

## **RNA-seq analysis of Lgr6<sup>+</sup> stem cells and identification of an Lgr6 isoform**

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### **Abstract**

We studied Lgr6<sup>+</sup> stem cells in experimental UV carcinogenesis in hairless mice. For further characterisation through RNA-seq, these stem cells were isolated by FACS from transgenic hairless mice bearing an *EGFP-Ires-CreERT2* reporter cassette inserted into exon 1 of the *Lgr6* gene (purity confirmed by human *ERT2* expression). Between Lgr6<sup>+</sup> and Lgr6<sup>-</sup> basal cells (Tg/wt) 682 RNAs were differentially expressed, indicating stemness and expression of cancer-related pathways in Lgr6<sup>+</sup> cells. We discovered that suspected ‘Lgr6 null’ mice (Tg/Tg) expressed RNA of an Lgr6 isoform (delta-Lgr6, lacking 74 N-terminal aa) which could be functional and explain the lack of a phenotype.

We investigated the fate of a novel class of  $Lgr6^+$  proliferative stem cells in UV carcinogenesis in hairless mice, a model closely mimicking the development of cutaneous squamous cell carcinoma in man [1]. Using transgenic mice with an *EGFP-Ires-CreERT2* reporter cassette inserted into exon 1 of *Lgr6*, we found - similar to what was found in haired mice [2] - that  $Lgr6^+$  stem cells appeared in large clusters in the interfollicular epidermis (IFE) and in very small clusters in the remnants of hair follicles of hairless mice [3]. Contrary to our expectation, the  $Lgr6^+$  cells dwindled in numbers in the hyperplastic IFE under chronic UV exposure, and did not appear to become tumor-initiating cells (TICs).

**Aim:** As part of this study we aimed to characterize the  $Lgr6^+$  stem cells further starting with RNA-seq analysis. The two main questions we wanted to address were: a) what is the gene expression profile of  $Lgr6^+$  stem cells and is there a unique expression of an alternative, more robustly expressed, (surface) marker for the  $Lgr6^+$  stem cells? And b) what is the status of the *Lgr6* gene in mice homozygous for the *EGFP-Ires-CreERT2* (Tg/Tg) which are supposedly 'Lgr6 null' mice? Despite this defect these mice appear to be healthy without any apparent phenotype.

**Set-up** (detailed Material and Methods in Supplement): Epidermal cell suspensions were obtained by trypsin digestion of skin sheets from dorsum, ventrum and flanks. Basal cells were labelled by anti- $\alpha 6$ -integrin-PE fluorescent conjugated monoclonal antibodies. We separated (green fluorescent)  $Lgr6^+$  from  $Lgr6^-$  basal cells by live-cell FACS (Figure S1). For robust sequencing, extracted RNA of 2 mice of similar age (male and female, both either Tg/wt or Tg/Tg) was pooled. For RNA-seq, pooled RNA samples (450 ng) were processed by an Illumina HiSeq-2000 (Illumina Inc., San Diego, CA, USA).

**Results & Discussion:** RNA-seq showed 682 genes to be differentially expressed (291 up, 391 down) with adjusted p-values (FDR) < 0.05 comparing  $Lgr6^+$  with  $Lgr6^-$  basal (Tg/wt) cells (Table S1 sorted according to FDR). Figure 1a depicts a heat map of the top most

differentially expressed genes (35 up and 35 down). Successful purification of Lgr6<sup>+</sup> basal cells could be confirmed by exclusive expression of *ERT2* (Figure S2), an engineered fragment of human *ESR1* coding for the tamoxifen binding domain. Also, the *Lgr6* expression was much higher in the sorted Lgr6<sup>+</sup> cells, but Lgr6<sup>-</sup> cells were not completely devoid of *Lgr6* transcripts (Figure S3; verified by qPCR). This could be due to stochastic hypermethylation of the promoter of the reporter cassette [3] which could silence *EGFP* expression and thus cause some leakage of expression of the accompanying wt *Lgr6* allele into the sorted Lgr6<sup>-</sup> (Tg/wt) cells. This would evidently affect the contrast in expression between the Lgr6<sup>+</sup> and Lgr6<sup>-</sup> sorted fractions.

As anticipated, the Lgr6<sup>+</sup> samples showed increased expression of several stem cell-related genes (e.g. *Kitl*, *Gas* family members, *Ctgf*) (see Figure 1a), and decreased expression of bulge stem cell markers (e.g. *Tcf4*, *Fzd3*, *Runx1*, *Sox9*, *Tnc*). DAVID and KEGG pathway mapping supported stemness of Lgr6<sup>+</sup> cells by increased expression of genes involved in pluripotency and decreased expression of genes controlling metabolic pathways (Supplementary Table S2). Also, highly significant increased expression of pathways related to cancer, particularly basal cell carcinoma, including the hedgehog pathway, was observed (Supplementary Table S2). In accordance with Lgr6 enhancement of Wnt signaling, several of these ‘Wnt genes’ (e.g. *Wnt7b*, *Lgr6*, *Znrf3*, *Axin2*; the latter verified by qPCR) showed increased expression in Lgr6<sup>+</sup> cells (see Figure 1c). Of Rspo1-4 as ligands of Lgr6, only Rspo3 was found to be expressed in Lgr6<sup>+</sup> and Lgr6<sup>-</sup> cells.

Strikingly, many of the top 35 RNAs with lower expression in the Lgr6<sup>+</sup> vs Lgr6<sup>-</sup> samples were non-coding (15/35). The most strongly differentially expressed protein-coding genes were *Sostdc1* and *Fst* (Figure 1a, arrow heads; down in Lgr6<sup>+</sup>); products of which inhibit signaling of BMPs and TGF-β family members, respectively. Among the top of higher expressed protein-coding genes in Lgr6<sup>+</sup> cells (e.g. *Igfbp3*, *Adam8*, *Nat8l*, *Skint7*, *Crispld2*,

*Adamts14*, *Ngfr*, *Slc2a12*) some may code for robust alternative surface markers of  $Lgr6^+$  stem cells. From scrutiny of [genecard.org](http://genecard.org) and [proteatlas.org](http://proteatlas.org), *Ngfr* (low affinity nerve growth factor receptor) and *Slc2a12* (glucose transporter 12), for example, would appear to be promising candidates: they are membrane-bound and show the anticipated partial to sparse staining of epidermal basal cells (in human skin with antibodies CAB000143 and 001995 for *Ngfr*, HPA031593 for *Slc2a12*). Further research is evidently called for on isolating from human skin cells bearing alternative markers and expressing *LGR6*.

After initial presentation of our work [4], Füllgrabe et al [2] published results on RNA-seq of  $Lgr6^+$  versus  $Lgr6^-$  cells from hair follicles and IFE of haired mice. Surprisingly, they found no distinct expression signature of  $Lgr6^+$  cells, and only differential expression in hair follicles, not in IFE (particularly not for *Lgr6*). Our samples contained mainly  $Lgr6^+$  cells from IFE and did show extensive differential expression. This may simply be attributed to the fact that our samples contained 450 fold more RNA and our read counts were at least 100x higher allowing more reliable quantification of low abundant transcripts and more rigorous statistical testing.

Contrary to expectation [5], RNA-seq results from homozygous knock-in mice (Tg/Tg) showed transcripts of *Lgr6*. These skipped exon 1 (with the knock-in cassette), started in close proximity to exon 2 (see Figure S4) and ran on through exon 18 (confirmed by qPCR, supplementary Table S3 for primers). This coded for an N-terminal truncated protein (delta-*Lgr6*) lacking 74 amino acids compared to full length *Lgr6*. A perfectly matching tryptic peptide (minus the N-terminal methionine) was found in dataset PRDB000032 (proteomicsDB) [6], indicating that the human delta-LGR6 homologue is expressed (see Figure S6) with post-translational removal of the N-terminal methionine. Based on sequence homology with LGR4, critical R-spondin binding residues in the ectodomain of LGR6 (aa 121-263) [7] are completely preserved in delta-LGR6/*Lgr6*. Thus, delta-*Lgr6* could be fully

functional and explain the lack of a phenotype in homozygous knock-in mice (Tg/Tg), suspected 'Lgr6 null' mice. Biological implications of truncated delta-LGR6 need to be explored.

We conclude that the RNA-seq data provided extensive leads on further characterization of Lgr6+ stem cells in the epidermis and on possible switching to expression of a delta-Lgr6 homologue.

### **Acknowledgement**

This research was supported by a grant of the Dutch Cancer Society (UL2010-4812). We thank prof. Hans Clevers and his team for starting us up with the transgenic mice and Heggert Rebel for assistance in performing the experiments. Paul Hensbergen suggested and supported searching the proteomics DB database. Yavuz Ariyurek carried out the RNA-seq.

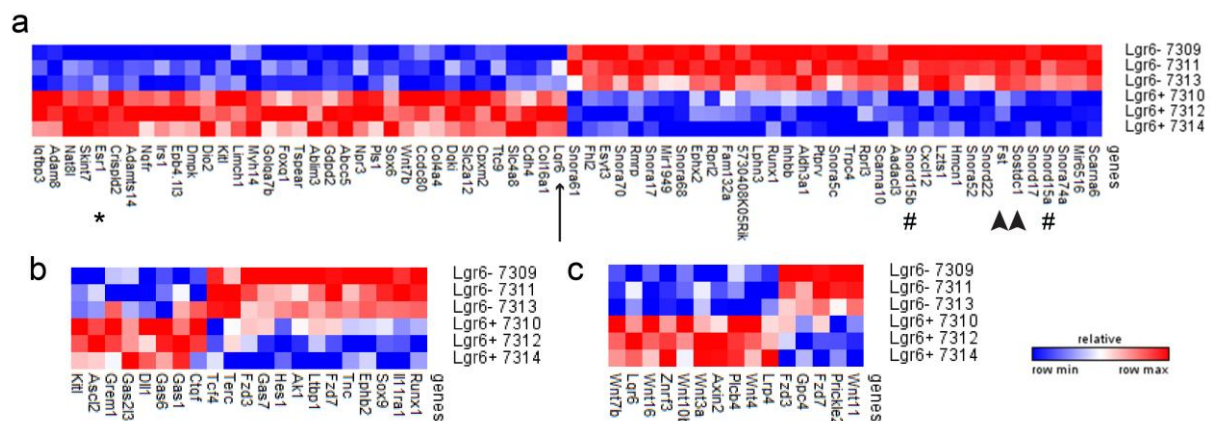
### **Accession Numbers**

RNA-seq data available at <http://www.ebi.ac.uk/ena/data/view/PRJEB15002>

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**Figure 1.** Heatmaps showing differentially expressed genes between Lgr6+ and Lgr6- cells from Tg/wt mice. (a) top 35 up- and downregulated genes (ranked on FDR) (\*=*Esr1*, arrow = *Lgr6*, arrow heads = *Fst* and *Sostdc1*, # = *Snord15a* and *b* non-coding in protein-coding *Rps3* gene, see Fig. S5). (b) shows stem cell-related genes and (c) genes from the Wnt pathway.

**SUPPLEMENTARY INFORMATION part 1 (M&M and Figures)**  
**RNA-seq analysis identifies an Lgr6 isoform and gene expression pattern characterizing adult skin stem cells**

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**MATERIALS AND METHODS**

**Mice**

Lgr6-EGFP-Ires-CreERT2/R26R-LacZ transgenic mice (kindly provided by Prof. Hans Clevers) were backcrossed into a hairless background using Crl:SKH1-HR hairless mice (Charles River, Sulzfeld, Germany). Both homozygous and heterozygous transgenic “Lgr6 mice” were obtained, not showing any phenotypic alterations despite Lgr6 gene disruption. Male and female mice were used in the experiments (see for details supplementary Table S4). They were kept individually in Macrolon type 1 cages at 25 ± 2°C with a humidity of 50% in a 12 hours light-12 hours dark cycle during experiments. Standard chow and tap water were available ad libitum. As legally required, all mouse experiments were performed with the approval of the Leiden University Medical Centers’ ethics committee (approval number DEC 10229) and executed according to EU regulations on animal experiments (Directive 2010/63/EU).

**Cell suspension preparation, antibody labelling and FACS sorting**

Mice were sacrificed by CO<sub>2</sub> asphyxiation, and back and belly skin was removed. The skin sample was incubated epidermal side up in 25 ml PBS containing trypsin (0.25%; T4799, Sigma-Aldrich, St. Louis, MO, USA) + D-glucose (0.1%; G5400, Sigma-Aldrich) over night at 4°C and at 37°C for 15 min. The epidermis was scraped off of the dermis and minced. The epidermis was digested using 8 ml PBS containing trypsin (0.25%) + D-glucose (0.1%) and repeated pipetting. 16 ml PBS with 5% BSA (A9647, Sigma-Aldrich), DNase I (200 Kunitz units/ml; DN25, Sigma-Aldrich) and MgCl<sub>2</sub>·6H<sub>2</sub>O (5mM; M2393, Sigma-Aldrich) was added and the suspension was put through a 70µm cell strainer. The strained cell suspension was incubated for 30 minutes at RT. Cells were spun down and resuspended in 300 µl of supernatant. 8 ml PBS with BSA (1%), DNase I (50 Kunitz units/ml) and MgCl<sub>2</sub>·6H<sub>2</sub>O (5mM) was added, spun down and again resuspended in 300 µl of the supernatant. The volume was brought to 2 ml with PBS containing BSA (0.2%), DNase I (50 Kunitz units/ml) and MgCl<sub>2</sub>·6H<sub>2</sub>O (5mM). Back and belly cell suspensions of the same animal were combined and cell viability and cell numbers were determined.

With this method we mainly isolated Lgr6<sup>+</sup> cells from interfollicular epidermis where they were abundantly present in large EGFP-fluorescent clusters 10, whereas only very few EGFP<sup>+</sup> cells were visible in the hair follicle remnants. For FACS analysis, cell suspensions were stained with anti-α6-integrin-PE conjugated monoclonal antibodies (CD49f clone GoH3,

BD Bioscience, San Jose, CA, USA) for 1 hour at 4°C. Cells were sorted using a FACS Aria III cell sorter (BD Bioscience) on the basis of single cell detection (pulse width), viability/integrity (scatter profile) and both EGFP and PE fluorescence. Sorting of PE+/EGFP+ and PE+/EGFP- cells (Lgr6+ and Lgr6- basal cells, respectively) was accomplished through very strict gating settings as shown in Supplementary Figure S1. Sorted cells were collected in sheath fluid on ice. FlowJo software version 7.2.5 (FlowJo, Ashland, OR, USA) was used to obtain FACS plots of raw data. RNA extraction was performed immediately after each sorting procedure.

### **RNA isolation**

Total RNA from sorted cells was extracted by using RNeasy Mini kit (74106, Qiagen, Hilden, Germany), which included on-column DNase digestion. All samples were eluted in 35 µl of RNase-free water. RNA concentration and purity were determined using a Nanodrop 1000 spectrophotometer (Thermo Fisher Scientific, Wilmington, DE, USA). In addition, integrity of RNA molecules was evaluated by using Agilent RNA 6000 Pico Kit on a 2100 Bioanalyzer (Agilent Technologies, Santa Clara, CA, USA). RNA samples with RIN scores above 8 were used for subsequent RNA-seq sample preparations. RNA isolated from female and male cell suspensions of matched ages (4, 12, 23 weeks) were pooled pairwise; no evident differences in expression profiles.

### **RNA precipitation, library preparation and RNA deep sequencing**

For RNA-seq, eight total RNA samples (450 ng) were processed. These samples were composed of 2 individual mice (a male and a female) bearing the same transgene zygosity. Combined RNA samples were concentrated by ethanol-mediated precipitation and resuspended in 10 µl RNase-free water for library preparation. Eight individual barcoded libraries were made, normalized and pooled to be sequenced in the same run. Library preparation (rRNA depletion by Ribo-zero magnetic kit, Illumina) and paired-end sequencing of 2 times 100 bp were performed by the Leiden Genome Technology Center (LGTC). Sequencing was performed on a Illumina HiSeq-2000 (Illumina Inc., San Diego, CA, USA) following the instructions of the manufacturer.

### **Data processing**

RNA-seq data was processed using bioinformatics pipelines of the Sequence Analysis Support Core (SASC) of our institute, LUMC, according following method. Sequencing adapters in the FastQ files were detected using FastQC version 0.10.1 and removed using the cutadapt tool (version 1.4.2). Base quality trimming was performed using the sickle tool (version 1.200). RNA paired-end reads were aligned to *Mus musculus* (murine) reference genome version mm10. (GSNAP version 2014-05-15; novel splicing flag set to true). The resulting alignment file was compressed, indexed, and name-sorted using samtools tool (version 0.1.19-44428cd). The count table was generated using htseq-count (HTSeq suite version 0.6.1p1). The UCSC genePredToGtf generated RefSeq annotation (raw database dump of the refGene table) was used as a GTF reference.

With this method, we were able to identify differentially expressed coding and (long) non coding transcripts.

### **Detection of differential mRNA and lncRNA expression**

Differential gene expression analysis was performed using edgeR 12 and R/Bioconductor (<https://www.R-project.org/>, <http://www.bioconductor.org>). The TMM method 13 was used to normalize gene counts. We selected statistically significantly differentially expressed genes



based on false discovery rates (FDR) obtained with the Benjamini-Hochberg procedure (correcting for multiple testing).

