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Supplemental Information

IL-17 Receptor Signaling in the Lung Epithelium

Is Required for Mucosal Chemokine Gradients

and Pulmonary Host Defense against *K. pneumoniae*

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Supplementary Fig 1, related to Figure 1. Characterization of the IL17R flox mice in vitro. (A) Ear skin fibroblasts were derived from the *Il17ra^{f/f}* mice and infected with adenovirus encoding CRE recombinase for 3 days. Cells treated with AdCRE or control virus were stimulated with TNF- α or the combination of TNF- α (1ng/mL) and IL-17 (10ng/mL) for 24h. Gene expression was determined by real-time RT-PCR. (B) Homozygotes *Il17ra^{f/f}* mice were sacrificed 5 days after receiving 10^8 Ad-CMV or Ad-CRE through intravenous injection. PCR using primers detecting recombined allele in the spleens were performed. Bands with no Cre-mediated recombination and Post-Cre in the spleens were indicated by arrows. (C) Peripheral blood from the *Il17ra^{f/f} E2a-Cre⁻* and *Il17ra^{f/f} E2a-Cre⁺* mice were collected from the tails and stained with IL-17RA and Gr-1 antibodies after red blood cell lysis. 3 mice for each genotype were shown.

Supplementary Fig 2 , related to Figure 1. Specific knock out of IL-17R in the flox mice. (A) Peripheral blood (PBL) from the *Il17ra^{f/f} E2a-Cre⁻* and *Il17ra^{f/f} E2a-Cre⁺* mice were collected from the tails and stained with IL-17RA and Gr-1 antibodies after red blood cell lysis. (B) Percentage of Gr-1+ cells in the PBL were graphed. (C) *Il17rc^{f/f}* and *Il17rc^{f/f} E2a-Cre⁺* mice were challenged with recombinant CXCL1 intranasally (1ug/mouse) for 24h and neutrophils as well as macrophage numbers were determined by FACS.

Supplementary Fig 3, related to Figure 2. *Scgb1a1-Cre* mediated recombination.

(A) PCR using primers detecting recombined allele in the lungs from *Il17ra^{fl/fl} Scgb1a1-Cre⁻* and *Il17ra^{fl/fl} Scgb1a1-Cre⁺* mice were performed. Bands with no Cre-mediated recombination and Post-Cre were indicated by arrows. (B) *Il17ra* expression in the bronchial brushes from *Il17ra^{fl/fl} Scgb1a1-Cre⁻* and *Il17ra^{fl/fl} Scgb1a1-Cre⁺* mice were determined by real-time RT-PCR.

Supplementary Fig 4, related to Figure 4. Real-time RT-PCR validation of RNA-seq findings.

Il17rc^{fl/fl} Scgb1a1-Cre⁻ and *Il17rc^{fl/fl} Scgb1a1-Cre⁺* mice were challenged with recombinant IL-17 intranasally (300ng/mouse) for 6h and bronchial brushings were harvested for RNA extraction and real-time RT-PCR analysis.

