

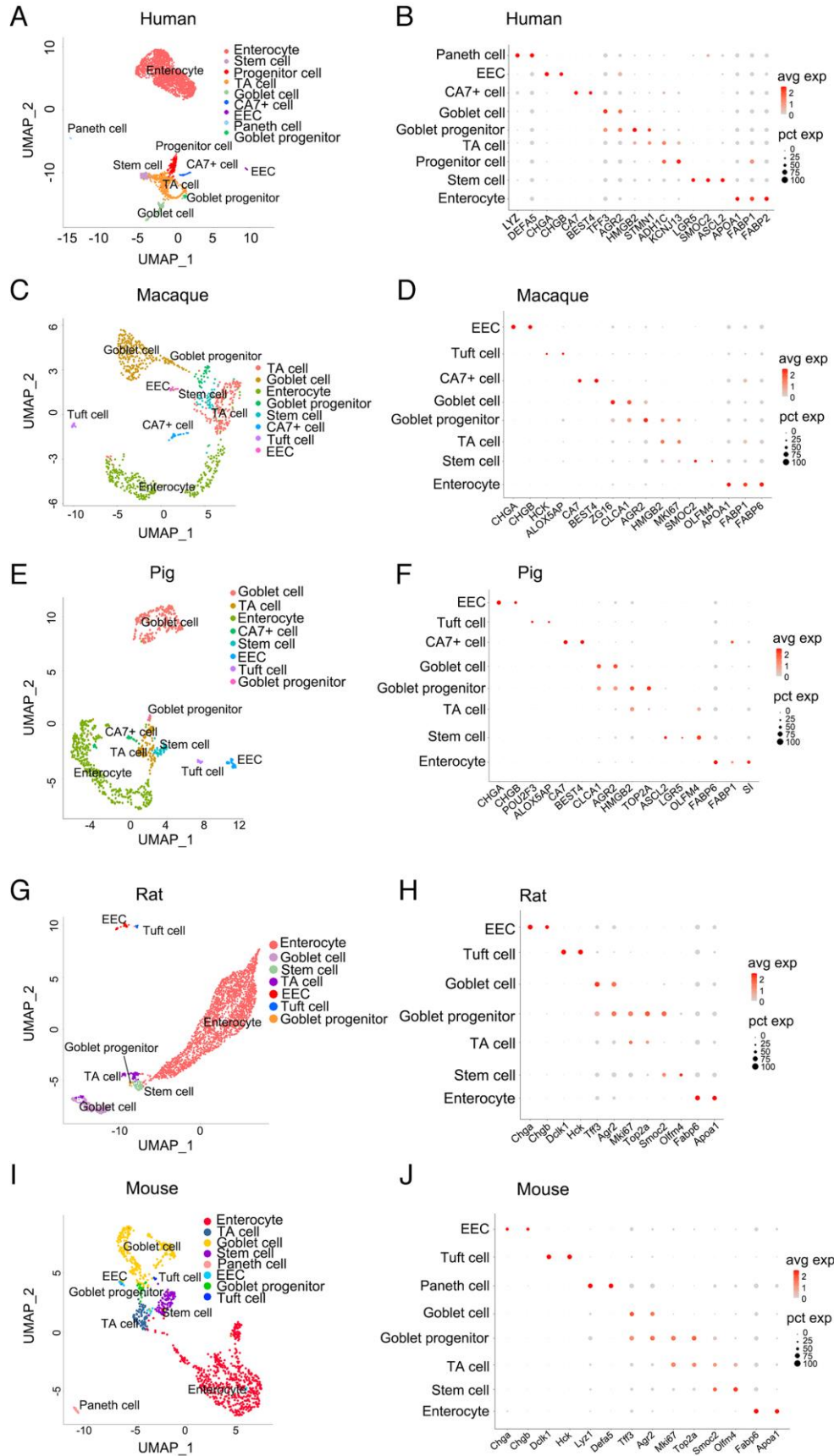
Supplementary Materials

Cross-species single-cell transcriptomic analysis reveals divergence of cell composition and functions in mammalian ileum epithelium