### **Visualization**

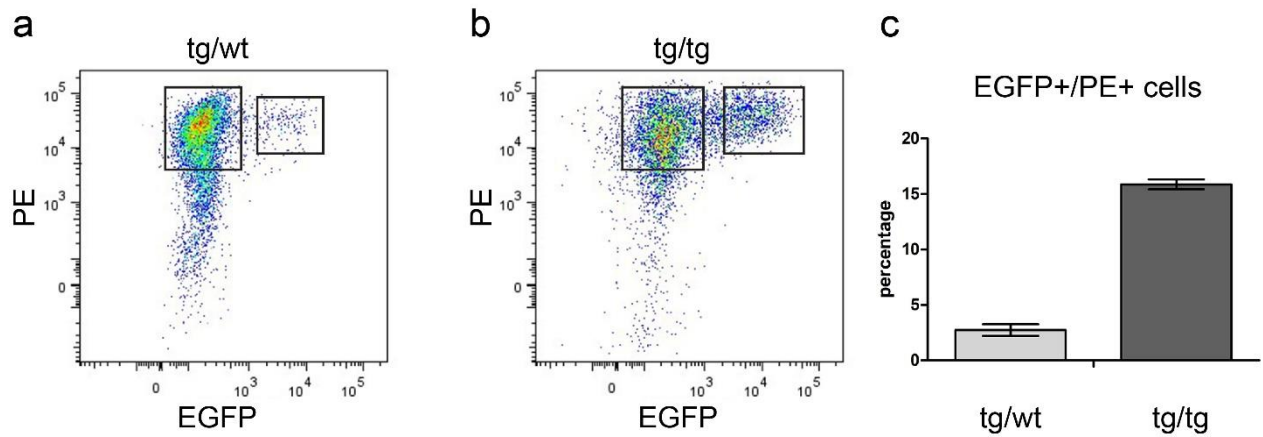
Sequencing results were visualized using the Integrative Genomics Viewer (IGV) 14. Heatmaps depicting log<sub>2</sub> transformed relative differentially expressed genes were created using Gene-E (Broad institute, [www.broadinstitute.org/cancer/software/GENE-E/](http://www.broadinstitute.org/cancer/software/GENE-E/) accessed September 9 2016)

### **Functional gene clustering**

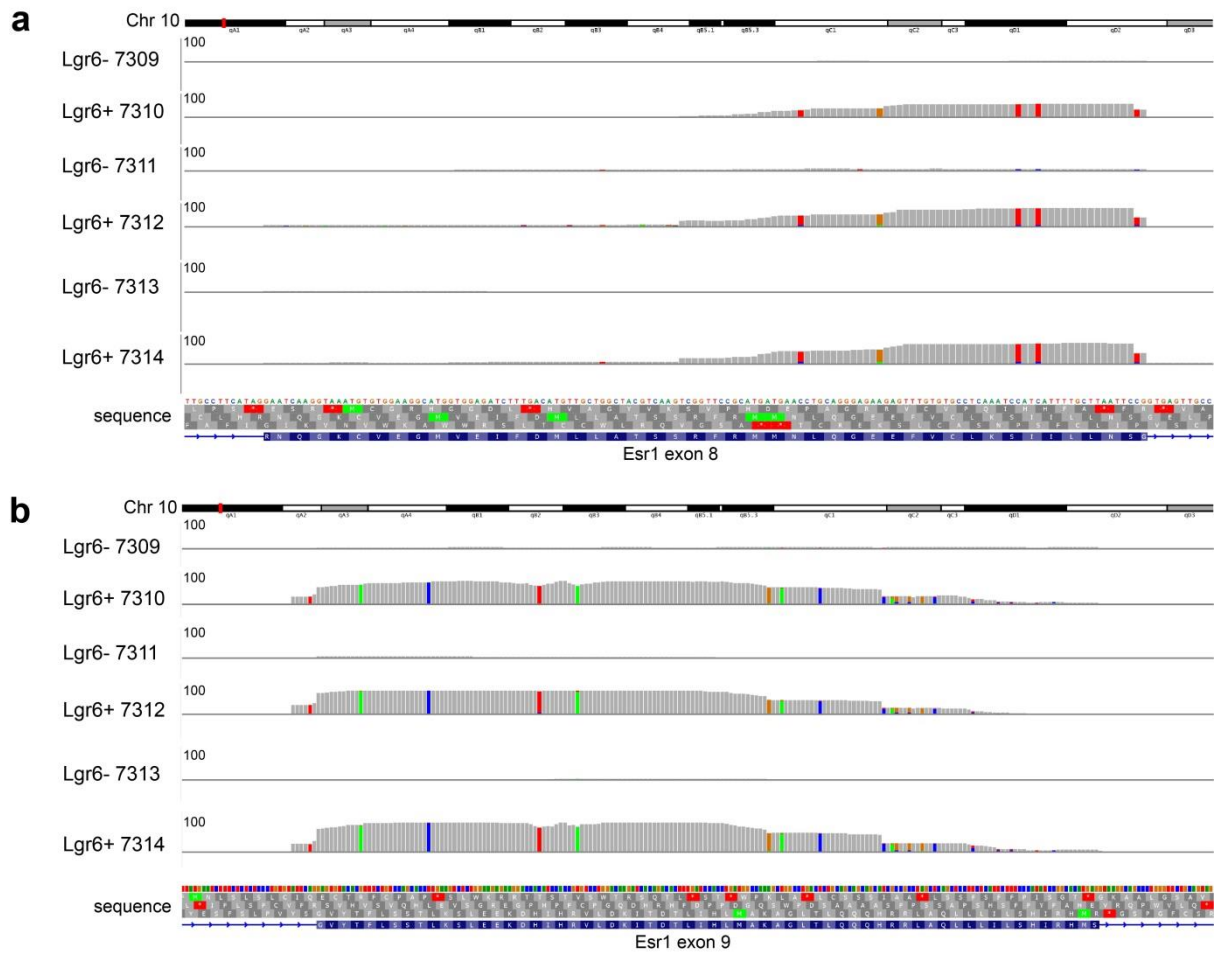
Biochemical pathways were analyzed using the web-based annotation tool DAVID v 6.8 (Database for Annotation, Visualization and Integrated Discovery; 15) to cluster statistically significantly differentially regulated genes by their common functionality. Upregulated and downregulated genes were subjected to DAVID analysis as two separate entities.

### **Reverse transcription and qPCR**

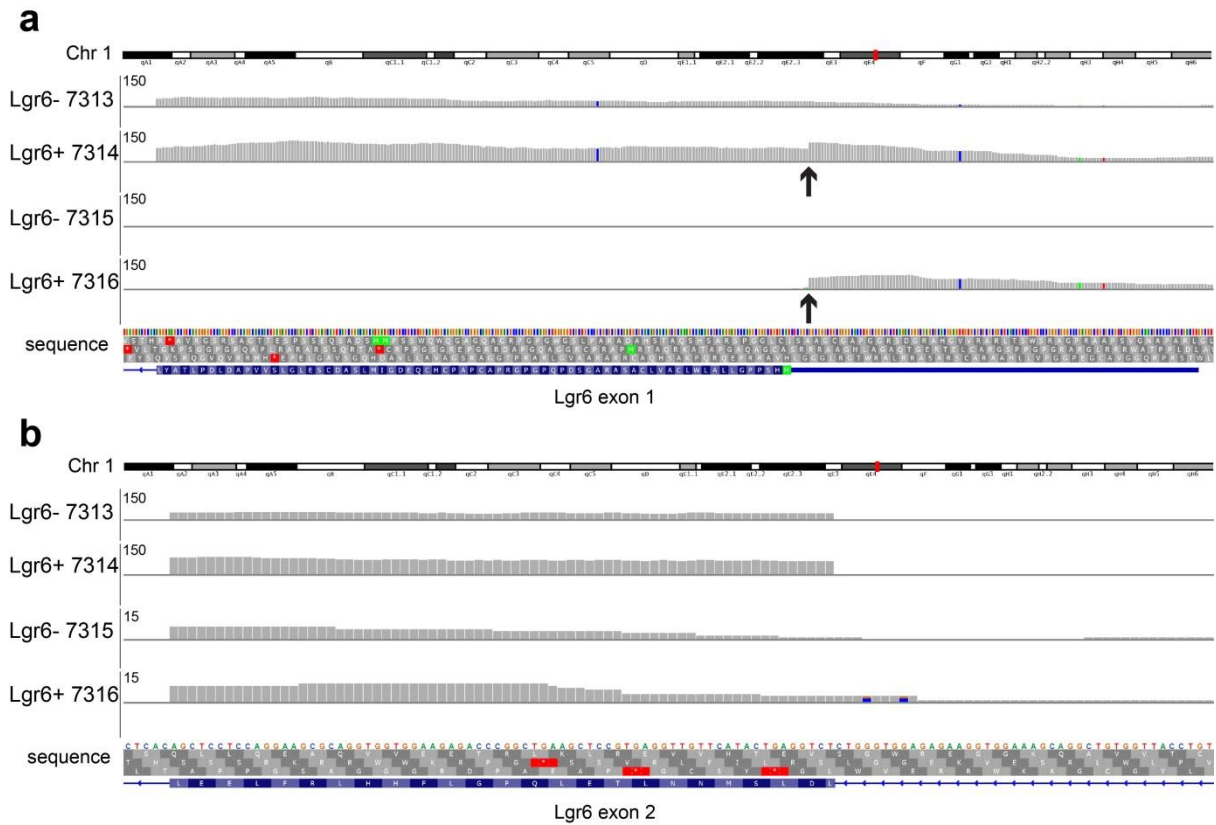
Total RNA was isolated from frozen skin using the RNeasy mini kit (74106, Qiagen, Hilden, Germany) including on-column DNase treatment. cDNA was synthesized from 1 µg total RNA using the iScript™ cDNA Synthesis Kit (170-8891, Biorad, Veenendaal, The Netherlands) according to manufacturer's instructions. qPCR for the different exons of Lgr6 was performed using the SYBR Green Supermix (Bio-Rad) on the CFX384™ real-time PCR detection system (Biorad). Cycle parameters were as follows: Hot start for 3 minutes at 95°C; denaturation for 15 seconds at 95°C, annealing and extension for 30 seconds at 60°C for 40 cycles. Specificity of the PCR products was confirmed by melting curve analysis. Data was normalized against reference genes Cyc1 and Ddx52 (see supplementary Table S3 for primers used) using the  $\Delta\Delta Cq$  method (Livak and Schmittgen, 2001) and is presented as relative mRNA expression (see supplementary figure S4).



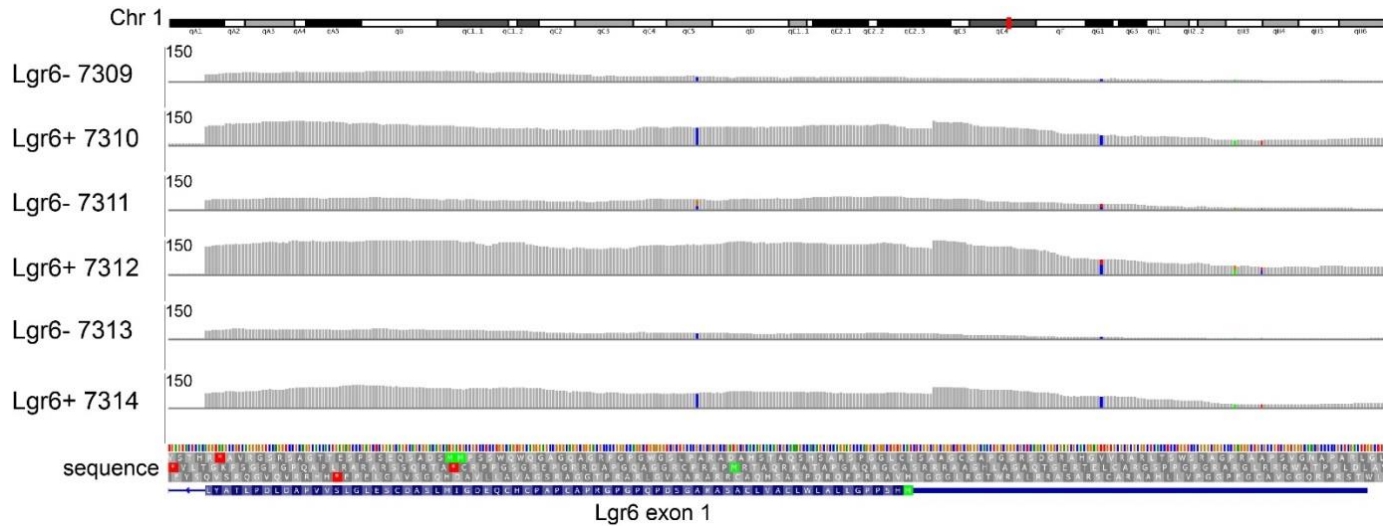
**Figure S1 FACS sorting of Lgr6<sup>+</sup> cells from murine skin** The FACS plots show three main distinguishable areas: apparent Lgr6<sup>+</sup> epidermal stem cells (PE<sup>+</sup>/EGFP<sup>+</sup>), cells that are negative for both markers (PE<sup>-</sup>/EGFP<sup>-</sup>) and basal layer epidermal cells (PE<sup>+</sup>/EGFP<sup>-</sup>); the latter group constituting the largest fraction of cells in suspension. a) FACS sorting of a heterozygous Lgr6<sup>+</sup> knock-in mouse and b) a homozygous Lgr6<sup>+</sup> knock-in mouse c) EGFP<sup>+</sup>/PE<sup>+</sup> cells constitute on average 2.5% and 15% of all cells in suspension in heterozygous and homozygous knock-in animals, respectively. Error Bars: Standard Error, Tg/wt (n=11), Tg/Tg (n=4).



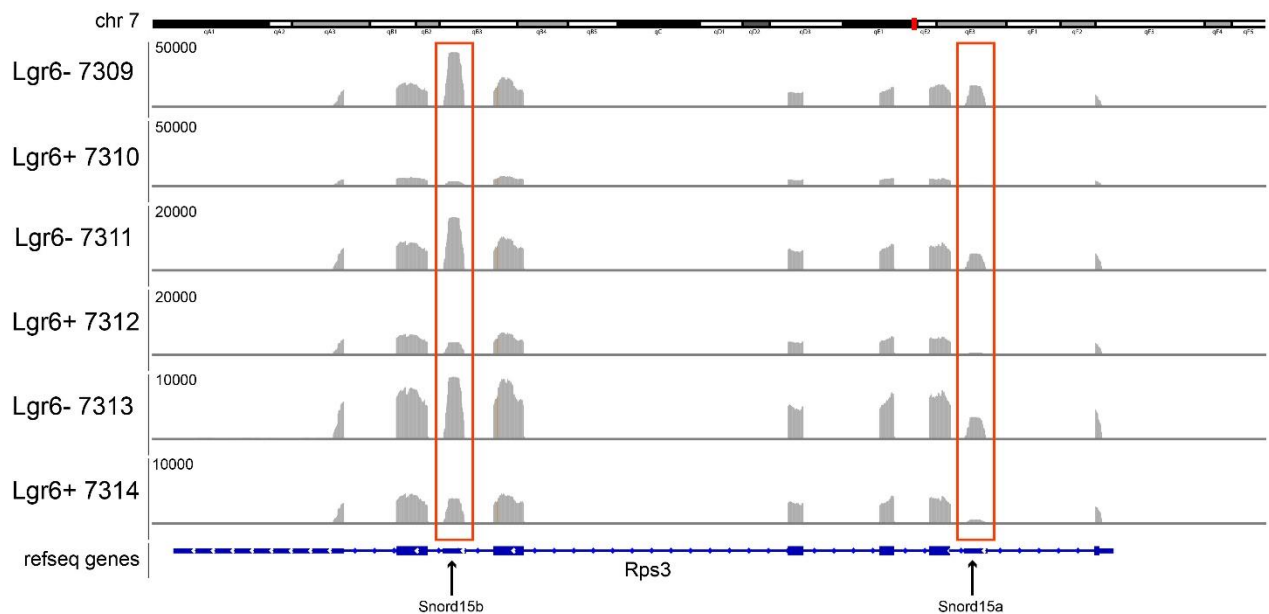
**Figure S2: RNA-seq reads mapped to Exon 8 (chr10: 4969159-4969292; a) and 9 (chr10:4997830-4998013; b) of the Esr1 gene for all heterozygous transgenic samples.** Screenshot from IG viewer of the base counts for both exons are shown (y-axis = 100), for Lgr6+ stem cells (even numbered samples) and for epidermal basal cells (Lgr6–, odd numbered samples). Coloured bars in the cumulative counts mark bases deviant from the reference mouse sequence but in accordance with the human sequence. Lgr6+ stem cells clearly express human ESR1 (present as ERT2 in the EGFP-Ires-CreERT2 cassette) while Lgr6– cells show very low counts mainly from (endogenous) Esr1.



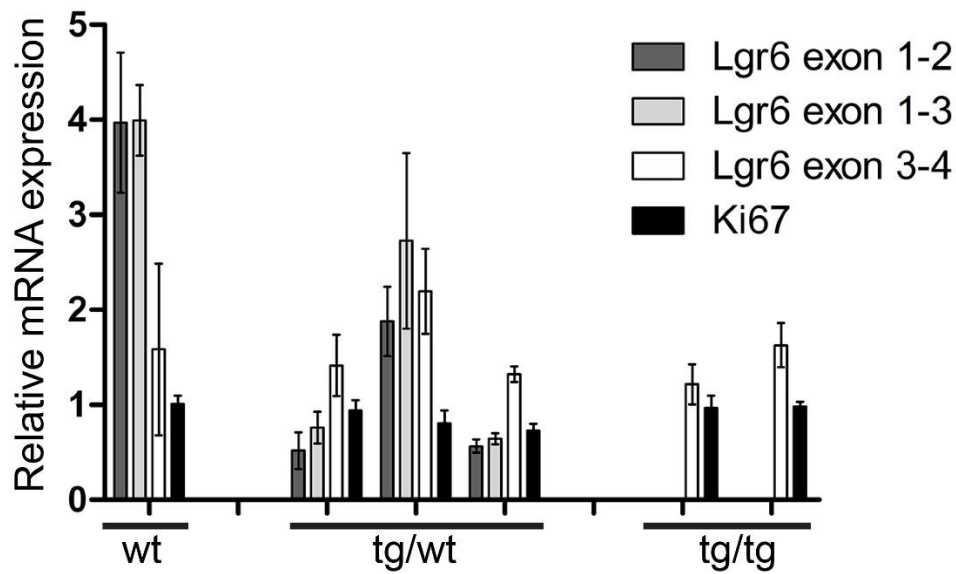
**Figure S3. Lgr6 expression of exon 1 and exon 2 in a heterozygous and a homozygous sample.** Screenshot from IG viewer of the base counts for Lgr6 exon 1 (a) and exon 2 (b) are depicted for epidermal basal cells (Lgr6<sup>-</sup>, odd samples) and for Lgr6<sup>+</sup> stem cells (even samples). Samples 7313 and 7314 are heterozygous and 7315 and 7316 are homozygous transgenic. The arrow (a) shows the position where the cassette (EGFP-Ires-CreERT2) is inserted. This results in no transcription of exon 1 in the homozygous sample. In the homozygous sample transcription starts in close proximity to exon 2 (b).



