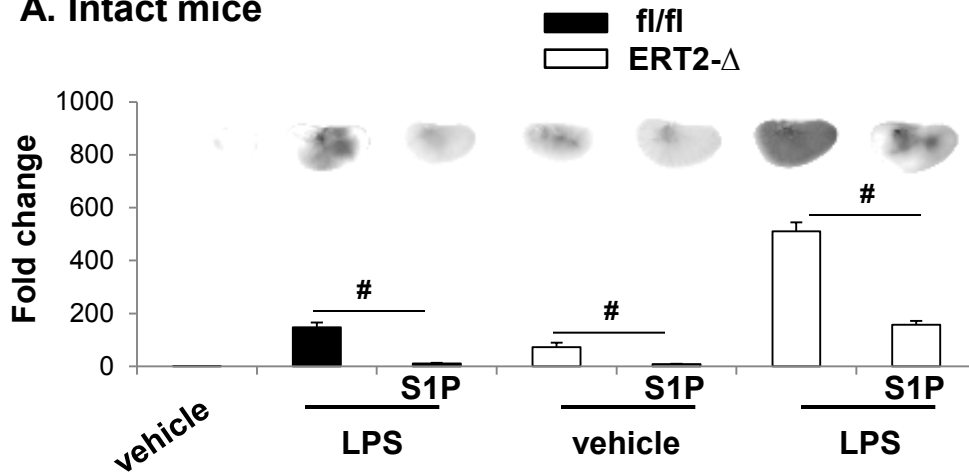
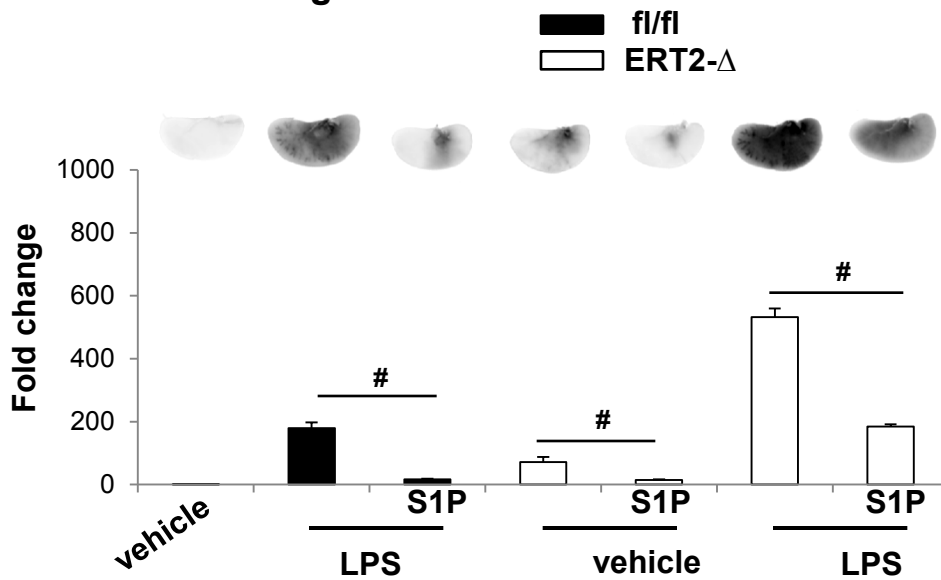


