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Short title:

scRNA sequencing of T cells in Crohn's disease

Authors:

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Statement of author contributions:

W.T.C.U.V. and M.D.V contributed equally to this work and are shared first authors. W.T.C.U.V. and M.D.V and E.A.M.F. participated in conception, design and coordination of the study. G.D., R.K.W. and E.A.M.F recruited patients. W.T.C.U.V., M.D.V. and B.H.J. performed the laboratory experiments. W.T.C.U.V., M.D.V., G.v.d.V., A.V.V and E.A.M.F. performed the data analyses and data interpretation. B.J., K.N.F., G.D., R.J.X., C.W. and D.B.G. provided support with data interpretation. All authors assisted in the writing and reviewing of the manuscript, and approved of sending it out for publication.

Abbreviations:

CD	Crohn’s disease
CTL	Cytotoxic T lymphocytes
IEL	Intraepithelial T lymphocytes
LPL	Lamina propria T lymphocytes
PBL	Peripheral blood T lymphocytes
scRNAseq	Single-cell RNA (ribonucleic acid) sequencing
Th17	T-helper 17
Treg	T-regulatory cell

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There are no (potential) conflicts of interest to declare.

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Introduction:

Crohn's disease (CD) is a chronic inflammatory disease predominantly affecting the terminal ileum. The ~200 CD-risk loci identified by genome-wide association studies (GWAS) are enriched for genes involved in T-cell signalling, highlighting the importance of T cells in CD pathology[1,2]. It is crucial to study T cells in their disease-relevant context: the intestinal mucosa. Although human single-cell atlases are in development[3], location- and disease-specific single-cell RNA sequencing (scRNAseq) datasets are still scarce. Here we use scRNAseq of disease-relevant cells to examine pathomechanisms and identify potential drug targets on a cellular level in CD.

Methods:

We performed flow-cytometry and scRNAseq of 5,292 CD3-positive T cells isolated from peripheral blood (PBL) and ileal biopsies of three CD patients with mild to moderate disease activity (**Figure 1, step 1**). Biopsies were dissociated and separated into intraepithelial T lymphocytes (IEL) and lamina propria T lymphocytes (LPL)[4]. We then integrated T-cell transcriptomes with GWAS CD-risk loci and drug-target identification resources. Through literature search and online database analysis, we identified 179 CD-risk genes and 2,712 drug-target genes that we aligned to differentially expressed genes. Finally, we selected genes encoding proteins targeted by drugs currently available for (clinical trials in) humans (**Supplementary Methods**).

Results:

After quality control, 4,070 T cells remained for analysis. These cells expressed 966 genes per cell, on average, and 41,134 distinct genes in total (**Figure 1, step 2**). IEL, LPL and PBL showed markedly different expression profiles (**Supplementary Figure 1, Supplementary Table 1**).

Unsupervised clustering of scRNAseq data identified 6 distinct T-cell types that have different distributions in IEL, LPL and PBL: cytotoxic T lymphocytes (CTL) dominate the IEL, quiescent T cells dominate the PBL reservoir, and T-helper 17 (Th17) cells dominate the LPL (**Figure 1, step 3**). In peripheral blood, Treg cells intermixed with effector T cells (Effector/Treg cells) and quiescent T cells (Treg/Quiescent cells). Treg/Quiescent cells were also present in the IEL and LPL. In both the IEL and LPL, we identified a cluster of cells of a previously undefined cell type characterized by expression of both *CD3* and *REG1A/B*, and confirmed this with immunofluorescence staining. All T-cell subtypes were present in all patients.

Strikingly, all cell-subtype clusters consisted of both epitopic CD8αβ-positive and –negative cells. Moreover, *CD8A* and *CD8B* transcripts were expressed in both epitopic CD8αβ-positive and -negative cells, which was confirmed in a publicly available naïve CD4+ T-cell scRNAseq dataset[5].

Using permutation analysis, we found that both IEL and LPL expressed significantly more CD-risk genes than expected by chance (*P*=0.00389 and *P*<0.00001, respectively), suggesting that cells within these compartments play a role in CD inflammation[2]. PBL were not enriched for CD-risk-gene expression (*P*=0.45954). Th17 cells show the highest number of overexpressed CD-risk genes and are most specifically enriched for CD-risk-gene expression (*P*<0.00001). Mucosal CTL and Treg/Quiescent and peripheral blood Effector/Treg cells are also significantly enriched for CD-risk-gene expression (*P*=0.0278, *P*=0.02477 and *P*=0.00081, respectively).

We investigated which drug targets are expressed by Th17 and CTL, both cell types with well-characterized expression signatures that play a central role in CD pathogenesis (**Table 1**). Th17 cells showed upregulation of *IL17A*, whose gene product is targeted by Secukinumab. *ITGAE*, whose gene product is targeted by Etrolizumab, is upregulated in mucosal CTL. *S1PR5*, upregulated in peripheral blood CTL, is a known drug target for Ozanimod. Potential targets for drug repositioning include: *PDE4D* in mucosal Th17 cells, a target for Apremilast, under investigation for treatment of ulcerative colitis; *ITGB2* in peripheral blood CTL, a target for Lifitegrast, approved for keratoconjunctivitis sicca; and *ALOX5AP* in mucosal CTL, a target for Fiboflapon, under investigation for asthma.

Discussion:

We have demonstrated that multiple ileal mucosal T-cell subtypes and one peripheral blood T-cell subtype from CD patients are enriched for CD-risk-gene expression. T-cell subtypes known to be involved in CD pathogenesis provide promising targets for future cell-type-specific therapies in CD patients. A limitation of our study is the small sample size, which may reduce the amount of variation covered. However, most cell-type-specific gene-expression signatures remained after correcting for inter-individual differences. As location- and disease-specific scRNAseq data are still limited, detailed datasets like ours are an important reference for furthering our understanding of the molecular processes leading to health and disease and identifying potential targets for drug development.

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Author names in bold designate shared co-first authorship.

Figure Legends:

Figure 1: Experimental flow chart. EDTA and collagenase are treatments used to isolate intraepithelial and lamina propria cells, respectively. T-cell-subtype characterization as described in **Supplementary Methods**. In brackets: number of epitopic CD8αβ-positive T cells measured by flow-cytometry. **IEL**: intraepithelial T lymphocyte. **LPL**: lamina propria T lymphocyte. **PBL**: peripheral blood T lymphocyte. **FACS**: fluorescence-activated cell sorting.

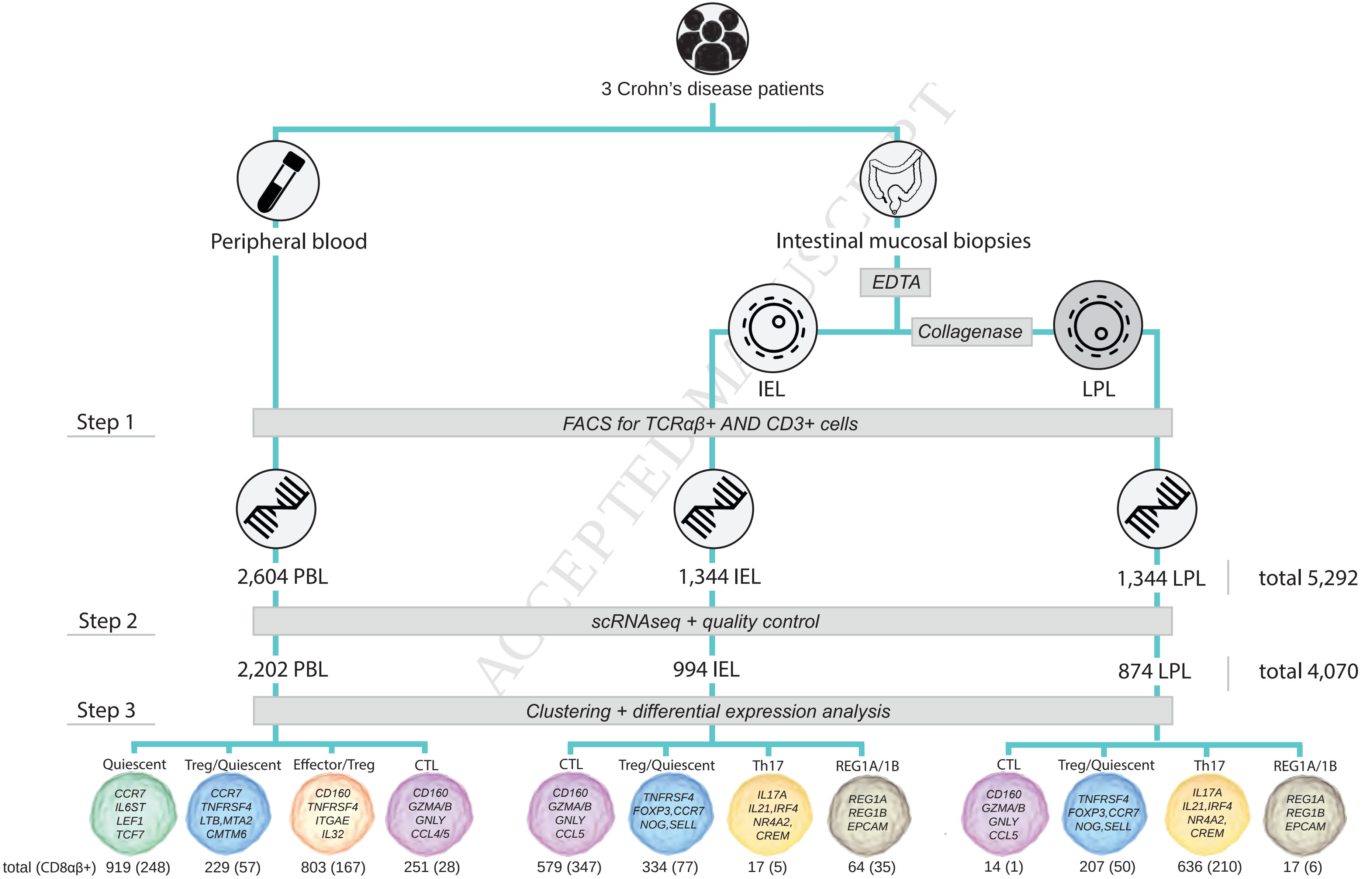
Table 1: Overexpression of CD-risk genes and genes encoding potential drug targets in ileal mucosal Th17 cells and cytotoxic T lymphocytes

	mucosal Th17 cells		**peripheral blood CTL**		**mucosal CTL**	
	Gene	**Function**	**Gene**	**Function**	**Gene**	**Function**
CD-risk gene	*CCL20*	Chemoattractant for various immune cells	*CTSW*	Regulation of T cell cytolytic activity	*PLCG2*	Transmembrane signaling of immune system receptors
	DNAJB4	Heat shock protein, involved in protein folding	*LSP1*	Adhesion and trans endothelial migration	*PTPN22*	Negative regulator of TCR signaling, positive regulator of TLR signaling
	IFNG	Cytokine, involved in adaptive/innate immunity	*PRKCB*	Apoptosis regulation	*SOCS1*	Cytokine-inducible negative regulation of cytokine signaling
	IRF4	Regulation of mucosal Th17 cell differentiation	*PTPRC*	T cell antigen receptor signaling regulation		
	MAP3K8	T-helper cell differentiation and IFNγ expression				
	Gene	**Drug or compound**	**Gene**	**Drug or compound**	**Gene**	**Drug or compound**
Known CD-drug target	*IL17A*	Secukinumab	*S1PR5*	Ozanimod	*CD3D/E/G*	NI-0401
			FCGR3A	IgG class mAbs*	*ITGAE*	Etrolizumab
					CCR9	Vercirnon
					TGFBR1	Mongersen***
Candidate for drug repositioning	*DNAJB1*	Apatorsen	*CCL5*	Heparin compounds	*CCL5*	Heparin compounds
	SIK1	Dabrafanib	*FGR*	Dasatinib	*ADRB1*	STD-101-D1
	HSP90AA1	Nedocromil	*FCGR3A*	IgG class mAbs**	*ALOX5AP*	Fiboflapon
	PTGER4	Rivenprost; Limaprost; Dinoproston	*ITGB2*	Lifitegrast	*SLAMF7*	Elotuzumab
	PDE4D	Apremilast	*ADRB2*	Beta-2 adrenergic receptor blockers	*MDM4*	ALRN-6924

Legend: Ileal mucosal Th17 cells, peripheral blood cytotoxic T lymphocytes (CTL) and ileal mucosal CTL show the highest number of significantly overexpressed **CD-risk genes**. The top 5 most significantly overexpressed **CD-risk genes** are shown in the first row of this table; Per cell type, the top 5 most significantly overexpressed **known CD-drug targets** and **candidates for drug repositioning** are shown. Selection of **CD-risk genes** is explained in ‘Supplementary Methods: CD-risk genes’. ‘**Known CD-drug target**’ refers to genes encoding targets for drugs currently approved or under investigation for treatment of CD in humans. **‘Candidate for drug repositioning’** refers to genes encoding targets for drugs currently approved or under investigation in humans for other diseases than CD. (see 'Supplementary Methods: Drug-target genes’)
CD: Crohn's disease; **Th17**: T-helper 17 cells; **CTL**: cytotoxic T lymphocyte

*[e.g. Adalimumab; Etanercept; Natalizumab]
**[e.g. Alefacept; Alemtuzumab]
***indirect target

Figure 1: Flow chart illustrating procedure of T-cell isolation and single-cell RNA sequencing



Supplementary Methods:

For details of antibodies, reagents, kits and software used see **Supplementary Table 2**.

Patient selection and sample collection

For this study, we recruited one male and two female patients (ages 36, 25, and 48, respectively) with mild to moderate Crohn's disease (CD). Written informed consent was obtained and ethical approval was granted by the University Medical Center Groningen Ethics Committee. All three patients had been diagnosed with histologically proven ileal CD at least five years earlier. None had undergone surgical resections. For each patient, five pinch biopsies were collected from mildly inflamed terminal ileum: the most common site of inflammation in CD and a clear anatomical landmark.

Biopsies were collected into RPMI 1640 medium on ice and processed immediately. 10 mL of peripheral blood was collected subsequently in tubes containing 158 USP units lithium-heparin.

Tissue processing

Ileal biopsies were dissociated into single cells following a previously published protocol[1], separating IEL and LPL fractions using EDTA+DTT and collagenase digestion. RNAse-mediated RNA degradation was limited by adding 15µl RNAse Superase™ before collagenase digestion. PBL were isolated using density gradient centrifugation with Lymphoprep™ solution. Tissue processing, except for collagenase incubation, was performed on ice.

Flow Cytometry of single-cell suspensions

All cell suspensions (IEL, LPL and PBL) were stained with the same antibody panel comprising propidium iodide and monoclonal antibodies to TCRαβ, CD3, CD8α, CD8β, CD19, CD45RO, CD62L and CD326.

Cells were sorted using the MoFlo Astrios (Beckman Coulter, Inc.), using forward- and side-scatter signals to define lymphocyte fraction and exclude unwanted events such as debris, non-viable cells and doublets. CD3+TCRαβ+ lymphocytes were sorted one-cell-per-well into 384-well plates containing cell lysis buffer, on ice (see 'Single-cell RNA library preparation and sequencing') (**Figure 1, step 1**). To minimize cell perturbation, sorting was performed at low pressures. After sorting, each cell was collected in a well containing lysis buffer consisting of dNTP mix, Oligo dT primer, Triton X-100 and RNase inhibitor.

Single-cell RNA library preparation and sequencing

Single-cell transcriptome libraries were created using a protocol based on Smart-Seq2 library preparation using 3'-paired-end sequencing[2]. After a 3-minute incubation/ligation step at 72°C, a TSO-primer containing Unique Molecular Identifiers (UMIs) was bound to the poly-A tail of RNA transcripts, after which these were reverse transcribed using SmartScribe reverse transcriptase. Next, the barcoded complementary DNA (cDNA) were amplified using BC-PCR primers. To eliminate short fragments, cDNA products were purified with 0.8X ratio Agencourt Ampure XP beads. Following purification, tagmented libraries were constructed with the Nextera XT DNA preparation kit. To allow multiplexed high-throughput sequencing, cells were pooled with N7xx Nextera primer barcoding, enabling *in silico* sorting. Following amplification, products were cleaned with 0.6X ratio Agencourt Ampure XP beads. To check for size distribution of the cDNA product, the product was measured repeatedly on a PerkinElmer LabChip GX high-sensitivity DNA chip. After final quality check of amplified and purified products, pools were combined into superpools (8 barcoded pools/superpool–672 cells/superpool) and sequenced on the Illumina NextSeq500 sequencer with 400M 75bp paired-end reads.

scRNAseq de-multiplexing pipeline

We obtained sequencing data for 5,292 single cells, with an average of ~400,000 reads per cell (**Figure 1, step 2)**. Sequencing data was processed through a de-multiplexing pipeline. Reads with a Hamming distance >1 and an average quality score ≤10 were excluded. Trimmed fastQ files were aligned to the human reference genome (Ensemble release 75, GRCh37) using STAR (v. 2.5.1b)[3] with default settings. Approximately 75% of reads mapped uniquely. Before gene quantification, Picardtools (v. 2.2.2)[4] was used to sort aligned reads and flag individual cells and UMIs. Gene level quantification was performed using Dropseq and filtering read count on unique UMIs, resulting in a gene/cell UMI count matrix.

Quality control

UMI counts were processed using Seurat[5]. To correct for cell-to-cell gene detection differences, we log-normalized UMI counts per cell and excluded genes expressed in <3 cells. To control for low quality cells and doublets, we excluded cells expressing <200 genes per cell, cells expressing >2500 genes per cell and cells with >5% mitochondrial genes. (**Figure 1, step 2**). We performed a principal component (PC) analysis and found that patient/batch, tissue-of-origin, and number of UMIs were the major drivers among the first 6 PCs. For our analyses, we regressed out the number of UMIs and percentage mitochondrial expression. Interpatient differences were assessed in differential expression analyses. Since differential expression between different tissues-of-origin may be partially driven by altered gene expression induced by collagenase digestion, we excluded 127 genes previously found to be influenced by collagenase digestion[6].

