SUPPORTING ONLINE MATERIAL

Analysis of changes in gene expression.

To identify changes in gene expression within each tissue, a multi-pronged approach was undertaken using the following analytical tools: Analysis of Variance (ANOVA), Database for Annotation, Visualization and Integrated Discovery (DAVID) (S*1*), Ingenuity Pathway Analysis (IPA) (S*2*), and Gene Set Enrichment Analysis (GSEA) (S*3*). The purpose of this approach was to identify differentially expressed genes associated with the loss of CFTR.

ANOVA.

To generate a list of differentially expressed genes, 'variance' of each gene was calculated across the two genotypes and ranked using *P*-value (uncorrected) and False Discovery Rate (FDR, q-value, normalized for multiple comparisons). This was done using commercially available software: Partek Genomics Suite (S*4*). Furthermore, successive filters were implemented to make the analysis more rigorous and to generate a list of differentially expressed genes with a high confidence of validation. Table S3 highlights the number of differentially expressed genes in each tissue, after the implementation of each filter, taking the analysis from baseline (*P*-value <0.05) to the most rigorous (q-value <0.1). The fold change is calculated as a ratio of *CFTR*-/- to *CFTR*+/+, thus a positive fold change indicates an increase in expression of the gene in *CFTR*-/- samples in comparison with *CFTR*+/+ samples, and vice versa. A gene list with a fold change cut-off >1.5 fold was generated by listing all genes that had a fold change value >+1.5 and <-1.5. The same applied to the gene list with a fold change cut-off >2 fold. The Affymetrix GeneChip is a one-color spotted cDNA microarray system that is based on the immunofluorescent detection of biotinylated nucleic acids. Thus by accounting for the difference in perfect and mismatched

probe intensities, gene expression is calculated as a measure of signal intensity. However, owing to hybridization biases, there is bound to be variation and a certain level of background hybridization (S*5-7*). To correct for this, a minimum signal intensity threshold was set at 100 for each gene in each sample. Thus, only if all samples in a tissue had a signal intensity of 100 or more for a gene, would that gene be considered a candidate.

IPA and DAVID.

To further mine the data for candidate enriched pathways or gene networks, nine gene lists generated with a fold change cutoff of >1.5 fold, >2 fold and signal intensity cutoff were analyzed using IPA and DAVID (indicated in Table S3 with an *). IPA is an extensive, manually curated proprietary database, classifying gene products based on their functional interactions with other gene products. Each network of genes generated by IPA is ranked by *P*-value based on the presence of listed genes within a curated gene network. In all nine analyses, no gene network was generated with a *P*-value <0.05. DAVID classifies genes into functionally-related gene groups based on their biological function, functional domains and motifs, interacting proteins, pathways and signaling cascade interactions. As was done with IPA, gene groups were ranked by *P*-value based on the presence of listed genes within a curated gene group. While genes were segregated into clusters based on functional domains and motifs, no pathway or signaling cascade was identified with a *P*-value <0.05 in any of the nine gene lists.

Gene Set Enrichment Analysis.

GSEA is an analysis program that: a) takes into account changes in expression of every gene in every sample analyzed in the experiment, and b) identifies up or down-regulation of a pathway

or network of genes owing to the cumulative effect of gene expression changes within that network or pathway. Two reference libraries were used to analyze the microarray data. The first was the 'Curated Gene Set' comprised of 1,892 gene sets, compiled from online databases, published literature, and knowledge of domain experts. The second reference library used was the 'Computational Gene Set' comprising 883 gene sets, compiled by mining large collections of cancer-oriented microarray data. Therefore, each of the three tissues was analyzed separately by GSEA against a reference library of 2,775 gene sets. Table S4 highlights the number of differentially expressed gene sets in each of the tissues. The finding that none of these curated gene sets were enriched at a FDR <0.25 lends support to the idea that there were no significant differences in gene expression between the two genotypes.

Differentially expressed genes in trachea, bronchus, and distal lung from wild-type and *CFTR*-/- newborn piglets.

One-way ANOVA was used to identify differentially expressed genes in each tissue compartment. Changes in expression were rated based both on the *P*-value as well as the false discovery rate calculated for each gene. Table S5 provides a list of differentially expressed genes selected based on a *P*-value cut-off <0.05 and a fold change >2 fold with no further correction for multiple comparisons. The fold change is represented as a ratio of *CFTR*-/- to *CFTR*+/+, thus a positive fold change indicates an increase in expression of the gene in *CFTR*-/- samples in comparison with *CFTR*+/+ samples, and vice versa. Overall, the numbers of differentially expressed genes predicted by this approach were small.

Comparison of microarray data for porcine tissue with other array profiles.

We further interrogated the porcine mRNA expression data sets for changes in gene expression that may be relevant to CF pathogenesis. We asked whether any differentially expressed genes in the present study intersected with results from previously published studies of expression profiling in CF. We focused on published studies that used *in vivo* tissues or primary cultures of airway epithelia (S*8-12*). We compared genes that were differentially expressed in *CFTR*-/- trachea, bronchus or distal lung to genes reported as differentially expressed in the published reports. Table S6 presents the differentially expressed genes from previous studies that overlap with our data. Those genes that were found to be significant in their differential expression in the current porcine study are indicated in bold. There were no genes common to these studies that were consistently differentially expressed across the *CFTR*-/- pig samples.

