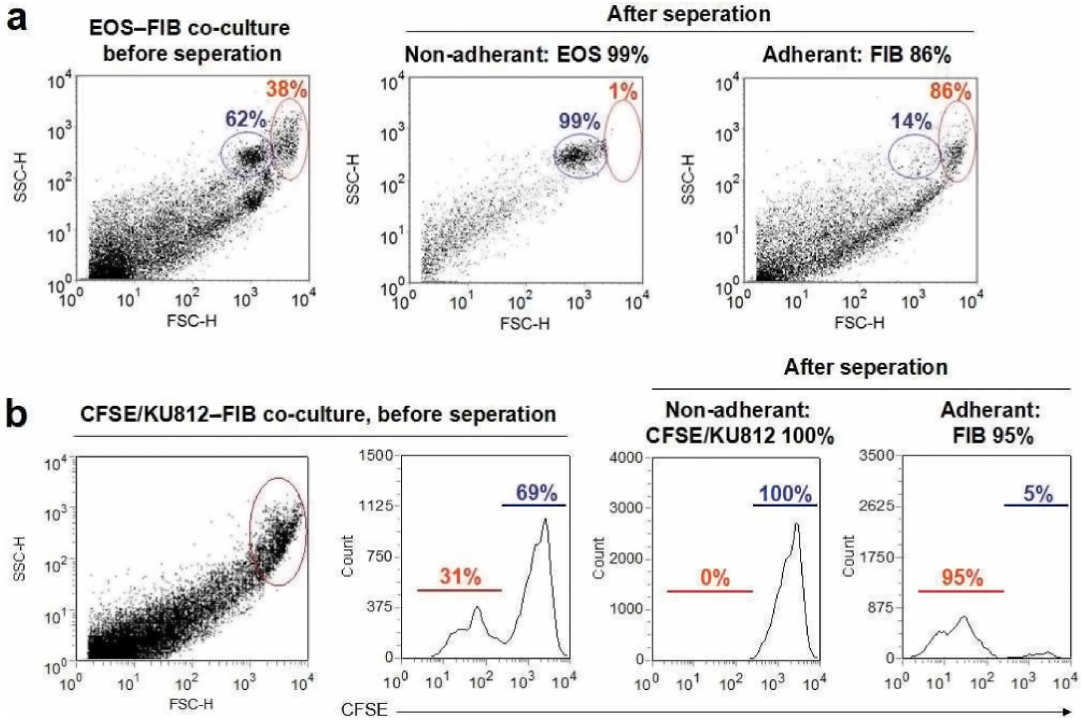
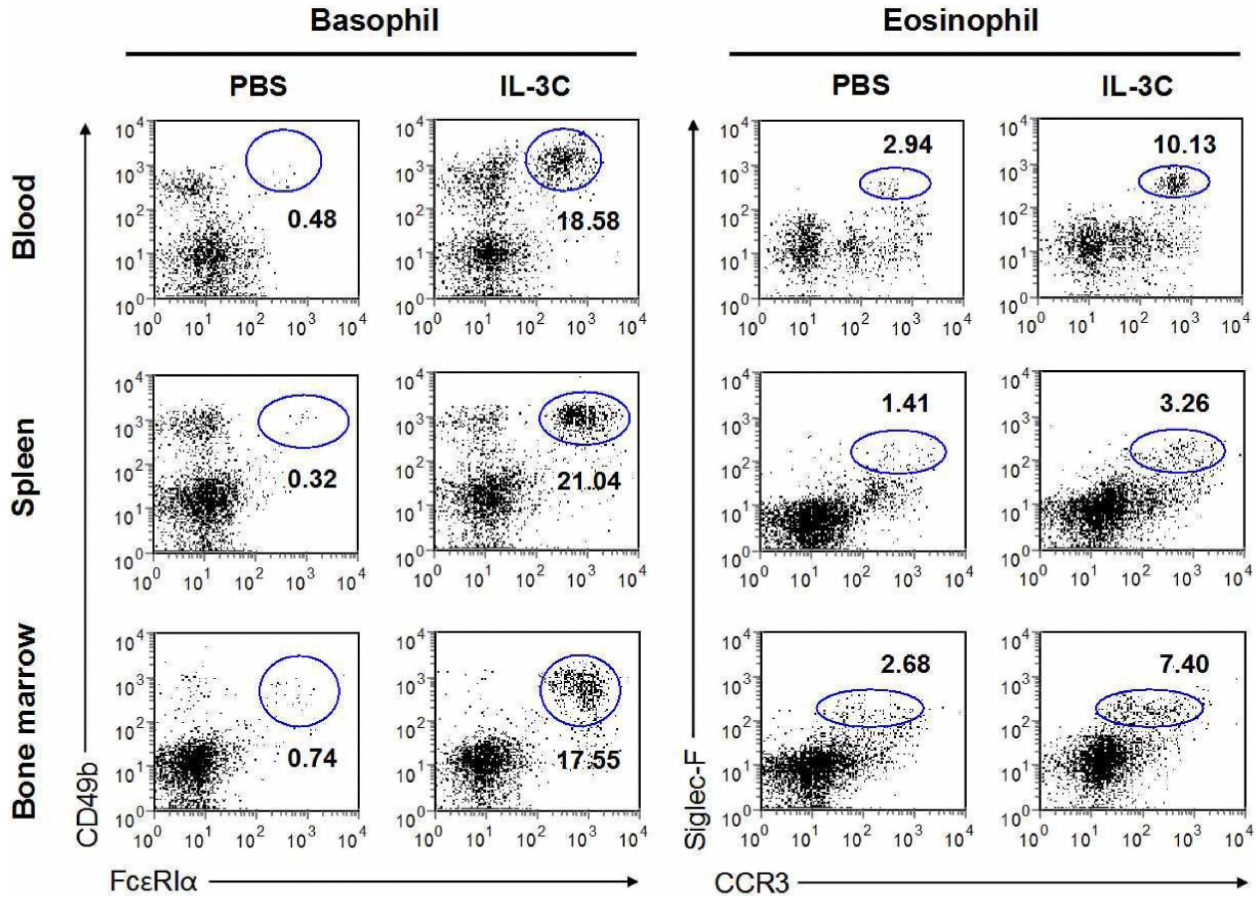
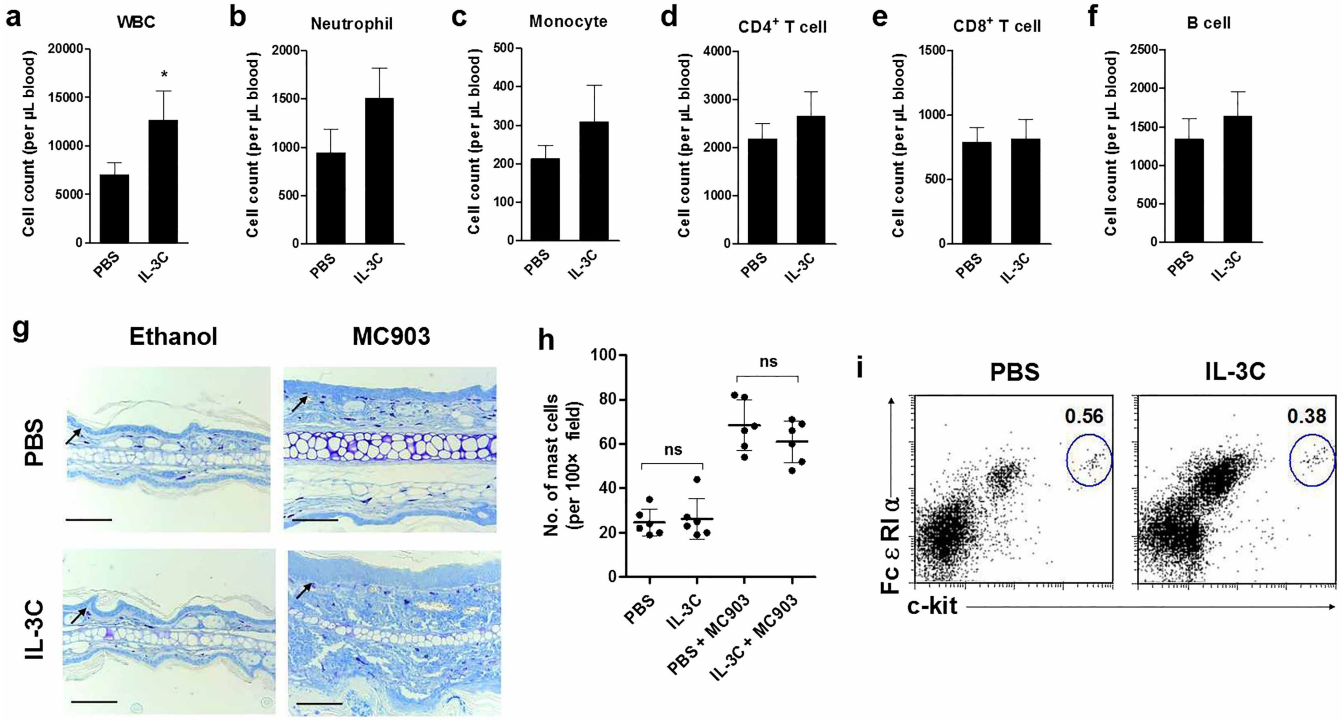


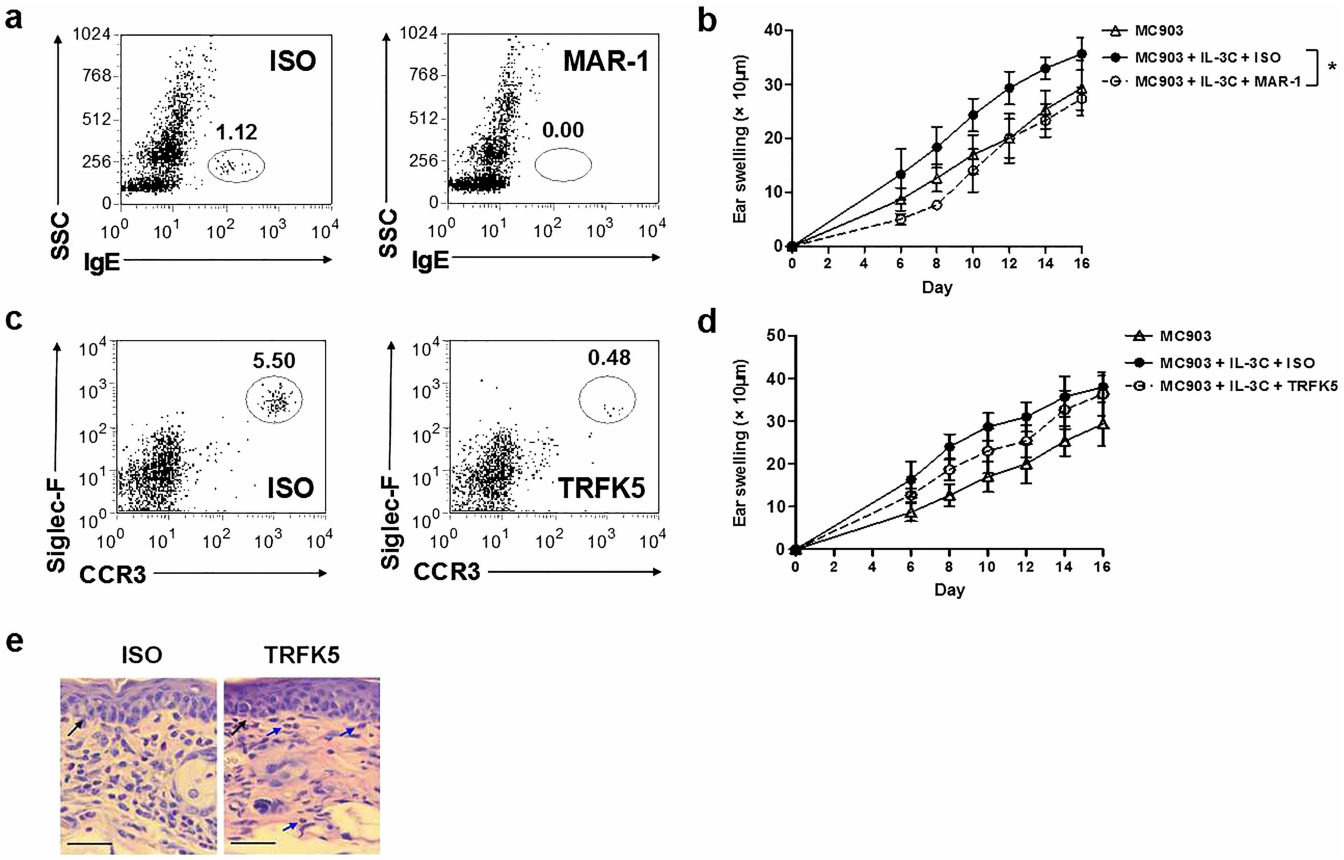
Supplementary Figure S1 Analysis of the purity of the separated cells in co-culture. (**a**) Co-cultured eosinophils and dermal fibroblasts were separated by rinsing five times with large volumes of ice-cold PBS, and the non-adherent and adherent cells were analyzed by flow cytometry and presented with representative dot plots. (**b**) Likewise, carboxyfluorescein succinimidyl ester (CFSE) tracing marker-labeled KU812 