Integrating flow-cytometry and RNA expression data

Flow-cytometry data was analyzed using Kaluza software (Beckman Coulter Inc.). Positivity for any epitope was determined by visual inspection of plots with staining intensities. This adjudication process was cross-checked by a flow-cytometry expert. We used Summit software (Beckman Coulter Inc.) to extract intensity data per cell into a CSV file format. Data on positivity for epitope per cell was merged with metadata of the Seurat data file.

Clustering

Cells were clustered using a K-nearest-neighbor-based method[5] (**Figure 1, step 3**). Clustering was done with the PCs that were significant in a null-distribution determined through JackStraw analysis. We varied clustering resolution between 0.6 and 1.2, and settled on 0.6 because higher resolution produced clusters defined by marginal differential gene expression. Different subsets (based on tissue-of-origin and the CD8αβ epitope) were clustered separately to check for subset-specific cell types and/or states. tSNE reduction was used for visualization purposes.

Identification of T-cell subtypes in intestinal mucosa

In order to stratify cell types, we first defined cells with a quiescent profile based on expression of *CCR7* and cells with an effector profile based on expression of *CD160*. The mucosal T cells could be divided into four T-cell subtypes: T-helper 17 (Th17) cells, Treg cells on a quiescent background (Treg/Quiescent), Cytotoxic T cells (CTL), and a group of *REG1A*/*1B*-expressing cells. (**Figure 1, Supplementary Figure 1, Supplementary Table 1**).

CTL were identified based on expression of *EOMES*, *PRF1* and *TBX21;* cytotoxic enzymes such as *GNLY*, *GZMH* and *GZMB*; and genes for cytokines with a strong chemoattractant function such as *CCL4* and *CCL5* or *XCL1, XCL2* and *ITGA1.* **Treg/Quiescent cells** were characterized by expression of *TNFRSF4, FOXP3, CCR7, IL6ST, NOG* and *SELL*. Th17 cells were characterized by expression of *IL17A, IL22* and *IRF4* and transcription factors typical for Th17 cell function such as *NR4A2* and *CREM*.

Finally, we identified a much smaller group of cells that could not be defined based on published genetic markers. These cells express high levels of ***REG1A/1B*** and show co-expression of *CD3E/G* and *EPCAM*. Immunofluorescence staining of ileal mucosa of CD patients confirmed the presence of these cells in the mucosa, expressing both CD3 and REG1A proteins.

Identification of T-cell subtypes in peripheral blood

Within the PBL population, we found CTL, Quiescent cells, Effector/Treg cells and Treg/Quiescent cells (**Figure 1, Supplementary Table 1)**. **Quiescent T cells** were characterized based on expression of *CCR7*, *IL6ST*, *SELL, NOG* and *TCF7* (**Supplementary Table 1)**. A second cluster of cells with a quiescent profile express *TNFRSF4,* and these were characterized as **Treg/Quiescent cells** through expression of *TNFRSF4* and *LTB*, *MTA2* and *HNRPH1*. **Effector/Treg** were characterized by expression of *TNFRSF4* and *ITGAE***,** *IL32*, *FOXP3*, *PRDM1* and *CMTM6*. Finally, **CTL** were characterized based on high expression of marker genes such as *EOMES*, *PRF1* and *TBX21* and the above-mentioned genes *GNLY, GZMH, GZMB, CCL4* and *CCL5* (**Supplementary Table 1**).

Differential expression analysis

Differential expression analysis was done using the MAST function in Seurat (**Figure 1, step 3**). Differential expression was calculated between tissues-of-origin and cell types. To classify only genes that are expressed at least moderately, we filtered out genes expressed in less than 1% of the cells. After Bonferroni correction for multiple testing, results were considered significant at an adjusted *P*-value <0.05. Regressing out the effects of individual patient and sex did not induce major differences in gene expression signatures: 94% of the T-cell-subtype-specific gene-expression signatures overlapped between analyses (data not shown). To capture subtle changes in expression, we used the non-regressed data for subsequent analyses.

CD-risk genes

Through literature search, we identified 179 CD-risk genes. From each genome-wide association study (GWAS) risk locus, we selected the gene implicated through coding variants or functional variants. If multiple genes were implicated within a locus, the genes implicated through functional evidence were selected. Three loci remained in which two genes were implicated, and all were included in further analysis. If no functional or coding data was available, the most likely implicated gene (generally implicated indirectly through functional studies) was selected. Since scRNAseq detects overexpression more robustly than underexpression, and a previous study showed that CD-risk genes dysregulated between CD intestinal mucosa and healthy intestinal mucosa are generally upregulated, we focus on upregulated genes[7].

Drug-target genes

We aligned IBD drug-target genes extracted from *OpenTargets*[8] (n=2,712) and *Drugbank*[9], to differentially expressed genes, and subsequently selected genes encoding proteins targeted by drugs currently available for (clinical trials in) humans.

Comparison with scRNAseq dataset of T cells from healthy subjects

We studied publicly available scRNAseq data of epitopic CD4-positive naïve T cells for their mRNA expression of genes typically associated with epitopic CD8$\alpha\beta$-positive T cells[10].

Enrichment for CD-risk gene expression

We assessed whether T-cell subtypes showed enrichment for expression of CD-risk genes. We created null-distributions by randomly selecting sets the size of the differentially expressed genes per cell type from the total set of 12,531 genes. Empirical *P*-values of overrepresentation of CD-risk genes within cell-type-specific differentially expressed gene sets were derived from the null-distributions generated from 10^5 rounds of random sampling.

Data and software availability

The scripts used can be found at https://github.com/WeersmaLabIBD/SingleCell. Summit can be obtained from Beckman Coulter. The raw data is available at https://ega-archive.org (EGAS00001002702).

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Supplementary Table 1: T-cell expression signatures specific to T-cell subsets

Legend: T-cell subsets were characterized based on marker genes (see Supplementary Methods). Genes shown are significantly overexpressed in the specified cell type relative to all other cell types. The 'Gene annotation' column indicates whether a gene is a CD-risk gene, a drug-target gene (as described Supplementary Methods sections: ‘CD-risk genes’ and ‘Drug-target genes’), a transcription factor or encodes a cytokine.

✘ : risk gene; ◁ : drug target; ⦿ : transcription factor; ✷ : cytokine

Gene	**Average log fold change**	**Adjusted p-value**	**Compartment**	**Cell type**	**Gene annotation**
GNLY	3.11E+00	3.60E-201	Peripheral blood	CTL	
GZMH	2.43E+00	3.23E-166	Peripheral blood	CTL	
NKG7	1.89E+00	2.24E-136	Peripheral blood	CTL	
PRF1	1.88E+00	2.44E-123	Peripheral blood	CTL	
GZMB	2.26E+00	2.41E-106	Peripheral blood	CTL	
ADGRG1	1.89E+00	1.56E-101	Peripheral blood	CTL	
S1PR5	1.94E+00	4.14E-82	Peripheral blood	CTL	◁
CX3CR1	1.64E+00	1.31E-67	Peripheral blood	CTL	
CCL5	9.36E-01	1.64E-66	Peripheral blood	CTL	✷
TBX21	1.28E+00	3.71E-64	Peripheral blood	CTL	⦿
FGR	1.55E+00	1.96E-58	Peripheral blood	CTL	
FGFBP2	1.77E+00	1.38E-57	Peripheral blood	CTL	
EFHD2	1.36E+00	2.61E-56	Peripheral blood	CTL	
TRGC2	1.57E+00	1.10E-54	Peripheral blood	CTL	
FCRL6	1.33E+00	1.87E-51	Peripheral blood	CTL	
FCGR3A	1.52E+00	5.86E-49	Peripheral blood	CTL	◁
PLEK	1.40E+00	1.11E-45	Peripheral blood	CTL	⦿
CST7	1.05E+00	1.28E-43	Peripheral blood	CTL	
ITGB2	9.32E-01	1.20E-42	Peripheral blood	CTL	
GZMA	1.48E+00	2.84E-42	Peripheral blood	CTL	
FLVCR2	5.21E-01	4.90E-38	Peripheral blood	CTL	
PRSS23	1.20E+00	1.63E-35	Peripheral blood	CTL	
CTSW	1.06E+00	3.00E-35	Peripheral blood	CTL	✘
CCL4	1.26E+00	1.35E-34	Peripheral blood	CTL	✷
ADRB2	1.23E+00	7.44E-33	Peripheral blood	CTL	
PFN1P1	2.53E-01	4.83E-32	Peripheral blood	CTL	
SPON2	1.38E+00	9.60E-31	Peripheral blood	CTL	
KLRD1	1.15E+00	2.67E-29	Peripheral blood	CTL	
TRGC1	7.60E-01	3.39E-29	Peripheral blood	CTL	
FLNA	8.16E-01	1.63E-28	Peripheral blood	CTL	
ARL4C	9.80E-01	2.40E-28	Peripheral blood	CTL	
SYT8	5.63E-01	1.40E-24	Peripheral blood	CTL	
SYNE2	7.85E-01	8.38E-23	Peripheral blood	CTL	
ZEB2	9.52E-01	3.86E-22	Peripheral blood	CTL	⦿

Gene	Average log fold change	Adjusted p-value	Compartment	Cell type	Gene annotation
ASCL2	6.95E-01	5.10E-22	Peripheral blood	CTL	⦿
LITAF	8.27E-01	3.08E-21	Peripheral blood	CTL	
ZNF683	1.05E+00	8.94E-21	Peripheral blood	CTL	⦿
EOMES	9.51E-01	1.39E-20	Peripheral blood	CTL	⦿
SAMD3	9.49E-01	2.17E-19	Peripheral blood	CTL	
HOPX	1.21E+00	9.28E-19	Peripheral blood	CTL	⦿
RAP1GAP2	6.39E-01	9.66E-19	Peripheral blood	CTL	
SH3BGRL3	5.61E-01	2.03E-18	Peripheral blood	CTL	
TXNIP	6.02E-01	4.08E-18	Peripheral blood	CTL	
C1orf21	8.99E-01	1.12E-17	Peripheral blood	CTL	
SLC9A3R1	6.93E-01	1.81E-17	Peripheral blood	CTL	
CD8A	8.40E-01	1.90E-17	Peripheral blood	CTL	
C12orf75	1.14E+00	2.26E-17	Peripheral blood	CTL	
SLC15A4	9.25E-01	3.17E-17	Peripheral blood	CTL	
PXN	9.43E-01	1.53E-16	Peripheral blood	CTL	
HLA.C	4.72E-01	1.05E-15	Peripheral blood	CTL	
MYO1F	7.75E-01	1.62E-15	Peripheral blood	CTL	
EMP3	3.90E-01	3.20E-14	Peripheral blood	CTL	
PPP2R5C	6.39E-01	4.80E-14	Peripheral blood	CTL	
RAP2A	7.15E-01	5.89E-14	Peripheral blood	CTL	
HLA.A	4.74E-01	1.03E-13	Peripheral blood	CTL	
AHNAK	8.24E-01	1.09E-13	Peripheral blood	CTL	
TSPAN32	9.25E-01	1.30E-13	Peripheral blood	CTL	
CMC1	1.01E+00	2.60E-13	Peripheral blood	CTL	
PATL2	9.03E-01	3.22E-13	Peripheral blood	CTL	
ITGAM	6.97E-01	4.74E-13	Peripheral blood	CTL	
KLRG1	8.36E-01	6.85E-13	Peripheral blood	CTL	
HLA.DPB1	9.00E-01	1.08E-12	Peripheral blood	CTL	
LCP1	6.13E-01	1.48E-12	Peripheral blood	CTL	
HCST	7.18E-01	1.71E-12	Peripheral blood	CTL	
CCND3	5.59E-01	2.45E-12	Peripheral blood	CTL	
APOBEC3G	8.46E-01	2.52E-12	Peripheral blood	CTL	
KLRF1	9.54E-01	4.13E-12	Peripheral blood	CTL	
PDGFD	5.94E-01	8.70E-12	Peripheral blood	CTL	✸
ZFP36L2	4.43E-01	1.05E-11	Peripheral blood	CTL	⦿
SLC20A1	7.61E-01	1.18E-11	Peripheral blood	CTL	
CLIC3	8.00E-01	1.32E-11	Peripheral blood	CTL	
RASSF1	7.47E-01	4.48E-11	Peripheral blood	CTL	
PYHIN1	8.95E-01	4.91E-11	Peripheral blood	CTL	
BIN2	6.01E-01	6.41E-11	Peripheral blood	CTL	

Gene	**Average log fold change**	**Adjusted p-value**	**Compartment**	**Cell type**	**Gene annotation**
RP11.81H14.2	5.22E-01	1.08E-10	Peripheral blood	CTL	
NCR1	3.79E-01	3.05E-10	Peripheral blood	CTL	
LPCAT1	5.39E-01	4.17E-10	Peripheral blood	CTL	
TPST2	6.94E-01	8.86E-10	Peripheral blood	CTL	
USP28	4.99E-01	1.04E-09	Peripheral blood	CTL	
CD8B	4.52E-01	1.34E-09	Peripheral blood	CTL	
CD300A	7.72E-01	2.28E-09	Peripheral blood	CTL	
RUNX3	7.44E-01	2.32E-09	Peripheral blood	CTL	⦿
CYTH4	6.20E-01	2.60E-09	Peripheral blood	CTL	
MAPK1	7.73E-01	2.87E-09	Peripheral blood	CTL	
LYAR	9.36E-01	4.91E-09	Peripheral blood	CTL	
PTGDR	8.27E-01	5.28E-09	Peripheral blood	CTL	
ID2	6.69E-01	1.13E-08	Peripheral blood	CTL	⦿
TOB1	3.65E-01	1.31E-08	Peripheral blood	CTL	
APOBEC3C	3.89E-01	2.11E-08	Peripheral blood	CTL	
VCL	6.67E-01	2.14E-08	Peripheral blood	CTL	
SYNE1	6.98E-01	2.38E-08	Peripheral blood	CTL	
ZNF276	5.07E-01	2.90E-08	Peripheral blood	CTL	⦿
PLAC8	6.36E-01	4.02E-08	Peripheral blood	CTL	
ITGAX	7.69E-01	5.67E-08	Peripheral blood	CTL	
ITGAL	6.07E-01	7.06E-08	Peripheral blood	CTL	
MED15	5.38E-01	8.56E-08	Peripheral blood	CTL	
RAP2B	3.85E-01	9.63E-08	Peripheral blood	CTL	
SLAMF6	5.69E-01	1.02E-07	Peripheral blood	CTL	
PRR5L	8.09E-01	1.05E-07	Peripheral blood	CTL	
C9orf142	6.06E-01	1.42E-07	Peripheral blood	CTL	
LSP1	4.45E-01	1.49E-07	Peripheral blood	CTL	✘
TGFBR3	5.09E-01	1.70E-07	Peripheral blood	CTL	
ANXA2	6.52E-01	1.70E-07	Peripheral blood	CTL	
MYO1G	4.95E-01	1.76E-07	Peripheral blood	CTL	
KRT72	4.31E-01	2.56E-07	Peripheral blood	CTL	
CTBP1	4.43E-01	2.88E-07	Peripheral blood	CTL	
OSBPL5	3.95E-01	3.63E-07	Peripheral blood	CTL	
ARHGAP25	6.05E-01	3.91E-07	Peripheral blood	CTL	
SERPINB6	7.05E-01	4.64E-07	Peripheral blood	CTL	
MBP	7.13E-01	5.55E-07	Peripheral blood	CTL	
TLN1	6.48E-01	5.72E-07	Peripheral blood	CTL	
SLAMF7	5.50E-01	6.36E-07	Peripheral blood	CTL	
CFL1	3.03E-01	6.43E-07	Peripheral blood	CTL	
RAB1B	5.15E-01	7.68E-07	Peripheral blood	CTL	

Gene	Average log fold change	Adjusted p-value	Compartment	Cell type	Gene annotation
LILRB1	5.59E-01	7.93E-07	Peripheral blood	CTL	
S1PR1	6.45E-01	7.96E-07	Peripheral blood	CTL	◁
RNF166	3.85E-01	1.44E-06	Peripheral blood	CTL	⊙
SH2D1A	6.52E-01	1.46E-06	Peripheral blood	CTL	
JAKMIP1	4.57E-01	1.58E-06	Peripheral blood	CTL	
CCL3	3.71E-01	1.76E-06	Peripheral blood	CTL	✸
UCP2	5.41E-01	1.79E-06	Peripheral blood	CTL	
HLA.B	3.39E-01	2.25E-06	Peripheral blood	CTL	
ARRDC3	2.85E-01	2.66E-06	Peripheral blood	CTL	
ADGRE5	6.15E-01	2.81E-06	Peripheral blood	CTL	
APMAP	6.46E-01	4.76E-06	Peripheral blood	CTL	
PREX1	3.87E-01	5.17E-06	Peripheral blood	CTL	
CLIC1	5.10E-01	5.76E-06	Peripheral blood	CTL	
H6PD	3.70E-01	6.76E-06	Peripheral blood	CTL	
ADAP1	5.15E-01	6.96E-06	Peripheral blood	CTL	
CHST12	5.31E-01	7.11E-06	Peripheral blood	CTL	
FAM49A	5.32E-01	7.18E-06	Peripheral blood	CTL	
MRFAP1L1	5.27E-01	7.47E-06	Peripheral blood	CTL	
STARD3NL	6.37E-01	8.76E-06	Peripheral blood	CTL	
CYBA	5.36E-01	8.83E-06	Peripheral blood	CTL	
PARP8	3.91E-01	9.71E-06	Peripheral blood	CTL	
MATK	6.05E-01	9.90E-06	Peripheral blood	CTL	
CMKLR1	3.10E-01	1.19E-05	Peripheral blood	CTL	
CD99	5.20E-01	1.38E-05	Peripheral blood	CTL	
FCRL3	4.54E-01	1.49E-05	Peripheral blood	CTL	
S100A4	5.82E-01	2.45E-05	Peripheral blood	CTL	
STK38	6.01E-01	2.61E-05	Peripheral blood	CTL	
ARRB2	3.67E-01	3.14E-05	Peripheral blood	CTL	
MYL6	3.46E-01	3.67E-05	Peripheral blood	CTL	
FBXW5	5.10E-01	4.19E-05	Peripheral blood	CTL	
LGR6	3.04E-01	5.76E-05	Peripheral blood	CTL	
GNAI2	6.15E-01	6.63E-05	Peripheral blood	CTL	
PRMT2	3.28E-01	6.89E-05	Peripheral blood	CTL	
TYROBP	7.17E-01	7.66E-05	Peripheral blood	CTL	
ABI3	4.90E-01	8.59E-05	Peripheral blood	CTL	
HCLS1	4.12E-01	9.20E-05	Peripheral blood	CTL	
TFEB	4.55E-01	9.88E-05	Peripheral blood	CTL	⊙
PTPRC	3.98E-01	1.07E-04	Peripheral blood	CTL	✘
CDC25B	3.44E-01	1.07E-04	Peripheral blood	CTL	
IL10RA	4.03E-01	1.08E-04	Peripheral blood	CTL	