Figure S1

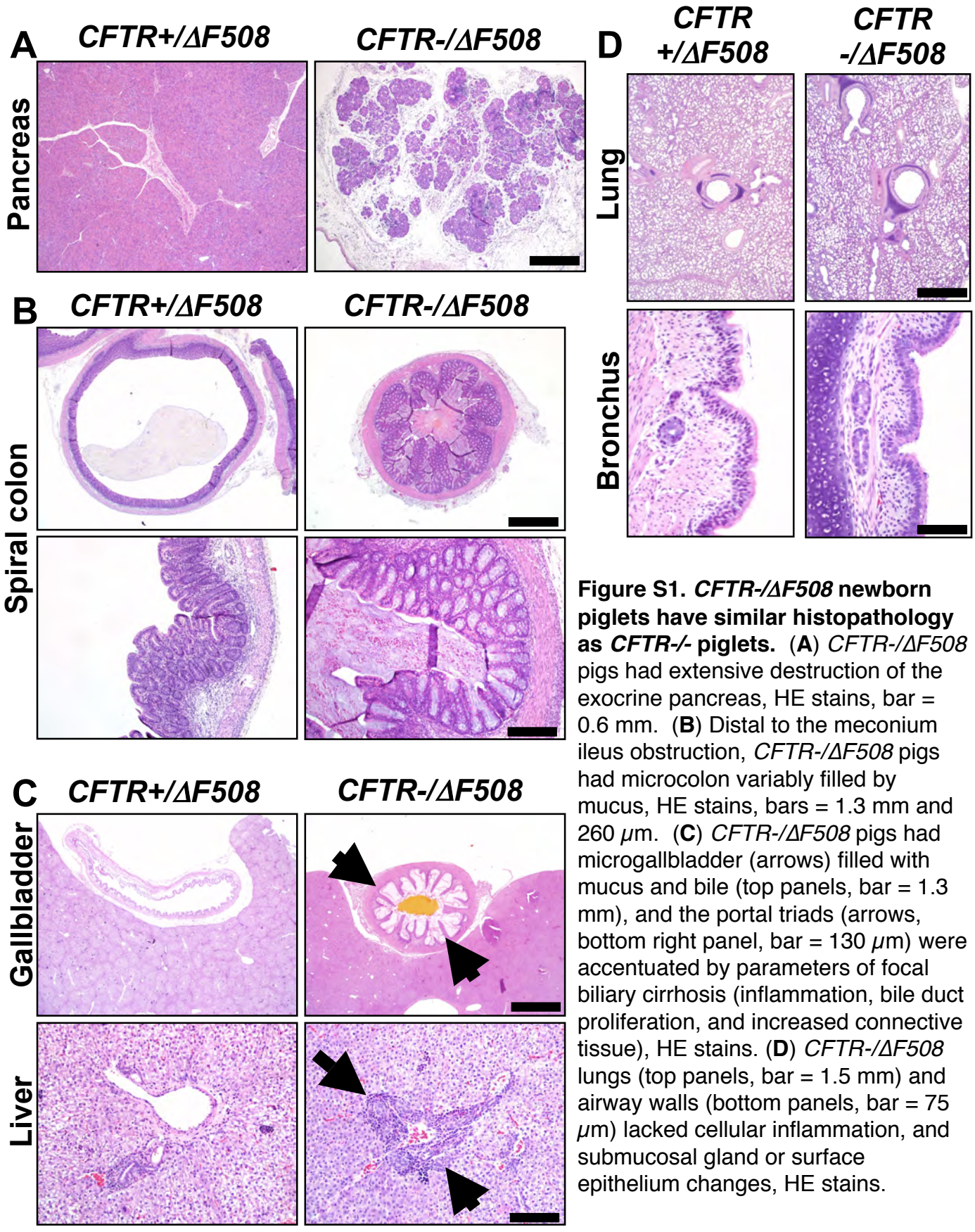


Figure S1. *CFTR-/ΔF508* newborn piglets have similar histopathology as *CFTR-/-* piglets. (**A**) *CFTR-/ΔF508* pigs had extensive destruction of the exocrine pancreas, HE stains, bar = 0.6 mm. (**B**) Distal to the meconium ileus obstruction, *CFTR-/ΔF508* pigs had microcolon variably filled by mucus, HE stains, bars = 1.3 mm and 260 μm. (**C**) *CFTR-/ΔF508* pigs had microgallbladder (arrows) filled with mucus and bile (top panels, bar = 1.3 mm), and the portal triads (arrows, bottom right panel, bar = 130 μm) were accentuated by parameters of focal biliary cirrhosis (inflammation, bile duct proliferation, and increased connective tissue), HE stains. (**D**) *CFTR-/ΔF508* lungs (top panels, bar = 1.5 mm) and airway walls (bottom panels, bar = 75 μm) lacked cellular inflammation, and submucosal gland or surface epithelium changes, HE stains.

Figure S2

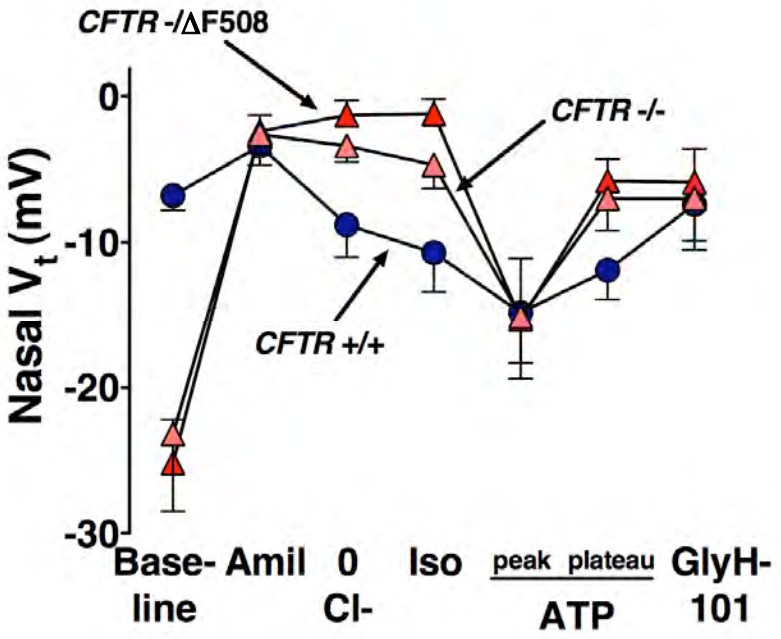


Figure S2. *CFTR-/ΔF508* newborn piglets have similar nasal electrophysiology as *CFTR-/-* piglets. *In vivo* nasal voltage (Vt) measured in newborn piglets. After baseline measurements, the following agents/solutions were sequentially added to the epithelial perfusate: amiloride (100 µM), Cl^--free solution, isoproterenol (10 µM), ATP (100 µM), and GlyH-101 (100 µM). Shown are average nasal Vt measurements as indicated. Data are from 5 *CFTR+/+*, 5 *CFTR-/-*, and 5 *CFTR-/ΔF508* piglets. Data from *CFTR-/-* piglets have been previously reported (S13) and are included for comparison to data from *CFTR−/ΔF508* pigs.