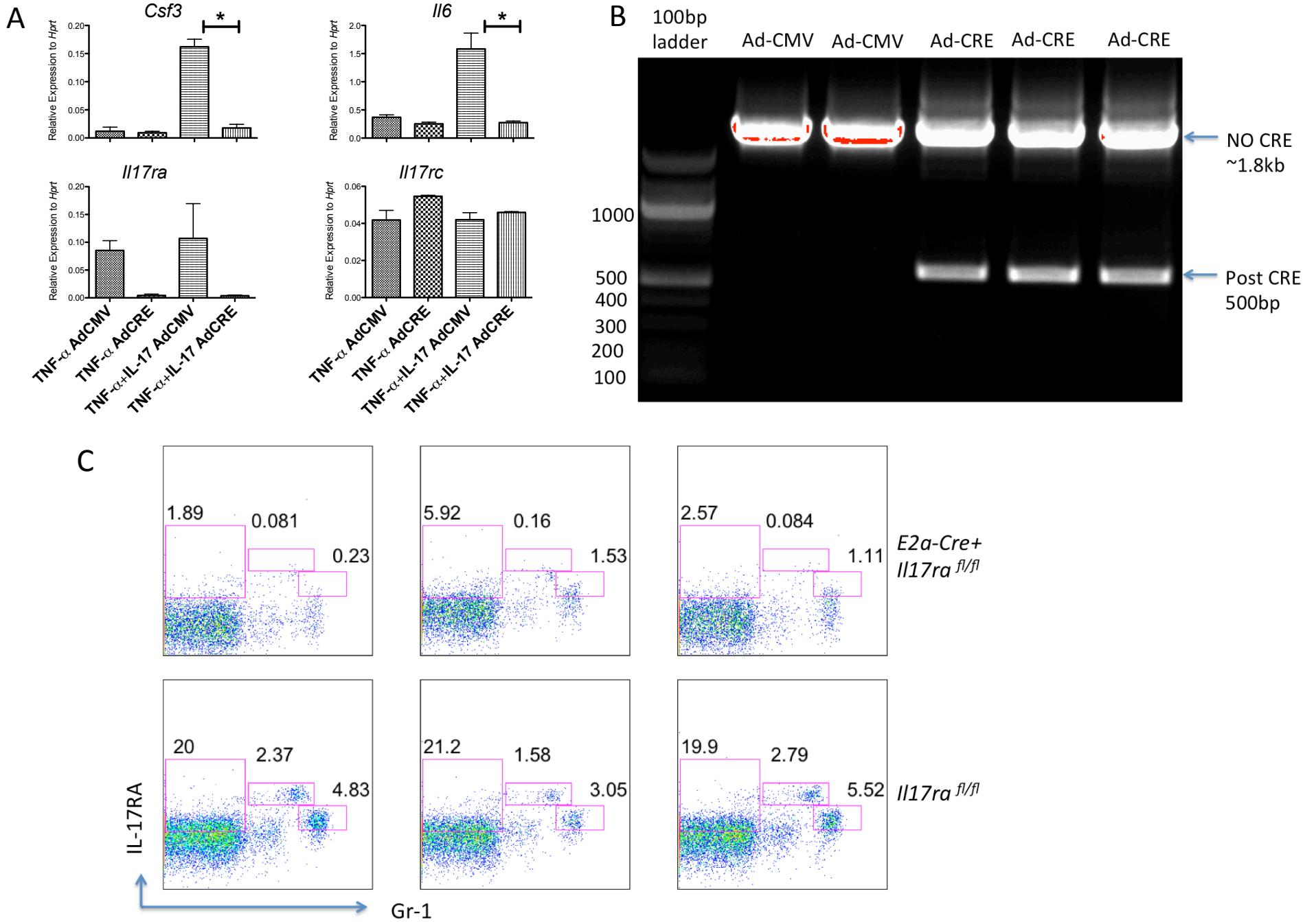
Supplementary Fig 5, related to Figure 5. Airway inflammation in CXCL5 rescued

***Il17ra^{fl/fl} x Scgb1a1-Cre⁺* after *K. pneumoniae* infection.** *Il17ra^{fl/fl} Scgb1a1-Cre⁻* and *Il17ra^{fl/fl} Scgb1a1-Cre⁺* mice were infected with 10⁴ KP43816 intranasally. 2h post infection, half of *Il17ra^{fl/fl} Scgb1a1-Cre⁺* the mice received 1ug recombinant CXCL5 (LIX). Mice were sacrificed 24h after infections. Airway inflammation was assessed by H&E staining.