cells were co-cultured, separated, and analyzed. Representative histograms were presented with relative cell counts and MFI.



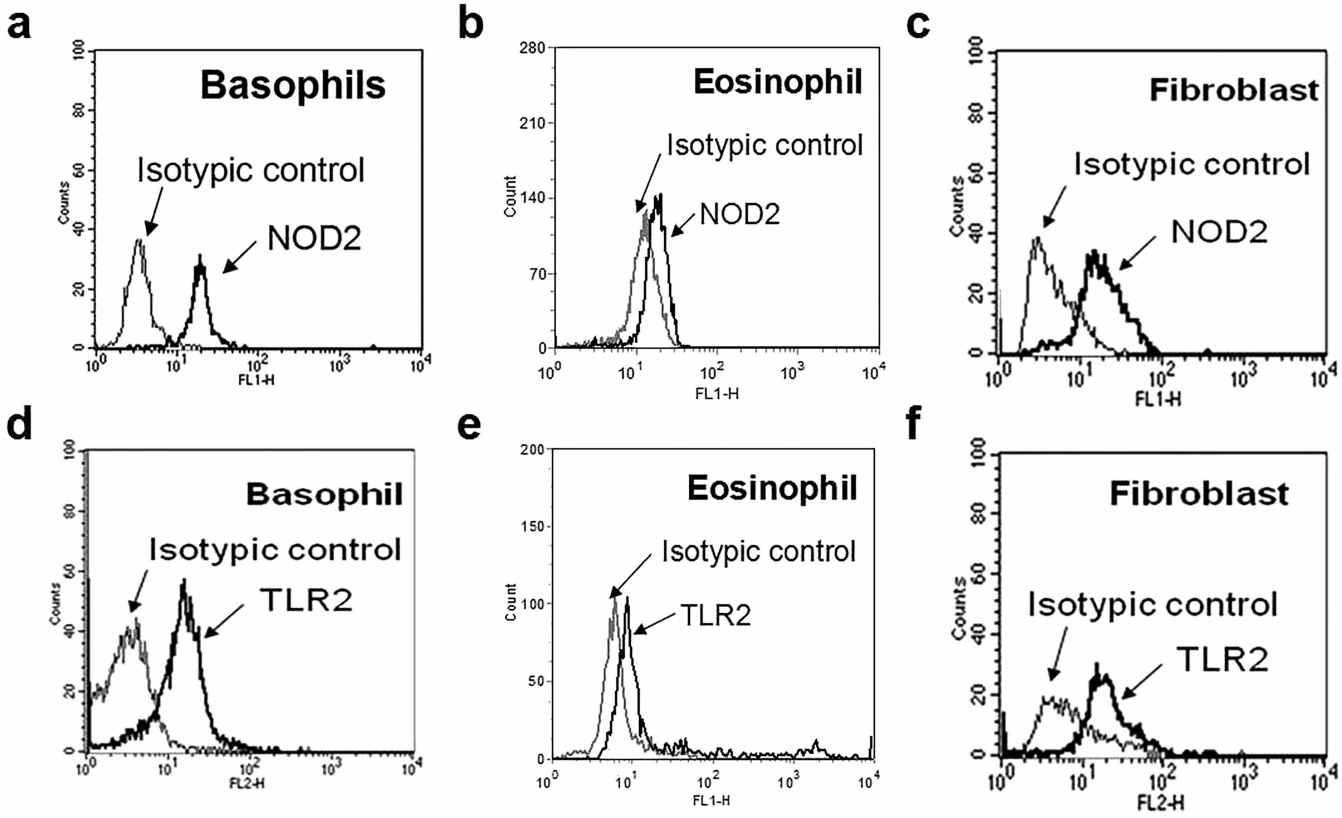
Supplementary Figure S2 Representative dot plots of the flow cytometric analysis of basophils and eosinophils in PBS/IL-3C-treated mice.



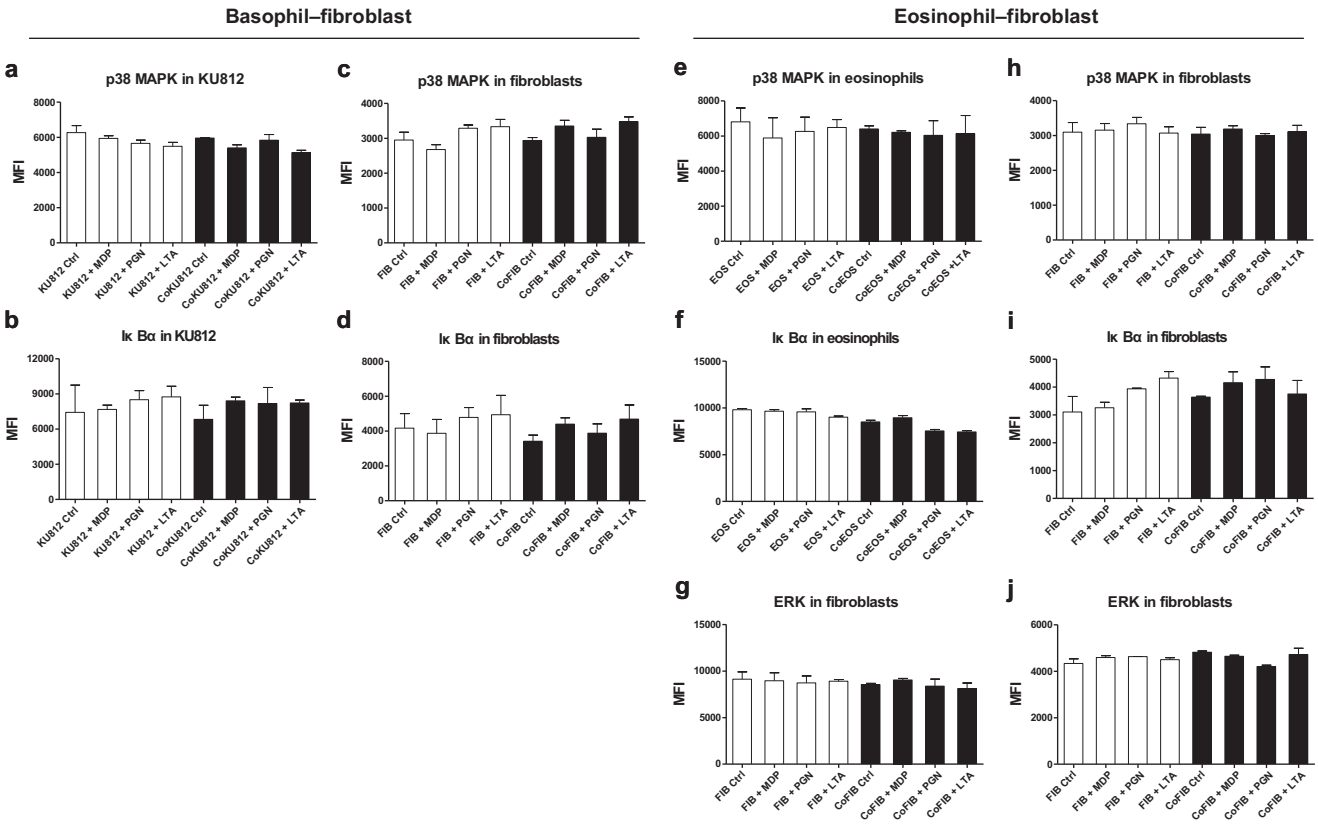
Supplementary Figure S3 IL-3C treatment does not affect non-basophilic, non-eosinophilic blood cells, and mast cells. (**a**–**f**) White blood cell counting (**a**) and blood cell counting of neutrophils (**b**), monocytes (**c**), CD4$^+$ T cells (**d**), CD8$^+$ T cells (**e**), and B cells (**f**) were performed for PBS/IL-3C-treated mice. (**g**) Detection of mast cells in the skin after the treatment of IL-3C and MC903 by using toluidine blue staining. Black arrows point to the dermal/epidermal junction. Scale bars = 150 μm. (**h**) Numbers of mast cells presented in the skin after the treatment of IL-3C and MC903. (**i**) Representative flow cytometric analysis of mast cells in the peritoneum. Results are shown as the arithmetic mean ± SD.



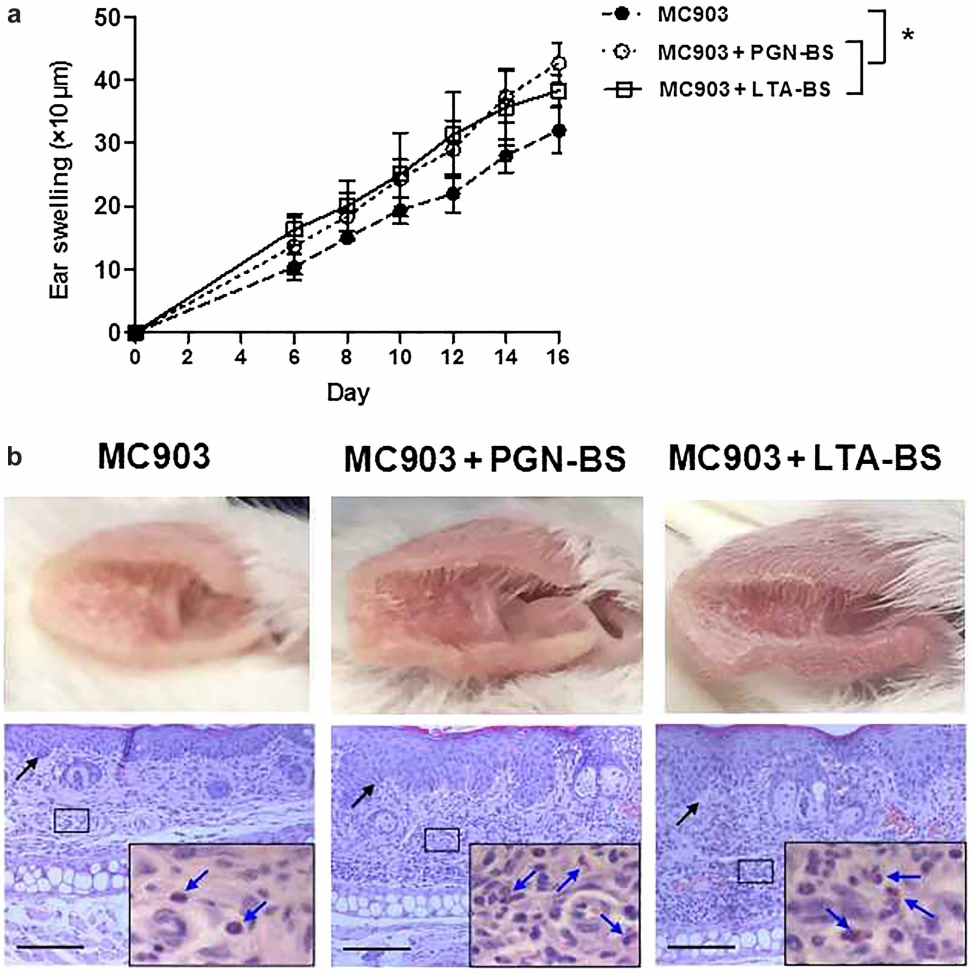
