Supplementary Materials

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Supplementary Table 1: Subject demographics for CF bronchial brushes

	Age (years)	Gender	Mutation1	Mutation2	Culture results
CF1	17	F	F508	N1303K	20,000 colony forming units/mL Staphylococcus aureus (MRSA)
CF2*	5	F	F508	F508	13000 colony forming units/mL Normal Flora 25000 colony forming units/mL Staphylococcus aureus (MRSA)
CF3*	5	F	F508	F508	13000 colony forming units/mL Normal Flora 25000 colony forming units/mL Staphylococcus aureus (MRSA)
CF4	12	F	F508	621+1 G>T	No Growth 2 Days
CF5	6	F	F508	F508	No Growth 2 Days, Positive for RSV B Virus. MRSA in sinus clulture taken on same date
CF6*	5	F	F508	F508	Less than 10,000 cfu/mL Normal Flora, Greater than 100,000 cfu/mL Staphylococcus aureus (MRSA) Less than 10,000 cfu/mL Stenotrophomonas maltophilia
*** same patient**					

Supplementary Table 2. Subject demographics for healthy control bronchial brushes (n=4)

Subject number	Healthy Control 1	Healthy Control 2	Healthy Control 3	Healthy Control 4
Demographic				
Age, yr	27	40	24	27
Gender, male/female	female	male	male	male
Race, AA/white/other	AA	white	white	white
BMI	29	31	23	29
Atopy	yes	yes	yes	yes
Baseline FEV1%p	78	105	95	n/a

Definition of abbreviations: AA= African American; BMI= body mass index; FEV1= forced expiratory volume in 1 second

Supplementary Table 3: Donor genotypes of CF HBE cells

CF HBE	Genotype
CF218	F508del/G542x
CF219	F508del/F508del
CF220	F508del/621+1g-t
CF225	F508del/F508del

Supplementary Table 4: Canonical pathways identified by IPA analysis (see attached Excel SS)