Figure S3

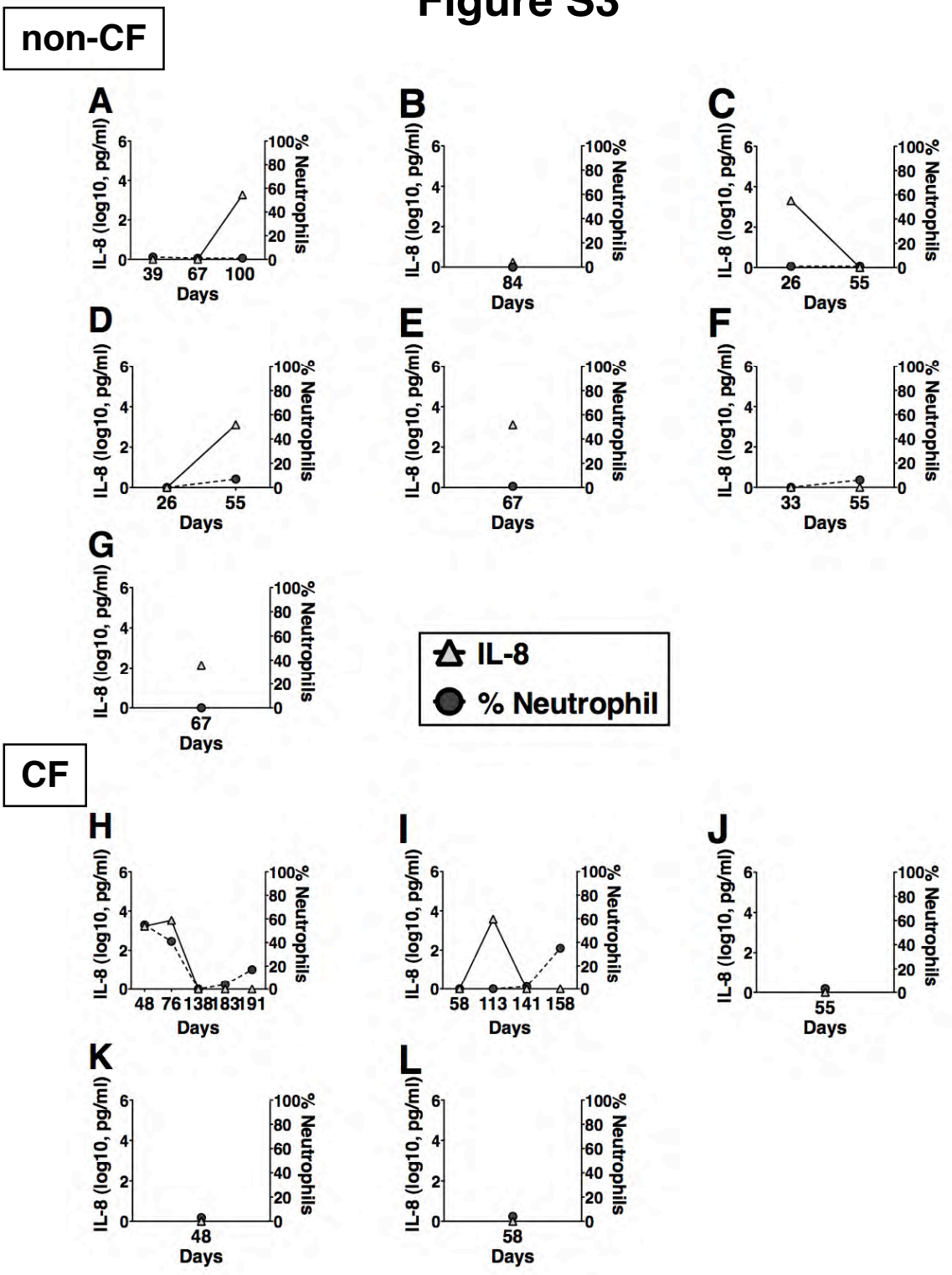


Figure S3. Bronchoalveolar lavage (BAL) neutrophil and IL-8 levels in non-CF and CF animals. BAL was performed at indicated time points and percent neutrophils and IL-8 levels were determined on recovered liquid from non-CF (Panels **A**-**G**) and CF (Panels **H**-**L**) pigs. Data are shown from individual animals. Levels of TNF-α also did not differ by genotype.

Figure S4

	BAL	
	non-CF, n=7	CF, n=5
Alpha hemolytic Streptococcus	3 (42%)	3 (60%)
Bordetella bronchiseptica	0	1 (20%)
Chryseobacterium indologenes	1 (14%)	0
Coagulase-negative Staphylococcus	4 (57%)	2 (40%)
Diphtheroids	0	1 (20%)
Escherichia coli	3 (42%)	2 (40%)
Enterococcus sp.	4 (57%)	3 (60%)
Haemophilus sp.	0	1 (20%)
Klebsiella pneumoniae	2 (28%)	2 (40%)
Moraxella catarrhalis	1 (14%)	1 (20%)
Neisseria sp.	0	1 (20%)
Pasteurella pneumotropica	1 (14%)	1 (20%)
Staphylococcus aureus	2 (28%)	3 (60%)

Figure S4. Microbiology profile of BAL liquid obtained from non-CF and CF animals. BAL was performed and all recovered bacterial species were identified by standard culture methods. Shown are the number of animals from each group with at least one lavage sample positive for the specified bacteria. The percentage of animals with a positive sample is noted in parentheses.

