Supplementary Figure 1. Phagocytosis of apoptotic cells by airway epithelial cells results in production of bioactive TGF-β.

a, Production of TGF-β, (n=5), and PGE₂, (n=4) by mouse (MLE-12) epithelial cells after apoptotic cell recognition, * p<0.05, student’s t-test. b, Luciferase assay measuring active TGF-β in supernatants collected from MLE-12 cells cultured with apoptotic cells (AC) in the presence or absence of annexin V (10 μg/ml), n=3, representative graph of at least two experiments performed in duplicate. The supernatants from MLE cells stimulated with apoptotic cells were incubated with a TGF-β responsive PE25 cell line. PE25 cells have been stably transfected with two tandems copies of a 36-base pair fragment containing Smad-binding elements (SBEs) of the human PAF promoter. Error bars indicate s.e.m.
Supplementary Figure 2. Generation of inducible Rac1 deficient mice in bronchial epithelial cells.

a, Schematic depicting the generation of conditional Rac1 transgenic mice. b, H&E staining of lung sections showing comparable appearance of a large airway from Control/Rac1^{fl/fl} and CCSP-Cre/Rac1^{fl/fl} mice. c, (Left) The basal levels of TGF-β production in BAL fluid was tested from naïve CCSP-Cre/Rac1^{fl/fl} mice treated with or without doxycycline for one week in drinking water (1mg ml^{-1}); (right), levels of TGF-β in BAL fluid of Rac1^{fl/fl} mice expressing either the cre transgene or the ccsp transgene. The data are from one experiment representative of two independent experiments, with n=3 mice/group. Error bars indicate s.e.m.
Supplementary Figure 3. Gating strategy for sorting bronchial epithelial cells.

Flow cytometry showing the sorting strategy used in the CCSP/Rac1<sup>fl/fl</sup> Rosa26<sup>STOP-YFP</sup> mice, a, or CCSP-Cre/Rac1<sup>fl/fl</sup> Rosa26<sup>STOP-YFP</sup> mice, b, Rac1 was successfully deleted in the YFP<sup>hi</sup> EpCAM<sup>hi</sup> population. This YFP<sup>hi</sup> EpCAM<sup>hi</sup> population was used to set the gate for some of the engulfment experiments in Figure 1, as this population shows the highest degree of Rac1 deletion. c, Comparable levels of Rac1 in CD45 positive cells purified from CCSP/Rac1<sup>fl/fl</sup> Rosa26<sup>STOP-YFP</sup> (white bars) or CCSP-Cre/Rac1<sup>fl/fl</sup> Rosa26<sup>STOP-YFP</sup> (red bars) mice, n=5 mice per group. Error bars indicates s.e.m.
Supplementary Figure 4. Rac1 deletion in bronchial epithelial cells does not affect the integrity of the airways.

**a.** Left, cultured monolayer of bronchial epithelial cells (Clara cells) purified from the lungs of Control/Rac1^{fl/fl} mice. We confirmed the purification of Clara cells by staining with nitrotetrazolium; right, graph showing comparable numbers of purified epithelial cells from Control/Rac1^{fl/fl} or CCSP-Cre/Rac1^{fl/fl} mice, n=4 mice per group of at least three independent experiments. **b.** Vascular permeability was measured using Evan’s blue method from the lungs of Control/Rac1^{fl/fl} or CCSP-Cre/Rac1^{fl/fl} mice, n=3 mice per group of two independent experiments. **c.** Epithelial cell monolayers showing occludin staining (green). We found no difference in the pattern of occludin staining between epithelial cells purified from Control/Rac1^{fl/fl} or CCSP-Cre/Rac1^{fl/fl} mice, CCSP (red) and Dapi (blue). This experiment was done at least two times with similar results. **d.** Representative immunofluorescence staining of occludin in lung sections from Control/Rac1^{fl/fl} or CCSP-Cre/Rac1^{fl/fl}; the micrograph shown is representative of at least two independent experiments, with two mice per group in each experiment.
Supplementary Figure 5. Rac1 deletion in bronchial epithelial cells does not compromise the formation of tight junctions or the ability to capture soluble antigen.

a, Transmission electron micrograph (TEM) of lung sections from Control/Rac1<sup>1<sup>−/−</sup></sup> or CCSP-Cre/Rac1<sup>1<sup>−/−</sup></sup> mice showing tight junctions and desmosomes (arrows), magnification 4,000x or 20,000x upper panels.

