, NC; notochord, NT; neural tube.



A
ENG
5kb
-8
P
+7
+9
B
Bry-GFP
ES cells
Day 3 EBs
Bry-GFP+FLK1-
(G+F-)
Bry-GFP+FLK1+
(G+F+)
C
Eng expression relative to bActin
40
20
***
G+F-
G+F+
D
H3K9Ac enrichment relative to IgG
80
50
20
10
5
**
**
**
**
-8
-4
P
+7
+9


Figure 1

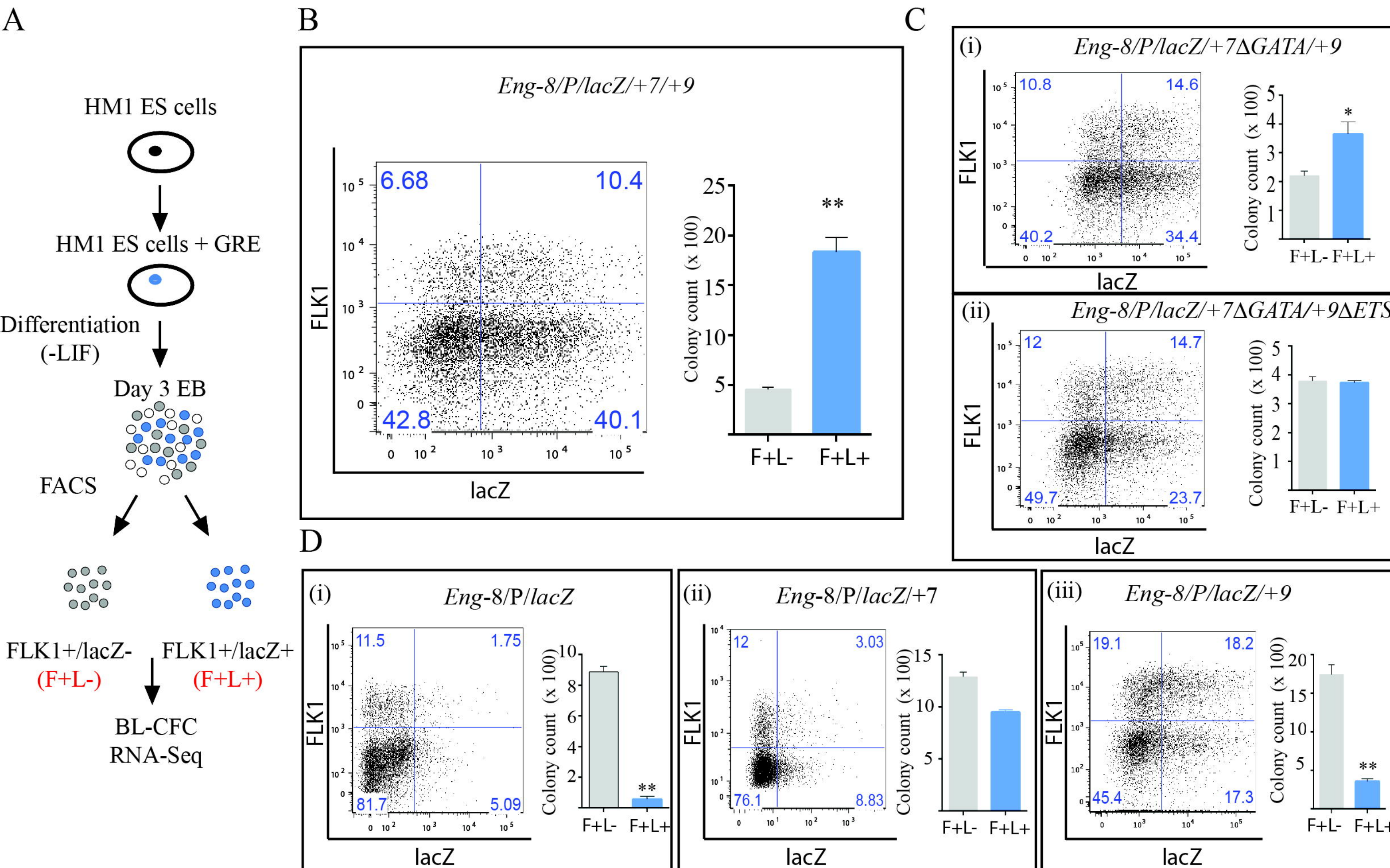

A
HM1 ES cells
HM1 ES cells + GRE
Differentiation
(-LIF)
Day 3 EB
FACS
FLK1+/lacZ-
(F+L-)
FLK1+/lacZ+
(F+L+)
BL-CFC
RNA-Seq
B
Eng-8/P/lacZ/+7/+9
FLK1
lacZ
6.68
10.4
42.8
40.1
Colony count (x 100)
**
F+L-
F+L+
C
(i)
Eng-8/P/lacZ/+7ΔGATA/+9
10.8
14.6
40.2
34.4
*
(ii)
Eng-8/P/lacZ/+7ΔGATA/+9ΔETS
12
14.7
49.7
23.7
D
(i)
Eng-8/P/lacZ
11.5
1.75
81.7
5.09
**
(ii)
Eng-8/P/lacZ/+7
12
3.03
76.1
8.83
(iii)
Eng-8/P/lacZ/+9
19.1
18.2
45.4
17.3
**

Figure 2

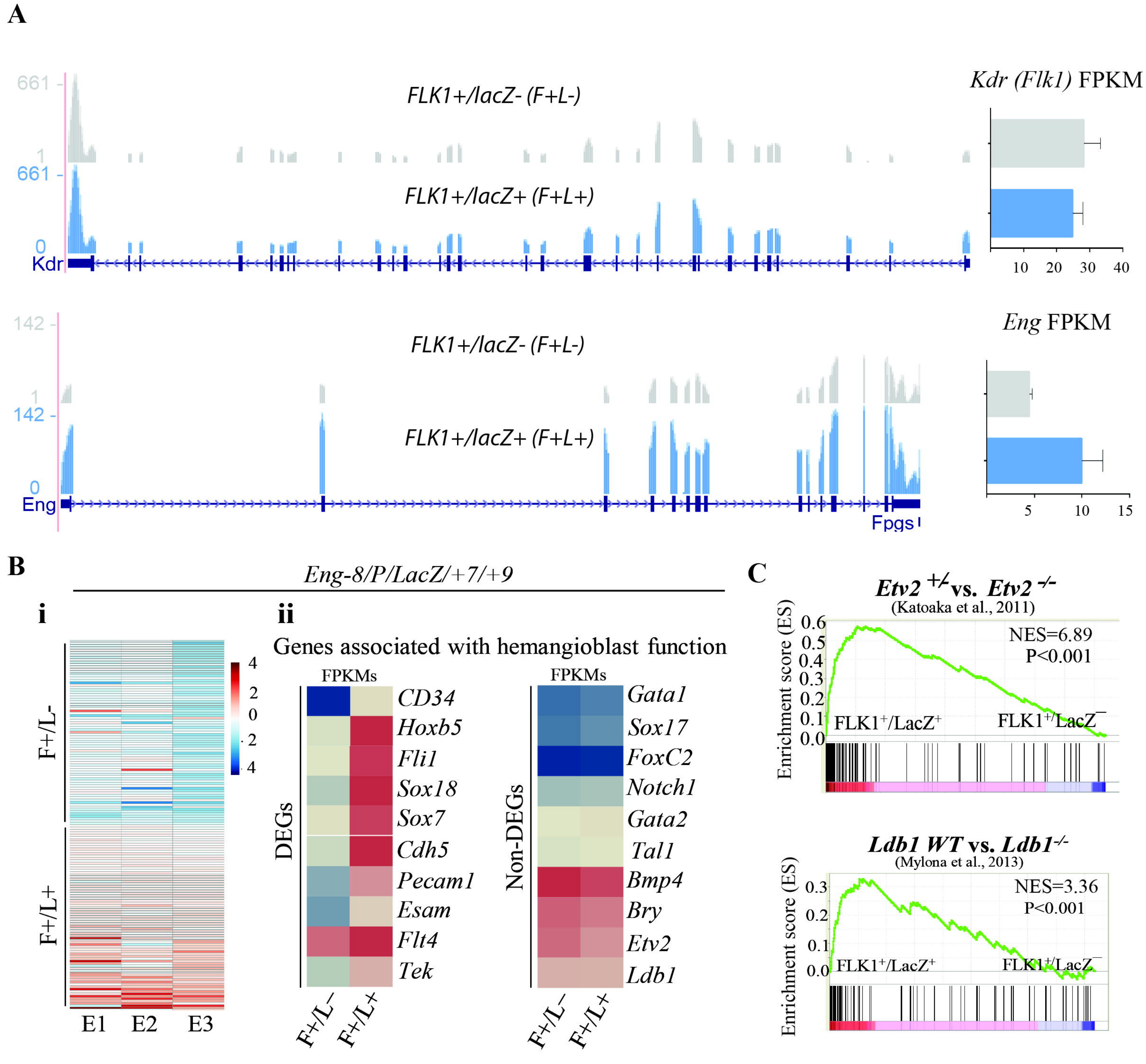

A
FLK1+/lacZ- (F+L-)
FLK1+/lacZ+ (F+L+)
Kdr
Kdr (Flk1) FPKM
Eng
Fpgs
Eng FPKM
B
Eng-8/P/LacZ/+7/+9
i
ii
F+/L-
F+/L+
E1
E2
E3
Genes associated with hemangioblast function
FPKMs
DEGs
Non-DEGs
CD34
Hoxb5
Fli1
Sox18
Sox7
Cdh5
Pecam1
Esam
Flt4
Tek
Gata1
Sox17
FoxC2
Notch1
Gata2
Tal1
Bmp4
Bry
Etv2
Ldb1
C
Etv2 +/- vs. Etv2 -/-
(Katoaka et al., 2011)
NES=6.89
P<0.001
Enrichment score (ES)
FLK1+/LacZ+
FLK1+/LacZ−
Ldb1 WT vs. Ldb1-/-
(Mylona et al., 2013)
NES=3.36
P<0.001

Figure 3

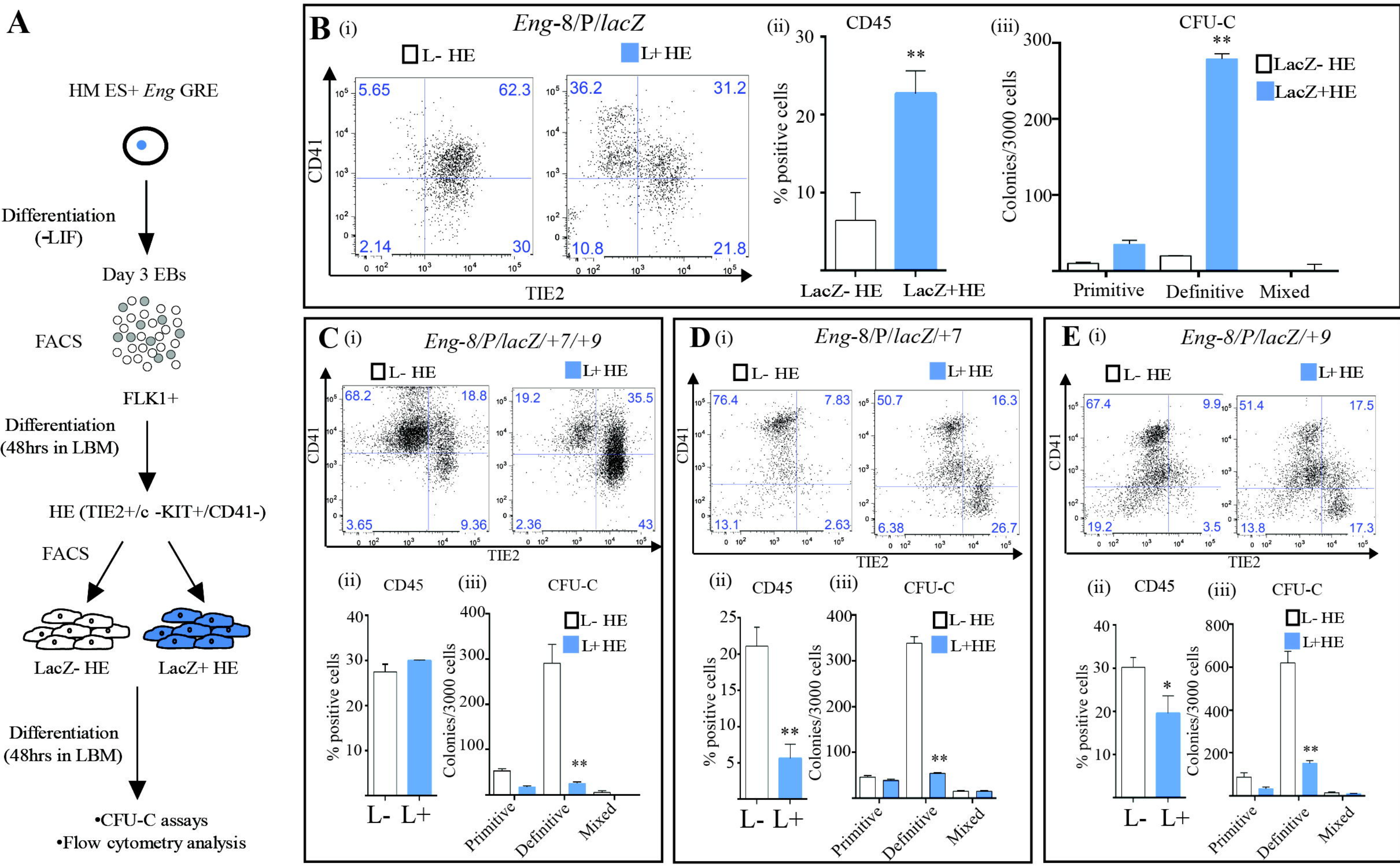

A
HM ES+ Eng GRE
Differentiation (-LIF)
Day 3 EBs
FACS
FLK1+
Differentiation (48hrs in LBM)
HE (TIE2+/c -KIT+/CD41-)
FACS
LacZ- HE
LacZ+ HE
Differentiation (48hrs in LBM)
•CFU-C assays
•Flow cytometry analysis
B (i) Eng-8/P/lacZ
L- HE
L+ HE
CD41
TIE2
5.65 62.3 2.14 30
36.2 31.2 10.8 21.8
(ii) CD45
% positive cells
LacZ- HE LacZ+HE
(iii) CFU-C
Colonies/3000 cells
LacZ- HE
LacZ+HE
Primitive Definitive Mixed
C (i) Eng-8/P/lacZ/+7/+9
68.2 18.8 3.65 9.36
19.2 35.5 2.36 43
(ii) CD45
(iii) CFU-C
L- HE
L+ HE
L- L+
D (i) Eng-8/P/lacZ/+7
76.4 7.83 13.1 2.63
50.7 16.3 6.38 26.7
E (i) Eng-8/P/lacZ/+9
67.4 9.9 19.2 3.5
51.4 17.5 13.8 17.3

Figure 4

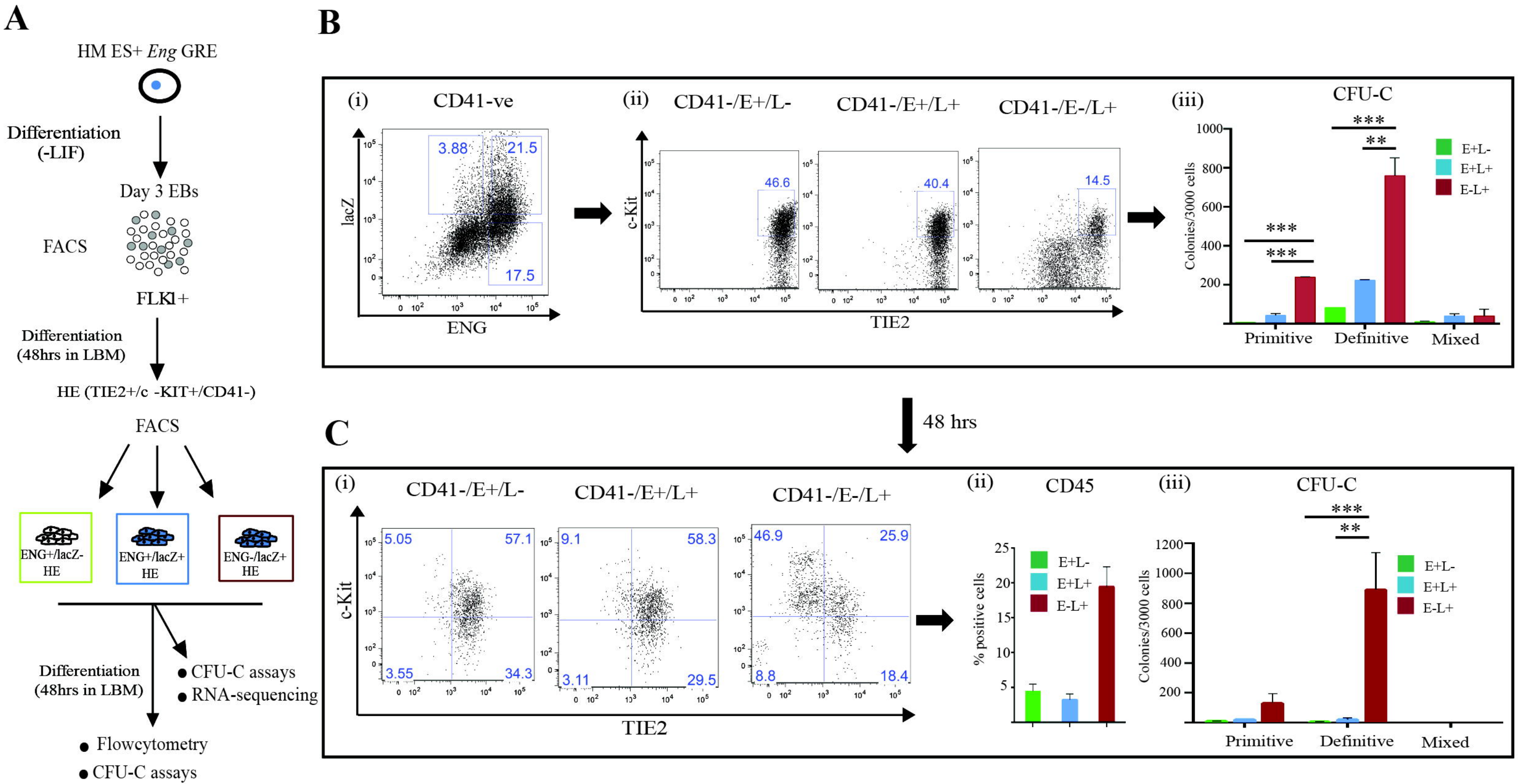
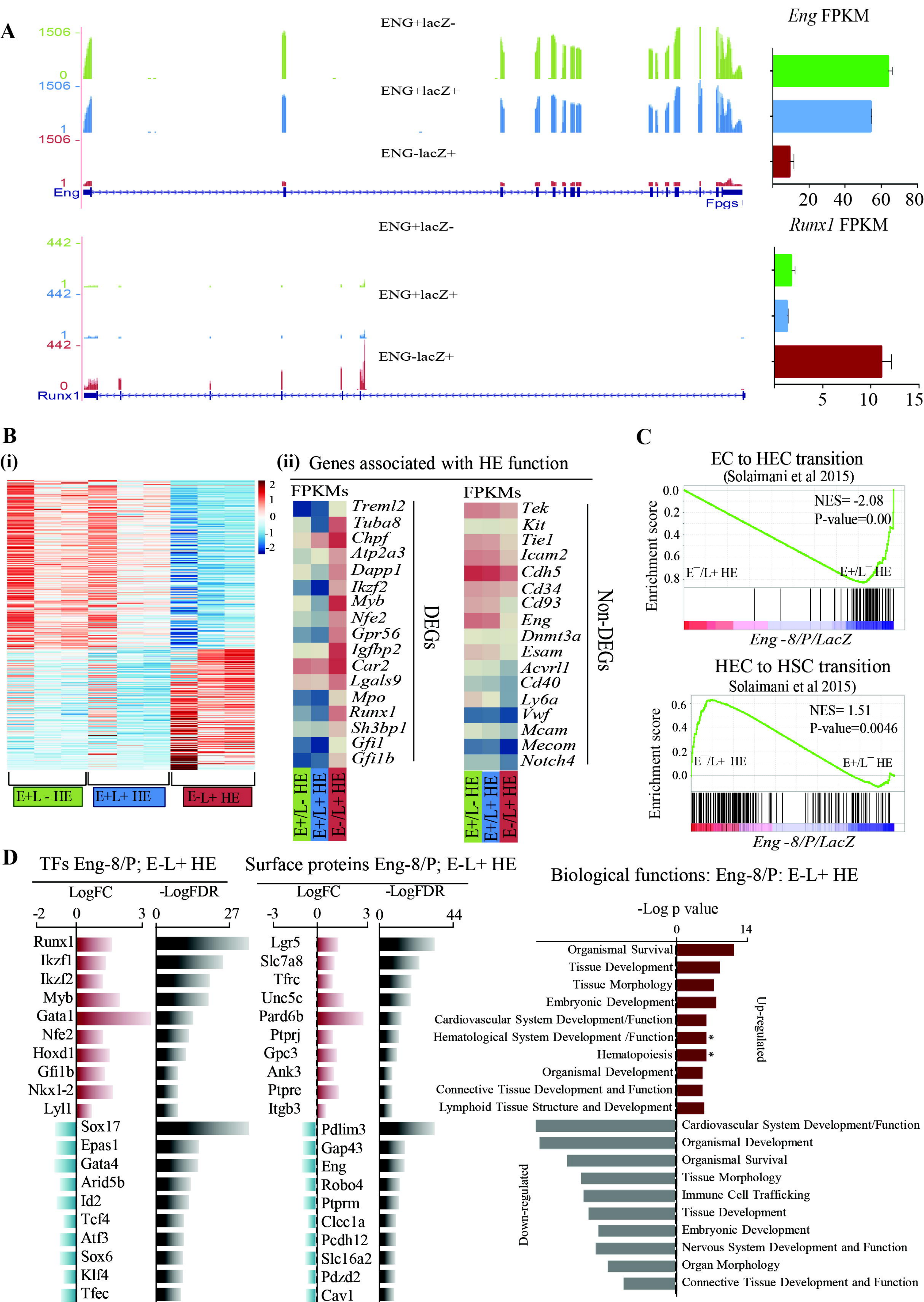

A
HM ES+ Eng GRE
Differentiation (-LIF)
Day 3 EBs
FACS
FLK1+
Differentiation (48hrs in LBM)
HE (TIE2+/c -KIT+/CD41-)
FACS
ENG+/lacZ- HE
ENG+/lacZ+ HE
ENG-/lacZ+ HE
Differentiation (48hrs in LBM)
CFU-C assays
RNA-sequencing
Flowcytometry
CFU-C assays
B
(i) CD41-ve
lacZ
ENG
3.88
21.5
17.5
(ii) CD41-/E+/L-
CD41-/E+/L+
CD41-/E-/L+
c-Kit
TIE2
46.6
40.4
14.5
(iii) CFU-C
Colonies/3000 cells
E+L-
E+L+
E-L+
Primitive
Definitive
Mixed
48 hrs
C
(i) CD41-/E+/L-
CD41-/E+/L+
CD41-/E-/L+
c-Kit
TIE2
5.05
57.1
3.55
34.3
9.1
58.3
3.11
29.5
46.9
25.9
8.8
18.4
(ii) CD45
% positive cells
E+L-
E+L+
E-L+
(iii) CFU-C
Colonies/3000 cells
E+L-
E+L+
E-L+
Primitive
Definitive
Mixed

Figure 5



A
ENG+lacZ-
ENG+lacZ+
ENG-lacZ+
1506
0
1506
1
1506
1
Eng
Fpgs
Eng FPKM
20 40 60 80
442
1
442
1
442
0
Runx1
Runx1 FPKM
5 10 15
B
(i)
E+L - HE
E+L+ HE
E-L+ HE
(ii) Genes associated with HE function
FPKMs
Treml2
Tuba8
Chpf
Atp2a3
Dapp1
Ikzf2
Myb
Nfe2
Gpr56
Igfbp2
Car2
Lgals9
Mpo
Runx1
Sh3bp1
Gfi1
Gfi1b
DEGs
Tek
Kit
Tie1
Icam2
Cdh5
Cd34
Cd93
Eng
Dnmt3a
Esam
Acvrl1
Cd40
Ly6a
Vwf
Mcam
Mecom
Notch4
Non-DEGs
E+/L- HE
E+/L+ HE
E-/L+ HE
C
EC to HEC transition
(Solaimani et al 2015)
NES= -2.08
P-value=0.00
Enrichment score
E⁻/L+ HE
E+/L⁻ HE
Eng -8/P/LacZ
HEC to HSC transition
Solaimani et al 2015)
NES= 1.51
P-value=0.0046
Eng -8/P/LacZ
D
TFs Eng-8/P; E-L+ HE
LogFC
-LogFDR
Runx1
Ikzf1
Ikzf2
Myb
Gata1
Nfe2
Hoxd1
Gfi1b
Nkx1-2
Lyl1
Sox17
Epas1
Gata4
Arid5b
Id2
Tcf4
Atf3
Sox6
Klf4
Tfec
Surface proteins Eng-8/P; E-L+ HE
Lgr5
Slc7a8
Tfrc
Unc5c
Pard6b
Ptprj
Gpc3
Ank3
Ptpre
Itgb3
Pdlim3
Gap43
Eng
Robo4
Ptprm
Clec1a
Pcdh12
Slc16a2
Pdzd2
Cav1
Biological functions: Eng-8/P: E-L+ HE
-Log p value
Organismal Survival
Tissue Development
Tissue Morphology
Embryonic Development
Cardiovascular System Development/Function
Hematological System Development /Function
Hematopoiesis
Organismal Development
Connective Tissue Development and Function
Lymphoid Tissue Structure and Development
Up-regulated
Cardiovascular System Development/Function
Organismal Development
Organismal Survival
Tissue Morphology
Immune Cell Trafficking
Tissue Development
Embryonic Development
Nervous System Development and Function
Organ Morphology
Connective Tissue Development and Function
Down-regulated


Figure 6

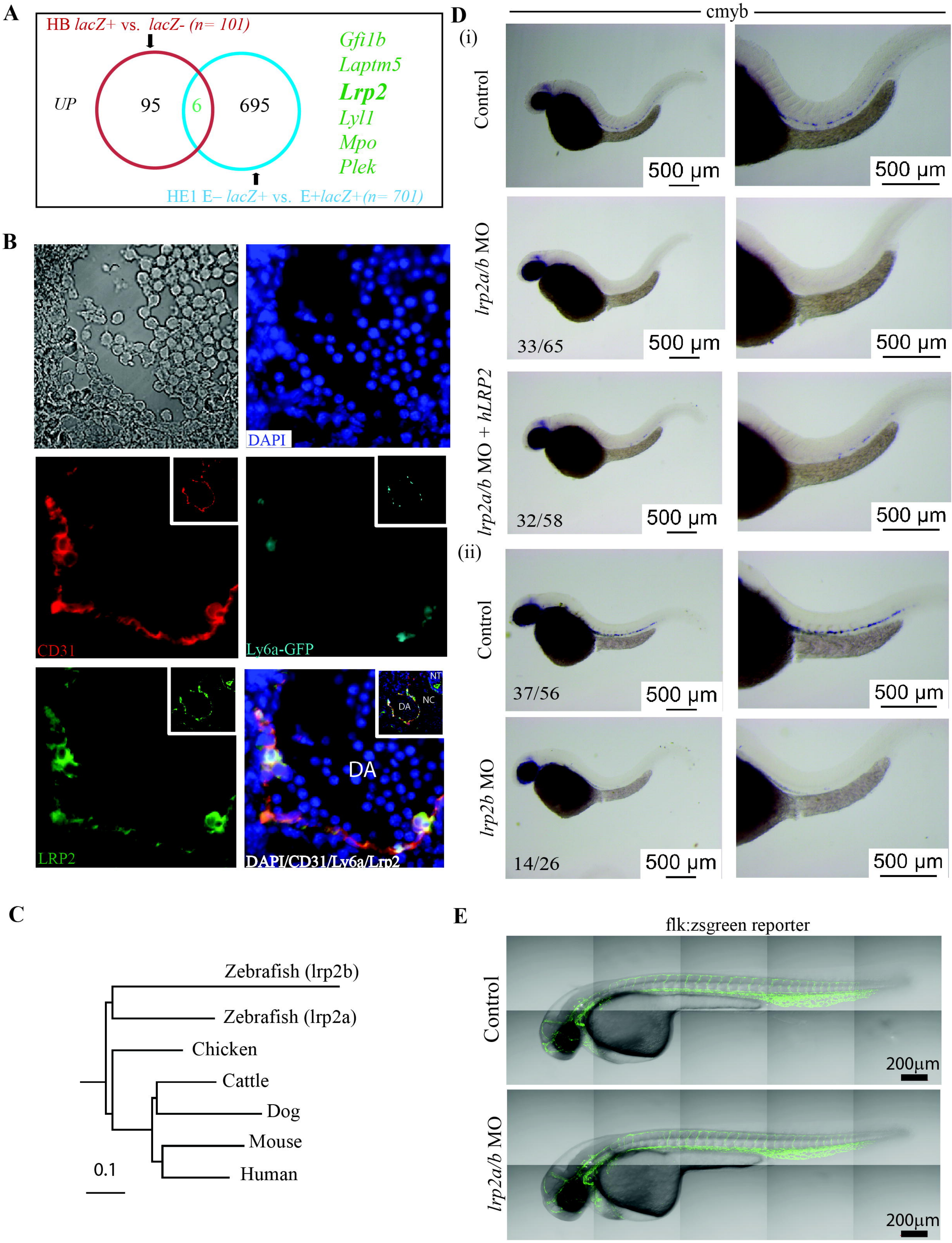

A
HB lacZ+ vs. lacZ- (n= 101)
UP
95
6
695
HE1 E– lacZ+ vs. E+lacZ+(n= 701)
Gfi1b
Laptm5
Lrp2
Lyl1
Mpo
Plek
B
DAPI
CD31
Ly6a-GFP
LRP2
NT
NC
DA
DAPI/CD31/Ly6a/Lrp2
C
Zebrafish (lrp2b)
Zebrafish (lrp2a)
Chicken
Cattle
Dog
Mouse
Human
0.1
D
cmyb
(i)
Control
lrp2a/b MO
33/65
lrp2a/b MO + hLRP2
32/58
(ii)
Control
37/56
lrp2b MO
14/26
500 µm
E
flk:zsgreen reporter
Control
lrp2a/b MO
200µm

Figure 7

## SUPPLEMENTAL METHODS

### Murine ES cell culture

The Bry/GFP [1] and HM1 ES cells [2] have been previously described. Murine ES cells were seeded on 6-well plates coated with irradiated mouse embryonic feeders, in media composed of 84% Dulbecco's Modified Eagle Medium (DMEM, PAA Laboratories), 15% Fetal Bovine serum (FBS, Invitrogen) pre-tested for maintenance of ES cells, 0.1% of 0.15M dilution of monothioglycerol (MTG, Sigma Aldrich) and 1000units/ml mouse recombinant Leukaemia inhibitory factor (Esgro, Millipore).

### Generating *Hprt* targeting constructs

To generate the *Hprt* targeting constructs DNA fragments corresponding to the *Eng -8, P, +7, +9* [3,4]*, mutant +7 (+7Δ, mutant Gata),* and *mutant +9 (+9Δ, mutant Ets)* regions (Fig. S1B) along with the *LacZ* reporter gene were ligated in multiple combinations into the pMP8 targeting vector. The DNA constructs cloned into pMP8 were sequenced using the following primers; Pmp8_F, 5'-AGAACGTCAGTAGTCATAG-3'; Pmp8_R, 5'-TGCAGTGAGCCAGACTGTG-3'. The generated targeting constructs are listed in supplementary figure S1C. A map for *Eng -8/P* in pMP8 can be found in Supplementary Fig. S2A (All other reporter constructs were cloned into the same region of the pMP8 vector).