Figure S5

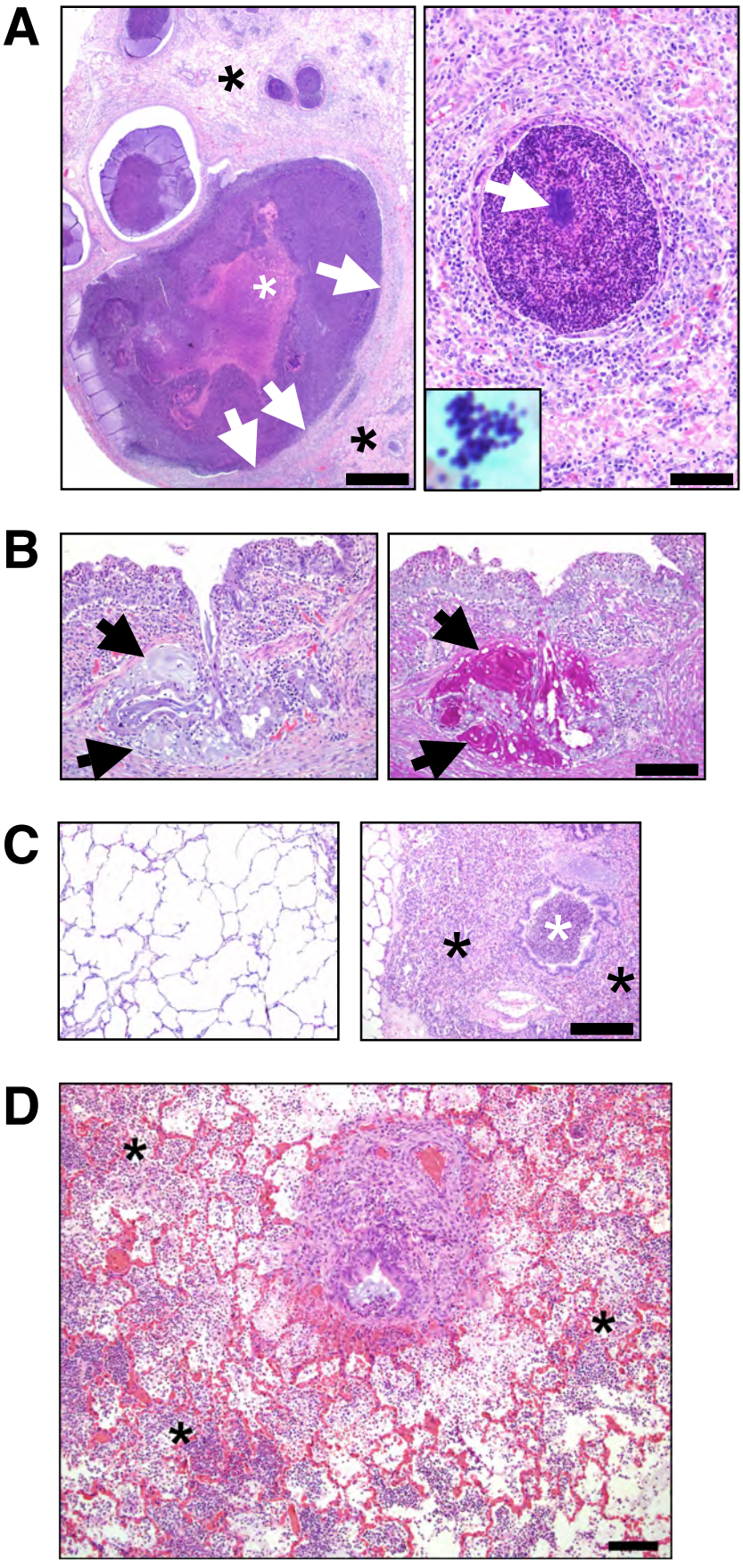


Figure S5. Airway wall ulceration, obstruction, atelectasis, and pneumonia. (**A**) Advanced lesions had ulceration of the airway wall (white arrows, left panel, HE stain, bar = 890 μm) to form parenchymal abscesses (white asterisk) with adjacent lung inflammation (black asterisks). Distended airways (right panel, HE stain, bar = 89 μm) were filled by degenerative neutrophils often surrounding Gram positive cocci (arrow) (inset, Gram stain). (**B**) Submucosal gland inflammation and destruction, Case #1. Severe neutrophilic inflammation of the airway walls sometimes resulted in pools of free mucus (black arrows) adjacent to degenerative submucosal glands, (HE and PAS stain, respectively, bar = 130 μm). (**C**) Airway obstruction, Case #1. Hyperinflation (left panel) and atelectasis (black asterisks, right panel) were often associated with airway obstruction (white asterisk, right panel), HE stains, bar = 300 μm. (**D**) Pneumonia, Case #4. Pneumonia (asterisks) was sometimes characterized by severe congestion, neutrophilic infiltrates, fibrin, and focal necrosis, HE stain, bar = 107 μm.

Figure S6

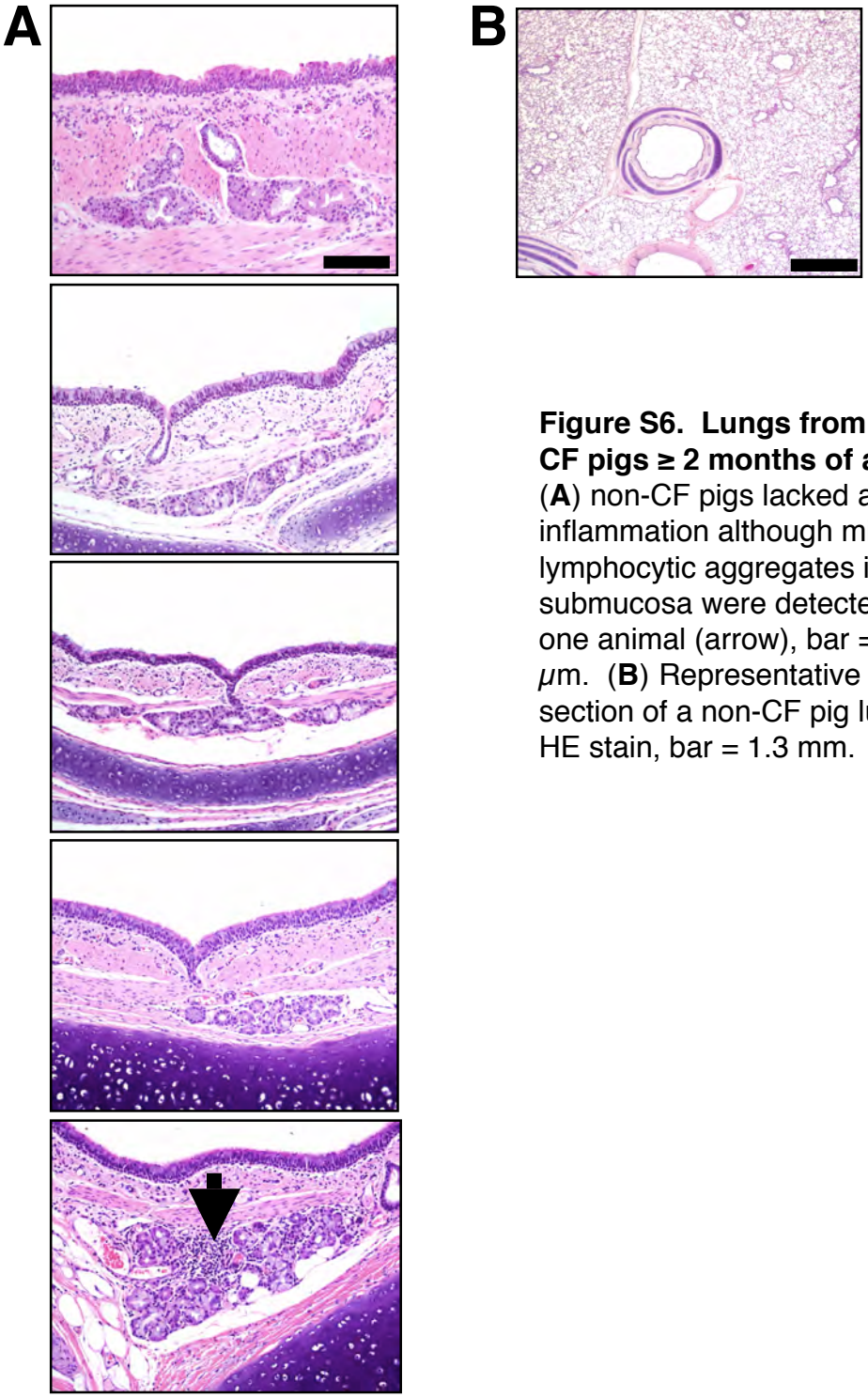
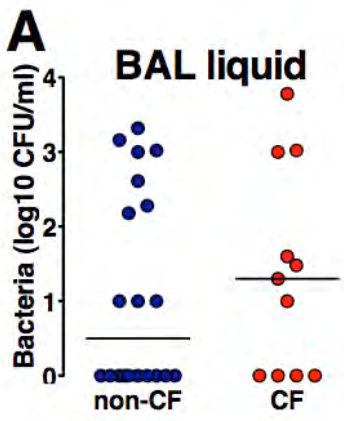


