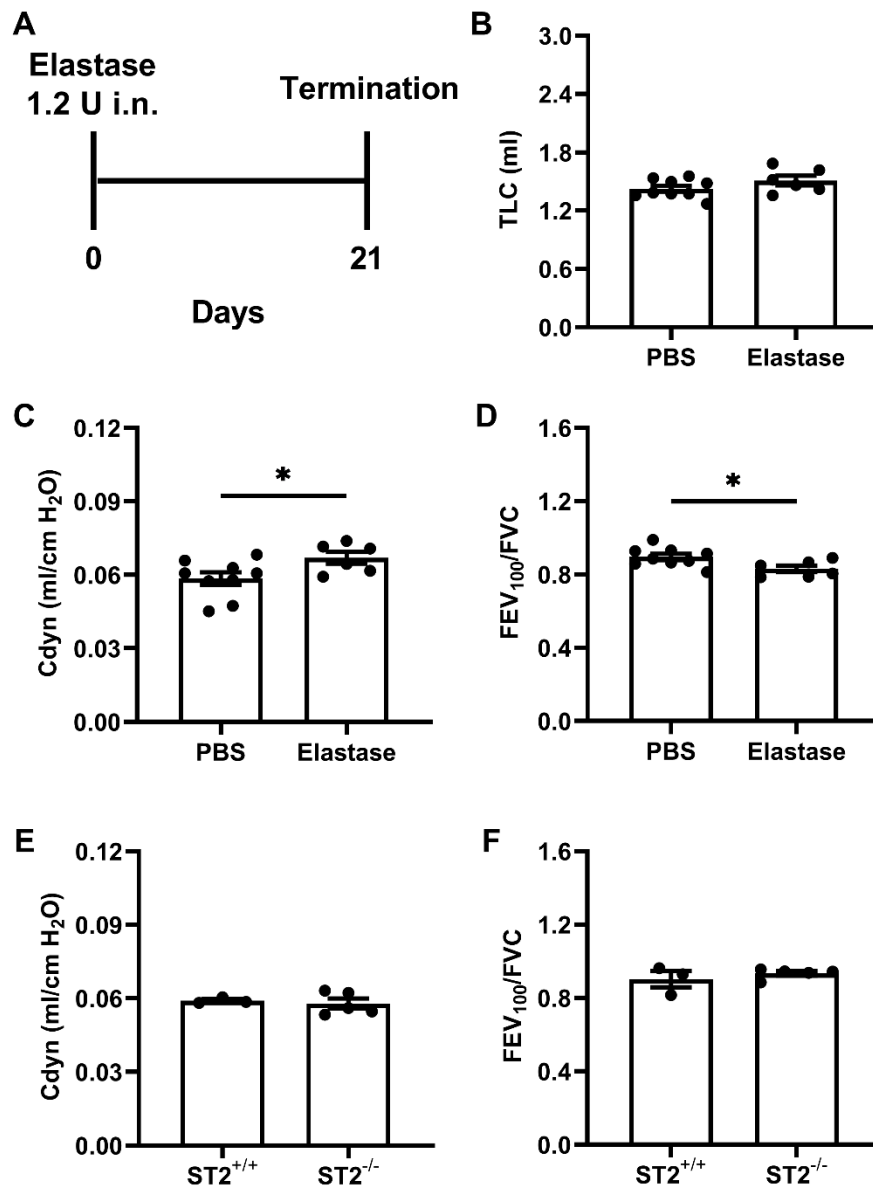
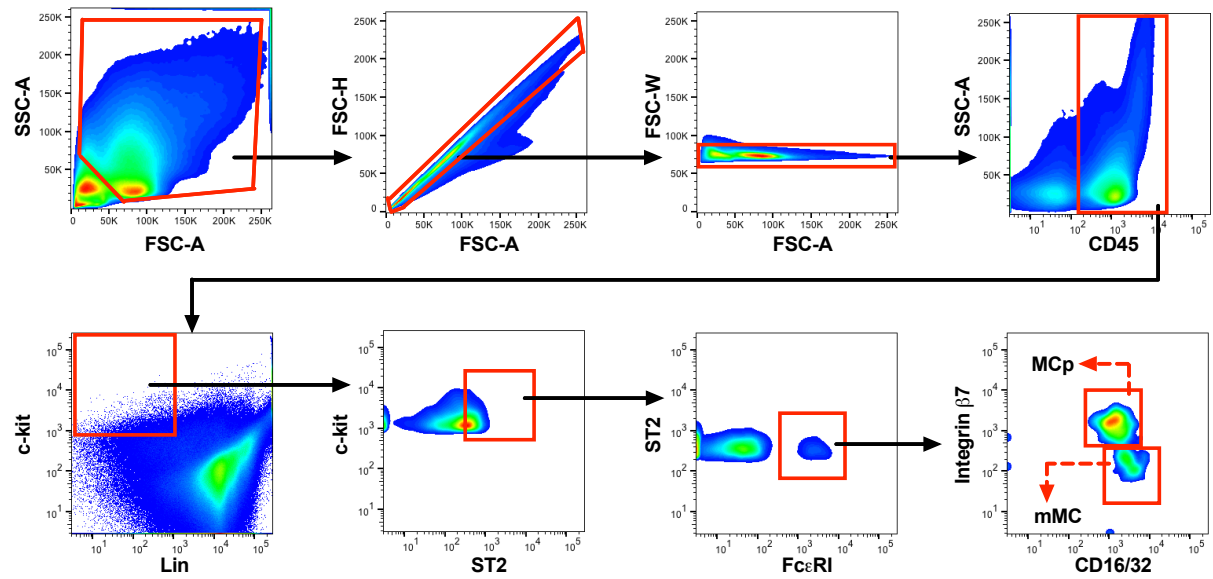