### *Hprt* targeting of HM1 ES cells

To prepare the cells for targeting, HM1 ES cells were cultured in DMEM-ES medium containing 1× 6-Thioguanine (6-TG, Sigma Aldrich) for a week before electroporation. The cells were grown to confluence, washed with PBS, and trypsinized to obtain a single cell suspension. $1\times10^8$ HM1 cells were resuspended in 900µl ice-cold PBS, mixed with 100µg of Pme1-linearized targeting vector and electroporated at 0.8Kv/3uF using a Gene Pulser (BioRad). Cells were centrifuged and the pellet was resuspended and distributed over 4x100mm gelatin-coated plates. 24 hours later, Hypoxanthine Aminopterin Thymidine (HAT, Sigma Aldrich-Aldrich) was added to the culture medium to select cells with successful integration of the targeting vector. After 7-10 days, over which the selection media was changed every 48 hours, HAT resistant colonies were picked into 96-well plates, and maintained in ES medium supplemented with Hypoxanthine-Thymidine (1×HT, Sigma Aldrich). Genomic DNA was extracted and analysed for successful recombination by PCR and southern blots.

**Isolation of Genomic DNA**

Cell pellets were lysed in 500µl of ES cell lysis buffer (10mM Tris pH7.4, 10mM EDTA, 10mM NaCl, and 0.5% Sarkosyl at 30% stock concentration) with freshly added 1mg/ml Proteinase K (20mg/ml stock) and incubated at 55°C O/N. Two phenol chloroform (Sigma Aldrich) extractions were performed using the Maxtract low density tubes (Qiagen) according to manufacturer's instructions. Cleanup of the genomic DNA was done by ethanol precipitation. The DNA pellet was washed with 70% ethanol, re-suspended in milliQ water and stored at -20. Genomic DNA isolated from recombinant ES cell clones was analysed for successful integration of the DNA fragments by qPCR using the following primers: LacZ_F, 5'-GCCATTGTCAGACATGTATAC-3'; LacZ_R, 5'-CTCAACCCTATAGCTCCAG-3'; *Hprt* exon2_F, 5'-GAACCAGGTTATGACCTAGA-3'; *Hprt* exon2_R, 5'-ATTGTGGCCCTCTGTGTGCT-3' (Fig. S2B-D).

**Southern blotting**

10μg of genomic DNA was digested with Hpa1 and Sac1 (NEB) at 37°C O/N. The DNA was separated on a 0.8% agarose gel (1xSYBR safe DNA stain, Invitrogen), run at 25V for 12-14 hours. The gel was subsequently washed with 0.25M HCl solution for 20min, and 0.4M NaOH for 30min. The DNA was then transferred O/N onto a Hybond membrane (Hybond-XL, Amersham) in a 0.4M NaOH solution. The membrane was washed in 0.4M NaOH for 10min, and 2xSSC for 10min. The membrane was then baked in an oven at 85°C for 2 hours to crosslink the DNA followed by incubation in a bottle containing 20ml of hybridisation buffer (0.5M NaP, 7% SDS, 1mM EDTA, and 1% crystalline grade BSA) for 2 hours at 65°C. During this time, the probe was labelled with alpha $^{32}$P-dCTP (PerkinElmer) using a Decaprime II kit (Applied biosystems), as per manufacturers description. The membrane was incubated with the labelled probe at 65°C O/N. Membranes were subsequently washed in 2xSSC at room temperature for 20min, then 0.1xSSC/0.1%SDS preheated to 65°C for 10min. The washed membranes were then developed using a phosphoimager.

**ES cell differentiation into EBs**

To generate EBs, ES cells were collected and cultured in media consisting of IMDM supplemented with 15% FBS (PAA laboratories) pretested for efficient embryonic stem cell differentiation, 1% L-Glutamine (Invitrogen), 1% penicillin-streptomycin, 0.3% of 0.15M MTG, 0.6% of 30mg/ml transferrin (Life Technologies) and 1% of 5mg/ml ascorbic acid (Sigma Aldrich). Cells were then seeded on ultra-low attachment 60mm plates (Sterilin) and placed in an incubator at 37°C and 5%$CO_2$. These culture conditions were optimal for growth of day 1-4 EBs [5].

**LacZ staining**

Fluorescein di-β-D-galactopyranoside (FDG, Sigma Aldrich) is a substrate for β-D-galactosidase enzyme that is encoded by the LacZ reporter gene. FDG powder was reconstituted to a 2mM stock solution according to manufacturer's instructions. Cells collected from day 3EB and D2 liquid blast cultures were dissociated and diluted in PBS/2% FBS at a concentration of $3 \times 10^6$ cells/0.1ml. On a 37C heat block, FDG was added to the cells at a 1:1 ratio and incubated at 37C for 1 min. The cell suspension was then added to IMDM/20%FBS and placed on ice for 1 hour. Further staining with primary and secondary antibodies was performed after the LacZ staining procedure.

**Flow cytometry and cell sorting**

Cells were collected from EBs and liquid blast cultures and dissociated into a single cell suspension. Cells were incubated on ice for 30 min either with a biotinylated or flurochrome-conjugated primary antibody. For cells stained with a primary biotinylated antibody this was followed with 30min incubation with SA-pecy7 secondary antibody. Dead cells were excluded from the analysis on the basis of Hoechst 33258 uptake (1µg/ml final concentration; Invitrogen). The following primary and secondary antibodies were used for staining; TIE2-biotin, TIE2-PE, Endoglin-Biotin, Endoglin-PE, CD117-eFluor780, FLK1-APC, FLK1-Biotin, FLK1-PE, CD41-Biotin, CD41-pecy7, CD41-APC, CD45-percp_cy5.5, CD144-AlexaFluor647, rabbit anti-mouse Lrp2-pecy7 (Bioss antibodies), streptavidin-pecy7 (eBiosciences), and anti-rabbit Alexa Fluor-647 (Invitrogen). Flow cytometry analysis was performed using standard flow cytometers; LSR or BD Canto II. FACS was performed on an Aria II, Influx or Jazz BD.

**Methylcellulose blast colony forming (BL-CFC) assay**

$2 \times 10^4$ FLK1+/LacZ- and FLK1+/LacZ+ cells sorted from day 3 EBs were seeded in methylcellulose mix which consisted of IMDM supplemented with 55% methylcellulose (BioScientific), 10% FBS pretested for efficient EB differentiation, 1% L-glutamine, 1% L-glutamine, 0.6% of 30mg/ml transferrin, 0.3% of 0.15M MTG, 0.5% of 5mg/ml ascorbic acid, 15% D4T conditioned media, 0.1% of 5µg/ml VEGF, and 0.1% of 10µg/ml IL-6. A 1ml syringe and 18 gauge blunt-end needle were used to aspirate the methylcellulose mix onto 35mm petri dishes. The blast potential in Flk1+ cells was assayed in triplicate dishes of 1ml. The plates were then placed in a humidified incubator 37°C and 5% $CO_2$. Colonies were scored following four days of culture [5].

**Liquid BL-CFC assay**

Day 3 EBs were dissociated into single cells using trypsin (Gibco), and stained with a Flk1-PE or Flk1-bio antibody (eBiosciences). Sorted FLK1+ cells were seeded on gelatin coated plates at a density of 7.5-8.5x$10^4$ cells/9.6$cm^2$ (in a humidified incubator 37°C, 5% $CO_2$). The culture medium consisted of IMDM supplemented with 10% FBS pre-tested for differentiation, 1% L-Glutamine, 0.6% of 30mg/ml transferrin, 0.3% of 0.15M MTG, 0.5% of 5mg/ml ascorbic acid, 15% D4T conditioned medium, 0.1% of 5µg/ml VEGF, and 0.1% of 10µg/ml IL-6 (R&D systems).

**Hematopoietic methylcellulose colony-forming assay**

Cells isolated from day 2 or 4 of liquid blast cultures were seeded in media containing IMDM supplemented with 55% methylcellulose, 15% plasma derived serum (PDS, Animal Technologies), 10% protein-free hybridoma medium (PFHMII, Invitrogen), 1% L-Glutamine, 0.6% of 30mg/ml transferrin, 0.3% of 0.15M MTG, 0.5% of 5mg/ml ascorbic acid, 1% of 10µg/ml kit ligand (KL), 0.1% of 1µg/ml IL-3, 0.3% of 10µg/ml G-CSF, 0.1% of 5µg/ml IL-

11, 0.2% erythropoietin at 2000 units/ml, 0.2% of 5µg/ml IL-6, 0.1% of 5µg/ml TPO, and 0.1% of 10µg/ml GM-CSF. Cells were seeded at a concentration of $3x10^4$cells/ml, and the assay was set up in triplicate dishes of 1ml. Primitive colonies were scored after 4-5 days of culture, whereas most definitive colonies were scored after 7-10 days. All cytokines used in this assay were purchased from R&D systems [5].

**RT-PCR**

Prior to RNA isolation from samples, all equipment was treated with RNaseZap (Ambion) to remove any contaminating RNases. RNA was extracted using and RNeasy extraction kit (Qiagen) following manufacturer's instructions. RNA was eluted with 30µl RNase-free water. cDNA was then synthesized using the GoScript Reverse Transcriptase (Promega) following manufacturer's guidelines. The cDNA was analysed for expression using the Express SYBR Green QPCR Supermix universal (Life Technologies). List of primers used for RT-PCR: *Eng*_F, 5'-AAATCCCGTTGCACTTGG-3'; Eng_R, 5'-ACTCTTGGCTGTCCTTGGAA-3'; *B-actin*_F, 5'-TGACAGGATGCAGAAGAAGA-3'; B-actin_R, 5'-CGCTCAGGAGGAGCAATG-3'; Lrp2_F; Lrp2_R.

**Chromatin immunoprecipitation (ChIP) assay**

ChIP assays were performed as detailed previously[3]. Briefly, FACS sorted *Bry*-GFP ES cells (+/+ and +/− cell fractions) were treated with 0.4% formaldehyde (Sigma Aldrich) and the cross-linked chromatin was retrieved by nuclei isolation and lysis. The chromatin was sonicated to yield an average fragment size of approximately 500 bp, pre-cleared with rabbit serum (anti-IgG, Millipore), and immunoprecipitated with an anti–acetyl H3K9 antibody (AcH3K9, Millipore) to recover acetylated histones and bound DNA. The DNA was then purified, and enrichment at the *Eng* locus was measured by real-time PCR. Expression levels were normalized to *Eng -4* (Negative control region). List of primers used to quantify enrichment; Eng-8_F, 5’-TGTCATTGTCTTCTGGTCTC-3’; Eng-8_R, 5’-ACACTCTCTGGGCATAGC-3’; Eng-4_F, 5’-AAGCGGCATTGGATATTG-3’; Eng-4_R, 5’-AAGGTTAGGTTCGTTTGG-3’; EngP_F, 5’-ACTTCTCCTGACTTCTCC-3’; EngP_R, 5’-CGGTATCCAGAGGTAAGG-3’; Eng+7_F, 5’-CCAGAGCAACTTGATGAC-3’; Eng+7_R, 5’-TACTCCTCCTCCTCCTTC-3’; Eng+9_F, 5’-TGGGTCAGGGTGAAATTCC -3’; Eng+9_R, 5’-AAGGCCGGTGATGTAGAGC-3’.

**Mouse embryo immunostaining and imaging**

10um thick cryosections of E10.5 fixed mouse embryos embedded in a gelation/sucrose solution were thawed and rehydrated in PBS prior to immunostaining. The sections were streptavidin/biotin blocked followed by serum blocking (PBS with 10% FCS, 0.05% Tween20 and of 10% goat serum (DAKO) for 1 hour before the sections were incubated with primary antibodies at 4°C overnight in blocking buffer. Immunostaining of E10.5 embryo sections was performed using purified rat anti mouse CD31 (553370, MEC13.3, BD Biosciences) (1/100) and guinea pig anti-mouse Lrp2 primary antibody (Dr Annette Hammes, Max-Delbrueck-Center for Molecular Medicine, Berlin). Sections were washed three times in PBST for 15 minutes each and then incubated with fluorochrome-conjugated secondary antibodies Alexa Fluor(r) 488 Goat Anti-Rat IgG (A11006, Life Technologies) and Alexa Fluor(r) 647 goat anti-guinea pig IgG (A-21450, Life Technologies) at a 1/400 dilution. Sections were further washed three times in PBS and mounted using Prolong Gold antifade reagent with DAPI (Life Technologies). Images were taken using a low-light time lapse microscope (Leica) using the Metamorph imaging software and processed using ImageJ.

**Generating zebrafish morpholinos and analysis**

Morpholinos against lrp2a (5′-AATCAGTGCTTGTGGTTTACCTGGG-3′,[6]), lrp2b (5′-CACCACTCATGCACTGACCTGACCTGCACA-3′,[7]) and p53 (5′-GCGCCATTGCTTTGCAAGAATTG -3′, [8]) were purchased from Gene Tools. Lrp2a/b morpholinos were injected at increasing doses of 1ng, 2ng and 4ng each. The p53 morpholino was injected at a previously determined optimal dose of 4ng (Zon lab). The Lrp2 rescue was performed using a Human lrp2 vector obtained from Origene. Plasmid was linearized with Sfo1 and *in-vitro* transcribed using mMessage mMACHINE T7 kit (Thermo Fisher). The mRNA was injected at two different doses "low" (20pg/embryo) and "high" (100pg/embryo). Embryos were fixed at 36hpf followed by analysis of runx1 and cmyb expression in the AGM which was analyzed by in situ hybridization (as previously described[9]). Zebrafish embryo images were taken with a Leica stereoscope. For the analysis of vascular integrity flk:zsgreen embryos were injected with the lowest effective MO dose of 2ng of each lrp2 morpholino (lrp2a and lrp2b) as determined by in situ hybridization. Embryos were aged to 32h. Ten embryos for each condition were anesthetized in 0.04 mg/ml Tricaine, mounted in 1% low-melting agarose and imaged with a Leica stereoscope. A high-resolution image for a representative embryo of each group was acquired on a Zeiss confocal microscope.

**Analysis of adult peripheral blood and bone marrow**

Blood samples were diluted in PBS and analyzed using an Ac · T Diff analyzer (Beckman Coulter) using equine setting. Suspensions of BM cells from the femurs were isolated and depleted of red blood cells by an ammonium chloride lysis step (STEMCELL Technologies, STEMCELL)). HSC and progenitor fractions were identified using the following antibodies: CD45-FITC or APC-Cy7 (Clone 30-F11 Biolegend), EPCR-PE (Clone RMEPCR1560, STEMCELL), CD150-Pacific Blue or PE-Cy7 (Clone TC15-12F12.2, Biolegend), CD48-APC (Clone HM48-1, Biolegend), Sca-1-Pacific Blue or PE (Clone E13- 161.7, Biolegend), FLT3-PE or PE-Cy5 (Clone A2F10, eBioscience), CD34-FITC (Clone RAM34, BD Biosciences), c-kit APC-Cy7 (Clone 2B8, Biolegend), and a panel of lineage markers (Hematopoietic Progenitor Enrichment Cocktail, STEMCELL) plus streptavidinV500 (BD Biosciences). See [10] for details.

**Statistical analysis**

RT-PCR data, BL-CFCs and hematopoietic colony counts were statistically analysed using Student's T-test or Paired Student's T-test. Significant differences are marked * for $p<0.05$, ** for $p<0.01$, *** for $p<0.001$ and not significant differences are marked NS.

**RNA sequencing and analysis**

Cells were sorted into IMDM/20%FCS and centrifuged. The cells were lysed in RNA lysis buffer/1% β-mercaptoethanol and snap frozen in liquid nitrogen. RNA was isolated from cells as per standard method (For details about samples refer to supplentary table S3), and amplified using the Ovation RNA amplification system V2 (Nugen). Single-stranded TruSeq cDNA libraries were generated and sequenced using the Illumina HiSeq2000 analyzer (BGI, Hong Kong). The sequencing reads were aligned to the mouse genome (GRCm38/mm10) using the software package TopHat. Transcript expression for FLK1+/LacZ- and FLK1+/LacZ+ samples sorted from day 3 EBs was quantified with the software suite HOMER using standard parameters and two characteristically different bioinformatics tools, GFOLD and DeSeq, were used to identify differentially expressed genes. GFOLD was used to identify genes with large fold changes (e.g. within the 1% and 99% percentiles of GFOLD estimates), and DeSeq was used to identify genes that significantly changed across sample populations (≤0.05). Samples were collected in triplicates, and each experiment was analysed independently to generate a list of DEGs. Heat maps were generated using the R package pheatmap [pheatmap: Pretty Heatmaps. R package version 061]. Patterns were generated based on normalized FPKM, with expression levels lower than 1/3 assigned as low (L), between 1/3 and 2/3 as intermediate (I), and more than 2/3 as high (H). Gene lists from each resulting category were analysed using Panther gene ontology program. The data has been deposited in GEO under the accession number GSE77390.

**Pathway and Gene-set enrichment analysis**

The Ingenuity IPA Core Analysis Tool (version 17199142) was used to establish 'Molecular and Cellular Functions' that correlate with the lists of differentially expressed genes. Gene-set enrichment analysis was performed using the GSEA Java Desktop tool (v 2.0.13). Gene-expression levels were obtained from RNA-seq, and ranked using the GFOLD algorithm. The GSEA pre-ranked tool was used to interrogate the enrichment of various biological pathways provided by publically available databases such as Kegg and Biocarta. Other datasets were obtained from the GEO NCBI website; Ldb1 WT vs. Ldb1-/- (Accession number: GSE43044), Etv2+/- vs. Etv2-/- (Accession number: GSE31743), EC vs. HEC, and HEC vs. HSC (Data from [11] provided by Professor Elaine Dzierzak).

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**SUPPLEMENTAL FIGURE LEGENDS**

**Figure S1 Characteristics and functional behaviour of Endoglin regulatory elements. (A)** Table listing combinations of *Eng* regulatory elements tested in mouse transgenic reporter assays {Pimanda, 2008 #621}. Tissues with hematopoietic and endothelial activity; placenta, yolk sac (YS), dorsal aorta (DA), fetal liver (FL) and heart tissue were investigated for *lacZ* reporter gene expression in endothelial (E) and hematopoietic (H) cells. **(B)** Table listing the mouse/human coordinates and size of the *Eng -8, P, +7, +9, +7Δ, +9Δ* regulatory elements {Pimanda, 2008 #621}. **(C)** Table listing the combinations of the *Eng* enhancer-driven LacZ reporter gene constructs which were used in this study.

**Figure S2. Generating recombinant mouse ES cell lines using combinations of the LacZ/Eng regulatory elements. (A)** Schematic representation of the Hprt targeting strategy. Reporter constructs were cloned into the pMP8 plasmid between the 5'-3' *Hprt* homology arms. After electroporation into HM1 ES cells, the respective 5'-3' sites recombined and integrated the construct into the genome. The *Eng -8/P/LacZ* construct was used as an example in this figure. **(B)** Schematic of the recombinant Hprt locus. Successful recombination was verified by PCR and sourthern blots. **(C)** PCR#1 verified the integration of the targeting construct into the genome. Size of the PCR product varied from 1-2Kb depending on the type of insert. (i) Size of the PCR product for Eng-8/P ES cells was 1Kb. (ii) Size of PCR product for Eng-8/P/LacZ/+7 or +9 was 1.5Kb. (iii) Size of PCR product for Eng-8/P/LacZ/+7/+9 was 2Kb. (iv) Size of PCR product for Eng-8/P/LacZ/+7Δ/+9 and Eng-8/P/LacZ/+7Δ/+9Δ was 2Kb. The positive control for each PCR was a pMP8 plasmid containing the corresponding construct. **(D)** PCR#2 verified the integration of the construct specifically into the *Hprt* locus. The PCR spanned from exon 2 in the targeting construct, to exon 3 in the endogenous *Hprt* locus. A 3.2Kb PCR product was detected for all successfully recombinant clones. No PCR product was detected for HM1 ES cells which lack exons 1 and 2. **(E)** The southern blot analysis quantified copy number integration. The probe was a 250bp fragment that binds to a region between exons 3 and 4 of the *Hprt* locus. We detected a 6.5Kb band for the successfully recombinant clones, and a 9Kb band for HM1 ES cells. The white boxes highlight the southern blot band for each recombinant ES cell line tested.

**Figure S3.** Bar charts showing BL-CFC numbers/3000 seeded cells sorted from day 3 EBs generated from recombinant ES cells. Experiments were performed in triplicate and repeated two times. Statistical analysis using students t-test, *P<0.05; **P<0.01; ***P<0.001; NS, not significant.

**Figure S4**. **RNA-sequencing comparative analysis of FLK1+/LacZ- and FLK1+/LacZ+ sorted fractions. (A)** List of up- and down-regulated receptors and transcription factors in the FLK1+/LacZ+ cell population. **(B)** Gene network diagram showing genes upregulated in the FLK1+/LacZ+ fraction that are associated with the angiogenic and vasculogenic development network. **(C)** Bar chart showing a list canonical pathways with highest p-values associated with genes up-regulated in the FLK1+/LacZ+ fraction. **(D)** Bar chart showing diseases and biological functions with highest p-value associated with genes up-regulated in the FLK1+/LacZ+ fraction. **(E)** Bar chart showing a list canonical pathways with highest p-values associated with genes down-regulated in the FLK1+/LacZ+ fraction. **(F)** Bar chart showing diseases and biological functions with highest p-value associated with genes down-regulated in the FLK1+/LacZ+ fraction.

**Figure S5. -8/P/LacZ/+7Δ/+9, and -8/P/LacZ/+7Δ/+9Δ mutant constructs do not enrich cells with hemogenic potential in HEI.** At day 2 of liquid blast cultures, HEI LacZ+/LacZ- fractions were sorted and re-seeded in liquid blast media for 2 days and then seeded into CFU-C assays. **(A)** Bar chart showing the number of hematopoietic colonies generated from Eng -8/P/LacZ/+7Δ/+9 ES cells. **(B)** Bar chart showing the number of hematopoietic colonies generated from Eng -8/P/LacZ/+7Δ/+9Δ ES cells. $3x10^4$ cells were seeded in methylcellulose mix. Primitive and definitive colonies were counted after four and nine days respectively. Experiments were performed in triplicate and repeated two times. Statistical analysis using students t-test, *P<0.05; **P<0.01; ***P<0.001; NS, not significant.

**Figure S6**. **RNA-sequencing analysis of ENG+/LacZ-, ENG+/LacZ+ and ENG-/LacZ+ HEI fractions sorted from day 2 liquid blast cultures. (A)** GSEA plots showing the overlap of genes that are differentially expressed between ENG+/LacZ- and ENG-/LacZ+ HEI and genes in the hypoxia via HIF1a pathway (upper panel) and cell cycle regulators (lower panel). **(B)** Network diagram of genes that are associated with hematopoietic development and function and are upregulated in ENG-/LacZ+ HEI cells. **(C-E)** Differentially expressed genes within each cell fraction were further analysed based on their relative expression pattern across the three HEI populations. The FPKM values for each gene were normalized across the three populations, which resulted in a specific expression pattern. H=High, I=Intermediate, L=Low. The genes within each fraction were further analysed in PANTHER for their association with GO biological functions. **(C)** Analysis of genes differentially expressed in the ENG+/LacZ- HEI fraction. (i) Histograms displaying the expression pattern of genes in the HLL, HIL, HHL, and HHI. (ii) Table listing the biological functions associated with genes in each group. **(D)** Analysis of genes differentially expressed in the ENG+/LacZ+ fraction. (i) Histograms displaying the expression pattern of genes in the

HHL, HHI, and IHL. (ii) Table listing the biological functions associated with genes in each group. **(E)** Analysis of genes differentially expressed in the ENG-/LacZ+ fraction. (i) Histograms displaying the expression pattern of genes in the LLH, IIH, LIH, and ILH. (ii) Table listing the biological functions associated with genes in each group.

**Figure S7. Functional and regulatory aspects of genes shared between FLK1+/LacZ+ cells from day 3 EBs and ENG-/LacZ+ HEI cells. (A)** (i) List of common genes categorized into genes upregulated in both cell fractions (green), genes downregulated in the FLK1+/LacZ+ cells and upregulated in the ENG-/LacZ+ HEI (red), genes upregulated in the FLK1+/LacZ+ cells and downregulated in the ENG-/LacZ+ HEI (yellow). (ii) Gene regulatory network association between all three gene sets. (iii) The genes listed in table S6A were further analysed based on their relative expression pattern across the FLK1+/LacZ-, FLK1+/LacZ+, ENG+/LacZ- HEI, ENG+/LacZ+ HEI, and ENG-/LacZ+ HEI populations. (i) The FPKM values for each gene were normalised across all populations, which resulted in a specific expression pattern. H=High, I=Intermediate, L=Low (ii) Each gene set was analysed using genes2Canvas for their association with specific cell types. The canvas associated with each gene set was overlaid. **(B)** Bar chart showing the molecular and cellular functions associated with each gene set. **(C)** Table listing genes that were up-regulated in FLK1 mesodermal (FLK1+/lacZ) and HE1 cells (ENG-/lacZ) that were targeted by *Eng* regulatory elements with a detailed description of their known functions and relation to hematopoietic development if known.

**Figure S8. Genes down-regulated in both FLK1+/LacZ+ cells from day 3 EBs and ENG-/LacZ+ HEI cells. (A)** Venn diagram showing the overlap and identity of genes that were down-regulated in FLK1 mesodermal (FLK1+/lacZ) and HE1 cells (ENG-/lacZ) cells. **(B)**

Table listing genes from (A) with a detailed description of their known functions and relation to hematopoietic development if known.

**Figure S9. Lrp2 a/b and tp53 morpholinos. (A)** Analysis of WT and *lrp2a/b* MO zebrafish for the presence of HSCs at 36 hpf following MO injections at 24 hpf. Low (left panel) and high (right panel) magnifications are shown and numbers in the panels indicate the number of embryos with the depicted phenotype. ISH for the HSC marker *runx1*. **(B)** ISH for *cmyb* following in *lrp2a/b* morphants co-injected with *tp53*MO to exclude non-specific cell death.

**Figure S10. LRP2 null FVB/N adult mice** *(*A) Peripheral blood counts (Mean (SD)) from 9 month old LRP2KO mice and littermates. (B) Bone marrow flowcytometry based assessment of MNC fractions. Differences were not significant.

**A**

| Endoglin transgenic construct | Placenta | YS | DA | Liver | | Heart | Reference |
|---|---|---|---|---|---|---|---|
| -8/P/LacZ | No | E | E | E | medium H | E | Pimanda et al Blood 2006 Jun 15;107(12) |
| -8/P/LacZ/+7 | No | E | E | E | High H | E | Pimanda et al Blood. 2008 Dec 1;112(12) |
| -8/P/LacZ/+9 | No | E | E | E | medium H | E | Pimanda et al Blood. 2008 Dec 1;112(12) |
| -8/P/LacZ/+7/+9 | E | E | N/A | E | High H | E | Pimanda et al Blood. 2008 Dec 1;112(12) |

E=Endothelial
H=Hematopoietic
No=No staining
N/A=No observed

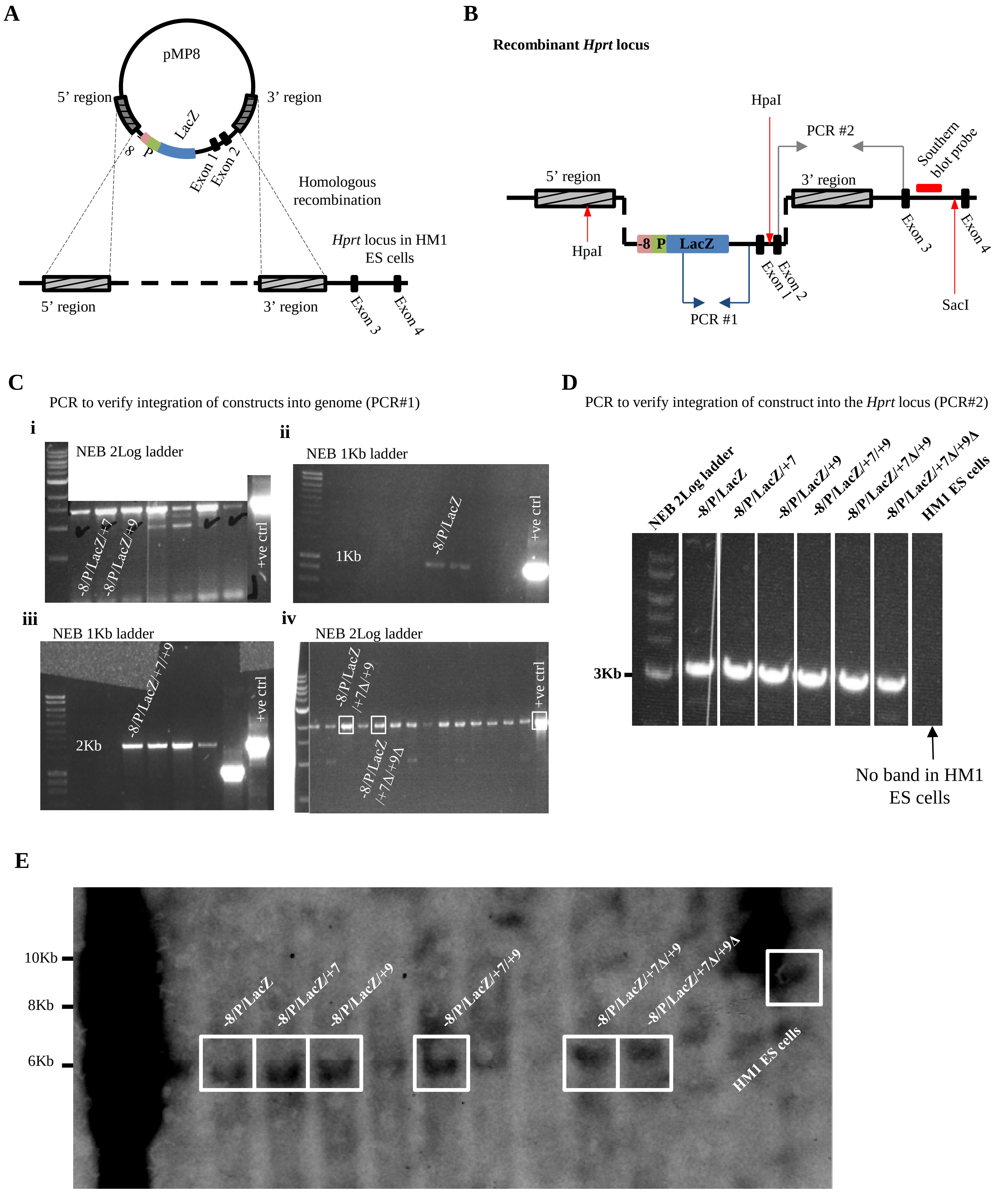
**B**

| Regulatory elements | Mouse sequence coordinates (mm7) | Size (bp) | Reference | Human sequence coordinates (hg18) |
|---|---|---|---|---|
| *Eng* -8 | Chr2:32645367-32645659 | 329 | Pimanda et al Blood 2006 Jun 15;107(12) | Chr9:129664306-129664634 |
| *Eng* P | Chr2:32653786-32654245 | 484 | Pimanda et al Blood 2006 Jun 15;107(12) | Chr9:129656479-129656962 |
| *Eng* +7 | Chr2:32661915-32662416 | 483 | Pimanda et al Blood. 2008 Dec 1;112(12) | Chr9:129648543-129649025 |
| *Eng* +9 | Chr2:32663000-32663504 | 500 | Pimanda et al Blood. 2008 Dec 1;112(12) | Chr9:129646983-129647482 |
| *Eng* +9Δ | Δ Gata sites | 453 | Pimanda et al Blood. 2008 Dec 1;112(12) | |
| *Eng* +7Δ | Δ Ets sites | 374 | Pimanda et al Blood. 2008 Dec 1;112(12) | |

**C**

| Construct | Schematic |
|---|---|
| -8/P | **-8 P LacZ** |
| -8/P/+7 | **-8 P LacZ +7** |
| -8/P/+9 | **-8 P LacZ +9** |
| -8/P/+7/+9 | **-8 P LacZ +7 +9** |
| -8/P/+7Δ/+9 | **-8 P LacZ +7Δ +9** |
| -8/P/+7Δ/+9Δ | **-8 P LacZ +7Δ +9Δ** |

