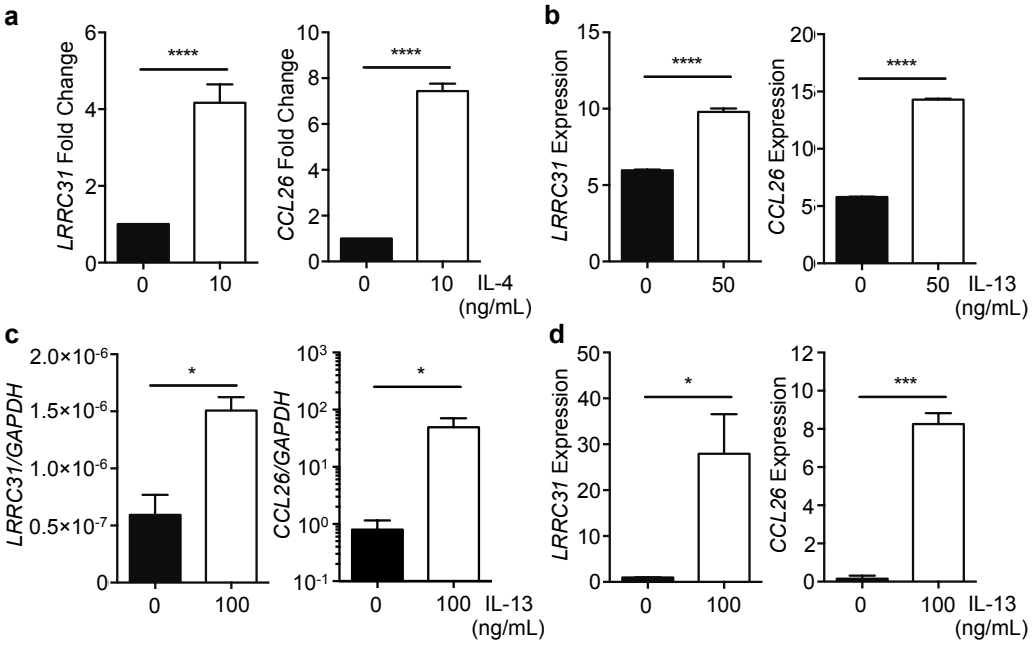
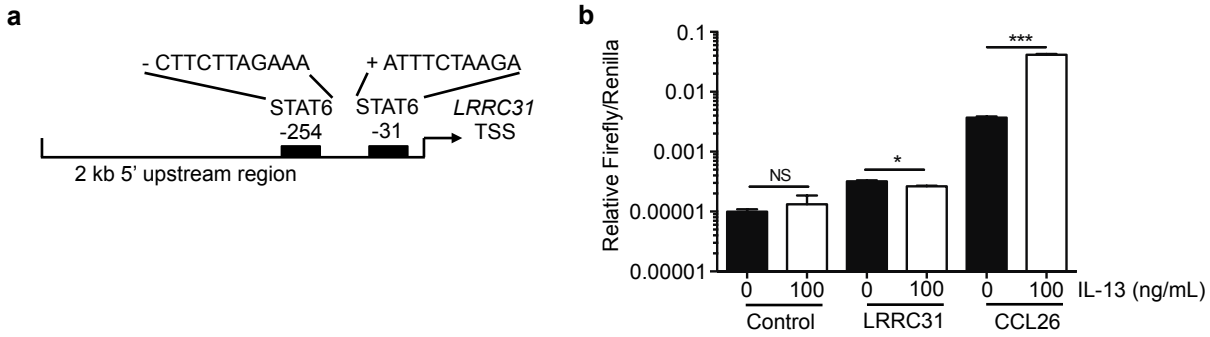
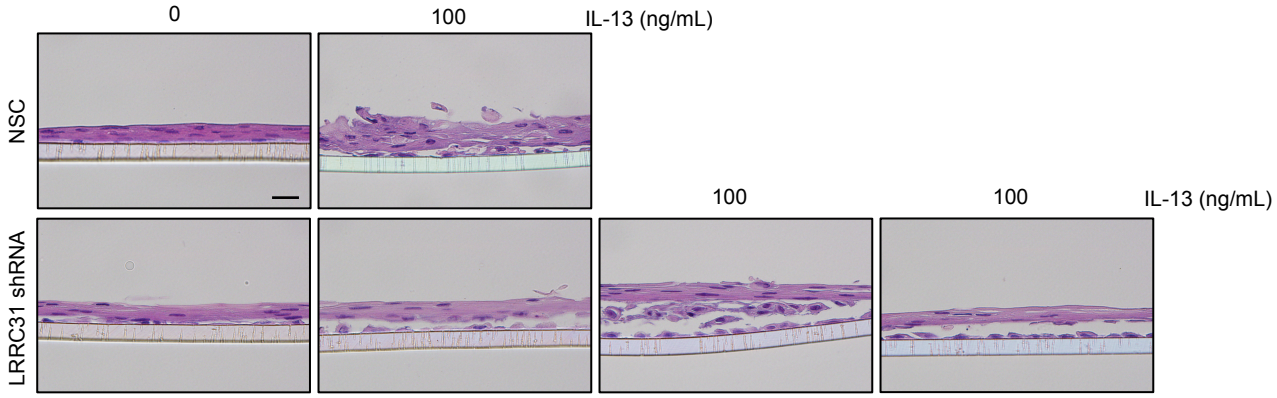