**Figure S4. IGV visualization of reads aligned to Exon 1 of the *Lgr6* gene for all heterozygous transgenic samples.** Read count for *Lgr6* exon 1 is shown (y-axis = 150) for epidermal basal cells (*Lgr6*<sup>-</sup>, odd samples) and *Lgr6*<sup>+</sup> stem cells (even samples). *Lgr6*<sup>+</sup> stem cells express higher counts (also after normalization), however the *Lgr6*<sup>-</sup> samples are not completely negative for *Lgr6*.



**Figure S5. IGV screenshot of (m)RNA expression corresponding to the region encoding the *Rps3* gene (including *Snord15a* and *Snord15b*) for all heterozygous transgenic samples.** The counts for the *Rps3* gene, *Snord15a* and *Snord15b* are represented (y-axis, values vary), for the epidermal basal cells (*Lgr6*<sup>-</sup>, odd numbering) and for the *Lgr6*<sup>+</sup> stem cells (even numbering). The *Lgr6*<sup>+</sup> cells show lower counts for *Rps3* compared to the *Lgr6*<sup>-</sup> cells. *Snord15a* and *Snord15b* are even more prominently downregulated in *Lgr6*<sup>+</sup> cells (see red boxes and arrows).



**Figure S6. Relative mRNA expression of *Lgr6* in hairless mice.** Gene expression of *Lgr6* and *Ki67* was measured by qPCR and normalized against stably expressed reference genes (see Methods above and Supplementary table S3 for used primers). RNA was isolated from SKH-1 mice (wt), heterozygous *Lgr6-EGFP-Ires-CreERT2/R26R-LacZ* mice (Tg/wt) and homozygous *Lgr6-EGFP-Ires-CreERT2/R26R-LacZ* mice (Tg/Tg). *Lgr6* gene expression was measured using different primer pairs. The primer pairs for exon 1-2 and exon 1-3 detect expression of the wt *Lgr6* allele, the primers for exon 3-4 detect expression of the wt allele and the alternative transcript. In homozygous *Lgr6-EGFP-Ires-CreERT2/R26R-LacZ* mice expression of exon 1-2 and exon 1-3 is not detected at all, however expression of *Lgr6* exon 3-4 was found. Error bars are SEMs.

**SUPPLEMENTARY INFORMATION Part 2**  
**RNA-seq analysis identifies an Lgr6 isoform and gene expression pattern characterizing adult skin stem cells**

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**Supplementary Table S1 All upregulated (a) and downregulated (b) genes in Lgr6<sup>+</sup> basal epidermal keratinocytes (FDR <0.05).**

**a. upregulated cells in Lgr6<sup>+</sup> cells**

genes	logFC	logCPM	LR	PValue	FDR	S7309	S7311	S7313	S7310	S7312	S7314
Igfbp3	1.7449e+00	9.54690426	72.978	1.31E-17	1.71E-14	324.1	403.13	304	1305.4	1300.2	850.83
Adam8	1.2265e+00	7.08857733	68.619	1.19E-16	1.31E-13	83.817	77.296	83.216	214.35	196.17	161.29
Nat8l	1.4536e+00	5.08290211	64.432	9.99E-16	9.08E-13	14.311	21.148	19.067	42.709	52.784	53.034
Esr1	2.2224e+00	3.66258455	62.661	2.46E-15	2.07E-12	3.1384	4.1264	6.3258	16.389	24.489	21.389
Skint7	1.1538e+00	6.89963398	62.646	2.47E-15	2.07E-12	64.024	82.012	76.177	154.93	165.88	172.95
Crispld2	1.1386e+00	5.18984284	61.572	4.27E-15	3.3E-12	21.258	22.99	24.145	53.043	48.977	48.125
Adamts14	1.1792e+00	7.04431775	59.966	9.65E-15	6.5E-12	69.045	84.665	89.007	165.02	203.61	180.23
Ngfr	1.4180e+00	5.25109094	49.561	1.92E-12	7.87E-10	19.207	23.948	18.977	55.546	70.264	40.148
Irs1	1.7518e+00	4.75758712	48.582	3.17E-12	1.23E-09	9.7082	17.463	9.9788	36.169	54.602	34.1
Epb4.1l3	1.2735e+00	4.92353235	48.021	4.22E-12	1.55E-09	16.655	19.6	16.928	45.292	49.583	33.574
Dmpk	1.6867e+00	4.08939534	46.435	9.47E-12	3.3E-09	6.4861	9.7265	8.0187	23.009	34.526	20.074
Dio2	1.3821e+00	5.05977374	45.085	1.89E-11	6.16E-09	15.525	16.211	23.878	40.045	44.304	59.872
Kitl	1.9530e+00	3.56224904	40.66	1.81E-10	5.11E-08	3.4313	5.7475	5.4349	25.432	18.431	12.097
Limch1	1.1370e+00	6.23916695	39.96	2.59E-10	7.12E-08	54.023	35.443	51.943	121.34	89.214	100.72
Myh14	8.7376e-01	6.19157637	39.737	2.91E-10	7.78E-08	57.705	48.632	48.023	92.684	92.33	98.53
Golga7b	1.8483e+00	4.95680827	36.684	1.39E-09	3.45E-07	9.7919	18.79	11.939	41.094	74.244	30.243
Foxq1	1.2222e+00	5.14092325	36.576	1.47E-09	3.57E-07	18.705	24.169	20.581	38.511	65.332	44.005
Tspear	1.6016e+00	3.90722155	36.229	1.75E-09	4.16E-07	6.0676	9.3581	6.8604	19.942	30.805	16.655
Ablim3	1.2686e+00	3.97220759	35.692	2.31E-09	5.25E-07	9.2479	8.6949	9.5333	19.861	19.037	27.35
Gdpd2	8.9909e-01	6.43633925	33.716	6.38E-09	1.33E-06	55.069	62.633	63.615	93.733	131.53	112.56
Abcc5	8.2111e-01	8.15482089	32.282	1.33E-08	2.63E-06	195.84	205.51	216.59	334.32	376.41	380.79
Npr3	1.5884e+00	3.25043551	32.221	1.38E-08	2.66E-06	4.5193	6.1896	3.3857	15.501	16.095	10.957
Pls1	1.3763e+00	3.71877907	31.88	1.64E-08	3.14E-06	6.5279	7.2949	8.1078	20.91	22.325	13.412
Sox6	9.7095e-01	6.96172020	31.497	2E-08	3.76E-06	70.008	82.159	100.59	142.17	154.98	197.59
Wnt7b	7.8482e-01	7.13482732	31.014	2.56E-08	4.78E-06	109.09	103.31	96.937	198.37	173.24	161.64
Ccdc80	1.4790e+00	3.70009250	30.74	2.95E-08	5.45E-06	8.3691	6.4843	5.4349	23.817	20.248	13.061
Col4a4	4.0657e+00	0.26775538	30.705	3E-08	5.5E-06	0.16738	0.073686	0.089096	4.1175	1.298	0.96426

Dgki	1.4240e+00	3.53588907	30.476	3.38E-08	6.11E-06	4.8123	8.1054	5.9694	17.439	19.383	13.5
Slc2a12	7.3833e-01	7.03039310	29.801	4.79E-08	8.19E-06	95.869	104.93	92.927	170.19	165.19	154.63
Cpxm2	7.7072e-01	6.28348319	29.56	5.42E-08	9.2E-06	61.681	53.496	57.2	109.96	91.032	93.358
Ttc9	1.1428e+00	4.00585268	28.475	9.49E-08	1.54E-05	9.8756	12.011	7.9296	21.314	25.354	19.373
Slc4a8	1.0628e+00	4.29885682	28.005	1.21E-07	1.93E-05	11.173	12.084	14.968	22.283	25.44	31.733
Cdh4	1.2123e+00	4.03202647	27.818	1.33E-07	2.08E-05	8.7039	9.2844	11.583	16.389	25.354	26.473
Col16a1	8.5712e-01	8.92759674	27.778	1.36E-07	2.11E-05	298.69	346.84	393.72	607.85	691.91	582.15
Lgr6	1.1048e+00	6.69144306	27.321	1.72E-07	2.61E-05	45.11	85.254	66.555	117.07	171.94	133.86
Phldb1	8.4835e-01	7.33632062	27.085	1.95E-07	2.93E-05	108.8	125.56	111.73	218.23	240.47	164.27
Ripply3	1.2454e+00	3.30258336	26.827	2.23E-07	3.3E-05	5.5655	5.8212	6.0585	14.048	15.922	11.308
Man1c1	1.1500e+00	5.94092811	26.389	2.79E-07	3.99E-05	23.978	44.211	46.508	65.476	97.608	90.553
Slc16a9	8.4731e-01	5.68169457	26.164	3.14E-07	4.43E-05	37.368	39.495	32.876	77.425	68.187	51.982
Ror1	1.3467e+00	3.85508008	25.794	3.8E-07	5.29E-05	7.2393	8.4738	8.7314	21.556	27.431	12.974
Col4a2	1.7095e+00	4.89805970	25.041	5.61E-07	7.56E-05	14.813	18.421	8.4641	56.595	59.361	20.775
Mmp28	6.7536e-01	6.59461898	24.832	6.26E-07	8.17E-05	66.2	75.749	81.345	115.29	119.33	121.41
Il12rb2	1.3919e+00	5.55491878	24.352	8.03E-07	0.000102	19.96	33.527	24.323	35.2	83.849	84.942
Abca4	1.8840e+00	1.19371517	24.302	8.24E-07	0.000104	0.83691	1.1053	0.89096	3.5523	3.8939	2.9804
Il20ra	7.3658e-01	7.69178939	23.334	1.36E-06	0.000165	137.21	168.52	159.48	224.85	284.34	265.61
Wnk2	7.5118e-01	6.83668084	23.206	1.46E-06	0.000175	80.093	95.644	79.652	120.46	165.36	144.03
Sntb2	6.8741e-01	5.81609181	22.999	1.62E-06	0.000192	39.879	43.548	45.974	61.036	70.697	76.352
Ccr4	9.9612e-01	3.66020631	22.93	1.68E-06	0.000198	9.1642	8.0317	7.8405	16.954	17.133	16.129
Crlf1	1.0861e+00	3.49677431	22.813	1.79E-06	0.00021	6.4442	6.558	8.6423	14.532	14.537	16.568
Nrp1	2.2311e+00	0.64570913	22.781	1.82E-06	0.000211	0.66953	0.36843	0.44548	2.9065	1.5576	2.8928
Xkr4	1.9450e+00	1.30727523	22.72	1.87E-06	0.000216	0.79507	1.5474	0.62367	4.1982	3.8939	3.3311
Lifr	7.1906e-01	7.10811403	22.677	1.92E-06	0.00022	113.74	104.93	93.729	183.11	144.34	187.24
Hsd3b7	7.5553e-01	4.97919105	22.507	2.09E-06	0.000236	20.672	24.906	24.769	36.573	39.286	42.515
Cysltr1	8.4317e-01	4.84837245	22.456	2.15E-06	0.000241	19.667	22.843	19.156	39.076	41.708	29.804
Wnt16	1.0968e+00	3.63043845	22.144	2.53E-06	0.000276	8.8713	7.2949	7.2168	20.103	16.614	13.587
Antxr1	6.9221e-01	8.14070762	22.14	2.53E-06	0.000276	203.62	219.44	224.17	309.94	364.39	371.24
Frmd4a	6.1125e-01	6.15764326	22.08	2.61E-06	0.000279	57.831	56.591	54.705	83.076	89.301	86.17
Phospho1	7.3031e-01	5.08024485	22.077	2.62E-06	0.000279	23.266	27.632	25.303	37.38	44.045	44.794
Zfp652	7.0529e-01	5.92200264	22.077	2.62E-06	0.000279	40.256	47.601	50.428	64.507	75.715	84.767
Ackr2	9.7986e-01	3.63668600	21.536	3.47E-06	0.000363	7.867	8.5475	8.5532	17.842	14.883	16.392
Igfbp7	9.7521e-01	4.36109562	21.331	3.86E-06	0.000401	10.629	12.969	18.087	30.679	24.402	26.123
Csrp2	1.3611e+00	2.97995669	20.822	5.04E-06	0.000518	3.0547	4.0527	6.2367	10.011	12.547	11.133
Znrf3	6.1328e-01	6.42678877	20.763	5.2E-06	0.000532	65.991	69.412	68.426	95.187	105.05	111.5
Camkk1	6.1839e-01	6.49327360	20.598	5.66E-06	0.000574	74.192	63.443	75.286	108.18	102.89	115.89
Shisa2	3.2563e+00	-0.51527234	20.527	5.88E-06	0.000593	0.041846	0.22106	0.089096	1.6147	1.1249	0.52596
Ikbke	5.9542e-01	6.51311568	20.465	6.07E-06	0.00061	69.506	74.349	74.217	101.65	111.89	115.8
Wipf3	1.4521e+00	2.15401507	20.153	7.15E-06	0.00069	2.2597	2.3579	2.4056	6.1359	5.1919	7.8894
Phka1	9.6263e-01	3.93234595	20.14	7.2E-06	0.00069	8.2018	11.2	11.672	17.52	22.152	20.425
Slc24a3	6.1925e-01	6.75810442	20.138	7.21E-06	0.00069	76.285	87.023	92.749	126.51	127.72	138.59
Col7a1	8.5312e-01	10.54820699	20.052	7.54E-06	0.000712	918.05	1128.3	1155	1852.8	2286.3	1643.3
4930412013Rik	6.9537e-01	5.13390235	19.979	7.83E-06	0.000737	25.777	27.632	26.818	38.107	49.669	42.077
Adrb1	1.4360e+00	3.65018024	19.498	1.01E-05	0.000927	4.9378	9.7265	5.6131	16.631	26.306	11.746



Cecr2	5.6707e-01	6.50847162	19.432	1.04E-05	0.000955	69.757	75.896	74.306	108.91	110.24	106.51
Mcc	6.5736e-01	7.59899258	19.404	1.06E-05	0.000965	167.76	156.21	126.87	237.28	242.9	231.51
Ctsl	7.8874e-01	5.51114432	19.249	1.15E-05	0.001029	35.36	31.98	32.698	73.792	54.602	44.531
Fras1	1.1795e+00	3.90031323	19.231	1.16E-05	0.001029	7.7415	6.6317	13.097	16.631	19.297	25.86
Golm1	1.5419e+00	2.71877841	18.882	1.39E-05	0.00121	2.9292	1.9158	5.2567	7.912	9.0859	12.097
Zfp503	8.2471e-01	5.44986683	18.865	1.4E-05	0.001216	23.183	37.58	33.946	52.074	65.678	49.352
Fuk	6.8438e-01	5.02160783	18.415	1.78E-05	0.001484	22.471	25.053	27.174	44.808	37.814	36.992
Col4a6	6.8641e-01	7.81764797	18.362	1.83E-05	0.001508	179.56	181.27	157.61	315.43	293.34	225.72
Lonrf3	9.4918e-01	4.70171198	18.325	1.86E-05	0.001522	13.935	16.506	22.898	27.288	32.276	42.866
Unc5b	5.9891e-01	6.02849452	18.287	1.9E-05	0.001544	45.821	51.506	58.447	82.188	75.369	77.754
Parppb	6.9086e-01	4.56167220	18.24	1.95E-05	0.001577	17.324	18.937	17.73	28.742	29.767	28.577
Slc27a3	7.5655e-01	8.08341986	18.221	1.97E-05	0.00158	163.83	233.51	207.77	350.79	391.47	279.55
Gpr64	8.2704e-01	4.16405476	18.016	2.19E-05	0.001733	14.604	13.411	10.335	24.705	22.239	21.564
Mef2a	6.5677e-01	7.21137745	17.946	2.27E-05	0.001777	97.626	118.93	128.57	161.31	178	204.25
Fam124b	3.0533e+00	-0.52336618	17.914	2.31E-05	0.001801	0.12554	0.22106	0	0.88809	1.8172	0.52596
Slc6a2	5.7604e-01	6.62445403	17.811	2.44E-05	0.001888	73.104	77.444	87.047	108.67	118.12	127.02
Trim47	6.0338e-01	6.58076592	17.747	2.52E-05	0.001938	66.158	77.886	83.929	108.02	110.76	127.02
Pbxip1	6.9589e-01	4.36990954	17.559	2.79E-05	0.002116	16.194	14.59	16.305	25.997	25.787	24.545
Col4a3	2.8084e+00	-0.05119185	17.455	2.94E-05	0.002218	0.33477	0.14737	0.089096	2.5835	1.471	0.52596
Wnt10b	1.0340e+00	3.89566953	17.437	2.97E-05	0.002232	10.671	10.316	8.0187	26.4	19.037	14.201
Ccng2	6.5757e-01	6.72863785	17.418	3E-05	0.002245	72.184	86.802	87.849	134.18	148.49	106.24
Cgnl1	2.5474e+00	0.26010348	17.386	3.05E-05	0.002276	0.37661	0.44211	0.089096	2.9872	1.9902	0.70128
Lama3	6.7165e-01	9.52688963	17.301	3.19E-05	0.002372	555.04	523.9	627.95	915.05	835.99	967.68
Afap111	1.2588e+00	2.72702413	17.271	3.24E-05	0.0024	2.8455	3.4632	5.4349	8.5579	9.7781	9.2919
Il22ra2	8.4908e-01	5.15336899	17.226	3.32E-05	0.00245	22.053	30.874	23.165	49.329	55.034	32.522
Psd3	5.7179e-01	6.22525551	17.178	3.4E-05	0.002502	61.597	59.096	59.516	82.592	85.58	99.844
Kdm5d	6.1870e-01	5.61600627	17.122	3.51E-05	0.002561	33.853	44.506	37.599	59.825	61.957	55.927
Trpc1	1.1107e+00	2.81462252	17.116	3.52E-05	0.002561	3.6406	4.4211	5.2567	9.3653	8.9128	10.169
Trim7	5.3833e-01	6.34188361	17.115	3.52E-05	0.002561	67.079	66.022	65.04	96.478	92.676	98.705
Ascl2	1.0205e+00	3.98287384	17.09	3.57E-05	0.002586	7.6159	12.748	10.959	21.718	25.613	15.779
Abcg1	5.7557e-01	5.63826626	16.992	3.75E-05	0.002704	36.615	40.527	42.766	55.788	60.572	61.975
Clu	9.0713e-01	4.68481688	16.961	3.81E-05	0.002738	21.676	18.79	12.741	39.722	34.699	25.947
Serpib2	6.7229e-01	8.71554538	16.855	4.03E-05	0.002885	290.28	300.78	381.42	579.11	478.52	491.6
Adck3	6.6179e-01	4.89576341	16.793	4.17E-05	0.002971	21.592	23.285	24.145	34.151	34.007	40.849
Il33	7.2241e-01	6.37327574	16.775	4.21E-05	0.00299	70.384	52.022	64.951	129.66	89.993	89.676
Ttc3	6.3101e-01	8.16291162	16.663	4.46E-05	0.00315	215.25	212.88	246.44	323.34	320.34	400.78
Pgm5	1.6585e+00	1.68268612	16.627	4.55E-05	0.003189	1.0043	1.9158	1.6928	2.9872	5.538	5.7855
Ccdc17	9.3177e-01	3.56787295	16.604	4.61E-05	0.003218	7.6578	9.6528	6.9495	13.241	16.355	16.743
Plcd2	7.7138e-01	4.10812856	16.552	4.73E-05	0.003295	13.809	12.821	11.226	21.072	23.71	20.162
Papln	6.2690e-01	6.07116605	16.482	4.91E-05	0.003407	44.9	56.001	57.645	68.948	88.349	87.046
Pdgfb	7.3172e-01	5.42533089	16.419	5.08E-05	0.003512	23.894	39.127	33.946	52.881	58.063	49.44
Rapgef4	8.6696e-01	4.25236975	16.379	5.19E-05	0.003574	10.001	15.474	15.057	28.661	21.806	22.879
Aknad1	9.5365e-01	3.83744680	16.316	5.36E-05	0.003683	8.0762	8.916	12.206	22.283	14.883	18.935
Enthd2	5.7019e-01	5.49777193	16.265	5.51E-05	0.003772	33.853	38.906	36.173	49.733	56.159	55.664
Cbr2	6.8320e-01	4.91730926	16.075	6.09E-05	0.004141	22.053	23.211	24.145	36.734	43.439	31.119