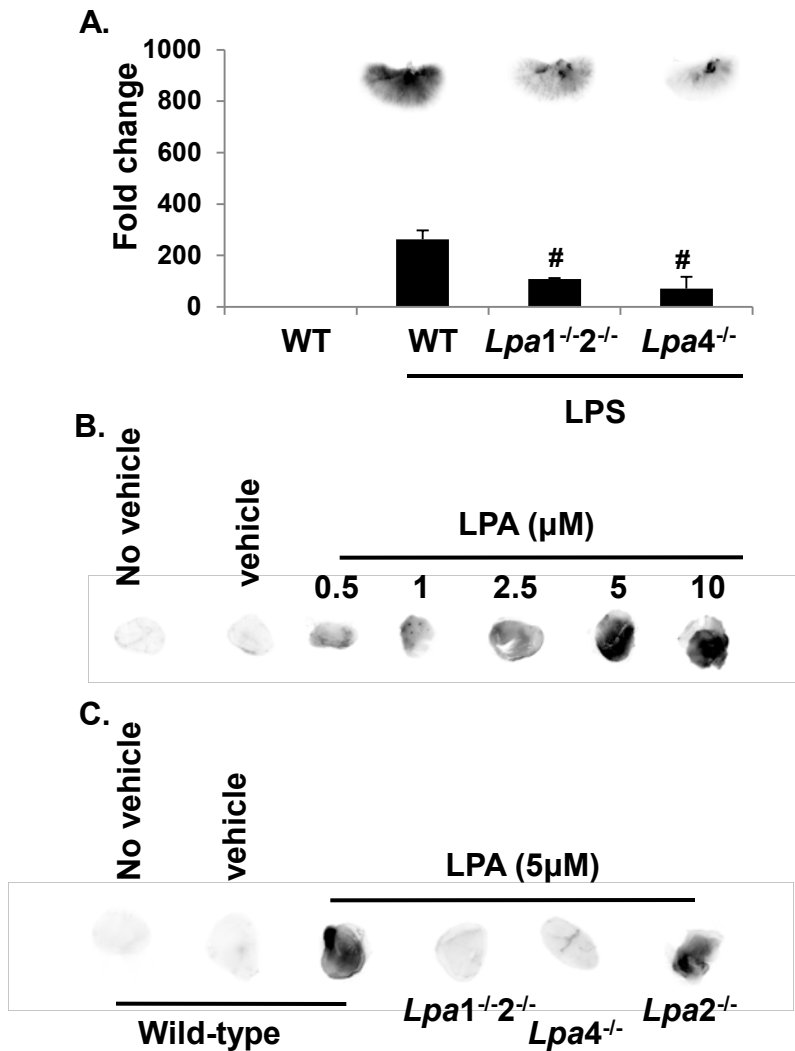
## A. Intact mice



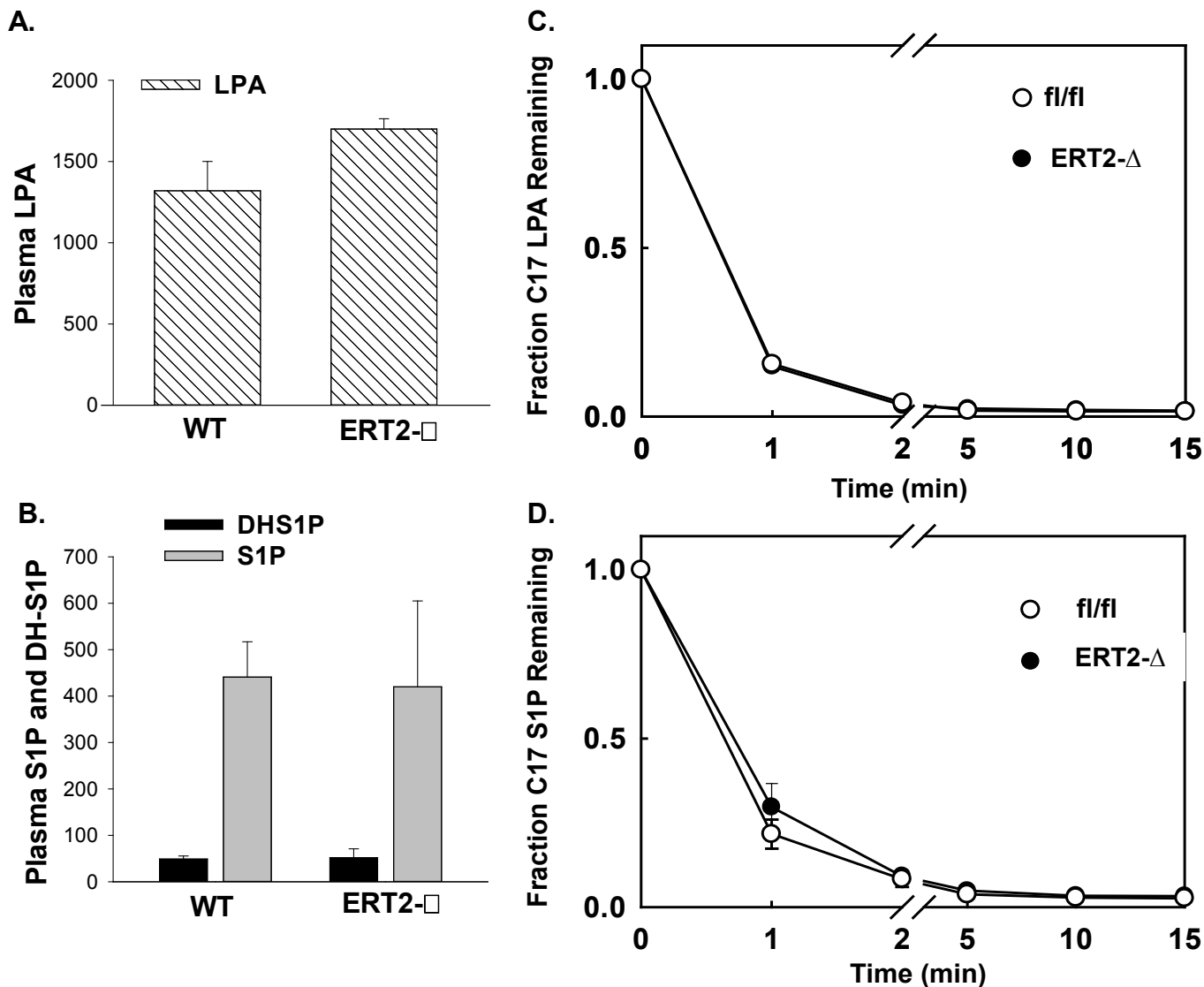
## B. Perfused Lung



**Supplemental Figure I. Lack of LPP3 does not alter the ability of S1P to protect endothelial barrier function .** (A) S1P was administered 60 min after LPS administration and protein leak in *Ppap2b<sup>fl/fl</sup>* (fl/fl) or *ERT2-Ppap2bΔ* (ERT2-Δ) lungs (n = 3/group/genotype) was measured with EBD as described. (B) S1P was administered to ventilated/perfused lungs prior to infusion of LPS via the pulmonary artery and protected from protein leak in fl/fl or ERT2-Δ lungs. # P<0.05 by ANOVA.



**Supplemental Figure II. LPA inhibits endothelial barrier function.** (A) *LPA1<sup>-/-2-/-</sup>* and *LPA4<sup>-/-</sup>* receptor mice were protected against LPS induced vascular permeability. (B) LPA induced permeability in a skin Miles assay. (C) *LPA1<sup>-/-2-/-</sup>* and *LPA4<sup>-/-</sup>* receptor mice were protected against LPA induced vascular permeability in the skin Miles assay. #  $P < 0.05$  by ANOVA.



**Supplemental Figure III.** Steady state plasma levels and rate of elimination of total LPA and S1P from the circulation of live mice is unaffected by endothelial cell LPP3 deficiency. A) Plasma total LPA and B) S1P and dihydro(DH)-S1P levels in sex and littermate-matched wild-type and ERT2-*Ppap2b*Δ mice (n = 2 – 3). Results are presented as mean values (± SD). A single ~500 pmol bolus intravenous dose of either C17-LPA (C) or C17-S1P (D) in combination with Evans Blue Dye was administered in *Ppap2b*<sup>fl/fl</sup> (fl/fl) or ERT2-*Ppap2b*Δ (ERT2-Δ) mice. Plasma samples were collected at the indicated times for determination of C17 LPA or C17 S1P levels by HPLC MS/MS or Evans Blue Dye by spectrophotometric detection. Measurements of Evans Blue Dye were used to correct for variation in dosing and sample collection as we have previously described (Salous AK et al. J Lipid Res. 2013;54:2775-84). The data shown are means SD of measurements made using at least three animals per experiment. The graphs for C17-LPA elimination (top) overlap in the fl/fl and ERT2-Δ mice.