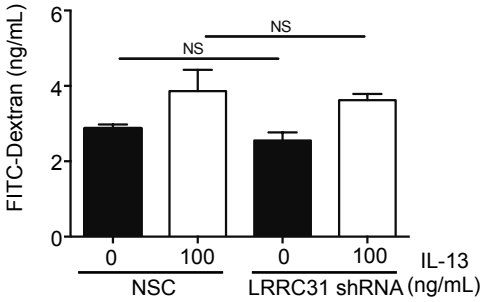
Supplemental Figure 1 | *LRRC31* expression in esophageal epithelial cells. a, Fold change in normalized *LRRC31* and *CCL26* mRNA expression in bronchial epithelial cells treated with IL-4 (10 ng/mL) for 18 hours determined by microarray gene expression analysis.[17] **b**, Normalized *LRRC31* and *CCL26* mRNA expression in tracheal epithelial cells treated with IL-13 (50 ng/mL) for 23 days determined by microarray gene expression analysis.[18] **c**, Normalized *LRRC31* and *CCL26* mRNA expression in Caco2-bbe colonic epithelial cells treated with IL-13 (100 ng/mL) for 48 hours determined by microarray gene expression analysis. **d**, Normalized *LRRC31* and *CCL26* mRNA expression in esophageal epithelial cells treated with IL-13 (100 ng/mL) for 48 hours determined by microarray gene expression analysis. For **a**-**d**, data are represented as the mean ± SEM; **P* < 0.05, ****P* < 0.001, *****P* < 0.0001.



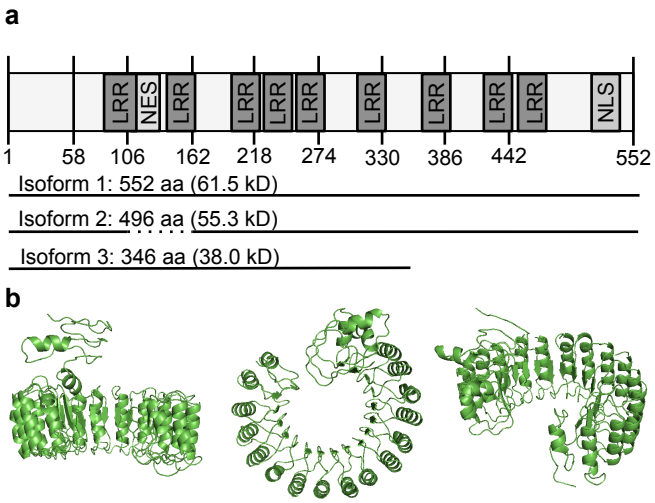
Supplemental Figure 2 | IL-13–STAT6 effect on *LRRC31* gene promoter activity. **a**, Identification of putative STAT6 binding sites within the 2 kb 5' upstream region of the *LRRC31* transcription start site (TSS) from publicly available ChIP-Seq data.[19] **b**, Normalized luciferase activity in empty vector control, *LRRC31* gene promoter (*LRRC31*), and *CCL26* gene promoter (*CCL26*) transfected TE-7 esophageal epithelial cells treated with IL-13 (100 ng/ml) for 48 hours. A representative experiment is shown (n = 3). For **b**, data are represented as the mean ± SEM; NS, not significant; **P* < 0.05, ****P* < 0.001.



