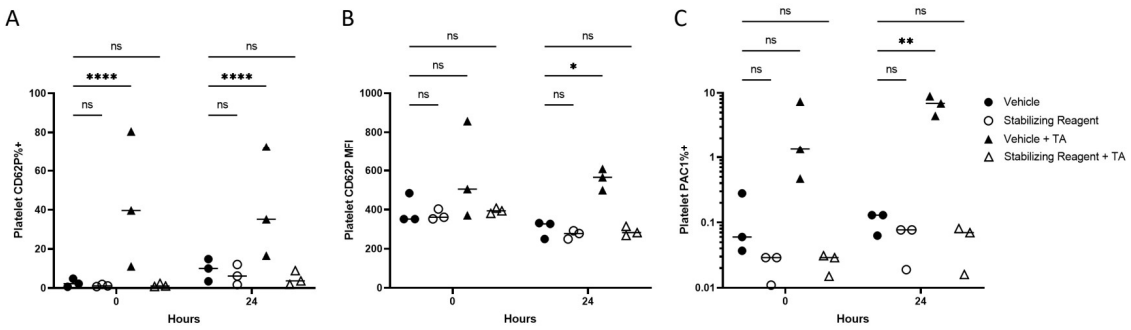
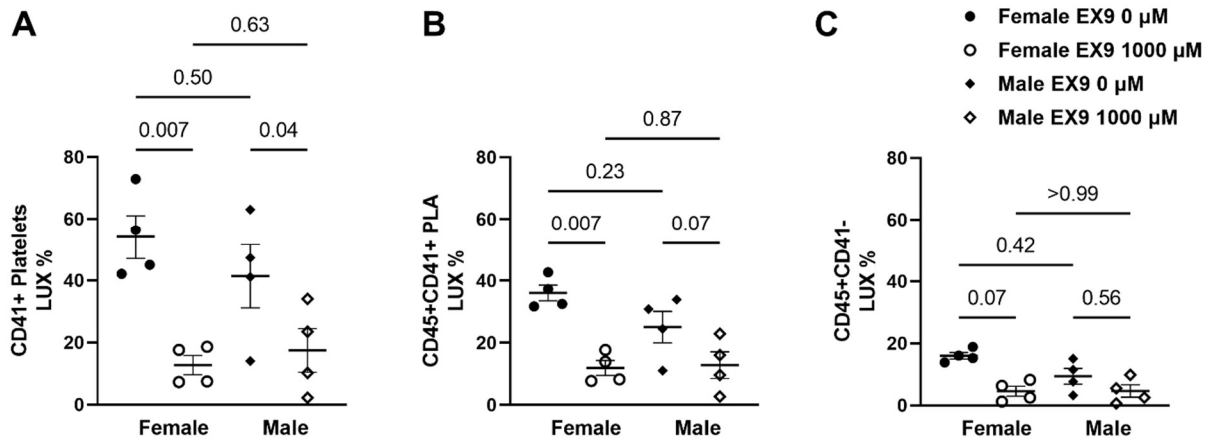
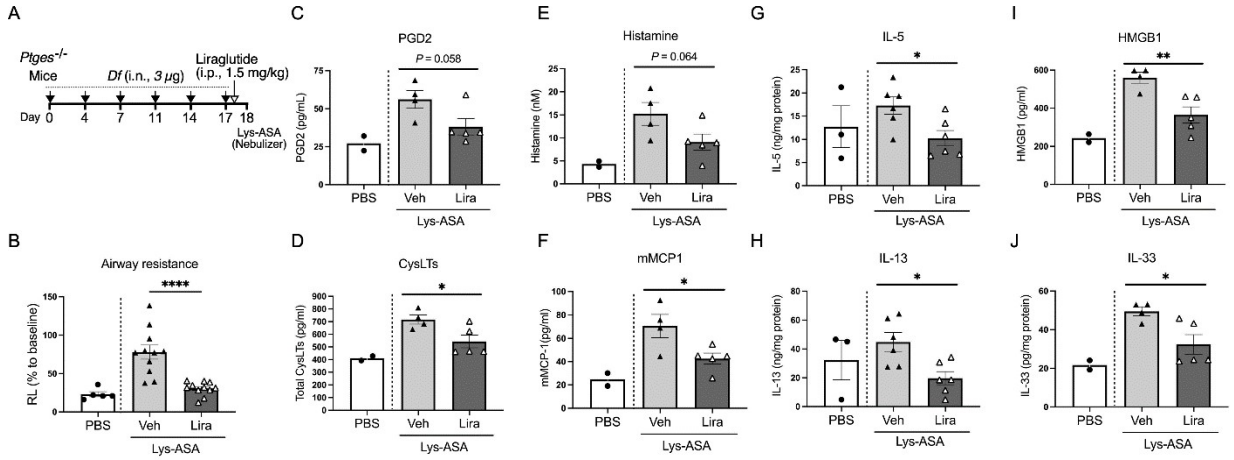


