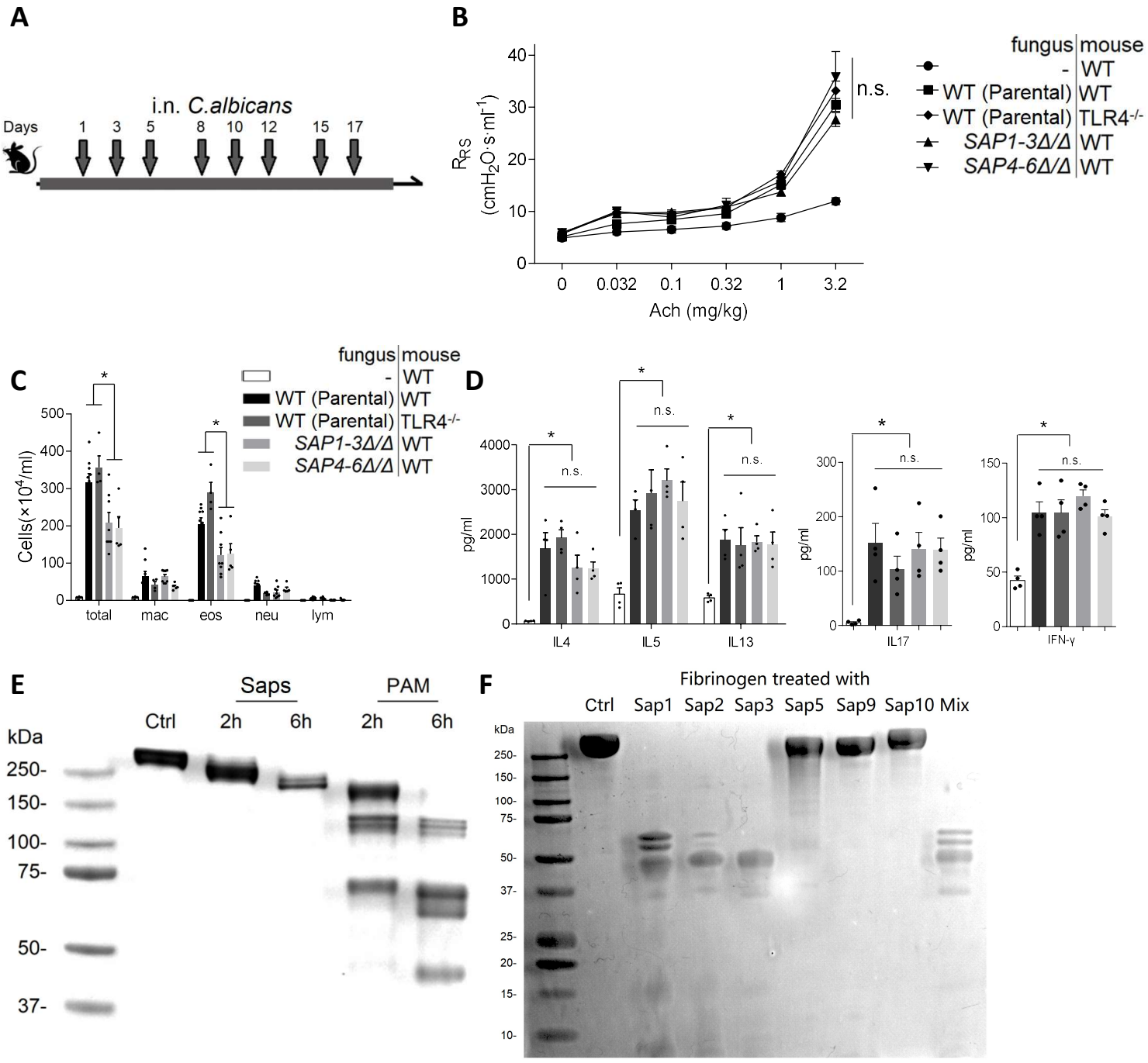
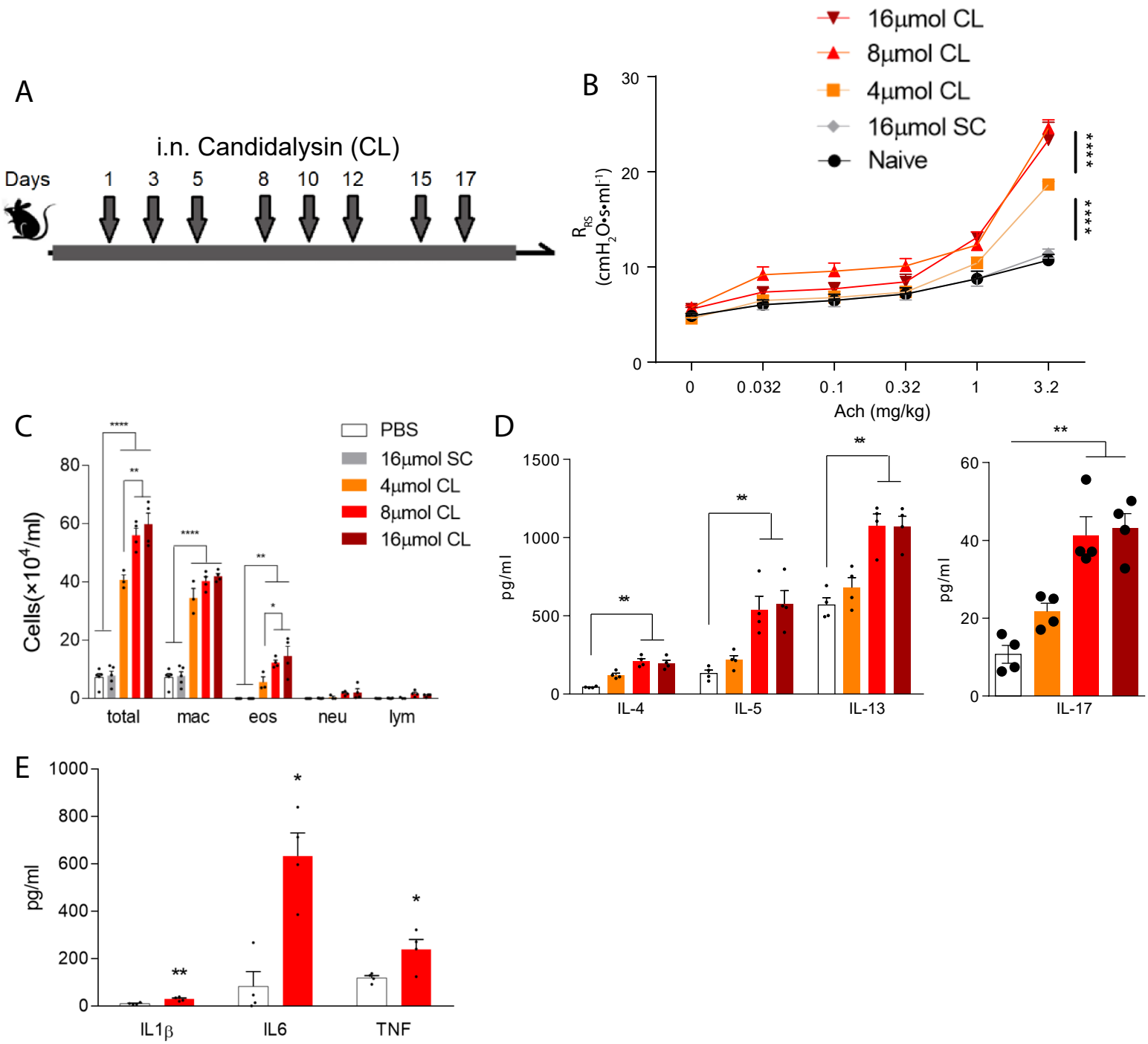
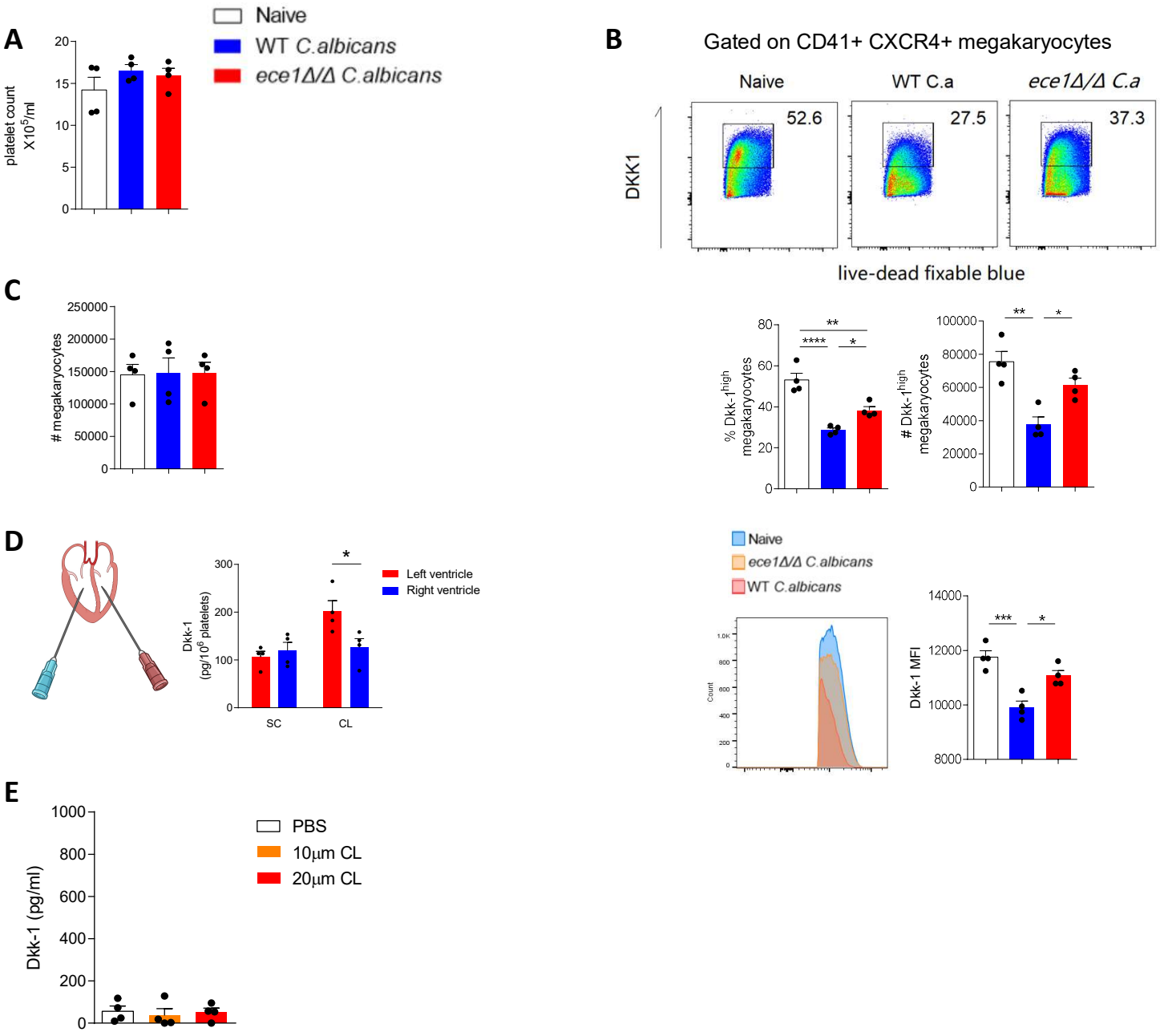


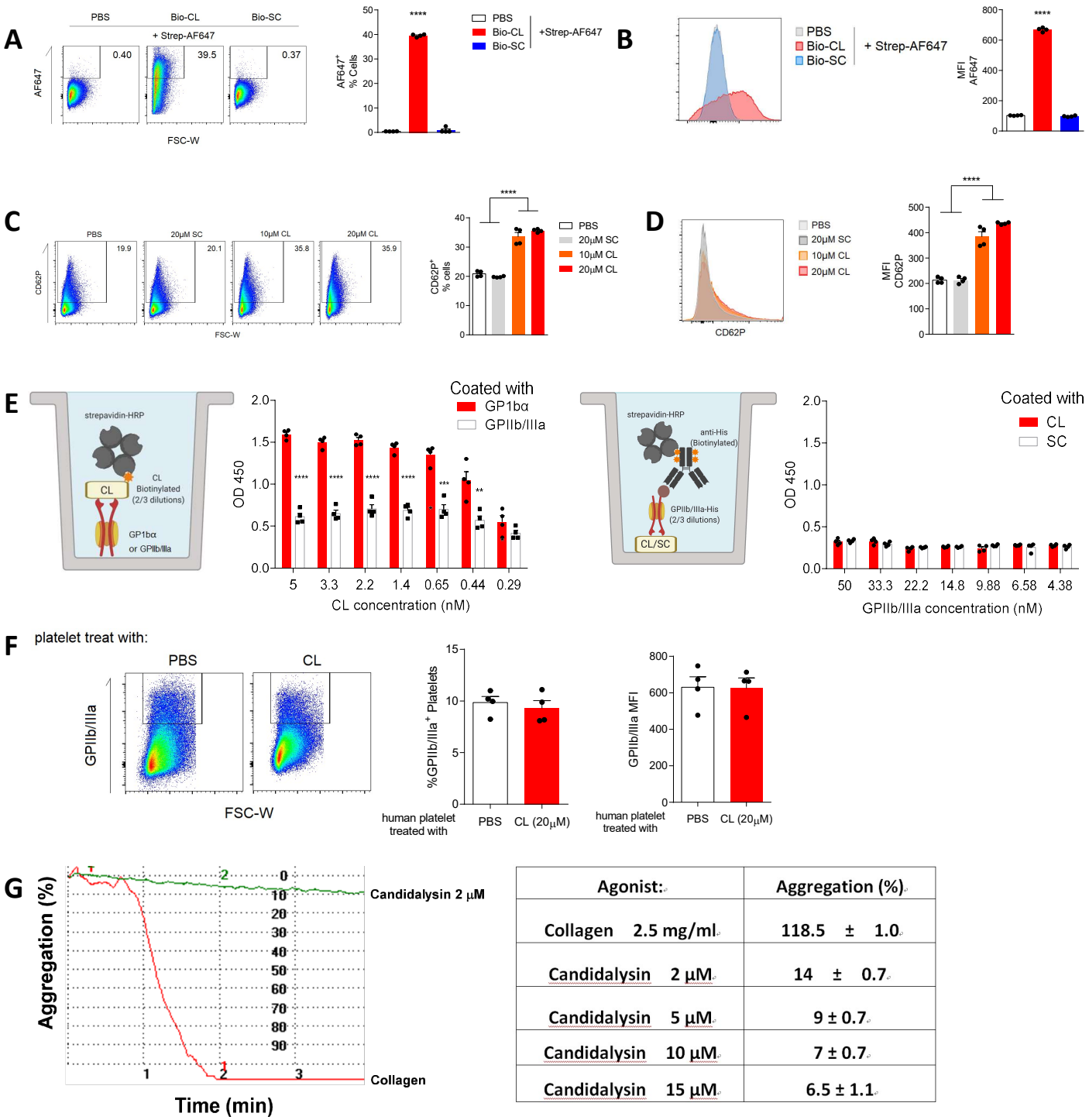
Extended Data Figure 1, related to Figure 1. Proteinase from *C. albicans* is not required for allergic airway disease. (A) Wild type (WT) or TLR4$^{-/-}$ C57BL/6 mice were challenged intranasally with 10^5 viable cells of WT (Parental control), secreted aspartic proteinase 1,2,3 triple deficient (*SAP1-3Δ/Δ* or *SAP4-6Δ/Δ*) *C. albicans* every two days over 17 days. **(B)** Respiratory system resistance (R_{RS}) was assessed in response to increasing intravenous acetylcholine (Ach) challenges. **(C)** Quantitation of cells from bronchoalveolar lavage fluid (mac: macrophages; eos: eosinophils; neu: neutrophils; lym: lymphocytes). **(D)** Cytokines quantitated by ELISA from deaggregated lung. **(E-F)** SDS-PAGE gel electrophoresis assay showing degradation of fibrinogen by purified secreted aspartic proteinases (Saps) from *C. albicans* or the proteinase from *Aspergillus melleus* (PAM) over the indicated times **(E)**, or by recombinant Saps individually or combined for 6 hours **(F)**. (n≥4, mean±S.E.M, n.s.: not significant, *p<0.05, **p<0.01, using one-way ANOVA followed by Tukey's test for multiple comparisons). Data are representative of three independent experiments



Extended Data Figure 2, related to Figure 1. Candidalysin induces allergic airway disease. **(A)** Protocol for administering synthetic candidalysin intranasally to anesthetized wildtype mice. **(B)** Respiratory system resistance (RRS), **(C)** BALF cells, and **(D-E)** lung cytokines were quantitated as in Figure 1. (n≥4, mean±S.E.M, *p<0.05, **p<0.01 and ****p<0.0001 using one-way ANOVA followed by Tukey's test for multiple comparison.) Data are representative of three independent experiments.