Cxcl14	7.9693e-01	6.48567631	16.002	6.33E-05	0.004291	62.015	79.728	54.438	124.57	136.89	79.42
Th	2.9242e+00	-1.0237201	15.857	6.83E-05	0.004573	0.083691	0.073686	0.089096	0.40368	0.86532	0.78894
Bcar3	6.1300e-01	5.24545962	15.81	7E-05	0.004643	31.635	29.916	28.065	51.186	46.208	39.885
Cpe	6.6499e-01	6.74590095	15.743	7.25E-05	0.004779	68.418	74.201	106.56	129.74	132.83	131.75
Sema3e	2.9131e+00	0.51471081	15.662	7.57E-05	0.004972	0.41846	0.36843	0.089096	4.7634	1.9037	0.4383
Grem1	3.0035e+00	-0.46575827	15.643	7.65E-05	0.004979	0.25107	0.073686	0	1.7762	1.2114	0.35064
Mrgprd	5.2808e+00	-1.77957399	15.643	7.65E-05	0.004979	0	0	0	0.48441	0.086532	0.4383
Abcb1b	6.7692e-01	5.73660233	15.5	8.25E-05	0.005335	36.029	34.19	52.923	61.682	64.034	70.566
Mafa	1.5517e+00	2.54288016	15.47	8.38E-05	0.005402	1.4646	3.3159	4.1875	7.6698	11.682	6.3992
Als2cl	6.6757e-01	8.17556771	15.216	9.59E-05	0.006035	199.35	211.18	259.63	300.58	342.58	420.94
Npr1	1.6176e+00	0.86709864	15.215	9.59E-05	0.006035	0.96245	0.73686	0.80187	3.3101	2.5094	2.0162
Raph1	5.4849e-01	6.64636641	15.179	9.78E-05	0.006115	81.85	78.549	83.394	110.2	108.86	137.54
Gpr116	2.0726e+00	0.18133361	15.066	0.000104	0.006437	0.54399	0.22106	0.35638	2.3413	1.8172	0.8766
Arhgef28	5.2405e-01	5.95698395	15.065	0.000104	0.006437	52.516	48.19	51.854	76.375	65.159	77.93
Ccna1	2.2580e+00	-0.48461602	15.042	0.000105	0.006496	0.20923	0.22106	0.17819	1.3725	0.77879	0.8766
Kcnip3	9.4433e-01	3.21716917	15.019	0.000106	0.006539	5.1889	7.2212	6.5931	12.352	12.807	11.133
Rhbd1	9.1382e-01	3.52495792	14.991	0.000108	0.006597	7.1556	9.0633	7.5732	13.16	18.345	13.237
Hs3st3a1	2.5340e+00	-0.330613	14.959	0.00011	0.006691	0.083691	0.073686	0.53458	0.72662	1.471	1.4026
Ankrd6	1.3524e+00	2.50861642	14.76	0.000122	0.007287	2.7618	2.9474	3.8311	5.8129	6.4034	12.009
Dnah8	7.2306e-01	4.77615668	14.739	0.000123	0.007346	19.416	19.306	23.165	28.661	30.892	42.427
Fgfr3	6.5852e-01	9.13775294	14.73	0.000124	0.00736	357.74	447.71	505.35	634.25	676.85	757.38
Rgs11	1.0329e+00	3.23480725	14.661	0.000129	0.00755	5.6492	4.7159	8.1078	10.98	11.509	15.077
Mfsd7b	5.4072e-01	5.85321068	14.609	0.000132	0.007718	41.846	48.632	50.785	76.133	62.043	66.797
2010016118Rik	1.2267e+00	2.45777619	14.552	0.000136	0.007899	2.3434	4.3474	3.1184	6.6203	8.3071	7.8017
Wnt3a	6.8910e-01	5.27551980	14.513	0.000139	0.008007	23.266	33.895	31.807	39.399	51.919	51.632
Slc12a4	5.1466e-01	7.41082967	14.498	0.00014	0.00805	139.93	135.88	144.34	200.87	191.75	207.58
Espl1	5.3674e-01	5.49909252	14.431	0.000145	0.008319	36.908	35.59	37.955	49.248	52.092	58.907
Klf12	1.3271e+00	2.23905763	14.396	0.000148	0.008408	2.8037	3.0948	1.9601	6.1359	4.8458	8.9413
Ddx3y	6.6155e-01	6.95732646	14.38	0.000149	0.008456	72.519	105.81	110.57	161.63	163.63	130.96
Adcy6	5.3063e-01	5.67828870	14.326	0.000154	0.008675	37.787	42.738	45.083	58.452	57.89	64.693
Fgfr2	5.8601e-01	9.18049115	14.212	0.000163	0.009095	425.28	503.57	462.94	651.61	743.4	694
Itga2	5.2405e-01	5.88092573	14.204	0.000164	0.00911	45.905	46.938	52.032	67.495	62.476	78.105
Slc16a3	1.2784e+00	3.60007701	14.171	0.000167	0.009205	4.1427	5.8948	11.315	16.712	12.201	22.266
Ccdc3	7.0845e-01	7.83788994	14.165	0.000167	0.009205	183.08	193.2	144.51	334.65	308.05	208.54
Lamc2	5.5791e-01	8.90939350	14.117	0.000172	0.009397	387.87	361.06	417.86	579.35	548.61	589.6
Gas2l3	6.3623e-01	5.38942546	14.111	0.000172	0.009397	36.699	26.379	35.015	46.746	46.727	59.258
Tgm7	1.5354e+00	2.44061092	14.04	0.000179	0.009734	2.4689	4.0527	1.6928	5.3285	12.461	6.1362
Zfr2	7.2175e-01	4.05350636	14.029	0.00018	0.009746	10.964	13.779	12.741	18.488	22.325	20.775
Ttc14	5.6735e-01	7.28176623	14.027	0.00018	0.009746	112.77	141.11	122.15	160.82	204.39	191.8
Axin2	5.2398e-01	7.07264361	13.978	0.000185	0.009933	107.33	115.61	108.07	138.86	169.17	167.96
Foxp1	7.0136e-01	5.18547545	13.928	0.00019	0.010166	23.475	24.758	34.926	38.914	41.622	54.174
Dll1	5.3065e-01	7.17675454	13.91	0.000192	0.010166	113.49	114.07	127.41	188.11	151.69	172.69
Cd55	5.2636e-01	5.97262576	13.852	0.000198	0.010404	50.466	52.612	51.052	69.028	67.235	85.731
Plcb4	7.8408e-01	3.74063143	13.81	0.000202	0.010611	11.173	9.9476	7.9296	17.6	16.268	16.568
Gm9926	4.7202e+00	-2.05079697	13.798	0.000204	0.010644	0	0	0	0.24221	0.17306	0.26298

Eif4e3	5.6062e-01	5.05229115	13.795	0.000204	0.010644	24.145	27.337	28.867	37.945	41.622	38.57
Ptch2	1.9268e+00	-0.09561434	13.748	0.000209	0.010859	0.41846	0.22106	0.35638	1.534	0.86532	1.5779
Incenp	5.7620e-01	6.08107320	13.706	0.000214	0.010962	54.567	46.201	62.1	69.271	82.811	90.64
Sema3f	5.2150e-01	7.80422310	13.692	0.000215	0.010973	185.46	196.89	167.95	270.87	268.51	250.71
Ttll7	7.4834e-01	3.96878696	13.609	0.000225	0.011357	9.499	12.084	13.454	19.376	18.777	20.249
Anpep	1.2613e+00	3.37543151	13.571	0.00023	0.011506	6.3187	8.9896	2.762	12.837	18.604	12.185
Gas6	5.5181e-01	8.79209299	13.509	0.000237	0.011805	364.18	378.45	335.63	560.22	544.81	475.73
G2e3	4.7913e-01	6.17864935	13.503	0.000238	0.011813	58.333	61.97	61.031	86.387	85.926	80.296
Smoc2	5.4161e-01	8.17982244	13.382	0.000254	0.012513	210.53	238.15	259.8	327.38	357.98	345.47
Aspm	5.4141e-01	7.59907070	13.359	0.000257	0.012636	171.44	140.59	161.35	213.14	220.74	255.35
Etv3	5.5829e-01	7.65862411	13.313	0.000264	0.012864	147.05	165.79	177.39	207.09	243.15	271.31
Lrrc7	2.0509e+00	-0.08850242	13.29	0.000267	0.012969	0.16738	0.66317	0.17819	1.211	1.7306	1.1396
Dlk2	6.1237e-01	5.60883789	13.289	0.000267	0.012969	31.259	42.222	42.321	58.129	67.495	50.843
Gm53	1.3606e+00	1.97764426	13.256	0.000272	0.013073	2.4689	2.6527	1.2473	4.9248	7.2687	4.4706
Chn2	1.8270e+00	1.29086324	13.167	0.000285	0.013589	0.62769	0.66317	1.9601	2.4221	3.2017	5.5226
Apol7a	1.2503e+00	2.52580974	13.162	0.000286	0.01359	3.5987	4.4948	1.871	9.9304	6.5764	7.4511
Fbxo32	5.0529e-01	6.24969300	13.127	0.000291	0.013816	59.839	71.033	57.556	86.548	89.301	91.604
Pla2g4f	6.5317e-01	7.40256202	13.116	0.000293	0.013867	119.01	138.6	136.85	150.01	224.03	246.15
N4bp2l1	7.8387e-01	3.89058408	13.042	0.000305	0.014232	10.378	9.8739	12.295	23.009	16.441	16.392
Sgsm2	5.1004e-01	5.91081619	12.949	0.00032	0.014817	48.708	48.632	51.319	61.278	69.312	81.085
Gas1	8.2573e-01	6.79358807	12.874	0.000333	0.015296	47.788	85.917	106.56	120.05	158.96	146.04
Man2b2	6.2485e-01	4.79196994	12.829	0.000341	0.015593	23.015	18.642	23.432	29.468	32.623	38.395
Reep1	1.2450e+00	3.95262417	12.77	0.000352	0.015924	12.386	8.3265	6.504	33.989	20.075	10.87
Ets1	5.3267e-01	6.48707048	12.751	0.000356	0.016053	75.49	75.896	68.248	124.33	104.01	89.501
5930430L01Rik	5.1666e-01	5.35461855	12.696	0.000366	0.016423	33.1	35.001	32.609	44.081	52.525	47.512
Tgfr1	5.3971e-01	5.41247980	12.669	0.000372	0.016594	32.012	33.453	38.579	51.186	44.218	55.489
Slc43a1	1.0753e+00	2.82577839	12.583	0.000389	0.01726	3.9753	5.8948	3.6529	8.3157	12.374	7.8017
Galnt1	5.8167e-01	6.43380812	12.561	0.000394	0.017431	57.454	66.538	83.84	117.87	97.608	94.848
Zdhc2	9.4806e-01	3.52443080	12.534	0.0004	0.017646	5.6492	6.9264	11.048	16.47	15.576	12.974
D6ErtD527e	1.0794e+00	2.37333317	12.5	0.000407	0.017851	3.3895	3.6843	2.6729	6.2166	8.2205	6.3115
Serp1nb7	8.4376e-01	5.65002298	12.472	0.000413	0.018089	28.748	25.937	53.19	66.929	50.881	75.212
Soat1	1.4559e+00	1.72456622	12.449	0.000418	0.018254	1.8412	1.2527	2.0492	6.0551	5.6246	2.4545
Tubb6	9.6001e-01	3.84613126	12.447	0.000419	0.018254	9.5827	11.2	8.2859	19.699	25.44	11.483
Helz2	7.5846e-01	4.99057385	12.418	0.000425	0.018462	23.81	20.042	26.818	31.002	33.747	54.787
Sirpa	5.3071e-01	6.82386990	12.328	0.000446	0.01929	110.01	84.223	83.216	139.51	124.26	137.71
Hspb2	4.7188e+00	-2.05103255	12.276	0.000459	0.019648	0	0	0	0.24221	0.34613	0.08766
Ncam1	2.5434e+00	-0.5000453	12.261	0.000463	0.019754	0.12554	0.14737	0.26729	1.6954	1.1249	0.26298
Btbd3	4.6658e-01	6.78033706	12.222	0.000472	0.020086	89.466	98.149	89.007	124.33	121.23	136.66
Gja1	5.5375e-01	8.39295298	12.175	0.000484	0.020513	233.88	264.68	318.7	370.25	415.27	413.58
Sestd1	7.0322e-01	4.20696460	12.131	0.000496	0.020851	13.432	12.969	15.592	22.364	18.258	27.613
B130006D01Rik	1.0732e+00	2.34163418	12.111	0.000501	0.021019	2.4689	3.6106	3.6529	6.4588	7.0956	6.6621
Abr	5.1630e-01	7.41711391	12.096	0.000505	0.02115	134.95	125.34	161.53	191.83	195.04	216.17
Bmp2	5.5609e-01	5.73046345	12.085	0.000508	0.021227	35.527	41.632	51.854	58.533	62.995	67.498
Dbhos	4.5354e+00	-2.12684133	12.078	0.00051	0.02123	0	0	0	0.16147	0.2596	0.17532
Gm5126	4.5354e+00	-2.12684133	12.078	0.00051	0.02123	0	0	0	0.16147	0.2596	0.17532

