Figure S1. Gating strategy and IL-33 expression across lung immune and structural cells. (A) Flow cytometry gating strategy used to identify and analyze distinct immune cell population from mouse lungs. Cell types were defined as follows: Neu ($CD45^+Ly6G^+$ from P4); B cells ($CD45^+Ly6G^-CD11b^-CD11c^-CD24^+MHC\text{-}II^+$); macrophage (MΦ: $CD64^+CD24^-$ from P7); Eos ($MHC\text{-}II^{low}CD11b^+$ from P14) and DCs ($MHC\text{-}II^{high}$ from P14). Proportions of (B) Macrophage (MΦ) and (C) B cells. Flow cytometric analysis of (D) $IL\text{-}33^+$ MΦ and (E) IL-33 MFI in macrophage. Flow cytometric analysis of (F) $IL\text{-}33^+$ DCs and (G) IL-33 MFI in DCs. (H and I) IL-33 MFI in epithelial cells, endothelial cells and fibroblasts. Data are presented as the mean ± standard deviation (n=6). $^*P<0.05$, $^{**}P<0.01$ and $^{***}P<0.001$ were obtained by one-way ANOVA followed post calculation. Neu, neutrophils; Eos, eosinophils; DCs, dendritic cells; MFI, mean fluorescence intensity.

