Supplementary data

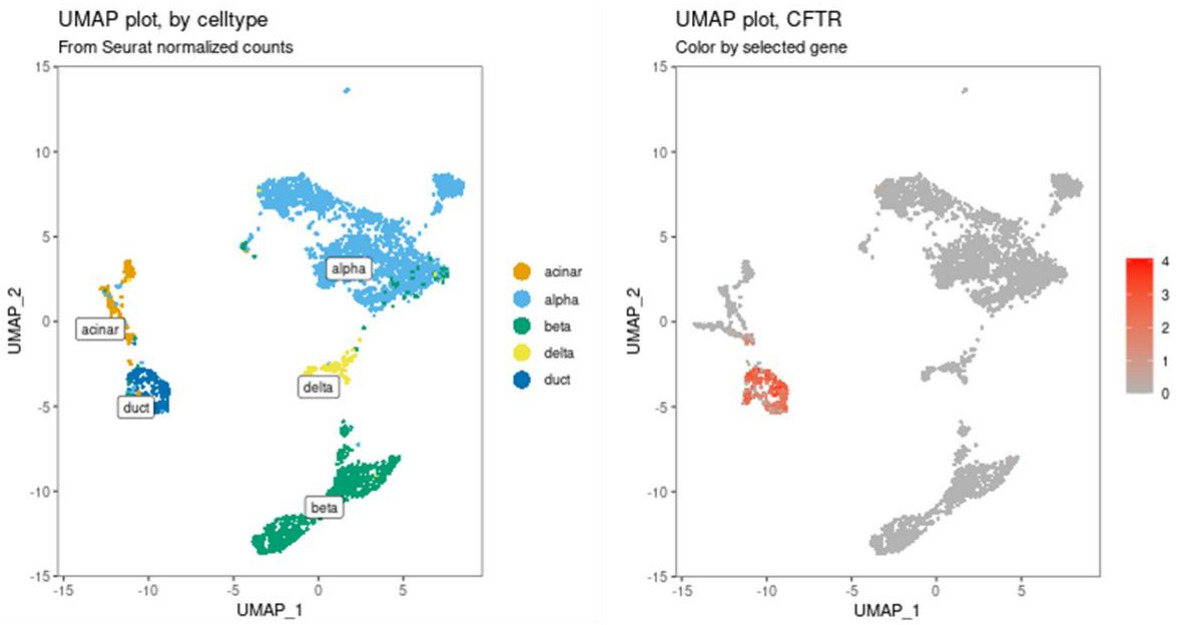

Figure S1. Single-cells CFTR expression.

Single-cell RNA-seq data from the PancrESS dataset [40]. Uniform Manifold Approximation and Projection (UMAP) of transcript abundances. On the left: cells are color-coded by cell type, demonstrating clustering by cell type. On the right: cells expressing the gene of interest, CFTR, are highlighted in red, with the color intensity representing transcript abundance levels.

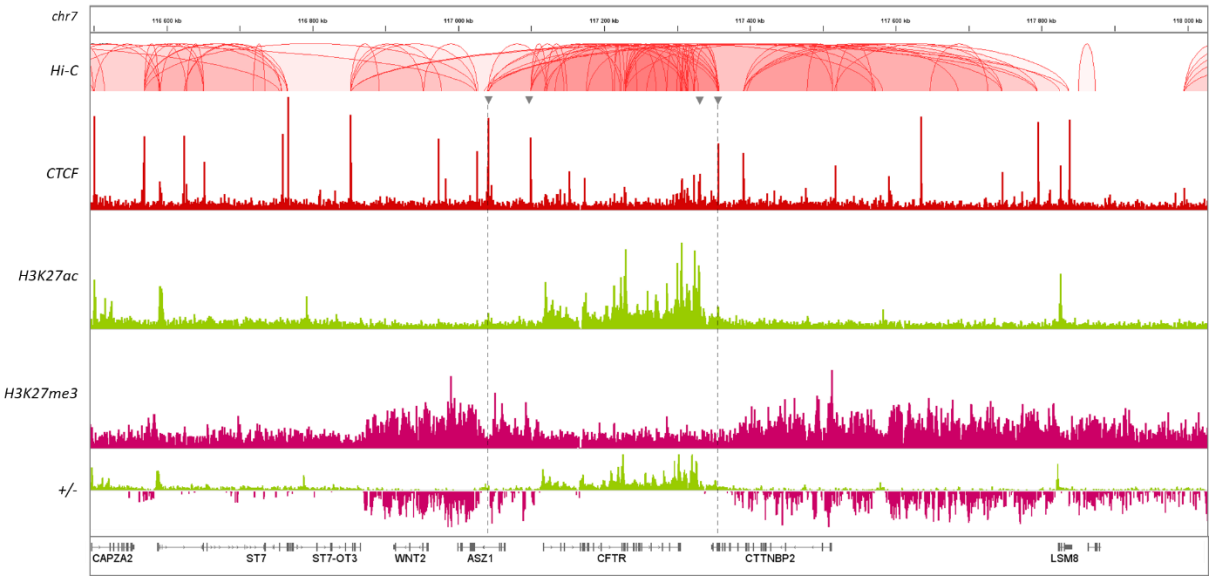

Figure S2. Chromatin data from Caco-2 cells.