Gene	Average log fold change	Adjusted p-value	Compartment	Cell type	Gene annotation
SELPLG	3.53E-01	1.11E-04	Peripheral blood	CTL	
DGKZ	3.95E-01	1.28E-04	Peripheral blood	CTL	
TES	4.89E-01	1.31E-04	Peripheral blood	CTL	
CEP78	6.67E-01	1.40E-04	Peripheral blood	CTL	
STAT6	4.51E-01	1.48E-04	Peripheral blood	CTL	⦿
TTC38	6.77E-01	1.63E-04	Peripheral blood	CTL	
KCNAB2	7.16E-01	2.38E-04	Peripheral blood	CTL	
NLRP1	4.91E-01	2.44E-04	Peripheral blood	CTL	
FUT11	6.25E-01	2.70E-04	Peripheral blood	CTL	
MYBL1	5.47E-01	2.79E-04	Peripheral blood	CTL	⦿
MSN	5.99E-01	2.79E-04	Peripheral blood	CTL	
CD52	3.09E-01	2.79E-04	Peripheral blood	CTL	
UQCRB	4.26E-01	4.42E-04	Peripheral blood	CTL	
SEPT7	5.15E-01	4.48E-04	Peripheral blood	CTL	
CDKN2D	6.33E-01	5.90E-04	Peripheral blood	CTL	
HNRNPD	3.12E-01	7.07E-04	Peripheral blood	CTL	
BTN3A2	3.10E-01	8.20E-04	Peripheral blood	CTL	
CYTOR	2.67E-01	8.53E-04	Peripheral blood	CTL	
CASP8	6.50E-01	8.95E-04	Peripheral blood	CTL	
CD63	5.35E-01	9.97E-04	Peripheral blood	CTL	
FADS2	3.98E-01	1.06E-03	Peripheral blood	CTL	
AKNA	5.57E-01	1.28E-03	Peripheral blood	CTL	⦿
RASA3	5.11E-01	1.30E-03	Peripheral blood	CTL	
DPP7	3.20E-01	1.37E-03	Peripheral blood	CTL	
LLGL2	4.21E-01	1.39E-03	Peripheral blood	CTL	
NPRL2	5.11E-01	1.39E-03	Peripheral blood	CTL	
PSMB8	4.32E-01	1.40E-03	Peripheral blood	CTL	
ADAM8	3.64E-01	1.70E-03	Peripheral blood	CTL	
PRKCB	4.20E-01	1.97E-03	Peripheral blood	CTL	✘ ◁
STK10	5.37E-01	2.11E-03	Peripheral blood	CTL	
S100A10	4.09E-01	2.49E-03	Peripheral blood	CTL	
RHOA	3.43E-01	2.55E-03	Peripheral blood	CTL	
ANKRD36BP1	3.31E-01	2.71E-03	Peripheral blood	CTL	
ZAP70	4.27E-01	2.84E-03	Peripheral blood	CTL	
DSTN	3.42E-01	3.08E-03	Peripheral blood	CTL	
PRELID1	4.10E-01	3.28E-03	Peripheral blood	CTL	
PTP4A2	3.61E-01	3.98E-03	Peripheral blood	CTL	
DLG5	3.29E-01	4.38E-03	Peripheral blood	CTL	
SAMHD1	2.98E-01	5.31E-03	Peripheral blood	CTL	
RP11.222K16.2	4.02E-01	5.50E-03	Peripheral blood	CTL	

Gene	Average log fold change	Adjusted p-value	Compartment	Cell type	Gene annotation
GSE1	3.72E-01	5.59E-03	Peripheral blood	CTL	
ARPC5L	4.34E-01	6.59E-03	Peripheral blood	CTL	
MIR4435.2HG	3.80E-01	6.86E-03	Peripheral blood	CTL	
LYPLA2	3.00E-01	7.59E-03	Peripheral blood	CTL	
MTATP6P1	3.80E-01	9.73E-03	Peripheral blood	CTL	
ARHGAP30	3.22E-01	1.04E-02	Peripheral blood	CTL	
PGAM1	3.34E-01	1.15E-02	Peripheral blood	CTL	
SLC25A20	4.36E-01	1.16E-02	Peripheral blood	CTL	
CYTH1	3.06E-01	1.17E-02	Peripheral blood	CTL	
RNF213	2.69E-01	1.17E-02	Peripheral blood	CTL	
SYTL1	5.87E-01	1.32E-02	Peripheral blood	CTL	
GAB3	5.56E-01	1.38E-02	Peripheral blood	CTL	
ACTB	2.86E-01	1.47E-02	Peripheral blood	CTL	
TPM3	4.14E-01	1.54E-02	Peripheral blood	CTL	
ATM	3.20E-01	1.58E-02	Peripheral blood	CTL	
BROX	2.70E-01	1.66E-02	Peripheral blood	CTL	
TTC16	5.03E-01	1.73E-02	Peripheral blood	CTL	
STX10	4.71E-01	1.88E-02	Peripheral blood	CTL	
PIK3R5	4.01E-01	1.94E-02	Peripheral blood	CTL	
ARHGEF1	3.85E-01	1.96E-02	Peripheral blood	CTL	
CAPN2	4.79E-01	1.97E-02	Peripheral blood	CTL	
MTND4P12	2.70E-01	2.08E-02	Peripheral blood	CTL	
PRKCH	3.21E-01	2.47E-02	Peripheral blood	CTL	◁
FAM65B	3.11E-01	2.63E-02	Peripheral blood	CTL	
STARD7	4.03E-01	2.75E-02	Peripheral blood	CTL	
IL2RB	4.62E-01	2.78E-02	Peripheral blood	CTL	◁
MOB3A	3.54E-01	2.93E-02	Peripheral blood	CTL	
ACTN4	5.91E-01	3.02E-02	Peripheral blood	CTL	
SLC2A1	4.24E-01	3.22E-02	Peripheral blood	CTL	
F2R	3.31E-01	3.40E-02	Peripheral blood	CTL	
FAM49B	4.98E-01	3.78E-02	Peripheral blood	CTL	
ANKRD20A11P	2.99E-01	4.46E-02	Peripheral blood	CTL	
RGS9	3.54E-01	4.52E-02	Peripheral blood	CTL	⦿
RPS27L	3.91E-01	4.65E-02	Peripheral blood	CTL	
C11orf21	4.50E-01	4.68E-02	Peripheral blood	CTL	
TAF10	4.29E-01	4.70E-02	Peripheral blood	CTL	
CCL5	1.14E+00	1.70E-120	Intestinal mucosa	CTL	✷
CD160	1.51E+00	3.82E-70	Intestinal mucosa	CTL	
TMSB4XP8	4.07E-01	3.00E-51	Intestinal mucosa	CTL	
ADRB1	1.06E+00	1.67E-43	Intestinal mucosa	CTL	

Gene	Average log fold change	Adjusted p-value	Compartment	Cell type	Gene annotation
XCL1	5.67E-01	4.30E-42	Intestinal mucosa	CTL	✷
XCL2	7.25E-01	9.84E-42	Intestinal mucosa	CTL	✷
CD8A	1.06E+00	2.59E-40	Intestinal mucosa	CTL	
ITGA1	8.30E-01	9.88E-40	Intestinal mucosa	CTL	
CKLF	8.62E-01	8.94E-38	Intestinal mucosa	CTL	✷
TMSB4X	2.84E-01	6.70E-35	Intestinal mucosa	CTL	
OSTF1	6.24E-01	3.04E-34	Intestinal mucosa	CTL	
CD3G	3.80E-01	5.68E-34	Intestinal mucosa	CTL	◁
RNF122	3.92E-01	2.21E-33	Intestinal mucosa	CTL	
PDCD4	5.63E-01	8.45E-33	Intestinal mucosa	CTL	
PLEKHF1	9.59E-01	1.23E-30	Intestinal mucosa	CTL	
CAPG	7.33E-01	4.69E-29	Intestinal mucosa	CTL	
CD2	7.03E-01	3.48E-27	Intestinal mucosa	CTL	
TMIGD2	8.13E-01	1.49E-26	Intestinal mucosa	CTL	
ITM2C	9.05E-01	4.59E-26	Intestinal mucosa	CTL	
STK17B	3.61E-01	3.95E-25	Intestinal mucosa	CTL	
CDV3	6.28E-01	1.38E-24	Intestinal mucosa	CTL	
STOM	8.13E-01	1.40E-24	Intestinal mucosa	CTL	
ABI3	9.20E-01	1.18E-22	Intestinal mucosa	CTL	
ITGAE	7.97E-01	6.31E-21	Intestinal mucosa	CTL	◁
CD8B	8.02E-01	3.58E-20	Intestinal mucosa	CTL	
ALOX5AP	7.42E-01	7.43E-20	Intestinal mucosa	CTL	
RGL4	7.22E-01	2.34E-19	Intestinal mucosa	CTL	
CD3D	5.01E-01	4.40E-19	Intestinal mucosa	CTL	◁
SMURF2	6.71E-01	9.98E-19	Intestinal mucosa	CTL	
PIP4K2A	2.95E-01	1.05E-18	Intestinal mucosa	CTL	
MBOAT1	4.94E-01	1.66E-17	Intestinal mucosa	CTL	
NMUR1	5.68E-01	3.30E-17	Intestinal mucosa	CTL	
PSD4	5.64E-01	1.03E-16	Intestinal mucosa	CTL	
PTPN22	6.44E-01	3.55E-16	Intestinal mucosa	CTL	✘
SCUBE1	4.85E-01	3.77E-16	Intestinal mucosa	CTL	
ABCA1	6.83E-01	3.94E-16	Intestinal mucosa	CTL	
CAPZA1	2.86E-01	3.11E-14	Intestinal mucosa	CTL	
MIAT	6.52E-01	1.73E-13	Intestinal mucosa	CTL	
CCR9	4.96E-01	5.88E-13	Intestinal mucosa	CTL	◁
CXCR6	8.95E-01	6.63E-13	Intestinal mucosa	CTL	
CTC.425F1.4	3.26E-01	1.90E-12	Intestinal mucosa	CTL	
SLAMF7	7.15E-01	2.28E-12	Intestinal mucosa	CTL	
TLE3	4.26E-01	3.52E-12	Intestinal mucosa	CTL	
APOBEC3C	3.44E-01	1.26E-11	Intestinal mucosa	CTL	

Gene	Average log fold change	Adjusted p-value	Compartment	Cell type	Gene annotation
RP11.94L15.2	6.82E-01	2.13E-11	Intestinal mucosa	CTL	
SAR1A	2.89E-01	4.62E-11	Intestinal mucosa	CTL	
DENND2D	4.37E-01	6.73E-11	Intestinal mucosa	CTL	
COTL1	5.56E-01	1.49E-10	Intestinal mucosa	CTL	
MDM4	4.08E-01	6.94E-10	Intestinal mucosa	CTL	
JAML	5.38E-01	7.68E-10	Intestinal mucosa	CTL	
SLC7A8	3.36E-01	9.89E-10	Intestinal mucosa	CTL	
CYBA	3.42E-01	1.25E-09	Intestinal mucosa	CTL	
AUTS2	4.64E-01	2.15E-09	Intestinal mucosa	CTL	
CALR	2.61E-01	7.04E-09	Intestinal mucosa	CTL	
AFAP1L2	3.57E-01	9.01E-09	Intestinal mucosa	CTL	
TBL1XR1	3.72E-01	1.20E-08	Intestinal mucosa	CTL	
CD3E	3.21E-01	1.93E-08	Intestinal mucosa	CTL	◁
RHOC	6.53E-01	1.99E-08	Intestinal mucosa	CTL	
CD244	4.98E-01	2.06E-08	Intestinal mucosa	CTL	
DAPK2	5.92E-01	2.83E-08	Intestinal mucosa	CTL	
TRAC	3.19E-01	2.98E-08	Intestinal mucosa	CTL	
CD96	3.60E-01	4.43E-08	Intestinal mucosa	CTL	
KLRB1	3.78E-01	5.35E-08	Intestinal mucosa	CTL	
MIDN	4.30E-01	2.67E-07	Intestinal mucosa	CTL	
YWHAH	6.03E-01	5.21E-07	Intestinal mucosa	CTL	
AC092580.4	5.70E-01	5.41E-07	Intestinal mucosa	CTL	
SEPT1	3.04E-01	1.41E-06	Intestinal mucosa	CTL	
PPP3CA	3.09E-01	1.48E-06	Intestinal mucosa	CTL	
FASLG	6.39E-01	8.39E-06	Intestinal mucosa	CTL	✸
CD248	3.08E-01	9.99E-06	Intestinal mucosa	CTL	
TMEM120B	3.22E-01	1.37E-05	Intestinal mucosa	CTL	
GAB3	3.92E-01	1.62E-05	Intestinal mucosa	CTL	
TGFBR1	5.06E-01	2.58E-05	Intestinal mucosa	CTL	
CTD.2369P2.2	2.68E-01	3.63E-05	Intestinal mucosa	CTL	
SBNO1	3.46E-01	3.81E-05	Intestinal mucosa	CTL	
FMNL3	2.68E-01	4.74E-05	Intestinal mucosa	CTL	
ERO1A	3.54E-01	4.88E-05	Intestinal mucosa	CTL	
PSME2	3.69E-01	5.49E-05	Intestinal mucosa	CTL	
CD101	4.68E-01	6.47E-05	Intestinal mucosa	CTL	
TRGC1	2.72E-01	7.17E-05	Intestinal mucosa	CTL	
TTI2	3.61E-01	9.01E-05	Intestinal mucosa	CTL	
RP11.841O20.2	3.57E-01	1.03E-04	Intestinal mucosa	CTL	
FKBP1A	4.29E-01	1.07E-04	Intestinal mucosa	CTL	◁
NABP1	3.31E-01	1.13E-04	Intestinal mucosa	CTL	

Gene	Average log fold change	Adjusted p-value	Compartment	Cell type	Gene annotation
BUB3	2.53E-01	1.28E-04	Intestinal mucosa	CTL	
FYN	3.77E-01	1.60E-04	Intestinal mucosa	CTL	
LAG3	3.12E-01	1.65E-04	Intestinal mucosa	CTL	
RHOF	2.87E-01	2.25E-04	Intestinal mucosa	CTL	
CEPT1	2.56E-01	2.38E-04	Intestinal mucosa	CTL	
TMEM33	3.38E-01	2.57E-04	Intestinal mucosa	CTL	
FNBP1	3.28E-01	2.93E-04	Intestinal mucosa	CTL	
IL18RAP	3.44E-01	3.06E-04	Intestinal mucosa	CTL	
GUK1	3.39E-01	3.24E-04	Intestinal mucosa	CTL	
AP1G1	2.89E-01	4.20E-04	Intestinal mucosa	CTL	
TRGC2	5.15E-01	4.26E-04	Intestinal mucosa	CTL	
ST3GAL5	3.32E-01	4.88E-04	Intestinal mucosa	CTL	
KLRC1	3.54E-01	5.28E-04	Intestinal mucosa	CTL	
DNAJC3	3.57E-01	6.14E-04	Intestinal mucosa	CTL	
SLC35F6	3.29E-01	6.31E-04	Intestinal mucosa	CTL	
GPR82	3.60E-01	6.73E-04	Intestinal mucosa	CTL	
DTX3L	4.27E-01	7.17E-04	Intestinal mucosa	CTL	
CD63	5.61E-01	9.29E-04	Intestinal mucosa	CTL	
AP4B1	3.02E-01	9.53E-04	Intestinal mucosa	CTL	
PTPN6	2.93E-01	1.20E-03	Intestinal mucosa	CTL	
TROVE2	2.87E-01	1.49E-03	Intestinal mucosa	CTL	
EIF1AD	3.55E-01	1.54E-03	Intestinal mucosa	CTL	
C9orf78	4.05E-01	2.44E-03	Intestinal mucosa	CTL	
PARP9	3.83E-01	3.13E-03	Intestinal mucosa	CTL	
PLCG2	3.43E-01	4.57E-03	Intestinal mucosa	CTL	✘
TMED2	3.23E-01	4.82E-03	Intestinal mucosa	CTL	
SPN	3.05E-01	5.05E-03	Intestinal mucosa	CTL	
FYCO1	2.60E-01	5.27E-03	Intestinal mucosa	CTL	
XYLT2	2.86E-01	5.65E-03	Intestinal mucosa	CTL	
AC020571.3	5.17E-01	5.86E-03	Intestinal mucosa	CTL	
DHRS7	4.46E-01	7.16E-03	Intestinal mucosa	CTL	
WDR41	4.20E-01	7.48E-03	Intestinal mucosa	CTL	
CD9	5.51E-01	8.02E-03	Intestinal mucosa	CTL	
TAPBP	2.81E-01	9.49E-03	Intestinal mucosa	CTL	
SOCS1	3.59E-01	9.51E-03	Intestinal mucosa	CTL	✘
ZSWIM1	3.15E-01	1.02E-02	Intestinal mucosa	CTL	
TNFSF14	4.70E-01	1.16E-02	Intestinal mucosa	CTL	✷
PSMA3	2.89E-01	1.21E-02	Intestinal mucosa	CTL	
ANAPC11	4.20E-01	1.70E-02	Intestinal mucosa	CTL	
GPR34	5.20E-01	1.73E-02	Intestinal mucosa	CTL	