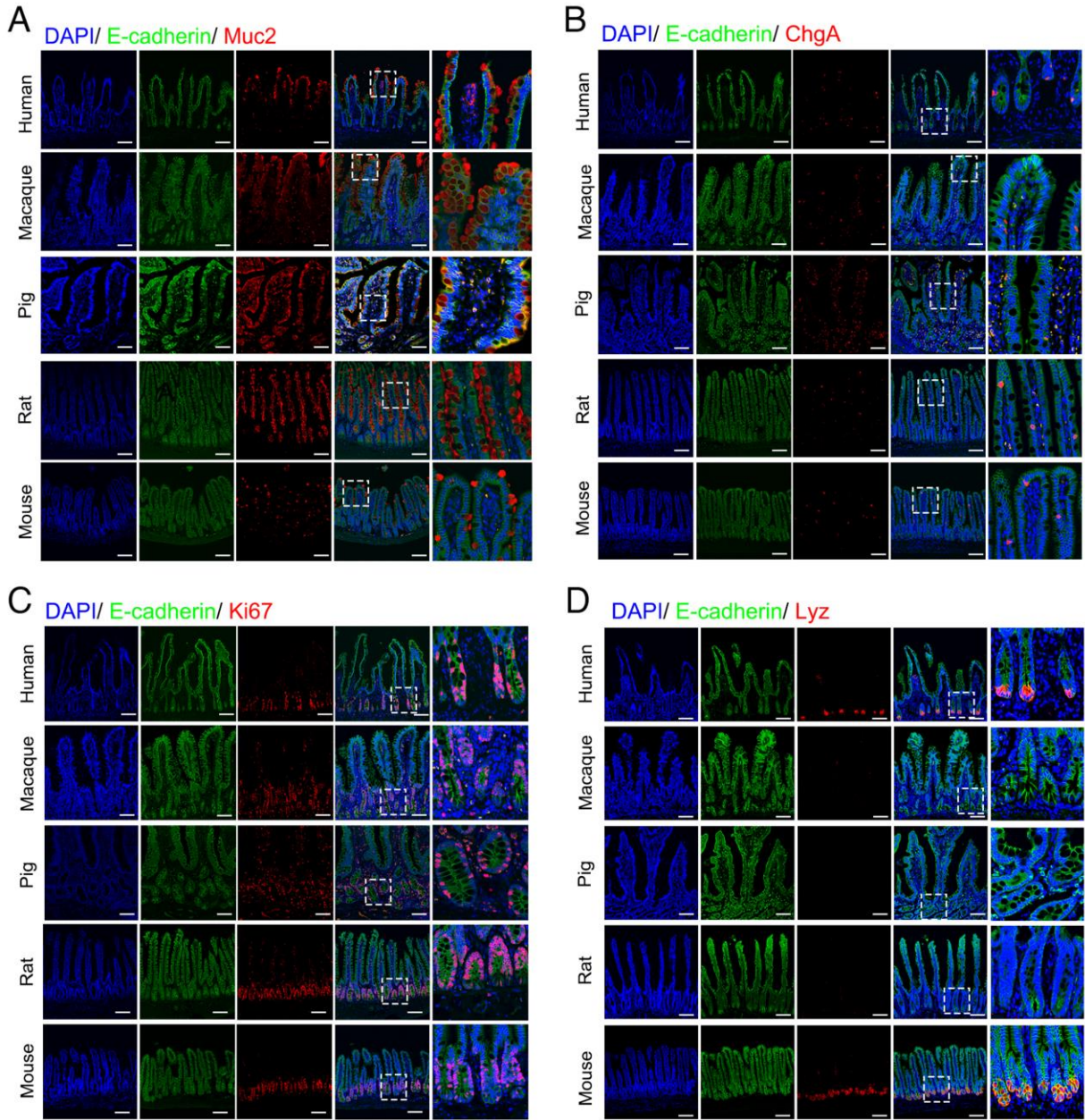
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Supplemental Figure S1-3