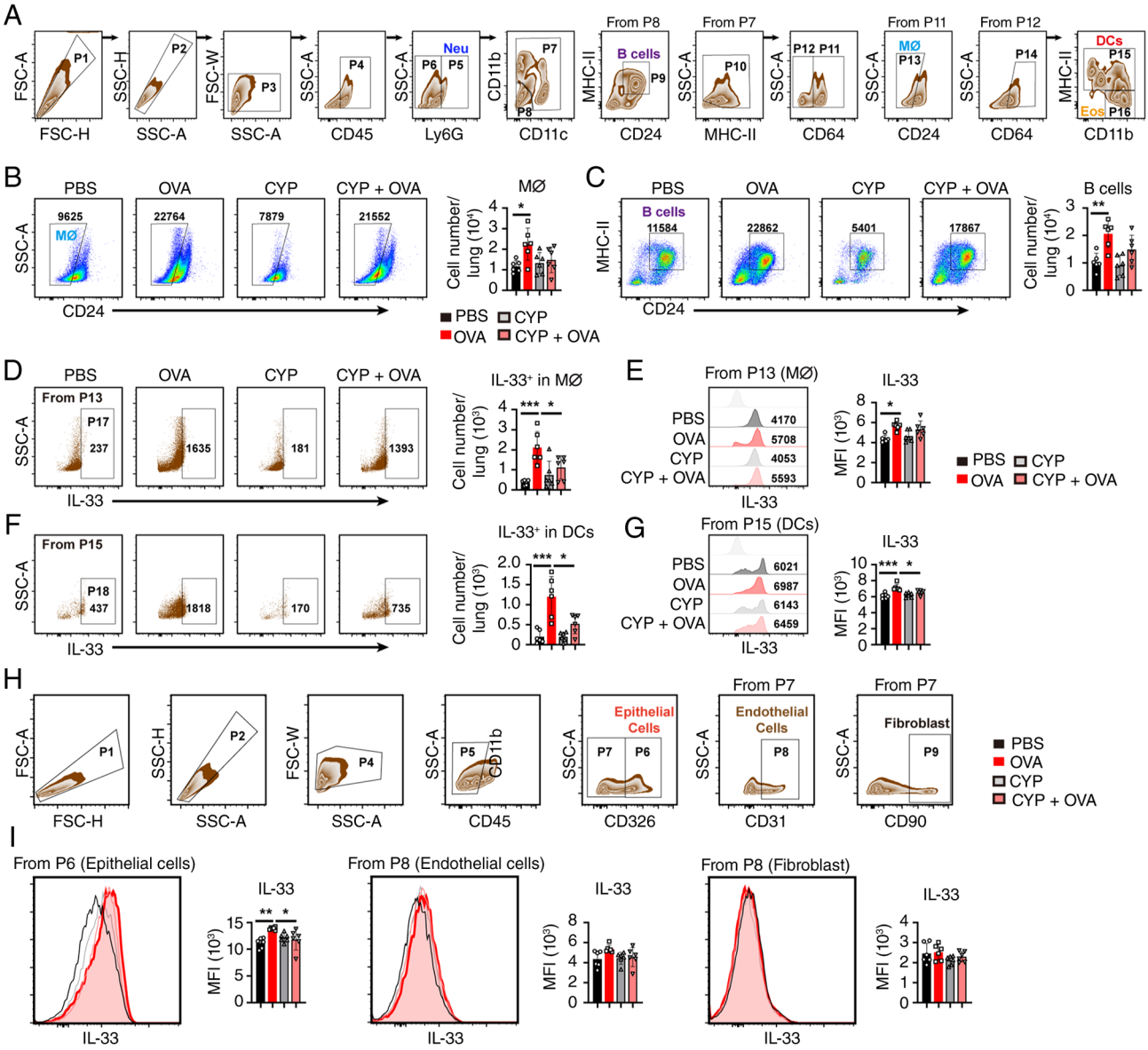

Figure S2. Flow cytometry gating strategies for mice lung tissue cells: (A) Gating strategy for Basophils (Lineage$^-$FcERI$^+$ CD11b$^+$c-Kit$^-$) and mast cells (Lineage$^-$FcERI$^+$CD11b$^-$c-Kit$^+$). (B) Identification of ILC2 (Lineage$^-$c-Kit$^-$SCA-1$^+$CD25$^+$). ILC2, group 2 innate lymphoid cells.

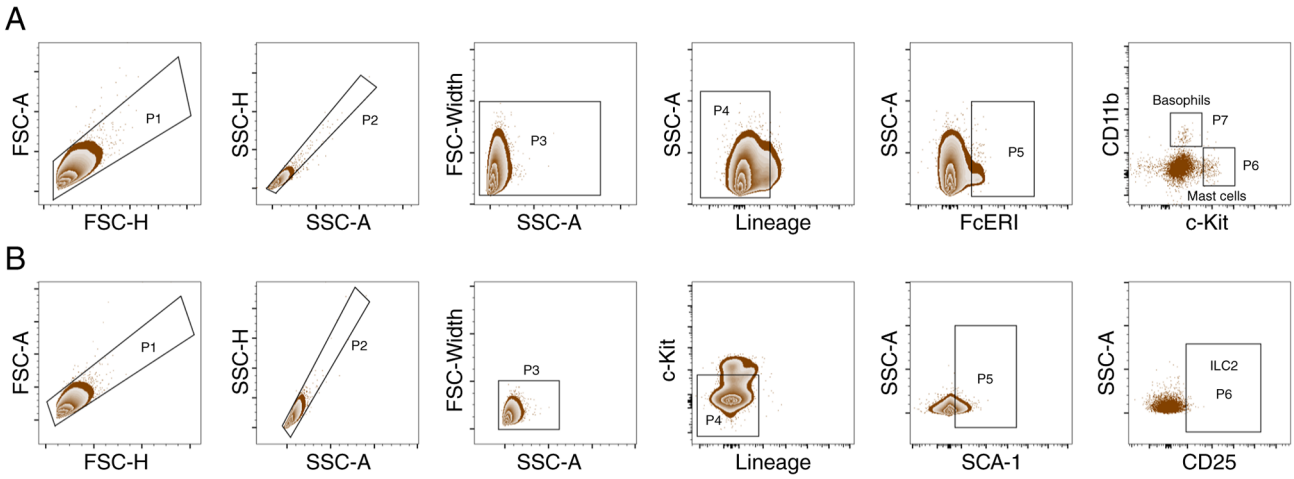

Figure S3. Western blot analysis of STAT5/6, p38 and ERK1/2 signaling in dendritic cells stimulated with OVA in the presence or absence of CYP. CYP, α-Cyperone; OVA, ovalbumin.

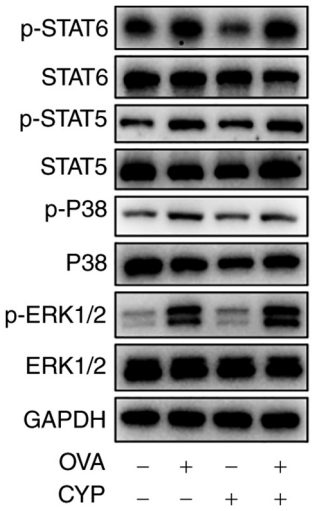

Figure S4. IL-33 inhibition attenuates OVA-induced allergic inflammation and immune cell maturation in asthmatic mouse lungs. An OVA-induced allergic asthma mouse model was utilized, with or without anti-mouse-IL-33 antibody treatment. (A and B) Representative H&E-stained and (C and D) PAS-stained lung tissue sections from the indicated experimental groups. The inflammation index and the percentage