Hi-C data provide information of genome-wide chromatin interaction. CTCF immunoprecipitation allows to map CTCF binding. H3K27ac and H3K27me3 provide information of the chromatin state, acetylation is for active chromatin and trimethylation is for repress chromatin. TAD boundaries and enhancer blocking sites are indicated by grey arrow. We noticed the correlation of chromatin state and epigenetic marks.

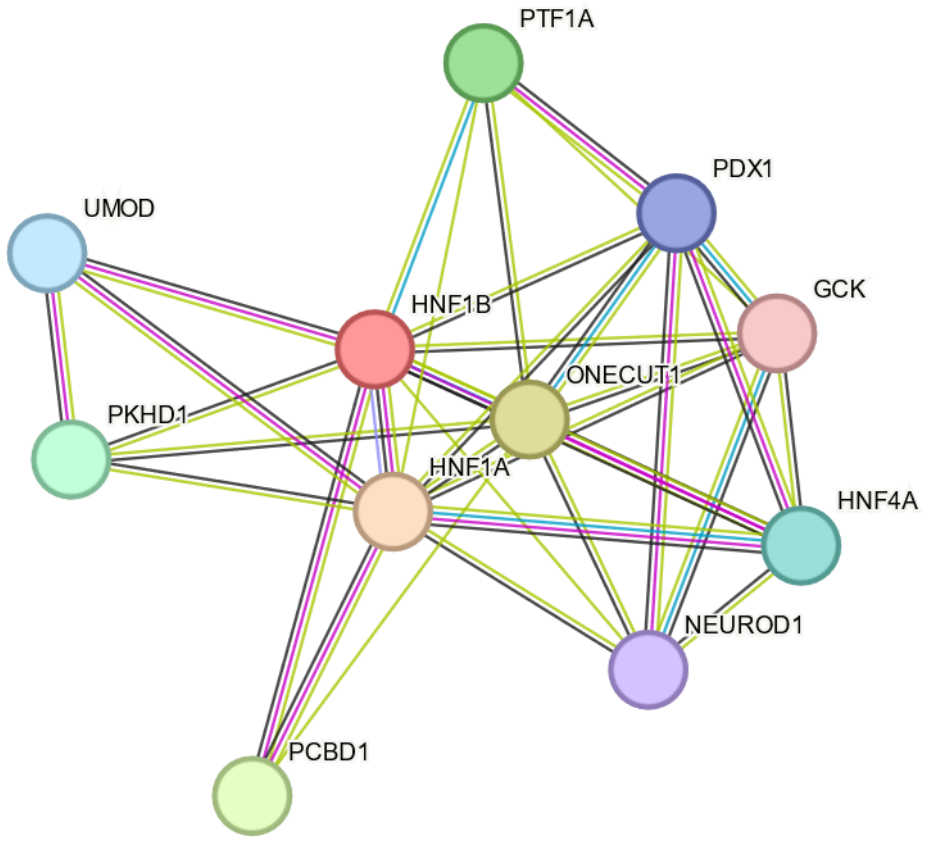

Figure S3. Transcription Factor Interaction Network.
The STRING database provides an interaction network with HNF1b as the bait. The edges represent protein-protein associations.

Table S1. PeakC analysis of 4C data from Capan-1 cells with the CFTR promoter as bait (chr7:117,039,879-117,356,81, hg19)

	CRE	Genomic coordinates (hg19)
1	-80.1 kb	chr7:117042598-117048074
2	-	chr7:117057283-117064712
3	Promoter	chr7:117113481-117125179
4	+15.6 kb	chr7:117310255-117329893

Table S2. 4C-seq primers

Primers Name	Primers Sequence
4C_pCFTR_reading	TACACGACGCTCTTCCGATCTGTCTTTCCATCATGAAATGCAC
4C_pCFTR_nonreading	ACTGGAGTTCAGACGTGTGCTCTTCCGATCTGAATTAAGCTCCAAAGAGGATC