Bnc1	4.9035e-01	6.20498898	12.054	0.000517	0.021453	61.597	55.927	66.288	81.865	80.388	95.9
Tgfb1	5.1785e-01	9.14732653	11.991	0.000535	0.022106	483.32	474.98	440.4	668.89	687.5	646.49
Hdac5	4.6153e-01	7.03472561	11.95	0.000546	0.022555	111.52	106.7	112.44	141.53	153.51	160.33
Acsbg1	5.5861e-01	6.90775896	11.935	0.000551	0.022695	112.1	96.012	82.681	164.38	142.52	121.93
Lmnb1	4.7742e-01	6.52938345	11.885	0.000566	0.023221	70.803	77.812	82.949	100.6	119.59	101.86
Dgkq	4.7219e-01	6.33766515	11.825	0.000585	0.023748	66.577	68.085	68.337	84.61	93.022	103.96
Ccdc88c	4.7789e-01	7.54822878	11.818	0.000587	0.023748	158.47	145.16	165.45	206.12	227.93	219.24
Ivns1abp	5.9961e-01	9.42547159	11.818	0.000587	0.023748	453.94	574.01	612.27	719.03	876.31	889.66
Etnk1	4.8131e-01	5.74889255	11.808	0.00059	0.023818	39.963	46.422	48.201	58.129	64.639	64.693
Kif13a	5.1903e-01	7.89434077	11.782	0.000598	0.02406	180.98	187.53	218.11	254.23	270.15	315.93
C2cd4b	1.4078e+00	0.79452277	11.737	0.000613	0.024557	0.66953	1.179	0.89096	2.3413	2.0768	2.7175
Hspb1	4.7363e-01	6.61268606	11.623	0.000651	0.025859	83.733	74.865	86.958	127.97	106.09	106.86
Gramd1b	1.0421e+00	2.73362720	11.616	0.000654	0.025911	4.059	5.3054	3.4748	9.5267	10.73	6.2238
Mmp1b	3.4287e+00	-1.77762523	11.595	0.000661	0.026054	0	0	0.089096	0.24221	0.43266	0.26298
Osmr	5.0057e-01	6.37465646	11.563	0.000673	0.026268	71.724	63.37	70.742	92.684	85.926	112.73
Mturn	8.3399e-01	2.98745260	11.542	0.00068	0.026458	5.3981	5.379	6.1476	10.657	10.211	9.2043
Hsf2	4.8897e-01	5.34917377	11.524	0.000687	0.026621	33.979	36.253	31.184	50.379	45.862	46.197
Scnn1g	1.3736e+00	1.06121084	11.506	0.000694	0.02683	1.3391	1.2527	0.62367	3.1487	3.2017	2.2792
Tmem194	5.6900e-01	4.51339026	11.44	0.000719	0.027538	17.91	17.979	19.067	30.276	24.835	26.298
Wnt4	4.8715e-01	8.04563977	11.421	0.000726	0.027722	234.34	212.44	212.94	334.32	307.53	283.05
Gpr62	4.5346e+00	-2.12737636	11.398	0.000735	0.028024	0	0	0	0.24221	0.086532	0.26298
Cidea	2.2858e+00	-0.39686976	11.339	0.000759	0.028799	0.12554	0.22106	0.35638	1.6954	1.2114	0.35064
Edar	1.1248e+00	1.88683416	11.335	0.000761	0.028799	2.0504	2.8737	1.871	5.3285	5.1054	4.383
Gpr27	1.5998e+00	2.06632706	11.334	0.000761	0.028799	0.58584	2.9474	2.762	5.8937	7.0091	5.6979
Cux1	4.8767e-01	6.25832156	11.299	0.000776	0.02927	64.066	66.464	60.318	77.021	101.59	89.15
Rasa3	4.4777e-01	7.02934027	11.293	0.000778	0.02927	112.61	109.28	109.32	140.72	151.34	159.8
Ms4a10	1.5783e+00	0.25492787	11.284	0.000782	0.029372	0.66953	0.22106	0.71277	1.6954	1.3845	1.8409
Uty	5.7962e-01	6.18943067	11.247	0.000798	0.029906	45.235	70.075	60.229	87.759	98.3	75.738
Nabp1	4.9645e-01	5.60260397	11.232	0.000804	0.030071	35.234	44.875	40.717	53.608	61.005	55.489
Mgll	6.4253e-01	6.26575129	11.23	0.000805	0.030071	65.698	69.559	44.548	87.598	116.56	76.965
Pif1	5.5726e-01	4.51511047	11.19	0.000822	0.030667	18.579	16.727	19.958	26.158	28.556	26.561
8030423F21Rik	3.3042e+00	-1.84387308	11.176	0.000829	0.030853	0	0.073686	0	0.32294	0.2596	0.26298
Frmd4b	4.5392e-01	6.60094715	11.161	0.000835	0.031042	77.707	81.275	86.601	100.84	122.44	112.91
D4Wsu53e	5.2464e-01	7.87031405	11.127	0.000851	0.031566	172.45	204.18	198.95	228.8	296.03	302.95
Nek2	4.9892e-01	5.38763086	11.063	0.000881	0.032499	30.296	35.001	38.757	49.894	51.313	45.32
Zfp804b	3.3042e+00	-1.84323067	11.051	0.000887	0.032543	0	0.073686	0	0.24221	0.34613	0.26298
Fgf13	1.1030e+00	2.02066156	11.04	0.000892	0.032678	2.3434	3.3159	1.871	5.0056	5.6246	5.6102
Rab11fip4	8.2465e-01	3.05425975	10.988	0.000917	0.033431	5.5655	6.2633	5.9694	12.272	9.5185	9.6426
Lrp4	5.5660e-01	9.39007626	10.97	0.000926	0.033645	532.78	501.36	594.98	716.28	747.29	932.44
Bhlhe41	1.6564e+00	-0.14316493	10.965	0.000928	0.033645	0.29292	0.36843	0.53458	1.4532	1.0384	1.1396
Mastl	4.6426e-01	5.19491712	10.921	0.000951	0.034231	31.259	30.211	30.56	43.92	39.805	43.304
Syne1	5.2868e-01	6.68714536	10.875	0.000975	0.034982	83.691	72.212	97.026	112.63	108.25	143.85
Lamc1	4.7764e-01	7.27436545	10.868	0.000979	0.035035	142.78	124.09	120.9	200.22	163.2	176.9
Grik4	2.0252e+00	-0.41232856	10.861	0.000982	0.035035	0.41846	0.14737	0.089096	1.4532	1.0384	0.61362
Lamb3	5.1210e-01	9.57124808	10.859	0.000983	0.035035	614.96	597.15	669.02	877.27	894.65	910.7

Nlrp5-ps	1.7306e+00	-0.12902879	10.842	0.000992	0.035241	0.20923	0.29474	0.71277	1.2918	1.2114	1.2272
Gmip	5.2893e-01	5.08007257	10.796	0.001017	0.03588	25.149	26.379	31.451	36.089	38.42	44.882
Cwh43	5.3965e-01	5.97161423	10.724	0.001058	0.036821	51.47	40.159	61.655	78.555	65.678	78.368
Ctgf	2.2523e+00	-0.55249766	10.711	0.001065	0.036853	0.29292	0.22106	0	1.3725	1.1249	0.35064
Cyp1a1	4.5362e+00	-2.12695956	10.69	0.001077	0.037009	0	0	0	0.16147	0.34613	0.08766
Ets2	4.9365e-01	8.57016429	10.683	0.001081	0.037084	301.54	310.22	335.09	414.09	418.64	500.27
Sorl1	4.5036e-01	6.56044213	10.592	0.001136	0.03882	86.411	79.065	73.326	101.32	104.62	120.8
Casc5	4.3913e-01	6.35508769	10.587	0.001139	0.038846	71.598	66.243	70.297	91.311	88.522	102.47
8430408G22Rik	1.2256e+00	2.26923790	10.581	0.001143	0.038864	3.0547	3.758	1.6037	4.4404	8.4801	7.0128
Tgfb3	4.5128e-01	6.91351168	10.57	0.00115	0.03904	95.994	105.37	103.98	124.82	142.43	150.07
Zfp518b	7.7123e-01	3.24619159	10.536	0.001171	0.039559	7.2812	6.1896	7.3059	11.384	10.47	13.675
Gramd2	5.3927e-01	4.40006655	10.526	0.001177	0.039631	17.031	17.39	16.928	22.848	26.565	25.246
Bmp4	4.6808e-01	5.53872366	10.525	0.001178	0.039631	38.121	37.948	40.717	49.087	60.832	51.544
Plekha3	6.3885e-01	4.16979522	10.524	0.001178	0.039631	11.173	15.179	15.859	23.09	21.114	21.038
Dock9	4.7820e-01	6.89852640	10.52	0.001181	0.039637	95.073	98.812	105.04	122.23	132.31	161.73
Tbc1d8b	5.0041e-01	4.98980049	10.473	0.001212	0.040225	23.434	28.222	27.174	37.057	35.651	38.483
Sema3c	5.2692e-01	9.04927593	10.454	0.001224	0.040448	465.91	440.93	395.05	721.85	604.34	549.89
Tjap1	4.5422e-01	5.62200992	10.446	0.001229	0.040562	43.017	43.106	38.133	54.012	61.611	54.875
Zdhhc18	4.2040e-01	6.23258383	10.44	0.001233	0.04063	64.484	62.854	65.307	85.095	84.628	88.098
Ccnf	4.6732e-01	5.29007947	10.418	0.001248	0.041022	35.36	30.58	32.164	44.404	47.679	43.83
Prodh	5.0823e-01	5.08856262	10.397	0.001262	0.041378	26.405	30.285	27.353	34.312	44.131	41.025
9030619P08Rik	4.3233e+00	-2.2074664	10.356	0.00129	0.041922	0	0	0	0.16147	0.17306	0.17532
Tmem100	4.3233e+00	-2.2074664	10.356	0.00129	0.041922	0	0	0	0.16147	0.17306	0.17532
Gna14	5.7212e-01	5.66059889	10.322	0.001314	0.042424	34.523	39.643	47.845	46.907	64.207	69.865
Slc9a1	4.7750e-01	6.35356356	10.304	0.001327	0.042781	65.991	67.496	71.366	79.443	96.57	109.14
Il1r1	4.2164e-01	6.20727007	10.193	0.00141	0.045065	63.187	63.001	62.991	80.251	82.465	90.728
Tmc4	8.2023e-01	2.75025694	10.166	0.00143	0.045608	4.9378	4.9369	4.4548	8.0735	8.9128	8.4153
Edaradd	4.2325e-01	7.15166385	10.159	0.001436	0.045693	120.18	126.96	116.98	166.31	168.13	153.84
Slco4a1	6.1398e-01	3.93101834	10.157	0.001437	0.045693	12.721	10.832	12.295	17.358	17.912	19.723
Tmprss11f	1.1148e+00	2.00352465	10.122	0.001465	0.046283	2.2597	3.0211	2.1383	5.9744	6.4034	3.6817
Kif14	5.1911e-01	5.02249884	10.103	0.001481	0.046709	25.442	28.001	26.462	32.052	38.593	43.83
Mt4	8.2638e-01	4.58266245	10.064	0.001512	0.047483	13.14	22.916	15.681	31.729	40.151	19.636
Nxpe3	1.7221e+00	1.03934831	10.05	0.001523	0.047669	1.0043	1.4	0.26729	2.9872	4.6727	1.4026
Tbc1d8	4.6745e-01	6.23013606	10.023	0.001546	0.048123	60.634	59.243	68.96	74.761	88.176	98.004
Zc3h7a	4.5453e-01	7.30416333	9.9773	0.001585	0.048962	124.87	133.08	141.93	161.71	183.19	202.84
Abca15	4.3217e+00	-2.20824065	9.9731	0.001588	0.049001	0	0	0	0.24221	0.17306	0.08766
Mia2	4.3219e+00	-2.20812208	9.956	0.001603	0.04924	0	0	0	0.24221	0.086532	0.17532
Arhgap22	7.0602e-01	3.43083747	9.9262	0.001629	0.04997	7.4485	9.3581	7.5732	12.03	14.191	13.5
Prss23	4.5787e-01	6.15867113	9.9225	0.001633	0.049999	63.815	61.454	54.883	85.175	91.724	70.829

LogFC = Log Fold change, LogCPM = Log count per million bases, LR = Log Ratio, FDR = BH corrected P-value, values in columns S7309-S7314 depict TMM normalized relative expression.

## b. downregulated genes in Lgr6<sup>+</sup> cells

genes	logFC	logCPM	LR	PValue	FDR	S7309	S7311	S7313	S7310	S7312	S7314
Scarna6	-2.4245	5.94731743	239.01	6.46E-54	1.35E-49	103.94	118.12	88.651	17.842	19.47	20.0
Mir6516	-2.8528	6.69509464	199.44	2.76E-45	2.88E-41	229.77	187.24	127.23	24.543	26.392	24.45
Snora74a	-2.7083	6.26491762	172.5	2.1E-39	1.46E-35	168.22	134.48	95.689	22.121	16.96	21.91
Snord15a	-3.0501	6.98047113	149.66	2.06E-34	1.08E-30	333.68	189.67	150.57	29.226	26.133	26.03
Snord17	-2.4889	7.13452249	136.44	1.6E-31	6.69E-28	249.19	284.65	180.24	36.977	34.44	55.83
Sostdc1	-1.7485	7.32403724	114.82	8.63E-27	3.01E-23	281.66	232.77	225.24	86.79	65.245	68.11
Fst	-2.2292	5.17236386	110.96	6.02E-26	1.8E-22	65.321	59.022	52.656	16.228	13.326	8.152
Snord22	-3.2174	6.94020400	110.12	9.23E-26	2.41E-22	323.89	231.52	107.63	20.265	23.969	27.08
Snora52	-2.702	5.07102299	91.082	1.38E-21	3.2E-18	78.21	64.401	30.293	9.5267	8.3071	8.76
Hmcn1	-1.8156	8.64596237	87.524	8.33E-21	1.74E-17	711.67	596.71	562.11	190.45	130.23	210.7
Lzts1	-1.6469	4.37415209	84.378	4.09E-20	7.76E-17	32.012	29.179	32.075	8.6387	10.211	10.95
Cxcl12	-2.4579	3.49316866	83.055	7.98E-20	1.39E-16	20.295	17.021	18.532	4.1175	2.0768	3.944
Snord15b	-1.9953	8.65610746	79.067	6.01E-19	9.65E-16	883.2	614.91	435.32	144.84	167.44	172.7
Aadacl3	-1.4765	5.51788602	77.642	1.23E-18	1.84E-15	69.966	68.38	62.813	19.053	24.056	29.27
Scarna10	-2.0741	8.32236244	77.048	1.67E-18	2.32E-15	454.44	663.1	433.36	161.39	124.09	82.75
Rprl3	-1.9896	7.63725499	71.701	2.5E-17	3.08E-14	312.34	374.91	265.77	71.935	113.88	54.17
Trpc4	-2.2411	3.89881518	69.096	9.38E-17	1.09E-13	29.543	25.2	17.641	6.9432	4.1535	4.207
Snora5c	-2.9615	4.00837572	67.249	2.39E-16	2.5E-13	41.009	29.843	12.652	4.279	3.2017	3.243
Ptprv	-1.4416	5.35214684	66.088	4.31E-16	4.29E-13	62.392	64.917	50.785	26.966	18.604	19.98
Aldh3a1	-1.5708	6.15322889	64.904	7.86E-16	7.46E-13	116.92	85.107	116.45	46.665	27.69	32.78
Inhbb	-2.4236	4.39248178	61.954	3.52E-15	2.82E-12	40.381	39.569	24.769	10.253	5.6246	3.594
Runx1	-1.7567	4.89986042	60.82	6.25E-15	4.66E-12	52.098	47.454	37.42	16.47	8.7397	15.3
Lphn3	-1.9446	5.96124373	60.665	6.77E-15	4.87E-12	125.08	100.95	69.228	36.573	21.72	18.40
S730408K05Rik	-1.4932	5.84555060	60.201	8.56E-15	5.96E-12	85.365	103.82	64.327	34.716	32.19	23.14
Fam132a	-1.7062	6.67563546	59.371	1.31E-14	8.52E-12	164.66	153.27	150.48	66.768	46.9	29.80
Rprl2	-2.5996	2.93948474	58.763	1.78E-14	1.13E-11	11.8	16.727	9.7115	1.7762	3.0286	1.490
Ephx2	-2.3102	3.78903813	58.162	2.41E-14	1.48E-11	27.702	22.548	17.285	6.2973	4.9323	2.366
Snora68	-2.7941	3.21601078	57.121	4.1E-14	2.45E-11	19.04	20.411	7.5732	2.3413	2.3364	2.103
Mir1949	-2.7708	3.28104116	56.087	6.93E-14	4.02E-11	23.141	17.832	8.0187	2.745	2.2498	2.191
Snora17	-2.1567	3.70751232	55.668	8.58E-14	4.84E-11	25.944	23.727	12.83	5.3285	3.8074	4.908
Rmrp	-1.8943	13.38180123	55.521	9.25E-14	5.08E-11	14861	19178	16428	5477.7	4995.4	3102.
Snora70	-2.1428	3.99932939	54.941	1.24E-13	6.65E-11	32.305	28.958	15.414	5.8937	4.3266	7.188
Esyt3	-1.3876	4.33164005	54.809	1.33E-13	6.83E-11	31.677	27.779	26.907	11.868	9.0859	12.09
Fhl2	-1.4977	4.45915414	54.79	1.34E-13	6.83E-11	38.205	28.516	29.58	13.321	9.1724	11.65
Snora61	-1.9231	4.47974657	52.168	5.1E-13	2.53E-10	35.778	48.19	20.67	8.5579	10.384	8.678
Prkcq	-1.9167	3.59063324	52.027	5.47E-13	2.66E-10	20.211	21.074	14.612	4.1175	4.067	6.662
Barx2	-1.0292	7.55479132	51.971	5.63E-13	2.67E-10	259.9	233.07	263.37	120.46	116.04	134.1
Fam117a	-1.3568	4.18477027	51.309	7.89E-13	3.66E-10	27.158	25.422	24.947	11.707	9.5185	9.02
Snora78	-2.4094	4.19056664	51.255	8.11E-13	3.68E-10	37.117	36.253	17.196	5.167	8.5667	3.331
Nt5dc2	-1.2541	4.97463750	51.162	8.51E-13	3.78E-10	49.503	46.938	35.371	17.681	17.826	19.89
Wnt11	-1.6922	3.75013343	51.045	9.03E-13	3.93E-10	22.639	21.443	16.394	7.7506	5.7976	5.171
Add2	-2.5762	3.96126203	50.374	1.27E-12	5.42E-10	38.414	26.085	13.632	6.2973	2.769	4.032
Dlc1	-1.2486	5.55254151	49.686	1.8E-12	7.53E-10	74.778	63.443	58.893	27.773	21.46	33.83