of goblet cells were quantified across six randomly selected fields per section used to quantify. (E-H) Flow cytometric analysis of pulmonary immune cells, gated according to previously described strategies: The immune cells are identified as: (E) Neu ($CD45^+Ly6G^+$ from P4); (F) Macrophage (MΦ, $CD64^+CD24^-$ from P7); (G) B cells ($CD45^+Ly6G^-CD11b^-CD11c^-CD24^+MHC\text{-}II^+$); (H) Eos ($MHC\text{-}II^{low}CD11b^+$ from P12) and DCs ($MHC\text{-}II^{high}$ from P12). (I) Flow cytometric quantification of $CD86^+$ mature DCs in the lung tissues. (J) Frequencies of basophils ($Lineage^-FcERI^+CD11b^+c\text{-}Kit^-$) and mast cells ($Lineage^-FcERI^+CD11b^-c\text{-}Kit^+$). Data are presented as the mean ± standard deviation (n=6). $^*P<0.05$, $^{**}P<0.01$ and $^{***}P<0.001$ were obtained by one-way ANOVA followed post calculation. OVA, ovalbumin; CYP, α-Cyperone; PAS, periodic acid-Schiff; Neu, neutrophils; Eos, eosinophils; DCs, dendritic cells; MHC-II, major histocompatibility complex class II.