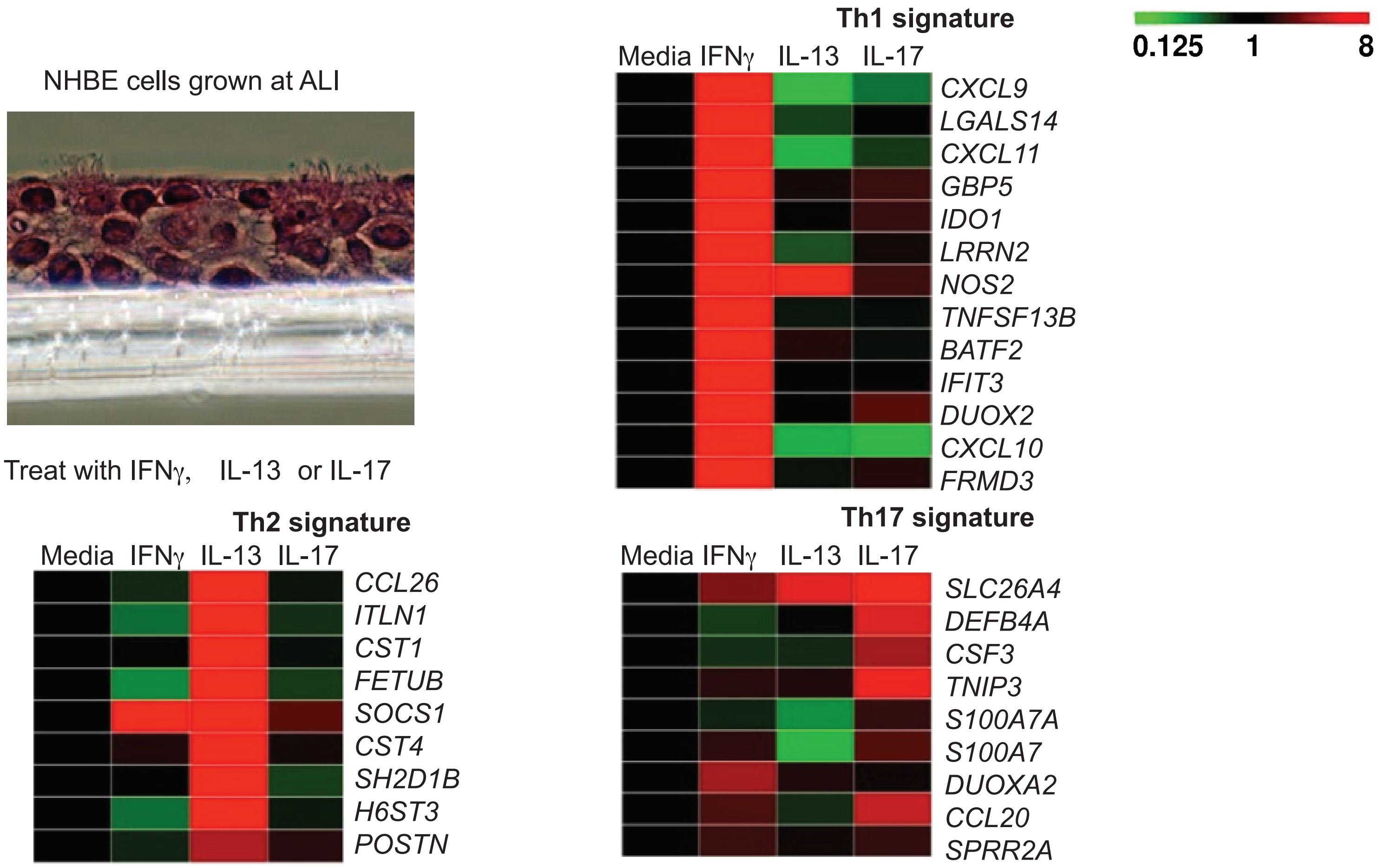


Fig. S1. Development of Th gene signature in NHBE cells.
RNA-seq was performed on normal polarized human bronchial epithelial cells treated with IFNγ (Th1), IL-13 (Th2), or IL-17 (Th17) for 48h. These data were used to develop T-cell signatures in the epithelium.