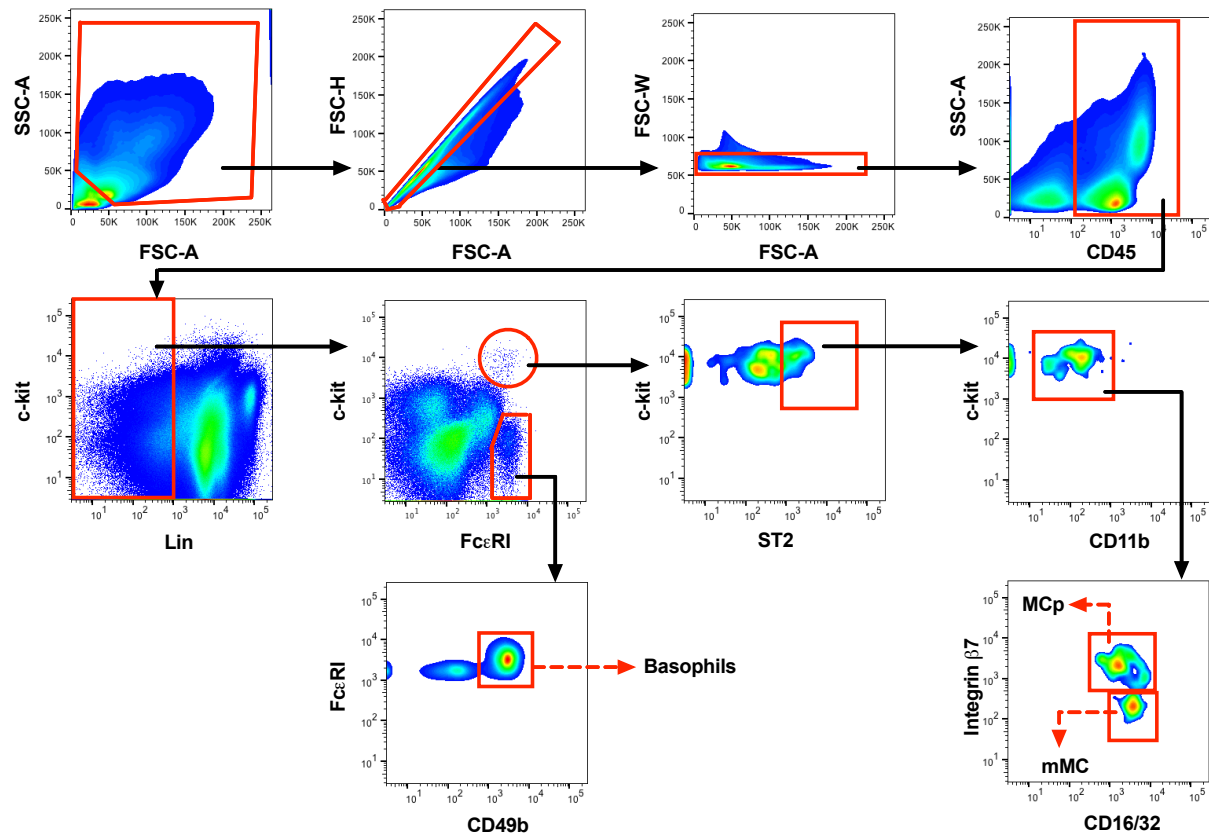
Supplementary Figure 1. Gating strategy for the identification of immune cells in BALF. BALF cells were stained using the antibodies described in Supplementary Table 1 and analyzed by flow cytometry. Alveolar macrophages were gated as CD45⁺ Siglec-F⁺ CD11c⁺ cells, eosinophils as CD45⁺ Siglec-F⁺ CD11c⁻ cells, neutrophils as CD45⁺ Siglec-F^{-/lo} CD11c^{-/lo} CD11b⁺ Ly6G⁺ cells, CD4⁺ T-cells as CD45⁺ Siglec-F^{-/lo} CD11c^{-/lo} CD11b^{-/lo} Ly6G^{-/lo} CD3⁺ CD4⁺ cells, and CD8⁺ T-cells as CD45⁺ Siglec-F^{-/lo} CD11c^{-/lo} CD11b^{-/lo} Ly6G^{-/lo} CD3⁺ CD8⁺ cells.