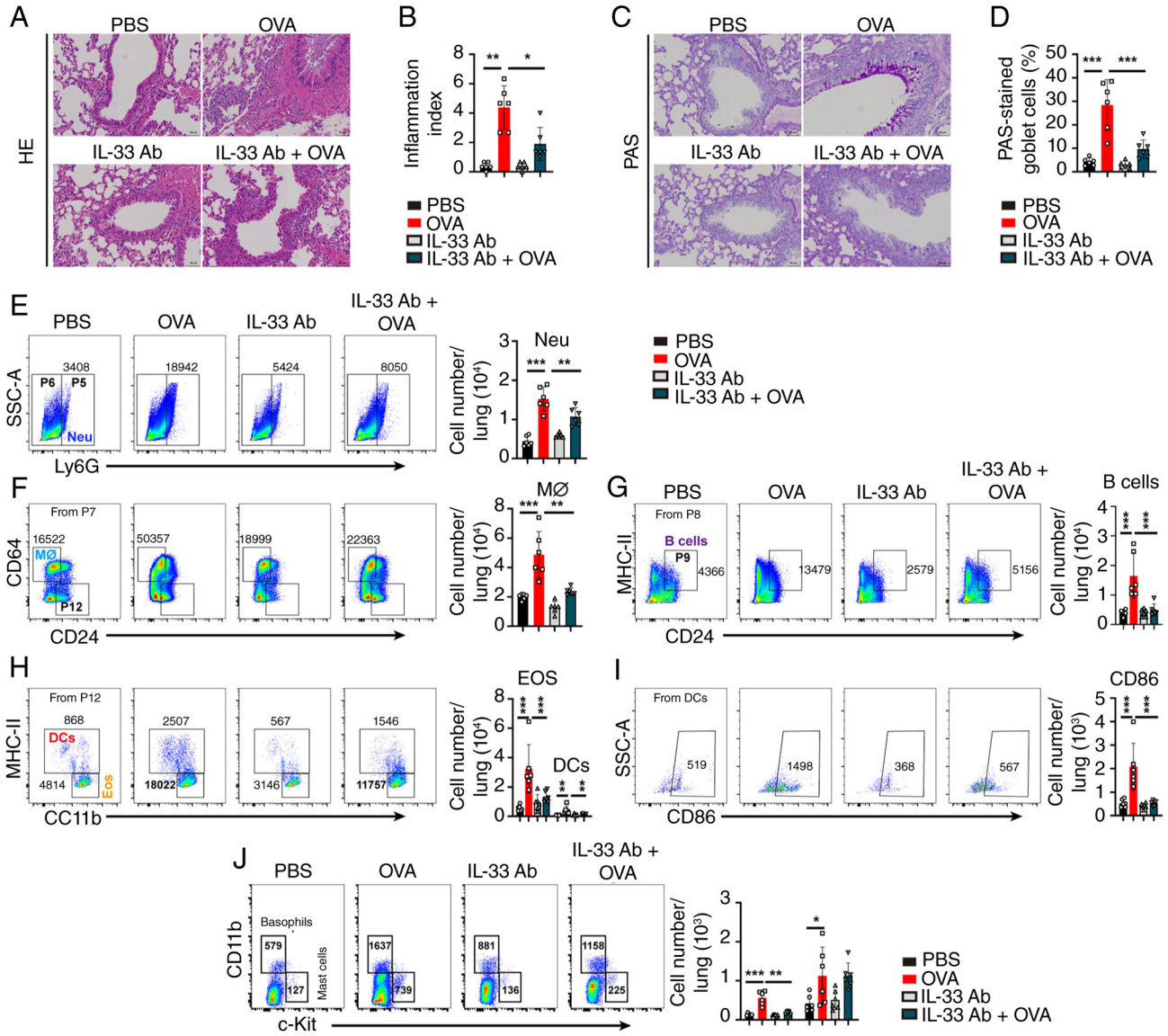

Figure S5. IL-33 regulates Th2/Th9 cell differentiation *in vivo*. (A) The flow cytometric analysis of T helper cell subtype from the lung tissue of the indicated experimental mouse groups. The primary gating strategy was applied as aforementioned to identify $CD45^+CD3^+CD4^+IFN\text{-}\gamma^+$ Th1, $CD45^+CD3^+CD4^+IL\text{-}4^+$ Th2, $CD45^+CD3^+CD4^+IL\text{-}9^+$ Th9 and $CD45^+CD3^+CD4^+IL\text{-}17A^+$ Th17 cells. (B) Absolute cell numbers of Th1/Th2/Th9/Th17 subsets in lung tissue. (C) Percentages of Th1/Th2/Th9/Th17 cells relative to the total $CD4^+CD3^+$ cell T cell population. (D) ELISA quantification of Il-4, Il-13 and Il-9 levels in mice lung homogenates. Data are shown as the mean ± standard deviation (n≥3). $^*P<0.05$, $^{**}P<0.01$ and $^{***}P<0.001$ were obtained by one-way ANOVA followed post analysis. OVA, ovalbumin; ns, not significant.

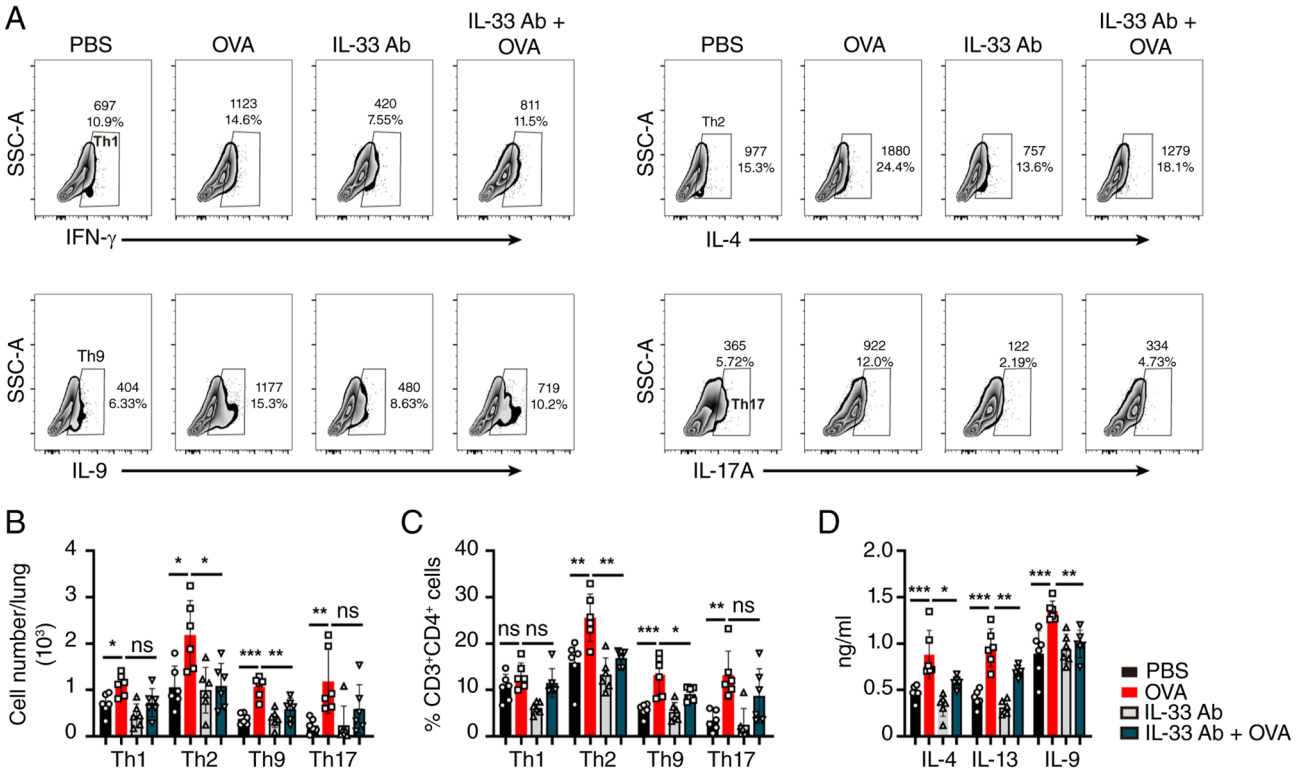

Figure S6. Molecular docking analysis of CYP binding to mouse PAK1 protein at positions (A) Lys141, (B) Ser402 and (C) Thr423. The binding energies (docking score) below threshold of -5 kcal/mol indicate strong binding affinity. CYP, α-Cyperone.