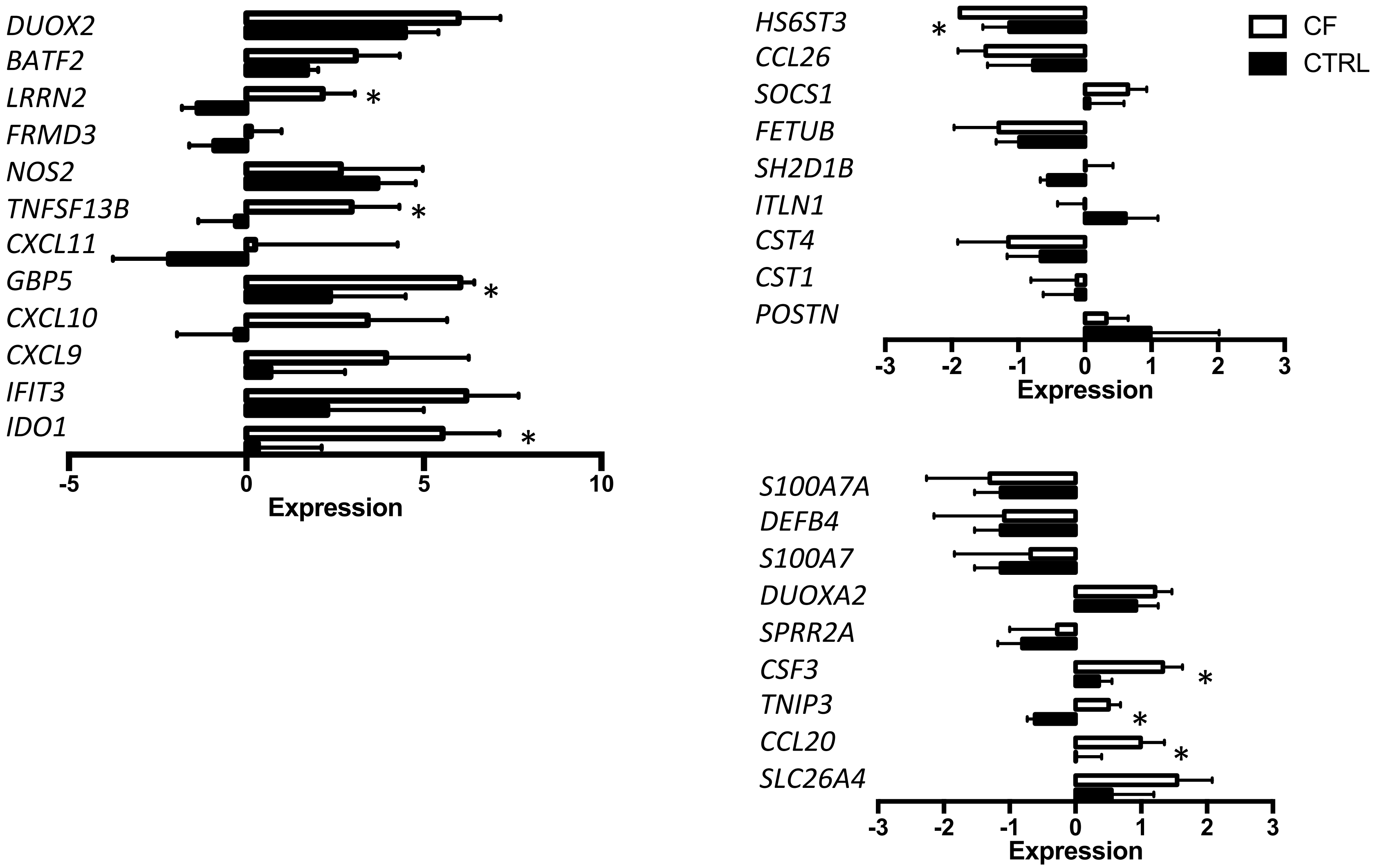