Gene	**Average log fold change**	**Adjusted p-value**	**Compartment**	**Cell type**	**Gene annotation**
GYG1	5.52E-01	1.86E-02	Intestinal mucosa	CTL	
GNGT2	4.30E-01	2.03E-02	Intestinal mucosa	CTL	
PDIA3	2.79E-01	2.91E-02	Intestinal mucosa	CTL	
MAN1A1	2.90E-01	3.13E-02	Intestinal mucosa	CTL	
GSTP1	4.04E-01	3.50E-02	Intestinal mucosa	CTL	
NOP10	2.90E-01	3.75E-02	Intestinal mucosa	CTL	
MARCH2	3.11E-01	4.57E-02	Intestinal mucosa	CTL	
DOCK5	3.62E-01	4.63E-02	Intestinal mucosa	CTL	
SELL	1.17E+00	3.05E-97	Peripheral blood	Quiescent	
CCR7	1.02E+00	5.98E-85	Peripheral blood	Quiescent	
NOG	1.22E+00	5.86E-72	Peripheral blood	Quiescent	
RP11.360D2.2	4.65E-01	7.01E-64	Peripheral blood	Quiescent	
RP11.234A1.1	3.96E-01	6.32E-59	Peripheral blood	Quiescent	
RP4.765C7.2	3.47E-01	2.27E-57	Peripheral blood	Quiescent	
RPS27	3.81E-01	9.92E-57	Peripheral blood	Quiescent	
RPS14P3	3.66E-01	1.43E-55	Peripheral blood	Quiescent	
RP11.543P15.1	2.89E-01	4.01E-53	Peripheral blood	Quiescent	
FAM65B	5.63E-01	1.78E-40	Peripheral blood	Quiescent	
C16orf54	4.27E-01	1.47E-38	Peripheral blood	Quiescent	
RPL34	3.88E-01	5.75E-37	Peripheral blood	Quiescent	
RPS14	3.10E-01	4.93E-36	Peripheral blood	Quiescent	
PCED1B.AS1	6.89E-01	1.32E-34	Peripheral blood	Quiescent	
RPL18A	3.17E-01	2.83E-34	Peripheral blood	Quiescent	
RPL3P4	3.10E-01	5.68E-34	Peripheral blood	Quiescent	
RPS25	3.60E-01	6.06E-34	Peripheral blood	Quiescent	
CDC42SE1	2.91E-01	2.47E-32	Peripheral blood	Quiescent	
RPS18	3.27E-01	3.76E-31	Peripheral blood	Quiescent	
RPL31	4.80E-01	1.59E-30	Peripheral blood	Quiescent	
RPS28	4.60E-01	1.21E-29	Peripheral blood	Quiescent	
RPL3	2.83E-01	1.49E-29	Peripheral blood	Quiescent	
C1orf56	2.92E-01	4.64E-28	Peripheral blood	Quiescent	
MYC	6.89E-01	2.67E-27	Peripheral blood	Quiescent	⊙
RPL23A	3.46E-01	3.09E-27	Peripheral blood	Quiescent	
NOSIP	6.46E-01	4.69E-27	Peripheral blood	Quiescent	
RP4.594I10.3	4.94E-01	6.23E-27	Peripheral blood	Quiescent	
TMSB10	3.17E-01	1.23E-26	Peripheral blood	Quiescent	
RCAN3	5.23E-01	1.94E-26	Peripheral blood	Quiescent	
RPS6	3.42E-01	7.94E-26	Peripheral blood	Quiescent	
RPL13A	3.40E-01	1.32E-24	Peripheral blood	Quiescent	
LEF1	6.36E-01	2.79E-24	Peripheral blood	Quiescent	⊙

Gene	Average log fold change	Adjusted p-value	Compartment	Cell type	Gene annotation
RPS15	4.14E-01	1.02E-23	Peripheral blood	Quiescent	
RPL32	4.24E-01	2.28E-23	Peripheral blood	Quiescent	
RPS11	2.84E-01	2.76E-23	Peripheral blood	Quiescent	
RPL37A	4.97E-01	2.98E-23	Peripheral blood	Quiescent	
RPL23	3.40E-01	7.86E-23	Peripheral blood	Quiescent	
RPS29	4.15E-01	1.81E-22	Peripheral blood	Quiescent	
RPL10P3	4.05E-01	6.72E-22	Peripheral blood	Quiescent	
LDHB	5.55E-01	2.62E-20	Peripheral blood	Quiescent	
IL6ST	4.22E-01	3.06E-20	Peripheral blood	Quiescent	✷
AES	3.82E-01	6.01E-20	Peripheral blood	Quiescent	
RPL13	3.01E-01	9.98E-20	Peripheral blood	Quiescent	
RPL30	4.69E-01	4.54E-19	Peripheral blood	Quiescent	
GIMAP7	3.68E-01	1.88E-18	Peripheral blood	Quiescent	
TRABD2A	5.92E-01	4.56E-18	Peripheral blood	Quiescent	
RPS3	3.16E-01	5.59E-18	Peripheral blood	Quiescent	
RPS28P7	3.84E-01	7.57E-18	Peripheral blood	Quiescent	
RPS13	4.57E-01	9.73E-18	Peripheral blood	Quiescent	
RPS21	4.48E-01	9.78E-18	Peripheral blood	Quiescent	
LINC00861	5.82E-01	5.17E-17	Peripheral blood	Quiescent	
MDS2	5.25E-01	1.18E-16	Peripheral blood	Quiescent	
RPL5	4.58E-01	1.90E-16	Peripheral blood	Quiescent	
RASSF3	3.72E-01	3.96E-15	Peripheral blood	Quiescent	
EIF2S3	3.18E-01	2.67E-14	Peripheral blood	Quiescent	
LIMD2	3.14E-01	4.62E-14	Peripheral blood	Quiescent	
RPL27A	3.37E-01	5.34E-14	Peripheral blood	Quiescent	
RPL19	3.82E-01	7.94E-14	Peripheral blood	Quiescent	
RPL15	2.99E-01	1.27E-13	Peripheral blood	Quiescent	
RPS16	3.56E-01	1.41E-13	Peripheral blood	Quiescent	
TOB1	4.13E-01	1.48E-13	Peripheral blood	Quiescent	
RPS12	3.85E-01	1.70E-13	Peripheral blood	Quiescent	
RPL14	3.64E-01	2.80E-13	Peripheral blood	Quiescent	
RPL39	3.63E-01	3.23E-13	Peripheral blood	Quiescent	
RPL28	3.93E-01	3.28E-13	Peripheral blood	Quiescent	
RPL11	4.53E-01	3.56E-13	Peripheral blood	Quiescent	
RPL27	3.39E-01	4.00E-13	Peripheral blood	Quiescent	
TCF7	3.73E-01	4.05E-13	Peripheral blood	Quiescent	⦿
RP11.415F23.2	4.99E-01	5.53E-13	Peripheral blood	Quiescent	
AC005944.2	4.02E-01	1.64E-12	Peripheral blood	Quiescent	
RPL9	2.85E-01	1.80E-12	Peripheral blood	Quiescent	
NELL2	5.30E-01	2.10E-12	Peripheral blood	Quiescent	

Gene	**Average log fold change**	**Adjusted p-value**	**Compartment**	**Cell type**	**Gene annotation**
CD27	3.79E-01	9.01E-12	Peripheral blood	Quiescent	
RPS20	3.03E-01	1.13E-11	Peripheral blood	Quiescent	
CTD.2031P19.5	2.70E-01	1.39E-11	Peripheral blood	Quiescent	
RPL38	4.09E-01	1.39E-11	Peripheral blood	Quiescent	
RPL10A	3.15E-01	1.53E-11	Peripheral blood	Quiescent	
LRRC75A.AS1	4.46E-01	2.57E-11	Peripheral blood	Quiescent	
FOXP1	3.25E-01	2.75E-11	Peripheral blood	Quiescent	⦿
S1PR1	5.11E-01	3.03E-11	Peripheral blood	Quiescent	◁
RPL26	3.76E-01	3.69E-11	Peripheral blood	Quiescent	
RPS15A	3.75E-01	6.71E-11	Peripheral blood	Quiescent	
RACK1	4.12E-01	7.37E-11	Peripheral blood	Quiescent	
RASGRP2	3.59E-01	1.32E-10	Peripheral blood	Quiescent	
RPLP2	3.16E-01	1.32E-10	Peripheral blood	Quiescent	
LRRC75A	4.33E-01	1.38E-10	Peripheral blood	Quiescent	
TXNIP	3.87E-01	1.58E-10	Peripheral blood	Quiescent	
PRKCA	5.04E-01	2.38E-10	Peripheral blood	Quiescent	◁
EIF4B	3.07E-01	2.43E-10	Peripheral blood	Quiescent	
RPL36	2.82E-01	3.66E-10	Peripheral blood	Quiescent	
RPS27A	2.80E-01	5.51E-10	Peripheral blood	Quiescent	
LDLRAP1	4.77E-01	5.52E-10	Peripheral blood	Quiescent	
C1orf162	5.86E-01	1.04E-09	Peripheral blood	Quiescent	
PIK3IP1	4.53E-01	2.67E-09	Peripheral blood	Quiescent	
DENND5A	3.80E-01	2.82E-09	Peripheral blood	Quiescent	
ADTRP	5.80E-01	5.46E-09	Peripheral blood	Quiescent	
RPL18	3.29E-01	8.19E-09	Peripheral blood	Quiescent	
RP4.635E18.8	3.91E-01	1.35E-08	Peripheral blood	Quiescent	
RP11.252A24.7	3.79E-01	1.42E-08	Peripheral blood	Quiescent	
RP11.458N5.1	3.88E-01	2.18E-08	Peripheral blood	Quiescent	
GAS5	4.47E-01	2.20E-08	Peripheral blood	Quiescent	
MAL	6.51E-01	2.91E-08	Peripheral blood	Quiescent	
IL7R	2.85E-01	4.34E-08	Peripheral blood	Quiescent	
RPS23	3.36E-01	7.98E-08	Peripheral blood	Quiescent	
RPL8	2.64E-01	3.56E-07	Peripheral blood	Quiescent	
PRKCQ.AS1	5.01E-01	3.81E-07	Peripheral blood	Quiescent	
RPS9	3.11E-01	4.72E-07	Peripheral blood	Quiescent	
NPM1	2.53E-01	7.45E-07	Peripheral blood	Quiescent	
TCEA3	4.72E-01	9.23E-07	Peripheral blood	Quiescent	
LINC01089	4.09E-01	9.79E-07	Peripheral blood	Quiescent	
PRMT2	3.40E-01	1.12E-06	Peripheral blood	Quiescent	
PFDN5	3.34E-01	1.18E-06	Peripheral blood	Quiescent	

Gene	**Average log fold change**	**Adjusted p-value**	**Compartment**	**Cell type**	**Gene annotation**
RPL37	3.65E-01	1.53E-06	Peripheral blood	Quiescent	
S100A8	5.75E-01	1.86E-06	Peripheral blood	Quiescent	
RPLP0	2.62E-01	2.04E-06	Peripheral blood	Quiescent	
RPL12	3.16E-01	2.10E-06	Peripheral blood	Quiescent	
FCN1	2.91E-01	2.36E-06	Peripheral blood	Quiescent	
PCED1B	5.26E-01	2.38E-06	Peripheral blood	Quiescent	
RPL29	3.11E-01	2.58E-06	Peripheral blood	Quiescent	
SVIL	3.91E-01	4.87E-06	Peripheral blood	Quiescent	
EEF1D	2.92E-01	5.91E-06	Peripheral blood	Quiescent	
SATB1	3.90E-01	1.14E-05	Peripheral blood	Quiescent	⦿
ADD3	3.22E-01	1.60E-05	Peripheral blood	Quiescent	
GIMAP4	3.17E-01	2.26E-05	Peripheral blood	Quiescent	
GLTSCR2	3.43E-01	2.58E-05	Peripheral blood	Quiescent	
SNORA12.2	3.27E-01	2.65E-05	Peripheral blood	Quiescent	
RP11.434H6.7	4.19E-01	5.27E-05	Peripheral blood	Quiescent	
CSF3R	2.53E-01	5.63E-05	Peripheral blood	Quiescent	◁
RASA3	4.09E-01	7.03E-05	Peripheral blood	Quiescent	
RPL7A	2.97E-01	9.90E-05	Peripheral blood	Quiescent	
ZNF516	3.29E-01	1.20E-04	Peripheral blood	Quiescent	⦿
SUSD3	3.53E-01	3.48E-04	Peripheral blood	Quiescent	
RPS4Y1	4.42E-01	4.10E-04	Peripheral blood	Quiescent	
RPS4X	2.59E-01	4.95E-04	Peripheral blood	Quiescent	
ITGB2.AS1	2.82E-01	5.50E-04	Peripheral blood	Quiescent	
SDK2	2.67E-01	5.71E-04	Peripheral blood	Quiescent	
IL16	2.61E-01	6.35E-04	Peripheral blood	Quiescent	✷
LYZ	5.78E-01	8.54E-04	Peripheral blood	Quiescent	
RPS5	3.08E-01	8.55E-04	Peripheral blood	Quiescent	
RPARP.AS1	3.44E-01	8.77E-04	Peripheral blood	Quiescent	
RPL35A	3.01E-01	1.00E-03	Peripheral blood	Quiescent	
TXK	3.42E-01	1.03E-03	Peripheral blood	Quiescent	
DSEL	4.16E-01	2.31E-03	Peripheral blood	Quiescent	
S100A9	6.25E-01	2.32E-03	Peripheral blood	Quiescent	
SLC40A1	2.75E-01	4.04E-03	Peripheral blood	Quiescent	
MORC2	3.33E-01	4.93E-03	Peripheral blood	Quiescent	
SRSF5	3.26E-01	5.69E-03	Peripheral blood	Quiescent	
BTF3	2.87E-01	5.80E-03	Peripheral blood	Quiescent	
PCMTD2	2.96E-01	6.22E-03	Peripheral blood	Quiescent	
TESPA1	3.02E-01	7.20E-03	Peripheral blood	Quiescent	
SORL1	3.19E-01	1.07E-02	Peripheral blood	Quiescent	
POLR3E	2.65E-01	1.11E-02	Peripheral blood	Quiescent	

Gene	**Average log fold change**	**Adjusted p-value**	**Compartment**	**Cell type**	**Gene annotation**
VCAN	2.53E-01	1.15E-02	Peripheral blood	Quiescent	
C10orf95	3.27E-01	1.34E-02	Peripheral blood	Quiescent	
RPL22	2.75E-01	1.50E-02	Peripheral blood	Quiescent	
ACTN1	2.98E-01	1.70E-02	Peripheral blood	Quiescent	
PIAS2	3.47E-01	2.25E-02	Peripheral blood	Quiescent	
EXOSC8	3.22E-01	2.48E-02	Peripheral blood	Quiescent	
BEX3	4.61E-01	2.52E-02	Peripheral blood	Quiescent	
SNHG8	4.14E-01	2.70E-02	Peripheral blood	Quiescent	
EIF3L	2.74E-01	3.56E-02	Peripheral blood	Quiescent	
FCGRT	3.21E-01	4.16E-02	Peripheral blood	Quiescent	
REG1B	1.84E+00	5.02E-94	Intestinal mucosa	REG1A/1B	
REG1A	2.11E+00	3.79E-89	Intestinal mucosa	REG1A/1B	✷
PIGR	1.88E+00	6.63E-83	Intestinal mucosa	REG1A/1B	
ANPEP	8.31E-01	2.25E-81	Intestinal mucosa	REG1A/1B	
DMBT1	9.04E-01	1.06E-76	Intestinal mucosa	REG1A/1B	
APOA1	8.54E-01	9.13E-70	Intestinal mucosa	REG1A/1B	
APOC3	5.28E-01	1.40E-68	Intestinal mucosa	REG1A/1B	
PHGR1	7.82E-01	4.47E-57	Intestinal mucosa	REG1A/1B	
ALDOB	1.17E+00	1.55E-54	Intestinal mucosa	REG1A/1B	
SLC15A1	6.94E-01	1.22E-52	Intestinal mucosa	REG1A/1B	
FABP1	1.02E+00	5.46E-50	Intestinal mucosa	REG1A/1B	
IFI27	3.57E-01	3.94E-37	Intestinal mucosa	REG1A/1B	
FABP6	3.47E-01	8.22E-37	Intestinal mucosa	REG1A/1B	
FABP2	5.56E-01	1.69E-30	Intestinal mucosa	REG1A/1B	
KRT19	3.51E-01	2.18E-29	Intestinal mucosa	REG1A/1B	
LGALS4	4.02E-01	2.97E-29	Intestinal mucosa	REG1A/1B	
SELENOP	1.08E+00	3.48E-29	Intestinal mucosa	REG1A/1B	
EPCAM	3.57E-01	8.27E-26	Intestinal mucosa	REG1A/1B	
TSPAN8	5.32E-01	1.21E-25	Intestinal mucosa	REG1A/1B	
MUC13	3.14E-01	6.08E-25	Intestinal mucosa	REG1A/1B	
APOB	3.70E-01	7.86E-24	Intestinal mucosa	REG1A/1B	
RARRES1	2.71E-01	2.02E-23	Intestinal mucosa	REG1A/1B	
LGALS3BP	4.42E-01	8.21E-19	Intestinal mucosa	REG1A/1B	
HLA.DRA	1.09E+00	1.88E-17	Intestinal mucosa	REG1A/1B	
SMIM24	6.08E-01	4.88E-17	Intestinal mucosa	REG1A/1B	
SPINK1	5.47E-01	3.82E-14	Intestinal mucosa	REG1A/1B	
KRT8	3.29E-01	5.06E-14	Intestinal mucosa	REG1A/1B	
TFF3	2.89E-01	3.91E-13	Intestinal mucosa	REG1A/1B	
HNF4A	3.23E-01	1.43E-12	Intestinal mucosa	REG1A/1B	⊙
AGR2	2.71E-01	1.90E-12	Intestinal mucosa	REG1A/1B	