Il11ra1	-1.0462	5.87628748	49.494	1.99E-12	7.99E-10	79.256	86.802	70.564	43.274	38.507	32.78
Igsf9	-1.0779	6.91060853	48.815	2.81E-12	1.11E-09	158.13	177.95	152.89	67.737	72.254	91.69
Nbea	-2.3158	4.40560132	48.399	3.48E-12	1.32E-09	47.872	39.938	16.305	8.235	7.7879	4.908
Krt73	-3.791	2.91818904	48.247	3.76E-12	1.4E-09	20.839	14.737	4.4548	0.96882	1.5576	0.3506
Gstm5	-1.3049	4.44686575	47.889	4.51E-12	1.62E-09	33.686	30.137	28.333	14.936	11.682	10.69
Smco4	-1.2374	5.08125663	46.714	8.21E-12	2.91E-09	43.268	53.496	45.083	21.718	23.104	15.25
Slco2b1	-2.5196	4.18946193	45.82	1.3E-11	4.44E-09	36.95	29.179	25.571	8.3964	5.8842	1.665
Snora21	-2.9291	3.77528598	45.665	1.4E-11	4.73E-09	36.113	25.643	8.7314	3.0679	1.9037	4.295
Susd2	-1.3282	7.84147011	45.325	1.67E-11	5.53E-09	410.46	335.79	236.64	126.03	114.22	151.3
Adh7	-1.0641	8.08113425	45.015	1.96E-11	6.28E-09	365.61	370.2	362.53	158.4	210.88	156.0
Dsc1	-1.2284	5.76672804	44.299	2.82E-11	8.92E-09	92.563	77.001	58.18	31.567	27.604	38.2
Snora43	-2.3416	3.47657071	44.068	3.17E-11	9.86E-09	28.455	15.474	9.9788	3.7138	3.8074	3.155
Scarna3a	-2.6009	3.33653567	44.045	3.21E-11	9.86E-09	24.982	17.832	7.3059	3.3101	2.6825	2.279
Nedd9	-1.1864	6.09400967	43.902	3.45E-11	1.05E-08	105.87	86.949	90.967	54.496	35.651	34.53
Sulf2	-2.0249	5.05338805	43.306	4.68E-11	1.4E-08	73.983	55.854	28.422	17.681	12.374	8.853
Sox9	-1.7671	4.38901675	43.219	4.89E-11	1.44E-08	37.745	33.38	24.769	13.886	8.3936	5.873
Aqp3	-1.0421	8.16438793	42.434	7.31E-11	2.12E-08	398.58	410.8	348.46	210.4	194.78	157.0
Klk8	-1.3421	6.90682417	42.233	8.1E-11	2.32E-08	228.94	160.41	125.63	78.555	69.139	55.57
Smpdl3a	-1.5715	5.57138943	40.538	1.93E-10	5.37E-08	90.638	63.517	58.002	24.059	14.71	32.69
Chil1	-2.3551	2.97300496	39.789	2.83E-10	7.67E-08	18.412	10.684	8.6423	3.7138	1.8172	1.840
Snora64	-2.0082	2.99097489	39.602	3.11E-10	8.23E-08	14.52	14.737	7.5732	2.745	3.1152	3.331
Clic4	-1.0188	7.58207682	39.576	3.16E-10	8.24E-08	294.09	232.48	242.25	147.34	110.07	122.1
Dpysl3	-2.2066	2.94324189	39.311	3.61E-10	9.32E-08	12.177	14.737	9.8006	1.9376	1.6441	4.38
Zfp365	-1.5454	3.57578686	38.82	4.65E-10	1.18E-07	20.337	17.537	14.255	7.2662	5.8842	4.733
Hoxc13	-2.4109	1.62925467	38.073	6.81E-10	1.71E-07	5.3144	4.4948	4.633	1.2918	0.60572	0.7889
Ccl2	-3.5745	0.22221791	36.644	1.42E-09	3.48E-07	1.8412	1.5474	1.9601	0.16147	0	0.2629
Vdr	-1.101	7.15708151	36.535	1.5E-09	3.6E-07	246.81	188.86	147.19	94.864	80.561	96.51
Emb	-1.8464	5.24292604	36.196	1.78E-09	4.19E-07	71.933	59.759	44.726	26.077	14.624	8.327
Rpph1	-1.6983	12.81501017	35.724	2.27E-09	5.25E-07	10748	12733	9570.3	4275	3986.6	1923.
Ephb2	-1.8157	4.08260886	35.689	2.31E-09	5.25E-07	33.644	21.369	22.809	9.2845	3.6343	9.204
Igals9	-1.2841	4.38389914	35.4	2.69E-09	6.03E-07	36.113	28.516	22.987	11.787	9.7781	14.55
Snora15	-2.7232	2.31291426	35.223	2.94E-09	6.53E-07	9.4571	10.463	4.4548	0.56515	1.1249	2.016
Angptl2	-1.2612	5.73545213	34.988	3.32E-09	7.29E-07	90.596	65.285	68.604	43.678	24.921	25.07
Egr2	-1.7902	5.91322282	34.578	4.1E-09	8.91E-07	99.969	106.7	72.613	41.256	27.171	12.27
Hpgd	-1.6964	2.94487716	34.346	4.61E-09	9.93E-07	13.307	11.642	9.1769	4.3597	3.4613	2.717
Pappa	-1.9332	2.59023372	34.059	5.35E-09	1.14E-06	11.173	7.5896	8.6423	2.9872	1.5576	2.629
Fam83a	-1.2124	4.11231589	33.736	6.31E-09	1.33E-06	26.07	23.432	22.007	8.8809	9.0859	12.97
Pdzk1ip1	-1.0422	5.31979118	33.686	6.48E-09	1.34E-06	58.542	49.369	52.478	22.525	22.066	33.39
Smpdl3b	-1.6452	3.43731212	33.367	7.63E-09	1.56E-06	18.287	11.569	18.354	5.9744	3.4613	5.960
Adamts1	-1.271	5.02426198	33.254	8.09E-09	1.64E-06	44.273	50.99	41.875	12.756	17.826	26.29
Snora44	-1.9663	3.52852042	32.911	9.65E-09	1.94E-06	25.861	18.2	9.4442	5.9744	3.9805	3.769
Lrrn1	-2.3854	1.57285668	32.84	1E-08	1.99E-06	4.2264	6.2633	3.3857	0.72662	0.95185	0.9642
Nudt4	-0.74315	6.17872150	32.219	1.38E-08	2.66E-06	88.043	93.507	89.898	55.949	53.996	52.15
Vsnl1	-1.6442	2.80055103	31.671	1.83E-08	3.47E-06	11.675	9.2844	9.6224	4.1982	2.5094	3.068
Cldn4	-1.4779	4.06294714	30.469	3.39E-08	6.11E-06	29.166	23.948	19.512	12.837	6.836	6.399

Orm1	-1.2777	3.65157140	30.433	3.46E-08	6.17E-06	20.63	15.327	16.394	8.3964	6.7495	6.486
Pdlim4	-2.0213	2.94977876	30.192	3.91E-08	6.93E-06	11.256	12.453	12.473	4.7634	2.9421	1.139
Otud7a	-2.243	3.34791627	30.137	4.03E-08	7.07E-06	8.8713	14.811	26.194	3.3101	1.9037	5.259
Ldhb	-0.98146	4.41409690	30.074	4.16E-08	7.24E-06	28.832	27.853	27.442	16.793	12.461	13.32
Gsdma3	-2.0685	2.49508418	29.924	4.49E-08	7.76E-06	9.4571	5.6738	11.137	2.8257	2.1633	1.227
Dach1	-0.98894	4.73738870	28.908	7.59E-08	1.28E-05	32.765	34.411	38.579	15.905	15.403	21.91
Itpkb	-0.98804	5.68808079	28.88	7.7E-08	1.29E-05	78.084	78.401	48.112	35.846	35.392	32.08
Bdh1	-0.88527	4.86305673	28.654	8.66E-08	1.43E-05	42.85	35.369	34.124	20.91	19.643	20.42
Stard5	-0.69431	6.56027038	28.598	8.91E-08	1.47E-05	121.19	117.09	110.92	74.518	69.399	71.96
Faah	-1.0099	6.12958356	28.496	9.39E-08	1.53E-05	91.014	89.675	99.253	38.43	36.949	63.64
Klhl29	-1.5304	2.68287255	28.046	1.18E-07	1.9E-05	8.7039	8.4002	10.692	3.5523	2.596	3.418
Mal2	-1.2815	4.30591540	27.94	1.25E-07	1.98E-05	36.406	26.822	19.601	11.626	8.9128	13.67
Mycl	-0.73761	7.32151333	27.85	1.31E-07	2.06E-05	212.74	207.79	178.55	119.89	123.05	116.
Flrt3	-0.76579	7.00010878	27.595	1.5E-07	2.3E-05	172.24	157.76	152.8	93.088	82.551	108.4
Shroom3	-1.2931	5.06434466	27.484	1.58E-07	2.42E-05	48.499	50.696	42.41	13.079	15.23	29.54
Ccl7	-4.768	-0.52674233	26.91	2.13E-07	3.18E-05	0.87876	0.58948	1.6037	0.080735	0	0
Ndrg2	-1.1024	5.45186435	26.628	2.47E-07	3.63E-05	72.184	66.464	39.381	32.133	28.209	22.70
Gprin3	-2.0443	2.94381743	26.607	2.49E-07	3.64E-05	17.492	11.642	6.4149	4.3597	2.2498	2.016
Fam84a	-0.78841	7.51031003	26.514	2.62E-07	3.8E-05	252.5	236.83	202.6	151.78	129.02	119.9
Acot1	-1.3445	4.87443394	26.402	2.77E-07	3.99E-05	41.678	49.517	34.124	23.817	15.835	9.642
Rnf152	-0.82811	5.16702367	26.35	2.85E-07	4.05E-05	44.022	45.096	48.112	22.444	23.883	30.94
Tbc1d30	-2.3591	0.67551284	26.111	3.22E-07	4.52E-05	1.9667	2.5053	2.6729	0.56515	0.43266	0.3506
Impdh1	-1.2243	4.07046700	25.662	4.07E-07	5.63E-05	23.978	20.632	25.125	8.4772	7.2687	14.11
Snord23	-2.2193	1.24756747	25.488	4.45E-07	6.12E-05	2.5107	4.5685	3.8311	0.56515	0.95185	0.7889
Scarna3b	-2.565	1.01417275	25.256	5.02E-07	6.81E-05	3.7661	3.758	1.5146	0.56515	0.60572	0.3506
Itpr1	-1.0998	4.40061270	25.256	5.02E-07	6.81E-05	34.606	28.369	22.363	15.986	13.932	9.993
Grin1	-2.2323	1.17328469	25.027	5.65E-07	7.56E-05	3.3058	3.5369	3.2966	0.24221	1.1249	0.7889
Psrc1	-0.81142	5.17009824	25.016	5.68E-07	7.56E-05	51.805	42.517	42.41	29.791	25.267	22.96
Prickle2	-0.8513	5.94839724	25.003	5.72E-07	7.57E-05	90.763	86.359	60.229	38.511	44.131	49.17
Lurap1l	-1.9709	2.65382145	24.95	5.88E-07	7.73E-05	12.554	11.274	4.8112	3.3101	2.2498	1.753
Pxdc1	-0.78122	5.59768935	24.806	6.34E-07	8.23E-05	60.969	52.685	69.406	37.138	30.892	38.39
Rps6ka6	-0.86877	4.75968575	24.626	6.96E-07	8.97E-05	38.038	36.695	29.402	20.91	19.21	17.00
Kif26b	-1.7031	4.76038273	24.537	7.29E-07	9.34E-05	43.603	33.969	45.795	8.8809	6.3168	22.70
Epcam	-0.88394	6.76887622	24.35	8.03E-07	0.000102	156.08	117.9	149.59	97.609	63.255	68.63
Scd2	-1.1942	5.20857298	24.136	8.98E-07	0.000112	60.425	59.759	33.055	19.296	17.739	30.06
Nqo1	-1.1127	4.47043557	23.927	1E-06	0.000124	35.694	29.99	24.234	18.811	11.509	11.30
Gfra1	-2.2732	3.17253588	23.817	1.06E-06	0.000131	23.643	12.969	6.3258	4.1982	3.4613	1.227
2010107E04Rik	-0.75958	5.85959543	23.608	1.18E-06	0.000145	75.113	77.222	65.931	49.41	45.602	33.92
Apobec1	-1.2694	3.86634032	23.478	1.26E-06	0.000154	25.568	19.895	15.235	11.303	7.3552	6.574
Chchd10	-1.4439	2.74392297	23.306	1.38E-06	0.000167	10.252	8.916	9.266	4.7634	3.1152	2.542
Flrt2	-1.1553	5.47385956	23.174	1.48E-06	0.000177	75.741	52.317	54.883	24.543	18.172	39.53
Mmp2	-0.92001	4.41281705	22.797	1.8E-06	0.00021	27.493	33.011	22.274	13.16	15.316	15.3
Fam167a	-0.80543	5.15202363	22.563	2.03E-06	0.000232	49.713	39.201	45.974	27.208	20.941	29.10
Sort1	-0.96141	6.41633994	22.513	2.09E-06	0.000236	141.44	119.81	76.177	56.272	50.102	67.14
Lrat	-1.9991	4.38469135	22.42	2.19E-06	0.000245	42.264	42.517	13.899	13.886	6.836	3.944



Aox4	-2.1787	2.87609483	22.38	2.24E-06	0.000248	14.269	16.874	3.3857	2.5835	2.4229	2.629
Ifitm2	-0.79582	5.84570837	22.301	2.33E-06	0.000258	76.787	71.107	70.297	51.105	43.612	30.94
Cplx2	-1.7254	1.65803546	22.273	2.36E-06	0.00026	4.6867	4.9369	3.9202	0.96882	1.3845	1.753
Snora16a	-1.619	4.06082922	22.084	2.61E-06	0.000279	35.234	28.443	10.335	8.4772	6.663	9.02
Tnc	-0.88522	6.08703999	21.841	2.96E-06	0.000314	109.38	72.801	81.434	56.03	35.997	50.84
Endod1	-1.173	5.74967778	21.564	3.42E-06	0.000361	100.26	71.18	50.963	46.1	24.315	28.31
4933431E20Rik	-1.163	3.45806326	21.557	3.44E-06	0.000361	18.036	14.369	12.117	6.2973	5.7111	7.97
Sox7	-0.95499	6.01039497	21.038	4.5E-06	0.000466	88.336	72.58	93.462	35.443	33.747	62.06
Eya2	-1.7817	3.91824714	20.615	5.62E-06	0.000572	30.38	23.948	14.523	10.98	6.4899	2.542
Apcdd1	-0.71178	7.07018131	20.4	6.28E-06	0.000628	189.98	158.65	151.11	106.89	84.369	114.0
Pls3	-0.63164	7.37207534	20.377	6.36E-06	0.000633	212.83	199.02	191.47	138.14	118.12	133.2
Runx2	-1.6671	2.63720401	20.322	6.54E-06	0.000648	12.261	8.3265	6.504	4.3597	2.2498	1.928
Snord8	-1.6647	1.98557796	20.286	6.67E-06	0.000657	6.8209	6.337	3.742	1.534	1.9902	1.840
Slc25a13	-0.59712	6.44382223	20.277	6.7E-06	0.000657	105.12	106.4	102.28	72.581	64.12	70.74
Ifngr2	-0.72051	5.45520399	20.254	6.78E-06	0.000662	61.304	51.506	50.161	38.914	29.334	30.76
Aqp9	-1.4799	2.80623143	20.164	7.11E-06	0.00069	8.7039	7.5896	13.899	2.5835	3.5478	4.64
Gsdmc	-1.1318	4.04597005	20.068	7.47E-06	0.000712	26.154	19.453	21.472	9.1231	7.0091	14.55
Gab2	-1.8409	1.31442166	20.059	7.51E-06	0.000712	3.515	3.9053	3.2966	0.96882	0.51919	1.490
Fzd7	-0.80048	6.10747604	19.895	8.18E-06	0.000766	91.266	93.433	77.335	65.557	45.429	39.44
Ntrk2	-0.68419	6.10368989	19.861	8.33E-06	0.000776	83.106	77.517	93.106	48.28	46.554	63.02
1700012P22Rik	-1.6265	1.67871268	19.713	9E-06	0.000835	4.059	3.979	5.7022	1.7762	1.2114	1.402
Mcf2l	-0.72405	5.61800232	19.555	9.78E-06	0.000903	74.485	56.296	51.765	38.753	34.613	37.43
Arhgef17	-0.99669	4.43199471	19.379	1.07E-05	0.000973	27.074	27.927	30.56	11.626	10.816	20.42
Irx3	-0.94216	5.47648768	19.37	1.08E-05	0.000973	49.964	51.875	73.326	27.692	22.585	40.76
Snord49b	-2.1244	1.70963344	19.294	1.12E-05	0.001009	7.3648	3.758	3.3857	0.40368	1.6441	1.314
Pianp	-3.4256	3.01833087	19.24	1.15E-05	0.001029	33.1	6.9264	1.4255	2.0991	1.0384	0.7012
BC021614	-1.8637	1.20652759	19.21	1.17E-05	0.001036	3.1384	2.3579	4.5439	0.80735	0.95185	0.9642
Plekha1	-0.63298	7.31080803	19.168	1.2E-05	0.001055	211.11	195.27	171.96	132.73	113.36	127.0
Serpina9	-2.6392	0.96773105	19.121	1.23E-05	0.001077	2.5526	1.4	5.3458	0.16147	0.51919	0.7889
9530059O14Rik	-1.7855	1.38021318	19.106	1.24E-05	0.001081	3.515	4.7896	2.8511	1.211	0.69226	1.314
Mpp7	-0.69851	6.14415848	18.803	1.45E-05	0.001251	90.889	89.823	81.078	49.975	44.477	66.97
Sepp1	-0.84774	6.68329127	18.715	1.52E-05	0.001305	158.09	146.63	90.611	85.256	71.216	63.37
Tmem159	-0.91964	6.11350065	18.653	1.57E-05	0.001342	108.17	98.149	64.417	60.148	48.285	34.80
Mark1	-1.2608	3.17139955	18.635	1.58E-05	0.001349	13.558	14.148	9.4442	6.2973	5.8842	3.331
Iqgap2	-1.1574	3.47329652	18.515	1.69E-05	0.001429	19.96	11.495	13.454	7.6698	5.538	7.012
Rgma	-0.66672	5.60724969	18.51	1.69E-05	0.001429	63.48	63.738	51.408	37.461	33.055	42.16
Klk5	-1.5144	2.85826903	18.464	1.73E-05	0.001458	15.023	9.4318	6.4149	4.7634	3.3747	2.717
Scarna13	-0.70156	7.68261646	18.422	1.77E-05	0.001484	286.89	259.37	216.15	152.99	181.37	134.6
Pdzrn3	-1.8622	2.77869384	18.396	1.79E-05	0.001493	16.738	8.4002	5.524	4.279	2.596	1.577
Gpr155	-0.84734	5.02061020	18.383	1.81E-05	0.001498	49.88	44.948	29.313	22.687	21.114	25.42
E030018B13Rik	-5.8497	-1.20891686	18.349	1.84E-05	0.001512	0.71138	0.14737	0.62367	0	0	0
Tmem229b	-1.8282	1.06008758	18.322	1.87E-05	0.001522	3.2221	2.8737	2.6729	0.80735	0.43266	1.227
Atp5e	-0.7138	6.60848658	18.229	1.96E-05	0.00158	132.86	121.07	108.96	79.766	85.926	55.66
Krtdap	-0.86041	8.02178830	18.143	2.05E-05	0.001635	446.7	325.03	232.63	194.25	175.57	183.6
Tsix	-2.5908	0.60562079	18.141	2.05E-05	0.001635	2.8037	0.73686	3.2075	0.48441	0.2596	0.3506