**Figure S1**



A
pMP8
5' region
3' region
LacZ
-8
P
Exon 1
Exon 2
Homologous recombination
Hprt locus in HM1 ES cells
5' region
3' region
Exon 3
Exon 4
B
Recombinant Hprt locus
HpaI
PCR #2
Southern blot probe
5' region
3' region
HpaI
-8
P
LacZ
Exon 1
Exon 2
Exon 3
Exon 4
SacI
PCR #1
C
PCR to verify integration of constructs into genome (PCR#1)
i
NEB 2Log ladder
-8/P/LacZ/+7
-8/P/LacZ/+9
+ve ctrl
ii
NEB 1Kb ladder
1Kb
-8/P/LacZ
+ve ctrl
iii
NEB 1Kb ladder
-8/P/LacZ/+7/+9
2Kb
+ve ctrl
iv
NEB 2Log ladder
-8/P/LacZ /+7Δ/+9
-8/P/LacZ /+7Δ/+9Δ
+ve ctrl
D
PCR to verify integration of construct into the Hprt locus (PCR#2)
NEB 2Log ladder
-8/P/LacZ
-8/P/LacZ/+7
-8/P/LacZ/+9
-8/P/LacZ/+7/+9
-8/P/LacZ/+7Δ/+9
-8/P/LacZ/+7Δ/+9Δ
HM1 ES cells
3Kb
No band in HM1 ES cells
E
10Kb
8Kb
6Kb
-8/P/LacZ
-8/P/LacZ/+7
-8/P/LacZ/+9
-8/P/LacZ/+7/+9
-8/P/LacZ/+7Δ/+9
-8/P/LacZ/+7Δ/+9Δ
HM1 ES cells


**Figure S2**

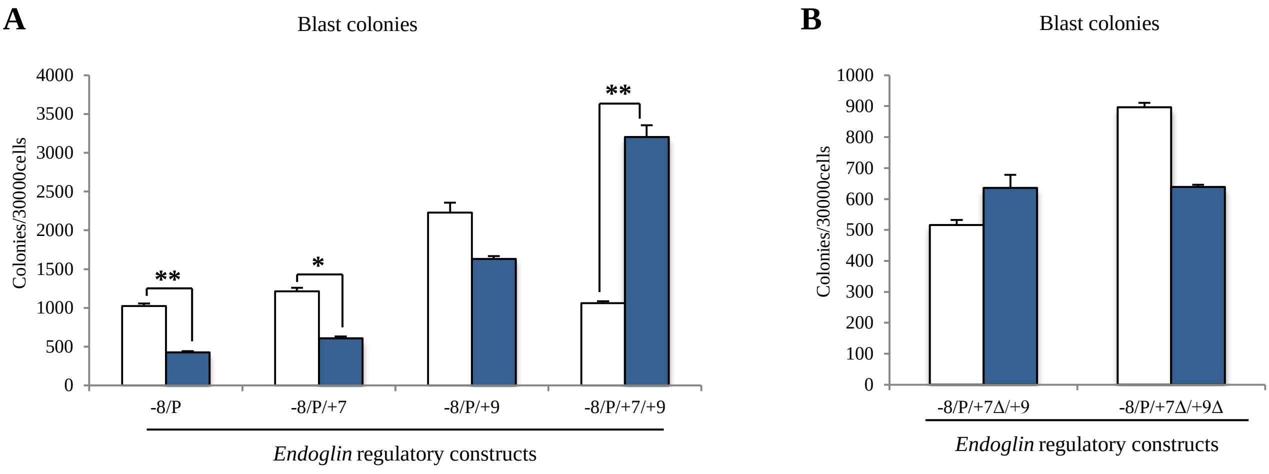
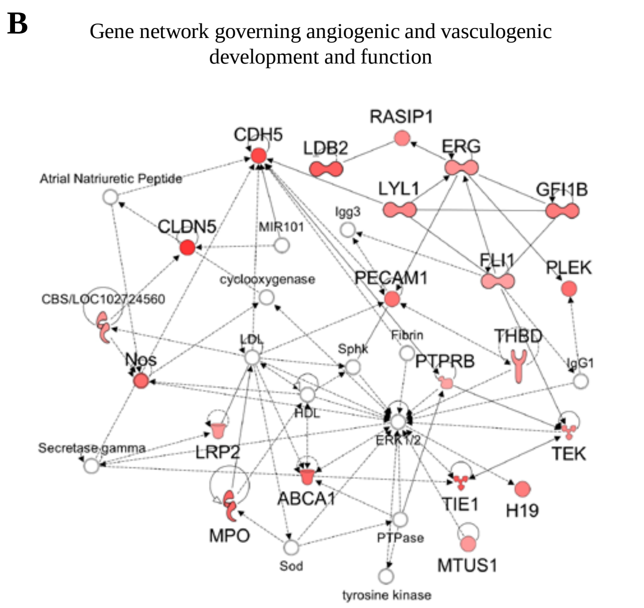

A
Blast colonies
4000
3500
3000
2500
2000
1500
1000
500
0
Colonies/30000cells
**
*
**
-8/P
-8/P/+7
-8/P/+9
-8/P/+7/+9
Endoglin regulatory constructs
B
Blast colonies
1000
900
800
700
600
500
400
300
200
100
0
Colonies/30000cells
-8/P/+7Δ/+9
-8/P/+7Δ/+9Δ
Endoglin regulatory constructs

**Figure S3**

**A**

| Up regulated cell surface receptors | LogFC | Upregulated transcription factors | LogFC |
|---|---|---|---|
| Disp2 | 5.774 | Utf1 | 4.471 |
| Cldn5 | 5.657 | Mecom | 3.468 |
| Tlr4 | 4.681 | Ldb2 | 3.166 |
| Ptchd1 | 4.602 | Gfi1b | 2.611 |
| Cdh5 | 3.583 | Hoxb5 | 2.543 |
| Tie1 | 3.352 | Lyl1 | 2.382 |
| Ednrb | 3.351 | Sox7 | 2.182 |
| Esam | 3.165 | Erg | 2.127 |
| Cd93 | 2.813 | Bcl6b | 2.082 |
| Pecam1 | 2.753 | Cbfa2t3 | 1.968 |
| Cd34 | 2.725 | Fli1 | 1.891 |
| Icam2 | 2.471 | Sox18 | 1.837 |
| Tek | 2.420 | Ptrf | 1.690 |
| Flt4 | 1.852 | Klf2 | 1.543 |

| Down regulated cell surface receptors | LogFC | Down regulated transcription factors | LogFC |
|---|---|---|---|
| Cxcr2 | -3.137 | Churc1 | -3.228 |
| H2-T23 | -3.035 | Znhit3 | -1.523 |
| Lepr | -2.193 | Pfdn5 | -1.435 |
| Ppp1r16b | -2.167 | Lhx1 | -0.961 |



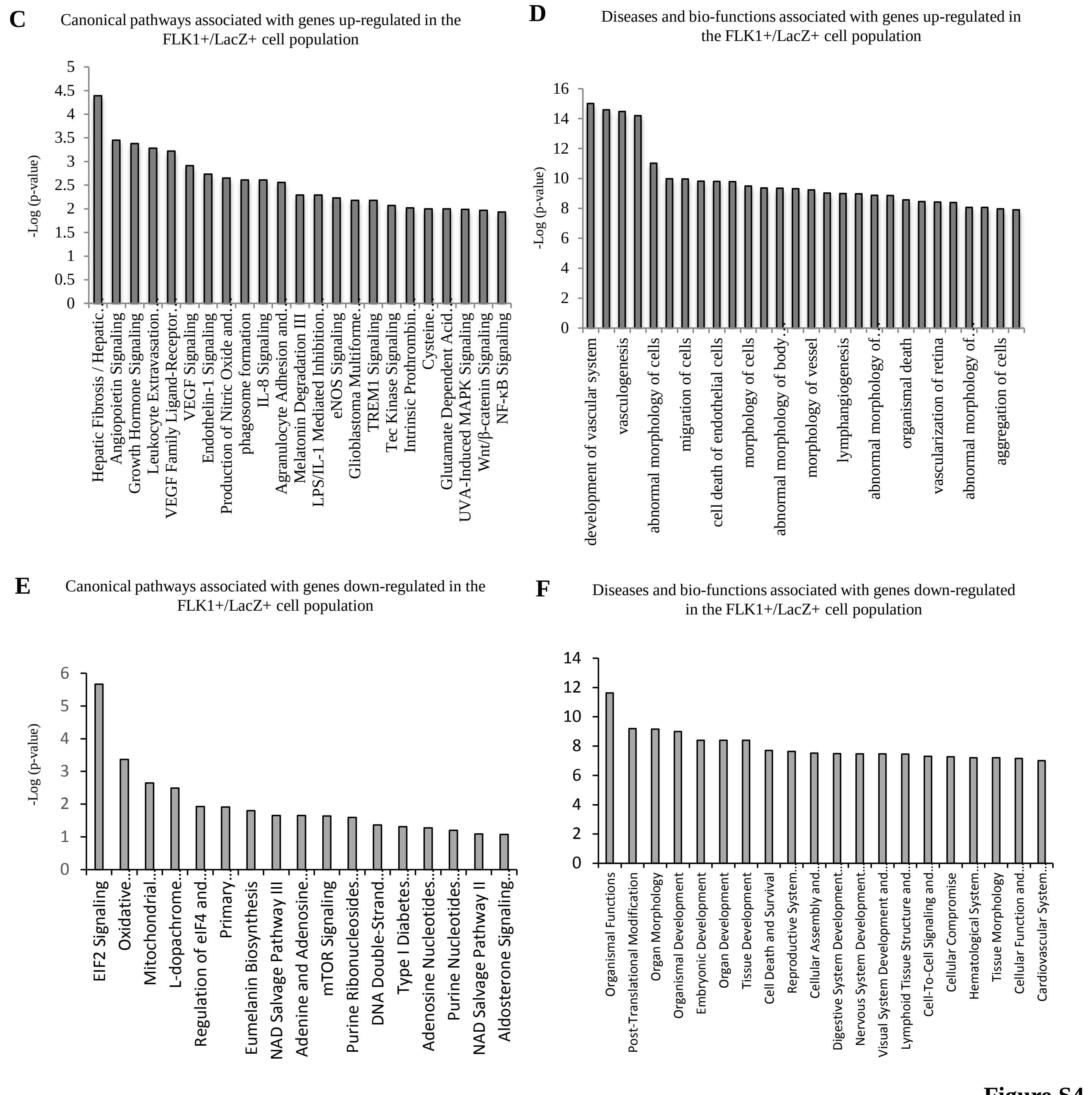




**Figure S4**

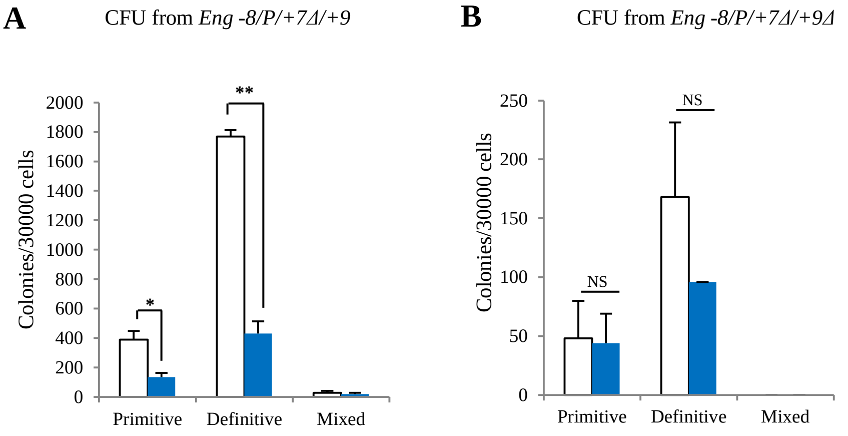
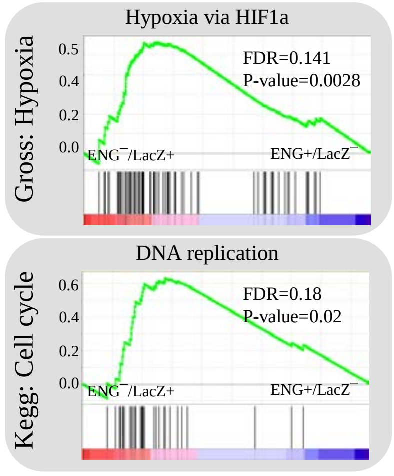
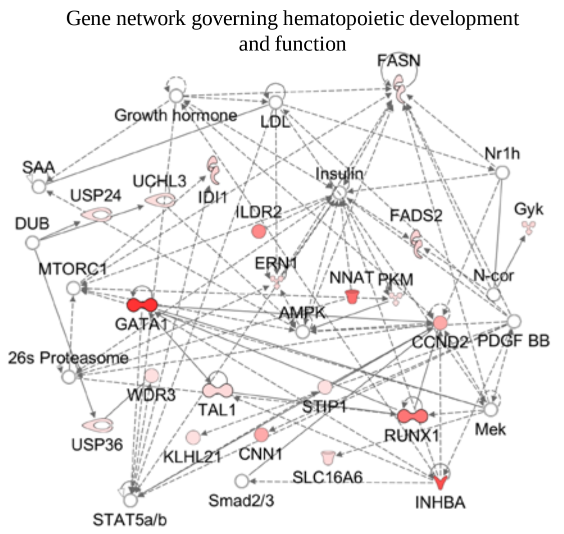

A
CFU from *Eng -8/P/+7Δ/+9*
Colonies/30000 cells
2000
1800
1600
1400
1200
1000
800
600
400
200
0
*
**
Primitive
Definitive
Mixed
B
CFU from *Eng -8/P/+7Δ/+9Δ*
Colonies/30000 cells
250
200
150
100
50
0
NS
NS
Primitive
Definitive
Mixed

**Figure S5**

**A**

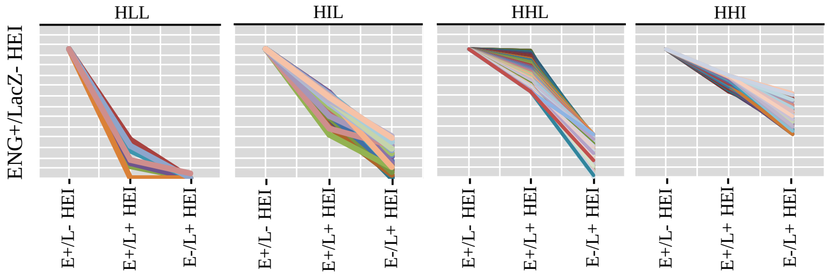



**B**




**C**

i

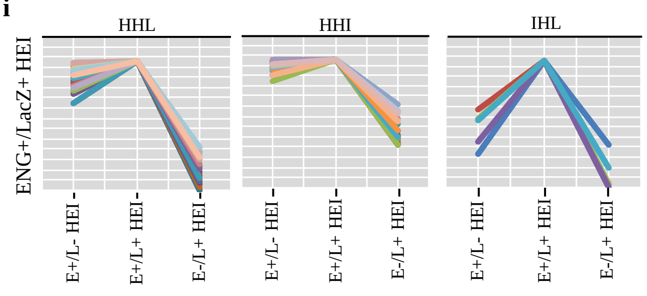



ii

| Gene Pattern | GO biological process complete | Log (p-value) |
|---|---|---|
| HHL | tube morphogenesis | 10.7 |
| | epithelial tube morphogenesis | 9.9 |
| | regulation of angiogenesis | 9.5 |
| | regulation of vasculature development | 9.5 |
| HHI | regulation of Ras protein signal transduction | 9.1 |
| | negative regulation of catabolic process | 8.9 |
| | muscle organ morphogenesis | 8.4 |
| | regulation of small GTPase mediated signal transduction | 8.3 |
| HIL | macromolecule metabolic process | 6.9 |
| | positive regulation of biosynthetic process | 6.4 |
| | positive regulation of cellular biosynthetic process | 6.4 |
| | regulation of actin filament-based process | 5.8 |

**D**

i

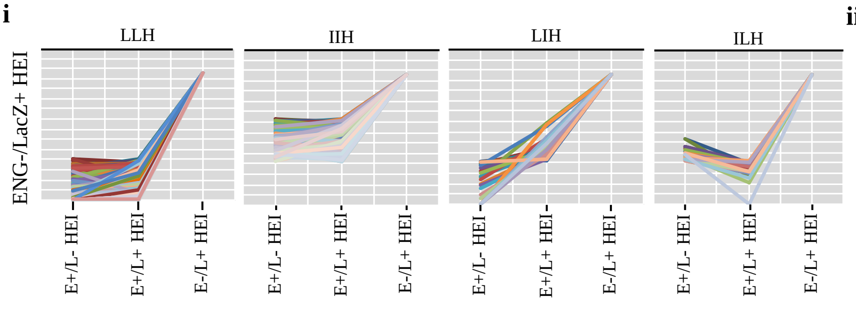



ii

| Gene pattern | GO biological process complete | Log (p-value) |
|---|---|---|
| HHL | positive regulation of developmental process | 5.7 |
| | regulation of developmental process | 5.7 |
| | regulation of cell differentiation | 4.9 |
| | regulation of localization | 4.8 |
| | negative regulation of cell differentiation | 4.8 |
| | negative regulation of developmental process | 4.8 |
| HHI-IHL | developmental process | 5.3 |
| | system development | 5.0 |
| | protein metabolic process | 4.9 |
| | cellular process | 4.8 |
| | regulation of molecular function | 4.5 |
| | regulation of catalytic activity | 4.5 |

**E**

i




ii

| Gene pattern | GO biological processes | Log (p-value) |
|---|---|---|
| LLH | positive regulation of immune system process | 11.7 |
| | myeloid cell differentiation | 9.9 |
| | immune system development | 9.8 |
| | hematopoietic or lymphoid organ development | 9.8 |
| IIH | leukocyte differentiation | 7.4 |
| | organ development | 7.03 |
| | cellular macromolecule localization | 6.9 |
| LIH | establishment of localization | 5.4 |
| | single-organism transport | 5.4 |
| ILH | regulation of protein phosphorylation | 5.3 |
| | regulation of cell migration | 5.3 |
| | regulation of cell motility | 4.9 |

**Figure S6**

A i

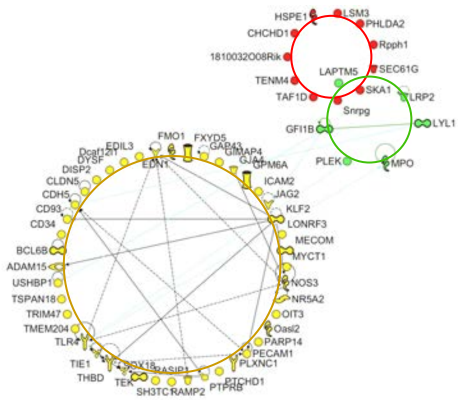
**Common genes between D3 EB and D2 HE**

| Genes Up in D3 EB and D2 HE |
|---|
| Gfi1b |
| Laptm5 |
| Lrp2 |
| Lyl1 |
| Mpo |
| Plek |

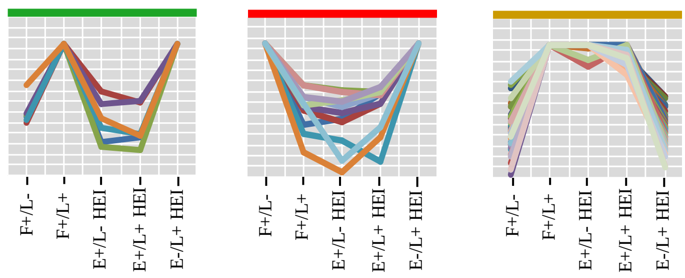
| Genes Down in D3 EB and up inD2 HE |
|---|
| 1810032O08Rik |
| Chchd1 |
| Hspe1 |
| Lsm3 |
| Phlda2 |
| Rpph1 |
| Sec61g |
| Ska1 |
| Snrpg |
| Taf1d |
| Tenm4 |

| Genes Up in D3 EB and down in D2 HE | |
|---|---|
| Adam15 | Mecom |
| Bcl6b | Myct1 |
| Cd34 | Nos3 |
| Cd93 | Nr5a2 |
| Cdh5 | Oasl2 |
| Cldn5 | Oit3 |
| Dcaf12l1 | Parp14 |
| Disp2 | Pecam1 |
| Dysf | Plxnc1 |
| Edil3 | Ptchd1 |
| Edn1 | Ptprb |
| Eltd1 | Ramp2 |
| Fmo1 | Rasip1 |
| Fxyd5 | Sh3tc1 |
| Gap43 | Sox18 |
| Gimap4 | Tek |
| Gja4 | Thbd |
| Gpm6a | Tie1 |
| Icam2 | Tlr4 |
| Jag2 | Tmem204 |
| Klf2 | Trim47 |
| Lonrf3 | Tspan18 |
| | Ushbp1 |

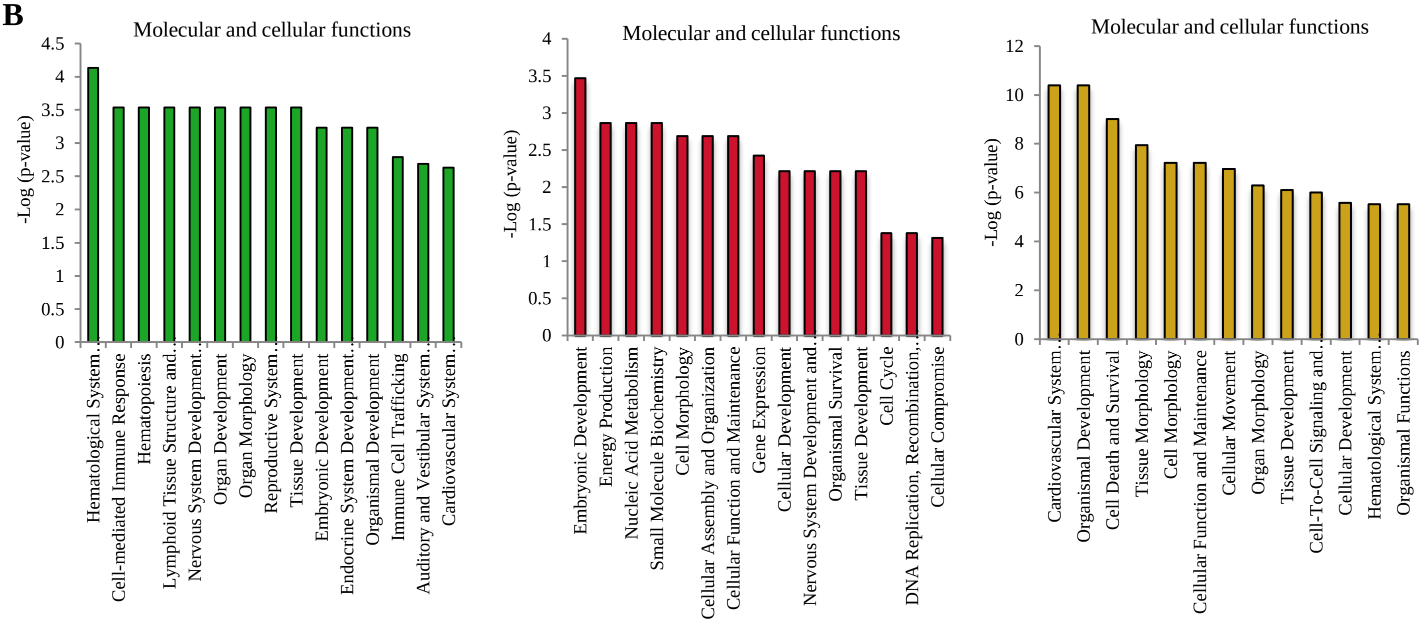
ii




iii




B

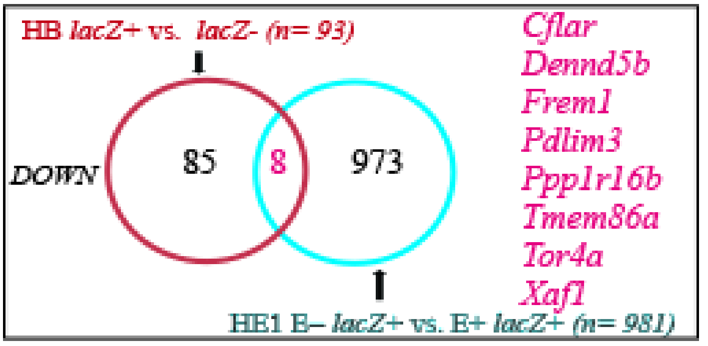



C

| UP in D3 EB and UP D2 HE | | | |
|---|---|---|---|
| Gene | Entrez Gene Name | Disease or function | Associated with hematopoiesis |
| Gfi1b | growth factor independent 1B transcription repressor | Development of blood, bone marrow, cardiovascular system, connective tissue, embryonic stem cells, hematopoiesis in embryo, hematopoietic progenitor cells, hematopoietic system and tissue, differentiation and maturation of blood and BM. | Yes |
| Laptm5 | lysosomal protein transmembrane 5 | Activation and prolifiration of blood cells (leukocytes, lymphocytes, T lymphocytes), delayed hypersensitive reaction. | Yes |
| Lrp2 | low density lipoprotein receptor-related protein 2 | Abnormal morphology of embryonic tissue, brain, CNS, embryonic body, telencephalic vesicles, loss of neurons, cancer,conventional melanoma | No |
| Lyl1 | lymphoblastic leukemia associated hematopoiesis regulator 1 | angiogenesis, apoptosis of blood and hematopoietic progenitor cells,development of blood cells, differentiation and function of hematopoietic progenitor cells, hematopoiesis of bone marrow, T cell development, thrombocytopenia | Yes |
| Mpo | myeloperoxidase | Abnormal metabolism, function of cardiovascular system, function and movement of blood cells, inflamatory response, | Yes |
| Plek | pleckstrin | Activation and aggregation of blood cells, coagulation, cytopenia, hemorrhagic disease, hemostasis, thrombocytopenia, | Yes |

**Figure S7**

**A**




**B**

| DOWN in D3 EB and DOWN in D2 HE | | | |
|---|---|---|---|
| **Gene** | **Entrez Gene Name** | **Disease or function** | **Association with hematopoiesis** |
| Pdlim3 | PDZ and LIM domain protein 3 | Transcription factor (non-motor actin binding protein) | No |
| Tmem86a | Lysoplasmalogenase-like protein TMEM86 A | | Expressed in hematopoietic stem cells of the lateral plate mesoderm and cardiovascular system |
| Cflar | CASP8 and FADD-like apoptosis regulator | Cysteine protease | Widely expressed. Higher expression in skeletal muscle, pancreas, heart, kidney, placenta, and peripheral blood leukocytes |
| Tor4a | Torsin-4a | Chaperone | No |
| Frem1 | FRAS1-related extracellular matrix protein 1 | cation transporter | No |
| Dennd5b | DENN domain-containing protein 5B | Ion channel, G-protein modulator, membrane-bound signaling molecule | Expressed in mature B cells |
| Xaf1 | XIAP-associated factor 1 | | Expressed in T Helper cells |

**Figure S8**

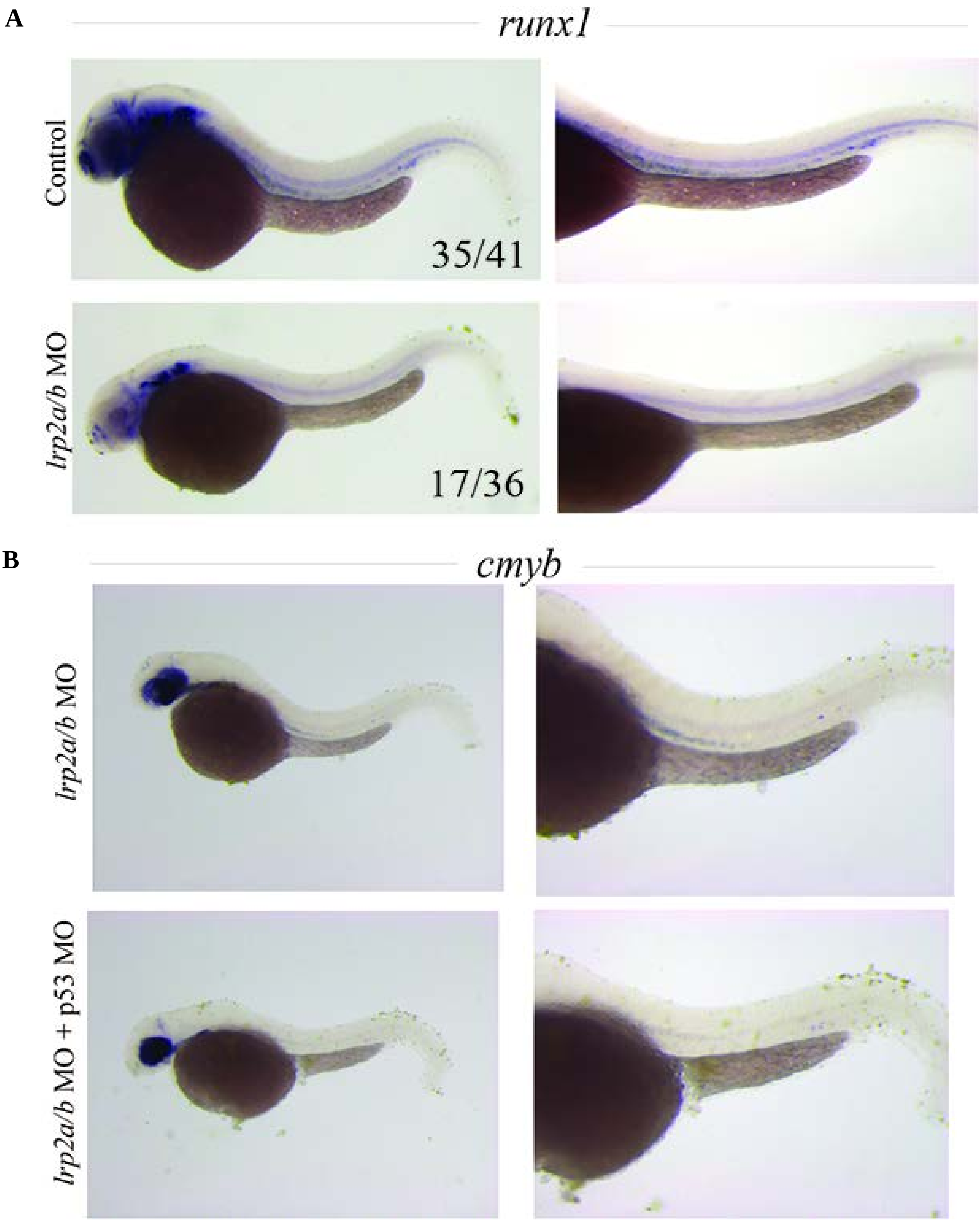

A
runx1
Control
35/41
lrp2a/b MO
17/36
B
cmyb
lrp2a/b MO
lrp2a/b MO + p53 MO

**Figure S9**

**A**

| | Hb | WCC | PLT |
|---|---|---|---|
| **LRP2 KO** | 13.9 (1.69) | 7.4 (2.12) | 1098.5 (49.39) |
| **WT** | 15.1 (1.55) | 7.1 (1.2) | 1118.3 (200.3) |