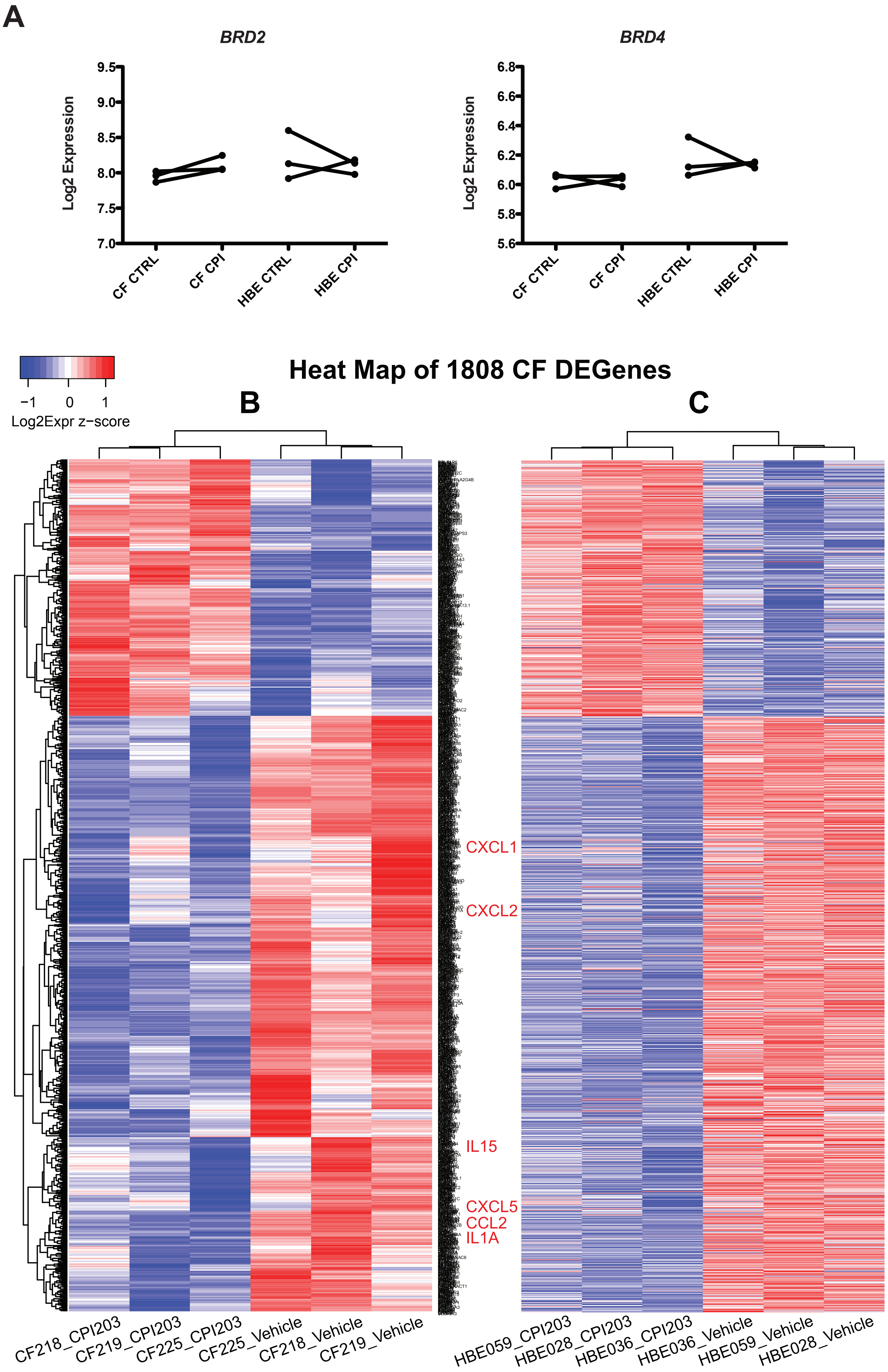