Figure S6. Lungs from non-CF pigs ≥ 2 months of age. (**A**) non-CF pigs lacked airway inflammation although mild lymphocytic aggregates in submucosa were detected in one animal (arrow), bar = 130 μm. (**B**) Representative section of a non-CF pig lung, HE stain, bar = 1.3 mm.

Figure S7



B

	Newborn			
	BAL		Lung Homogenate	
	non-CF, n=20	CF, n=11	non-CF, n=18	CF, n=12
Alpha hemolytic Streptococcus	6 (30%)	1 (9%)	1 (5%)	3 (25%)
Bacillus sp.	0	1 (9%)	0	0
Coagulase-negative Staphylococcus	7 (35%)	3 (27%)	2 (11%)	6 (50%)
Escherichia coli	3 (15%)	2 (18%)	4 (22%)	2 (16%)
Enterococcus sp.	1 (5%)	2 (18%)	2 (11%)	5 (41%)
Haemophilus sp.	0	0	0	1 (8%)
Micrococcus sp.	0	1 (9%)	1 (5%)	0
Neisseria sp.	1 (5%)	0	0	1 (8%)
Pasteurella pneumotropica	1 (5%)	1 (9%)	3 (16%)	1 (8%)
Staphylococcus aureus	3 (15%)	0	3 (16%)	4 (33%)
Stenotrophomonas maltophilia	0	0	0	1 (8%)

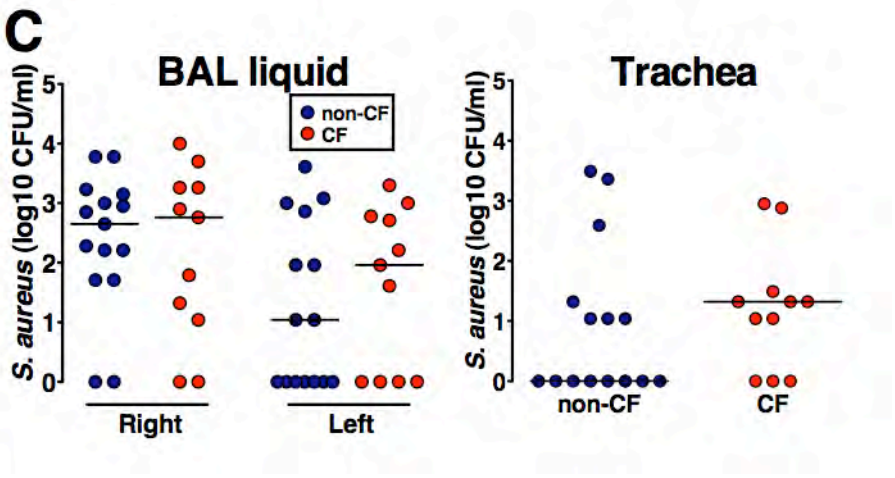


Figure S7. Lung microbiology in newborn CF pigs. (**A**) Quantitative microbiology on BAL liquid from newborn piglets. 6-12 h old piglets were euthanized and lungs were sterilely removed and BAL performed. Each point represents a sample from an individual animal. Bar denotes median. (**B**) Microbiology profile of bronchoalveolar lavage liquid and lung tissue homogenates obtained sterilely from newborn piglets within 6-12 h following birth. All recovered bacterial species were identified by standard culture methods. Shown are the number of animals from each group with a positive sample for the specified bacteria. The percentage of animals with a positive sample is noted in parentheses. (**C**) Bacteria recovered from right and left BAL liquid and tracheal wash following *S. aureus* intratracheal challenge. Each point represents a different animal. Bar denotes median. Newborn non-CF and CF pigs received an intrapulmonary challenge with *S. aureus* (average inoculum 1.9 x 10^5 cfu) delivered in 0.1 ml of 0.45% saline using an atomizer positioned just distal to the vocal cords. n = 15 non-CF and 11 CF animals from a total of 5 litters.

Table S1. Summary of CF pigs.

ID	Sex	Genotype	Lifespan	Reason for Euthanasia
Case 1	M	-/-	55 d	*Staphylococcus aureus* lung infection
Case 2	F	-/ΔF508	63 d	gastric ulcer
Case 3	M	-/ΔF508	58 d	gastric ulcer
Case 4	M	-/-	160 d	*Bordetella bronchiseptica* lung infection
Case 5	F	-/-	191 d	gastric ulcer

Table S2.