**B**

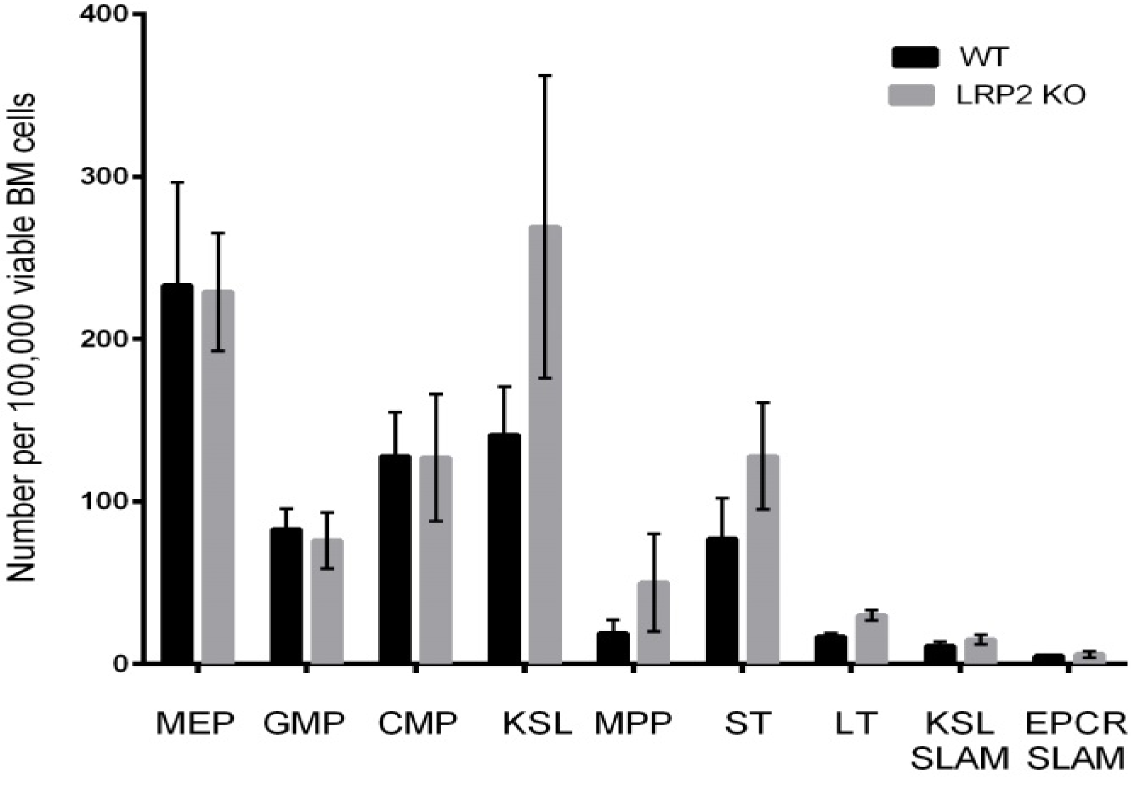



**Figure S10**

# Supplemental Table S1

Genes Up-regulated in the FLK1+/LacZ- fraction

| Gene symbol | LogFC | P-value |
|---|---|---|
| Edn1 | 1.087052505 | 0.544645462 |
| Adam15 | 1.096967974 | 0.057858206 |
| Klf2 | 1.552579775 | 0.043804917 |
| Calcrl | 1.65397083 | 0.009454124 |
| Tnfaip2 | 1.678923375 | 0.007076656 |
| Col18a1 | 1.680188937 | 0.000105422 |
| Sh3tc1 | 1.68266225 | 0.239405654 |
| Ptrf | 1.686370299 | 0.020360381 |
| Tmem204 | 1.698010214 | 0.364754734 |
| Ddah1 | 1.701268811 | 0.002344438 |
| Plxnc1 | 1.77132956 | 0.029150256 |
| Ptprb | 1.798755188 | 0.001642291 |
| Hapln1 | 1.803827939 | 0.000180533 |
| Flt4 | 1.81507194 | 7.60458E-05 |
| Sox18 | 1.827185378 | 0.000253912 |
| Parp14 | 1.830079852 | 0.003615943 |
| Fmo1 | 1.880601627 | 0.662464724 |
| Fli1 | 1.891716668 | 5.73862E-05 |
| Arap3 | 1.934430362 | 0.000112014 |
| Cbfa2t3 | 1.970349548 | 0.000457988 |
| Jag2 | 2.028158816 | 0.01367377 |
| Gap43 | 2.033613246 | 0.018886073 |
| Erg | 2.044460628 | 0.009601111 |
| Oasl2 | 2.046144561 | 0.001696947 |
| Car8 | 2.057906159 | 0.096011129 |
| Gstm1 | 2.064067907 | 1.3604E-05 |
| Plcg2 | 2.066293945 | 0.001221338 |
| Rhoj | 2.094338859 | 0.000155802 |
| Glrx | 2.119153348 | 0.001790813 |
| Cbs | 2.119967127 | 0.007751582 |
| Myct1 | 2.120605065 | 0.108486122 |
| Thbd | 2.139519925 | 0.041800621 |
| Lrp2 | 2.139519925 | 0.006199094 |
| Pik3cb | 2.142194059 | 0.001769992 |
| Bcl6b | 2.147425123 | 0.0003317 |
| Gca | 2.150555447 | 0.014679821 |
| Dcaf12l1 | 2.16566234 | 0.045560884 |
| Sox7 | 2.174728023 | 2.03373E-06 |

| | | |
|---|---|---|
| Gja4 | 2.188335841 | 0.021281851 |
| Mageb16 | 2.201764164 | 0.028264699 |
| Laptm5 | 2.205074479 | 0.00279795 |
| Mtus1 | 2.260979437 | 0.001639892 |
| Prrg4 | 2.287077113 | 0.0083592 |
| Chchd10 | 2.292194746 | 3.08535E-06 |
| Gcnt2 | 2.292862042 | 0.018055141 |
| Tspan18 | 2.310009471 | 4.49457E-06 |
| Ramp2 | 2.321386599 | 3.87678E-06 |
| Lonrf3 | 2.333967245 | 0.080567576 |
| Edil3 | 2.338014078 | 0.043433878 |
| Tek | 2.352213212 | 6.55371E-05 |
| Rasip1 | 2.354911982 | 4.21616E-06 |
| Lyl1 | 2.364162096 | 0.008989919 |
| Slain1 | 2.367160424 | 0.016180347 |
| Dysf | 2.378863287 | 0.000146065 |
| Spns2 | 2.454037875 | 0.000663005 |
| Igfbp3 | 2.454515995 | 5.20963E-07 |
| Gpm6a | 2.465564128 | 0.372363712 |
| Cd34 | 2.471393207 | 0.031684002 |
| Icam2 | 2.472706197 | 0.000425494 |
| Nefl | 2.475228664 | 3.2853E-05 |
| Smagp | 2.530659156 | 0.022321854 |
| Ushbp1 | 2.537713914 | 0.224722744 |
| H19 | 2.53859547 | 2.89424E-10 |
| C77370 | 2.53956471 | 0.002352499 |
| Wipf3 | 2.59109501 | 0.000309686 |
| Utf1 | 2.624496018 | 0.000790117 |
| Hoxb5 | 2.6345403 | 0.04801989 |
| Gfi1b | 2.64244189 | 0.009106872 |
| Ahr | 2.658209206 | 0.037305532 |
| Wscd1 | 2.678412777 | 0.029159008 |
| Mt1 | 2.696325413 | 3.06058E-07 |
| Thsd1 | 2.713341868 | 0.000693889 |
| Pecam1 | 2.748445669 | 5.52696E-06 |
| Gypc | 2.775693652 | 0.000884256 |
| Mir675 | 2.784317975 | 0.002039881 |
| Mt2 | 2.797161886 | 4.91321E-08 |
| Igf1 | 2.811136808 | 0.002047082 |
| Cd93 | 2.83041587 | 0.001829152 |
| Plek | 2.852587251 | 0.0477939 |
| Gad2 | 2.889245722 | 0.000556938 |
| Ednrb | 2.974577776 | 0.057961662 |
| Abca1 | 3.002163607 | 0.07276324 |

| | | |
|---|---|---|
| Rinl | 3.031910951 | 0.049704245 |
| F2rl2 | 3.068905158 | 0.044838631 |
| Esam | 3.118761365 | 0.000276056 |
| Mpo | 3.240857841 | 0.026627781 |
| Ldb2 | 3.248207297 | 0.009031311 |
| Nos3 | 3.319713262 | 0.020452161 |
| Fxyd5 | 3.350086911 | 0.008404157 |
| Cdh5 | 3.523106166 | 3.47251E-12 |
| Tie1 | 3.53897007 | 6.02652E-06 |
| Oit3 | 3.672015006 | 0.015333772 |
| Nr5a2 | 3.728598534 | 0.023161499 |
| Trim47 | 3.734750761 | 0.087328428 |
| Mfng | 3.76512441 | 0.040224814 |
| Disp2 | 3.812282387 | 2.30535E-05 |
| Eltd1 | 3.870658824 | 6.35113E-05 |
| Ccdc85a | 3.908082364 | 0.006066936 |
| Clic5 | 4.087052505 | 0.014790403 |
| Mecom | 4.110899247 | 0.002374777 |
| Ptchd1 | 4.954948969 | 0.009799116 |
| Ltc4s | 5.520011912 | 0.022456113 |
| Gimap4 | 6.050526629 | 0.003415153 |
| Zp3 | 6.153103569 | 2.73733E-05 |
| Cldn5 | 6.224556029 | 0.001564233 |
| C130074G19Rik | 6.554975456 | 2.88197E-07 |
| Tlr4 | 6.762764396 | 7.9993E-12 |

# Supplemental Table S1

Genes Down-regulated in the FLK1+/LacZ- fraction

| Gene symbol | LogFC | P-value |
|---|---|---|
| Omd | -3.443644727 | 1.43099E-07 |
| Pbld1 | -3.33667787 | 9.42527E-07 |
| 1500012F01Rik | -3.32524751 | 8.76912E-15 |
| Cxcr2 | -3.116079542 | 1.5724E-06 |
| Zim1 | -3.079224719 | 0.000273567 |
| Rpph1 | -3.035344126 | 0.000624533 |
| Mpv17l | -3.029685259 | 4.94891E-06 |
| Snhg6 | -2.901632182 | 5.03045E-06 |
| Gm16702 | -2.881238635 | 1.63224E-05 |
| Tmem86a | -2.83821662 | 0.037478878 |
| Pcgf1 | -2.766596069 | 0.000444155 |
| Tyr | -2.707363361 | 0.017659225 |
| Snhg1 | -2.606178717 | 3.48776E-10 |
| AA465934 | -2.599303616 | 1.78453E-08 |
| Tsacc | -2.534435872 | 0.015862459 |
| Slc7a14 | -2.475189919 | 0.000255652 |
| Smim4 | -2.459369534 | 0.00250001 |
| Snhg12 | -2.454883391 | 3.96865E-08 |
| Mrpl33 | -2.369692173 | 6.23265E-07 |
| Nmrk1 | -2.286351807 | 0.00020267 |
| 2810001G20Rik | -2.273010719 | 0.034753041 |
| 2500004C02Rik | -2.199542517 | 0.004688877 |
| Rpl41 | -2.195751742 | 1.59473E-08 |
| Tnnc1 | -2.191806868 | 0.009249219 |
| Atp5l | -2.176233922 | 6.19553E-08 |
| Phlda2 | -2.174697829 | 1.18531E-07 |
| AI450353 | -2.170672062 | 3.44592E-05 |
| 2810008D09Rik | -2.166344208 | 0.001119544 |
| Rab33b | -2.137786335 | 3.49429E-05 |
| 2410006H16Rik | -2.111274338 | 1.31921E-07 |
| Gm11974 | -2.104206638 | 1.12476E-05 |
| 1600020E01Rik | -2.074410918 | 0.011711608 |
| Lepr | -2.067148144 | 0.029084436 |
| 1810032O08Rik | -2.059788883 | 2.83772E-05 |
| Grb10 | -2.045972914 | 9.4691E-07 |
| H2-T23 | -2.02743351 | 0.015336305 |
| Polr2k | -1.943826808 | 0.000988815 |
| Rps24 | -1.912715704 | 7.20553E-07 |
| Usmg5 | -1.90756694 | 0.000121479 |

| | | |
|---|---|---|
| Chchd1 | -1.861472579 | 0.000234435 |
| Mnf1 | -1.851159702 | 0.000475386 |
| Tmem208 | -1.846219535 | 0.000288931 |
| Frem1 | -1.835779635 | 0.029421539 |
| 4930412O13Rik | -1.832493391 | 0.000685628 |
| Tnnt3 | -1.831810732 | 0.014886289 |
| Timm8b | -1.82503165 | 3.94814E-05 |
| Rpl35 | -1.81840748 | 3.01365E-06 |
| Uqcrh | -1.803074561 | 1.23805E-05 |
| Rpl13a | -1.794963422 | 3.84567E-06 |
| 1110059E24Rik | -1.793815299 | 0.000347094 |
| 2410004N09Rik | -1.754403645 | 0.001418213 |
| Lsm3 | -1.752929722 | 4.3554E-05 |
| Acyp1 | -1.752581652 | 0.003432837 |
| Commd2 | -1.749448763 | 0.001491238 |
| Wdr38 | -1.732902454 | 0.003299264 |
| Ppp1r16b | -1.718392827 | 0.004212779 |
| Ada | -1.716744598 | 0.049697011 |
| Ndufa7 | -1.712511296 | 7.87568E-05 |
| N6amt1 | -1.70718029 | 0.034158685 |
| Ccdc107 | -1.705505415 | 0.035432788 |
| 2810408A11Rik | -1.694307209 | 0.025011997 |
| Snrpe | -1.685820743 | 6.01685E-05 |
| Gnptg | -1.677097919 | 0.003908131 |
| Cdkn1c | -1.671891458 | 0.004903075 |
| Xaf1 | -1.670731561 | 0.010160461 |
| Taf1d | -1.653252435 | 0.000114362 |
| Rps27l | -1.651472254 | 3.71671E-05 |
| Rpl17 | -1.617675036 | 2.56901E-05 |
| Dnajc15 | -1.605713285 | 0.004843374 |
| Mrpl53 | -1.605713285 | 0.002009382 |
| A230046K03Rik | -1.589611808 | 0.000115813 |
| Loxl2 | -1.5752049 | 0.000796307 |
| Trnau1ap | -1.574986219 | 0.005760675 |
| Slfn5 | -1.571567037 | 0.008555419 |
| Cox7b | -1.558384248 | 0.00011155 |
| Rps18 | -1.544226652 | 5.6259E-05 |
| Mfsd11 | -1.543184076 | 0.002973958 |
| Myeov2 | -1.522099461 | 0.002501949 |
| Ndufb8 | -1.515810209 | 0.000503508 |
| Ska1 | -1.513220541 | 0.003933932 |
| Znhit3 | -1.495699452 | 0.002465377 |
| Mrps35 | -1.495365239 | 0.003322679 |
| Tenm4 | -1.493120394 | 0.013235397 |

| | | |
|---|---|---|
| Snrpg | -1.489592463 | 0.000147658 |
| Far2 | -1.48840291 | 0.01000884 |
| Sec61g | -1.48254913 | 0.000229356 |
| Churc1 | -1.475573666 | 0.014071031 |
| Dclre1c | -1.460417142 | 0.001742686 |
| Pdlim3 | -1.437809204 | 0.000747407 |
| Pfdn5 | -1.433673376 | 0.000465634 |
| Hspe1 | -1.358444684 | 0.000475662 |
| Rpl36 | -1.341678038 | 0.000419801 |
| Gm15645 | -1.34094818 | 0.007839282 |
| Tmem69 | -1.330831373 | 0.014474118 |
| Casc4 | -1.218342117 | 0.004189447 |
| Tor4a | -1.19925168 | 0.034050492 |
| Dennd5b | -1.165928236 | 0.02212856 |
| Tmem206 | -1.109755791 | 0.01054391 |
| Cflar | -1.043723213 | 0.0278312 |
| Lhx1 | -1.027683631 | 0.016250115 |
| Irak1 | -0.151310873 | 0.82384325 |

# Supplemental Table S2

Genes Up-regulated in the ENG-/LacZ+ HEI population

| Gene Symbol | logFC | FDR |
|---|---|---|
| Trim33 | -0.3573469 | 0.04650547 |
| Gspt1 | -0.3605518 | 0.04987142 |
| Sqle | -0.3611902 | 0.04749712 |
| Tardbp | -0.3666847 | 0.0450795 |
| Tcerg1 | -0.376228 | 0.04692825 |
| Psmb6 | -0.3846357 | 0.03435802 |
| Hnrnph1 | -0.3850724 | 0.04138392 |
| Orc3 | -0.386385 | 0.04950145 |
| Sf3a1 | -0.3926086 | 0.02979202 |
| Med14 | -0.3953839 | 0.03534769 |
| Ola1 | -0.396888 | 0.03082871 |
| Stip1 | -0.3980127 | 0.02573146 |
| Rrm1 | -0.40015 | 0.04897333 |
| Set | -0.4020976 | 0.01963419 |
| Pdcd11 | -0.4036084 | 0.03644631 |
| Pkm | -0.4037588 | 0.03312645 |
| Ncapd2 | -0.4068065 | 0.03463265 |
| Xpo5 | -0.4114309 | 0.04382674 |
| Utp6 | -0.4115701 | 0.03127257 |
| Wdr75 | -0.4123941 | 0.03276747 |
| Tyms | -0.4180273 | 0.03074998 |
| Mybbp1a | -0.4199431 | 0.02769257 |
| Smarcc1 | -0.4207404 | 0.01059255 |
| U2af2 | -0.4218187 | 0.03635639 |
| Nup62 | -0.4218858 | 0.03659348 |
| Epb4.1l5 | -0.4222133 | 0.03493345 |
| Ddx18 | -0.4238809 | 0.01903771 |
| Cops5 | -0.4239614 | 0.04751996 |
| Znrf3 | -0.4252158 | 0.03912092 |
| Cirh1a | -0.4273012 | 0.02573146 |
| Plagl2 | -0.4287221 | 0.03711419 |
| Ttll4 | -0.4302274 | 0.03645358 |
| Rae1 | -0.4322049 | 0.02672746 |
| Fam210a | -0.4326129 | 0.03337002 |
| Larp7 | -0.4335868 | 0.01353108 |
| Hnrnpc | -0.433706 | 0.04463755 |
| Cpsf6 | -0.4344144 | 0.0310876 |
| Nsun2 | -0.4344325 | 0.0494033 |
| Nme1 | -0.4416846 | 0.0185303 |

| | | |
|---|---|---|
| Aifm1 | -0.4417268 | 0.03947684 |
| Denr | -0.4420595 | 0.04877194 |
| Mre11a | -0.4431858 | 0.03997574 |
| Nup160 | -0.445214 | 0.01700972 |
| Nup155 | -0.4457544 | 0.01493718 |
| Psmb3 | -0.4494857 | 0.02443424 |
| Snrnp70 | -0.4500929 | 0.0349515 |
| Smn1 | -0.4510802 | 0.04776154 |
| Fasn | -0.4512933 | 0.01263781 |
| Plcl2 | -0.4526148 | 0.0450795 |
| Fastkd2 | -0.4526201 | 0.04305208 |
| Dtl | -0.4527959 | 0.0459797 |
| Gins2 | -0.4540335 | 0.04249431 |
| Ppat | -0.4559212 | 0.01150381 |
| Fus | -0.4564607 | 0.0163981 |
| Dhfr | -0.4572799 | 0.0368505 |
| Atic | -0.457867 | 0.03899655 |
| Acaca | -0.458071 | 0.03301159 |
| Mms22l | -0.458251 | 0.04369371 |
| Wdr3 | -0.4585454 | 0.04762262 |
| Utp11l | -0.4591145 | 0.04692825 |
| Hat1 | -0.459847 | 0.03971781 |
| Usp24 | -0.4598783 | 0.01399932 |
| Hells | -0.4618291 | 0.019913 |
| Rsl1d1 | -0.4630114 | 0.00897587 |
| Tacc3 | -0.4632733 | 0.02304744 |
| C1qbp | -0.4654797 | 0.01928416 |
| Khsrp | -0.4659537 | 0.02543228 |
| Erh | -0.4663217 | 0.01225007 |
| Nudc | -0.4675083 | 0.02315338 |
| Eif4e | -0.4700993 | 0.01482001 |
| Ruvbl2 | -0.4714274 | 0.01715585 |
| Frs2 | -0.4737451 | 0.02003154 |
| Fgfr1op | -0.4764688 | 0.02174393 |
| Rsl24d1 | -0.4794557 | 0.03088623 |
| Gatad1 | -0.4821751 | 0.00481321 |
| Phb | -0.4823853 | 0.026337 |
| Park7 | -0.4844912 | 0.03428394 |
| Tsr1 | -0.4870355 | 0.02543228 |
| Chaf1b | -0.4875325 | 0.03194556 |
| Myo19 | -0.4878522 | 0.04125506 |
| Trmt6 | -0.4884361 | 0.0349515 |
| Cct3 | -0.4887553 | 0.00537465 |
| Chek1 | -0.4912268 | 0.03306718 |

| | | |
|---|---|---|
| Rcc2 | -0.4921252 | 0.01422541 |
| Cacybp | -0.4933062 | 0.0278088 |
| 0610007P14Rik | -0.4934913 | 0.03218175 |
| Ticrr | -0.4936432 | 0.01544719 |
| Oat | -0.494166 | 0.00510136 |
| Ing5 | -0.4949474 | 0.02626481 |
| Psmg1 | -0.4960053 | 0.01868596 |
| Tuba1c | -0.4960215 | 0.00190905 |
| Cks1b | -0.4983408 | 0.01006836 |
| Dkc1 | -0.500082 | 0.0255021 |
| Mlec | -0.5010375 | 0.00379324 |
| Wdr18 | -0.5016548 | 0.02760258 |
| Eef1d | -0.5016561 | 0.00502959 |
| Gpn1 | -0.50166 | 0.03127257 |
| Kif20a | -0.5021924 | 0.02025168 |
| Gfpt2 | -0.5025914 | 0.03889119 |
| C330027C09Rik | -0.503346 | 0.0207671 |
| Rrp1b | -0.5039365 | 0.0041559 |
| Jade3 | -0.5045377 | 0.04865351 |
| Phlda1 | -0.511139 | 0.01548462 |
| Mrps30 | -0.5112446 | 0.03023915 |
| Nsdhl | -0.5131118 | 0.00403504 |
| Emg1 | -0.514678 | 0.03023915 |
| Pitrm1 | -0.5148078 | 0.03672314 |
| Dazap1 | -0.5151004 | 0.04344302 |
| Pcna | -0.5155391 | 0.00610925 |
| Eno1b | -0.5159822 | 0.02790907 |
| Pspc1 | -0.5165724 | 0.02684948 |
| Cenph | -0.5175012 | 0.03473194 |
| Srm | -0.5186396 | 0.01289603 |
| Uhrf1 | -0.5191902 | 0.00229883 |
| Nol10 | -0.5216314 | 0.03622576 |
| Eif5a | -0.5225901 | 0.00090198 |
| Rfc5 | -0.5234656 | 0.04012009 |
| Seh1l | -0.523609 | 0.00115992 |
| Mycbp | -0.5236966 | 0.023239 |
| Sf3b4 | -0.5257505 | 0.01150381 |
| Gemin5 | -0.5259505 | 0.01236071 |
| Pno1 | -0.5261394 | 0.00501727 |
| Mrpl18 | -0.5270604 | 0.00714937 |
| Hspd1 | -0.5276276 | 0.0162064 |
| Phykpl | -0.5278217 | 0.01967461 |
| Nop58 | -0.5278991 | 0.00264092 |
| Hsp90aa1 | -0.5285458 | 0.00455905 |

| | | |
|---|---|---|
| Klhl21 | -0.5298036 | 0.02020045 |
| Rspo3 | -0.5305875 | 0.00367767 |
| Magoh | -0.5325781 | 0.0217567 |
| Pfkp | -0.5343331 | 0.03711419 |
| Casc5 | -0.5346706 | 0.01063502 |
| Katna1 | -0.5392394 | 0.04053541 |
| Haus1 | -0.5416084 | 0.0184151 |
| Ddx20 | -0.5419028 | 0.00725007 |
| Zwilch | -0.5423232 | 0.0035169 |
| D8Ertd738e | -0.5444438 | 0.0362936 |
| Ppa1 | -0.545403 | 0.04828985 |
| Isoc1 | -0.5481145 | 0.0163981 |
| Lin28a | -0.5484315 | 0.00615527 |
| Cse1l | -0.5488957 | 0.00026741 |
| Lss | -0.5497879 | 0.01150381 |
| Mad2l1 | -0.5499787 | 0.01318802 |
| E2f4 | -0.5500669 | 0.01668018 |
| Cep76 | -0.5505935 | 0.03034652 |
| Noc3l | -0.5510514 | 0.00893186 |
| Rap1b | -0.5510983 | 0.02978328 |
| Ddx21 | -0.551379 | 0.00206249 |
| Zfp850 | -0.5528011 | 0.03489856 |
| Mrps22 | -0.5561946 | 0.0331987 |
| Ranbp1 | -0.5567163 | 0.0046022 |
| Umps | -0.5584059 | 0.0069547 |
| Dut | -0.5585744 | 0.00184012 |
| Mcm7 | -0.5601798 | 0.0006588 |
| Cep290 | -0.5611988 | 0.0289515 |
| Mif | -0.5644379 | 0.02222295 |
| Usp36 | -0.5669756 | 0.02926058 |
| Ppp1r14b | -0.5692128 | 0.00604927 |
| Hdgf | -0.5709078 | 0.00033317 |
| Hist1h1e | -0.5717303 | 0.01421933 |
| Cluh | -0.5718228 | 0.01021717 |
| Cks2 | -0.5722872 | 0.03797658 |
| Gcsh | -0.5728595 | 0.00190905 |
| Ahsa1 | -0.574962 | 0.0013853 |
| Pold1 | -0.5749853 | 0.01981412 |
| Sms | -0.5751655 | 0.00384989 |
| Jmjd6 | -0.5756012 | 0.00729657 |
| Fbl | -0.5758456 | 0.00085362 |
| Prps1 | -0.5765977 | 0.04076364 |
| Nop56 | -0.5766727 | 0.03773238 |
| Homer1 | -0.5783565 | 0.03549961 |

| | | |
|---|---|---|
| Nhp2 | -0.582946 | 0.00138054 |
| Nasp | -0.5832083 | 0.0001497 |
| Noc2l | -0.5835108 | 0.00115149 |
| Rcc1 | -0.5838483 | 0.01150381 |
| Atad5 | -0.5839931 | 0.00074499 |
| Snrpd2 | -0.5845768 | 0.04959674 |
| Gsg2 | -0.5887483 | 0.02480468 |
| Mdk | -0.5925585 | 0.03677938 |
| Maz | -0.5930999 | 0.03107751 |
| Mrpl3 | -0.5936589 | 0.01062553 |
| Naf1 | -0.5942042 | 0.00565761 |
| Mid1 | -0.5945538 | 0.01015109 |
| Cenpn | -0.5953636 | 0.00738044 |
| Pprc1 | -0.595594 | 0.01073499 |
| Dis3 | -0.5961683 | 0.00051683 |
| Naa10 | -0.5967393 | 0.01483212 |
| Ankrd27 | -0.5970243 | 0.03643087 |
| Rpp14 | -0.5981019 | 0.03203946 |
| Gnl3 | -0.6009705 | 0.00426017 |
| Pa2g4 | -0.6011336 | 7.3392E-05 |
| Kmt2b | -0.60144 | 0.03572526 |
| Ddx39 | -0.6014412 | 0.00136878 |
| Nop10 | -0.60184 | 0.00626164 |
| Snapc4 | -0.6024253 | 0.00972513 |
| Sppl2a | -0.6039032 | 0.01632944 |
| Bop1 | -0.6056497 | 0.00679395 |
| Psat1 | -0.6060635 | 0.00091311 |
| E2f1 | -0.6070543 | 0.01963896 |
| Cap2 | -0.6076249 | 0.00050595 |
| Polr1b | -0.6098149 | 0.00253093 |
| Naa50 | -0.6103831 | 0.02790907 |
| Nup35 | -0.6118891 | 0.03855556 |
| Timeless | -0.6145758 | 0.00215836 |
| Pfas | -0.616097 | 0.00089948 |
| Rps12 | -0.6173728 | 0.03182126 |
| Aste1 | -0.618063 | 0.03142146 |
| Zmym1 | -0.6181706 | 0.01059225 |
| Dtymk | -0.6182236 | 0.02642009 |
| Kif15 | -0.6183403 | 0.00027944 |
| Haus3 | -0.6188925 | 0.00930685 |
| Mrpl52 | -0.6198458 | 0.04870071 |
| P2ry1 | -0.6275068 | 0.02693819 |
| Dusp18 | -0.628064 | 0.0128828 |
| Ccdc124 | -0.6290632 | 0.02040009 |

| | | |
|---|---|---|
| Ell2 | -0.6296718 | 0.01841746 |
| Tk1 | -0.6301929 | 0.03728596 |
| Shmt2 | -0.630889 | 7.9875E-05 |
| Abcb10 | -0.6330012 | 0.00130076 |
| D030056L22Rik | -0.6356704 | 0.01811323 |
| Akt2 | -0.6369274 | 0.02134294 |
| L2hgdh | -0.6389627 | 0.00550733 |
| Rreb1 | -0.6400927 | 9.9507E-05 |
| Elac2 | -0.6413754 | 0.00215836 |
| Etl4 | -0.6415104 | 0.00152996 |
| 2410002F23Rik | -0.6417525 | 0.01963896 |
| Nkrf | -0.6418171 | 0.00353932 |
| Mrpl47 | -0.6420686 | 0.03473194 |
| Lsm2 | -0.6427002 | 0.01253675 |
| 9430015G10Rik | -0.6469001 | 0.02885122 |
| Uchl3 | -0.6487112 | 0.0089163 |
| Dhodh | -0.6498502 | 0.02416471 |
| Pole | -0.6524743 | 0.00118802 |
| Nmral1 | -0.653271 | 0.04645893 |
| Rad51 | -0.653761 | 0.00406655 |
| Urb1 | -0.6553645 | 0.00627884 |
| Mob1b | -0.6574739 | 0.00245262 |
| Nolc1 | -0.6576932 | 8.6466E-06 |
| Bckdhb | -0.6580894 | 0.02211293 |
| Bag2 | -0.6645741 | 0.02505003 |
| Smyd5 | -0.6656635 | 0.02672146 |
| Ndufs6 | -0.6699754 | 0.01536491 |
| Itga2b | -0.6727368 | 0.02027658 |
| Tsen2 | -0.6775487 | 0.04646687 |
| Edrf1 | -0.6829337 | 0.00804993 |
| Ppan | -0.6850071 | 0.03564443 |
| Ptgr1 | -0.6889211 | 0.02285697 |
| Cdc6 | -0.6929623 | 0.00174087 |
| 3110082I17Rik | -0.6937728 | 0.01223807 |
| Diablo | -0.6948298 | 0.02997505 |
| Rybp | -0.6951969 | 0.04477566 |
| Dctd | -0.7007772 | 0.0025433 |
| Mob3c | -0.7061391 | 0.0292513 |
| Ippk | -0.7063486 | 0.01195282 |
| Rab11fip1 | -0.7064745 | 0.00787161 |
| Mrpl22 | -0.7076716 | 0.01843504 |
| Sod2 | -0.7101316 | 0.00083047 |
| Srxn1 | -0.7117592 | 0.02027658 |
| Tlcd1 | -0.7161115 | 0.0349515 |

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|---|---|---|
| Mtrr | -0.7165168 | 0.00942764 |
| Uqcr10 | -0.7168167 | 0.00711417 |
| Heatr2 | -0.7168978 | 0.00627968 |
| Fancd2 | -0.7181052 | 0.0012332 |
| Tcof1 | -0.718714 | 0.00017748 |
| Trip13 | -0.7194061 | 0.000102 |
| Rad54l | -0.7201007 | 0.00644358 |
| Rpp40 | -0.720515 | 0.00872237 |
| Tal1 | -0.7243217 | 0.03500468 |
| Ccdc18 | -0.7250853 | 0.02243067 |
| Zfp36l2 | -0.7253139 | 0.00185707 |
| Setd8 | -0.7259416 | 0.00026996 |
| Prkab1 | -0.729529 | 0.00012967 |
| Zbtb43 | -0.7306579 | 0.03843164 |
| Gins1 | -0.7321125 | 0.00943833 |
| Sf3b6 | -0.7375405 | 0.02223724 |
| Cep152 | -0.7386925 | 0.03594749 |
| Ung | -0.7392586 | 0.01686781 |
| Snrpa1 | -0.741571 | 0.00020826 |
| Slc16a6 | -0.7451852 | 0.01005037 |
| Ska3 | -0.746177 | 0.00597189 |
| Egln3 | -0.7466605 | 4.2368E-05 |
| Bcor | -0.7480644 | 1.9447E-06 |
| Zik1 | -0.7482625 | 0.02993161 |
| Srf | -0.7496534 | 0.00348084 |
| Snhg5 | -0.7520657 | 0.00095124 |
| Uqcr11 | -0.7552484 | 0.01150381 |
| Ddx11 | -0.7563069 | 0.00417648 |
| Psmc3ip | -0.7568939 | 0.00041982 |
| 1110038B12Rik | -0.7581591 | 0.00127361 |
| Helb | -0.7590714 | 0.02052056 |
| Hsd17b7 | -0.7599393 | 0.00067447 |
| Prkcd | -0.7609372 | 0.04692825 |
| Smim3 | -0.7616062 | 0.01132173 |
| Notch2 | -0.7648085 | 0.00160718 |
| Hmgn2 | -0.7648535 | 0.00365518 |
| Lsm5 | -0.7653828 | 0.02076879 |
| Tfb2m | -0.7675262 | 0.016153 |
| Anapc11 | -0.7680224 | 0.03422569 |
| Ppih | -0.7682877 | 0.01636778 |
| H2afx | -0.7685989 | 0.00059415 |
| Fancb | -0.7713014 | 0.04139186 |
| Gyk | -0.7715793 | 0.0468364 |
| Polr2i | -0.7720022 | 0.01984889 |