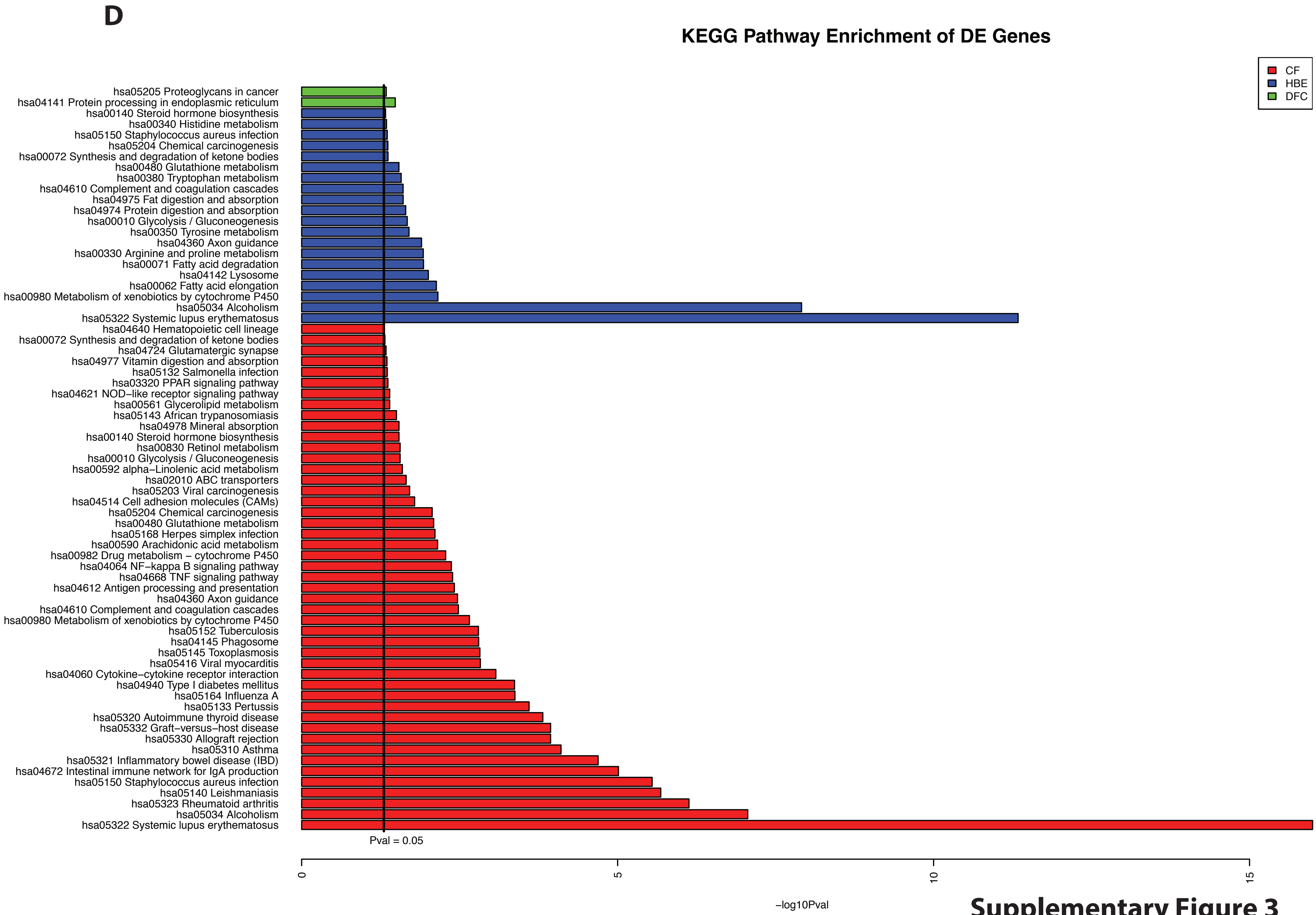