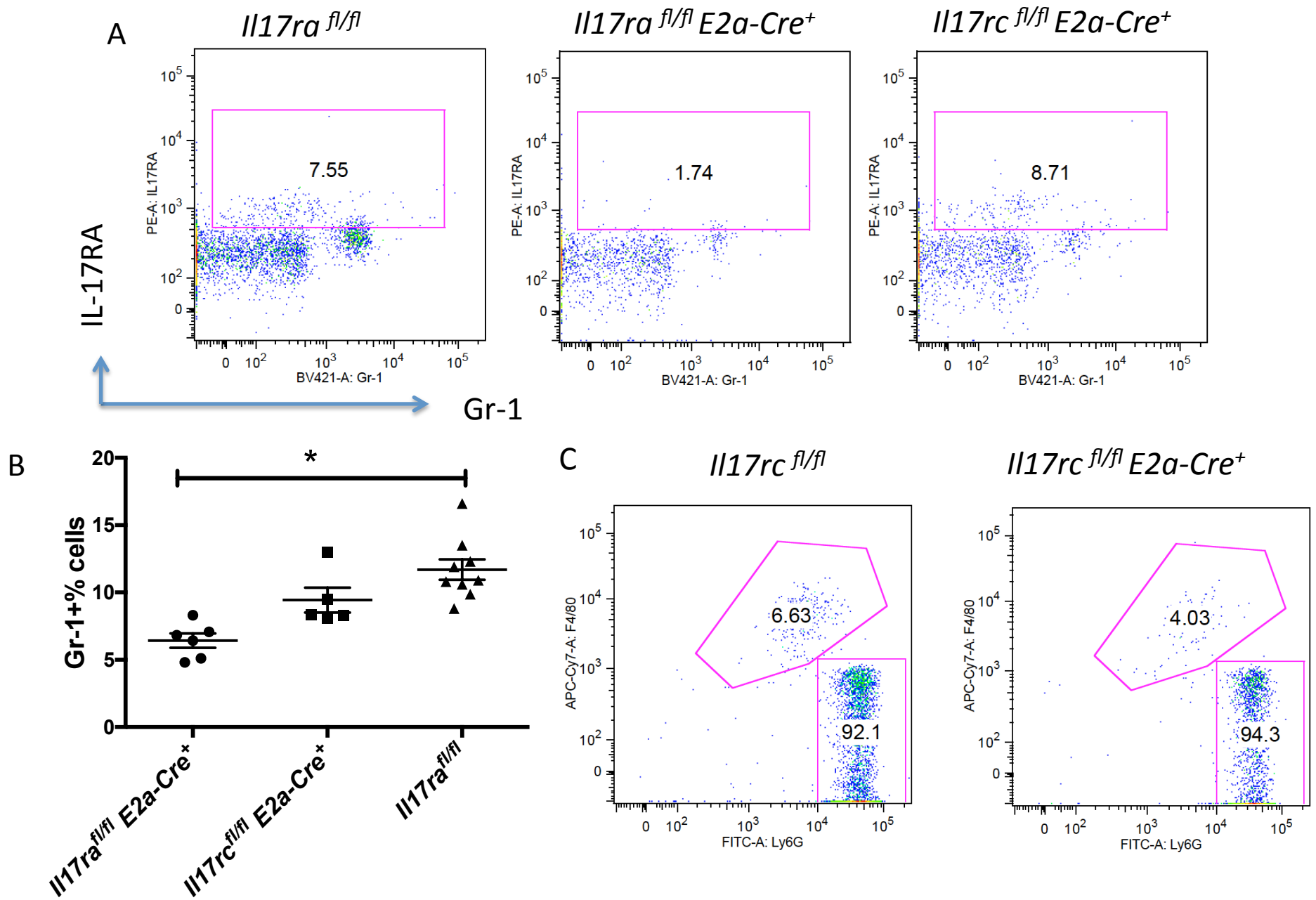
Supplementary Fig 6, related to Figure 6. Role of IL-17RE in IL-17 mediated

airway inflammation. RNAseq analysis was conducted on NHBE cells stimulated with recombinant human IL-17 (100ng/mL) for 48h (N=3-4). Heat map of the expression for IL-17 family cytokines and IL-17 receptor family were shown (A). *Il17c* expression in naïve unchallenged B6, WT or *Il17re^{+/-}* as well as littermates *Il17re^{-/-}* mice 24h post intranasal IL-17 challenge, and B6 mice 24h post KP infection were determined by real-time RT-PCR (B). BAL cell infiltration from control littermates and *Il17re^{-/-}* mice 24h post intranasal IL-17 challenge were measured by FACS (C). Gene expression of IL-17 downstream chemokines and cytokines were determined by real-time RT-PCR (D).