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|---|---|---|
| Depdc1b | -0.7720366 | 0.00170735 |
| Zcchc10 | -0.7745844 | 0.00524108 |
| Snrpg | -0.7818499 | 0.04215328 |
| Klhl12 | -0.7832182 | 0.00181501 |
| E2f8 | -0.78417 | 0.00018093 |
| Epb4.1 | -0.7849334 | 1.3779E-05 |
| Wbscr16 | -0.79124 | 0.01821397 |
| Fth1 | -0.7925434 | 0.00031048 |
| Troap | -0.7972141 | 0.0231519 |
| Hspe1 | -0.7988842 | 0.01963896 |
| Rnd2 | -0.8016923 | 0.02263465 |
| Ern1 | -0.8027457 | 0.0042741 |
| Mtx3 | -0.8052675 | 0.04224171 |
| Suv39h2 | -0.8053629 | 0.00026429 |
| Tcf7 | -0.8056699 | 3.7094E-05 |
| Lyar | -0.806388 | 5.6751E-06 |
| Smtnl2 | -0.8080904 | 0.0132248 |
| Tnfaip8 | -0.8116157 | 0.00189608 |
| Peo1 | -0.8136152 | 0.00721895 |
| Speg | -0.81617 | 0.0217567 |
| Fut8 | -0.8166749 | 0.00010455 |
| D2Wsu81e | -0.8168487 | 0.00815552 |
| H2afz | -0.8234957 | 3.0782E-08 |
| Laptm5 | -0.8267113 | 0.04336512 |
| Ubxn2a | -0.8271654 | 0.00022276 |
| Stra13 | -0.8316425 | 0.01229853 |
| Rrp12 | -0.8351638 | 0.00010987 |
| Gcnt1 | -0.8393189 | 2.3531E-05 |
| Tsc1 | -0.8417155 | 0.00012396 |
| Trmt61a | -0.8425698 | 0.00089333 |
| Polr2f | -0.8473131 | 0.00719128 |
| Utp23 | -0.8561307 | 0.01021231 |
| Mrto4 | -0.8586158 | 0.00010066 |
| Fads2 | -0.8661943 | 4.8134E-06 |
| Tm7sf2 | -0.8688088 | 0.02543228 |
| Nbeal2 | -0.8716841 | 0.00662327 |
| Ska1 | -0.8730391 | 0.03653303 |
| Traip | -0.8757748 | 0.02069251 |
| Psph | -0.8766564 | 0.00684254 |
| Inip | -0.8770961 | 0.00171834 |
| Ormdl1 | -0.8771678 | 0.00814927 |
| Srl | -0.8787499 | 0.02313439 |
| C530008M17Rik | -0.8817309 | 0.02435718 |
| Hist1h1b | -0.883334 | 5.4691E-05 |

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|---|---|---|
| Caprin2 | -0.8843534 | 0.00565763 |
| Rbmx | -0.8861848 | 0.00045963 |
| Grap2 | -0.8868077 | 0.0243308 |
| Sssca1 | -0.8898676 | 0.00050595 |
| Gas5 | -0.8931038 | 0.00100565 |
| Melk | -0.8938092 | 0.00074806 |
| Idi1 | -0.8942903 | 0.00062584 |
| Bcat1 | -0.9044063 | 0.00614126 |
| Mdm1 | -0.9053117 | 7.9056E-05 |
| Rps6ka6 | -0.9072983 | 2.512E-06 |
| Prmt1 | -0.9141192 | 0.00027692 |
| Fkbp11 | -0.9174265 | 0.03022019 |
| Slc19a1 | -0.9234819 | 0.01292404 |
| Ppil3 | -0.9241589 | 0.03307018 |
| Gtf3c5 | -0.9250698 | 8.0921E-08 |
| Hist1h2bb | -0.9256411 | 0.03473194 |
| Spc24 | -0.9296335 | 9.0055E-05 |
| Itga4 | -0.9299064 | 0.00012351 |
| Hist1h2be | -0.9304375 | 0.02222295 |
| Pola2 | -0.9380601 | 1.6172E-05 |
| Ahi1 | -0.9508248 | 2.5154E-05 |
| Acy1 | -0.9528935 | 0.04380506 |
| Ctla2a | -0.9543965 | 0.04970076 |
| Cenpp | -0.9595026 | 0.01722529 |
| Gpc6 | -0.9623014 | 0.01029804 |
| Shroom3 | -0.9652569 | 0.03815161 |
| Zfp692 | -0.9781341 | 0.00385429 |
| Tmem158 | -0.9823048 | 0.02592136 |
| Cited2 | -0.9926737 | 1.7574E-06 |
| Taf1d | -0.9953624 | 0.03696605 |
| Acot11 | -1.0008928 | 0.00777375 |
| Lsm7 | -1.0009126 | 0.00430527 |
| Slc7a5 | -1.0036 | 2.178E-06 |
| Tmem86b | -1.0039618 | 0.01746706 |
| Ifi30 | -1.0044766 | 0.04870071 |
| Psd3 | -1.0174544 | 0.03534982 |
| Wdsub1 | -1.0239369 | 0.04895047 |
| 1810032O08Rik | -1.0328231 | 0.02993161 |
| Hist1h4d | -1.0383794 | 0.00550733 |
| Dctpp1 | -1.0393153 | 0.00031738 |
| Plscr1 | -1.039389 | 0.00461492 |
| Pmp22 | -1.0535001 | 0.00984758 |
| Mgat4a | -1.0568436 | 0.00777681 |
| C77080 | -1.0585692 | 0.00018931 |

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|---|---|---|
| Snhg3 | -1.0648738 | 0.01026912 |
| Sec61g | -1.0666418 | 0.01710869 |
| Psmg4 | -1.0676331 | 0.04632492 |
| Sdc1 | -1.0753188 | 0.00099975 |
| Fzd2 | -1.0778418 | 0.02796823 |
| Lhpp | -1.0879831 | 0.02047849 |
| Gse1 | -1.0939363 | 2.3134E-11 |
| Zfp930 | -1.0940181 | 0.0006457 |
| Lsm3 | -1.0963022 | 0.00452377 |
| Tagln | -1.1030145 | 0.0347611 |
| Car2 | -1.1035294 | 0.03598601 |
| Kcnj5 | -1.1045913 | 0.00054441 |
| Med30 | -1.1093461 | 0.01936224 |
| Dsp | -1.1110028 | 0.00991782 |
| Lpar1 | -1.1156382 | 0.0338615 |
| Kalrn | -1.1171644 | 1.0778E-06 |
| Ccdc134 | -1.1231804 | 0.02068478 |
| Xk | -1.1366802 | 0.00784992 |
| Dyrk2 | -1.1426776 | 0.00974385 |
| Irs1 | -1.1430887 | 0.00296595 |
| Kctd15 | -1.1434019 | 0.02817557 |
| Lyl1 | -1.1442502 | 0.00095854 |
| Apitd1 | -1.1442509 | 0.00232128 |
| Ank3 | -1.1478545 | 5.4748E-07 |
| Etv2 | -1.1482494 | 0.00335705 |
| Arhgap6 | -1.1576452 | 1.2625E-05 |
| Tpm2 | -1.1599192 | 0.00522762 |
| Cth | -1.1612232 | 0.03283644 |
| Mtfp1 | -1.162728 | 0.01029804 |
| Chchd1 | -1.1640701 | 0.04268792 |
| Fam109b | -1.1687442 | 0.03442235 |
| Snrnp25 | -1.1795927 | 8.6466E-06 |
| Tfrc | -1.1817508 | 1.4296E-15 |
| Fzd10 | -1.1850427 | 0.01202788 |
| Robo2 | -1.1976152 | 0.02796823 |
| Rab27b | -1.2026754 | 0.00026257 |
| Hist1h3e | -1.207497 | 0.00202841 |
| Hist1h2bm | -1.2087727 | 0.00016605 |
| Pde4dip | -1.2117548 | 2.2216E-08 |
| Myl9 | -1.2154017 | 0.00896662 |
| Col5a1 | -1.2365169 | 0.02412473 |
| Nfix | -1.2439774 | 0.02885122 |
| Plek | -1.2460721 | 0.02967711 |
| Hist1h2ac | -1.2654033 | 0.04800539 |

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|---|---|---|
| Sh3bp1 | -1.2655429 | 3.8227E-06 |
| Slc35f2 | -1.2714037 | 0.00447928 |
| Med12l | -1.2776314 | 5.1885E-08 |
| Eno3 | -1.2819185 | 0.00053602 |
| Gria2 | -1.2929235 | 0.01273978 |
| Prtg | -1.2975163 | 3.8001E-10 |
| Samd14 | -1.3126027 | 0.03439808 |
| Gfra2 | -1.3188517 | 0.00121213 |
| Hist2h2ac | -1.3249293 | 0.04380506 |
| Hist1h2bl | -1.3323982 | 3.9428E-06 |
| Hist1h4c | -1.3424522 | 0.03677938 |
| Lgals9 | -1.3443204 | 0.00115378 |
| Phgdh | -1.3465429 | 1.0238E-06 |
| Hist1h4a | -1.3568512 | 0.04092191 |
| Hspb8 | -1.3581106 | 0.04765362 |
| Hist1h2bf | -1.3608963 | 9.8475E-05 |
| Lama1 | -1.3748046 | 0.01053971 |
| Ptpre | -1.3799639 | 6.3333E-07 |
| Mpl | -1.383543 | 0.00145656 |
| Gfi1 | -1.3873919 | 0.0297813 |
| Tenm3 | -1.3946725 | 0.03673257 |
| Klf8 | -1.398728 | 1.0931E-09 |
| Cyp26b1 | -1.4037073 | 0.0103534 |
| Hist1h2ak | -1.4072807 | 0.00027529 |
| Pitx2 | -1.410157 | 0.00313612 |
| Dyrk3 | -1.4106397 | 0.00457984 |
| Nap1l2 | -1.4284217 | 0.04125506 |
| Ston2 | -1.4291669 | 0.00010666 |
| Hist1h3g | -1.4334317 | 0.00190905 |
| Ifitm1 | -1.4344149 | 5.8211E-05 |
| Adamts9 | -1.4390785 | 0.02008021 |
| Mrvi1 | -1.439407 | 0.0163981 |
| Sfrp2 | -1.4502113 | 0.03473194 |
| Lrr1 | -1.45511 | 0.00446531 |
| Mpo | -1.4663655 | 0.01179793 |
| Ryr2 | -1.4690604 | 0.016935 |
| Unc5c | -1.4771939 | 4.1464E-15 |
| Egfl8 | -1.4885643 | 0.04839119 |
| Fam117a | -1.4937007 | 0.00425314 |
| Hist1h2bh | -1.4980855 | 4.3762E-05 |
| Syt7 | -1.5153341 | 0.01778145 |
| Gpc3 | -1.5323008 | 7.1689E-09 |
| Sall3 | -1.5370094 | 1.5078E-17 |
| Wnt5a | -1.5468432 | 0.0007608 |

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|---|---|---|
| Hist1h3i | -1.5483412 | 0.02672146 |
| Plcxd1 | -1.5523584 | 0.0381536 |
| Hist1h2bp | -1.5681605 | 0.00989979 |
| Hist1h2bk | -1.5735921 | 0.00043405 |
| Snord99 | -1.5909402 | 0.01629015 |
| AI467606 | -1.5969964 | 0.02294639 |
| Ptprj | -1.6077737 | 1.0931E-09 |
| Ctse | -1.6078993 | 0.00243166 |
| Prkca | -1.6098811 | 3.3616E-10 |
| Rgs10 | -1.6222642 | 0.01325467 |
| Wisp1 | -1.63618 | 0.00067447 |
| Hist1h1a | -1.6408645 | 0.00010791 |
| Dlg3 | -1.6444894 | 0.03846739 |
| Krt19 | -1.6450808 | 0.00471472 |
| Pappa | -1.6741823 | 0.02022074 |
| Cnn1 | -1.6778678 | 0.0287664 |
| Dapp1 | -1.7240331 | 1.2642E-07 |
| Ccnd2 | -1.7249129 | 8.4849E-05 |
| Sdc2 | -1.7252224 | 0.00129517 |
| Slc30a3 | -1.7763864 | 0.02078334 |
| Hist1h2ai | -1.8043194 | 0.04861388 |
| Nrgn | -1.8055743 | 0.0099646 |
| Aif1l | -1.8075623 | 0.00011715 |
| Atp2a3 | -1.8125327 | 2.5755E-06 |
| Rps6kl1 | -1.8244938 | 0.0494033 |
| Gm16982 | -1.848031 | 0.03181333 |
| Tmem62 | -1.8548086 | 0.01330257 |
| Thsd4 | -1.867671 | 0.00223766 |
| Col1a2 | -1.8752501 | 0.00086706 |
| Kcnj2 | -1.8778166 | 0.00938174 |
| Itgb3 | -1.904678 | 1.0396E-06 |
| Snord47 | -1.908005 | 0.03506548 |
| Hist1h4k | -1.9096921 | 0.00594326 |
| Gng7 | -1.9207414 | 0.01967723 |
| Ackr3 | -1.9236598 | 0.00111278 |
| Fam46a | -1.9265152 | 0.00730926 |
| Cdh11 | -1.9347074 | 0.00368123 |
| Acta2 | -1.9431264 | 0.00108295 |
| Igsf11 | -1.9730923 | 0.0032421 |
| Hbb-y | -1.9748359 | 4.584E-05 |
| Ubxn11 | -1.983615 | 0.00684254 |
| Ikzf2 | -1.9955979 | 8.666E-16 |
| Epcam | -1.9977628 | 0.01015501 |
| Was | -1.9990616 | 8.5009E-05 |

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|---|---|---|
| Acat3 | -2.0060747 | 0.02734464 |
| Mcoln3 | -2.0135873 | 0.03269587 |
| Hist1h4j | -2.0168569 | 0.03711419 |
| Gli2 | -2.0256238 | 0.0017032 |
| Smyd1 | -2.0480579 | 0.01838017 |
| Pde11a | -2.0583309 | 0.02803373 |
| Map7d2 | -2.0666869 | 0.03246469 |
| Wwc1 | -2.0764389 | 0.00047185 |
| Hba-x | -2.0906682 | 3.159E-07 |
| Irs2 | -2.0961118 | 5.8778E-20 |
| Pdgfrb | -2.1019287 | 0.00743475 |
| Ptpn13 | -2.1059753 | 4.7899E-08 |
| Nfe2 | -2.1065983 | 4.4655E-08 |
| Smim1 | -2.1151748 | 0.01490303 |
| Fgf10 | -2.1307131 | 1.5168E-05 |
| Wnt4 | -2.1362897 | 0.00140192 |
| Snord15b | -2.157675 | 0.00934557 |
| Sytl5 | -2.1590435 | 0.00044028 |
| Syne4 | -2.1602438 | 0.00603873 |
| Lrp2 | -2.1683193 | 0.00012169 |
| Kcnd3 | -2.1909069 | 0.00690389 |
| Kif26b | -2.2020228 | 0.03473194 |
| Tspan32 | -2.2086198 | 8.0245E-06 |
| Gfi1b | -2.2107003 | 1.6969E-06 |
| Cgn | -2.2139564 | 0.00221779 |
| Chpf | -2.2346358 | 0.02143951 |
| Col12a1 | -2.2377922 | 1.3079E-05 |
| Mir1949 | -2.252971 | 0.0065173 |
| Reep6 | -2.2591005 | 0.00044188 |
| Gucy1a3 | -2.2596713 | 3.0558E-09 |
| Fam110c | -2.2660124 | 0.04749712 |
| Pkd1l3 | -2.2721338 | 0.02464859 |
| Col8a1 | -2.275621 | 0.00458619 |
| Ikzf1 | -2.2786084 | 1.5466E-16 |
| Phlda2 | -2.2808251 | 0.00054441 |
| Sdk2 | -2.3005852 | 0.00178985 |
| Cort | -2.3033757 | 0.04319604 |
| F3 | -2.3463844 | 0.00249194 |
| Ildr2 | -2.3554778 | 0.02541073 |
| Cnksr2 | -2.4145604 | 0.00174087 |
| Adamts3 | -2.4415041 | 1.1435E-16 |
| Slit3 | -2.4443195 | 0.01676172 |
| Ccl17 | -2.4618337 | 0.00565698 |
| Scube2 | -2.4633338 | 1.2498E-05 |

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|---|---|---|
| P2rx1 | -2.4648688 | 4.2409E-06 |
| Plbd1 | -2.4842592 | 0.04380506 |
| Nog | -2.4867721 | 0.03074998 |
| Evx1 | -2.5070756 | 0.00710432 |
| Pard6b | -2.5132174 | 7.0216E-11 |
| Dlk1 | -2.5174664 | 0.01117957 |
| Lypd6 | -2.527006 | 0.01207909 |
| Slc16a10 | -2.5476922 | 1.0481E-05 |
| Igfbp2 | -2.5554076 | 1.8526E-05 |
| Epb4.2 | -2.5598202 | 1.8021E-05 |
| Krt8 | -2.5741038 | 1.0158E-06 |
| Terc | -2.5834174 | 0.01929542 |
| Hoxd1 | -2.621979 | 8.1501E-07 |
| Myl4 | -2.630741 | 0.00770151 |
| 5330426P16Rik | -2.6446846 | 0.02899933 |
| Adamts15 | -2.6619076 | 0.00183546 |
| Klhl34 | -2.6888257 | 0.0243308 |
| Snord65 | -2.6966047 | 0.01369938 |
| Zic3 | -2.7075066 | 0.01007745 |
| Chac1 | -2.7158122 | 0.03425189 |
| Car12 | -2.7161838 | 0.0125579 |
| Runx1 | -2.7256084 | 1.6576E-27 |
| Gpr56 | -2.7306544 | 6.1352E-12 |
| Lypd1 | -2.7503944 | 0.02958715 |
| Bdnf | -2.7569741 | 0.01706797 |
| Cemip | -2.7597959 | 0.00972513 |
| Psd2 | -2.7685594 | 0.04023191 |
| Bhlhe22 | -2.7788676 | 0.04589984 |
| Nkx1-2 | -2.8116603 | 4.8282E-06 |
| Krt18 | -2.8300695 | 1.9496E-05 |
| Fgf15 | -2.8448297 | 0.00074499 |
| Ripk4 | -2.8502852 | 0.03564443 |
| Acta1 | -2.8507773 | 0.00670684 |
| Mfsd2b | -2.8581726 | 3.3044E-10 |
| Hbb-bh1 | -2.8585705 | 2.1373E-10 |
| Nnat | -2.870562 | 0.00943661 |
| 1700024P16Rik | -2.9094172 | 0.04618593 |
| Treml2 | -2.9188545 | 0.01644824 |
| Il18rap | -2.9367721 | 0.02558671 |
| Cdh22 | -2.9609251 | 0.04793262 |
| Lgr5 | -2.9755872 | 4.1171E-26 |
| Rgs4 | -3.045216 | 0.00427405 |
| Bmp8a | -3.0462458 | 0.00051332 |
| Enpp1 | -3.0546272 | 4.1166E-06 |

| | | |
|---|---|---|
| Asic4 | -3.0661955 | 0.00893186 |
| Col11a2 | -3.1009018 | 0.02666483 |
| Igfbp5 | -3.1027981 | 5.0016E-11 |
| Scube3 | -3.1383901 | 0.00062887 |
| Crabp2 | -3.2575996 | 0.00615527 |
| Kcnk1 | -3.2686447 | 3.722E-05 |
| Rpph1 | -3.281995 | 2.1394E-05 |
| Lmod1 | -3.2934985 | 0.02731732 |
| Cacna1d | -3.3339941 | 0.01548462 |
| Dpf3 | -3.3366168 | 0.00736531 |
| Gm14204 | -3.3480536 | 0.00322228 |
| Cdh3 | -3.3515719 | 4.8587E-06 |
| Svep1 | -3.3665107 | 0.0246003 |
| Plac8 | -3.3850148 | 0.03516285 |
| Ppp1r14a | -3.3875344 | 0.02733033 |
| Snord11 | -3.4033326 | 0.03447524 |
| Col2a1 | -3.4043366 | 0.00770291 |
| Krtap5-4 | -3.4274958 | 0.01385011 |
| Tenm4 | -3.4333517 | 0.00039229 |
| Postn | -3.4429613 | 8.2311E-10 |
| Myb | -3.4543925 | 8.3365E-09 |
| Inhba | -3.4548191 | 0.00071399 |
| Tgfb3 | -3.4614945 | 0.00489641 |
| Slc32a1 | -3.4787561 | 0.01146119 |
| Twist2 | -3.486109 | 0.01341197 |
| Vgll3 | -3.5369871 | 4.2262E-07 |
| Actc1 | -3.5579124 | 7.5035E-08 |
| Bnc2 | -3.5880639 | 0.00947273 |
| Reln | -3.6170028 | 3.5E-25 |
| Krt14 | -3.6405079 | 0.03969407 |
| Sycp2 | -3.6541894 | 0.03473194 |
| Olfr893 | -3.6656714 | 0.04406622 |
| Col1a1 | -3.6976688 | 4.9544E-05 |
| Slc7a8 | -3.7032242 | 5.5358E-19 |
| Snord49b | -3.7060819 | 0.01634423 |
| 5830432E09Rik | -3.7217186 | 0.0184344 |
| Mir3473 | -3.7421314 | 0.04317957 |
| 1700019A02Rik | -3.8088791 | 0.01171316 |
| Loxl1 | -3.8129879 | 0.00049731 |
| Mfap4 | -3.8436132 | 1.6274E-06 |
| Slc14a1 | -3.9021836 | 0.03207504 |
| Ms4a4d | -3.9106388 | 0.00987801 |
| Arpp21 | -3.9845324 | 0.01348456 |
| Tuba8 | -4.0014776 | 0.00446531 |

| | | |
|---|---|---|
| B4galnt3 | -4.0405548 | 0.0170189 |
| Mir1188 | -4.0457792 | 0.04714171 |
| Cbln1 | -4.0779217 | 1.7455E-06 |
| Bzrap1 | -4.0941697 | 0.02551107 |
| Mycbpap | -4.1183436 | 0.01331954 |
| Tacstd2 | -4.1381791 | 0.0168138 |
| Mir6516 | -4.1802058 | 0.00018038 |
| Nrip3 | -4.2215567 | 6.594E-12 |
| Pdzk1ip1 | -4.2568504 | 4.6365E-06 |
| Ajap1 | -4.2816439 | 0.04380506 |
| Ccl3 | -4.4113143 | 0.00739012 |
| Muc13 | -4.4403089 | 4.5577E-05 |
| Cobl | -4.4440277 | 0.01229853 |
| Dlx5 | -4.4620843 | 0.0226765 |
| Col8a2 | -4.5076296 | 0.02801605 |
| D830026I12Rik | -4.542468 | 0.00273577 |
| Smoc2 | -4.5827836 | 0.04994031 |
| Mir6940 | -4.5833125 | 0.02009453 |
| Sema5b | -4.5908909 | 0.00018517 |
| Ndufa4l2 | -4.6090649 | 0.00112525 |
| Slc1a6 | -4.6456547 | 0.00116 |
| Pgm5 | -4.6485806 | 0.02672146 |
| Gabra4 | -4.7118276 | 0.04261054 |
| Alx3 | -4.8471877 | 0.01150381 |
| A4gnt | -5.1071371 | 0.03788653 |
| Vat1l | -5.1080698 | 0.0032421 |
| Slitrk2 | -5.1635952 | 0.0041559 |
| Pip5kl1 | -5.1675678 | 0.01401483 |
| Mir1940 | -5.2146295 | 0.03653303 |
| Dppa5a | -5.2384808 | 2.2469E-06 |
| Tph1 | -5.285813 | 0.01755235 |
| Bmp7 | -5.3633196 | 0.00053602 |
| Atp6v0d2 | -5.5623301 | 0.000386 |
| Pitx1 | -5.5980066 | 0.01330257 |
| Olfml1 | -5.6903819 | 0.00127361 |
| Prr15l | -5.7339197 | 0.01788615 |
| BC027072 | -5.7931802 | 0.01183079 |
| Zfp641 | -5.8463841 | 0.04897333 |
| Gata1 | -5.9307033 | 1.1428E-08 |
| Fgf3 | -5.9991188 | 1.1575E-07 |
| Rnase6 | -6.0909008 | 0.04215328 |
| Lum | -6.1112301 | 0.0207671 |
| Vmn2r2 | -6.1502481 | 0.02629604 |
| Atp6v0a4 | -6.270693 | 0.0248442 |

| | | |
|---|---|---|
| Clec18a | -6.5983151 | 3.5931E-05 |
| Elfn2 | -6.6897525 | 0.00171301 |
| Cd164l2 | -7.1662694 | 0.00307347 |
| Wfdc17 | -7.1680774 | 0.00025308 |
| Fstl3 | -7.2822667 | 0.00190905 |
| Tmem54 | -7.5876681 | 0.00015351 |
| Orm1 | -7.628743 | 0.00086706 |
| Sema4f | -8.0860262 | 0.00217464 |

## Supplemental Table S2

Genes Down-regulated in the ENG-/LacZ+ HEI population

| Gene Symbol | logFC | FDR |
|---|---|---|
| Crybb3 | 6.25650192 | 0.000354722 |
| Cxcl17 | 6.15729044 | 0.006121384 |
| Ly6g6e | 6.14113513 | 0.015207308 |
| Clcf1 | 6.12886931 | 0.000344337 |
| Ccdc87 | 6.01920364 | 0.002263224 |
| Kcnma1 | 5.81748514 | 0.00052578 |
| Gja5 | 5.73413275 | 4.32555E-09 |
| Slc41a2 | 5.54592025 | 6.60249E-06 |
| Pcdhb14 | 5.41579617 | 0.005325232 |
| Cftr | 5.33818775 | 0.006788754 |
| Hc | 5.20317026 | 0.02040009 |
| Fbxo40 | 5.13542033 | 0.014225415 |
| Adamtsl5 | 5.10235581 | 0.01616849 |
| Nlrp1b | 5.04492195 | 0.015260874 |
| Il7 | 4.93619933 | 7.33334E-05 |
| Bmx | 4.91850392 | 0.000121367 |
| B230119M05Rik | 4.85139145 | 0.019634188 |
| Tbx3os2 | 4.78746119 | 0.046854014 |
| Yipf7 | 4.78451146 | 0.015219914 |
| Gbp11 | 4.78136599 | 0.020574987 |
| Ido1 | 4.76348461 | 0.041332448 |
| Eva1a | 4.76262161 | 0.000251395 |
| D930020B18Rik | 4.75115005 | 0.03177312 |
| E230025N22Rik | 4.74596006 | 0.023740855 |
| Tmem82 | 4.73257398 | 0.048941292 |
| Fam19a3 | 4.69408279 | 0.000136769 |
| Snph | 4.57833549 | 0.041747333 |
| Fam19a2 | 4.51858612 | 0.04735918 |
| Trpm3 | 4.50268817 | 0.032075036 |
| C1qtnf2 | 4.39069707 | 0.009430587 |
| Clvs1 | 4.38407592 | 0.005507327 |
| Gpihbp1 | 4.36945782 | 0.005771646 |
| Pcdh9 | 4.35360008 | 1.47967E-09 |
| S1pr4 | 4.21985657 | 0.00743091 |
| Ifit1 | 4.18072192 | 0.01150381 |
| Ccbe1 | 4.09615522 | 0.006109254 |
| Ablim3 | 4.02702263 | 0.00216256 |
| C1qtnf1 | 3.97657648 | 5.84737E-06 |
| Abcd2 | 3.70273365 | 0.000520706 |

| | | |
|---|---|---|
| Npvf | 3.70199549 | 0.029404986 |
| Trnp1 | 3.6755603 | 0.024192528 |
| Dpp4 | 3.66117546 | 0.008422956 |
| 9030617O03Rik | 3.63402294 | 0.010635018 |
| Ifit3 | 3.63391696 | 0.04613748 |
| Scn3a | 3.62772869 | 0.000267407 |
| Sct | 3.62674208 | 0.022430669 |
| Slc2a13 | 3.57917944 | 4.57639E-07 |
| Pdlim3 | 3.57766279 | 2.16822E-44 |
| Cyp1a1 | 3.57720408 | 0.001905685 |
| S100a16 | 3.5477518 | 2.13634E-11 |
| Ly6a | 3.42207613 | 2.62151E-12 |
| Wbscr17 | 3.39468348 | 0.000355265 |
| Pgbd5 | 3.38836145 | 1.56978E-05 |
| Il1r1 | 3.34347429 | 6.40325E-07 |
| Nr5a2 | 3.29320254 | 0.005750421 |
| Cabp1 | 3.2728878 | 0.001120493 |
| Grik3 | 3.26096666 | 0.018407656 |
| Grin2c | 3.24189718 | 0.005374654 |
| Tmem53 | 3.22142009 | 0.034324076 |
| Ramp3 | 3.20739422 | 0.048766901 |
| Fst | 3.19328629 | 2.98063E-08 |
| Frrs1l | 3.12797418 | 0.000686358 |
| Tmem150c | 3.12351529 | 0.037114187 |
| Art3 | 3.08782442 | 0.012536686 |
| Disp2 | 3.08746265 | 0.000118107 |
| Rgs17 | 3.0588474 | 7.52981E-05 |
| Clec1a | 3.05635354 | 6.05317E-14 |
| Gbp6 | 3.03879822 | 0.022181358 |
| Slc4a8 | 3.02118734 | 0.001524407 |
| D430019H16Rik | 3.01525558 | 0.000230621 |
| Dusp26 | 2.9637332 | 0.01634546 |
| Prnd | 2.92446708 | 0.013206311 |
| 2700070H01Rik | 2.88477997 | 0.032301302 |
| Arhgap22 | 2.8796337 | 0.048204754 |
| Pdlim4 | 2.85391918 | 0.00816996 |
| Sorcs1 | 2.85196135 | 0.001475148 |
| Col13a1 | 2.84329058 | 0.019212038 |
| Adrb1 | 2.8354098 | 0.000456481 |
| Add2 | 2.80979515 | 2.00059E-07 |
| Bcl11b | 2.80191944 | 0.012637806 |
| Tifa | 2.77963433 | 0.008198429 |
| Lsamp | 2.77214612 | 0.023419121 |
| Robo4 | 2.76257106 | 9.41069E-17 |