Review of pulmonary lesions in human CF infants (less than 6 months) and CF pigs.

Site	Lesion	Birth to 1 month	1 to 6 months	Birth to 4 months	1 wk to 6 months	CF pigs
	Reference	1	1	2	3	-
Airway	Airway obstruction	D	D	+++ (10/15)	+++ (19/19)	CF#1, 4 (2/5)
	Airway inflammation	+ (4/21)	+++ (24/24)	+++ (11/15)	+++ (19/19)	CF#1-5 (5/5)
	Bronchiectasis	0 (0/21)	++ (14/24)	+ (3/15)	+++ (13/19)	0 (0/5)
	Surface epithelium, mucinous change/goblet cell hyperplasia	NA	NA	D "common"	NA	CF#1, 4 (2/5)
	Airway ulceration / abscess formation	NA	NA	NA	++ (7/19)	CF#1 (1/5)
	Submucosal gland hypertrophy/hyperplasia/ dilation	+ (6/21)	+++ (20/24)	D	NA	CF#1, 4 (2/5, rare)
	Squamous metaplasia	0 (0/21)	+ (1/24)	++ (8/15)	+ (5/19)	0
Parenchyma	Pneumonia (necrotizing, organizing/fibrosing, bronchopneumonia)	++ (11/21)	+++ (20/24)	+++ (11/15)	+++ (13/19)	CF#1, 4 (2/5)
	Air trapping/hyperinflation	D	D	D	NA	CF#1, 4 (2/5)
	"Emphysema" – in many old papers term often refers to air trapping (see above)	0 (0/21)	+ (2/24)	0 (0/15)	D	0 (0/5)
	Atelectasis	NA	NA	NA	D	CF#1, 4 (2/5)
	Hemorrhage	NA	NA	+ (3/15)	NA	CF#1, 4 (2/5)

"NA" not assessed; "0" none detected; "D" detected, but incidence not stated; "+" detected at <33% incidence; "++" detected at 33-<66% incidence; "+++" detected at >=66% incidence; numbers in parentheses indicate # observed / # studied

References for Table S2.

1) Esterly JR, Oppenheimer EH. Observations in cystic fibrosis of the pancreas. 3. Pulmonary lesions. Johns Hopkins Med J. 1968 Feb;122(2):94-101.

2) Bedrossian CW, Greenberg SD, Singer DB, Hansen JJ, Rosenberg HS. The lung in cystic fibrosis. A quantitative study including prevalence of pathologic findings among different age groups. Hum Pathol. 1976 Mar;7(2):195-204.

3) Andersen DH: Cystic fibrosis of the pancreas and its relation to celiac disease: a clinical and pathologic study. Am J Dis Child 1938, 56:344-399.

Table S3. Number of differentially expressed genes in each tissue, after the implementation of filters

FILTER	TRACHEA	BRONCHUS	DISTAL LUNG
***P*-value <0.05**	1531	1740	1632
Fold change >1.5	170*	181*	114*
Fold change >2.0	61*	51*	35*
Signal intensity	38*	34*	21*
q-value <0.1	0	0	4

Table S4. Gene set enrichment analysis of data from CF and non-CF tissues.

	TRACHEA		BRONCHUS		DISTAL LUNG	
	Increased in *CFTR+/+*	**Increased in *CFTR-/-***	**Increased in *CFTR+/+***	**Increased in *CFTR-/-***	**Increased in *CFTR+/+***	**Increased in *CFTR-/-***
Gene sets enriched at *P*<0.1	0	14	5	7	10	6
Gene sets enriched at *P*<0.05	0	0	0	0	0	0
Gene sets enriched at FDR<0.25	0	0	0	0	0	0

Table S5. Differentially expressed genes in each tissue selected based on a *P*-value cut-off < 0.05 and a >2-fold change (with no further correction for multiple comparisons).

Gene Name	TRACHEA Fold Change (CF vs non-CF)	BRONCHUS Fold Change (CF vs non-CF)	DISTAL LUNG Fold Change (CF vs non-CF)
ADAMTS1	2.03		
ALAS2	2.10		
AMY2B	-2.16		
ANKRD1			2.30
ANXA8L1			3.02
AQP4	2.55	3.24	
ARMC3	-2.14	-1.72	
ASPN		-2.69	
BNP			2.00
C10orf49		-2.27	
C14orf37	-2.11	-2.02	
C2orf40		-2.78	
C5	3.95		
C6orf189	2.81		
C8orf4		1.88	2.29
CAMP			2.67
CAPSL		-2.00	
CAV2	2.15		
CCDC80		-2.59	
CD24		2.05	1.71
CD61	2.01		
CDH5	2.13		
CDON		-3.20	
CHI3L1	4.16		
CHN1	2.04		
COL16A1		-2.00	
COL1A1		-2.10	
COL1A2		-2.04	
COL2A1		-3.65	
Col8a1		-3.00	
CPE		-2.15	
CRISPLD1		-3.65	
CXCL14	2.36		-2.57
CYP1A1			-2.72
CYP2A13	-2.14		
CYP2B7P1	-2.07		
CYP7B1	2.08		
CYR61		1.97	2.15

Table S5. (con't)

Gene Name	TRACHEA Fold Change (CF vs non-CF)	BRONCHUS Fold Change (CF vs non-CF)	DISTAL LUNG Fold Change (CF vs non-CF)
ECM2		-2.29	
EEF1D	2.09		
EGR1			2.09
ENPP3	-2.08	-2.04	
ERRFI1			2.19
FAM81B	-2.12		
FKBP5			2.13
FOS			4.34
FOXF1	2.04		
FUT2	-2.08		
FZD4			5.58
GABRP		-2.01	
GADD45G		2.34	2.64
GATA6	2.38		
GLUL	-2.32		
GNAS	-2.29		
GPRC5A	3.16		
GRHL2	-2.02	-1.73	
Gsta4	-3.47	-4.52	
Hapln1		-2.95	
HK2		2.22	
HP	5.99		
HSPA1A		-1.98	-2.27
HSPH1		-2.10	-1.84
IGFBP6		-2.04	
Inmt	3.69	3.40	2.94
ISCU		2.28	1.97
ISLR		-2.01	
KCTD12		-1.75	-2.26
LAMP2			2.69
LCN1L1	-3.66	-3.49	
LIMCH1	2.25		
LOC253012	-2.27		
LOC396871	2.78		
LOC508078	2.18		
LOC511674			-2.03
LOC647979	2.66		
LOC654323	-2.25	-1.96	-2.07
LOC728320			3.09
LPL		2.06	1.78
LRRC17	-1.72	-2.26	
LRRN3			-2.66
LUM		-1.68	2.06
LY6H	-3.05	-2.83	