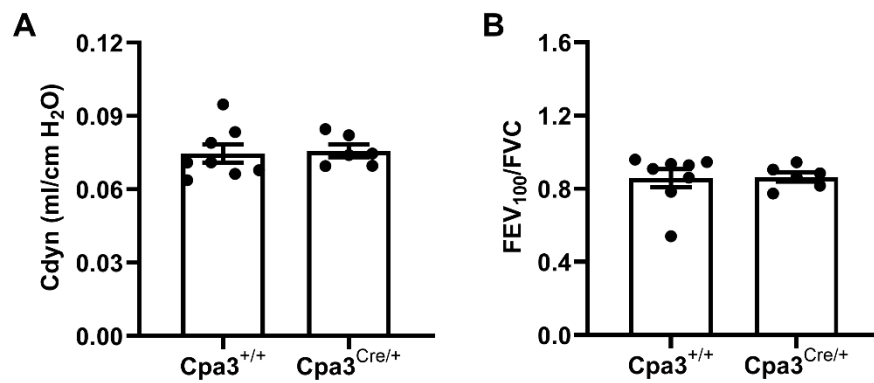
Supplementary Figure 2. A single elastase instillation causes slightly increased Cdyn and decreased FEV₁₀₀/FVC independently the ST2 receptor. (A) Mice received a single elastase or PBS administration and were analyzed 21 days later. (B) TLC, (C, E) Cdyn, and (D, F) FEV₁₀₀/FVC were determined. The data are shown as means \pm SEM. Data in (B-D) were obtained from 6-9 mice per group pooled from 2 individual experiments, and in (E, F) from 3-5 mice per group pooled from 2 individual experiments. Statistical significance was tested by unpaired Student's t-test. * $p < 0.05$.