| | | |
|---|---|---|
| Pth1r | 2.76119957 | 0.001401918 |
| Cyp2j9 | 2.75723043 | 0.032898869 |
| Thrb | 2.74835614 | 0.028183712 |
| Mamld1 | 2.72417862 | 3.71113E-10 |
| Gabrb2 | 2.68033058 | 2.17158E-05 |
| Tmem51 | 2.67281111 | 0.019634188 |
| Pcdh20 | 2.66722287 | 0.001611227 |
| Bean1 | 2.65069942 | 0.012145624 |
| Ceacam1 | 2.6373882 | 1.44202E-05 |
| Sema3g | 2.61765129 | 0.043021926 |
| Gpr85 | 2.59638848 | 0.03182126 |
| Pde1b | 2.58961839 | 0.002762568 |
| Sspn | 2.58675237 | 0.015013314 |
| Gdap1l1 | 2.58446104 | 0.042010661 |
| Tmem255a | 2.57903553 | 4.55639E-07 |
| Sh3rf3 | 2.55311261 | 0.00123892 |
| Pipox | 2.55237606 | 0.0035214 |
| Prokr2 | 2.54834849 | 0.000884339 |
| B3galt1 | 2.50824272 | 0.00062887 |
| Clec14a | 2.495834 | 1.60049E-20 |
| Slc12a8 | 2.48508379 | 0.028101691 |
| Zmynd15 | 2.4581337 | 0.000147643 |
| H2-Q4 | 2.41962659 | 0.012238072 |
| Tmem154 | 2.41479517 | 0.006344249 |
| Eng | 2.40375217 | 1.18852E-20 |
| Ahrr | 2.40185551 | 0.024671776 |
| Ccdc110 | 2.40159921 | 0.047583515 |
| Il13ra1 | 2.39997595 | 0.000174021 |
| Itga2 | 2.38701229 | 0.001931815 |
| 9630013A20Rik | 2.37734364 | 0.033826138 |
| Fam78b | 2.36416915 | 0.001063811 |
| Cadps | 2.36025135 | 0.046676127 |
| Mrgpre | 2.35622134 | 0.003300233 |
| Gimap6 | 2.35545309 | 0.000497308 |
| Pi16 | 2.35324086 | 2.97701E-05 |
| Hgf | 2.34764215 | 0.039717815 |
| Plekhg1 | 2.34189511 | 4.95345E-11 |
| Cntn1 | 2.32195392 | 0.018974153 |
| Cxcl16 | 2.31527239 | 2.17805E-06 |
| Cnr2 | 2.30573281 | 0.003227649 |
| Edn1 | 2.29334971 | 1.65091E-37 |
| Emcn | 2.2678929 | 1.20303E-09 |
| Cldn5 | 2.26712542 | 0.01179793 |
| Apba1 | 2.25723727 | 0.00481876 |

| | | |
|---|---|---|
| Rnft2 | 2.25079995 | 0.00099635 |
| Mdfi | 2.24735098 | 0.002126928 |
| Madcam1 | 2.24125549 | 7.8355E-07 |
| Patl2 | 2.23629909 | 0.00515282 |
| Nod1 | 2.22755616 | 0.017552353 |
| D030045P18Rik | 2.22492453 | 0.024330801 |
| Sqrdl | 2.22463208 | 0.01064127 |
| Rgs16 | 2.2179511 | 1.7526E-06 |
| Ddx60 | 2.21568307 | 0.038891191 |
| Prickle2 | 2.21311122 | 5.94511E-14 |
| Ptpn3 | 2.1918109 | 0.005325232 |
| Sgk3 | 2.17972228 | 1.70099E-10 |
| Cybrd1 | 2.17942797 | 0.036779379 |
| Nfil3 | 2.17816349 | 9.43137E-05 |
| Adam11 | 2.17718593 | 0.005319159 |
| Gcnt4 | 2.16602276 | 0.00761664 |
| Serpina3h | 2.16119221 | 0.039303536 |
| Dmrt3 | 2.15965709 | 0.022820026 |
| Sparcl1 | 2.15468423 | 0.000784538 |
| Adhfe1 | 2.1482248 | 0.007585006 |
| Six3os1 | 2.14355335 | 4.33993E-05 |
| Nrxn3 | 2.14053022 | 0.00347995 |
| Slc35f1 | 2.11849147 | 4.76936E-05 |
| Arhgap26 | 2.11760508 | 0.016344227 |
| Pcdh17 | 2.10986521 | 0.002889373 |
| Sh3gl3 | 2.10505529 | 0.034707678 |
| Astn1 | 2.10033507 | 0.021058067 |
| Cav1 | 2.09925614 | 2.47467E-12 |
| Tnfaip8l3 | 2.09249146 | 0.007404196 |
| Tchh | 2.08068758 | 0.02013666 |
| Tm4sf1 | 2.07157777 | 0.021439509 |
| Oasl2 | 2.0665172 | 0.0320633 |
| Chrdl1 | 2.06647352 | 0.015290546 |
| Tnfrsf23 | 2.05117221 | 0.003416577 |
| Pcdhga6 | 2.04796979 | 0.017445656 |
| Gpr116 | 2.04274007 | 2.62151E-12 |
| Fam181b | 2.03893273 | 0.004535041 |
| AI661453 | 2.02767285 | 0.011431788 |
| Col14a1 | 2.00867795 | 0.014440187 |
| Stx1b | 2.00249944 | 0.023957118 |
| Parp14 | 2.00240406 | 0.000385376 |
| Cdh13 | 1.98465913 | 0.031087599 |
| Map3k8 | 1.9826497 | 0.024648589 |
| Pcdhb17 | 1.97473016 | 0.048005393 |

| | | |
|---|---|---|
| Qpct | 1.97061125 | 0.010734992 |
| Sost | 1.95634788 | 1.97168E-06 |
| P2rx7 | 1.95587017 | 0.005716443 |
| Stc1 | 1.95258907 | 0.000216839 |
| Cyyr1 | 1.94995899 | 7.75173E-07 |
| Ace | 1.94926618 | 0.000154083 |
| Zbtb7c | 1.94059935 | 0.024431012 |
| Serpina3i | 1.93230914 | 0.026420093 |
| Mmp15 | 1.93131858 | 2.63802E-05 |
| Rassf4 | 1.9211141 | 0.041461583 |
| Nr2f2 | 1.91962709 | 5.46909E-05 |
| Foxp2 | 1.905238 | 0.001840115 |
| Rtn1 | 1.89810313 | 0.001200266 |
| Stab1 | 1.89248725 | 2.62151E-12 |
| Pdzd2 | 1.88789589 | 1.49745E-13 |
| Nos3 | 1.88237258 | 0.000100201 |
| Bend7 | 1.8759542 | 0.001789848 |
| Gpr182 | 1.87323757 | 0.013116394 |
| Dmd | 1.87144785 | 3.33051E-06 |
| Cttnbp2 | 1.86703161 | 3.99574E-07 |
| Lor | 1.86532742 | 0.01963896 |
| Rab3b | 1.85978302 | 0.00047339 |
| Rnd1 | 1.85755109 | 0.041040905 |
| Plekha6 | 1.85140994 | 0.031042368 |
| Pde10a | 1.84042583 | 0.010050368 |
| Psmb8 | 1.83743045 | 0.027786063 |
| Lhfpl2 | 1.83134969 | 1.4092E-06 |
| Kcna6 | 1.82511296 | 0.000713988 |
| Gap43 | 1.82032402 | 5.1548E-21 |
| 4933412E12Rik | 1.81999082 | 0.035906793 |
| Reep2 | 1.81576473 | 0.000671371 |
| Nrxn2 | 1.81220385 | 0.019511153 |
| Efna1 | 1.80689469 | 0.000608615 |
| Ptprt | 1.79154996 | 3.67473E-06 |
| Rgs7bp | 1.78985215 | 0.001521679 |
| Cd93 | 1.78781028 | 1.47462E-09 |
| Sh3bp5 | 1.78110259 | 5.89188E-08 |
| Slc1a2 | 1.77465572 | 2.90794E-07 |
| Gata4 | 1.77361085 | 1.4264E-11 |
| Zfp658 | 1.76190117 | 0.006038733 |
| Frem1 | 1.76071677 | 0.005881318 |
| Dach1 | 1.75932814 | 0.043196035 |
| Prex2 | 1.75415238 | 2.71593E-11 |
| Xaf1 | 1.7535399 | 0.014937183 |

| | | |
|---|---|---|
| Tmem86a | 1.75231894 | 0.030928756 |
| Aqp1 | 1.74957919 | 1.0118E-05 |
| Whrn | 1.74534522 | 0.037114597 |
| 6330419J24Rik | 1.74351345 | 0.004789365 |
| Lgr6 | 1.73169891 | 0.000136049 |
| Jag2 | 1.72948941 | 0.001174005 |
| Mmrn2 | 1.72862416 | 6.0269E-06 |
| Gpm6a | 1.72616942 | 5.13097E-09 |
| Dock4 | 1.72485324 | 1.76263E-08 |
| Tmem44 | 1.7247415 | 0.002530932 |
| Tmem204 | 1.72410478 | 7.78332E-12 |
| Filip1 | 1.71678234 | 9.92226E-05 |
| Fes | 1.7156733 | 0.001740874 |
| Gpm6b | 1.71382644 | 6.7478E-08 |
| Tshz3 | 1.70197523 | 0.001896077 |
| Mansc1 | 1.69808565 | 0.002520927 |
| Pcdhga3 | 1.69647693 | 0.006793952 |
| Eml1 | 1.68342858 | 2.31344E-11 |
| Cd97 | 1.68075811 | 2.15219E-13 |
| Skida1 | 1.67905073 | 0.049871418 |
| Grin3a | 1.67260577 | 1.27927E-05 |
| Bace2 | 1.67258507 | 7.14205E-05 |
| Rtn4rl1 | 1.67004782 | 0.035545165 |
| Ptprm | 1.67001425 | 5.32352E-16 |
| Hpgd | 1.66644196 | 0.046158644 |
| Ocln | 1.66423534 | 0.003780024 |
| Ago4 | 1.66418307 | 0.033067184 |
| Sox17 | 1.66352056 | 4.86361E-17 |
| Bmf | 1.65824119 | 7.16797E-07 |
| Plcd1 | 1.65246216 | 0.005508605 |
| Arhgef28 | 1.64188196 | 0.004154036 |
| Ccdc120 | 1.63713556 | 0.003731318 |
| Gnai1 | 1.63104051 | 2.78741E-12 |
| Epas1 | 1.62674831 | 1.54656E-16 |
| Nrep | 1.6241192 | 1.60062E-20 |
| Dhrs3 | 1.61872683 | 4.9319E-05 |
| Fzd1 | 1.61781646 | 3.26112E-08 |
| Adcy4 | 1.61753975 | 5.52292E-10 |
| Slc40a1 | 1.60771557 | 7.62751E-05 |
| Kctd12b | 1.60298537 | 7.39103E-08 |
| Mturn | 1.59050795 | 0.016730548 |
| Ndrg2 | 1.58502795 | 0.012945763 |
| Klhl8 | 1.58422961 | 0.001909046 |
| Tnnt2 | 1.57898015 | 0.005477122 |

| | | |
|---|---|---|
| Met | 1.57897949 | 0.000141575 |
| Gm20748 | 1.56772455 | 0.000484413 |
| Naalad2 | 1.56349374 | 0.011969237 |
| Eltd1 | 1.56326302 | 3.64109E-07 |
| Cxx1a | 1.56195873 | 0.009435987 |
| Dgkk | 1.55921393 | 1.7379E-05 |
| 1810011O10Rik | 1.55803329 | 2.83423E-06 |
| Npdc1 | 1.55318398 | 0.007309947 |
| Slc16a2 | 1.54823787 | 1.38332E-13 |
| Lrrn2 | 1.54572792 | 0.000118107 |
| Id2 | 1.53972139 | 5.81204E-09 |
| Pdk4 | 1.53886892 | 0.009747462 |
| Sema3a | 1.53813239 | 1.66242E-06 |
| Lrrk2 | 1.53395858 | 1.67821E-10 |
| Ppp1r16b | 1.53365855 | 5.76626E-09 |
| Trim47 | 1.52365175 | 0.007798689 |
| 6430548M08Rik | 1.517959 | 0.003489248 |
| 2510009E07Rik | 1.50602202 | 0.000267407 |
| Dok4 | 1.50596452 | 0.000513324 |
| Oit3 | 1.5047518 | 0.000127365 |
| Itpr3 | 1.50208177 | 2.87372E-06 |
| Ankrd6 | 1.50197519 | 0.023957118 |
| St8sia4 | 1.49910183 | 0.020200454 |
| Cyp39a1 | 1.49807854 | 0.044400618 |
| Erbb2 | 1.49752692 | 6.00543E-11 |
| LOC102636514 | 1.48547575 | 0.003300233 |
| B630019K06Rik | 1.48122346 | 0.041391858 |
| Adcy2 | 1.48104462 | 0.029844293 |
| Tm6sf1 | 1.47720907 | 1.47462E-09 |
| Fxyd5 | 1.47565629 | 0.008119747 |
| Rgs2 | 1.47522281 | 1.38332E-13 |
| Ramp2 | 1.4730347 | 6.55888E-06 |
| Ube2l6 | 1.46985536 | 0.01150381 |
| Emb | 1.46430329 | 6.98299E-07 |
| Angptl2 | 1.45622852 | 0.00019519 |
| Klhl4 | 1.45505394 | 0.000394479 |
| Cish | 1.45430575 | 0.014270424 |
| Rab15 | 1.4529967 | 0.022289537 |
| Hecw2 | 1.45168155 | 3.97907E-08 |
| Gimap8 | 1.44923421 | 0.003171631 |
| Akr1b8 | 1.4480994 | 0.000354722 |
| Rgs3 | 1.44669161 | 2.79034E-07 |
| N4bp3 | 1.44325245 | 0.001014064 |
| Nedd9 | 1.44126253 | 0.000682966 |

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| Acer2 | 1.43991526 | 0.001950725 |
| Kctd21 | 1.43725253 | 0.017552353 |
| Parp8 | 1.43446184 | 1.16695E-07 |
| Pcdh12 | 1.43441496 | 8.06968E-14 |
| Chst11 | 1.43216905 | 0.000491398 |
| F8 | 1.43126819 | 8.64663E-06 |
| Cpt1a | 1.43019018 | 9.66042E-05 |
| Hoxa1 | 1.42944378 | 0.036779379 |
| Ctsl | 1.42932441 | 2.78741E-12 |
| Limch1 | 1.42881176 | 3.30849E-06 |
| Gimap4 | 1.42612128 | 4.80559E-07 |
| Acvrl1 | 1.41594839 | 3.91822E-08 |
| Ptchd1 | 1.41513888 | 4.9372E-07 |
| Gabrb3 | 1.41110383 | 0.001412391 |
| 5730409E04Rik | 1.41066928 | 0.025586714 |
| Bmp6 | 1.40916486 | 1.00348E-09 |
| Tgfbr2 | 1.39565726 | 2.07504E-06 |
| Cubn | 1.3950718 | 0.012238072 |
| Notch4 | 1.39434678 | 4.55768E-05 |
| Ube2ql1 | 1.39284044 | 0.047761325 |
| Upp1 | 1.39204852 | 3.57082E-06 |
| Lpar4 | 1.38897623 | 2.34423E-09 |
| Dab2 | 1.38709916 | 0.001707355 |
| Icam1 | 1.38513664 | 5.82923E-05 |
| Icam2 | 1.38476952 | 0.000439071 |
| Rasgrp3 | 1.38203471 | 2.62151E-12 |
| Mcam | 1.38184493 | 6.96898E-06 |
| Ehd2 | 1.38165765 | 1.28373E-07 |
| Gprc5a | 1.3813017 | 0.007857311 |
| Prkch | 1.38094944 | 0.004465313 |
| Scrn1 | 1.37909994 | 0.025410734 |
| Ctsh | 1.37331548 | 0.000942925 |
| Nav3 | 1.37169696 | 0.02505003 |
| Atl1 | 1.37126786 | 1.29486E-06 |
| Slc8b1 | 1.37035742 | 0.005082306 |
| Spred3 | 1.36909934 | 0.01482001 |
| Antxr2 | 1.36625734 | 0.004418737 |
| Grrp1 | 1.3648216 | 0.000603886 |
| Sema6d | 1.36347571 | 5.29662E-08 |
| Rgmb | 1.36015967 | 0.004766197 |
| Parvb | 1.3598599 | 0.000213304 |
| Sema3f | 1.35666009 | 0.002533692 |
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| Capn5 | 1.34397931 | 0.000152011 |
| Cttnbp2nl | 1.34265528 | 1.08006E-19 |
| Adam12 | 1.34233974 | 0.000623682 |
| Itpkb | 1.33568824 | 2.03771E-05 |
| Bgn | 1.33373234 | 1.31763E-07 |
| Pld1 | 1.33141477 | 7.46474E-07 |
| Cyp4v3 | 1.32340215 | 0.010515006 |
| Plagl1 | 1.32121121 | 0.000761453 |
| Arid5b | 1.31915449 | 2.34423E-09 |
| Sgsh | 1.31853498 | 3.23703E-05 |
| Rcan3 | 1.31116263 | 0.000190286 |
| Kctd17 | 1.31029115 | 5.46315E-06 |
| Pdk1 | 1.30864086 | 0.000946184 |
| Helz2 | 1.30753826 | 0.011276152 |
| Atf3 | 1.30473364 | 4.0506E-08 |
| Itga1 | 1.30115946 | 9.11806E-09 |
| Fmo1 | 1.29472153 | 1.14916E-16 |
| Adam23 | 1.29284152 | 1.69365E-06 |
| Sox6 | 1.29150052 | 1.00407E-07 |
| Prom1 | 1.2904929 | 0.015321403 |
| Ppm1j | 1.28898246 | 0.047736329 |
| Slit2 | 1.28258055 | 0.00032164 |
| Plvap | 1.27866926 | 0.000509457 |
| Fmo5 | 1.27415737 | 0.021229611 |
| Tmem159 | 1.2686847 | 2.48102E-05 |
| Gbp9 | 1.26835918 | 0.027665722 |
| Psen2 | 1.26813081 | 0.019284155 |
| Tmem173 | 1.26774222 | 0.013769531 |
| Plcb1 | 1.26498936 | 3.06527E-05 |
| Chrnb1 | 1.26357764 | 0.024844203 |
| Ehd3 | 1.25677014 | 0.01482001 |
| Cd40 | 1.25564798 | 1.04773E-05 |
| Kdm7a | 1.25316491 | 6.67987E-08 |
| Hmcn1 | 1.24948206 | 4.9372E-07 |
| Pcdh1 | 1.24821296 | 1.22328E-06 |
| Timp1 | 1.24713649 | 0.043937948 |
| Ppap2a | 1.24317985 | 0.002303112 |
| Dock8 | 1.23892721 | 0.000148873 |
| Tfec | 1.23820736 | 4.36716E-07 |
| Dusp22 | 1.23817215 | 3.64109E-07 |
| Rps6ka2 | 1.23780729 | 2.57761E-06 |
| Mical2 | 1.23514769 | 0.000331948 |
| Osbpl6 | 1.23223577 | 0.03023915 |
| Rab3il1 | 1.23010403 | 0.008988872 |

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| Efnb2 | 1.22584467 | 2.74734E-12 |
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| Rarg | 1.21113647 | 0.012145624 |
| Entpd1 | 1.20279758 | 0.035626622 |
| Dnajb5 | 1.20061997 | 0.004435643 |
| Ntn3 | 1.19496915 | 4.14625E-05 |
| Rnf144a | 1.19357888 | 4.43976E-05 |
| Arsa | 1.19298159 | 0.002530932 |
| Arhgef15 | 1.18893214 | 7.14205E-05 |
| Eps8 | 1.18844868 | 0.000134139 |
| Tnks1bp1 | 1.18720037 | 0.001125329 |
| Cerk | 1.18674938 | 0.005050143 |
| Gbp4 | 1.18608431 | 0.01858609 |
| Ly96 | 1.18476099 | 0.045726424 |
| Dennd5b | 1.184206 | 7.51897E-07 |
| Fbxl7 | 1.18064294 | 0.000529909 |
| Elovl4 | 1.17998447 | 0.000442539 |
| Tgfbi | 1.17819143 | 0.030828711 |
| D1Ertd622e | 1.1708281 | 0.01179793 |
| Gatm | 1.16890665 | 0.002303112 |
| Rgl1 | 1.16709318 | 1.04659E-11 |
| Tie1 | 1.16496502 | 0.012145624 |
| Ctgf | 1.16010458 | 0.002370819 |
| Cbx6 | 1.15982767 | 0.025410734 |
| Epn2 | 1.15805733 | 3.92099E-12 |
| Rnf165 | 1.15781922 | 0.00341342 |
| Prdm1 | 1.15756418 | 0.019634188 |
| Dysf | 1.15635916 | 0.001690251 |
| Usp27x | 1.15446047 | 0.020712294 |
| Itsn1 | 1.15339098 | 2.74734E-12 |
| Cdh5 | 1.14956573 | 0.007024169 |
| Mecom | 1.1474593 | 0.00046904 |
| Dtx3l | 1.14619799 | 0.004151397 |
| Ghr | 1.14443005 | 1.16037E-10 |
| Mfap3l | 1.14063473 | 0.001320575 |
| Rhpn2 | 1.13471415 | 8.84809E-05 |
| Slc9a3r2 | 1.13254832 | 8.27541E-06 |
| Filip1l | 1.1321366 | 2.35311E-05 |
| Tnfaip1 | 1.12721741 | 4.35839E-07 |
| Sema6b | 1.12467937 | 0.043443023 |
| Rhou | 1.1222825 | 8.03697E-08 |
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| Plekha1 | 1.11979284 | 5.76626E-09 |
| Stap2 | 1.11946019 | 0.000776078 |
| Arhgef3 | 1.11938832 | 0.001529963 |
| Fat4 | 1.11909352 | 3.34289E-07 |
| AW551984 | 1.11908907 | 0.007970266 |
| Ccdc80 | 1.11603822 | 2.42344E-05 |
| Tmc8 | 1.11280255 | 0.031340642 |
| Ccnjl | 1.11244286 | 9.29763E-06 |
| Ypel2 | 1.11039245 | 0.001306038 |
| Abhd6 | 1.10911504 | 0.006734222 |
| Sash1 | 1.10646508 | 1.34103E-08 |
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| Endod1 | 1.10538157 | 0.001393788 |
| Sox18 | 1.10425759 | 0.025088085 |
| Pced1b | 1.1009767 | 0.004942393 |
| Parp9 | 1.10007273 | 0.022590568 |
| Parp10 | 1.09553229 | 0.046324916 |
| C1qtnf6 | 1.0943025 | 0.003161654 |
| 40422 | 1.0923483 | 1.85027E-06 |
| Zfp382 | 1.0912224 | 0.0406944 |
| S1pr1 | 1.08836574 | 5.18886E-09 |
| Acsf2 | 1.08560817 | 0.003227649 |
| Mdfic | 1.08416514 | 0.001233198 |
| Trim16 | 1.07769101 | 0.001032334 |
| Ptprd | 1.07514088 | 8.71795E-07 |
| Heg1 | 1.07463882 | 0.00010943 |
| Glul | 1.07355443 | 7.25498E-11 |
| Flrt2 | 1.07101031 | 1.05183E-09 |
| Armcx1 | 1.06964681 | 1.16037E-10 |
| Nipal3 | 1.06883569 | 0.044565478 |
| Sft2d2 | 1.06801998 | 3.96543E-07 |
| Gpr126 | 1.06463852 | 0.047141713 |
| Fbn1 | 1.06250049 | 4.67821E-06 |
| Fstl1 | 1.05755394 | 4.3809E-09 |
| Zfp618 | 1.05376379 | 0.028880357 |
| Cers6 | 1.05354182 | 0.010272676 |
| Prickle3 | 1.05255551 | 0.012461136 |
| Klf4 | 1.05032488 | 3.34249E-07 |
| Arhgap31 | 1.04630502 | 3.25179E-05 |
| Ap1s2 | 1.0448927 | 9.42993E-07 |
| Gja4 | 1.04113201 | 0.043941057 |
| Hand2 | 1.03844154 | 2.03771E-05 |
| Asb4 | 1.02904765 | 0.026253214 |
| Mxi1 | 1.02840984 | 0.000569955 |

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| Slc17a5 | 1.02556749 | 0.009523916 |
| Bcl2 | 1.02445677 | 0.00882067 |
| Tlr3 | 1.02388561 | 7.66505E-05 |
| Rhob | 1.02378506 | 0.000358687 |
| Meis2 | 1.02254553 | 0.019922414 |
| Gpr146 | 1.02105459 | 0.011179574 |
| Fam114a1 | 1.02104151 | 6.58615E-08 |
| Cd109 | 1.02066387 | 0.015844706 |
| Vash1 | 1.01960591 | 0.000539094 |
| Lmf1 | 1.01835716 | 0.047145219 |
| Peli2 | 1.017516 | 0.001315988 |
| Maf | 1.01633322 | 0.044860977 |
| Mroh1 | 1.01533484 | 0.00173172 |
| Plat | 1.01210985 | 0.025681478 |
| Trim2 | 1.00916577 | 0.028999329 |
| Tcf4 | 1.00896003 | 1.76263E-08 |
| Rcsd1 | 1.00162662 | 0.014440187 |
| Thbd | 1.00146299 | 0.03023915 |
| Slc26a10 | 1.00080202 | 0.002174643 |
| Elk3 | 1.00021479 | 1.28227E-05 |
| Cpne8 | 0.99605113 | 0.024692245 |
| Rusc1 | 0.99581914 | 0.039975742 |
| Peg10 | 0.99468146 | 1.01047E-05 |
| Lipa | 0.99340069 | 1.24628E-07 |
| Pdgfb | 0.99193709 | 0.001178785 |
| Tmem2 | 0.99150421 | 3.05746E-06 |
| Prrg3 | 0.99149258 | 0.000596048 |
| Atg10 | 0.99136987 | 0.019634188 |
| Kank1 | 0.98701352 | 0.007340664 |
| Myct1 | 0.98380908 | 0.023446821 |
| Fblim1 | 0.98165366 | 0.000130731 |
| Pitpnc1 | 0.98138227 | 0.001690251 |
| Camk2d | 0.98066506 | 2.17158E-05 |
| Spats2l | 0.97784568 | 0.000264676 |
| Plp2 | 0.97773516 | 1.0606E-09 |
| Phyh | 0.97773444 | 0.027919545 |
| Pik3r3 | 0.97521746 | 3.45092E-06 |
| Anxa5 | 0.97421157 | 4.41668E-10 |
| St3gal6 | 0.97298244 | 0.001053936 |
| Bcl6b | 0.97270841 | 0.00912701 |
| Arap2 | 0.97066286 | 0.000237722 |
| Plod1 | 0.97031481 | 1.95941E-07 |
| H2-D1 | 0.97008472 | 0.018813997 |
| Ushbp1 | 0.96956833 | 0.003222281 |

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| Cd55 | 0.9675418 | 0.000195384 |
| Id1 | 0.96676281 | 1.91118E-06 |
| 2900026A02Rik | 0.96611254 | 6.67852E-06 |
| Kif3c | 0.962524 | 0.002407405 |
| Smad6 | 0.96122668 | 0.001840092 |
| Gnal | 0.95992629 | 0.01006963 |
| Marveld1 | 0.95928409 | 0.000491459 |
| Asap2 | 0.95866243 | 1.61566E-07 |
| Dusp1 | 0.95834233 | 1.95941E-07 |
| Slc5a3 | 0.95613095 | 8.27149E-06 |
| Vim | 0.95304285 | 1.14278E-08 |
| Slc16a13 | 0.95140597 | 0.021745481 |
| Slc43a3 | 0.95098653 | 0.00252015 |
| Bmper | 0.94912401 | 0.025921359 |
| App | 0.94760363 | 0.000198842 |
| Otud1 | 0.94066555 | 0.019591334 |
| Wbscr27 | 0.93455272 | 0.025668121 |
| Leprel2 | 0.93089559 | 0.025464706 |
| Ece1 | 0.92701377 | 8.23016E-07 |
| Acvr1 | 0.92537402 | 0.001690251 |
| Zeb1 | 0.92283183 | 0.000413386 |
| Prnp | 0.92205661 | 0.006862971 |
| Atp11a | 0.91993892 | 9.81911E-08 |
| Crybg3 | 0.91509299 | 0.000399004 |
| Pqlc1 | 0.91466376 | 0.01323112 |
| Plxnd1 | 0.91335683 | 3.94278E-06 |
| Rasip1 | 0.91306805 | 0.031221634 |
| Slc6a6 | 0.91284416 | 1.05547E-06 |
| Asah2 | 0.91209642 | 0.000475057 |
| Ndrg1 | 0.91198646 | 0.042754269 |
| Mboat2 | 0.9107657 | 0.003756264 |
| Hexb | 0.91047392 | 0.018134441 |
| Apbb2 | 0.90950282 | 0.000638892 |
| Dcbld1 | 0.90927245 | 0.015219914 |
| Myo6 | 0.90924173 | 0.002158363 |
| Nfkbia | 0.90666537 | 0.029404986 |
| Edil3 | 0.90292285 | 0.02174393 |
| Mcc | 0.89900153 | 4.53883E-05 |
| Znfx1 | 0.89539114 | 0.004942393 |
| Armcx4 | 0.89529063 | 3.74857E-11 |
| Ankrd44 | 0.89363822 | 0.011299418 |
| Plk2 | 0.89271298 | 2.3896E-06 |
| Jup | 0.88980737 | 1.0674E-06 |
| Prkce | 0.88971728 | 0.000242988 |

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| Trib1 | 0.88855817 | 0.000164087 |
| Sirpa | 0.88847172 | 0.0032421 |
| Sh3rf1 | 0.88714516 | 7.95249E-05 |
| Herc3 | 0.88713647 | 0.02040009 |
| 9430020K01Rik | 0.88711749 | 1.00867E-05 |
| Nfib | 0.88684759 | 0.006734222 |
| Bcl2l11 | 0.88607971 | 3.79149E-07 |
| Nagk | 0.88524847 | 0.001014064 |
| Peg3 | 0.88415645 | 0.001693132 |
| Ttc28 | 0.88037653 | 0.00047339 |
| Tbc1d9 | 0.87763921 | 0.005050143 |
| Lcp1 | 0.87577972 | 0.017552353 |
| Fbxo10 | 0.87553724 | 0.000484413 |
| Dhx57 | 0.87543092 | 9.81911E-08 |
| Tor4a | 0.87431145 | 0.014140212 |
| Tanc1 | 0.87249721 | 1.15752E-07 |
| Fgd5 | 0.87024341 | 5.29662E-08 |
| Rras | 0.87010233 | 3.52916E-05 |
| Klhl13 | 0.86815254 | 1.01595E-05 |
| Klf2 | 0.8669513 | 0.000232828 |
| Fam69a | 0.86321708 | 0.010592548 |
| Wsb2 | 0.8629341 | 0.000353186 |
| Rims2 | 0.86275048 | 0.015219914 |
| Dusp6 | 0.86100696 | 7.86127E-05 |
| 4931406P16Rik | 0.85821535 | 1.14463E-06 |
| Gng11 | 0.85577535 | 0.00010029 |
| Col4a1 | 0.85572026 | 1.27974E-08 |
| Fyn | 0.85458237 | 0.030073173 |
| Vegfc | 0.85317872 | 0.00912701 |
| Mllt6 | 0.85243076 | 5.50239E-05 |
| Tmem176b | 0.85234919 | 0.00759766 |
| Dgkh | 0.85065338 | 0.005557702 |
| Id3 | 0.84983369 | 8.69853E-07 |
| Ltbp1 | 0.84714648 | 0.01858609 |
| Klf6 | 0.84618231 | 0.007412582 |
| Procr | 0.84381173 | 0.021201829 |
| Jag1 | 0.84337645 | 0.04692825 |
| Zfp532 | 0.84197757 | 4.20211E-05 |
| Tapbp | 0.83940005 | 0.016952314 |
| Col4a2 | 0.8384229 | 1.59634E-07 |
| Dlc1 | 0.83789397 | 1.50457E-07 |
| Creb3 | 0.83774535 | 0.008378562 |
| Nid1 | 0.83665967 | 0.016884793 |
| Pcdhgc3 | 0.83645238 | 0.003073471 |