Fig. S2. RNA-seq analysis of control and CF bronchial brushings.
Individual Th1, Th2 and Th17 signature genes were shown by histogram for both CF and control groups ($p<0.05$ by student t-test).



Supplementary Figure 3



Supplementary Figure 3

E

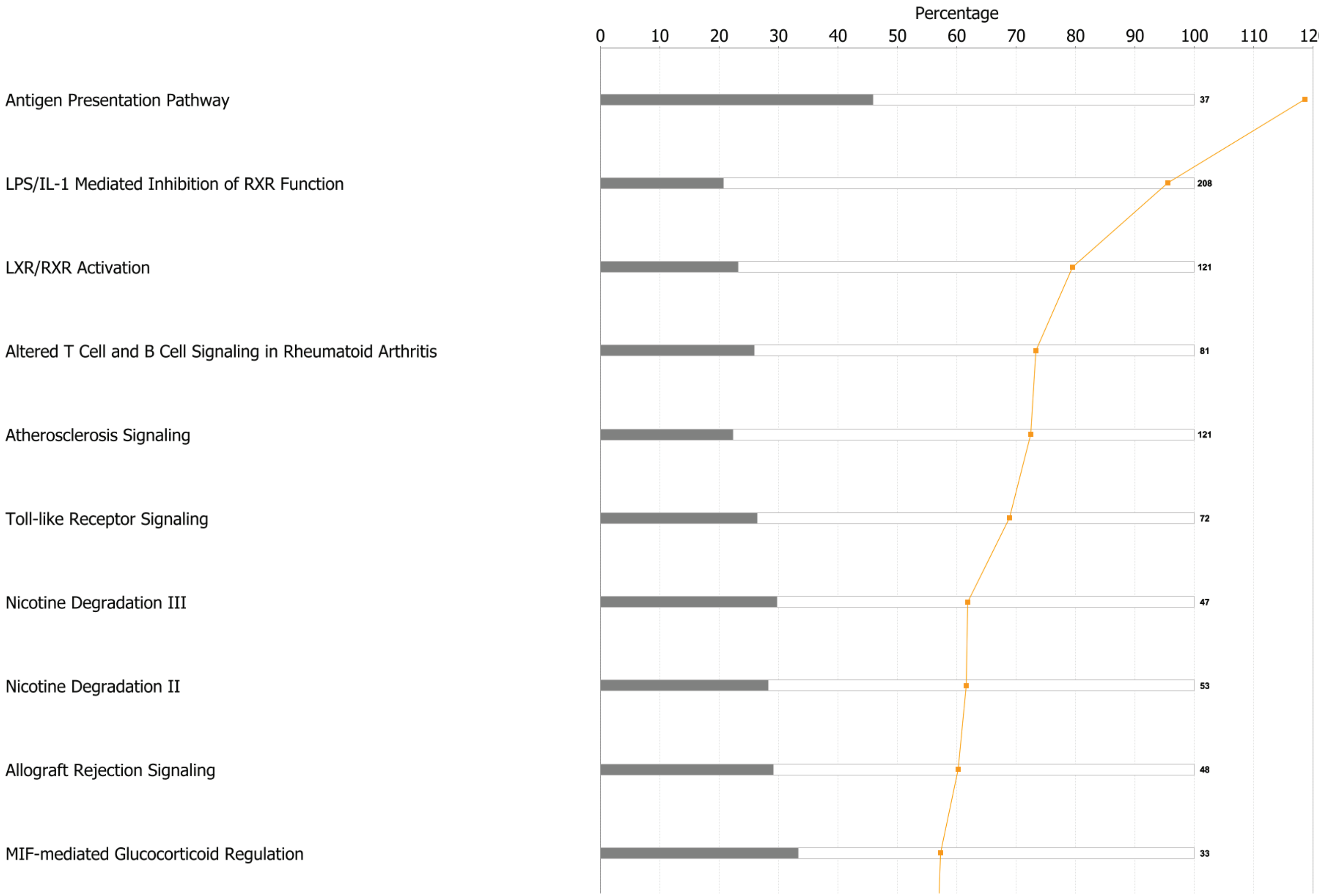


Fig. S3. RNA-seq analysis of HBE cells treated with CPI-203.
HBE cell lines from 3 CF and 3 non-CF (labeled as HBE) donors were established in air-liquid interface culture and treated with 200nM CPI-203 for 3 days. Cells were harvested in Qiagen RLT buffer andRNA-seq was conducted. 1808 genes were differentially expressed in CF cells after CPI-203 treatment ($p<0.05$ by student t-test). (A) BRD2 and BRD4 were found to be highly expressed in these cells and were not affected by CPI-203 treatment. Heat map of bi-clustering genes (row) and samples (column) in CF cells are shown in (B) with CXCL1, CXCL2, CXCL5, IL1A, IL15 and CCL2 highlighted. Heat map of the same 1808 genes as in (B) of HBE cells are shown (C). Significantly enriched KEGG (Kyoto Encyclopedia of Genes and Genomes) pathways of various biological processes are shown (D). X axis was -log10 scaled p-value of Fisher's Exact test. QIAGEN 's Ingenuity ® Pathway Analysis for the differentially expressed genes are shown (E). A full list of canonical pathways is summarized in Supplementary Table 4.