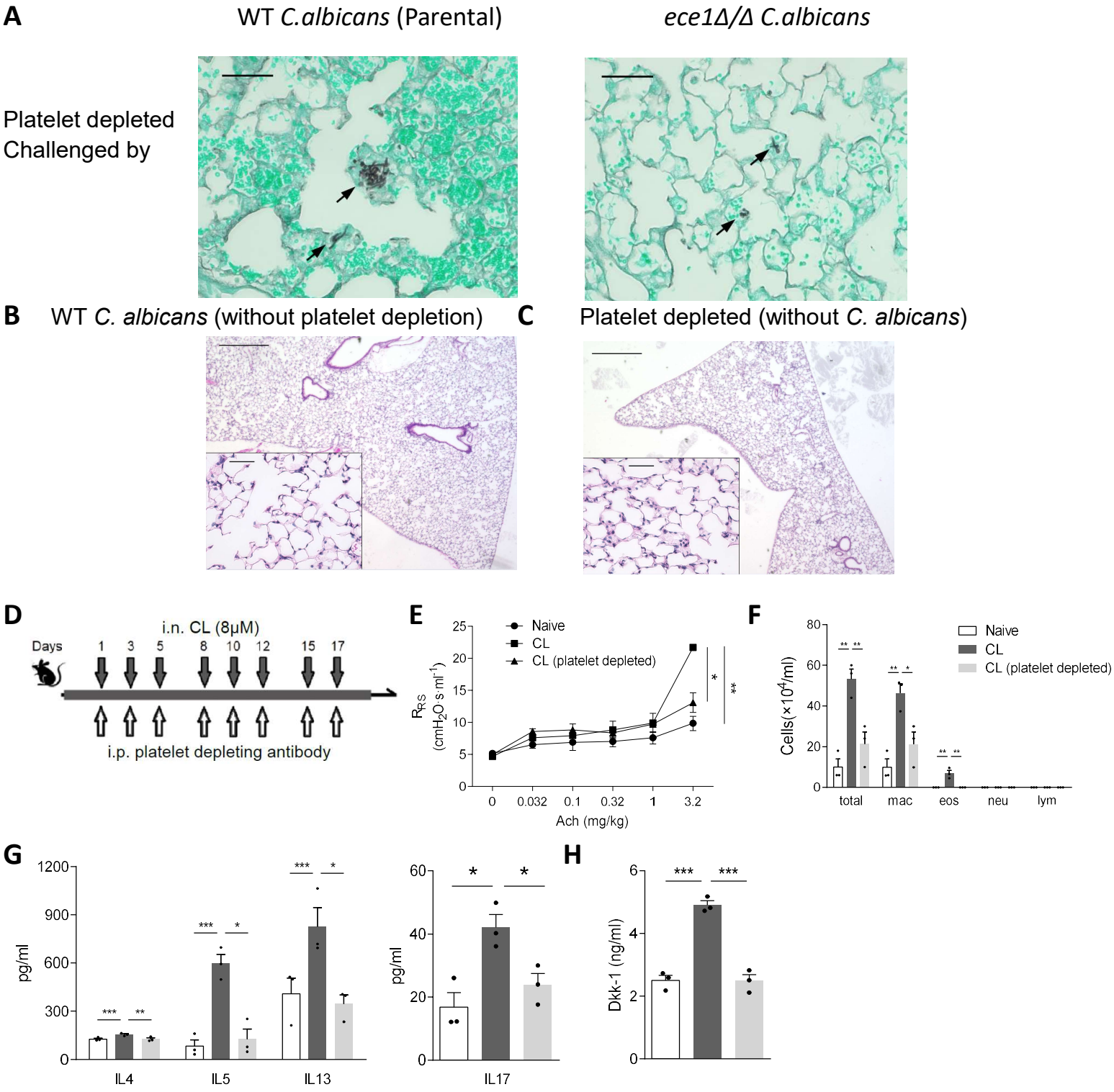


Extended Data Figure 3, related to Figure 2. Platelet and pulmonary megakaryocytes reacts to Candidalysin. (A-C) Anesthetized wildtype C57BL/6 mice were challenged intranasally 8 times over 17 days with WT (parenta) or *ece1Δ/Δ C. albicans*. **(A)** Platelet count from mice post challenge. Lungs were removed 24 hours after the final challenge and **(B)** quantified for Dkk-1^{high} megakaryocytes (as indicated by the gating box) and Dkk-1 MFI. **(C)** Total megakaryocytes were quantified by flow cytometry. **(D)** Mice are challenge intranasally with 16µmol of candidalysin (CL) or scrambled control (SC) and platelets were isolated from left and right ventricle 2 hours post challenge. Dkk-1 quantified from platelets from the left and right ventricle. **(E)** EOMA cells were treated with candidalysin at 10 and 20µM. Dkk-1 was quantified in the supernatant Illustrative figures generated at biorenders.com (n≥4, mean±S.E.M, n.s.: not significant, *p<0.05, **p<0.01, ***p<0.001, ****p<0.0001 using one-way ANOVA followed by Tukey's test for multiple comparisons)

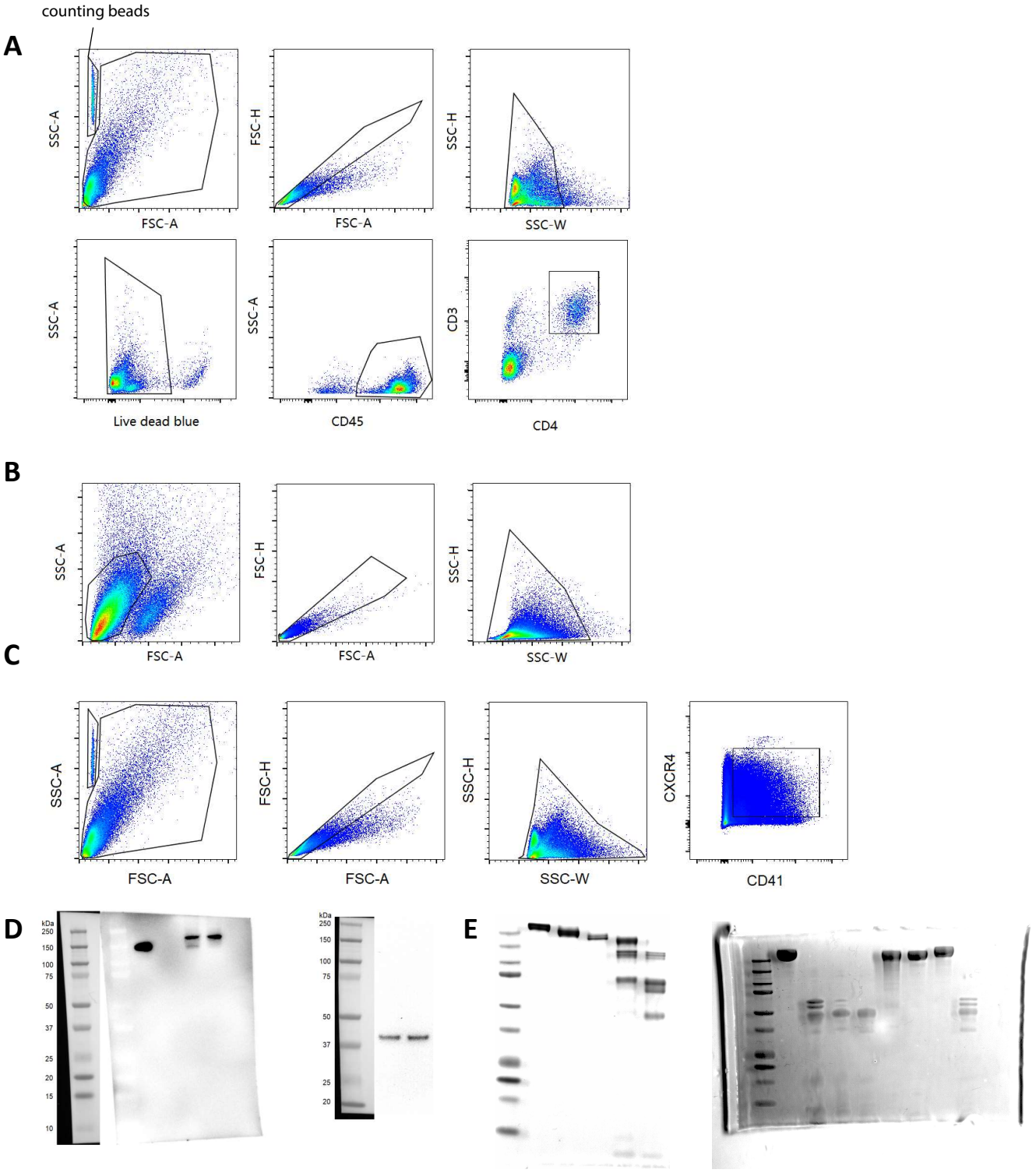


Agonist:	Aggregation (%)
Collagen 2.5 mg/ml	118.5 ± 1.0
Candidalysin 2 μM	14 ± 0.7
Candidalysin 5 μM	9 ± 0.7
Candidalysin 10 μM	7 ± 0.7
Candidalysin 15 μM	6.5 ± 1.1