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| Tspan18 | 0.83628395 | 0.032760213 |
| Arhgef5 | 0.8333038 | 0.001135402 |
| Tmc6 | 0.83177248 | 0.014936968 |
| Cdr2l | 0.83123085 | 0.000689689 |
| Gpr137b | 0.8308372 | 0.01399787 |
| Amotl1 | 0.83002043 | 2.79154E-05 |
| Arhgap27 | 0.82950263 | 0.001339082 |
| Lpar6 | 0.82549977 | 0.002249377 |
| Osbpl3 | 0.82535908 | 0.039860331 |
| Ermp1 | 0.82500645 | 5.20026E-05 |
| Unc13b | 0.82464396 | 0.004253621 |
| Cd38 | 0.8242372 | 0.005069433 |
| Rin2 | 0.8241474 | 0.01146119 |
| Lrrc8c | 0.82394381 | 0.000134139 |
| Palld | 0.82388517 | 0.000702081 |
| Ralgapa2 | 0.82382984 | 0.013376559 |
| Rragd | 0.82216875 | 0.009409538 |
| Hyal2 | 0.82155336 | 0.001091906 |
| Creb3l2 | 0.82147014 | 7.94869E-05 |
| Zfp462 | 0.82053886 | 0.035502939 |
| Btbd3 | 0.82036163 | 0.00057821 |
| Nxpe3 | 0.81835438 | 0.007625924 |
| Hspa12a | 0.81816773 | 0.000497308 |
| Spag9 | 0.81544543 | 6.30049E-05 |
| Sh3tc1 | 0.81403036 | 0.001037751 |
| Pam | 0.81334126 | 3.52916E-05 |
| Pim3 | 0.80868711 | 0.003911677 |
| Pros1 | 0.80804587 | 0.000529909 |
| Fam115a | 0.80737277 | 0.000643508 |
| Anxa3 | 0.80582012 | 0.00759766 |
| Notch1 | 0.80494113 | 3.83317E-05 |
| Crmp1 | 0.80486172 | 0.02670682 |
| Rasal2 | 0.80465513 | 3.53388E-05 |
| Sparc | 0.80441467 | 0.000108353 |
| Mef2a | 0.80342491 | 0.003423088 |
| Nhsl1 | 0.8027688 | 0.00046271 |
| Camk4 | 0.8025306 | 0.005352197 |
| Tek | 0.80198983 | 0.025731459 |
| 5031439G07Rik | 0.80153495 | 0.022986871 |
| Tbc1d12 | 0.80113584 | 0.024554354 |
| Dcxr | 0.79980701 | 0.014862217 |
| Kdr | 0.79919545 | 0.000147643 |
| Pde1c | 0.79849955 | 0.035981062 |
| Klf9 | 0.79835413 | 0.049000364 |

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| 3110043O21Rik | 0.79722091 | 0.045899837 |
| Hsd17b11 | 0.7968532 | 0.008376881 |
| Wwtr1 | 0.79563496 | 3.1261E-06 |
| Mtch1 | 0.79150964 | 4.57888E-07 |
| 4930402H24Rik | 0.78917036 | 0.003071407 |
| Ankrd50 | 0.78902273 | 3.65637E-06 |
| Ppp3ca | 0.78851049 | 7.03897E-05 |
| Pgap1 | 0.78722922 | 0.011690857 |
| Man1a | 0.78141342 | 0.000204243 |
| Ezh1 | 0.7813293 | 0.000650618 |
| Serpinf1 | 0.77974119 | 0.020078977 |
| Fam43a | 0.77910444 | 0.000544414 |
| Lcorl | 0.77650167 | 0.000106664 |
| Cntln | 0.77580148 | 0.034255696 |
| Pvr | 0.77573143 | 0.0007004 |
| Pcyt1a | 0.77081897 | 0.001756583 |
| Rnf157 | 0.76917696 | 0.000185175 |
| Srgap1 | 0.76881999 | 1.88927E-05 |
| Unc5b | 0.76821385 | 0.023645943 |
| Gpr19 | 0.76784159 | 0.022322881 |
| Adarb1 | 0.7638246 | 0.019634188 |
| Crip2 | 0.76264077 | 0.000603523 |
| Enox2 | 0.76209522 | 0.003227649 |
| Tnc | 0.76201871 | 0.012079092 |
| Myo1b | 0.75987452 | 0.001370017 |
| Lama4 | 0.75747045 | 0.013495977 |
| Palm | 0.75488996 | 0.010068361 |
| Mef2c | 0.75433857 | 0.047869168 |
| Obfc1 | 0.75209303 | 0.000770405 |
| Gsto1 | 0.75191683 | 0.048700709 |
| Adam15 | 0.75179566 | 0.000459628 |
| Clip2 | 0.75089598 | 0.012250073 |
| Rilpl1 | 0.75064451 | 0.023134393 |
| B2m | 0.75057654 | 0.000235722 |
| Crip1 | 0.75031877 | 0.002889373 |
| Mageh1 | 0.74814737 | 0.014737269 |
| Prr5l | 0.74490322 | 0.034017929 |
| Atp2b4 | 0.7420747 | 0.046466866 |
| Ets1 | 0.7412154 | 0.000303905 |
| Hpcal1 | 0.73952115 | 0.012987777 |
| Pecam1 | 0.73847653 | 0.037844023 |
| Pbxip1 | 0.73775555 | 0.005000647 |
| Camsap2 | 0.7373141 | 0.009287807 |
| Elmo1 | 0.7370861 | 0.005507327 |

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| Pcnx | 0.73615789 | 3.94535E-05 |
| Tmem176a | 0.73606916 | 0.036898442 |
| Srr | 0.73201569 | 0.02533065 |
| Akap12 | 0.73179423 | 0.013115436 |
| Vegfa | 0.73158639 | 0.004535041 |
| Uap1l1 | 0.73105184 | 0.002278496 |
| Hykk | 0.72645343 | 0.000945975 |
| Ephb4 | 0.72564068 | 9.43137E-05 |
| Man2a1 | 0.72442335 | 2.48102E-05 |
| Rab11fip3 | 0.72286423 | 0.000264676 |
| Dse | 0.72239888 | 0.017934181 |
| Klf3 | 0.7220224 | 0.000852713 |
| Gria3 | 0.72143183 | 0.011027841 |
| Renbp | 0.7185534 | 0.002433371 |
| Vwa5a | 0.7183543 | 0.000185665 |
| Arhgef12 | 0.71826823 | 2.64054E-07 |
| Dscr3 | 0.71820235 | 0.013373111 |
| Klf12 | 0.71801859 | 0.042038097 |
| Mest | 0.71748714 | 0.02435718 |
| Add3 | 0.71507281 | 0.012250073 |
| Tnip1 | 0.71391741 | 0.046323861 |
| Foxp1 | 0.71179306 | 0.007440962 |
| Agtpbp1 | 0.7110216 | 0.047479631 |
| Atxn1 | 0.70765713 | 0.047746792 |
| Ublcp1 | 0.70538133 | 0.001442801 |
| Slc36a1 | 0.70482982 | 0.034707678 |
| Ecscr | 0.70482623 | 0.00114924 |
| Nfkbiz | 0.70403005 | 0.03182126 |
| Ltbr | 0.70389335 | 0.013710817 |
| Ift122 | 0.70383341 | 0.0163981 |
| Ptprb | 0.70281707 | 0.012058309 |
| Ehd4 | 0.70160983 | 0.001007446 |
| Shroom2 | 0.70152849 | 0.002080608 |
| Caskin2 | 0.70133712 | 0.000825178 |
| Jun | 0.69962255 | 0.001690251 |
| Colec12 | 0.69953303 | 0.00064055 |
| Usp29 | 0.69942113 | 0.021813981 |
| Dcaf12l1 | 0.69936957 | 0.030760077 |
| Thsd7a | 0.69934142 | 0.006517304 |
| Ralb | 0.6988076 | 6.72988E-05 |
| Rffl | 0.69851775 | 0.028467784 |
| Gcc1 | 0.69814953 | 0.036533027 |
| Diap2 | 0.6974635 | 0.000107239 |
| Hivep1 | 0.69726877 | 0.001151491 |

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| 0610031J06Rik | 0.69448255 | 0.001056958 |
| Nrp1 | 0.69364745 | 0.000413386 |
| Hdgfrp3 | 0.69162281 | 0.017150534 |
| Pdlim1 | 0.69026258 | 0.00588207 |
| Cmtm6 | 0.6882245 | 0.007776813 |
| Tbc1d24 | 0.68781396 | 0.000761453 |
| Grina | 0.68632164 | 0.03875513 |
| Ssfa2 | 0.68422394 | 0.000529909 |
| Slc31a2 | 0.68153524 | 0.030759745 |
| Crebrf | 0.67763436 | 0.01150381 |
| Rab31 | 0.67591862 | 5.17294E-05 |
| Nfatc1 | 0.67566145 | 0.000358201 |
| Ankrd46 | 0.6737142 | 0.014225415 |
| Eogt | 0.67287239 | 0.000279617 |
| Tmem136 | 0.67127123 | 0.020783337 |
| Tmtc2 | 0.67104799 | 0.02269917 |
| Zfp423 | 0.66883462 | 0.000868266 |
| Nhsl2 | 0.66800437 | 0.045635912 |
| Phactr2 | 0.66526633 | 0.000168442 |
| Aplp2 | 0.66374113 | 0.002158363 |
| Plxnc1 | 0.66342244 | 0.046158644 |
| Zfp37 | 0.66136321 | 0.046466866 |
| Maged2 | 0.66117415 | 0.001690251 |
| Gdpd1 | 0.6590052 | 0.012339667 |
| Spats2 | 0.65873136 | 0.012461136 |
| Abhd17a | 0.65611991 | 0.042241708 |
| Rnf19a | 0.65543242 | 0.011892489 |
| 2810025M15Rik | 0.65526736 | 0.03018424 |
| Trerf1 | 0.6552643 | 0.032909333 |
| Phldb1 | 0.65390566 | 0.033454148 |
| Cmtm3 | 0.65378612 | 0.002099005 |
| Map4k5 | 0.65273535 | 0.000682966 |
| Rftn1 | 0.65088843 | 0.007188629 |
| Mapre2 | 0.65072114 | 3.04588E-05 |
| Car13 | 0.6501821 | 0.029781297 |
| Rap2a | 0.6495413 | 0.00012727 |
| Sorbs1 | 0.64864152 | 0.005769709 |
| Anxa6 | 0.64795673 | 0.005050143 |
| Aldh3a2 | 0.64686485 | 0.007871539 |
| Trp53inp2 | 0.64632375 | 0.006543975 |
| Dock11 | 0.64291223 | 0.001077678 |
| Fermt2 | 0.64276518 | 0.001317511 |
| 2010111I01Rik | 0.64226543 | 0.023531808 |
| Kdelc2 | 0.64148983 | 0.032128846 |

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|---|---|---|
| Rnf185 | 0.64126914 | 0.006954703 |
| Cpped1 | 0.64121622 | 0.020014143 |
| Acox1 | 0.64033263 | 0.003251755 |
| P4ha1 | 0.64031227 | 0.023531808 |
| Ucp2 | 0.63959579 | 0.013484556 |
| Litaf | 0.6387186 | 0.000584105 |
| Klhl24 | 0.63412857 | 0.000617457 |
| Ddx26b | 0.63165374 | 0.000923543 |
| Tbx3 | 0.6314738 | 0.01128909 |
| Neo1 | 0.63074852 | 0.001151491 |
| Dcaf6 | 0.62954061 | 0.02505003 |
| Tmbim1 | 0.62939469 | 0.003961101 |
| Sin3b | 0.62730055 | 0.00687311 |
| Ctns | 0.62718535 | 0.024164708 |
| 1700017B05Rik | 0.62710297 | 0.006939776 |
| Stk39 | 0.62697845 | 0.029616385 |
| Pabpc4l | 0.62383771 | 0.039717815 |
| Psap | 0.62363956 | 0.002904454 |
| Bcorl1 | 0.62358615 | 0.044217964 |
| Rcan1 | 0.62350671 | 0.007890401 |
| D8Ertd82e | 0.62298176 | 0.020080206 |
| Pald1 | 0.62157232 | 0.004155895 |
| Hspg2 | 0.62080375 | 0.023583472 |
| Mfsd1 | 0.62021811 | 0.014816049 |
| Tram2 | 0.62013336 | 0.017156973 |
| Timp3 | 0.62007929 | 0.045270638 |
| Large | 0.61708174 | 0.00070527 |
| Mrps18a | 0.61666294 | 0.01963896 |
| Ap1b1 | 0.61648275 | 0.026554312 |
| Atp7a | 0.61478233 | 0.000656631 |
| Cdk19 | 0.61444285 | 0.003519578 |
| Ddah2 | 0.61139152 | 0.000539094 |
| Pcmtd2 | 0.61134989 | 0.041391858 |
| Wdr59 | 0.61015405 | 0.001261071 |
| Txndc12 | 0.60745129 | 0.017302164 |
| Sh2d3c | 0.6070239 | 0.046485043 |
| Ctsb | 0.60682587 | 0.002415398 |
| Coro2b | 0.60484299 | 0.015178259 |
| Sntb2 | 0.60408587 | 0.023485284 |
| Dram2 | 0.60395019 | 0.003681232 |
| Snx33 | 0.60357863 | 0.042833276 |
| Ctsz | 0.60319387 | 0.042038097 |
| Dpysl3 | 0.60275999 | 0.023848921 |
| Hbp1 | 0.60202876 | 0.001246888 |

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|---|---|---|
| Pygb | 0.60159009 | 0.024938826 |
| B4galt1 | 0.60021312 | 0.009472726 |
| Chst2 | 0.59935197 | 0.044317282 |
| Itm2a | 0.59934598 | 0.016952314 |
| Fam3c | 0.59884264 | 0.002171325 |
| Lrp5 | 0.59853274 | 0.004574116 |
| Dst | 0.59845677 | 0.04029844 |
| Tjp1 | 0.59775217 | 0.002024504 |
| Tulp4 | 0.59769468 | 0.042038097 |
| Ankrd12 | 0.59745828 | 0.031663064 |
| Magi3 | 0.59609837 | 0.000744992 |
| Cds2 | 0.59605618 | 0.003453483 |
| Agap1 | 0.5959778 | 0.000824873 |
| Snx30 | 0.59496096 | 0.001178785 |
| Tirap | 0.59184831 | 0.04215328 |
| Laptm4b | 0.59147045 | 0.016153005 |
| Nckap1 | 0.59012864 | 0.000861761 |
| Trio | 0.58716907 | 0.001049105 |
| Ccser2 | 0.58667636 | 0.012536686 |
| Ctsa | 0.58558901 | 0.002521886 |
| Zfp365 | 0.58450017 | 0.010050368 |
| Mrps6 | 0.58421779 | 0.015953899 |
| Dip2a | 0.58319374 | 0.012216594 |
| Msn | 0.58263225 | 0.002146891 |
| Fuca1 | 0.58182629 | 0.030945311 |
| Myl12b | 0.58058091 | 0.003073471 |
| C1galt1 | 0.58014878 | 0.044217964 |
| Arhgap32 | 0.58007553 | 0.019465196 |
| Cd81 | 0.57997559 | 0.002473598 |
| Bin1 | 0.57985951 | 0.022188608 |
| Ppm1f | 0.57934618 | 0.009875557 |
| Slc35f5 | 0.57639734 | 0.011713162 |
| Frmd4b | 0.57613481 | 0.001740874 |
| Nbea | 0.57567119 | 0.013359638 |
| Fam149a | 0.57540988 | 0.031478578 |
| Gas6 | 0.57495921 | 0.024093476 |
| Ttc21b | 0.57463453 | 0.047145219 |
| Cflar | 0.57426542 | 0.010484254 |
| Tet2 | 0.57397044 | 0.021805972 |
| Abca3 | 0.57208283 | 0.039347379 |
| Cdc42bpb | 0.57079366 | 0.002730013 |
| Kank2 | 0.56893831 | 0.000687737 |
| Pea15a | 0.56454173 | 0.007986298 |
| Tmeff1 | 0.56339126 | 0.002796434 |

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| Map4k3 | 0.56184021 | 0.007739628 |
| Calcoco1 | 0.55926819 | 0.021813981 |
| Lphn2 | 0.55915459 | 0.028792274 |
| Frmd4a | 0.55909661 | 0.009381743 |
| She | 0.55727128 | 0.014278091 |
| Bex2 | 0.55682153 | 0.017018905 |
| Fam222b | 0.55582617 | 0.003171631 |
| Tjp2 | 0.55518464 | 0.047736269 |
| Gabarapl1 | 0.55411434 | 0.027968234 |
| Bcl2l2 | 0.55379105 | 0.025731459 |
| Macf1 | 0.55359979 | 0.008348814 |
| Cyth3 | 0.55158306 | 0.017107797 |
| Tcf7l2 | 0.54950471 | 0.019670119 |
| Mapk3 | 0.54926569 | 0.012042675 |
| Sypl | 0.54779776 | 0.002164505 |
| Casd1 | 0.54730099 | 0.004621678 |
| Ndel1 | 0.54515163 | 0.032707262 |
| Elovl5 | 0.54455376 | 0.007198543 |
| Zfyve1 | 0.5429496 | 0.034501245 |
| Gm16515 | 0.54253368 | 0.030750353 |
| Oxct1 | 0.53889576 | 0.003227649 |
| Hexa | 0.53755868 | 0.010353402 |
| Hip1 | 0.53669525 | 0.003779115 |
| Akt3 | 0.5358331 | 0.002640916 |
| Ctnnb1 | 0.53480571 | 0.002134974 |
| Gna12 | 0.53476745 | 0.036457407 |
| Tmem106b | 0.53293082 | 0.00983404 |
| Kctd10 | 0.53232996 | 0.005050143 |
| Dlg5 | 0.53052194 | 0.026201187 |
| Copg2 | 0.52907354 | 0.007441806 |
| Klhl6 | 0.52885112 | 0.043764027 |
| Bmpr2 | 0.52816564 | 0.012806133 |
| Arhgef11 | 0.52804764 | 0.04460364 |
| Tenc1 | 0.5270311 | 0.046485043 |
| Exoc4 | 0.52598929 | 0.013850109 |
| Grn | 0.52512264 | 0.017073221 |
| Sccpdh | 0.52503297 | 0.020276582 |
| Asah1 | 0.5240867 | 0.004107884 |
| Adipor1 | 0.52219677 | 0.027909075 |
| Cd34 | 0.52113702 | 0.044968769 |
| Sptbn1 | 0.52107557 | 0.011841617 |
| Dmwd | 0.51969525 | 0.034731938 |
| Steap2 | 0.51959855 | 0.016884793 |
| Acbd5 | 0.5192529 | 0.010635018 |

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| Fam129b | 0.51726306 | 0.045007815 |
| Sri | 0.51476517 | 0.027981567 |
| Myo1c | 0.51023212 | 0.026664828 |
| Anapc2 | 0.5094904 | 0.047761325 |
| Clip1 | 0.50854321 | 0.045970845 |
| Usp32 | 0.50601689 | 0.006862971 |
| Lrrc58 | 0.50208572 | 0.014354849 |
| Lrrc8a | 0.50131466 | 0.015484623 |
| Numb | 0.50039981 | 0.038467385 |
| Tgoln1 | 0.49960455 | 0.020080206 |
| Hdac7 | 0.4984747 | 0.021512228 |
| Yipf3 | 0.49814051 | 0.04568778 |
| Rab12 | 0.4976599 | 0.016680184 |
| Lamp2 | 0.49504798 | 0.00331656 |
| Cdh2 | 0.49261398 | 0.044437726 |
| Slk | 0.49239968 | 0.04613748 |
| Cobll1 | 0.49228499 | 0.046238274 |
| Sptan1 | 0.4915641 | 0.006608602 |
| Ctsd | 0.49134742 | 0.006278841 |
| Slc44a2 | 0.49073396 | 0.014312804 |
| Nav1 | 0.48608593 | 0.012488255 |
| Pxdn | 0.48546871 | 0.047497123 |
| Dock6 | 0.48544075 | 0.026055774 |
| Cnppd1 | 0.48498683 | 0.036442504 |
| Srgap2 | 0.4838278 | 0.015024717 |
| Mpzl1 | 0.48375674 | 0.004183166 |
| Smad1 | 0.4829588 | 0.0470535 |
| Il6st | 0.47740513 | 0.016300121 |
| Pik3c2a | 0.47232209 | 0.020342359 |
| Ppp1r9a | 0.47205388 | 0.032031301 |
| Fkbp9 | 0.47062321 | 0.031063557 |
| Lgals8 | 0.47012918 | 0.037800364 |
| Atp2b1 | 0.46992678 | 0.005771646 |
| Npc1 | 0.46778791 | 0.030749983 |
| Atp2c1 | 0.46589562 | 0.02782276 |
| Yes1 | 0.46384103 | 0.032301302 |
| Tspan9 | 0.4601918 | 0.019634188 |
| Nrp2 | 0.45803467 | 0.031478578 |
| Dusp16 | 0.45754214 | 0.046634435 |
| Iqgap1 | 0.45699364 | 0.039120924 |
| Map3k3 | 0.45523166 | 0.016592229 |
| Qk | 0.45351265 | 0.031272574 |
| Dock1 | 0.4495832 | 0.047761325 |
| Btg1 | 0.44955823 | 0.038726639 |

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| Actn4 | 0.44890813 | 0.010940718 |
| Carhsp1 | 0.44872969 | 0.022590568 |
| Adcy6 | 0.44322494 | 0.027909075 |
| Ptk7 | 0.44099911 | 0.046270724 |
| Itga5 | 0.43983133 | 0.019283968 |
| Man2b1 | 0.43442997 | 0.020610191 |
| Ugp2 | 0.4328997 | 0.035589807 |
| Map3k11 | 0.43032825 | 0.034398076 |
| Fam135a | 0.42739733 | 0.04226346 |
| Pdlim5 | 0.42663236 | 0.036732568 |
| Triobp | 0.41876773 | 0.02533065 |
| Gng12 | 0.41696342 | 0.042038097 |
| Ptpn14 | 0.41348236 | 0.039033139 |
| Piezo1 | 0.40509281 | 0.036447588 |
| Skil | 0.39370361 | 0.04302612 |
| Map4k4 | 0.39335155 | 0.043693615 |
| Lamp1 | 0.37683457 | 0.044951032 |
| Maged1 | 0.37170291 | 0.041391858 |
| Trim33 | -0.3573469 | 0.046505472 |
| Gspt1 | -0.3605518 | 0.049871418 |
| Sqle | -0.3611902 | 0.047497123 |
| Tardbp | -0.3666847 | 0.0450795 |
| Tcerg1 | -0.376228 | 0.04692825 |
| Psmb6 | -0.3846357 | 0.034358015 |
| Hnrnph1 | -0.3850724 | 0.041383915 |
| Orc3 | -0.386385 | 0.049501447 |
| Sf3a1 | -0.3926086 | 0.029792015 |
| Med14 | -0.3953839 | 0.035347688 |
| Ola1 | -0.396888 | 0.030828711 |
| Stip1 | -0.3980127 | 0.025731459 |
| Rrm1 | -0.40015 | 0.048973333 |
| Set | -0.4020976 | 0.019634188 |
| Pdcd11 | -0.4036084 | 0.036446307 |
| Pkm | -0.4037588 | 0.033126447 |
| Ncapd2 | -0.4068065 | 0.034632648 |
| Xpo5 | -0.4114309 | 0.043826737 |
| Utp6 | -0.4115701 | 0.031272574 |
| Wdr75 | -0.4123941 | 0.032767466 |
| Tyms | -0.4180273 | 0.030749983 |
| Mybbp1a | -0.4199431 | 0.027692569 |
| Smarcc1 | -0.4207404 | 0.010592548 |
| U2af2 | -0.4218187 | 0.036356386 |
| Nup62 | -0.4218858 | 0.03659348 |
| Epb4.1l5 | -0.4222133 | 0.034933449 |

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| Ddx18 | -0.4238809 | 0.019037708 |
| Cops5 | -0.4239614 | 0.047519961 |
| Znrf3 | -0.4252158 | 0.039120924 |
| Cirh1a | -0.4273012 | 0.025731459 |
| Plagl2 | -0.4287221 | 0.037114187 |
| Ttll4 | -0.4302274 | 0.036453576 |
| Rae1 | -0.4322049 | 0.02672746 |
| Fam210a | -0.4326129 | 0.033370023 |
| Larp7 | -0.4335868 | 0.01353108 |
| Hnrnpc | -0.433706 | 0.04463755 |
| Cpsf6 | -0.4344144 | 0.031087599 |
| Nsun2 | -0.4344325 | 0.049403296 |
| Nme1 | -0.4416846 | 0.018530298 |
| Aifm1 | -0.4417268 | 0.039476839 |
| Denr | -0.4420595 | 0.048771943 |
| Mre11a | -0.4431858 | 0.039975742 |
| Nup160 | -0.445214 | 0.017009718 |
| Nup155 | -0.4457544 | 0.014937183 |
| Psmb3 | -0.4494857 | 0.024434239 |
| Snrnp70 | -0.4500929 | 0.034951497 |
| Smn1 | -0.4510802 | 0.047761545 |
| Fasn | -0.4512933 | 0.012637806 |
| Plcl2 | -0.4526148 | 0.0450795 |
| Fastkd2 | -0.4526201 | 0.043052075 |
| Dtl | -0.4527959 | 0.045979705 |
| Gins2 | -0.4540335 | 0.042494308 |
| Ppat | -0.4559212 | 0.01150381 |
| Fus | -0.4564607 | 0.0163981 |
| Dhfr | -0.4572799 | 0.036850504 |
| Atic | -0.457867 | 0.038996551 |
| Acaca | -0.458071 | 0.033011588 |
| Mms22l | -0.458251 | 0.043693714 |
| Wdr3 | -0.4585454 | 0.047622621 |
| Utp11l | -0.4591145 | 0.04692825 |
| Hat1 | -0.459847 | 0.039717815 |
| Usp24 | -0.4598783 | 0.013999324 |
| Hells | -0.4618291 | 0.019912997 |
| Rsl1d1 | -0.4630114 | 0.008975873 |
| Tacc3 | -0.4632733 | 0.023047439 |
| C1qbp | -0.4654797 | 0.019284155 |
| Khsrp | -0.4659537 | 0.025432283 |
| Erh | -0.4663217 | 0.012250073 |
| Nudc | -0.4675083 | 0.023153375 |
| Eif4e | -0.4700993 | 0.01482001 |

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|---|---|---|
| Ruvbl2 | -0.4714274 | 0.017155849 |
| Frs2 | -0.4737451 | 0.020031543 |
| Fgfr1op | -0.4764688 | 0.02174393 |
| Rsl24d1 | -0.4794557 | 0.030886228 |
| Gatad1 | -0.4821751 | 0.004813209 |
| Phb | -0.4823853 | 0.026336996 |
| Park7 | -0.4844912 | 0.03428394 |
| Tsr1 | -0.4870355 | 0.025432283 |
| Chaf1b | -0.4875325 | 0.031945563 |
| Myo19 | -0.4878522 | 0.041255062 |
| Trmt6 | -0.4884361 | 0.034951497 |
| Cct3 | -0.4887553 | 0.005374654 |
| Chek1 | -0.4912268 | 0.033067184 |
| Rcc2 | -0.4921252 | 0.014225415 |
| Cacybp | -0.4933062 | 0.027808796 |
| 0610007P14Rik | -0.4934913 | 0.032181752 |
| Ticrr | -0.4936432 | 0.015447187 |
| Oat | -0.494166 | 0.005101356 |
| Ing5 | -0.4949474 | 0.026264805 |
| Psmg1 | -0.4960053 | 0.018685955 |
| Tuba1c | -0.4960215 | 0.001909046 |
| Cks1b | -0.4983408 | 0.010068361 |
| Dkc1 | -0.500082 | 0.025502096 |
| Mlec | -0.5010375 | 0.003793243 |
| Wdr18 | -0.5016548 | 0.027602575 |
| Eef1d | -0.5016561 | 0.005029593 |
| Gpn1 | -0.50166 | 0.031272574 |
| Kif20a | -0.5021924 | 0.020251678 |
| Gfpt2 | -0.5025914 | 0.038891191 |
| C330027C09Rik | -0.503346 | 0.020767104 |
| Rrp1b | -0.5039365 | 0.004155895 |
| Jade3 | -0.5045377 | 0.04865351 |
| Phlda1 | -0.511139 | 0.015484623 |
| Mrps30 | -0.5112446 | 0.03023915 |
| Nsdhl | -0.5131118 | 0.004035043 |
| Emg1 | -0.514678 | 0.03023915 |
| Pitrm1 | -0.5148078 | 0.036723138 |
| Dazap1 | -0.5151004 | 0.043443023 |
| Pcna | -0.5155391 | 0.006109254 |
| Eno1b | -0.5159822 | 0.027909075 |
| Pspc1 | -0.5165724 | 0.026849481 |
| Cenph | -0.5175012 | 0.034731938 |
| Srm | -0.5186396 | 0.012896026 |
| Uhrf1 | -0.5191902 | 0.002298833 |

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|---|---|---|
| Nol10 | -0.5216314 | 0.036225763 |
| Eif5a | -0.5225901 | 0.000901976 |
| Rfc5 | -0.5234656 | 0.040120088 |
| Seh1l | -0.523609 | 0.001159918 |
| Mycbp | -0.5236966 | 0.023238999 |
| Sf3b4 | -0.5257505 | 0.01150381 |
| Gemin5 | -0.5259505 | 0.012360708 |
| Pno1 | -0.5261394 | 0.005017275 |
| Mrpl18 | -0.5270604 | 0.007149373 |
| Hspd1 | -0.5276276 | 0.016206396 |
| Phykpl | -0.5278217 | 0.01967461 |
| Nop58 | -0.5278991 | 0.002640916 |
| Hsp90aa1 | -0.5285458 | 0.004559047 |
| Klhl21 | -0.5298036 | 0.020200454 |
| Rspo3 | -0.5305875 | 0.003677673 |
| Magoh | -0.5325781 | 0.021756697 |
| Pfkp | -0.5343331 | 0.037114187 |
| Casc5 | -0.5346706 | 0.010635018 |
| Katna1 | -0.5392394 | 0.040535413 |
| Haus1 | -0.5416084 | 0.018415097 |
| Ddx20 | -0.5419028 | 0.007250069 |
| Zwilch | -0.5423232 | 0.003516898 |
| D8Ertd738e | -0.5444438 | 0.036293603 |
| Ppa1 | -0.545403 | 0.048289851 |
| Isoc1 | -0.5481145 | 0.0163981 |
| Lin28a | -0.5484315 | 0.006155268 |
| Cse1l | -0.5488957 | 0.000267407 |
| Lss | -0.5497879 | 0.01150381 |
| Mad2l1 | -0.5499787 | 0.01318802 |
| E2f4 | -0.5500669 | 0.016680184 |
| Cep76 | -0.5505935 | 0.030346521 |
| Noc3l | -0.5510514 | 0.008931862 |
| Rap1b | -0.5510983 | 0.029783277 |
| Ddx21 | -0.551379 | 0.002062486 |
| Zfp850 | -0.5528011 | 0.034898561 |
| Mrps22 | -0.5561946 | 0.033198701 |
| Ranbp1 | -0.5567163 | 0.004602199 |
| Umps | -0.5584059 | 0.006954703 |
| Dut | -0.5585744 | 0.001840115 |
| Mcm7 | -0.5601798 | 0.000658803 |
| Cep290 | -0.5611988 | 0.0289515 |
| Mif | -0.5644379 | 0.022222952 |
| Usp36 | -0.5669756 | 0.029260583 |
| Ppp1r14b | -0.5692128 | 0.006049266 |

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|---|---|---|
| Hdgf | -0.5709078 | 0.000333168 |
| Hist1h1e | -0.5717303 | 0.014219326 |
| Cluh | -0.5718228 | 0.010217169 |
| Cks2 | -0.5722872 | 0.037976577 |
| Gcsh | -0.5728595 | 0.001909046 |
| Ahsa1 | -0.574962 | 0.001385299 |
| Pold1 | -0.5749853 | 0.019814115 |
| Sms | -0.5751655 | 0.003849886 |
| Jmjd6 | -0.5756012 | 0.007296571 |
| Fbl | -0.5758456 | 0.00085362 |
| Prps1 | -0.5765977 | 0.040763638 |
| Nop56 | -0.5766727 | 0.037732378 |
| Homer1 | -0.5783565 | 0.035499608 |
| Nhp2 | -0.582946 | 0.00138054 |
| Nasp | -0.5832083 | 0.0001497 |
| Noc2l | -0.5835108 | 0.001151491 |
| Rcc1 | -0.5838483 | 0.01150381 |
| Atad5 | -0.5839931 | 0.000744992 |
| Snrpd2 | -0.5845768 | 0.049596743 |
| Gsg2 | -0.5887483 | 0.024804679 |
| Mdk | -0.5925585 | 0.036779379 |
| Maz | -0.5930999 | 0.031077508 |
| Mrpl3 | -0.5936589 | 0.010625531 |
| Naf1 | -0.5942042 | 0.005657614 |
| Mid1 | -0.5945538 | 0.010151093 |
| Cenpn | -0.5953636 | 0.007380439 |
| Pprc1 | -0.595594 | 0.010734992 |
| Dis3 | -0.5961683 | 0.000516827 |
| Naa10 | -0.5967393 | 0.014832121 |
| Ankrd27 | -0.5970243 | 0.036430871 |
| Rpp14 | -0.5981019 | 0.032039462 |
| Gnl3 | -0.6009705 | 0.004260171 |
| Pa2g4 | -0.6011336 | 7.33916E-05 |
| Kmt2b | -0.60144 | 0.035725263 |
| Ddx39 | -0.6014412 | 0.001368778 |
| Nop10 | -0.60184 | 0.006261636 |
| Snapc4 | -0.6024253 | 0.009725129 |
| Sppl2a | -0.6039032 | 0.01632944 |
| Bop1 | -0.6056497 | 0.006793952 |
| Psat1 | -0.6060635 | 0.00091311 |
| E2f1 | -0.6070543 | 0.01963896 |
| Cap2 | -0.6076249 | 0.000505951 |
| Polr1b | -0.6098149 | 0.002530932 |
| Naa50 | -0.6103831 | 0.027909075 |