Krt23	-2.048	2.01620999	18.027	2.18E-05	0.00173	8.0762	7.8844	2.1383	1.8569	1.298	1.227
Psph	-0.94168	5.88235449	17.996	2.21E-05	0.001738	89.55	83.338	58.893	52.639	42.055	26.03
Flot2	-0.98711	3.24087314	17.996	2.21E-05	0.001738	12.512	12.305	12.117	6.9432	5.8842	5.785
Scube2	-1.1822	3.50684793	17.826	2.42E-05	0.001879	18.454	16.432	11.404	9.1231	6.5764	4.733
Ebp	-0.61016	5.69802244	17.764	2.5E-05	0.001927	64.652	62.633	60.229	46.503	40.757	35.5
Nradd	-0.75548	4.66437731	17.731	2.54E-05	0.001946	34.857	31.537	28.333	21.798	18.085	16.30
Hip1	-1.2712	3.68781050	17.723	2.56E-05	0.001948	17.994	15.621	20.225	4.6019	5.8842	11.83
Cd5	-1.6232	1.55484184	17.527	2.83E-05	0.002144	4.5193	4.5685	3.2075	1.0496	1.9037	1.051
Itgb5	-0.69009	6.44611657	17.021	3.7E-05	0.002672	114.24	105.22	102.73	59.582	55.294	84.94
Sec14l2	-0.558	6.53252425	16.761	4.24E-05	0.003002	116.96	100.58	112.53	73.63	69.399	81.26
Phyh	-0.58894	5.43693344	16.63	4.54E-05	0.003189	55.487	47.085	52.834	33.505	37.209	32.69
Rgs10	-1.3696	3.53136531	16.161	5.82E-05	0.003972	21.132	14.884	12.83	9.5267	6.4034	2.980
Cebpd	-0.71305	4.43859334	15.953	6.49E-05	0.004389	23.727	25.348	31.273	17.197	15.749	15.86
Atp13a2	-0.5578	6.78353742	15.942	6.53E-05	0.004399	136.92	142.58	113.33	87.436	88.349	91.25
Pramef12	-1.7097	1.02197887	15.917	6.62E-05	0.004445	3.1803	3.1685	1.9601	0.72662	1.1249	0.7012
Gns	-0.77362	4.76996831	15.847	6.87E-05	0.004582	37.452	34.337	30.649	16.551	17.653	25.8
Plagl1	-0.9014	3.87960651	15.818	6.98E-05	0.004639	17.91	21.59	17.285	7.4276	11.076	11.92
P2rx7	-0.95281	3.29807405	15.766	7.17E-05	0.004738	13.6	10.905	13.632	6.3781	5.7976	7.538
Gm6251	-0.70004	5.12081345	15.642	7.65E-05	0.004979	51.805	38.611	37.866	25.512	30.546	23.14
Pkd1l3	-2.4724	0.44671149	15.578	7.92E-05	0.005136	2.971	0.66317	2.0492	0.32294	0.51919	0.1753
Nupr1	-1.2086	3.27435304	15.448	8.48E-05	0.00545	18.579	11.2	9.5333	7.5084	4.8458	4.733
Fibin	-1.483	3.22593055	15.436	8.53E-05	0.005466	16.404	16.063	7.6623	6.3781	5.7976	2.191
Tgm1	-1.4406	2.69958542	15.374	8.82E-05	0.005633	13.516	8.1054	5.524	3.8753	2.3364	3.85
Tpm2	-0.54133	6.58570172	15.31	9.12E-05	0.005808	117.38	105	118.59	81.785	83.763	68.72
Slc39a10	-0.51641	6.09948573	15.305	9.15E-05	0.005808	80.176	83.486	77.87	59.825	56.765	52.24
Slc37a2	-1.1035	3.95427137	15.238	9.48E-05	0.006	26.907	24.243	11.137	9.6882	9.3455	10.08
Snora23	-1.5217	2.66979324	15.189	9.73E-05	0.006101	6.4442	14.737	6.3258	2.6643	2.5094	4.38
Rassf9	-0.71439	5.76801814	15.166	9.85E-05	0.006138	79.423	69.338	53.458	47.553	44.131	31.73
Ifi27l2a	-0.73358	4.17414565	15.021	0.000106	0.006539	24.354	21.295	21.205	13.483	15.23	11.57
Atp10b	-0.94308	4.50295606	14.994	0.000108	0.006597	35.945	31.832	20.67	12.675	12.72	20.77
Col8a1	-1.2257	3.32628286	14.93	0.000112	0.006773	17.24	15.4	8.375	7.6698	5.9707	3.944
Apoc1	-0.56398	7.16981858	14.925	0.000112	0.006773	179.94	167.41	167.32	135.31	107.47	105.3
Ltbp1	-1.891	3.54811718	14.854	0.000116	0.007013	28.455	14.737	10.424	8.7194	4.4131	1.314
Gcnt2	-0.69924	6.21077203	14.833	0.000117	0.007069	102.9	83.633	87.671	57.16	41.276	70.56
Dpysl5	-1.9845	0.43342199	14.777	0.000121	0.00726	2.4271	1.7685	1.1583	0.24221	0.43266	0.7012
Blnk	-1.0967	3.09494079	14.76	0.000122	0.007287	11.508	14.074	8.4641	4.1982	5.1054	6.662
E030044B06Rik	-3.8587	-1.1113751	14.684	0.000127	0.007522	0.79507	0.44211	0.26729	0	0.086532	0
Stbd1	-1.9065	0.28683248	14.67	0.000128	0.00755	2.0923	1.4	1.2473	0.32294	0.51919	0.438
Gstm1	-0.84973	3.63991943	14.662	0.000129	0.00755	14.437	15.253	17.819	8.1542	7.8744	10.25
F730043M19Rik	-1.2621	1.87196043	14.62	0.000132	0.007693	4.3938	5.379	4.9894	1.9376	2.0768	2.103
Gm6402	-0.94945	5.77022903	14.601	0.000133	0.007727	107.04	54.527	52.923	36.412	45.602	29.27
Ift43	-0.7129	4.70695289	14.549	0.000137	0.007899	38.498	31.169	26.729	21.314	20.508	17.18
Epas1	-0.86581	6.05860908	14.539	0.000137	0.00792	108.51	89.675	58.982	59.744	48.198	33.31
Lmo1	-0.71569	4.81583501	14.422	0.000146	0.008337	37.745	32.864	33.678	25.754	21.806	15.95
Hdac11	-0.70242	4.78114503	14.399	0.000148	0.008408	36.113	39.127	26.105	21.233	22.066	19.1

Neurl1b	-0.5302	7.45285305	14.322	0.000154	0.008675	211.7	211.92	196.81	143.87	130.49	155.3
Ispd	-0.79917	3.60326008	14.305	0.000155	0.008727	15.567	13.927	16.126	9.1231	8.3071	8.76
Rgs20	-1.239	2.38152658	14.257	0.000159	0.00893	7.9507	8.0317	4.9894	2.6643	3.5478	2.717
Ilf5	-0.64306	5.65410543	14.238	0.000161	0.008997	70.677	63.517	49.092	42.224	42.66	32.69
BC100530	-0.71383	8.48242569	14.183	0.000166	0.009188	435.61	350.96	545.98	237.76	247.74	326.8
Ctsz	-1.1593	3.04608953	14.168	0.000167	0.009205	12.679	11.937	8.6423	6.2166	5.7976	2.892
2410015M20Rik	-0.70399	6.26614978	14.114	0.000172	0.009397	113.03	91.223	80.988	67.575	65.332	42.3
Tomm7	-0.63099	6.14011525	14.023	0.000181	0.009746	97.752	82.454	76.088	64.104	58.928	42.60
2900060B14Rik	-0.90291	3.51503024	14.018	0.000181	0.009749	17.408	14.148	12.206	9.2845	6.5764	7.626
Lif	-1.4734	1.56537418	13.923	0.00019	0.010166	2.7618	4.8632	4.8112	1.6147	1.1249	1.665
Rgs2	-0.78744	4.30794769	13.915	0.000191	0.010166	30.129	18.864	25.392	16.793	13.326	13.06
Olah	-2.6286	-0.26282765	13.91	0.000192	0.010166	1.2972	1.2527	0.71277	0	0	0.5259
Enox1	-1.4326	2.77276271	13.865	0.000196	0.010385	13.265	10.979	4.3657	3.956	4.067	2.629
Ank	-0.62954	5.06676281	13.858	0.000197	0.0104	40.716	44.801	35.906	23.655	23.537	31.38
Cbr3	-0.58769	5.42726128	13.77	0.000207	0.010758	51.847	53.348	49.181	36.169	39.112	27.43
Gjb4	-1.046	5.23560478	13.727	0.000211	0.010935	68.334	53.717	29.045	31.971	25.267	16.04
Slc6a15	-2.3371	-0.31068955	13.726	0.000212	0.010935	1.3809	0.66317	0.98006	0.32294	0.086532	0.1753
Kalrn	-1.2823	5.00138599	13.711	0.000213	0.010962	59.546	43.18	32.253	31.244	15.662	8.590
D10Bwg1379e	-1.6826	0.53830427	13.704	0.000214	0.010962	2.0923	1.5474	2.1383	0.48441	0.43266	0.876
Ak1	-0.80153	4.96390658	13.698	0.000215	0.010962	48.081	31.095	38.935	30.033	19.729	18.05
Gpc4	-0.56904	6.15647548	13.698	0.000215	0.010962	98.337	77.886	78.583	59.986	49.064	62.9
Cmb1	-5.2397	-1.64119205	13.648	0.00022	0.011204	0.16738	0.5158	0.35638	0	0	0
Acat3	-2.1379	0.91043330	13.638	0.000222	0.011234	2.72	1.2527	4.3657	0.64588	1.0384	0.1753
Krt17	-0.99119	9.35848871	13.609	0.000225	0.011357	1211.6	766.85	640.78	627.47	376.33	313.9
Lrrc8c	-1.5391	0.85267126	13.585	0.000228	0.011475	2.6781	2.579	1.871	0.80735	0.86532	0.7889
Gulp1	-2.2238	-0.23491717	13.574	0.000229	0.011506	1.4228	1.0316	0.71277	0.24221	0.34613	0.0876
Heph	-0.51765	6.77146766	13.553	0.000232	0.011587	137.97	127.92	119.3	97.528	79.177	92.48
Ceacam2	-3.0632	-1.10046814	13.546	0.000233	0.0116	0.50215	0.5158	0.62367	0	0	0.1753
Skint4	-1.0912	5.80688397	13.475	0.000242	0.011963	102.77	78.107	46.508	55.142	25.7	25.94
Mllt4	-0.57992	8.83851318	13.385	0.000254	0.012513	612.87	548.29	483.7	362.42	334.19	404.0
Fabp5	-0.61816	6.96801049	13.354	0.000258	0.012643	143.95	168.15	142.11	89.858	124.35	81.69
Snx22	-1.5807	3.34433017	13.341	0.00026	0.012697	25.819	7.1475	11.137	5.3285	6.836	2.629
Hes1	-0.51136	6.38776433	13.283	0.000268	0.01298	109.51	90.265	94.709	70.885	64.207	71.70
Mir703	-0.9481	3.79551687	13.275	0.000269	0.013001	21.843	14.737	17.374	9.6882	12.201	6.136
Bglap3	-2.5934	0.07071951	13.263	0.000271	0.013054	2.0923	1.7685	0.26729	0.16147	0.34613	0.1753
Rnf122	-0.88426	3.13133422	13.193	0.000281	0.01349	11.842	10.095	11.404	6.1359	5.2784	6.662
Lama4	-1.1526	3.90662293	13.177	0.000283	0.013575	20.128	12.748	28.511	12.433	5.4515	9.642
Adamts5	-2.3604	0.81208501	13.167	0.000285	0.013589	4.059	2.6527	0.62367	0.72662	0.17306	0.5259
Skint2	-1.7678	1.48785762	13.098	0.000296	0.013967	4.5193	5.8212	1.5146	0.96882	1.1249	1.402
Fkbp1a	-0.68563	4.51574887	13.092	0.000297	0.013979	30.547	31.758	21.472	16.631	17.826	17.79
Nrep	-1.1318	3.42287541	13.083	0.000298	0.014013	15.943	16.506	10.781	9.1231	7.0956	3.506
Slc9a7	-1.6979	0.70149916	13.069	0.0003	0.01409	1.7994	1.7685	3.2075	0.72662	0.43266	0.876
Cachd1	-0.50654	7.45579661	13.065	0.000301	0.01409	218.85	211.04	187.55	138.7	142.35	153.7
Ptn	-0.4758	5.91347411	12.986	0.000314	0.014628	69.38	67.054	73.415	53.285	51.313	46.19
Lrrfip1	-0.49813	5.76473053	12.974	0.000316	0.014689	69.548	58.506	62.189	44.243	47.766	42.86

Pcsk5	-1.7706	2.10205773	12.953	0.000319	0.014817	9.6664	5.6738	3.1184	3.0679	1.471	0.876
Fn1	-1.1276	4.86398028	12.946	0.000321	0.014817	61.639	37.138	19.69	21.233	13.672	19.4
Cox8a	-0.61612	6.83394104	12.916	0.000326	0.015018	150.64	135.07	127.76	94.622	107.73	67.49
Cygb	-1.3458	1.35236437	12.884	0.000331	0.015245	3.4732	3.979	2.6729	1.3725	1.471	1.139
Apex1	-0.62045	6.30415627	12.836	0.00034	0.015576	104.78	92.991	88.74	74.034	66.543	45.84
Slc41a2	-2.1621	1.17089406	12.805	0.000346	0.015766	2.3852	1.6948	6.3258	1.0496	0.17306	1.051
Atxn7l1	-0.76806	4.05081290	12.785	0.000349	0.015901	20.546	19.527	21.918	11.868	9.0859	15.42
Ndufa4	-0.79918	6.48742389	12.776	0.000351	0.015924	144.33	111.27	85.265	78.313	74.677	43.04
Foxg1	-2.6698	3.47871460	12.771	0.000352	0.015924	45.528	7.5159	1.871	2.9872	3.9805	1.665
Myh2	-2.3722	-0.32582749	12.739	0.000358	0.016122	0.83691	0.73686	1.6928	0.24221	0	0.3506
Hadh	-0.53094	7.40980989	12.716	0.000363	0.016285	207.76	212.66	181.85	136.28	157.4	123.2
Cyp17a1	-1.2833	2.67018060	12.669	0.000372	0.016594	11.508	9.137	5.2567	3.5523	2.3364	4.821
Rps15a-ps6	-0.7092	5.37251385	12.622	0.000381	0.016977	58.417	51.138	43.835	40.045	31.671	22.17
Hdac7	-0.76103	5.29287899	12.596	0.000387	0.017178	49.587	46.053	51.587	19.942	26.133	40.84
Crot	-0.49185	6.53235971	12.515	0.000404	0.017782	111.69	116.57	95.6	77.829	82.032	70.56
Ttc22	-0.62276	4.31461191	12.512	0.000404	0.017782	25.944	24.537	21.116	14.936	15.662	16.04
Ii34	-0.55219	5.31466380	12.438	0.000421	0.018301	46.7	51.211	43.39	27.45	32.969	36.02
Snord33	-3.4833	-1.3827301	12.337	0.000444	0.019244	0.41846	0.5158	0.26729	0	0.086532	0
Gm5148	-1.8476	2.19913873	12.313	0.00045	0.019405	9.8337	3.3159	7.1277	2.5028	2.6825	0.438
Slc39a8	-0.51771	6.35227208	12.301	0.000453	0.019491	94.488	110.68	82.77	62.57	70.437	68.19
Qrich2	-1.5416	1.10804288	12.287	0.000456	0.019606	3.2221	3.3895	2.0492	0.64588	1.5576	0.7889
Lphn2	-0.57966	6.54666603	12.275	0.000459	0.019648	132.69	108.1	94.353	81.462	61.351	81.69
Ccl27a	-0.82556	6.25559837	12.24	0.000468	0.019936	109.13	115.83	67.179	70.643	58.149	36.11
Gas7	-0.83922	5.40896471	12.187	0.000481	0.020427	69.338	47.232	45.974	44.001	24.662	22.26
Ifitm3	-0.76376	6.30752092	12.17	0.000486	0.020532	132.48	93.36	72.168	72.096	60.053	43.56
C1qtnf7	-1.5427	0.75936631	12.143	0.000493	0.020793	2.4271	1.5474	2.762	0.72662	0.60572	0.9642
Pglyrp4	-1.6229	3.11726169	12.13	0.000496	0.020851	18.119	15.695	4.0093	4.9248	5.2784	2.103
Bnc2	-0.73385	3.62958131	12.051	0.000518	0.021453	14.646	14.811	16.305	8.3964	9.0859	9.993
Gm10677	-1.5564	0.71703630	11.897	0.000562	0.023115	2.4689	1.6948	2.3165	0.96882	0.86532	0.3506
Map2	-0.69767	5.17099462	11.876	0.000569	0.023252	47.704	42.222	43.033	25.593	19.383	37.0
Ccl8	-1.2225	2.16058599	11.875	0.000569	0.023252	5.7747	5.8212	6.4149	1.6954	2.1633	3.85
Arl15	-0.5192	5.34874020	11.862	0.000573	0.023371	51.428	50.548	41.252	32.375	32.969	34.80
Tbx18	-3.6675	-0.55746389	11.845	0.000578	0.023534	1.7994	0.44211	0.089096	0.16147	0	0
Snord12	-1.9012	-0.22204903	11.779	0.000599	0.02406	0.96245	1.4	0.89096	0.32294	0.2596	0.2629
Fxyd5	-1.6935	0.21354576	11.779	0.000599	0.02406	1.9249	1.2527	1.1583	0.48441	0.43266	0.438
4930473A02Rik	-2.2085	0.14319899	11.701	0.000625	0.024993	2.0923	0.5158	1.7819	0.080735	0.51919	0.3506
Igsf10	-1.5103	1.23744893	11.675	0.000633	0.025251	4.352	2.9474	2.0492	0.96882	0.77879	1.577
Tec	-0.71423	4.70349269	11.671	0.000635	0.025251	39.753	30.506	25.927	24.463	16.614	17.70
Prss12	-1.154	1.89329918	11.671	0.000635	0.025251	4.4775	4.9369	5.2567	1.8569	1.9037	2.805
Snora7a	-1.0089	2.42871678	11.612	0.000655	0.02592	7.1556	7.737	5.8803	3.7138	3.5478	3.068
Lipg	-0.80558	3.72833069	11.594	0.000662	0.026054	19.249	18.127	12.295	10.576	7.9609	9.993
Dctpp1	-0.71797	4.60612106	11.592	0.000662	0.026054	36.782	28.664	24.501	20.83	20.335	13.67
Srgn	-2.9934	-1.12410776	11.588	0.000664	0.026058	0.62769	0.58948	0.26729	0	0	0.1753
Dgat2	-0.6858	4.72339970	11.57	0.00067	0.026256	35.82	36.548	24.501	17.6	18.518	24.28
Adamts18	-2.0382	0.49139956	11.563	0.000673	0.026268	1.5064	0.88423	3.742	0.40368	0.34613	0.7012