b, Gating strategy used for identifying epithelial cells, alveolar macrophages and dendritic cells.

c, Fluorescently labeled-HDM or Ovalbumin was delivered intranasally to Control/Rac1<sup>1<sup>−/−</sup></sup> or CCSP-Cre/Rac1<sup>1<sup>−/−</sup></sup> mice for 1 hour; dendritic cells, alveolar macrophages and epithelial cells were gated based on surface markers and analyzed for antigen uptake by flow cytometry. Data shown are representative histograms of two independent experiments performed with three mice in each group.
Supplementary Figure 6. Airway epithelial cells from Rac1 deficient mice have impaired phagocytosis of apoptotic cells in vivo.

a, Left, gating strategy used for analyzing engulfment of apoptotic cells by lung epithelial cells. Right, graph showing the percentage of internalized apoptotic cells by YFP^+ bronchial epithelial cells form CCSP-Cre/Rac1^fl/fl (red bars) or Control/Rac1^fl/fl (open bars) mice, n=9 mice combined from 2 independent experiments.

b, Left, gating strategy for analyzing engulfment of apoptotic cells by alveolar macrophages. Right, graph showing the percentage of internalized apoptotic cells by alveolar macrophages, n=6 mice from 2 independent experiments. *P < 0.05, unpaired student’s t-test with Welch’s correction. Error bars represent s.e.m.
Supplementary figure 7. Exacerbated inflammation and Th2 response in Rac1 deficient mice sensitized via the peritoneal route.

(a) Schematic depicting the protocol used for inducing airway inflammation. **b**, Absolute numbers of infiltrating CD4 T cells, eosinophils, levels of TGF-β in BAL fluid of Control/Rac1+/− or CCSP-Cre/Rac1+/−, n=8-9 mice combined from 3 independent experiments. The levels of IgE in the serum were also higher in mice deficient in Rac1, n=3 mice per group. (c) Cytokine production by MLN cells restimulated in vitro for 5d with 10 μg ml−1 of HDM. n=6 mice per group, combined from two independent experiments. (d) Lung function analysis of airway resistance, compliance and pulmonary pressure in CCSP-Cre/Rac1+/− mice (red triangles) or Control/Rac1+/− (open triangles), n=7-10 mice per group combined from 2 independent experiments. (e) Representative H&E staining of lung sections showing increased inflammation in CCSP-Cre/Rac1+/− mice challenged with HDM. The mice were sensitized and challenged with the cysteine protease Der p1. (f) IgE and IgG1 levels in the serum of mice sensitized and challenge with Der p1, n=5 mice per group combined from 2 experiments. *P < 0.05, **P < 0.01, unpaired student’s t-test with Welch’s correction (b,c,d,f).
Supplementary figure 8. Deletion of Rac1 in myeloid cells does not result in exacerbated airway inflammation.

a, Rac1 and Rac2 mRNA expression in bone marrow derived macrophages (BMDM) from Lys-M/Cre-Rac1 mice (for deletion of Rac1 in myeloid cells), n=2 mice per group from two independent experiments performed in duplicates. 
b, Levels of IL-10 and TGF-β in BAL fluid of Lys-M/Cre-Rac1fl/wt or Lys-M/Cre-Rac1fl/fl mice that received apoptotic cells intranasally for 18h, n=5 mice per group combined from 2 experiments. 
c, Schematic depicting the protocol used to induce airway inflammation in Lys-M/Cre-Rac1 mice. 
d, BAL fluid analysis of infiltrating T-cells, eosinophils and Th2-type cytokines in Lys-M/Cre-Rac1fl/wt or Lys-M/Cre-Rac1fl/fl mice, n=6 mice per group, from two experiments. *P < 0.05, unpaired student’s t-test (d). Error bars represent s.e.m.
Supplementary Figure 9. Rac1 expression is necessary during the priming stage for preventing airway the sensitization to allergens.

