

Description of Additional Supplementary Files

Supplementary Data 1: scRNA-seq Pathway Analysis of CF Airway Epithelial Cells from Human Lung Tissue. Publicly available scRNA-Seq datasets from human lung tissue were analyzed to identify differentially expressed genes using predefined statistical significance ($P < 0.05$) and fold-change thresholds. P values were adjusted for multiple comparisons using false discovery rate (FDR) correction. Genes meeting these criteria were subjected to pathway enrichment analysis using DAVID with KEGG pathway annotations, focusing on routes involved in pyrimidine metabolism, cell proliferation, fibrosis and mitochondrial function. Statistical significance of pathway enrichment was assessed using DAVID's modified Fisher's exact test (EASE score), with P values adjusted for multiple comparisons using the Benjamini–Hochberg false discovery rate (FDR) procedure.

Supplementary Data 2: Bulk-RNA-seq Pathway enrichment analysis of CF epithelial cell lines. Publicly available bulk RNA-seq datasets obtained from primary cells and cell lines grown *ex vivo* were analyzed to identify differentially expressed genes using predefined statistical significance ($P < 0.05$) and fold-change thresholds. P values were adjusted for multiple hypothesis testing using false discovery rate (FDR) correction. Pathway enrichment analysis was performed using DAVID with KEGG pathway annotations, putting special emphasis on those related to pyrimidine metabolism, cell proliferation, fibrotic signaling and mitochondrial function. Statistical significance of pathway enrichment was assessed using DAVID's modified Fisher's exact test (EASE score), with P values adjusted for multiple comparisons using the Benjamini–Hochberg false discovery rate (FDR) procedure.

Supplementary Data 3: NCBI entry numbers of *P. aeruginosa* genomes used for genetic analyses on pyrimidine metabolism.

Supplementary Data 4: Primers used in the study.