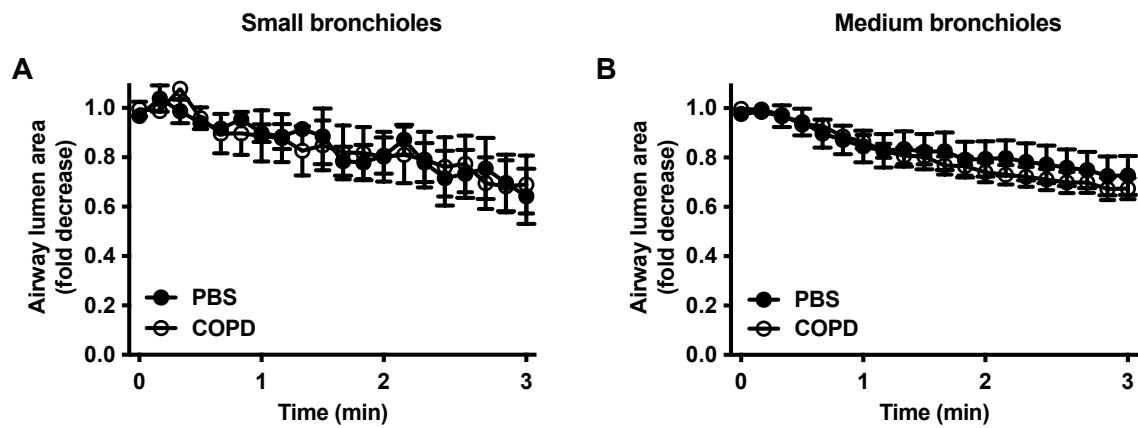
Supplementary Figure 3. Gating strategy for the identification of mature MCs and MC progenitors. Cells from dissociated lungs were stained using the antibodies described in Supplementary Table 1 and analyzed by flow cytometry. Mature MCs (mMC; CD45⁺ Lin⁻ c-kit^{hi} ST2⁺ FcεRI⁺ CD16/32⁺ Integrin β7^{lo} cells) and their progenitors (MCp; CD45⁺ Lin⁻ c-kit^{hi} ST2⁺ FcεRI⁺ CD16/32⁺ Integrin β7^{hi}) were identified.



Supplementary Figure 4. Gating strategy for the identification of mature MCs, MC progenitors, and basophils. Cells from dissociated lungs were stained using the antibodies described in Supplementary Table 1, and analyzed by flow cytometry. Mature MCs (mMC) were gated as CD45⁺ Lin⁻ c-kit^{hi} CD11b⁻ ST2⁺ FcεRI⁺ CD16/32⁺ Integrin β7^{lo} cells, MC progenitors (MCp) as CD45⁺ Lin⁻ c-kit^{hi} CD11b⁻ ST2⁺ FcεRI⁺ CD16/32⁺ Integrin β7^{hi} cells, and basophils as CD45⁺ Lin⁻ c-kit⁺ FcεRI⁺ CD49b⁺ cells.



Supplementary Figure 5. A single elastase instillation causes slightly increased Cdyn and decreased FEV₁₀₀/FVC independently of MCs. Mice received a single elastase administration and were analyzed 21 days later. **(A)** Cdyn and **(B)** FEV₁₀₀/FVC were determined. The data are shown as means \pm SEM. Data were obtained from 6-8 mice per group from a single experiment. Statistical significance was tested by unpaired Student's t-test. No statistically significant differences were found.



Supplementary Figure 6. Small- and medium-sized bronchioles from elastase/LPS-treated mice do not show AHR in response to methacholine challenge. PCLS were obtained from wildtype Balb/c mice subjected to elastase/LPS-induced COPD-like disease or given PBS as control. Time-lapse images of individual bronchioles were recorded every 10 s for 1 min before **(A)** small- ($<5\,000\,\mu\text{m}^2$ airway lumen area) and **(B)** medium-sized ($5\,000\text{--}15\,000\,\mu\text{m}^2$ airway lumen area) bronchioles were challenged with methacholine (MCh) and recorded for 3 more min. Airway narrowing after MCh challenge was determined as fold decrease from baseline. Data are shown as means \pm SEM from **(A)** 6–11 PCLS per group obtained from 3 PBS and 5 COPD mice pooled from four individual experiments, and **(B)** 19–37 PCLS per group obtained from 6 PBS and 10 COPD mice pooled from four individual experiments.