a, Schematic showing the protocol used to induce airway inflammation and the temporal deletion of Rac1 in the airways. CCSP-Cre/Rac1<sup>fl/fl</sup> mice exposed to doxycycline to delete Rac1 either in the priming or the challenge phases were primed and challenged with low-endotoxin HDM. b, BAL fluid analysis of infiltrating CD4<sup>+</sup> T cells and eosinophils in to the airways. Deleting Rac1 during the priming stage is sufficient to induce exacerbated leukocyte infiltration. c, Cytokine analysis of IL-4, IL-5 and IL-13 in BAL fluid of CCSP-Cre/Rac1<sup>fl/fl</sup> mice. b and c, n=5 mice, combined from 2 independent experiments. *P < 0.05, **P < 0.01, unpaired student’s t-test (b and c). Error bars represent s.e.m.
Supplementary Figure 10. Respond to methacholine challenge in Control/Rac1<sup>fl/fl</sup> and CCSP-Cre/Rac1<sup>fl/fl</sup> mice.

**a.** Increased airway resistance in 8-week-old CCSP-Cre/Rac1<sup>fl/fl</sup> (red triangles) compared to Control/Rac1<sup>fl/fl</sup> (open triangles) mice after challenged with increasing doses of methacholine. **b.** Control/Rac1<sup>fl/fl</sup> mice either primed and challenged with HDM (open triangles) or PBS (red squares) responded to methacholine at higher doses, (a, b, n=5 mice per group of 2 independent experiments). Error bars represent s.e.m.
**Supplementary Figure 11. Intranasal priming with ovalbumin in wild type mice results in minimal airway inflammation.**

*a*, Production of IL-4, IL-5 and IL-13 in the airways of Control/Rac1<sup>+/−</sup> mice primed with ovalbumin either intranasally or via the peritoneal route. Mice primed intranasally produced lower levels of Th2 cytokines compared to Control/Rac1<sup>+/−</sup> mice primed in the peritoneum, n=5 mice per group, and data combined from two independent experiments. *P < 0.05*, unpaired student’s *t*-test.
Supplementary Figure 12. Rac1 deficient mice contain higher levels of IL-5 expressing nuocytes, and treatment with anti-IL-33 antibody reduces Rac1-dependent inflammation.

a, Left, Bar graph showing increased IL-5 production in BAL fluid from CCSP-Cre/Rac1<sup>−/−</sup> (red bars) or control (open mice) after HDM priming (for 5 days, see schematic in Figure 2a). Right, representative graph showing increased frequency of lung IL-5<sup>+</sup> nuocytes in CCSP-Cre/Rac1<sup>−/−</sup> (red bars) compared to control (open bars) mice. Data shown are from 6 mice per group, combined from two independent experiments. b, Representative plot showing the percentage of CD4<sup>+</sup> T cells expressing IL-5 in the lung does not change after HDM priming. c, Upper, mediastinal lymph nodes excised from control and CCSP-Cre/Rac1<sup>−/−</sup> mice that were treated intranasally with anti-IL-33 (6.5 μg/mouse/dose) during HDM priming and challenge. Below, combined data from two independent experiments showing the cellularity of mediastinal lymph nodes from control (open triangles) or CCSP-Cre/Rac1<sup>−/−</sup> mice primed and challenge with HDM and treated with anti-IgG (red squares) or anti-IL-33 antibody (open squares). d, Absolute numbers of infiltrating activated T cells and eosinophils from control (open triangles) or CCSP-Cre/Rac1<sup>−/−</sup> mice, primed and challenge with HDM and treated with anti-IgG (red squares) or anti-IL-33 antibody (open squares). Data from seven mice per group (from two independent experiments) were combined. *<i>P</i> < 0.05, unpaired student’s <i>t</i>-test. Error bars represent s.e.m.
Supplementary Figure 13. IL-33 expression in response to apoptotic cells depends on Rac1 signaling.
IL-33 (a) or TGF-β (b) expression in mouse alveolar epithelial cells treated with a specific Rac1 inhibitor EHT1864 (30 μM) and stimulated with HDM or apoptotic cells. n=5, representative of three independent experiments. * P < 0.05, student’s t-test, error bars indicate s.e.m.
Supplementary Figure 14. Gating strategy for the identification of activated CD4⁺ T cells and eosinophils.

Cells recovered from the BAL fluid or total lungs were stained for CD4⁺ T cells and eosinophils (CD11b⁺ Siglec F⁺ CD11c⁻ cells). The absolute numbers were derived using reference particles (Spherotec), right.