Extended Data Figure 4, related to Figures 2,4,5. **Candidalysin binds to and activates human platelets. (A-B)** Human platelets were treated with 10μM biotinylated candidalysin (Bio-CL) or scrambled control (Bio-SC), followed by Streptavidin-Alexafluor 647 after which flow cytometry was used to determine binding as (**A**) AF647 % positive cells and (**B**) median fluorescence intensity (MFI). **(C-D)** Human platelets were prepared with candidalysin (CL) (10 or 20μM), scrambled control (SC) or PBS after which flow cytometry was used to determine the change in expression of the activation marker P-selectin (CD62P) expressed as (**C**) % positive cells and (**D**) mean fluorescence intensity (MFI). **(E)** Schematic diagrams and aggregate data depicting in vitro assays in which the dose-dependent binding of plate-bound GP1bα or GPIIb/IIIa to candidalysin was determined colorimetrically. **(F)** Human platelets were prepared with 20μM candidalysin (CL) or PBS after which flow cytometry was used to determine the change in expression of the activation marker GPIIb/IIIa expressed as % positive cells and mean fluorescence intensity (MFI). **(G)** Percentage aggregation for platelets in response to the indicated doses of collagen or candidalysin Data are representative of three independent experiments. (n≥4, mean±S.E.M, n.s.: not significant, **p<0.01,



Extended Data Figure 5, related to Figure 6. Lung histology of mice after platelet depletion or *C.albicans* challenge, and candidalysin failed to induce airway hyperreactivity to platelet depleted mice. (A) GMS staining on lung sections from wildtype plateled depleted mice after *C.albicans* challenge.