Supplementary Table 1. List of antibodies used in flow cytometry.

| Supplementary Figure 1 | | | |
|------------------------|-----------------|------------|----------------|
| Target molecule | Fluorochrome | Clone | Company |
| CD3 | PE | 17A2 | BD Biosciences |
| CD4 | PE-Cy5 | GK1.5 | Invitrogen |
| CD8b | BV510 | H35-17.2 | BD Biosciences |
| CD11b | FITC | M1/70 | BD Biosciences |
| CD11c | PE-Cy5 | N418 | Invitrogen |
| CD45 | Alexa Fluor 700 | 30-F11 | Invitrogen |
| Ly-6G | BV605 | 1A8 | BD Biosciences |
| Siglec-F | BV421 | E50-2440 | BD Biosciences |
| Supplementary Figure 3 | | | |
| Target molecule | Fluorochrome | Clone | Company |
| CD45 | Alexa Fluor 700 | 30-F11 | Invitrogen |
| c-kit | PE-Cy7 | 2B8 | Invitrogen |
| Lin: CD3 | PE-Cy5 | 17A2 | BD Biosciences |
| Lin: CD4 | PE-Cy5 | GK1.5 | Invitrogen |
| Lin: CD19 | PE-Cy5 | 1D3 | Invitrogen |
| Lin: B220 | PE-Cy5 | RA3-6B2 | Invitrogen |
| Lin: TER-119 | PE-Cy5 | TER-119 | Invitrogen |
| Lin: Gr-1 | PE-Cy5 | RB6-8C5 | Invitrogen |
| Lin: CD8b | PE-Cy5 | H35-17.2 | Invitrogen |
| Lin: CD11b | PE-Cy5 | M1/70 | Invitrogen |
| ST2 | BV421 | DIH9 | BioLegend |
| IgG2a (isotype) | BV421 | RTK2758 | BioLegend |
| FceRI | PE | MAR-1 | Invitrogen |
| IgG (isotype) | PE | eBio299Arm | eBioscience |
| CD16/32 | BV605 | 2.4G2 | BD Biosciences |
| Integrin B7 | FITC | FIB504 | Invitrogen |
| Supplementary Figure 4 | | | |
| Target molecule | Fluorochrome | Clone | Company |
| CD45 | Alexa Fluor 700 | 30-F11 | Invitrogen |
| c-kit | PE-Cy7 | 2B8 | Invitrogen |
| Lin: CD3 | BV510 | 17A2 | BD Biosciences |
| Lin: CD4 | BV510 | GK1.5 | BD Biosciences |
| Lin: CD19 | BV510 | 1D3 | BD Biosciences |
| Lin: B220 | BV510 | RA3-6B2 | BD Biosciences |
| Lin: TER-119 | BV510 | TER-119 | BD Biosciences |
| Lin: Gr-1 | BV510 | RB6-8C5 | BD Biosciences |
| Lin: CD8b | BV510 | H35-17.2 | BD Biosciences |
| FceRI | PE | MAR-1 | Invitrogen |
| IgG (isotype) | PE | eBio299Arm | eBioscience |

| | | | |
|-----------------|--------|--------|----------------|
| CD11b | PE-Cy5 | M1/70 | BD Biosciences |
| ST2 | BV786 | U29-93 | BD Biosciences |
| IgG2a (isotype) | BV786 | R35-95 | BD Biosciences |
| CD16/32 | BV605 | 2.4G2 | BD Biosciences |
| Integrin B7 | FITC | FIB504 | Invitrogen |
| CD49b | V450 | DX5 | BD Biosciences |