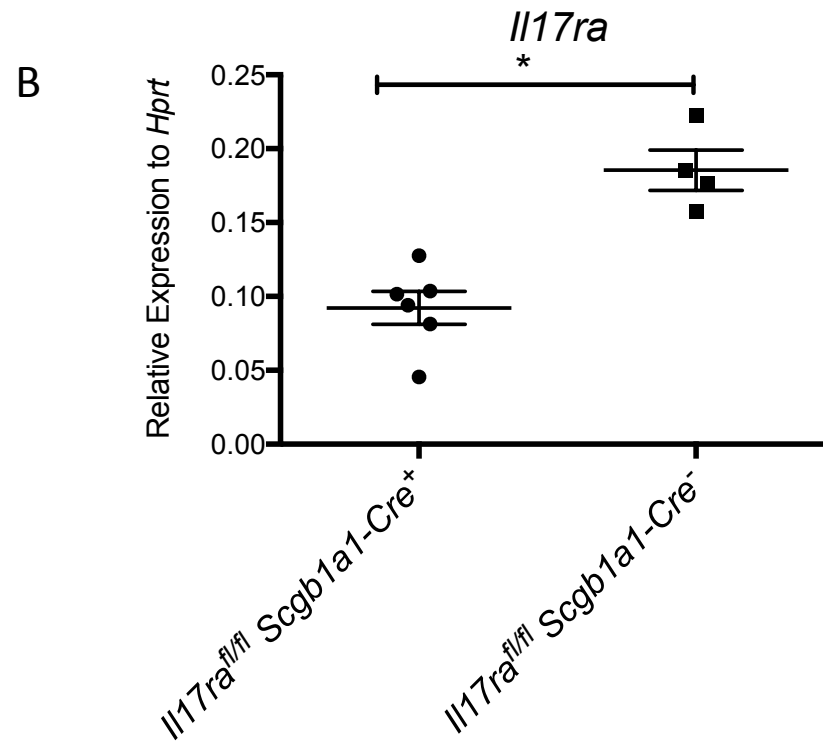
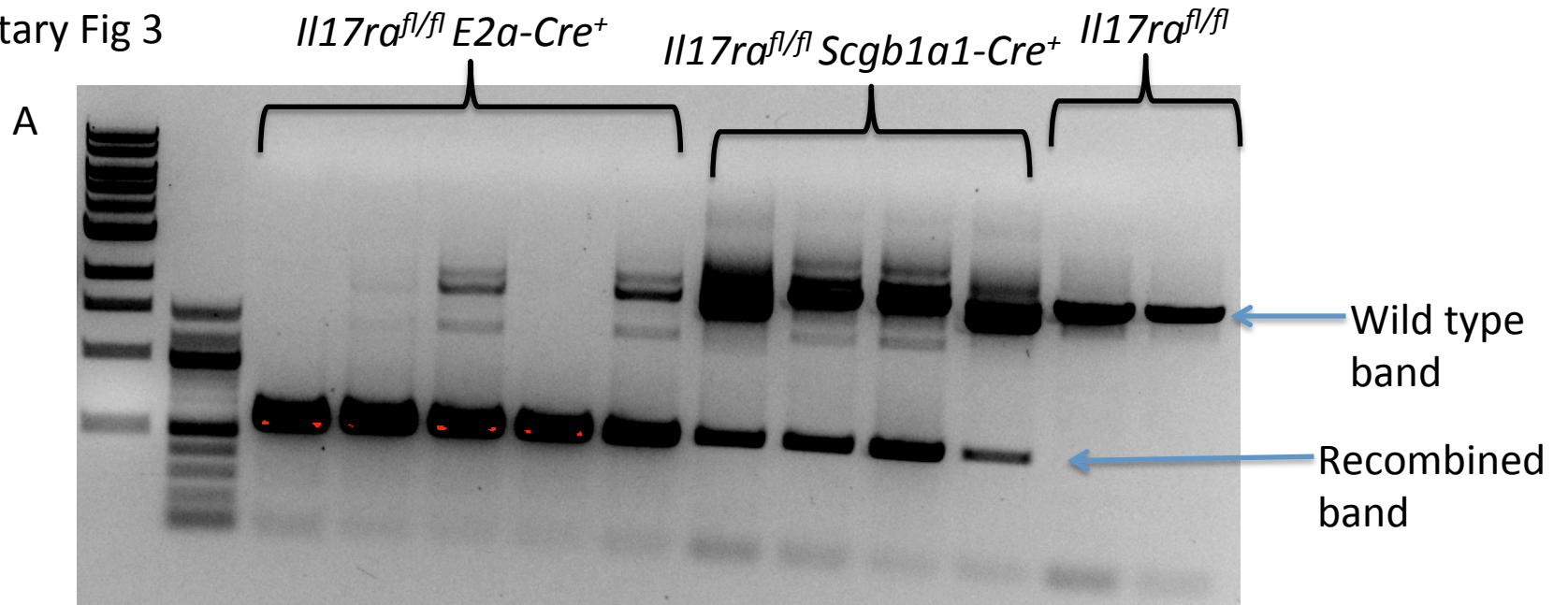
Supplementary Fig 1