Supplementary Figure S4 Role of basophils and eosinophils in IL-3C-aggravated skin inflammation. (**a**) Representative flow cytometric analysis of basophils in MAR-1-treated mice. (**b**) Ear thickness was measured before topical administration of MC903 in IL-3C and MAR-1-treated mice. (**c**) Representative flow cytometric analysis of eosinophils in TRFK5-treated mice. (**d**) Ear thickness was measured before topical administration of MC903 in IL-3C and TRFK5-treated mice. (**e**) The detection of eosinophils in the skin after the treatment with MC903 and TRFK5 by using H&E staining. Black arrows point to the dermal/epidermal junction, blue arrows point to the eosinophils. Scale bars = 50 μm. Results are shown as the arithmetic mean ± SD. *$P < 0.05$.



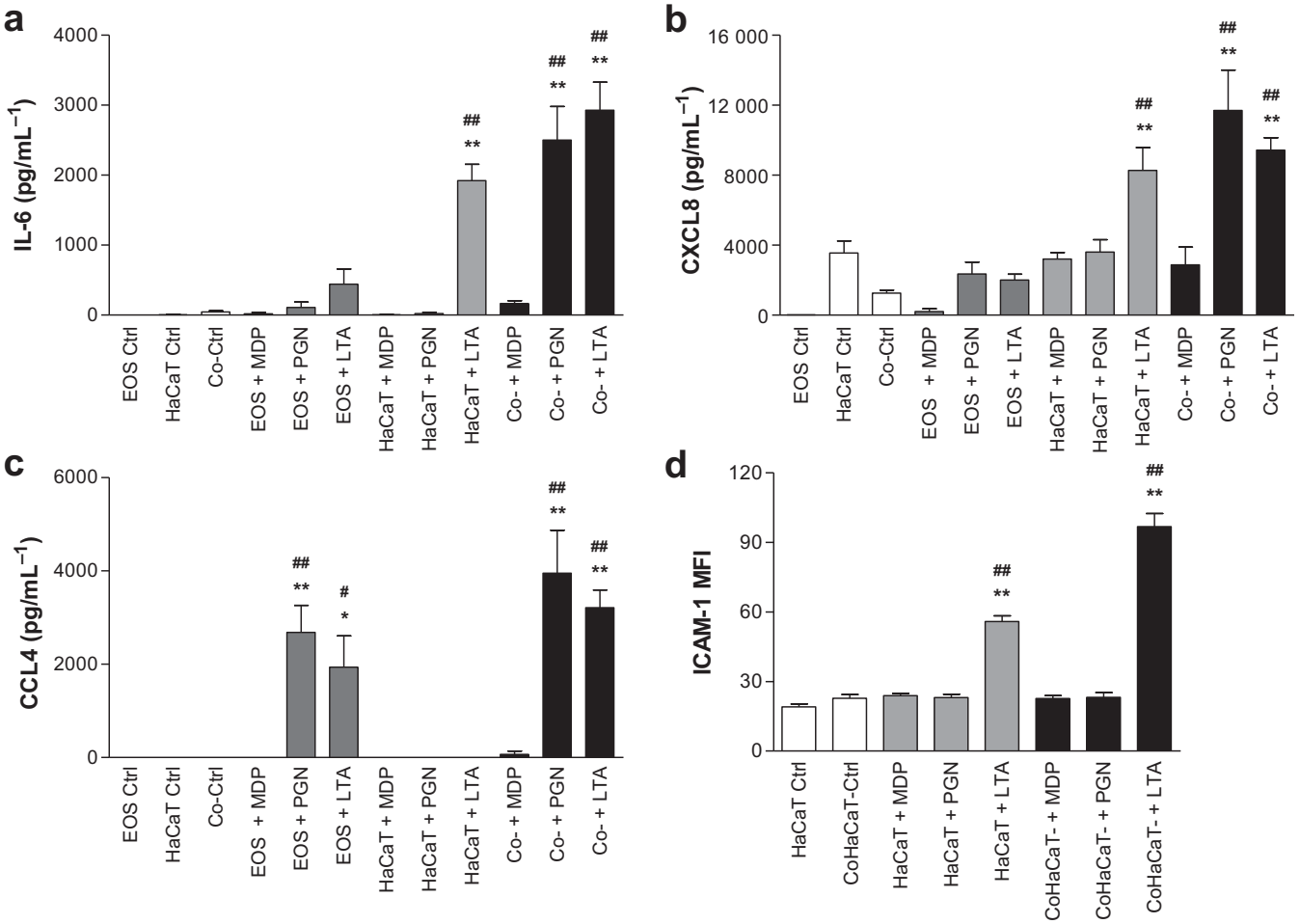
Supplementary Figure S5 Human basophils, eosinophils and dermal fibroblasts constitutively express NOD2 and TLR2. Intracellular expression of NOD2 and surface expression of TLR2 were determined by flow cytometry. Representative histograms were presented with relative cell counts and MFI.



Supplementary Figure S6 Measurements of the intracellular total signaling molecules shown in Figure 