(**B-C**) Wildtype, platelet-sufficient mice were challenged once with *C. albicans* intranasally (**B**) or platelet depleted without *C. albicans* challenge (**C**). Lungs were removed 4 hours after either challenge and H&E staining on 5 μm lung sections was performed. Reference bar: 500 and 50μm, respectively. Magnification: **A**: 200x, **B-C**: 40× (Inset: 200×). **(D)** Wild type mice were challenged intranasally with 8μM of recombinant candidalysin intranasally, with or without platelet depleting antibody intraperitoneally every two days over 17 days. **(E)** Respiratory system resistance (R_{RS}) was assessed in response to increasing intravenous acetylcholine (Ach) challenges. **(F)** Quantitation of cells from bronchoalveolar lavage fluid (mac: macrophages; eos: eosinophils; neu: neutrophils; lym: lymphocytes). **(G)** Cytokines quantitated by ELISA from deaggregated lung. **(H)** Dkk-1 quantitated by ELISA from mouse plasma. (n=3, mean±S.E.M, n.s.: not significant, *p<0.05, **p<0.01, ***p<0.001, using one-way ANOVA followed by Tukey's test for multiple comparisons). Data are representative of two independent experiments



Extended Data Figure 6, related to STARR Methods. Gating strategy for **(A)** TH cells, (**B**) Platelets and (**C**) megakaryocytes. Uncropped membranes from western blot of GP1Bα pulldown and **(D)** cleavage product from Saps or PAM