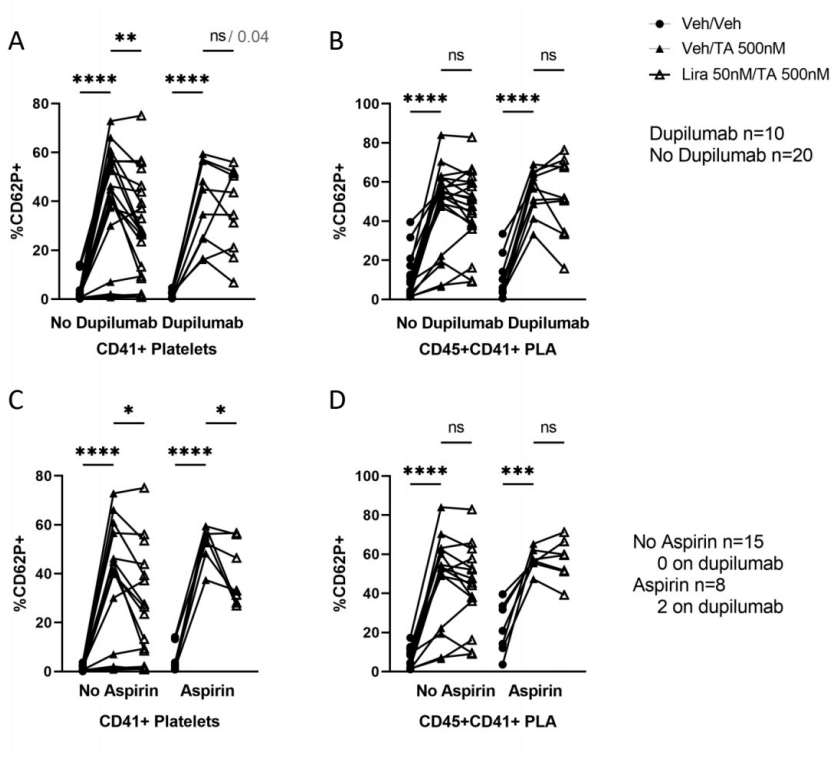
Supplemental Fig. 1: Platelet stabilizing reagent inhibits in vitro platelet activation of platelets from subjects with AERD after 30 minutes or 24 hours of exposure. In subjects with AERD (n=3), whole blood samples were treated with or without the platelet stabilizing reagent (open symbols) or vehicle (solid symbols) for 30 minutes then stimulated with the thromboxane receptor agonist, U46619 (500 nM, triangles) or vehicle (circles) for 30 minutes or 24 hours and stained for flow cytometry. Effect of treatment with the platelet stabilizing or vehicle on platelet activation as assess by **A)** $CD41^+$ platelet % CD62P expression, **B)** $CD41^+$ platelet CD62P mean fluorescent intensity (MFI) and **C)** $CD41^+$ platelet % PAC-1 expression. Two-way ANOVA with post-hoc uncorrected Fisher's least squared difference from vehicle for each time point reported. *=$p<0.05$, ** = $p<0.01$, **** = $p<0.05$



Supplemental Fig. 2: GLP-1 receptor expression does not differ by sex. LUXendin645 signal following the selective GLP-1 receptor antagonist exendin-9-39 (EX9) pretreatment on **A)** CD41+ platelets, **B)** CD45+CD41+ platelet-leukocyte aggregates and **C)** CD45+ leukocytes from 8 adult wild-type C57B6 mice stratified by sex (4 females and 4 males). One-way ANOVA with post-hoc group comparisons reported.



Supplemental Fig. 3. GLP-1 receptor agonists attenuate type-2 inflammation and mast cell mediator production following aspirin challenge in the *Ptges*$^{-/-}$ AERD mouse model. A) Protocol for intranasal administration of *Df* (3 μg) followed by Lysine-aspirin (Lys-ASA) challenge. Liraglutide or PBS was administered 24 hours prior to Lys-ASA challenge. **B)** Airway resistance (R_L) in response to Lys-ASA was assessed with an Invasive Pulmonary Function Device and compared across treatment groups. (PBS/Veh: n =5, Veh/Lys-ASA: n=11, Liraglutide/Lys-ASA: n=11 mice from 3 experiments). Values are mean ± SEMs. ****=p<.0.0001, by unpaired t-test **C-J)** Mast cell mediators and HMGB1 were measured in BAL fluids and IL-5, IL-13, and IL-33 were measured in the lung. (PBS/Veh: n =2, Veh/Lys-ASA: n=4, Liraglutide/Lys-ASA: n=5 mice from one experiment). Values are mean ± SEMs. *= p<0.05, **=p<.0.01 by unpaired t-test. P=0.0635 (Histamine), by Mann Whitney test.



Supplemental Fig. 4: Effect of dupilumab and aspirin exposure on thromboxane-induced platelet activation in subjects with AERD. In subjects with aspirin-exacerbated respiratory disease, whole blood samples were treated with the GLP-1R agonist liraglutide (Lira 50 nM) or vehicle (Veh) for 30 minutes then stimulated with the thromboxane receptor agonist, U46619 (TA 500 nM) for 30 minutes and stained for flow cytometry. **A)** Effect of pre-treatment with liraglutide or vehicle on TA-induced $CD41^+$ platelet CD62P expression and **B)** $CD45^+CD41^+$ platelet-leukocyte aggregates (PLA) CD62P expression in individuals on dupilumab treatment. Gray p-value reflects analysis with outlier excluded. **C)** Effect of pre-treatment with liraglutide or vehicle on TA-induced $CD41^+$ platelet CD62P expression and **D)** $CD45^+CD41^+$ PLA CD62P expression in individuals on aspirin treatment. One-way ANOVA with post-hoc group comparisons reported.** = $p<0.01$, **** = $p<0.0001$