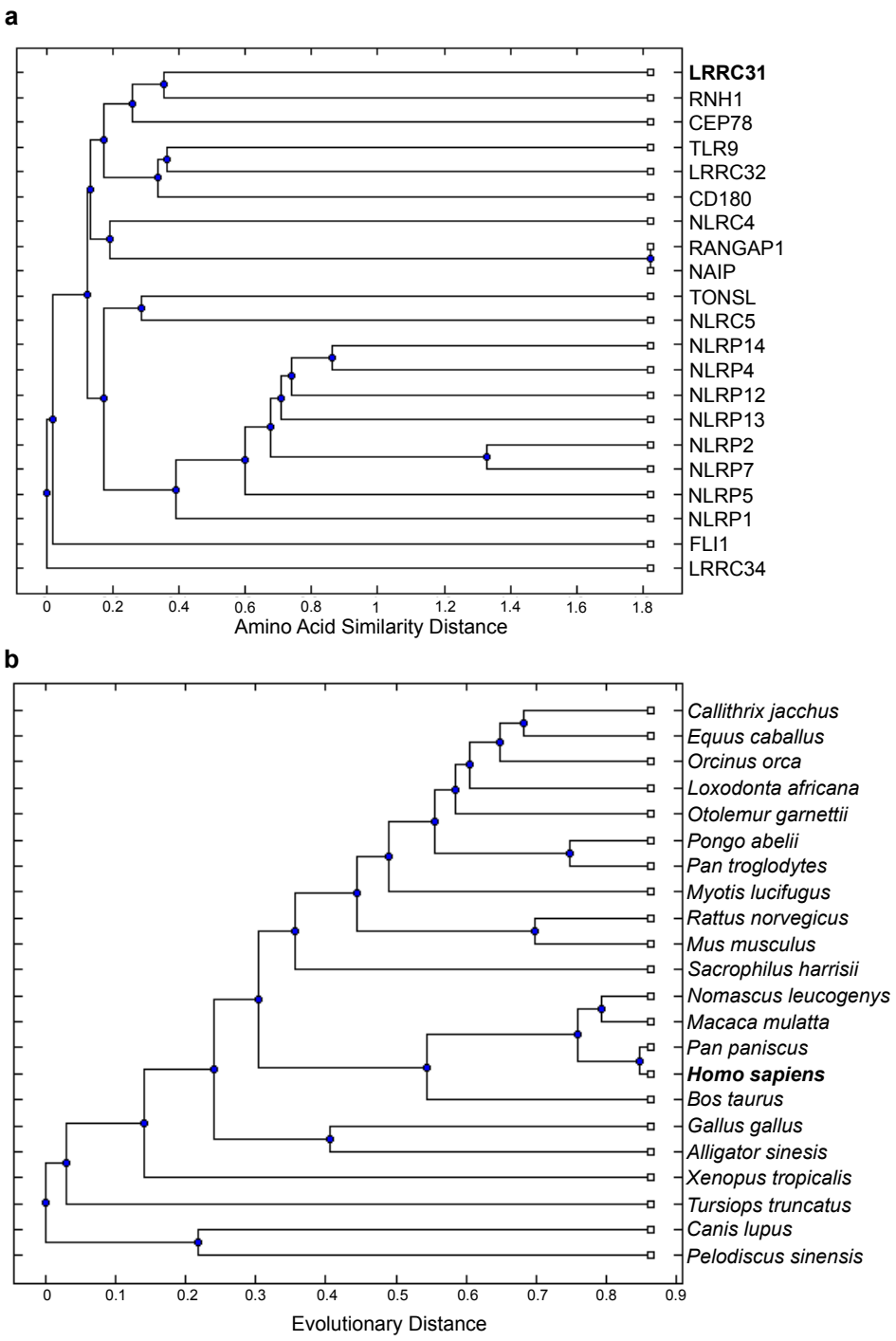
Supplementary Figure 3 | *LRRC31* gene-silenced EPC2s. Additional images of H&E-stained sections from differentiated NSC and LRRC31 shRNA EPC2s at day 14.



Supplemental Figure 4 | Paracellular flux measurements in *LRRC31* gene silenced, differentiated EPC2 cells. FITC-dextran (3-5 kD) paracellular flux measured at 3 hours after FITC-dextran was added to luminal surface of differentiated NSC and LRR31 shRNA EPC2s at day 14. A representative experiment is shown (n = 3). Data are represented as the mean ± SEM; NS, not significant.



Supplementary Figure 5 | LRRC31 structure. a, Representation of LRRC31 protein amino acid primary sequence with 9 exons indicated and putative domains (LRR, leucine-rich repeat; NES, nuclear export signal; NLS, nuclear localization signal).[25,26] **b**, Images representing predicted tertiary structure of LRRC31 generated using I-TASSER Online Protein Structure and Function Predictions.[27]



Supplementary Figure 6 | LRRC31 homology and phylogeny. a, Analysis of LRRC31 amino acid similarity to pBLAST-predicted homologous human proteins using Jukes Cantor modeling.[28] **b**, Analysis of LRRC31 amino acid similarity to eggNOG-predicted orthologous proteins using Jukes Cantor modeling.[33]

Supplementary Table 1

Gene	Amplicon	Forward Primer	Reverse Primer
GAPDH	351 bp	TGGAAATCCCATCACCATCT	GTCTTCTGGGTGGCAGTGAT
CCL26	151 bp	AACTCCGAAACAATTGTACTCAGCTG	GTAACTCTGGGAGGAAACACCCTCTCC
LRRC31	131 bp	CAAAAGAGTGTCAAAATATTGGATG	TGCTTTAGCATGACCAACTGA
KRT10	126 bp	AGCATGGCAACTCACATCAG	TGTCGATCTGAAGCAGGATG
KLK1	89 bp	GTGCTCACAGCTGCTCATTG	AACTGGGCTGTGTTTTCGTC
KLK5	155 bp	AGTCAGAAAAGGTGCGAGGA	TAATCTCCCCAGGACACGAG
KLK7	122 bp	CGTCCTGGTCAATGAGCG	ACTTCGAGGCCTTGATCCTC
KLK11	101 bp	CACCAGCTGCCTCATTTCC	TCTGGTGCTCAATGATGGTG
KLK13	82 bp	CCTAGTGATCGCCTCCCTG	GGTCCCATTGGTGTTGAGAA