Gene	Average log fold change	Adjusted p-value	Compartment	Cell type	Gene annotation
GOLIM4	2.80E-01	5.38E-12	Intestinal mucosa	REG1A/1B	
KRT18	2.63E-01	8.39E-11	Intestinal mucosa	REG1A/1B	
SLC6A19	2.66E-01	2.33E-10	Intestinal mucosa	REG1A/1B	
HLA.DRB1	5.80E-01	2.24E-09	Intestinal mucosa	REG1A/1B	
CCDC152	3.27E-01	2.65E-08	Intestinal mucosa	REG1A/1B	
ATP1B1	3.74E-01	3.38E-08	Intestinal mucosa	REG1A/1B	
IGHA1	2.63E+00	1.89E-06	Intestinal mucosa	REG1A/1B	
CD74	4.92E-01	4.24E-06	Intestinal mucosa	REG1A/1B	
LGALS3	5.32E-01	4.52E-06	Intestinal mucosa	REG1A/1B	
ALDH2	3.23E-01	1.13E-05	Intestinal mucosa	REG1A/1B	
TSPAN3	7.87E-01	2.07E-05	Intestinal mucosa	REG1A/1B	
OAT	4.68E-01	3.09E-05	Intestinal mucosa	REG1A/1B	
JCHAIN	2.85E+00	4.19E-05	Intestinal mucosa	REG1A/1B	
IGHG1	2.50E-01	8.06E-05	Intestinal mucosa	REG1A/1B	
GCNT3	3.26E-01	8.95E-05	Intestinal mucosa	REG1A/1B	
MS4A10	4.80E-01	1.38E-04	Intestinal mucosa	REG1A/1B	
CST3	9.40E-01	1.48E-04	Intestinal mucosa	REG1A/1B	
HLA.DPA1	3.73E-01	6.53E-04	Intestinal mucosa	REG1A/1B	
ACO2	3.07E-01	2.06E-03	Intestinal mucosa	REG1A/1B	
IGKC	1.70E+00	2.22E-03	Intestinal mucosa	REG1A/1B	
CTSD	7.31E-01	2.28E-03	Intestinal mucosa	REG1A/1B	
TM9SF3	3.32E-01	2.68E-03	Intestinal mucosa	REG1A/1B	
IGHA2	1.86E+00	3.12E-03	Intestinal mucosa	REG1A/1B	
DDAH1	3.12E-01	3.37E-03	Intestinal mucosa	REG1A/1B	
RNF24	1.84E+00	4.40E-03	Intestinal mucosa	REG1A/1B	
ENAM	2.07E+00	4.78E-03	Intestinal mucosa	REG1A/1B	
STK17B	5.04E-01	1.02E-02	Intestinal mucosa	REG1A/1B	
IGLC2	1.23E+00	1.09E-02	Intestinal mucosa	REG1A/1B	
MUC2	2.75E-01	1.14E-02	Intestinal mucosa	REG1A/1B	
TAPBP	5.61E-01	1.88E-02	Intestinal mucosa	REG1A/1B	
ECHS1	6.72E-01	2.22E-02	Intestinal mucosa	REG1A/1B	
OLFM4	4.49E-01	4.22E-02	Intestinal mucosa	REG1A/1B	
RASGEF1B	2.44E+00	4.33E-294	Intestinal mucosa	Th17	
RGS1	2.55E+00	1.69E-247	Intestinal mucosa	Th17	
CD69	2.36E+00	1.04E-244	Intestinal mucosa	Th17	
TNFAIP3	2.28E+00	4.02E-237	Intestinal mucosa	Th17	✘
DUSP2	2.33E+00	4.67E-186	Intestinal mucosa	Th17	
DNAJB1	2.22E+00	2.19E-184	Intestinal mucosa	Th17	
MIR24.2	1.89E+00	1.40E-150	Intestinal mucosa	Th17	
NR4A2	1.93E+00	4.10E-143	Intestinal mucosa	Th17	⦿

Gene	Average log fold change	Adjusted p-value	Compartment	Cell type	Gene annotation
YPEL5	1.73E+00	5.60E-142	Intestinal mucosa	Th17	
FAM46C	1.68E+00	2.10E-106	Intestinal mucosa	Th17	
PTGER4	1.67E+00	1.15E-96	Intestinal mucosa	Th17	✘ ◁
SIK1	9.65E-01	8.05E-93	Intestinal mucosa	Th17	
CYTIP	1.16E+00	1.35E-85	Intestinal mucosa	Th17	
CXCR4	1.53E+00	6.82E-79	Intestinal mucosa	Th17	
SLC2A3	1.49E+00	1.73E-78	Intestinal mucosa	Th17	
HSP90AA1	1.33E+00	5.06E-76	Intestinal mucosa	Th17	
PHLDA1	1.63E+00	3.02E-75	Intestinal mucosa	Th17	
CREM	1.33E+00	4.48E-73	Intestinal mucosa	Th17	⦿
PFKFB3	1.26E+00	5.93E-63	Intestinal mucosa	Th17	
RGS2	1.69E+00	8.00E-61	Intestinal mucosa	Th17	
ZNF331	1.51E+00	2.32E-60	Intestinal mucosa	Th17	⦿
DUSP5	7.63E-01	4.76E-57	Intestinal mucosa	Th17	
TSC22D3	1.23E+00	9.20E-56	Intestinal mucosa	Th17	⦿
CLEC2D	7.86E-01	2.29E-55	Intestinal mucosa	Th17	
SELENOK	1.28E+00	9.48E-55	Intestinal mucosa	Th17	
CLK1	8.28E-01	3.30E-50	Intestinal mucosa	Th17	
DUSP4	1.18E+00	1.29E-48	Intestinal mucosa	Th17	
CSRNP1	1.14E+00	1.89E-45	Intestinal mucosa	Th17	
PPP1CB	7.14E-01	4.04E-45	Intestinal mucosa	Th17	
PABPC1	8.12E-01	5.78E-44	Intestinal mucosa	Th17	
SRGN	8.04E-01	2.30E-43	Intestinal mucosa	Th17	
HNRNPLL	9.31E-01	9.65E-43	Intestinal mucosa	Th17	
SPRY1	1.39E+00	1.27E-42	Intestinal mucosa	Th17	
HSPH1	1.12E+00	2.29E-39	Intestinal mucosa	Th17	
KLF6	9.43E-01	1.80E-37	Intestinal mucosa	Th17	⦿
BIRC3	1.23E+00	1.98E-37	Intestinal mucosa	Th17	
FTH1	7.55E-01	3.01E-37	Intestinal mucosa	Th17	
PER1	8.30E-01	8.37E-37	Intestinal mucosa	Th17	
MPZL3	1.05E+00	7.70E-35	Intestinal mucosa	Th17	
THBS1	6.66E-01	9.88E-34	Intestinal mucosa	Th17	
KDM6B	7.36E-01	3.01E-33	Intestinal mucosa	Th17	
MORF4L2	7.79E-01	5.98E-33	Intestinal mucosa	Th17	
ETF1	7.92E-01	2.71E-32	Intestinal mucosa	Th17	
DNAJA1	1.14E+00	7.72E-31	Intestinal mucosa	Th17	
CDKN1A	8.15E-01	2.44E-30	Intestinal mucosa	Th17	
DNAJA4	1.24E+00	6.98E-30	Intestinal mucosa	Th17	
DUSP10	5.10E-01	1.84E-29	Intestinal mucosa	Th17	
PDE4D	1.04E+00	2.66E-29	Intestinal mucosa	Th17	◁

Gene	Average log fold change	Adjusted p-value	Compartment	Cell type	Gene annotation
CD96	1.07E+00	6.39E-28	Intestinal mucosa	Th17	
LDLRAD4	1.20E+00	1.35E-27	Intestinal mucosa	Th17	
USP36	9.61E-01	5.33E-27	Intestinal mucosa	Th17	
STN1	7.47E-01	7.24E-27	Intestinal mucosa	Th17	
RANBP2	6.00E-01	2.00E-26	Intestinal mucosa	Th17	
ABCA1	9.81E-01	2.35E-26	Intestinal mucosa	Th17	
SNORD99	6.28E-01	8.66E-26	Intestinal mucosa	Th17	
KMT2E	6.81E-01	1.33E-25	Intestinal mucosa	Th17	
ZFP36L2	7.49E-01	1.82E-25	Intestinal mucosa	Th17	⦿
ZNF250	6.73E-01	2.30E-25	Intestinal mucosa	Th17	⦿
ZSWIM4	4.11E-01	2.35E-25	Intestinal mucosa	Th17	
CCNH	8.71E-01	1.97E-24	Intestinal mucosa	Th17	
BCAS2	1.00E+00	4.49E-24	Intestinal mucosa	Th17	
VMP1	6.84E-01	1.55E-23	Intestinal mucosa	Th17	
EML4	8.37E-01	8.40E-23	Intestinal mucosa	Th17	
MAPK1IP1L	6.59E-01	1.43E-22	Intestinal mucosa	Th17	
ASB2	7.19E-01	5.20E-22	Intestinal mucosa	Th17	
CCL20	7.56E-01	5.46E-22	Intestinal mucosa	Th17	✘ ✷
PMAIP1	8.42E-01	6.61E-22	Intestinal mucosa	Th17	
IL22	1.00E+00	4.75E-21	Intestinal mucosa	Th17	✷
NAMPT	3.24E-01	1.07E-20	Intestinal mucosa	Th17	✷
SAT1	8.17E-01	2.65E-20	Intestinal mucosa	Th17	
SDCBP	9.11E-01	4.94E-20	Intestinal mucosa	Th17	
RP11.138A9.2	6.81E-01	2.82E-19	Intestinal mucosa	Th17	
AC008440.5	2.64E-01	3.08E-19	Intestinal mucosa	Th17	
IRF2BP2	7.69E-01	3.36E-19	Intestinal mucosa	Th17	
SNHG16	7.47E-01	4.81E-19	Intestinal mucosa	Th17	
CD55	7.44E-01	1.47E-18	Intestinal mucosa	Th17	
ARL5B	7.57E-01	3.02E-18	Intestinal mucosa	Th17	
ADAM19	5.04E-01	1.48E-17	Intestinal mucosa	Th17	
RPL21	5.67E-01	2.37E-17	Intestinal mucosa	Th17	
PTP4A1	8.26E-01	5.76E-17	Intestinal mucosa	Th17	
MBOAT1	6.35E-01	1.28E-16	Intestinal mucosa	Th17	
MAP3K8	8.01E-01	2.02E-16	Intestinal mucosa	Th17	✘
YWHAZ	4.16E-01	7.91E-16	Intestinal mucosa	Th17	
EZR	5.74E-01	1.14E-15	Intestinal mucosa	Th17	
FMNL3	5.78E-01	2.05E-15	Intestinal mucosa	Th17	
IFRD1	7.10E-01	3.02E-15	Intestinal mucosa	Th17	
PDCD4	4.13E-01	3.12E-15	Intestinal mucosa	Th17	
CCL5	4.99E-01	4.01E-15	Intestinal mucosa	Th17	✷

Gene	**Average log fold change**	**Adjusted p-value**	**Compartment**	**Cell type**	**Gene annotation**
HSP90AB1	7.36E-01	1.22E-14	Intestinal mucosa	Th17	
ICOS	8.82E-01	2.59E-14	Intestinal mucosa	Th17	
PRMT9	8.69E-01	5.56E-14	Intestinal mucosa	Th17	
STAT1	6.65E-01	2.33E-13	Intestinal mucosa	Th17	⊙
PIM3	7.52E-01	3.22E-13	Intestinal mucosa	Th17	
PPP1R15B	5.32E-01	4.10E-12	Intestinal mucosa	Th17	
IL17A	1.04E+00	1.10E-11	Intestinal mucosa	Th17	✷ ◁
VPS37B	4.82E-01	1.29E-11	Intestinal mucosa	Th17	
HSPE1	9.28E-01	1.33E-11	Intestinal mucosa	Th17	
IRF4	5.31E-01	2.02E-11	Intestinal mucosa	Th17	✘ ⊙
RORA	6.06E-01	2.80E-11	Intestinal mucosa	Th17	⊙
NFE2L2	7.10E-01	3.08E-11	Intestinal mucosa	Th17	⊙
IFNG	7.86E-01	5.22E-11	Intestinal mucosa	Th17	✘ ✷
HLA.J	3.67E-01	6.82E-11	Intestinal mucosa	Th17	
HSPA8	5.68E-01	8.03E-11	Intestinal mucosa	Th17	
TSPYL1	4.34E-01	8.10E-11	Intestinal mucosa	Th17	
AHSA1	3.97E-01	1.21E-10	Intestinal mucosa	Th17	
NUP98	4.89E-01	1.43E-10	Intestinal mucosa	Th17	
SRSF3	4.46E-01	1.91E-10	Intestinal mucosa	Th17	
CHD1	6.84E-01	2.29E-10	Intestinal mucosa	Th17	⊙
LINC.PINT	4.89E-01	3.95E-10	Intestinal mucosa	Th17	
RP11.631M6.2	3.95E-01	1.55E-09	Intestinal mucosa	Th17	
ANKHD1	6.47E-01	1.71E-09	Intestinal mucosa	Th17	
SNHG12	2.86E-01	3.06E-09	Intestinal mucosa	Th17	
CLDND1	6.63E-01	1.45E-08	Intestinal mucosa	Th17	
TSC22D2	4.38E-01	2.21E-08	Intestinal mucosa	Th17	⊙
ISG15	6.10E-01	2.42E-08	Intestinal mucosa	Th17	
PTPN22	4.53E-01	3.13E-08	Intestinal mucosa	Th17	✘
TP53INP1	5.00E-01	1.56E-07	Intestinal mucosa	Th17	
CHD2	5.33E-01	1.87E-07	Intestinal mucosa	Th17	⊙
HES4	3.99E-01	1.99E-07	Intestinal mucosa	Th17	⊙
RP11.138A9.1	5.05E-01	2.49E-07	Intestinal mucosa	Th17	
GNL3	5.16E-01	2.71E-07	Intestinal mucosa	Th17	
AC092580.4	4.92E-01	3.48E-07	Intestinal mucosa	Th17	
DNAJB4	4.84E-01	4.24E-07	Intestinal mucosa	Th17	✘
GFPT2	3.76E-01	4.30E-07	Intestinal mucosa	Th17	
TIPARP	7.20E-01	4.66E-07	Intestinal mucosa	Th17	⊙
DHX36	4.05E-01	6.87E-07	Intestinal mucosa	Th17	
CYCS	8.36E-01	7.24E-07	Intestinal mucosa	Th17	
PTGES3	5.18E-01	9.72E-07	Intestinal mucosa	Th17	

Gene	**Average log fold change**	**Adjusted p-value**	**Compartment**	**Cell type**	**Gene annotation**
STRN3	4.36E-01	3.24E-06	Intestinal mucosa	Th17	
LRRC1	4.00E-01	4.56E-06	Intestinal mucosa	Th17	
PTBP2	3.99E-01	6.32E-06	Intestinal mucosa	Th17	
UBE2B	3.62E-01	6.48E-06	Intestinal mucosa	Th17	
ARHGEF7	4.56E-01	7.35E-06	Intestinal mucosa	Th17	
RP11.727F15.9	5.28E-01	7.46E-06	Intestinal mucosa	Th17	
RHOH	4.87E-01	7.91E-06	Intestinal mucosa	Th17	
LDLR	4.20E-01	8.22E-06	Intestinal mucosa	Th17	
ZBTB10	4.10E-01	9.07E-06	Intestinal mucosa	Th17	⦿
CTB.131B5.2	3.62E-01	9.32E-06	Intestinal mucosa	Th17	
H3F3B	4.60E-01	9.46E-06	Intestinal mucosa	Th17	
DEFA5	2.99E-01	1.04E-05	Intestinal mucosa	Th17	✷
TANK	4.51E-01	1.06E-05	Intestinal mucosa	Th17	
ERN1	5.39E-01	1.32E-05	Intestinal mucosa	Th17	
ZBTB25	4.18E-01	1.56E-05	Intestinal mucosa	Th17	⦿
HECA	5.08E-01	1.56E-05	Intestinal mucosa	Th17	
NOP58	3.89E-01	1.58E-05	Intestinal mucosa	Th17	
NASP	3.57E-01	2.40E-05	Intestinal mucosa	Th17	
GPR34	5.99E-01	2.73E-05	Intestinal mucosa	Th17	
DOCK11	4.54E-01	2.83E-05	Intestinal mucosa	Th17	
SYTL3	7.15E-01	2.99E-05	Intestinal mucosa	Th17	
RP11.297H3.3	6.31E-01	3.56E-05	Intestinal mucosa	Th17	
CCL4	9.08E-01	3.66E-05	Intestinal mucosa	Th17	✷
TSPYL2	7.38E-01	3.93E-05	Intestinal mucosa	Th17	
WDR74	3.58E-01	5.73E-05	Intestinal mucosa	Th17	
CHMP1B	5.35E-01	6.03E-05	Intestinal mucosa	Th17	
STRAP	4.98E-01	7.87E-05	Intestinal mucosa	Th17	
OSTF1	3.75E-01	9.02E-05	Intestinal mucosa	Th17	
CTD.2636A23.2	2.54E-01	1.43E-04	Intestinal mucosa	Th17	
LZTFL1	3.36E-01	1.60E-04	Intestinal mucosa	Th17	
KLRB1	5.69E-01	2.27E-04	Intestinal mucosa	Th17	
SH2D2A	5.69E-01	2.63E-04	Intestinal mucosa	Th17	
SHISA2	4.90E-01	2.78E-04	Intestinal mucosa	Th17	
DDX3X	3.11E-01	2.81E-04	Intestinal mucosa	Th17	
HSPA6	4.77E-01	3.12E-04	Intestinal mucosa	Th17	
STIP1	4.22E-01	3.50E-04	Intestinal mucosa	Th17	
PIK3R1	7.36E-01	3.53E-04	Intestinal mucosa	Th17	
ETV3	4.55E-01	4.25E-04	Intestinal mucosa	Th17	⦿
ZNF267	4.35E-01	4.54E-04	Intestinal mucosa	Th17	⦿
UBB	4.68E-01	6.99E-04	Intestinal mucosa	Th17	