6. (**a**–**d**) KU812 cells and dermal fibroblasts were cultured either together or separately with or without NOD2/TLR2 ligands for 10 min. Intracellular total p38 MAPK and IκBα in KU812 cells and fibroblasts were determined by using Multiplex assay. (**e**–**j**) Likewise, eosinophils and dermal fibroblasts were cultured and stimulated. Intracellular total p38 MAPK, IκBα, and ERK in eosinophils and fibroblasts were determined. Results are expressed as MFI and shown as arithmetic mean ± SD.



Supplementary Figure S7 Topical *Bacillus subtilis* (BS)-derived PGN and LTA exacerbate AD-like symptoms. (**a**) Ear thickness was measured before the topical application of MC903 or MC903 plus PGN/LTA from BS. (**b**) Photographs were taken and H&E staining was performed for the ears on day 16. Blue arrows point to eosinophils. Black arrows point to the dermal/epidermal junction. Scale bars = 150 μm. Results are shown as the arithmetic mean ± SD. $*P < 0.05$.



Supplementary Figure S8 NOD2/TLR2 ligands activate human eosinophils in co-culture with human keratinocyte HaCaT cells. (**a**–**d**) Eosinophils and HaCaT cells were cultured either together or separately with or without NOD2/TLR2 ligands for 20 h. Release of IL-6 (**a**), CXCL8 (**b**), and CCL4 (**c**) was determined. (**d**) ICAM-1 expression on HaCaT cells was analyzed by flow cytometry and shown as MFI. EOS, eosinophils; Co, co-culture of HaCaT cells with eosinophils; CoHaCaT, HaCaT cells in co-culture. Results are shown as arithmetic mean ± SD. $*P < 0.05$, $**P < 0.01$ when compared between denoted groups and eosinophil (**a**–**c**), or HaCaT cell (**d**) control groups. $^{\#}P < 0.05$, $^{\#\#}P < 0.01$ when compared between denoted groups and co-culture control groups.