Table S3. Primers for plasmid constructs

CRE	Forward/reverse	Primers sequence
-44 KB	F	AAATCGATAAGGATCCGGTCATAGATGTGGAACATTCTG
	R	GATCAGATGTGGGATCCCCGCAAAATCTGCCATCATC
-35 KB	F	AAATCGATAAGGATCCCTCATGTAGCAGGCATTTGTG
	R	ATCGGTCGACGGATCCGTGTTTCCAATTTCTACCCAGAC
+15,6 KB	F	AAATCGATAAGGATCCCAGTGCCTGGCCAAGAATC
	F	ATCGGTCGACGGATCCGAGGTATCAGAAATCAGTGTGAG
+37,7 KB	R	AAATCGATAAGGATCCTACCACGTAAGTGAGATTATGTGG
	F	ATCGGTCGACGGATCCGAGTGGCTTCAAACCTTACTTATTC
-44 KB / -35 KB	R	CTAGCCCGGGCTCGAGGGTCATAGATGTGGAACATTCTG
	F	CAAATGCCTGCTACATGAGCCGCAAAATCTGCCATCATC
	F	GATGATGGCAGATTTTGCGGCTCATGTAGCAGGCATTTG
	R	GATCGCAGATCTCGAGCCAGAAGTTCACAAGACTG
+15,6 KB / +37,7 KB	F	AAATCGATAAGGATCCCAGTGCCTGGCCAAGAATC
	R	CATAATCTCACTTACGTGGTAGGAGGTATCAGAAATCAGTGTG
	F	CACACTGATTTCTGATACCTCCTACCACGTAAGTGAGATTATG
	R	AAATCGATAAGGATCCTACCACGTAAGTGAGATTATGTGG
-3,4 KB	F	AAATCGATAAGGATCCCTTTAGCACCCAAGCTCTTG
	R	ATCGGTCGACGGATCCCCTTATGGTTGTTGGTCACTTAC
Intron 11	F	AAATCGATAAGGATCCCTTAGTTCTCATGCTTTCTAGTGG
	R	ATCGGTCGACGGATCCGCAGTGGAGGATGGTTTGAAAG
Intron 12	F	AAATCGATAAGGATCCTGGAGAAGGTGGAATCACACTG
	R	ATCGGTCGACGGATCCGAAGACAGTATGCAAGAGCTACAT
Intron 18	F	AAATCGATAAGGATCCCTCCCCATTTCCCTCTCTCC
	R	ATCGGTCGACGGATCCGCTGGGCATTCGTCTTGGAG
Intron 24	F	AAATCGATAAGGATCCGCATTTCTCACTCTGGCTGG
	R	ATCGGTCGACGGATCCCCTGTCCAAACTAAGAAGACTTC
Intron 12-24	F	AAATCGATAAGGATCCTGGAGAAGGTGGAATCACACTG
	R	TACTGTCTTCGGATCCTCGACGCATTTCTCACTCTGGCTGG
	F	AAGGGCATCGTCGACCCTGTCCAAACTAAGAAGACTTC
	R	ATCGGTCGACGGATCCCCTGTCCAAACTAAGAAGACTTC
Intron 26	F	AAATCGATAAGGATCCATCTGAGCCATGTGGTGAGGTTGA
	R	ATCGGTCGACGGATCCTTCCTTTGAGCCTGTGCCAGTTTC
+484,2 KB	F	AAATCGATAAGGATCCGTACGAAGTATCAACTAGGAGAGC
	R	ATCGGTCGACGGATCCTCTTAGATAATTTAAAAAGCC
+507,6 KB	F	AAATCGATAAGGATCCGTGCCACAGAAAAAGATGGCC
	R	ATCGGTCGACGGATCCGAATAATGTAAGAAGGTATATAG
+513,7 KB	F	AAATCGATAAGGATCCGAGCATTACTTTGAGAGGTTTCGAC
	R	ATCGGTCGACGGATCCGTGTCTTCCGCTAATGAAAGAAC

Table S4. gRNA and PCR primers for CRISPR/cas9 deletion of -44 kb region

gRNA name	**gRNA sequence**
sgRNA-CRE1_F	CAGAGAGGCCTGGGCTATCC
sgRNA-CRE1_R	GATATCAGACAACAAGTCTA
PCR primers name	**Primers sequence**
Cis_CFTR_-44kb_Ext_F	GGAAACAGGTAAGTTTTGTTCTG
Cis_CFTR_-44kb_Ext_R	GCTTTGTTCTCTGACCTAACC
qPCR primers name	**Primers sequence**
CFTR_qPCR_F	ATGCCCTTCGGCGATGTTTT
CFTR_qPCR_R	TGATTCTTCCCAGTAAGAGAGGC
Actin_qPCR_F	CTGGAACGGTGAAGGTGACA
Actin_qPCR_R	AAGGGACTTCCTGTAACAATGCA