Gene	**Average log fold change**	**Adjusted p-value**	**Compartment**	**Cell type**	**Gene annotation**
CFAP20	6.38E-01	8.83E-04	Intestinal mucosa	Th17	
G3BP2	4.94E-01	9.43E-04	Intestinal mucosa	Th17	
ZC3H12A	5.09E-01	9.88E-04	Intestinal mucosa	Th17	
ITGA1	7.52E-01	1.24E-03	Intestinal mucosa	Th17	
RP3.370M22.8	4.11E-01	1.26E-03	Intestinal mucosa	Th17	
PPP3CA	3.55E-01	1.69E-03	Intestinal mucosa	Th17	
AUTS2	3.08E-01	1.73E-03	Intestinal mucosa	Th17	
SOCS1	6.59E-01	1.78E-03	Intestinal mucosa	Th17	✘
CEBPZ	2.89E-01	2.43E-03	Intestinal mucosa	Th17	⊙
REL	3.88E-01	4.08E-03	Intestinal mucosa	Th17	✘ ⊙
FAM177A1	5.57E-01	4.57E-03	Intestinal mucosa	Th17	
TAGAP	5.94E-01	6.05E-03	Intestinal mucosa	Th17	✘
RNF19A	3.25E-01	9.96E-03	Intestinal mucosa	Th17	
GABARAPL1	3.19E-01	1.02E-02	Intestinal mucosa	Th17	
NABP1	2.73E-01	1.16E-02	Intestinal mucosa	Th17	
GALK2	4.63E-01	1.18E-02	Intestinal mucosa	Th17	
BTG3	5.26E-01	1.40E-02	Intestinal mucosa	Th17	
COCH	2.63E-01	1.64E-02	Intestinal mucosa	Th17	
ZFP36L1	3.82E-01	2.02E-02	Intestinal mucosa	Th17	✘ ⊙
DCTN6	3.41E-01	2.20E-02	Intestinal mucosa	Th17	
PAPOLA	5.16E-01	2.39E-02	Intestinal mucosa	Th17	
IL2	3.81E-01	2.59E-02	Intestinal mucosa	Th17	✷
ZC3H12D	3.08E-01	2.74E-02	Intestinal mucosa	Th17	
KPNA2	4.57E-01	3.42E-02	Intestinal mucosa	Th17	
GPR35	2.99E-01	3.68E-02	Intestinal mucosa	Th17	
ARL4D	4.03E-01	4.22E-02	Intestinal mucosa	Th17	
NUP58	4.79E-01	4.40E-02	Intestinal mucosa	Th17	
S100A4	6.18E-01	3.44E-67	Peripheral blood	Effector/Treg	
LTB	7.50E-01	6.76E-62	Peripheral blood	Effector/Treg	✷
TOB1	5.29E-01	8.63E-45	Peripheral blood	Effector/Treg	
C16orf54	3.13E-01	7.21E-43	Peripheral blood	Effector/Treg	
CD52	4.09E-01	2.02E-41	Peripheral blood	Effector/Treg	
IL32	3.94E-01	2.07E-39	Peripheral blood	Effector/Treg	✷
TMSB10	3.63E-01	3.36E-36	Peripheral blood	Effector/Treg	
EMP3	2.58E-01	2.64E-33	Peripheral blood	Effector/Treg	
TNFRSF25	3.83E-01	2.37E-29	Peripheral blood	Effector/Treg	
RAP2B	3.64E-01	2.35E-28	Peripheral blood	Effector/Treg	
RASSF3	2.66E-01	2.52E-28	Peripheral blood	Effector/Treg	
S100A11	4.07E-01	4.78E-25	Peripheral blood	Effector/Treg	
PRDM1	3.98E-01	1.43E-24	Peripheral blood	Effector/Treg	✘ ⊙

Gene	**Average log fold change**	**Adjusted p-value**	**Compartment**	**Cell type**	**Gene annotation**
CALM1	2.96E-01	1.48E-24	Peripheral blood	Effector/Treg	
RPL13A	3.30E-01	6.10E-24	Peripheral blood	Effector/Treg	
TTC39C	2.73E-01	9.43E-23	Peripheral blood	Effector/Treg	
RUNX2	6.60E-01	8.29E-22	Peripheral blood	Effector/Treg	⊙
ADAM19	3.99E-01	1.67E-21	Peripheral blood	Effector/Treg	
FAM65B	3.16E-01	2.22E-21	Peripheral blood	Effector/Treg	
SH3BGRL3	3.48E-01	1.02E-19	Peripheral blood	Effector/Treg	
AES	2.73E-01	1.75E-18	Peripheral blood	Effector/Treg	
TTC39C.AS1	4.49E-01	1.21E-17	Peripheral blood	Effector/Treg	
FLNA	4.53E-01	6.53E-17	Peripheral blood	Effector/Treg	
FUT7	3.14E-01	2.06E-16	Peripheral blood	Effector/Treg	
SOCS2	6.58E-01	2.85E-16	Peripheral blood	Effector/Treg	
PIM1	5.37E-01	2.92E-16	Peripheral blood	Effector/Treg	
MORC2.AS1	3.79E-01	3.47E-16	Peripheral blood	Effector/Treg	
PSME1	2.80E-01	1.42E-15	Peripheral blood	Effector/Treg	
MORC2	4.93E-01	8.75E-15	Peripheral blood	Effector/Treg	
TESPA1	3.74E-01	1.36E-14	Peripheral blood	Effector/Treg	
RPL5	2.80E-01	6.17E-14	Peripheral blood	Effector/Treg	
PCED1B.AS1	2.70E-01	9.66E-14	Peripheral blood	Effector/Treg	
PLP2	5.98E-01	1.38E-13	Peripheral blood	Effector/Treg	
PTPN13	4.66E-01	1.47E-13	Peripheral blood	Effector/Treg	
CMTM6	4.78E-01	1.93E-13	Peripheral blood	Effector/Treg	✷
S1PR1	4.97E-01	2.43E-13	Peripheral blood	Effector/Treg	◁
RPLP0	2.57E-01	2.75E-13	Peripheral blood	Effector/Treg	
TNFRSF4	4.85E-01	8.03E-13	Peripheral blood	Effector/Treg	✘
ANXA2	4.32E-01	9.76E-13	Peripheral blood	Effector/Treg	
S100A10	5.28E-01	1.29E-12	Peripheral blood	Effector/Treg	
CTSH	5.95E-01	1.98E-12	Peripheral blood	Effector/Treg	
P2RY8	4.81E-01	2.34E-12	Peripheral blood	Effector/Treg	
BIN2	4.23E-01	4.11E-12	Peripheral blood	Effector/Treg	
C21orf33	2.61E-01	4.25E-12	Peripheral blood	Effector/Treg	
SLC25A6	3.23E-01	5.05E-12	Peripheral blood	Effector/Treg	
NOSIP	6.04E-01	5.06E-12	Peripheral blood	Effector/Treg	
USP10	5.74E-01	3.09E-11	Peripheral blood	Effector/Treg	
TSPO	6.49E-01	3.11E-11	Peripheral blood	Effector/Treg	
IL7R	2.83E-01	4.13E-11	Peripheral blood	Effector/Treg	
RPL4	2.84E-01	9.82E-11	Peripheral blood	Effector/Treg	
TIMP1	5.64E-01	1.13E-10	Peripheral blood	Effector/Treg	
NPDC1	3.83E-01	1.38E-10	Peripheral blood	Effector/Treg	
SELPLG	4.92E-01	1.73E-10	Peripheral blood	Effector/Treg	

Gene	Average log fold change	Adjusted p-value	Compartment	Cell type	Gene annotation
RPL18	2.56E-01	1.28E-09	Peripheral blood	Effector/Treg	
TRAT1	4.50E-01	1.38E-09	Peripheral blood	Effector/Treg	
MAP3K1	5.20E-01	3.08E-09	Peripheral blood	Effector/Treg	
CAPN2	4.85E-01	5.43E-09	Peripheral blood	Effector/Treg	
GBP5	4.51E-01	1.05E-08	Peripheral blood	Effector/Treg	
SVIL	4.19E-01	1.16E-08	Peripheral blood	Effector/Treg	
HSD11B1	3.86E-01	1.33E-08	Peripheral blood	Effector/Treg	
AQP3	4.76E-01	1.77E-08	Peripheral blood	Effector/Treg	
CDC25B	3.66E-01	4.66E-08	Peripheral blood	Effector/Treg	
GTF3A	4.03E-01	5.53E-08	Peripheral blood	Effector/Treg	⊙
C12orf75	6.12E-01	7.35E-08	Peripheral blood	Effector/Treg	
CISH	5.24E-01	8.45E-08	Peripheral blood	Effector/Treg	
GLUL	5.11E-01	9.62E-08	Peripheral blood	Effector/Treg	
MFNG	3.79E-01	1.26E-07	Peripheral blood	Effector/Treg	
PDIA4	2.81E-01	2.34E-07	Peripheral blood	Effector/Treg	
LDHB	2.59E-01	2.97E-07	Peripheral blood	Effector/Treg	
RP11.356J5.12	5.69E-01	3.68E-07	Peripheral blood	Effector/Treg	
IL10RA	3.29E-01	6.00E-07	Peripheral blood	Effector/Treg	
ARPC1B	2.70E-01	6.26E-07	Peripheral blood	Effector/Treg	
ITGB2	2.74E-01	7.35E-07	Peripheral blood	Effector/Treg	
PDCD5	5.30E-01	7.94E-07	Peripheral blood	Effector/Treg	
SLC40A1	3.77E-01	8.32E-07	Peripheral blood	Effector/Treg	
YWHAQ	2.85E-01	2.17E-06	Peripheral blood	Effector/Treg	
ELK3	4.46E-01	2.71E-06	Peripheral blood	Effector/Treg	⊙
NECAP2	4.12E-01	3.59E-06	Peripheral blood	Effector/Treg	
ELOVL4	3.71E-01	4.33E-06	Peripheral blood	Effector/Treg	
MOSPD3	3.37E-01	5.23E-06	Peripheral blood	Effector/Treg	
PSMB8	3.76E-01	5.97E-06	Peripheral blood	Effector/Treg	
TRADD	4.01E-01	7.02E-06	Peripheral blood	Effector/Treg	
SSR4	2.66E-01	2.17E-05	Peripheral blood	Effector/Treg	
TXN	3.24E-01	2.26E-05	Peripheral blood	Effector/Treg	
MYC	4.04E-01	3.83E-05	Peripheral blood	Effector/Treg	⊙
TEX264	5.62E-01	1.17E-04	Peripheral blood	Effector/Treg	
JAKMIP1	2.71E-01	1.18E-04	Peripheral blood	Effector/Treg	
RNASET2	3.30E-01	1.27E-04	Peripheral blood	Effector/Treg	✘
LTK	2.74E-01	1.67E-04	Peripheral blood	Effector/Treg	
PLEKHG3	2.65E-01	1.74E-04	Peripheral blood	Effector/Treg	
CNN2	2.68E-01	1.76E-04	Peripheral blood	Effector/Treg	
MT.TT	2.81E-01	2.00E-04	Peripheral blood	Effector/Treg	
AHNAK	2.84E-01	2.01E-04	Peripheral blood	Effector/Treg	

Gene	Average log fold change	Adjusted p-value	Compartment	Cell type	Gene annotation
BIN1	3.85E-01	2.25E-04	Peripheral blood	Effector/Treg	
C10orf54	4.48E-01	2.46E-04	Peripheral blood	Effector/Treg	
REXO2	3.75E-01	3.66E-04	Peripheral blood	Effector/Treg	
TC2N	3.17E-01	4.28E-04	Peripheral blood	Effector/Treg	
DPP4	2.50E-01	5.66E-04	Peripheral blood	Effector/Treg	
ENO1	3.00E-01	6.73E-04	Peripheral blood	Effector/Treg	
NSG1	3.90E-01	7.02E-04	Peripheral blood	Effector/Treg	
HINT1	2.60E-01	7.02E-04	Peripheral blood	Effector/Treg	
SIT1	3.32E-01	1.78E-03	Peripheral blood	Effector/Treg	
TRAF3IP3	2.91E-01	2.04E-03	Peripheral blood	Effector/Treg	
SEC61B	2.59E-01	2.44E-03	Peripheral blood	Effector/Treg	
CCR2	2.93E-01	2.56E-03	Peripheral blood	Effector/Treg	✘
ICAM2	4.66E-01	3.01E-03	Peripheral blood	Effector/Treg	
ATP5F1	2.98E-01	5.84E-03	Peripheral blood	Effector/Treg	
RIPK2	4.75E-01	6.17E-03	Peripheral blood	Effector/Treg	✘
CBLL1	3.34E-01	6.32E-03	Peripheral blood	Effector/Treg	⦿
LRRFIP1	2.80E-01	6.58E-03	Peripheral blood	Effector/Treg	
S1PR4	3.74E-01	7.70E-03	Peripheral blood	Effector/Treg	◁
EIF4EBP2	2.69E-01	8.50E-03	Peripheral blood	Effector/Treg	
CPT1A	2.54E-01	9.14E-03	Peripheral blood	Effector/Treg	
SYTL1	2.86E-01	1.06E-02	Peripheral blood	Effector/Treg	
SLIRP	3.02E-01	1.25E-02	Peripheral blood	Effector/Treg	
TNFAIP8	2.91E-01	1.29E-02	Peripheral blood	Effector/Treg	
RSU1	3.85E-01	1.64E-02	Peripheral blood	Effector/Treg	
ARL14EP	2.70E-01	1.79E-02	Peripheral blood	Effector/Treg	
CYTH1	2.57E-01	1.90E-02	Peripheral blood	Effector/Treg	
MAT2B	3.02E-01	2.12E-02	Peripheral blood	Effector/Treg	
LPAR6	3.77E-01	2.42E-02	Peripheral blood	Effector/Treg	
EAF1	2.78E-01	2.58E-02	Peripheral blood	Effector/Treg	
CARD16	3.12E-01	2.76E-02	Peripheral blood	Effector/Treg	
SMDT1	2.67E-01	3.69E-02	Peripheral blood	Effector/Treg	
MYO1F	3.07E-01	4.61E-02	Peripheral blood	Effector/Treg	
CDC42SE1	9.05E-01	8.32E-44	Peripheral blood	Treg/Quiescent	
C1orf56	9.03E-01	3.44E-42	Peripheral blood	Treg/Quiescent	
HNRNPH1	7.20E-01	1.88E-37	Peripheral blood	Treg/Quiescent	
MTA2	6.33E-01	1.15E-12	Peripheral blood	Treg/Quiescent	⦿
C16orf54	7.99E-01	8.09E-12	Peripheral blood	Treg/Quiescent	
HNRNPL	5.86E-01	2.67E-11	Peripheral blood	Treg/Quiescent	
SRSF6	5.83E-01	2.37E-07	Peripheral blood	Treg/Quiescent	
RASSF3	8.64E-01	4.41E-07	Peripheral blood	Treg/Quiescent	

Gene	Average log fold change	Adjusted p-value	Compartment	Cell type	Gene annotation
EIF5A	4.91E-01	1.62E-06	Peripheral blood	Treg/Quiescent	
CTNNB1	5.27E-01	7.67E-06	Peripheral blood	Treg/Quiescent	
CTBP1	7.36E-01	3.51E-05	Peripheral blood	Treg/Quiescent	
SAR1A	3.91E-01	4.35E-05	Peripheral blood	Treg/Quiescent	
MPRIP	8.35E-01	4.67E-04	Peripheral blood	Treg/Quiescent	
GIGYF1	6.07E-01	6.64E-04	Peripheral blood	Treg/Quiescent	
PCBP2	4.81E-01	1.06E-03	Peripheral blood	Treg/Quiescent	
POLR2J3	4.20E-01	1.43E-03	Peripheral blood	Treg/Quiescent	
B4GALT1	4.09E-01	6.54E-03	Peripheral blood	Treg/Quiescent	
RAB12	7.70E-01	7.50E-03	Peripheral blood	Treg/Quiescent	
WTAP	4.85E-01	2.68E-02	Peripheral blood	Treg/Quiescent	
C6orf62	4.52E-01	3.14E-02	Peripheral blood	Treg/Quiescent	
NOG	9.18E-01	3.82E-02	Peripheral blood	Treg/Quiescent	
FLVCR2	6.93E-01	4.00E-96	Intestinal mucosa	Treg/Quiescent	
SYT8	7.73E-01	2.91E-54	Intestinal mucosa	Treg/Quiescent	
MTND4P12	6.81E-01	1.20E-43	Intestinal mucosa	Treg/Quiescent	
CXCR5	1.02E+00	2.40E-35	Intestinal mucosa	Treg/Quiescent	✘
ICA1	8.77E-01	4.83E-24	Intestinal mucosa	Treg/Quiescent	
ST8SIA1	8.56E-01	1.68E-22	Intestinal mucosa	Treg/Quiescent	
RPL13P12	2.96E-01	2.98E-20	Intestinal mucosa	Treg/Quiescent	
ACTB	3.58E-01	2.90E-19	Intestinal mucosa	Treg/Quiescent	
TIGIT	7.33E-01	2.18E-18	Intestinal mucosa	Treg/Quiescent	
PDCD1	7.20E-01	5.88E-17	Intestinal mucosa	Treg/Quiescent	
CTLA4	6.18E-01	1.73E-16	Intestinal mucosa	Treg/Quiescent	
TOX2	4.45E-01	3.35E-14	Intestinal mucosa	Treg/Quiescent	⦿
TRPS1	1.11E+00	6.72E-13	Intestinal mucosa	Treg/Quiescent	⦿
KIAA1551	6.39E-01	8.18E-13	Intestinal mucosa	Treg/Quiescent	
IL6ST	7.54E-01	1.62E-12	Intestinal mucosa	Treg/Quiescent	✷
CTD.2031P19.5	6.75E-01	1.80E-11	Intestinal mucosa	Treg/Quiescent	
DPP7	4.42E-01	1.13E-10	Intestinal mucosa	Treg/Quiescent	
MAF	5.92E-01	7.40E-10	Intestinal mucosa	Treg/Quiescent	⦿
RP11.157G21.2	4.63E-01	7.70E-10	Intestinal mucosa	Treg/Quiescent	
CHRM3.AS2	5.49E-01	2.58E-09	Intestinal mucosa	Treg/Quiescent	
CD38	4.19E-01	2.66E-09	Intestinal mucosa	Treg/Quiescent	
RBM6	4.69E-01	3.13E-09	Intestinal mucosa	Treg/Quiescent	⦿
RNU4.2	3.23E-01	7.10E-09	Intestinal mucosa	Treg/Quiescent	
TBC1D4	6.45E-01	3.48E-08	Intestinal mucosa	Treg/Quiescent	
HNRNPD	6.03E-01	3.89E-08	Intestinal mucosa	Treg/Quiescent	
SDR39U1	4.53E-01	4.67E-08	Intestinal mucosa	Treg/Quiescent	
CNOT6L	5.03E-01	5.65E-08	Intestinal mucosa	Treg/Quiescent	