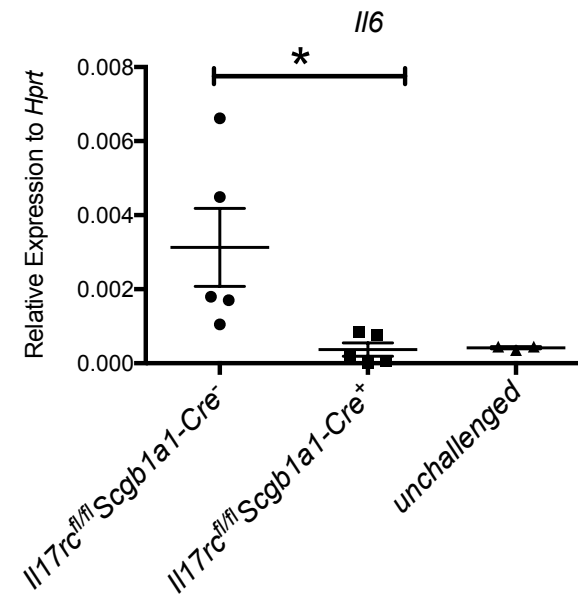
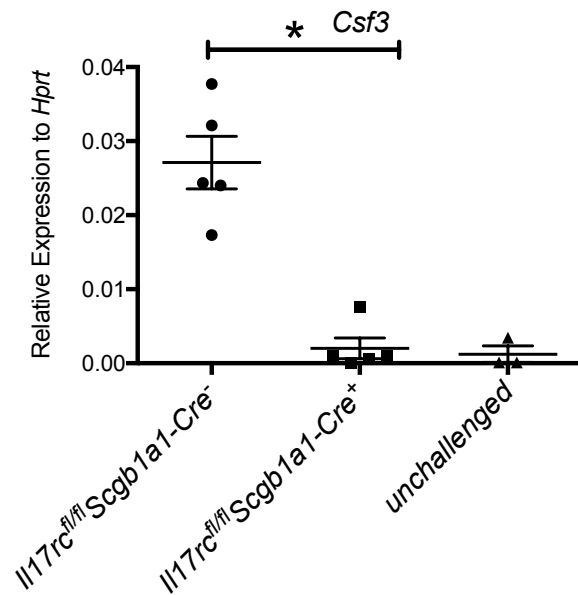
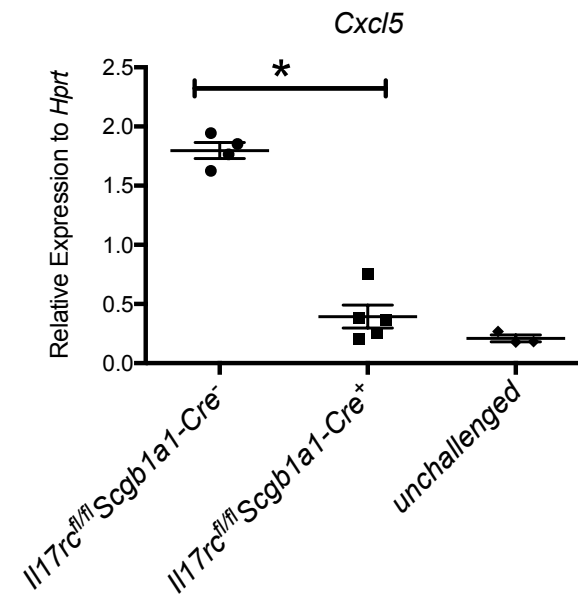
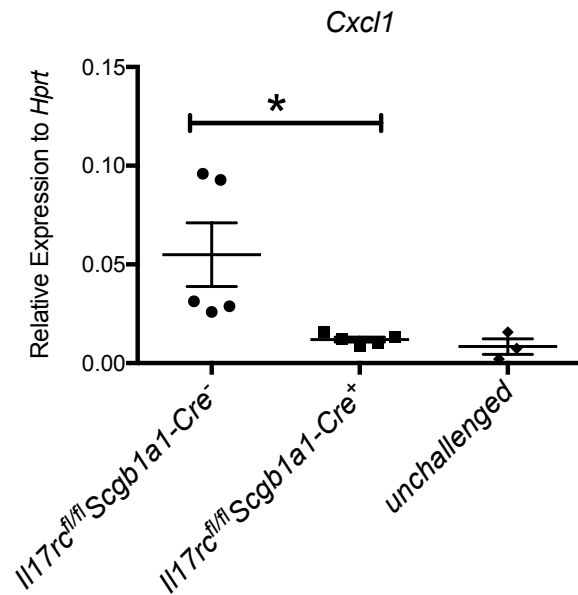
Supplementary Fig 2