Cyp7b1	-2.309	0.96900575	11.556	0.000675	0.026309	1.8412	1.5474	5.7913	0.080735	0.51919	1.227
Fzd3	-1.1205	4.05796208	11.527	0.000686	0.026621	29.418	23.285	14.612	15.097	10.73	5.171
Tmem180	-1.5876	0.27348107	11.49	0.0007	0.027013	1.632	1.5474	1.4255	0.64588	0.60572	0.2629
Ado	-0.48291	6.38232597	11.46	0.000711	0.0274	97.375	103.16	90.611	78.071	68.62	61.62
Syt12	-0.86989	3.61983182	11.446	0.000717	0.027538	18.287	13.484	15.057	11.707	7.0956	6.837
Spata13	-1.4502	1.33714667	11.439	0.000719	0.027538	4.3101	3.1685	2.5838	1.7762	1.298	0.6136
Pcbd1	-1.7438	0.41128330	11.437	0.00072	0.027538	2.5526	1.3263	1.1583	0.40368	0.69226	0.438
Ggh	-0.63714	6.64138130	11.393	0.000737	0.028049	141.52	133.74	88.383	89.051	82.984	61.97
Pnpla1	-0.79539	5.00792241	11.293	0.000778	0.02927	53.521	43.622	24.234	23.978	20.941	25.24
Clic3	-0.85768	3.88998822	11.122	0.000853	0.031595	23.434	20.927	11.939	11.707	10.73	8.76
Ung	-0.61727	4.38069970	11.071	0.000877	0.032408	25.693	23.579	25.749	16.712	19.21	12.97
Mrpl41	-0.56081	4.70278650	11.057	0.000883	0.032504	32.723	29.253	30.471	22.929	21.72	18.05
Terc	-0.97164	3.89336108	11.056	0.000884	0.032504	13.516	22.769	22.274	11.303	12.72	5.697
Angpt1	-2.0069	0.34033586	11.033	0.000895	0.032735	1.3809	3.0948	0.71277	0.40368	0.60572	0.2629
Eif4ebp1	-0.60814	4.67662825	11.004	0.000909	0.033201	34.439	31.39	26.016	22.444	21.027	16.91
Insig2	-0.53484	5.94510951	10.967	0.000928	0.033645	81.474	73.98	62.456	61.116	45.083	44.35
Mir3074-1	-2.9183	-1.1684016	10.963	0.00093	0.033645	0.66953	0.44211	0.26729	0.080735	0	0.0876
Atp6v1b2	-0.49805	5.78974370	10.94	0.000941	0.033999	69.757	69.264	54.527	49.491	40.93	46.8
Pdzd4	-0.4875	5.15195146	10.93	0.000946	0.034138	43.31	42.296	38.222	31.81	29.075	27.52
Ninj1	-0.68759	4.03057187	10.888	0.000968	0.034785	23.015	18.053	18.621	15.017	11.163	10.95
Nop10	-0.57906	5.25099439	10.865	0.00098	0.035035	49.755	49.075	37.242	34.393	32.19	24.63
Adamts9	-1.1135	2.99068066	10.847	0.00099	0.03521	12.261	8.2528	11.226	7.5084	4.4131	2.717
Hebp2	-0.53405	5.97075729	10.808	0.00101	0.035764	80.72	80.465	60.585	50.863	59.274	43.21
Fscn1	-0.48345	5.45610128	10.808	0.001011	0.035764	51.679	44.58	56.754	35.523	35.911	37.95
Astn2	-3.6179	-0.5780098	10.805	0.001012	0.035764	1.7575	0.5158	0	0.080735	0	0.0876
Pkib	-0.68854	4.55810429	10.786	0.001023	0.036019	33.435	31.685	21.205	20.507	14.537	18.67
Nme1	-0.61495	6.14660382	10.768	0.001033	0.036277	99.76	82.159	74.395	62.812	65.245	39.44
Gstp1	-0.5974	4.67760664	10.767	0.001034	0.036277	34.272	28.811	28.6	23.009	21.2	16.4
Rbms3	-1.2407	3.93399139	10.761	0.001037	0.036327	27.702	23.064	12.473	14.694	8.0475	4.032
Bzw2	-0.51892	6.79530244	10.756	0.001039	0.036357	150.35	130.72	110.57	99.062	96.656	77.84
Fdft1	-0.55001	5.85459737	10.752	0.001042	0.036386	83.357	70.37	51.587	49.571	46.035	44.96
Atp5o	-0.56768	7.06823611	10.73	0.001054	0.036752	185.29	155.33	139.35	125.54	115.17	83.27
Icam2	-1.9391	-0.44874724	10.711	0.001065	0.036853	0.83691	0.81054	1.0692	0.16147	0.17306	0.3506
Fhdc1	-0.44462	6.24538890	10.711	0.001065	0.036853	93.483	88.865	79.296	62.085	64.812	65.5
Aldh3b2	-0.5985	6.31588324	10.706	0.001068	0.036853	117.63	99.77	69.495	70.401	63.428	55.92
Rarres1	-0.92021	4.66483306	10.703	0.00107	0.036853	26.112	31.169	41.786	11.949	13.153	27.17
Tcf4	-0.43772	6.07507490	10.703	0.00107	0.036853	76.494	78.475	77.157	52.559	55.986	62.85
Dnm3	-1.1564	2.69344153	10.7	0.001071	0.036853	9.7501	8.0317	8.1078	2.745	2.5094	6.399
Txnrd3	-0.46276	5.97912817	10.613	0.001123	0.038448	77.959	73.317	67.357	59.502	52.611	46.63
Galt	-0.52552	4.95287714	10.585	0.00114	0.038846	38.665	38.095	32.164	27.208	26.219	22.35
Sardh	-1.4242	1.18571662	10.563	0.001154	0.039122	3.3477	2.3579	3.3857	1.4532	1.471	0.438
Capn2	-0.78262	6.57262303	10.557	0.001157	0.039176	117.42	95.497	147.63	58.614	47.852	103.0
Nme4	-1.0425	1.93500979	10.518	0.001182	0.039637	5.3563	4.6422	4.633	2.5835	2.1633	2.366
Fbln2	-1.6683	0.81720876	10.492	0.001199	0.040044	3.5987	1.2527	2.0492	1.0496	0.51919	0.6136
Stxbp6	-1.3718	1.12709477	10.49	0.0012	0.040044	3.7243	2.579	2.1383	1.3725	1.2114	0.7012

Ccr2	-3.6462	-1.19945372	10.49	0.0012	0.040044	0.87876	0.22106	0.17819	0	0	0.0876
Tomm5	-0.52017	5.13687748	10.482	0.001206	0.040131	44.482	38.759	40.45	31.406	31.152	23.75
Cyp27a1	-0.84982	3.82810998	10.48	0.001207	0.040131	18.538	16.063	19.512	14.209	9.3455	6.399
Pycard	-0.54687	7.60325655	10.468	0.001215	0.040234	245.8	238.67	207.42	172.45	179.73	121.1
Angptl1	-4.5753	-1.95962314	10.467	0.001216	0.040234	0.25107	0.14737	0.17819	0	0	0
Bola2	-0.63301	4.66815278	10.416	0.001249	0.041022	33.477	30.801	27.709	21.556	23.277	14.55
Rnu11	-0.69128	3.94289578	10.382	0.001272	0.041646	20.672	19.821	15.681	11.061	14.018	9.817
Nipal1	-0.97702	2.83657539	10.372	0.00128	0.041825	11.926	8.6212	6.8604	5.8129	3.8074	4.38
Lypd5	-1.9532	-0.16417976	10.368	0.001282	0.041835	1.2972	1.5474	0.44548	0.24221	0.2596	0.3506
Uqcr10	-0.66929	5.99082141	10.356	0.001291	0.041922	93.4	76.265	63.704	60.955	53.304	32.60
Cacnb4	-2.1016	-0.45951801	10.34	0.001302	0.042227	1.2554	0.73686	0.53458	0.24221	0.086532	0.2629
Slc39a2	-1.3581	2.71703180	10.333	0.001307	0.042317	11.508	11.495	4.1875	5.5707	2.8556	2.191
Bmp7	-0.43559	5.89394169	10.325	0.001313	0.042424	76.243	65.875	62.189	49.733	51.66	49.96
Paqr8	-1.1773	1.29679112	10.259	0.00136	0.043767	3.6406	2.9474	2.762	1.3725	1.298	1.490
Cox6b2	-1.8455	-0.37652433	10.233	0.001379	0.044279	1.0043	0.81054	0.98006	0.32294	0.34613	0.0876
Isyna1	-0.60988	4.69712523	10.232	0.00138	0.044279	34.062	34.485	24.68	23.252	20.595	17.35
Sptb	-1.5607	2.08370151	10.203	0.001402	0.044918	4.1009	3.0948	11.315	2.0184	1.3845	2.805
Mrpl55	-0.72111	3.94594043	10.191	0.001411	0.045065	23.517	16.211	16.928	12.837	12.461	9.204
Itgb8	-1.455	3.79424449	10.132	0.001457	0.046243	27.409	19.969	12.295	13.079	6.663	2.016
Ostc	-0.55365	5.81071730	10.13	0.001459	0.046243	72.686	66.833	60.051	51.428	51.4	33.22
Gm6548	-0.74895	6.91707501	10.124	0.001464	0.046283	227.72	114.58	111.1	99.466	92.676	77.9
Cox6b1	-0.6047	6.82034343	10.079	0.001499	0.047229	163.74	132.27	112.17	105.76	97.175	65.65
Trpm4	-0.45699	5.61803849	10.072	0.001505	0.047342	53.855	52.833	63.347	39.641	39.805	44.26
Rpl39	-0.58443	9.27183977	10.049	0.001525	0.047669	835.66	759.48	629.11	571.77	519.28	392.4
Cat	-0.64997	6.36640274	10.049	0.001525	0.047669	132.23	98.149	70.921	76.941	55.38	59.95
Pyy	-1.5281	0.94721100	10.04	0.001532	0.04783	3.5569	2.579	1.3364	1.0496	0.51919	1.051
Snrpd3	-0.69662	4.06415058	10.026	0.001543	0.048111	24.061	22.474	14.612	11.707	13.326	12.88
Scel	-0.53809	8.80933311	10.013	0.001555	0.048313	626.26	545.72	421.07	365.57	346.73	385.0
Hoxc8	-0.62127	3.87345495	10.007	0.001559	0.048345	18.998	16.211	17.374	12.11	10.816	11.30
Pcsk6	-0.65327	5.69329852	10.006	0.00156	0.048345	83.399	63.001	42.321	45.212	37.468	37.60
Fgfbp1	-0.50292	7.82660279	9.9896	0.001574	0.04871	306.69	256.79	234.23	211.69	186.74	164.7
Cers2	-0.60243	4.04633395	9.9659	0.001595	0.049123	22.095	19.674	17.196	12.433	13.412	13.14
Ndufa12	-0.61666	5.13679580	9.9616	0.001598	0.049163	50.173	42.59	34.124	31.002	31.325	20.

LogFC = Log Fold change, LogCPM = Log count per million bases, LR = Log Ratio, FDR = BH corrected P-value, values in columns S7309-S7314 depict TMM normalized relative expression.

**Supplementary Table S2 Pathway analysis of upregulated (A) and downregulated (B) genes in Lgr6<sup>+</sup> basal epidermal keratinocytes.**

**A.**

KEGG_PATHWAY analysis using DAVID 6.8: Genes upregulated in Lgr6 <sup>+</sup> basal epidermal keratinocytes					
Term	Genes	Count	%	P-Value	Benjamini Hochberg corrected
Pathways in cancer	FGFR2, WNT16, FGFR3, PDGFB, WNT3A, ADCY6, FGF13, LAMB3, WNT4, PLCB4, AXIN2, MMP1B, BMP4, COL4A4, COL4A3, BMP2, WNT10B, COL4A2, TGFBR1, ITGA2, KITL, COL4A6, WNT7B, LAMA3, LAMC2, LAMC1, PTCH2	27	9,4	1,70E-10	2,90E-08
Amoebiasis	COL4A4, GNA14, COL4A3, IL1R1, COL4A2, COL4A6, LAMB3, PLCB4, LAMA3, SERPINB2, HSPB1, LAMC2, LAMC1	13	4,5	1,90E-07	1,60E-05
Hedgehog signaling pathway	BMP4, WNT16, WNT10B, BMP2, WNT7B, WNT4, WNT3A, GAS1, PTCH2	9	3,1	5,40E-07	3,10E-05
Basal cell carcinoma	BMP4, WNT16, WNT10B, BMP2, WNT7B, WNT4, WNT3A, PTCH2, AXIN2	9	3,1	1,60E-06	6,80E-05
Small cell lung cancer	COL4A4, COL4A3, COL4A2, LAMB3, LAMA3, ITGA2, LAMC2, LAMC1, COL4A6	9	3,1	3,90E-05	1,30E-03
Signaling pathways regulating pluripotency of stem cells	FGFR2, BMP4, WNT16, WNT10B, BMP2, WNT7B, WNT4, FGFR3, WNT3A, LIFR, AXIN2	11	3,8	4,60E-05	1,30E-03
ECM-receptor interaction	COL4A4, COL4A3, COL4A2, LAMB3, LAMA3, ITGA2, LAMC2, LAMC1, COL4A6	9	3,1	5,50E-05	1,30E-03
PI3K-Akt signaling pathway	FGFR2, COL4A4, COL4A3, COL4A2, FGFR3, PDGFB, OSMR, ITGA2, FGF13, KITL, IRS1, COL4A6, LAMB3, LAMA3, LAMC2, NGFR, LAMC1	17	5,9	8,10E-05	1,70E-03
Cytokine-cytokine receptor interaction	IL12RB2, IL1R1, CXCL14, PDGFB, OSMR, CCR4, IL20RA, TGFBR1, LIFR, EDAR, NGFR, KITL, IL22RA2	13	4,5	3,40E-04	6,40E-03
Hippo signaling pathway	BMP4, WNT16, WNT10B, BMP2, WNT7B, WNT4, CTGF, TGFBR1, WNT3A, AXIN2	10	3,5	4,60E-04	7,90E-03
119 of 291 upregulated genes were categorized in a pathway					

**B.**

KEGG_PATHWAY analysis using DAVID 6.8: Genes downregulated in Lgr6 <sup>+</sup> basal epidermal keratinocytes					
Term	Genes	Count	%	P-Value	Benjamini Hochberg corrected
Metabolic pathways	LDHB, ATP5E, GCNT2, OLAH, ACOT1, ITPKB, ADH7, ATP6V1B2, PSPH, CMBL, FDFT1, ALDH3A1, ISYNA1, UQCR10, CERS2, COX6B1, ATP5O, COX6B2, HADH, SARDH, BDH1, IMPDH1, DCTPP1, NDUFA4, EBP, AK1, COX8A, GALT, EPHX2, ALDH3B2, CBR3, NDUFA12, GNS, NME4, CYP17A1, ADO, CYP27A1, DGAT2, NME1, LIPG, AOX4	41	10,6	3,30E-05	6,00E-03
Metabolism of xenobiotics by cytochrome P450	GSTM1, ALDH3B2, ADH7, CBR3, GSTM5, GSTP1, ALDH3A1	7	1,8	9,70E-05	8,90E-03
Drug metabolism - cytochrome P450	GSTM1, ALDH3B2, AOX4, ADH7, GSTM5, GSTP1, ALDH3A1	7	1,8	1,40E-04	8,60E-03
Oxidative phosphorylation	NDUFA4, ATP5E, UQCR10, COX8A, COX6B1, ATP5O, ATP6V1B2, COX6B2, NDUFA12	9	2,3	2,30E-03	1,00E-01
Alzheimer's disease	NDUFA4, ATP5E, UQCR10, COX8A, GRIN1, COX6B1, ATP5O, COX6B2, CAPN2, NDUFA12	10	2,6	2,90E-03	1,00E-01

131 of 391 down regulated genes were categorized in a pathway



**Supplementary Table S3 Primers used for qPCR.**

Gene	Primer sequence (5'→ 3')	Amplicon size	Exonic Location	Accession No.	Amplification efficiency	Correlation (R <sup>2</sup> )
<i>Cyc1</i>	GATGTCGCCACCTTCCTTCGC	136	6, 7	NM_025567.2	98.6%	0.99
	GGACTGACCACTTATGCCGCTTC					
<i>Ddx52</i>	CACAGCAGCAGCGAGATAACAC	177	10-11, 11-12	NM_030096	107.0%	0.99
	CTCTTCCAGTCCGACCTATCCTATG					
<i>Lgr6 ex1-2</i>	GCTGTCCGCTGACTGCTC	102	1, 2	NM_001033409	95.0%	0.97
	AGCTCCGTGAGGTTGTTTCAT					
<i>Lgr6 ex1-3</i>	GGACCCCCTGACGGCTTA	120	1, 3	NM_001033409	95.0%	0.97
	TGTGAGAGGTGGTTCCTGA					
<i>Lgr6 ex3-4</i>	TCAGGGAACCACCTCTACA	113	3, 4	NM_001033409	92.0%	0.95
	CATAGTGCCTCTGCTGGGAT					
<i>Mki67</i>	CAGAAGAAATGGAAGCCAAAA	110	12, 13	NM_001081117.2	96.5%	0.99
	TGCAGATGCATCAAACCTTGG					

**Supplementary Table S4. Sample information RNA-seq**

Mouse code	Gender	Genotype	Age (days)	sample IDs
701	M	Lgr6-EGFP-IRES-CreERT2 heterozygous	28	7309/ 7310
721	F	Lgr6-EGFP-IRES-CreERT2 heterozygous	31	
720	M	Lgr6-EGFP-IRES-CreERT2 heterozygous	31	7311/ 7312
722	F	Lgr6-EGFP-IRES-CreERT2 heterozygous	31	
565	M	Lgr6-EGFP-IRES-CreERT2 heterozygous	95	7313/ 7314
774	F	Lgr6-EGFP-IRES-CreERT2 heterozygous	90	
508	M	Lgr6-EGFP-IRES-CreERT2 homozygous	147	7315/ 7316
550	F	Lgr6-EGFP-IRES-CreERT2 homozygous	176	