Gene	**Average log fold change**	**Adjusted p-value**	**Compartment**	**Cell type**	**Gene annotation**
NFATC1	4.20E-01	1.32E-07	Intestinal mucosa	Treg/Quiescent	✘ ⦿
HNRNPH3	4.94E-01	2.12E-07	Intestinal mucosa	Treg/Quiescent	
FOXP3	3.57E-01	4.14E-07	Intestinal mucosa	Treg/Quiescent	⦿
TUBA4A	3.10E-01	6.72E-07	Intestinal mucosa	Treg/Quiescent	
PLK3	3.52E-01	1.85E-06	Intestinal mucosa	Treg/Quiescent	
SIRPG	4.06E-01	2.96E-06	Intestinal mucosa	Treg/Quiescent	
TOX	4.11E-01	3.82E-06	Intestinal mucosa	Treg/Quiescent	⦿
EPHB6	4.86E-01	3.83E-06	Intestinal mucosa	Treg/Quiescent	
NABP1	5.00E-01	5.93E-06	Intestinal mucosa	Treg/Quiescent	
PASK	5.30E-01	6.62E-06	Intestinal mucosa	Treg/Quiescent	
DGKA	5.52E-01	2.47E-05	Intestinal mucosa	Treg/Quiescent	
FAN1	2.62E-01	3.71E-05	Intestinal mucosa	Treg/Quiescent	
SP110	6.01E-01	4.94E-05	Intestinal mucosa	Treg/Quiescent	⦿
CMTM7	5.50E-01	7.78E-05	Intestinal mucosa	Treg/Quiescent	✷
DNPH1	4.84E-01	8.22E-05	Intestinal mucosa	Treg/Quiescent	
PTPN7	2.52E-01	1.03E-04	Intestinal mucosa	Treg/Quiescent	
ACAD10	2.98E-01	1.23E-04	Intestinal mucosa	Treg/Quiescent	
FCMR	4.05E-01	1.81E-04	Intestinal mucosa	Treg/Quiescent	
CTSB	4.70E-01	7.16E-04	Intestinal mucosa	Treg/Quiescent	
CDK5R1	3.16E-01	7.16E-04	Intestinal mucosa	Treg/Quiescent	
PVT1	3.51E-01	7.28E-04	Intestinal mucosa	Treg/Quiescent	
AHI1	3.73E-01	7.32E-04	Intestinal mucosa	Treg/Quiescent	
TLK1	4.47E-01	7.88E-04	Intestinal mucosa	Treg/Quiescent	
ZNF251	3.00E-01	9.69E-04	Intestinal mucosa	Treg/Quiescent	⦿
RNA28S5	4.14E-01	1.02E-03	Intestinal mucosa	Treg/Quiescent	
TMEM2	3.63E-01	1.03E-03	Intestinal mucosa	Treg/Quiescent	
PTPRCAP	4.02E-01	1.15E-03	Intestinal mucosa	Treg/Quiescent	
SESN3	5.10E-01	1.27E-03	Intestinal mucosa	Treg/Quiescent	
AFTPH	2.81E-01	1.76E-03	Intestinal mucosa	Treg/Quiescent	
UBA6.AS1	2.87E-01	1.87E-03	Intestinal mucosa	Treg/Quiescent	
FYB	4.33E-01	3.79E-03	Intestinal mucosa	Treg/Quiescent	
TSEN34	2.54E-01	4.12E-03	Intestinal mucosa	Treg/Quiescent	
SELENOM	3.23E-01	4.65E-03	Intestinal mucosa	Treg/Quiescent	
PVALB	2.96E-01	5.27E-03	Intestinal mucosa	Treg/Quiescent	
RPL10	2.50E-01	6.18E-03	Intestinal mucosa	Treg/Quiescent	
MBOAT1	2.53E-01	8.03E-03	Intestinal mucosa	Treg/Quiescent	
RPS5	3.32E-01	1.33E-02	Intestinal mucosa	Treg/Quiescent	
ZC2HC1A	3.14E-01	2.14E-02	Intestinal mucosa	Treg/Quiescent	
SYPL1	4.76E-01	2.24E-02	Intestinal mucosa	Treg/Quiescent	
STX16	2.90E-01	2.30E-02	Intestinal mucosa	Treg/Quiescent	

Gene	**Average log fold change**	**Adjusted p-value**	**Compartment**	**Cell type**	**Gene annotation**
MTATP6P1	3.58E-01	2.69E-02	Intestinal mucosa	Treg/Quiescent	
LINC00847	3.50E-01	2.91E-02	Intestinal mucosa	Treg/Quiescent	
VWA5A	2.77E-01	3.01E-02	Intestinal mucosa	Treg/Quiescent	
CD59	4.71E-01	3.23E-02	Intestinal mucosa	Treg/Quiescent	
C1orf228	2.52E-01	3.84E-02	Intestinal mucosa	Treg/Quiescent	

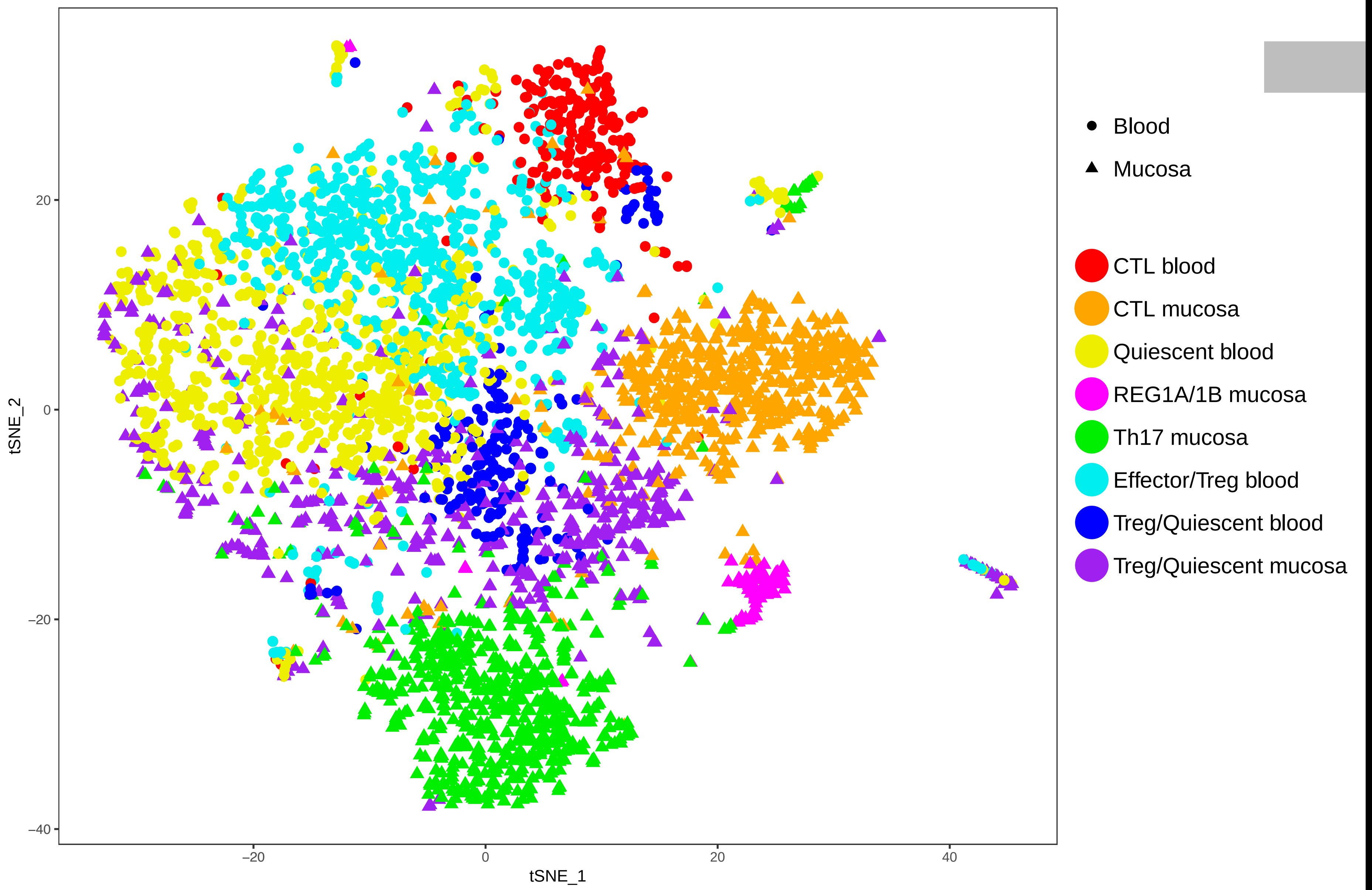
Supplementary Table 2: Specification for materials and resources

	Reagent or resource	Source	Identifier/version
Antibodies	Anti-Human CD3 APC e780	eBioscience	47-0036-42
	Anti-Human CD8α APC	Biolegend	300912
	Anti-Human CD8β APC	BD Biosciences	641058
	Anti-Human CD19 APC r700	BD Biosciences	564977
	Anti-Human CD45RO BV421	BD Biosciences	562641
	Anti-Human CD62L PE	Biolegend	304806
	Anti-Human CD326 PercpCy5.5	Biolegend	324214
	Anti-Human αβTCR FITC	eBioscience	11-9986-42
	Propidium iodide	Sigma	4170
	Anti-Human REG1A monoclonal antibody	Thermo Fisher Scientific	MA5-15524
	Anti-Human CD3 polyclonal antibody	Abcam	ab5690
Commercial kits	Nextera XT DNA sample preparation kit	Illumina	FC-131-1096
	Nextera XT 24-index kit	Illumina	FC-131-1001
	HT DNA HiSense extended range labchip	PerkinElmer	760517
	High output flowcell cartridge v2, 75bp kit.	Illumina	15065973
Reagents	Lymphoprep solution	STEMCELL	7801
	RPMI 1640 (+nil)	Thermo Fisher Scientific	61870-010
	HBSS -CMF	Thermo Fisher Scientific	14175-053
	EDTA (0.5M)	Sigma-Aldrich	3690
	DTT (0.5M)	Thermo Fisher Scientific	
	Collagenase IV	Sigma	C1889
	DNAse II type V	Sigma	D8764
	SUPERase•In™ RNase Inhibitor	Thermo Fisher Scientific	AM2696
	PW1	Illumina	in Sequencing Kit
	KAPA HiFi HotStart ReadyMix	Sopachem- KAPA Biosystems	KK2601
	EB solution 10 mM Tris-Cl, pH 8.5	Qiagen	19086
	Ethanol		

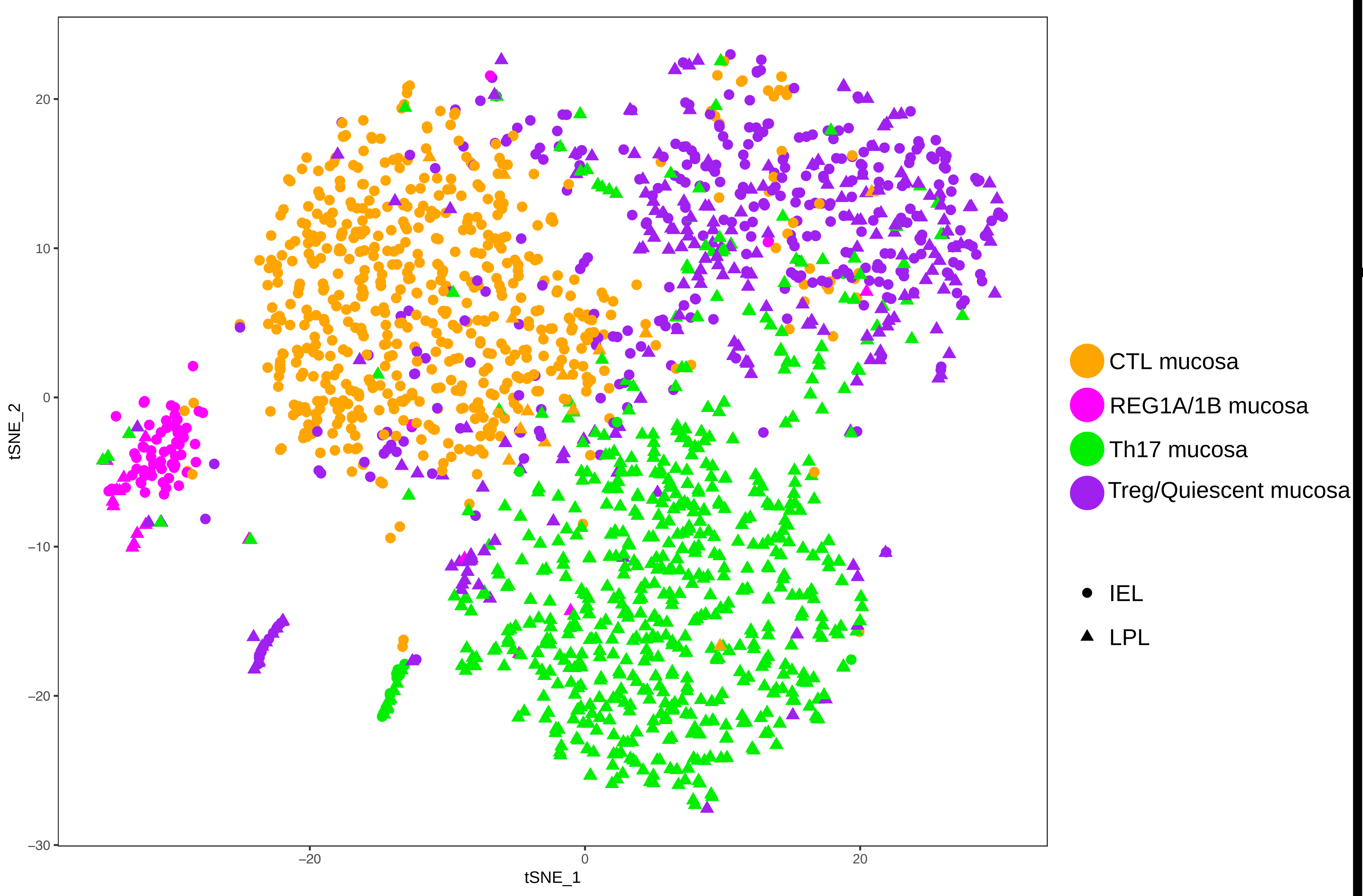
	Agencourt Ampure XP beads	Beckman Coulter	A 63881
	Betaine BioUltra ≥99.0%	Sigma-Aldrich	61962
	Triton X-100	Sigma-Aldrich	T9284
	dNTP mix	Westburg-Fermentas	R0192
	Recombinant RNase inhibitor	Westburg-Clontech	2313A
	SmartScribe reverse transcriptase	Westburg-Clontech	CL639537
	DNA-OFF	Westburg-Takara Bio	9036
	First-strand buffer	LifeTechnologies	18064-014
	DTT	LifeTechnologies	18064-014
	RNaseZap	LifeTechnologies	AM9780
Oligonucleotides	BC-TSO: AAGCAGTGGTATCAACGCAGAGTGAATrGrG+G	Biolegio	Custom design
	BC-PCR: AAGCAGTGGTATCAACGCAGAGT	Biolegio	Custom design
	BC-Read1Primer: GCCTGTCCGCGGAAGCAGTGGTATCAACGCAGAGTAC	Biolegio	Custom design
	P5-TSO-hybrid: AATGATACGGCGACCACCGAGATCTACAC - GCCTGTCCGCGGAAGCAGTGGTATCAACGCAGAGT*A*C	Biolegio	Custom design
Software	Summit	Beckman Coulter	v. 6.3.1
	DropSeq	Macosko, 2015	v. 1.12
	STAR	Dobin, 2013	v 2.5
	Picard	http://broadinstitute.github.io/picard/	v. 2.10
	R	https://www.r-project.org/	3.4.2
	Seurat	Macosko, 2015	2.1.0
	SCDE	Kharchenko and Fan, 2016	1.99.4
	SCONE	Cole and Risso, 2017	v 1.1.3
	Kaluza	Beckman Coulter	v 1.5a
	ReactomePA	Yu and He, 2016	1.22.0

Supplementary Figure Legends:

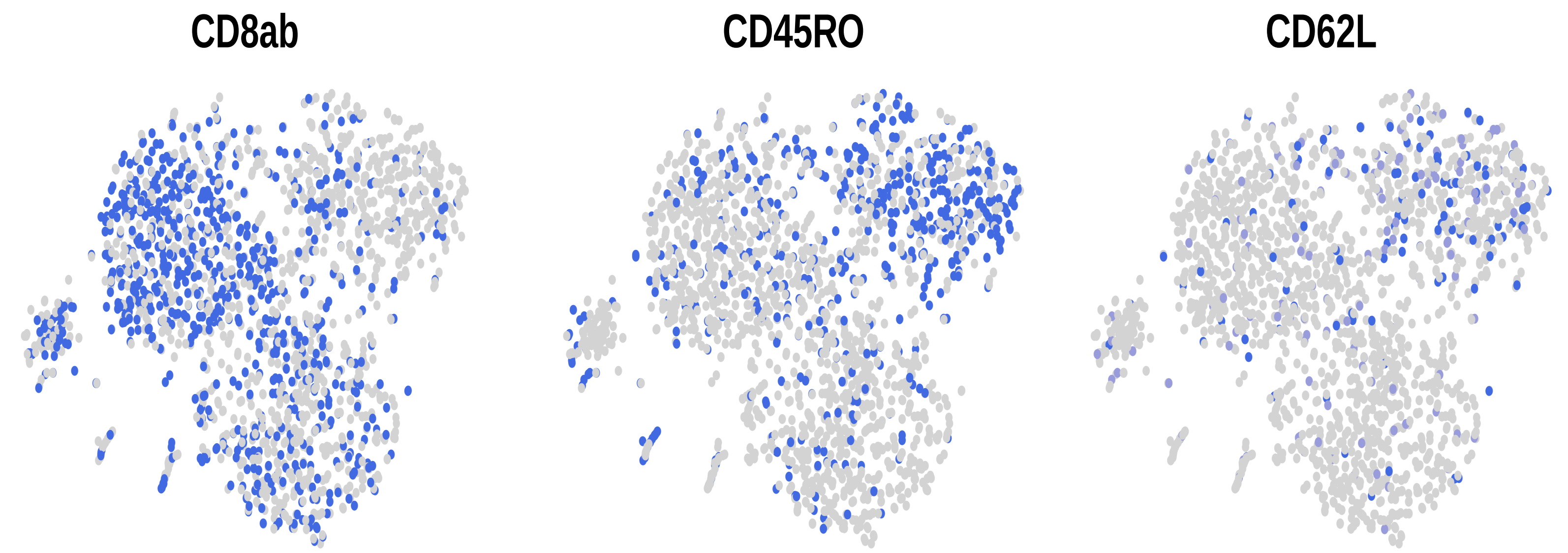
Supplementary Figure 1: t-SNE plots representing T cells pooled from three individual patients with Crohn's disease. **A)** t-SNE plot representing transcriptomes from T cells in peripheral blood (circles) and intestinal mucosa (triangles). **B)** t-SNE plot representing transcriptomes from intestinal mucosal T cells as depicted in panel A. IEL are presented as circles, LPL as triangles. **C)** t-SNE plot indicating the presence of surface markers on intestinal mucosal T cells, measured by flow-cytometry, in a binary fashion. **D-G)** t-SNE plots featuring expression of cellular marker genes in intestinal mucosal T cells. Plots represent gene expression values of a particular gene, measured by single-cell RNA sequencing, ranging from Q0-Q75 of normalized expression values per gene. **IEL**: intraepithelial T lymphocyte. **LPL**: lamina propria T lymphocyte. **CTL:** Cytotoxic T lymphocytes. **Quiescent:** Quiescent T lymphocytes. **REG1A/1B**: cells highly expressing REG1A/1B, without expressing Paneth cell markers. **Th17**: T-helper 17 cells**. Effector/Treg:** T-regulatory lymphocytes on an effector memory background. **Treg/Quiescent:** T-regulatory lymphocytes on a quiescent background.