Supplementary Fig 3

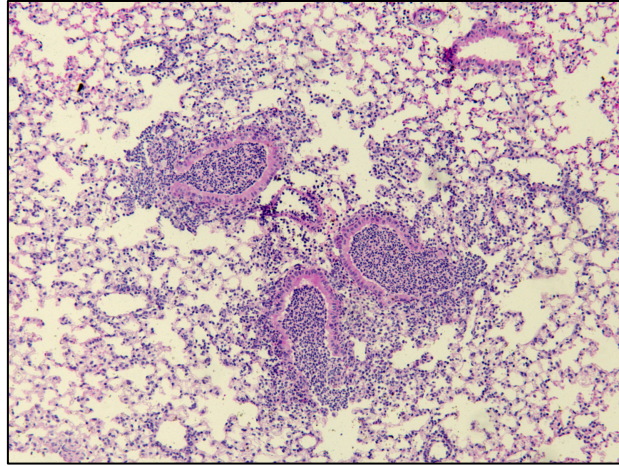


Supplementary Fig 4

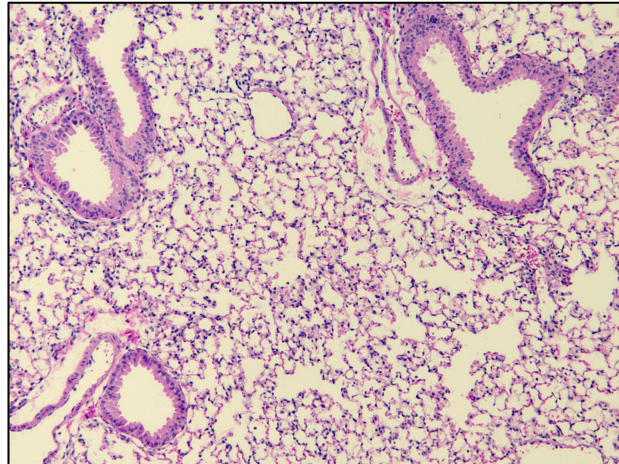


Supplementary Fig 5

Il17ra^{fl/fl} x Scgb1a1-Cre⁺ +K. pneumoniae



+ PBS



+ CXCL5
(LIX)

Supplementary Fig 6