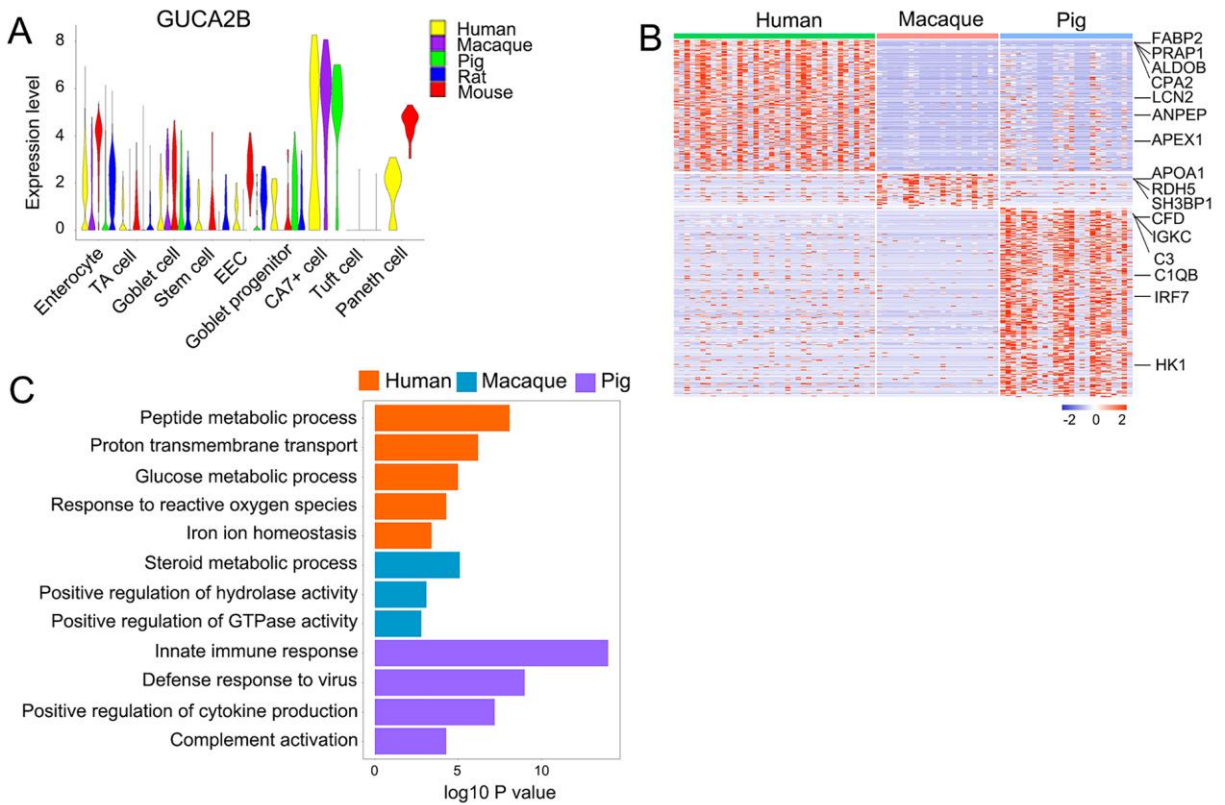
Supplemental Table S1-10



Figures S1 Cell landscapes of ileum epithelial cells in each species based on single-cell RNA-seq data. A, C, E, G, I, UMAP plots showing different cell types from ileum epithelial cells in human (A), macaque (C), pig (E), rat (G) and mouse (I). B, D, F, H, J, Dot Plot showing cell type-specific genes in human (B), macaque (D), pig (F), rat (H) and mouse (J) ileum. Each dot represents a gene. The color indicates the average gene expression and the size shows the percentage of cells expressing this gene.



Figures S2 Cell type identification by marker gene expression across species. A-D Muc2 staining (A), ChgA staining (B), Ki67 staining (C), Lyz staining (D) in ileum sections from mouse, rat, pig, macaque and human to show goblet cells, enteroendocrine cells, TA cells and Paneth cells, respectively. Scale bars, 100 μ m.



Figures S3 Differential expression patterns and functions in CA7⁺ cells across species. A, Violin plots showing expression distributions of *GUCA2B* across species. **B, C,** Expression heatmap (**B**) and functional enrichments (**C**) of signature genes in CA7⁺ cells of human, macaque and pig ileum. A subset of differentially expressed genes was shown in the heatmap.

Table S1 shows an overview of the scRNA-seq database and cell type distribution from each species.

Table S2 shows genes in different cell types of macaque, pig, rat and mouse ileum in Fig. S1.

Table S3 shows conserved and distinct gene modules across five species in Fig. 2E.

Table S4 shows differentially expressed genes in EECs between human and other species in Fig. 3A.

Table S5 shows differentially expressed genes in murine and human Paneth cells in Fig. 3C.

Table S6 shows differentially expressed genes in CA7⁺ cells in human, macaque and pig in Fig. S3B.

Table S7 shows conserved and differentially expressed genes in enterocytes across five species in Fig. 6A.

Table S8 shows correlation score in drug metabolism and transport between human and other species in Fig. 6B.

Table S9 shows orthologous gene lists in mouse, rat, pig, macaque and human .

Table S10 shows quantitative PCR primers.