Table S5. (con't)

Gene Name	TRACHEA Fold Change (CF vs non-CF)	BRONCHUS Fold Change (CF vs non-CF)	DISTAL LUNG Fold Change (CF vs non-CF)
MFAP5		-2.06	
MMP8			3.58
MUT			-2.03
MYC			2.00
MYOC		-2.04	
NCL		-2.40	-2.21
NOV		-2.69	
NPNT	2.46		
NTRK2		-2.76	
OB1	3.14		
PALM2-AKA	2.02		
PCOLCE		-2.40	
PCOLCE2		-2.25	
PDGFRL		-2.16	
PDK4		2.19	
PDPN	2.29		
PIGR	-2.46		
PLAT	2.23		
PLTP	2.73		
PODXL	2.08		
POSTN		-2.83	
PPP1R12A		2.30	
PRRX1		-2.39	
PSAT1			2.47
QPCT	-1.97	-2.21	
RHOU			2.12
RPS27	2.23		
S100A9	4.46		
SCRG1		-3.31	
SERPINE1	2.88		
SFRP2		-3.39	
SFTPC	4.73		
SLC1A4			2.03
SLC5A5	-2.17	-1.85	
SLC7A11			2.29
SMOC2		-2.31	
SPOCK3	2.17		
TCF21	2.66		
TF			-2.15
TGM2	2.07		
THBD	2.53		
THBS1			2.74
TIMP1	2.36		
TMC5		-2.32	
TMEM100	3.33		
TMEM119	2.47		
TMEM46	2.53		
TNFRSF12A	2.57		
UBD			-2.09
UGP2			2.07
UPTI		-2.22	
VSIG2	3.02		

Table S6. Comparison of microarray data for porcine tissue with array profiles from other studies.

	Trachea (CF vs. non-CF)			Bronchus (CF vs. non-CF)			Distal Lung (CF vs. non-CF)		
	***P*-value**	**q-value**	**Fold-Change**	***P*-value**	**q-value**	**Fold-Change**	***P*-value**	**q-value**	**Fold-Change**
Xu et al., 2003.									
Genes most significantly differentially expressed in lungs of $Cftr^{-/-}$ adult mice compared with $Cftr^{+/+}$ littermates									
Genes up in CF									
CEBPD	**0.02**	**0.60**	**1.20**	0.14	0.73	1.11	0.13	0.79	1.12
CHIA	0.70	0.94	1.16	0.11	0.69	1.74	0.38	0.94	-1.36
CLDN8	0.12	0.69	-1.17	0.73	0.97	-1.03	0.96	1.00	-1.00
IL1B	0.31	0.80	1.13	0.84	0.98	-1.02	0.89	1.00	-1.01
IL4	0.10	0.67	1.03	0.57	0.94	-1.01	0.34	0.93	1.02
KLF1	0.54	0.89	-1.02	0.35	0.87	1.03	0.11	0.77	1.06
NPR3	0.08	0.66	1.09	0.41	0.90	1.04	0.14	0.81	1.06
PEG3	0.37	0.83	1.02	0.79	0.98	1.01	0.95	1.00	1.00
PGAM2	0.71	0.94	1.02	0.77	0.97	-1.01	0.32	0.92	-1.05
PSMC3	0.09	0.66	1.14	**0.05**	**0.58**	**1.15**	0.30	0.91	1.07
S100A8	**0.05**	**0.63**	**1.31**	0.19	0.77	1.17	0.07	0.69	1.25
S100A9	**0.04**	**0.62**	**4.46**	0.34	0.87	1.88	0.08	0.72	3.23
SLC38A4	0.94	0.99	-1.00	0.73	0.97	-1.01	0.61	0.99	-1.01
Genes down in CF									
ARF5	0.38	0.84	-1.06	0.41	0.90	-1.05	0.37	0.94	-1.06
CFTR	0.85	0.98	-1.02	0.14	0.73	-1.13	**0.00**	**0.06**	**-1.47**
COL5A1	0.98	1.00	1.00	0.76	0.97	-1.02	0.45	0.96	-1.04
GJA4	0.77	0.96	1.03	0.64	0.95	1.05	0.15	0.82	1.15
IGFBP2	0.89	0.98	-1.02	0.08	0.65	-1.20	0.44	0.96	1.08
IGFBP7	0.19	0.73	1.07	0.75	0.97	1.01	0.54	0.98	1.03
IRF1	0.77	0.96	1.06	**0.02**	**0.48**	**-1.51**	0.06	0.65	-1.39
JAK3	0.37	0.83	1.10	0.09	0.66	1.19	0.51	0.98	1.07
KIF3A	0.84	0.97	-1.03	0.99	1.00	-1.00	0.79	1.00	-1.03
LIPE	0.32	0.81	-1.11	0.66	0.95	-1.04	0.75	1.00	-1.03
NR2F1	0.18	0.72	1.25	0.59	0.94	1.08	**0.00**	**0.27**	**-1.59**
PSME3	0.72	0.95	1.03	0.83	0.98	-1.02	0.41	0.95	-1.07
PTH	0.55	0.90	-1.01	0.43	0.90	1.01	0.13	0.80	-1.02
TDO2	0.91	0.99	1.00	0.45	0.91	-1.01	0.71	1.00	1.01
Haston et al., 2006									
Genes most significantly differentially expressed in lungs of 12-wk-old $Cftr^{-/-}$ mice compared with $Cftr^{+/+}$ littermates									
Genes up in CF									
BIRC5	0.20	0.73	-1.06	0.95	0.99	1.00	0.73	1.00	-1.01
KIF23	0.73	0.95	1.03	0.98	1.00	-1.00	0.25	0.89	1.10
RACGAP1	0.98	1.00	1.00	0.71	0.97	-1.05	0.79	1.00	1.03
RRM2	0.17	0.71	1.18	0.40	0.90	-1.09	0.57	0.98	-1.06
TK1	0.43	0.86	-1.06	0.59	0.94	-1.03	0.59	0.98	-1.03
UCP2	0.68	0.94	1.03	0.08	0.65	1.13	0.56	0.98	1.04
Genes down in CF									
CCDC25	0.12	0.69	1.17	0.47	0.92	1.07	0.47	0.96	1.07
MAP1LC3B	0.85	0.98	-1.02	0.86	0.98	1.02	0.18	0.84	1.13
MYO10	1.00	1.00	1.00	0.15	0.74	-1.24	**0.00**	**0.07**	**-1.99**
TOB2	0.08	0.66	1.19	0.14	0.73	1.14	0.39	0.95	1.08