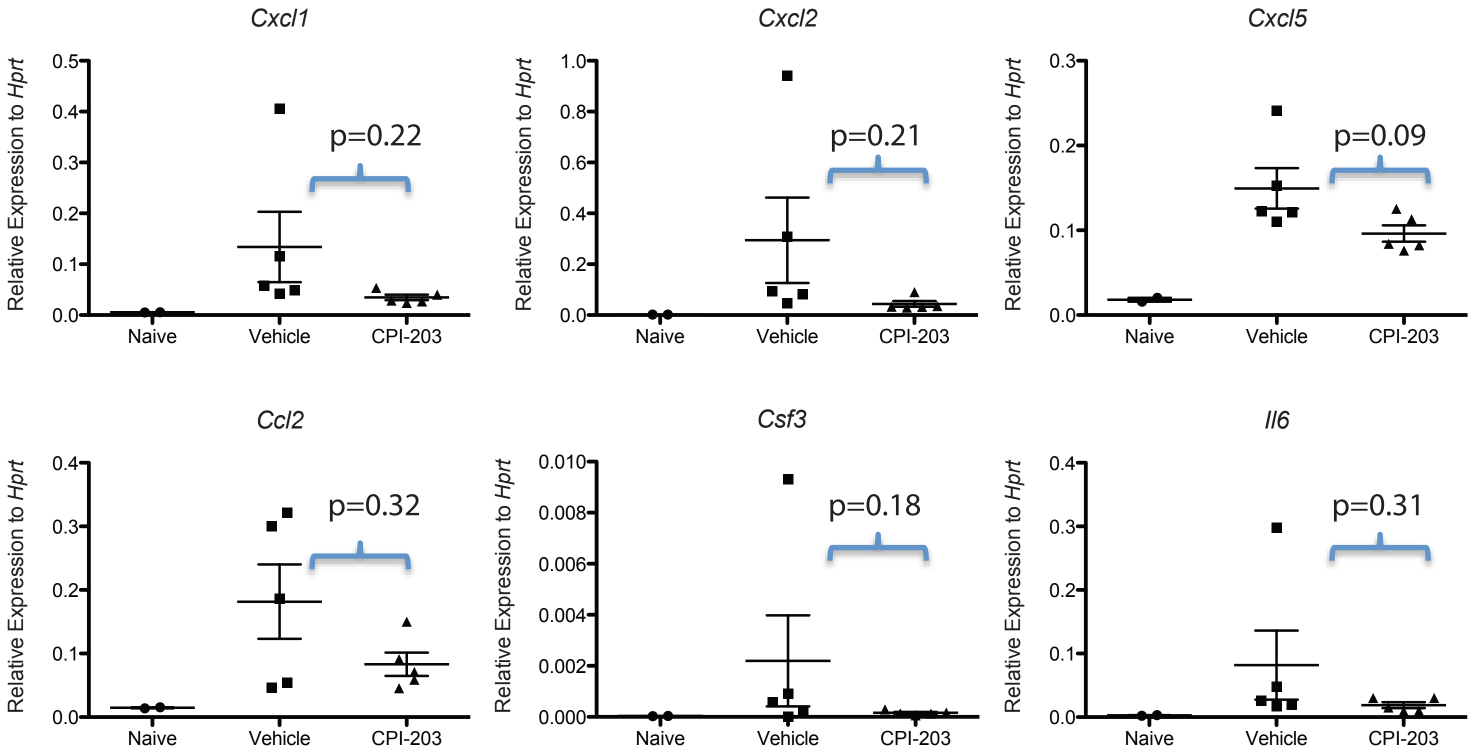


Fig. S4. Gene expression profiles in PA infected and CPI treated mice.
Gene expression of proinflammatory chemokines and cytokines in the lungs of mice that were inoculated with PA with and without CPI-203 treatment as described in Fig 4.

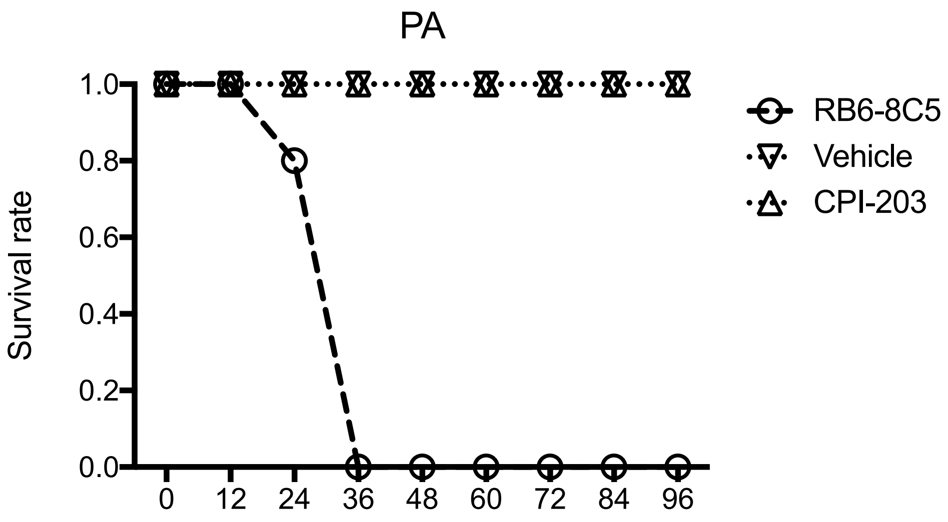


Fig. S5. CPI-203 does not exacerbate PA infection. Female 6-8 week old mice (n=5 per group) were randomized to treatment with vehicle or compound by i.p. administration followed by inoculation with PAO1. Mice were infected with PAO1 via o.p. aspiration (10^6 organisms). As a positive control for susceptibility mice underwent neutrophil-depletion by i.p. injection of antibody clone RB6-8C5 (0.6mg per mouse) one day prior to infection. Survival of the animals were monitored for 4 days.