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|---|---|---|
| Nup35 | -0.6118891 | 0.038555559 |
| Timeless | -0.6145758 | 0.002158363 |
| Pfas | -0.616097 | 0.000899475 |
| Rps12 | -0.6173728 | 0.03182126 |
| Aste1 | -0.618063 | 0.031421462 |
| Zmym1 | -0.6181706 | 0.010592254 |
| Dtymk | -0.6182236 | 0.026420093 |
| Kif15 | -0.6183403 | 0.000279445 |
| Haus3 | -0.6188925 | 0.00930685 |
| Mrpl52 | -0.6198458 | 0.048700709 |
| P2ry1 | -0.6275068 | 0.026938192 |
| Dusp18 | -0.628064 | 0.012882798 |
| Ccdc124 | -0.6290632 | 0.02040009 |
| Ell2 | -0.6296718 | 0.018417458 |
| Tk1 | -0.6301929 | 0.037285962 |
| Shmt2 | -0.630889 | 7.98755E-05 |
| Abcb10 | -0.6330012 | 0.001300759 |
| D030056L22Rik | -0.6356704 | 0.018113235 |
| Akt2 | -0.6369274 | 0.021342939 |
| L2hgdh | -0.6389627 | 0.005507327 |
| Rreb1 | -0.6400927 | 9.95066E-05 |
| Elac2 | -0.6413754 | 0.002158363 |
| Etl4 | -0.6415104 | 0.001529963 |
| 2410002F23Rik | -0.6417525 | 0.01963896 |
| Nkrf | -0.6418171 | 0.00353932 |
| Mrpl47 | -0.6420686 | 0.034731938 |
| Lsm2 | -0.6427002 | 0.012536752 |
| 9430015G10Rik | -0.6469001 | 0.028851222 |
| Uchl3 | -0.6487112 | 0.008916301 |
| Dhodh | -0.6498502 | 0.024164708 |
| Pole | -0.6524743 | 0.001188025 |
| Nmral1 | -0.653271 | 0.046458929 |
| Rad51 | -0.653761 | 0.004066553 |
| Urb1 | -0.6553645 | 0.006278841 |
| Mob1b | -0.6574739 | 0.002452616 |
| Nolc1 | -0.6576932 | 8.64663E-06 |
| Bckdhb | -0.6580894 | 0.022112927 |
| Bag2 | -0.6645741 | 0.02505003 |
| Smyd5 | -0.6656635 | 0.026721458 |
| Ndufs6 | -0.6699754 | 0.015364912 |
| Itga2b | -0.6727368 | 0.020276582 |
| Tsen2 | -0.6775487 | 0.046466866 |
| Edrf1 | -0.6829337 | 0.00804993 |
| Ppan | -0.6850071 | 0.035644434 |

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|---|---|---|
| Ptgr1 | -0.6889211 | 0.022856973 |
| Cdc6 | -0.6929623 | 0.001740874 |
| 3110082I17Rik | -0.6937728 | 0.012238072 |
| Diablo | -0.6948298 | 0.029975046 |
| Rybp | -0.6951969 | 0.044775658 |
| Dctd | -0.7007772 | 0.002543299 |
| Mob3c | -0.7061391 | 0.029251299 |
| Ippk | -0.7063486 | 0.011952822 |
| Rab11fip1 | -0.7064745 | 0.00787161 |
| Mrpl22 | -0.7076716 | 0.018435039 |
| Sod2 | -0.7101316 | 0.00083047 |
| Srxn1 | -0.7117592 | 0.020276582 |
| Tlcd1 | -0.7161115 | 0.034951497 |
| Mtrr | -0.7165168 | 0.009427644 |
| Uqcr10 | -0.7168167 | 0.00711417 |
| Heatr2 | -0.7168978 | 0.006279683 |
| Fancd2 | -0.7181052 | 0.001233198 |
| Tcof1 | -0.718714 | 0.000177483 |
| Trip13 | -0.7194061 | 0.000102004 |
| Rad54l | -0.7201007 | 0.006443575 |
| Rpp40 | -0.720515 | 0.008722369 |
| Tal1 | -0.7243217 | 0.035004677 |
| Ccdc18 | -0.7250853 | 0.022430669 |
| Zfp36l2 | -0.7253139 | 0.001857072 |
| Setd8 | -0.7259416 | 0.000269964 |
| Prkab1 | -0.729529 | 0.000129675 |
| Zbtb43 | -0.7306579 | 0.038431642 |
| Gins1 | -0.7321125 | 0.009438331 |
| Sf3b6 | -0.7375405 | 0.022237244 |
| Cep152 | -0.7386925 | 0.035947492 |
| Ung | -0.7392586 | 0.016867812 |
| Snrpa1 | -0.741571 | 0.000208255 |
| Slc16a6 | -0.7451852 | 0.010050368 |
| Ska3 | -0.746177 | 0.005971886 |
| Egln3 | -0.7466605 | 4.23684E-05 |
| Bcor | -0.7480644 | 1.94473E-06 |
| Zik1 | -0.7482625 | 0.029931613 |
| Srf | -0.7496534 | 0.003480838 |
| Snhg5 | -0.7520657 | 0.000951237 |
| Uqcr11 | -0.7552484 | 0.01150381 |
| Ddx11 | -0.7563069 | 0.004176478 |
| Psmc3ip | -0.7568939 | 0.000419823 |
| 1110038B12Rik | -0.7581591 | 0.001273613 |
| Helb | -0.7590714 | 0.020520561 |

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|---|---|---|
| Hsd17b7 | -0.7599393 | 0.000674468 |
| Prkcd | -0.7609372 | 0.04692825 |
| Smim3 | -0.7616062 | 0.011321729 |
| Notch2 | -0.7648085 | 0.001607176 |
| Hmgn2 | -0.7648535 | 0.003655177 |
| Lsm5 | -0.7653828 | 0.020768793 |
| Tfb2m | -0.7675262 | 0.016153005 |
| Anapc11 | -0.7680224 | 0.034225692 |
| Ppih | -0.7682877 | 0.016367779 |
| H2afx | -0.7685989 | 0.000594153 |
| Fancb | -0.7713014 | 0.041391858 |
| Gyk | -0.7715793 | 0.046836397 |
| Polr2i | -0.7720022 | 0.01984889 |
| Depdc1b | -0.7720366 | 0.001707355 |
| Zcchc10 | -0.7745844 | 0.005241081 |
| Snrpg | -0.7818499 | 0.04215328 |
| Klhl12 | -0.7832182 | 0.001815011 |
| E2f8 | -0.78417 | 0.000180926 |
| Epb4.1 | -0.7849334 | 1.37786E-05 |
| Wbscr16 | -0.79124 | 0.018213973 |
| Fth1 | -0.7925434 | 0.000310477 |
| Troap | -0.7972141 | 0.023151903 |
| Hspe1 | -0.7988842 | 0.01963896 |
| Rnd2 | -0.8016923 | 0.022634645 |
| Ern1 | -0.8027457 | 0.004274098 |
| Mtx3 | -0.8052675 | 0.042241708 |
| Suv39h2 | -0.8053629 | 0.000264292 |
| Tcf7 | -0.8056699 | 3.70941E-05 |
| Lyar | -0.806388 | 5.67508E-06 |
| Smtnl2 | -0.8080904 | 0.013224797 |
| Tnfaip8 | -0.8116157 | 0.001896077 |
| Peo1 | -0.8136152 | 0.007218947 |
| Speg | -0.81617 | 0.021756697 |
| Fut8 | -0.8166749 | 0.000104545 |
| D2Wsu81e | -0.8168487 | 0.008155523 |
| H2afz | -0.8234957 | 3.07822E-08 |
| Laptm5 | -0.8267113 | 0.043365121 |
| Ubxn2a | -0.8271654 | 0.000222764 |
| Stra13 | -0.8316425 | 0.012298527 |
| Rrp12 | -0.8351638 | 0.000109874 |
| Gcnt1 | -0.8393189 | 2.35311E-05 |
| Tsc1 | -0.8417155 | 0.00012396 |
| Trmt61a | -0.8425698 | 0.000893326 |
| Polr2f | -0.8473131 | 0.007191282 |

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|---|---|---|
| Utp23 | -0.8561307 | 0.010212308 |
| Mrto4 | -0.8586158 | 0.000100664 |
| Fads2 | -0.8661943 | 4.81338E-06 |
| Tm7sf2 | -0.8688088 | 0.025432283 |
| Nbeal2 | -0.8716841 | 0.006623268 |
| Ska1 | -0.8730391 | 0.036533027 |
| Traip | -0.8757748 | 0.020692508 |
| Psph | -0.8766564 | 0.006842544 |
| Inip | -0.8770961 | 0.001718342 |
| Ormdl1 | -0.8771678 | 0.00814927 |
| Srl | -0.8787499 | 0.023134393 |
| C530008M17Rik | -0.8817309 | 0.02435718 |
| Hist1h1b | -0.883334 | 5.46909E-05 |
| Caprin2 | -0.8843534 | 0.005657628 |
| Rbmx | -0.8861848 | 0.000459628 |
| Grap2 | -0.8868077 | 0.024330801 |
| Sssca1 | -0.8898676 | 0.000505951 |
| Gas5 | -0.8931038 | 0.001005654 |
| Melk | -0.8938092 | 0.000748058 |
| Idi1 | -0.8942903 | 0.000625845 |
| Bcat1 | -0.9044063 | 0.006141257 |
| Mdm1 | -0.9053117 | 7.9056E-05 |
| Rps6ka6 | -0.9072983 | 2.512E-06 |
| Prmt1 | -0.9141192 | 0.000276921 |
| Fkbp11 | -0.9174265 | 0.030220191 |
| Slc19a1 | -0.9234819 | 0.012924042 |
| Ppil3 | -0.9241589 | 0.033070183 |
| Gtf3c5 | -0.9250698 | 8.09209E-08 |
| Hist1h2bb | -0.9256411 | 0.034731938 |
| Spc24 | -0.9296335 | 9.00545E-05 |
| Itga4 | -0.9299064 | 0.000123511 |
| Hist1h2be | -0.9304375 | 0.022222952 |
| Pola2 | -0.9380601 | 1.61723E-05 |
| Ahi1 | -0.9508248 | 2.51545E-05 |
| Acy1 | -0.9528935 | 0.043805059 |
| Ctla2a | -0.9543965 | 0.049700762 |
| Cenpp | -0.9595026 | 0.01722529 |
| Gpc6 | -0.9623014 | 0.010298045 |
| Shroom3 | -0.9652569 | 0.038151613 |
| Zfp692 | -0.9781341 | 0.00385429 |
| Tmem158 | -0.9823048 | 0.025921359 |
| Cited2 | -0.9926737 | 1.75743E-06 |
| Taf1d | -0.9953624 | 0.036966046 |
| Acot11 | -1.0008928 | 0.00777375 |

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|---|---|---|
| Lsm7 | -1.0009126 | 0.004305268 |
| Slc7a5 | -1.0036 | 2.17805E-06 |
| Tmem86b | -1.0039618 | 0.017467063 |
| Ifi30 | -1.0044766 | 0.048700709 |
| Psd3 | -1.0174544 | 0.03534982 |
| Wdsub1 | -1.0239369 | 0.048950469 |
| 1810032O08Rik | -1.0328231 | 0.029931613 |
| Hist1h4d | -1.0383794 | 0.005507327 |
| Dctpp1 | -1.0393153 | 0.000317381 |
| Plscr1 | -1.039389 | 0.004614916 |
| Pmp22 | -1.0535001 | 0.009847584 |
| Mgat4a | -1.0568436 | 0.007776813 |
| C77080 | -1.0585692 | 0.000189306 |
| Snhg3 | -1.0648738 | 0.010269121 |
| Sec61g | -1.0666418 | 0.017108692 |
| Psmg4 | -1.0676331 | 0.046324916 |
| Sdc1 | -1.0753188 | 0.000999753 |
| Fzd2 | -1.0778418 | 0.027968234 |
| Lhpp | -1.0879831 | 0.02047849 |
| Gse1 | -1.0939363 | 2.31344E-11 |
| Zfp930 | -1.0940181 | 0.000645702 |
| Lsm3 | -1.0963022 | 0.004523766 |
| Tagln | -1.1030145 | 0.034761101 |
| Car2 | -1.1035294 | 0.035986008 |
| Kcnj5 | -1.1045913 | 0.000544414 |
| Med30 | -1.1093461 | 0.019362238 |
| Dsp | -1.1110028 | 0.009917825 |
| Lpar1 | -1.1156382 | 0.033861499 |
| Kalrn | -1.1171644 | 1.07783E-06 |
| Ccdc134 | -1.1231804 | 0.020684784 |
| Xk | -1.1366802 | 0.007849919 |
| Dyrk2 | -1.1426776 | 0.009743851 |
| Irs1 | -1.1430887 | 0.002965951 |
| Kctd15 | -1.1434019 | 0.028175567 |
| Lyl1 | -1.1442502 | 0.000958535 |
| Apitd1 | -1.1442509 | 0.00232128 |
| Ank3 | -1.1478545 | 5.47484E-07 |
| Etv2 | -1.1482494 | 0.003357049 |
| Arhgap6 | -1.1576452 | 1.26249E-05 |
| Tpm2 | -1.1599192 | 0.005227615 |
| Cth | -1.1612232 | 0.032836443 |
| Mtfp1 | -1.162728 | 0.010298045 |
| Chchd1 | -1.1640701 | 0.042687922 |
| Fam109b | -1.1687442 | 0.034422349 |

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| Snrnp25 | -1.1795927 | 8.64663E-06 |
| Tfrc | -1.1817508 | 1.42962E-15 |
| Fzd10 | -1.1850427 | 0.012027882 |
| Robo2 | -1.1976152 | 0.027968234 |
| Rab27b | -1.2026754 | 0.000262575 |
| Hist1h3e | -1.207497 | 0.002028412 |
| Hist1h2bm | -1.2087727 | 0.000166046 |
| Pde4dip | -1.2117548 | 2.22157E-08 |
| Myl9 | -1.2154017 | 0.008966617 |
| Col5a1 | -1.2365169 | 0.024124732 |
| Nfix | -1.2439774 | 0.028851222 |
| Plek | -1.2460721 | 0.029677111 |
| Hist1h2ac | -1.2654033 | 0.048005393 |
| Sh3bp1 | -1.2655429 | 3.82269E-06 |
| Slc35f2 | -1.2714037 | 0.004479282 |
| Med12l | -1.2776314 | 5.18855E-08 |
| Eno3 | -1.2819185 | 0.00053602 |
| Gria2 | -1.2929235 | 0.012739783 |
| Prtg | -1.2975163 | 3.8001E-10 |
| Samd14 | -1.3126027 | 0.034398076 |
| Gfra2 | -1.3188517 | 0.001212132 |
| Hist2h2ac | -1.3249293 | 0.043805059 |
| Hist1h2bl | -1.3323982 | 3.94278E-06 |
| Hist1h4c | -1.3424522 | 0.036779379 |
| Lgals9 | -1.3443204 | 0.001153782 |
| Phgdh | -1.3465429 | 1.0238E-06 |
| Hist1h4a | -1.3568512 | 0.040921913 |
| Hspb8 | -1.3581106 | 0.047653617 |
| Hist1h2bf | -1.3608963 | 9.84748E-05 |
| Lama1 | -1.3748046 | 0.010539709 |
| Ptpre | -1.3799639 | 6.33328E-07 |
| Mpl | -1.383543 | 0.00145656 |
| Gfi1 | -1.3873919 | 0.029781297 |
| Tenm3 | -1.3946725 | 0.036732568 |
| Klf8 | -1.398728 | 1.0931E-09 |
| Cyp26b1 | -1.4037073 | 0.010353402 |
| Hist1h2ak | -1.4072807 | 0.000275295 |
| Pitx2 | -1.410157 | 0.003136119 |
| Dyrk3 | -1.4106397 | 0.004579839 |
| Nap1l2 | -1.4284217 | 0.041255062 |
| Ston2 | -1.4291669 | 0.000106664 |
| Hist1h3g | -1.4334317 | 0.001909046 |
| Ifitm1 | -1.4344149 | 5.82107E-05 |
| Adamts9 | -1.4390785 | 0.020080206 |

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|---|---|---|
| Mrvi1 | -1.439407 | 0.0163981 |
| Sfrp2 | -1.4502113 | 0.034731938 |
| Lrr1 | -1.45511 | 0.004465313 |
| Mpo | -1.4663655 | 0.01179793 |
| Ryr2 | -1.4690604 | 0.016935002 |
| Unc5c | -1.4771939 | 4.14642E-15 |
| Egfl8 | -1.4885643 | 0.048391189 |
| Fam117a | -1.4937007 | 0.00425314 |
| Hist1h2bh | -1.4980855 | 4.37625E-05 |
| Syt7 | -1.5153341 | 0.017781453 |
| Gpc3 | -1.5323008 | 7.16894E-09 |
| Sall3 | -1.5370094 | 1.50775E-17 |
| Wnt5a | -1.5468432 | 0.000760804 |
| Hist1h3i | -1.5483412 | 0.026721458 |
| Plcxd1 | -1.5523584 | 0.038153598 |
| Hist1h2bp | -1.5681605 | 0.009899788 |
| Hist1h2bk | -1.5735921 | 0.00043405 |
| Snord99 | -1.5909402 | 0.016290154 |
| AI467606 | -1.5969964 | 0.022946391 |
| Ptprj | -1.6077737 | 1.0931E-09 |
| Ctse | -1.6078993 | 0.002431662 |
| Prkca | -1.6098811 | 3.36158E-10 |
| Rgs10 | -1.6222642 | 0.013254674 |
| Wisp1 | -1.63618 | 0.000674468 |
| Hist1h1a | -1.6408645 | 0.00010791 |
| Dlg3 | -1.6444894 | 0.038467385 |
| Krt19 | -1.6450808 | 0.004714719 |
| Pappa | -1.6741823 | 0.020220736 |
| Cnn1 | -1.6778678 | 0.028766399 |
| Dapp1 | -1.7240331 | 1.26418E-07 |
| Ccnd2 | -1.7249129 | 8.48488E-05 |
| Sdc2 | -1.7252224 | 0.001295174 |
| Slc30a3 | -1.7763864 | 0.020783337 |
| Hist1h2ai | -1.8043194 | 0.048613885 |
| Nrgn | -1.8055743 | 0.009964598 |
| Aif1l | -1.8075623 | 0.000117149 |
| Atp2a3 | -1.8125327 | 2.57553E-06 |
| Rps6kl1 | -1.8244938 | 0.049403296 |
| Gm16982 | -1.848031 | 0.031813334 |
| Tmem62 | -1.8548086 | 0.013302571 |
| Thsd4 | -1.867671 | 0.002237663 |
| Col1a2 | -1.8752501 | 0.000867063 |
| Kcnj2 | -1.8778166 | 0.009381743 |
| Itgb3 | -1.904678 | 1.03962E-06 |

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|---|---|---|
| Snord47 | -1.908005 | 0.035065481 |
| Hist1h4k | -1.9096921 | 0.00594326 |
| Gng7 | -1.9207414 | 0.01967723 |
| Ackr3 | -1.9236598 | 0.001112783 |
| Fam46a | -1.9265152 | 0.007309261 |
| Cdh11 | -1.9347074 | 0.003681232 |
| Acta2 | -1.9431264 | 0.001082949 |
| Igsf11 | -1.9730923 | 0.0032421 |
| Hbb-y | -1.9748359 | 4.58395E-05 |
| Ubxn11 | -1.983615 | 0.006842544 |
| Ikzf2 | -1.9955979 | 8.66601E-16 |
| Epcam | -1.9977628 | 0.010155013 |
| Was | -1.9990616 | 8.50094E-05 |
| Acat3 | -2.0060747 | 0.027344644 |
| Mcoln3 | -2.0135873 | 0.03269587 |
| Hist1h4j | -2.0168569 | 0.037114187 |
| Gli2 | -2.0256238 | 0.001703197 |
| Smyd1 | -2.0480579 | 0.018380174 |
| Pde11a | -2.0583309 | 0.028033733 |
| Map7d2 | -2.0666869 | 0.032464685 |
| Wwc1 | -2.0764389 | 0.000471852 |
| Hba-x | -2.0906682 | 3.15899E-07 |
| Irs2 | -2.0961118 | 5.87776E-20 |
| Pdgfrb | -2.1019287 | 0.007434748 |
| Ptpn13 | -2.1059753 | 4.78986E-08 |
| Nfe2 | -2.1065983 | 4.46548E-08 |
| Smim1 | -2.1151748 | 0.014903031 |
| Fgf10 | -2.1307131 | 1.51684E-05 |
| Wnt4 | -2.1362897 | 0.001401918 |
| Snord15b | -2.157675 | 0.00934557 |
| Sytl5 | -2.1590435 | 0.000440282 |
| Syne4 | -2.1602438 | 0.006038733 |
| Lrp2 | -2.1683193 | 0.000121691 |
| Kcnd3 | -2.1909069 | 0.006903889 |
| Kif26b | -2.2020228 | 0.034731938 |
| Tspan32 | -2.2086198 | 8.02448E-06 |
| Gfi1b | -2.2107003 | 1.69686E-06 |
| Cgn | -2.2139564 | 0.002217795 |
| Chpf | -2.2346358 | 0.021439509 |
| Col12a1 | -2.2377922 | 1.30785E-05 |
| Mir1949 | -2.252971 | 0.006517304 |
| Reep6 | -2.2591005 | 0.000441881 |
| Gucy1a3 | -2.2596713 | 3.05581E-09 |
| Fam110c | -2.2660124 | 0.047497123 |

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|---|---|---|
| Pkd1l3 | -2.2721338 | 0.024648589 |
| Col8a1 | -2.275621 | 0.004586186 |
| Ikzf1 | -2.2786084 | 1.54656E-16 |
| Phlda2 | -2.2808251 | 0.000544414 |
| Sdk2 | -2.3005852 | 0.001789848 |
| Cort | -2.3033757 | 0.043196035 |
| F3 | -2.3463844 | 0.002491942 |
| Ildr2 | -2.3554778 | 0.025410734 |
| Cnksr2 | -2.4145604 | 0.001740874 |
| Adamts3 | -2.4415041 | 1.14347E-16 |
| Slit3 | -2.4443195 | 0.016761722 |
| Ccl17 | -2.4618337 | 0.005656976 |
| Scube2 | -2.4633338 | 1.24981E-05 |
| P2rx1 | -2.4648688 | 4.24094E-06 |
| Plbd1 | -2.4842592 | 0.043805059 |
| Nog | -2.4867721 | 0.030749983 |
| Evx1 | -2.5070756 | 0.00710432 |
| Pard6b | -2.5132174 | 7.02155E-11 |
| Dlk1 | -2.5174664 | 0.011179574 |
| Lypd6 | -2.527006 | 0.012079092 |
| Slc16a10 | -2.5476922 | 1.04806E-05 |
| Igfbp2 | -2.5554076 | 1.85263E-05 |
| Epb4.2 | -2.5598202 | 1.80207E-05 |
| Krt8 | -2.5741038 | 1.01582E-06 |
| Terc | -2.5834174 | 0.019295424 |
| Hoxd1 | -2.621979 | 8.15008E-07 |
| Myl4 | -2.630741 | 0.007701513 |
| 5330426P16Rik | -2.6446846 | 0.028999329 |
| Adamts15 | -2.6619076 | 0.001835464 |
| Klhl34 | -2.6888257 | 0.024330801 |
| Snord65 | -2.6966047 | 0.013699384 |
| Zic3 | -2.7075066 | 0.010077455 |
| Chac1 | -2.7158122 | 0.03425189 |
| Car12 | -2.7161838 | 0.0125579 |
| Runx1 | -2.7256084 | 1.65762E-27 |
| Gpr56 | -2.7306544 | 6.13521E-12 |
| Lypd1 | -2.7503944 | 0.029587149 |
| Bdnf | -2.7569741 | 0.017067973 |
| Cemip | -2.7597959 | 0.009725129 |
| Psd2 | -2.7685594 | 0.040231909 |
| Bhlhe22 | -2.7788676 | 0.045899837 |
| Nkx1-2 | -2.8116603 | 4.82819E-06 |
| Krt18 | -2.8300695 | 1.94958E-05 |
| Fgf15 | -2.8448297 | 0.000744992 |

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|---|---|---|
| Ripk4 | -2.8502852 | 0.035644434 |
| Acta1 | -2.8507773 | 0.006706841 |
| Mfsd2b | -2.8581726 | 3.30438E-10 |
| Hbb-bh1 | -2.8585705 | 2.13735E-10 |
| Nnat | -2.870562 | 0.009436605 |
| 1700024P16Rik | -2.9094172 | 0.046185933 |
| Treml2 | -2.9188545 | 0.016448242 |
| Il18rap | -2.9367721 | 0.025586714 |
| Cdh22 | -2.9609251 | 0.04793262 |
| Lgr5 | -2.9755872 | 4.11712E-26 |
| Rgs4 | -3.045216 | 0.004274047 |
| Bmp8a | -3.0462458 | 0.000513324 |
| Enpp1 | -3.0546272 | 4.11656E-06 |
| Asic4 | -3.0661955 | 0.008931862 |
| Col11a2 | -3.1009018 | 0.026664828 |
| Igfbp5 | -3.1027981 | 5.0016E-11 |
| Scube3 | -3.1383901 | 0.00062887 |
| Crabp2 | -3.2575996 | 0.006155268 |
| Kcnk1 | -3.2686447 | 3.72197E-05 |
| Rpph1 | -3.281995 | 2.1394E-05 |
| Lmod1 | -3.2934985 | 0.027317316 |
| Cacna1d | -3.3339941 | 0.015484623 |
| Dpf3 | -3.3366168 | 0.00736531 |
| Gm14204 | -3.3480536 | 0.003222281 |
| Cdh3 | -3.3515719 | 4.85866E-06 |
| Svep1 | -3.3665107 | 0.024600296 |
| Plac8 | -3.3850148 | 0.035162852 |
| Ppp1r14a | -3.3875344 | 0.02733033 |
| Snord11 | -3.4033326 | 0.03447524 |
| Col2a1 | -3.4043366 | 0.007702911 |
| Krtap5-4 | -3.4274958 | 0.013850109 |
| Tenm4 | -3.4333517 | 0.000392286 |
| Postn | -3.4429613 | 8.23112E-10 |
| Myb | -3.4543925 | 8.33645E-09 |
| Inhba | -3.4548191 | 0.000713988 |
| Tgfb3 | -3.4614945 | 0.004896411 |
| Slc32a1 | -3.4787561 | 0.01146119 |
| Twist2 | -3.486109 | 0.013411972 |
| Vgll3 | -3.5369871 | 4.22616E-07 |
| Actc1 | -3.5579124 | 7.50346E-08 |
| Bnc2 | -3.5880639 | 0.009472726 |
| Reln | -3.6170028 | 3.50005E-25 |
| Krt14 | -3.6405079 | 0.039694071 |
| Sycp2 | -3.6541894 | 0.034731938 |

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|---|---|---|
| Olfr893 | -3.6656714 | 0.044066221 |
| Col1a1 | -3.6976688 | 4.95442E-05 |
| Slc7a8 | -3.7032242 | 5.53584E-19 |
| Snord49b | -3.7060819 | 0.016344227 |
| 5830432E09Rik | -3.7217186 | 0.018434404 |
| Mir3473 | -3.7421314 | 0.043179572 |
| 1700019A02Rik | -3.8088791 | 0.011713162 |
| Loxl1 | -3.8129879 | 0.000497308 |
| Mfap4 | -3.8436132 | 1.62745E-06 |
| Slc14a1 | -3.9021836 | 0.032075036 |
| Ms4a4d | -3.9106388 | 0.009878012 |
| Arpp21 | -3.9845324 | 0.013484556 |
| Tuba8 | -4.0014776 | 0.004465313 |
| B4galnt3 | -4.0405548 | 0.017018905 |
| Mir1188 | -4.0457792 | 0.047141713 |
| Cbln1 | -4.0779217 | 1.74552E-06 |
| Bzrap1 | -4.0941697 | 0.025511069 |
| Mycbpap | -4.1183436 | 0.013319538 |
| Tacstd2 | -4.1381791 | 0.016813797 |
| Mir6516 | -4.1802058 | 0.000180383 |
| Nrip3 | -4.2215567 | 6.59402E-12 |
| Pdzk1ip1 | -4.2568504 | 4.63652E-06 |
| Ajap1 | -4.2816439 | 0.043805059 |
| Ccl3 | -4.4113143 | 0.007390122 |
| Muc13 | -4.4403089 | 4.55768E-05 |
| Cobl | -4.4440277 | 0.012298527 |
| Dlx5 | -4.4620843 | 0.022676496 |
| Col8a2 | -4.5076296 | 0.028016048 |
| D830026I12Rik | -4.542468 | 0.00273577 |
| Smoc2 | -4.5827836 | 0.049940314 |
| Mir6940 | -4.5833125 | 0.020094533 |
| Sema5b | -4.5908909 | 0.000185175 |
| Ndufa4l2 | -4.6090649 | 0.00112525 |
| Slc1a6 | -4.6456547 | 0.001159997 |
| Pgm5 | -4.6485806 | 0.026721458 |
| Gabra4 | -4.7118276 | 0.042610543 |
| Alx3 | -4.8471877 | 0.01150381 |
| A4gnt | -5.1071371 | 0.03788653 |
| Vat1l | -5.1080698 | 0.0032421 |
| Slitrk2 | -5.1635952 | 0.004155895 |
| Pip5kl1 | -5.1675678 | 0.014014826 |
| Mir1940 | -5.2146295 | 0.036533027 |
| Dppa5a | -5.2384808 | 2.24686E-06 |
| Tph1 | -5.285813 | 0.017552353 |

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|---|---|---|
| Bmp7 | -5.3633196 | 0.00053602 |
| Atp6v0d2 | -5.5623301 | 0.000386004 |
| Pitx1 | -5.5980066 | 0.013302571 |
| Olfml1 | -5.6903819 | 0.001273613 |
| Prr15l | -5.7339197 | 0.017886152 |
| BC027072 | -5.7931802 | 0.011830787 |
| Zfp641 | -5.8463841 | 0.048973333 |
| Gata1 | -5.9307033 | 1.14278E-08 |
| Fgf3 | -5.9991188 | 1.15752E-07 |
| Rnase6 | -6.0909008 | 0.04215328 |
| Lum | -6.1112301 | 0.020767104 |
| Vmn2r2 | -6.1502481 | 0.026296039 |
| Atp6v0a4 | -6.270693 | 0.024844203 |
| Clec18a | -6.5983151 | 3.59311E-05 |
| Elfn2 | -6.6897525 | 0.001713009 |
| Cd164l2 | -7.1662694 | 0.003073471 |
| Wfdc17 | -7.1680774 | 0.000253078 |
| Fstl3 | -7.2822667 | 0.001909046 |
| Tmem54 | -7.5876681 | 0.000153509 |
| Orm1 | -7.628743 | 0.000867063 |
| Sema4f | -8.0860262 | 0.002174643 |