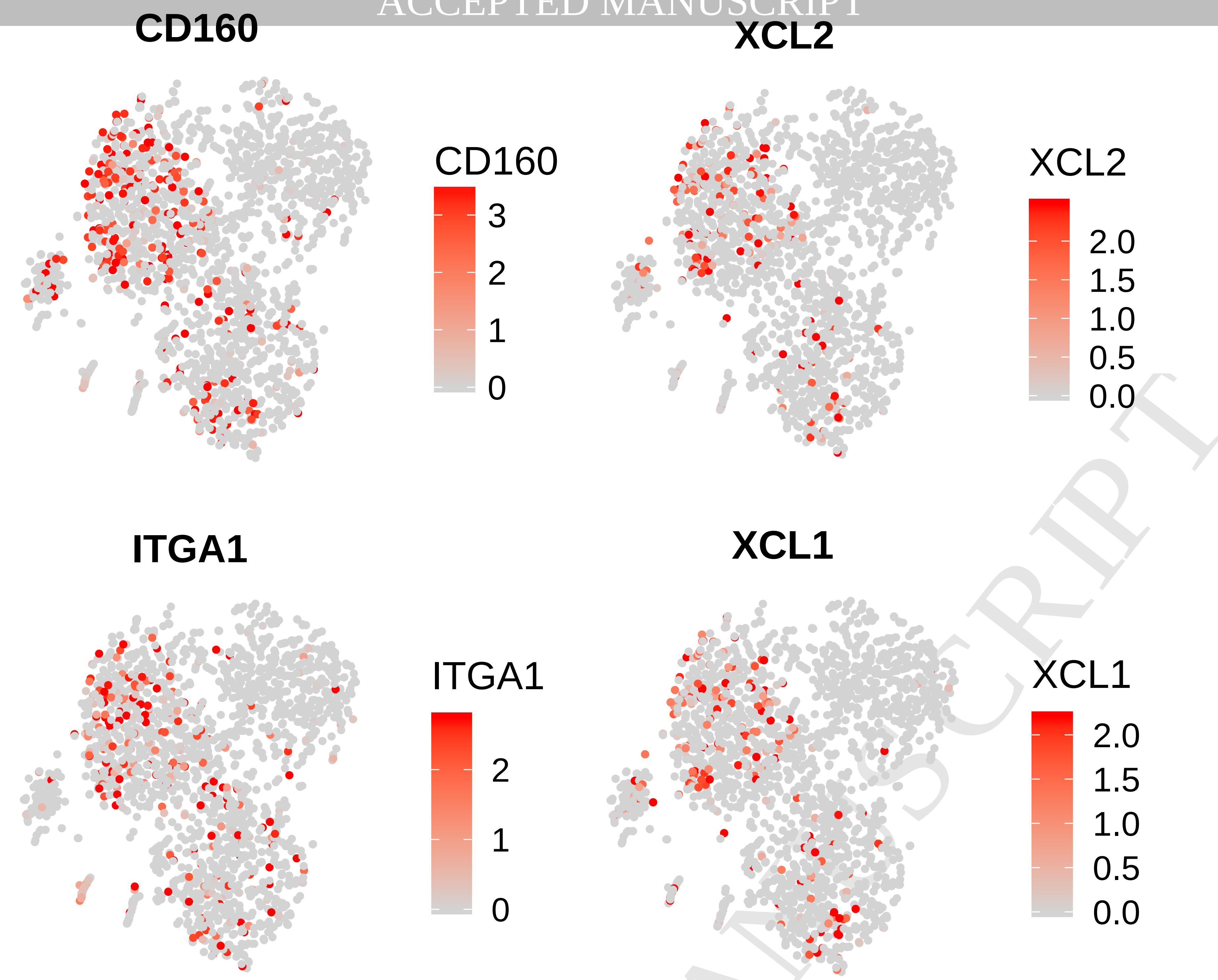
1A: T-cell subtypes in blood and mucosa



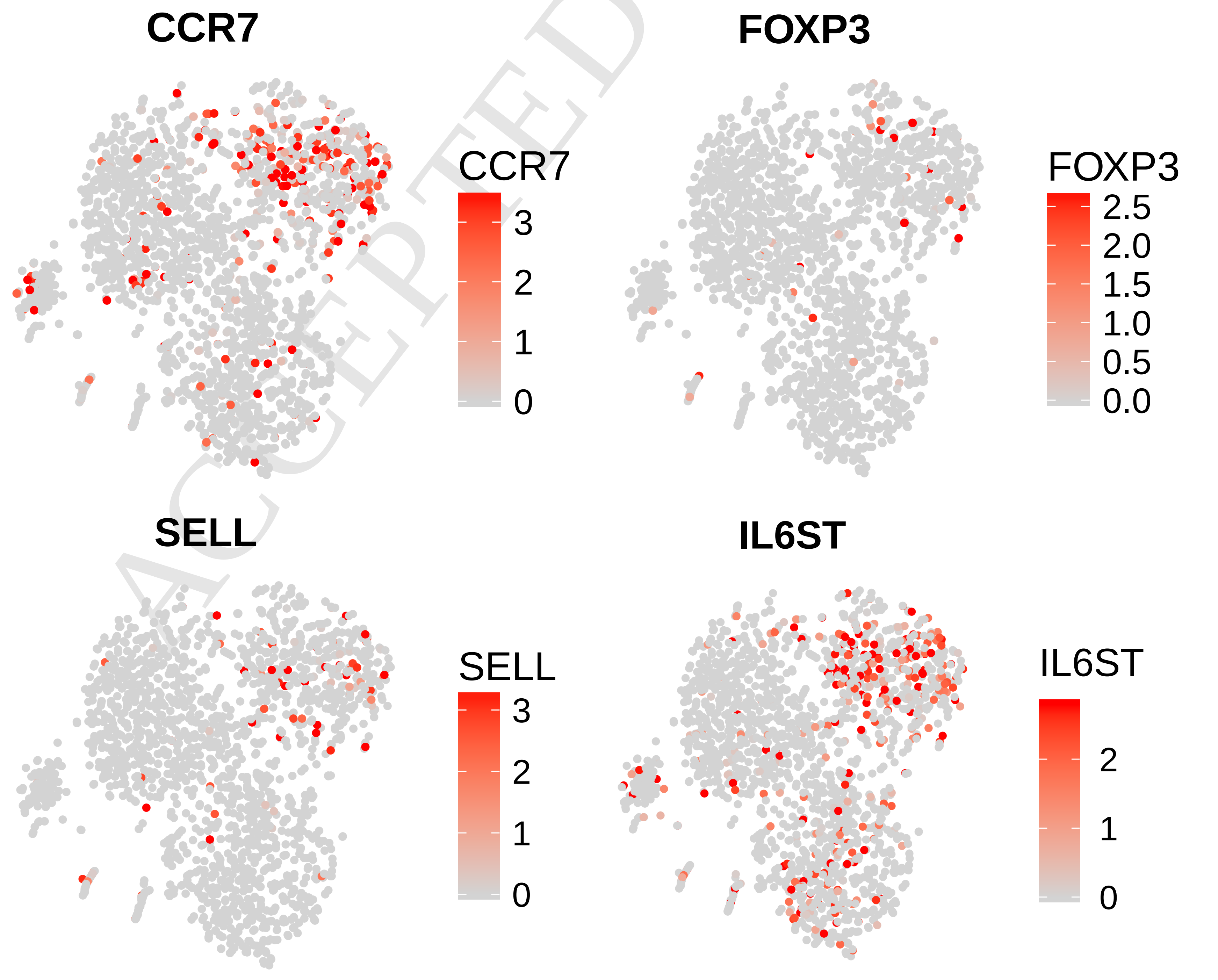
1B: T-cell subtypes in IEL and LPL mucosa



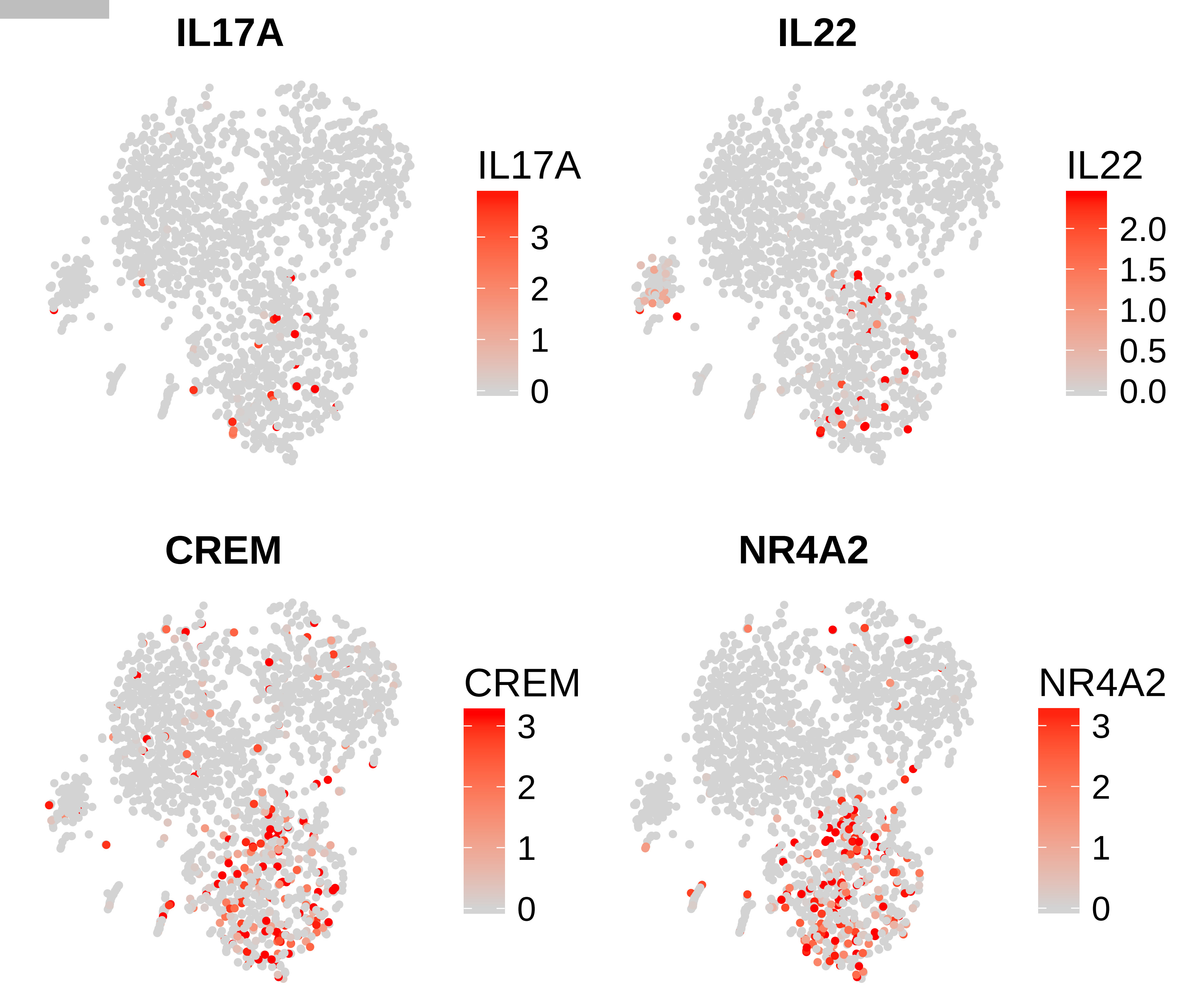
1C: Surface-marker expression in mucosa



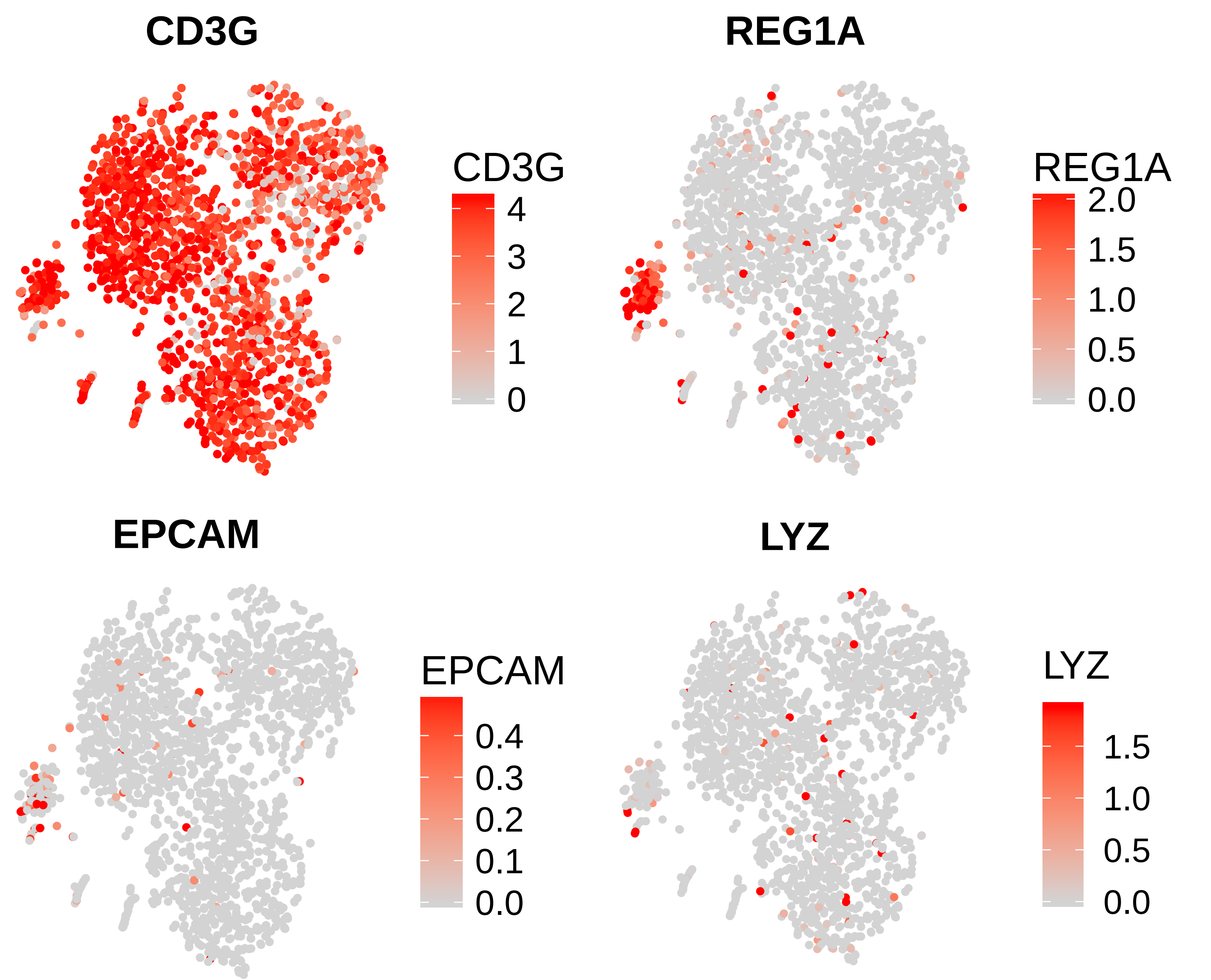
1D: Marker-gene expression in mucosal CTL



1E: Marker-gene expression in mucosal Treg/Quiescent T cells



1F: Marker-gene expression in mucosal Th17 cells



1G: REG1A/REG1B-cell gene expression, no Paneth cell marker-gene expression