Table S6. (con't)

	Trachea (CF vs. non-CF)			Bronchus (CF vs. non-CF)			Distal Lung (CF vs. non-CF)		
	***P*-value**	**q-value**	**Fold-Change**	***P*-value**	**q-value**	**Fold-Change**	***P*-value**	**q-value**	**Fold-Change**
Xu et al., 2006.									
Genes most significantly differentially expressed in lungs of $Cftr^{\Delta F/\Delta F}$ adult mice compared with $Cftr^{+/+}$ littermates									
Genes up in CF									
CES1	0.25	0.77	-1.60	0.38	0.89	-1.39	0.66	0.99	-1.18
KTN1	0.30	0.80	1.11	0.35	0.87	1.09	0.42	0.95	1.08
PIK3CA	0.22	0.75	-1.03	0.71	0.96	1.01	0.82	1.00	1.00
SEMA4B	0.31	0.80	-1.06	0.20	0.78	1.07	0.47	0.96	1.04
Genes down in CF									
CYP7B1	**0.02**	**0.59**	**2.08**	0.57	0.94	-1.16	0.61	0.99	-1.15
DHX30	0.86	0.98	1.02	0.90	0.99	1.01	0.59	0.98	-1.05
DRD2	0.28	0.79	-1.05	0.61	0.95	1.02	0.79	1.00	-1.01
FAAH	0.73	0.95	-1.02	1.00	1.00	1.00	0.70	1.00	-1.02
FOXP1	0.12	0.69	1.14	0.16	0.74	1.11	0.86	1.00	1.01
MLF1	0.08	0.66	-1.63	**0.05**	**0.58**	**-1.65**	0.94	1.00	1.02
NUP50	0.76	0.96	-1.03	0.99	1.00	-1.00	0.60	0.98	1.04
SHC1	0.50	0.88	1.06	0.59	0.94	-1.04	0.83	1.00	1.02
SOAT1	**0.00**	**0.38**	**-1.18**	**0.01**	**0.45**	**-1.11**	0.30	0.91	-1.04
Zabner et al., 2005.									
Genes most significantly differentially expressed in primary airway epithelia cultures from human $CFTR^{\Delta F/\Delta F}$ patients compared to normal controls									
Genes up in CF									
GLDC	0.98	1.00	1.00	0.38	0.89	1.03	0.97	1.00	1.00
PSKH1	0.91	0.99	1.00	**0.03**	**0.51**	**1.09**	0.33	0.93	1.04

Table S6. (con't)

	Trachea (CF vs. non-CF)			Bronchus (CF vs. non-CF)			Distal Lung (CF vs. non-CF)		
	***P*-value**	**q-value**	**Fold-Change**	***P*-value**	**q-value**	**Fold-Change**	***P*-value**	**q-value**	**Fold-Change**
Wright et al., 2006									
Genes most significantly differentially expressed in nasal respiratory epithelial cells collected by nasal brushing from human CF patients compared to normal controls									
Genes up in CF									
ADIPOQ	**0.02**	**0.60**	**-1.60**	0.60	0.94	-1.10	0.90	1.00	1.02
COL7A1	0.10	0.67	-1.19	0.48	0.92	1.07	0.95	1.00	-1.01
FXYD2	0.21	0.74	1.42	0.07	0.63	1.59	0.78	1.00	-1.07
HTR2A	0.28	0.79	1.03	0.89	0.99	-1.00	0.71	1.00	-1.01
LRRN1	0.73	0.95	-1.01	0.30	0.85	1.03	0.88	1.00	1.00
PGF	0.56	0.90	1.04	0.30	0.85	1.07	0.84	1.00	1.01
PPP2CA	0.29	0.79	1.11	0.54	0.93	1.06	0.39	0.94	1.08
SCAMP1	**0.04**	**0.62**	**-1.22**	0.88	0.99	-1.01	0.24	0.88	1.11
SFTPB	0.07	0.65	3.69	0.40	0.89	1.71	0.97	1.00	-1.02
SLC9A2	0.45	0.87	-1.02	0.84	0.98	-1.00	0.07	0.71	-1.04
Genes down in CF									
ACTB	0.80	0.97	1.02	0.98	1.00	1.00	0.58	0.98	-1.04
CALR	0.21	0.74	-1.05	0.63	0.95	1.02	0.63	0.99	1.02
CD2	0.94	0.99	-1.00	0.79	0.98	1.01	0.95	1.00	1.00
CD74	0.16	0.71	1.50	0.68	0.96	1.12	0.18	0.85	-1.42
CSN2	0.19	0.73	-1.06	0.61	0.95	1.02	0.64	0.99	1.02
CTSB	0.12	0.69	1.14	0.51	0.92	-1.05	0.16	0.82	-1.12
DAZAP2	0.41	0.85	-1.10	0.85	0.98	1.02	0.17	0.84	1.16
DUOX2	0.85	0.97	1.02	0.95	0.99	-1.01	0.99	1.00	-1.00
FBP1	0.15	0.71	-1.17	0.11	0.68	-1.18	0.78	1.00	-1.03
IFITM1	0.39	0.84	1.21	0.82	0.98	-1.04	0.53	0.98	1.13
IGFBP3	0.68	0.94	1.06	0.86	0.98	-1.02	0.78	1.00	1.04
ITM2A	0.59	0.91	-1.08	0.96	1.00	1.01	0.54	0.98	-1.09
LRRC1	0.66	0.93	-1.03	0.20	0.78	1.09	0.17	0.84	1.09
MYH9	0.24	0.76	-1.03	0.60	0.94	1.01	0.23	0.88	1.03
PRKACB	**0.02**	**0.59**	**1.20**	0.72	0.97	1.03	0.61	0.99	-1.04
SP110	0.10	0.67	-1.12	0.36	0.87	-1.06	0.96	1.00	1.00

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