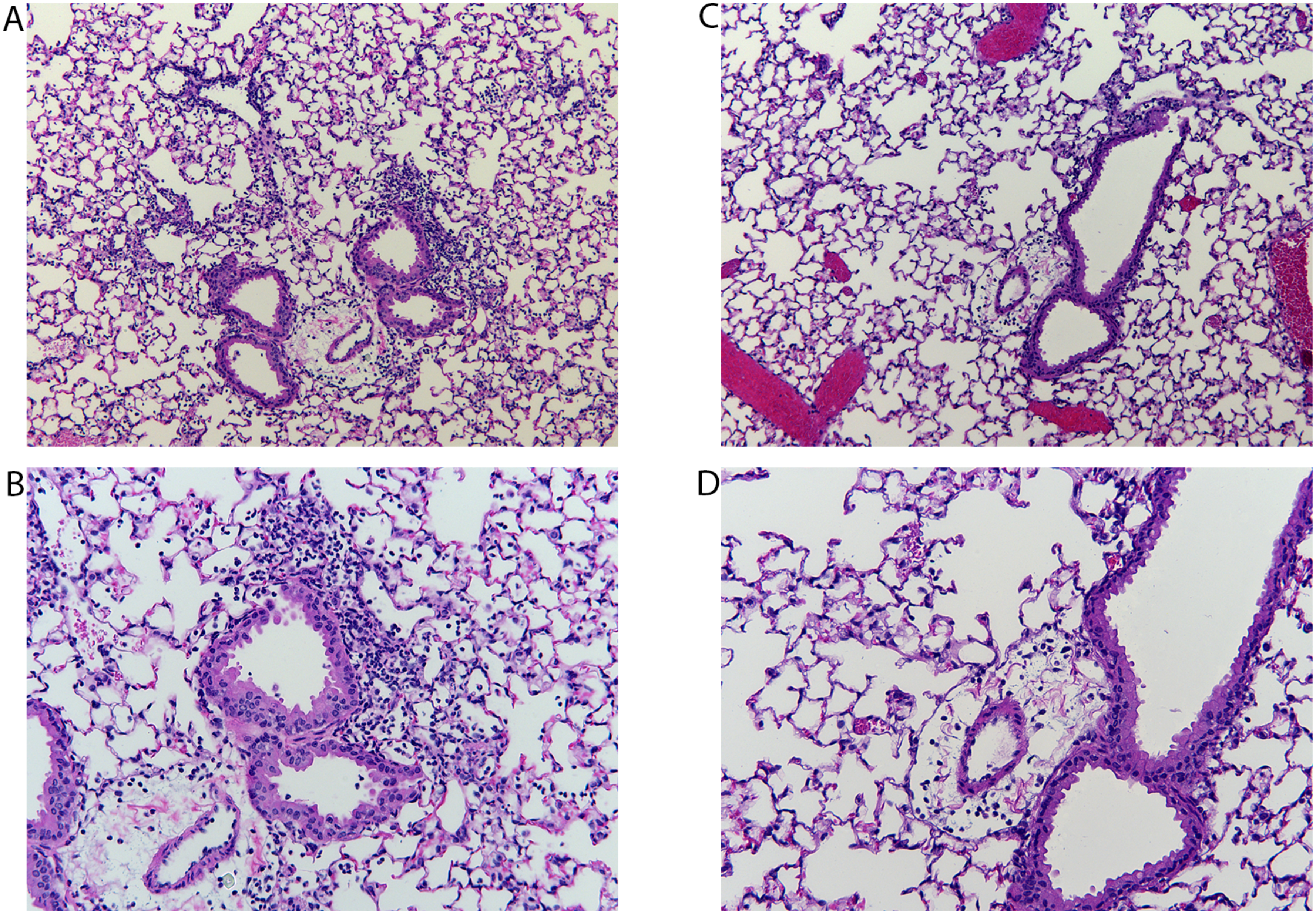


Fig. S6. Lung histopathology from PAO1 infected mice is attenuated with BET inhibition. Female 6-8 week old mice (n=5 per group) were randomized to treatment with vehicle or compound by i.p. administration followed by inoculation with PAO1. Representative images from mice infected with PAO1 and treated with vehicle control at 10x (A) and 20X (B) or CPI-203 (BET inhibitor) at 10x (C) and 20X (D).