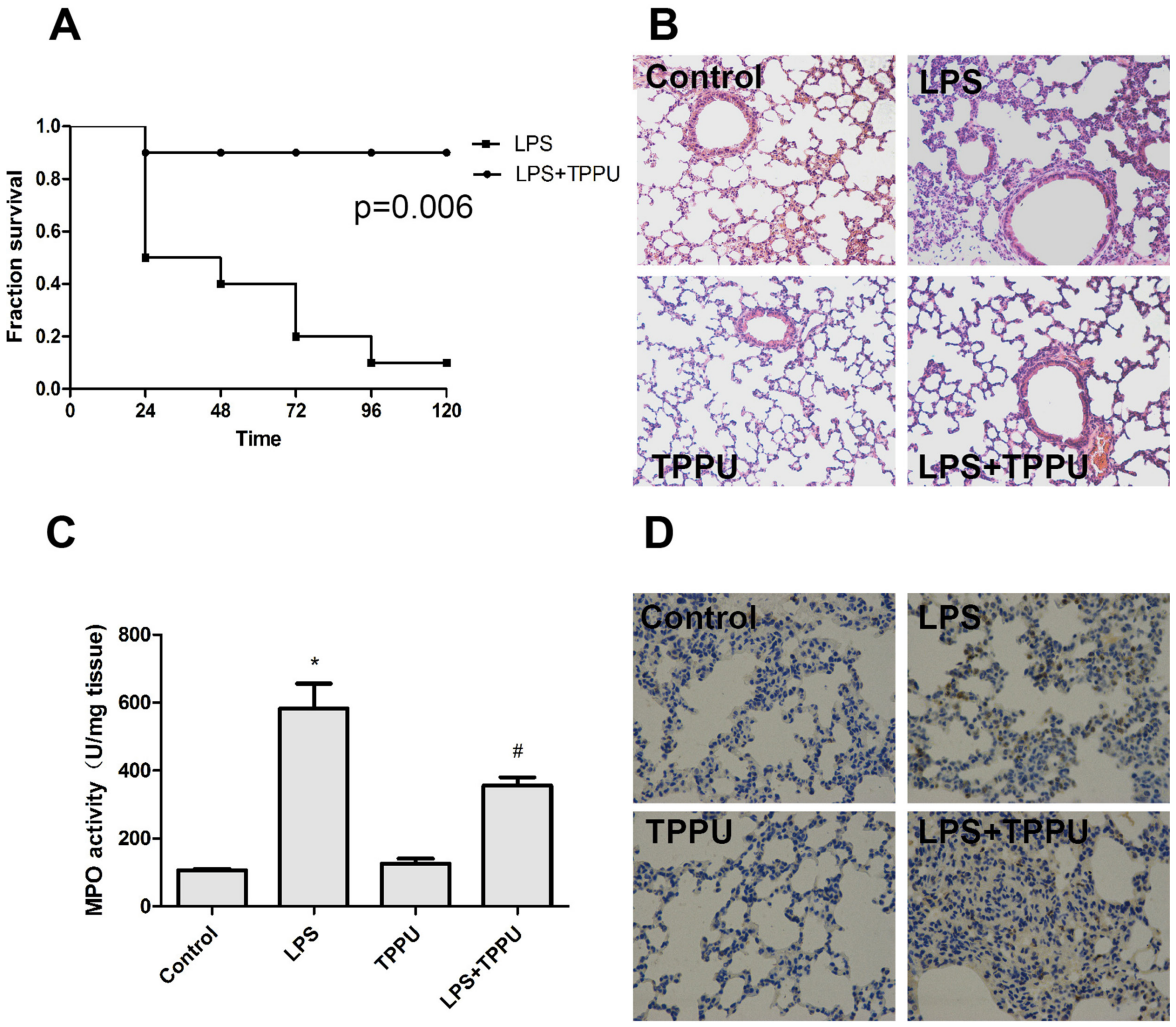
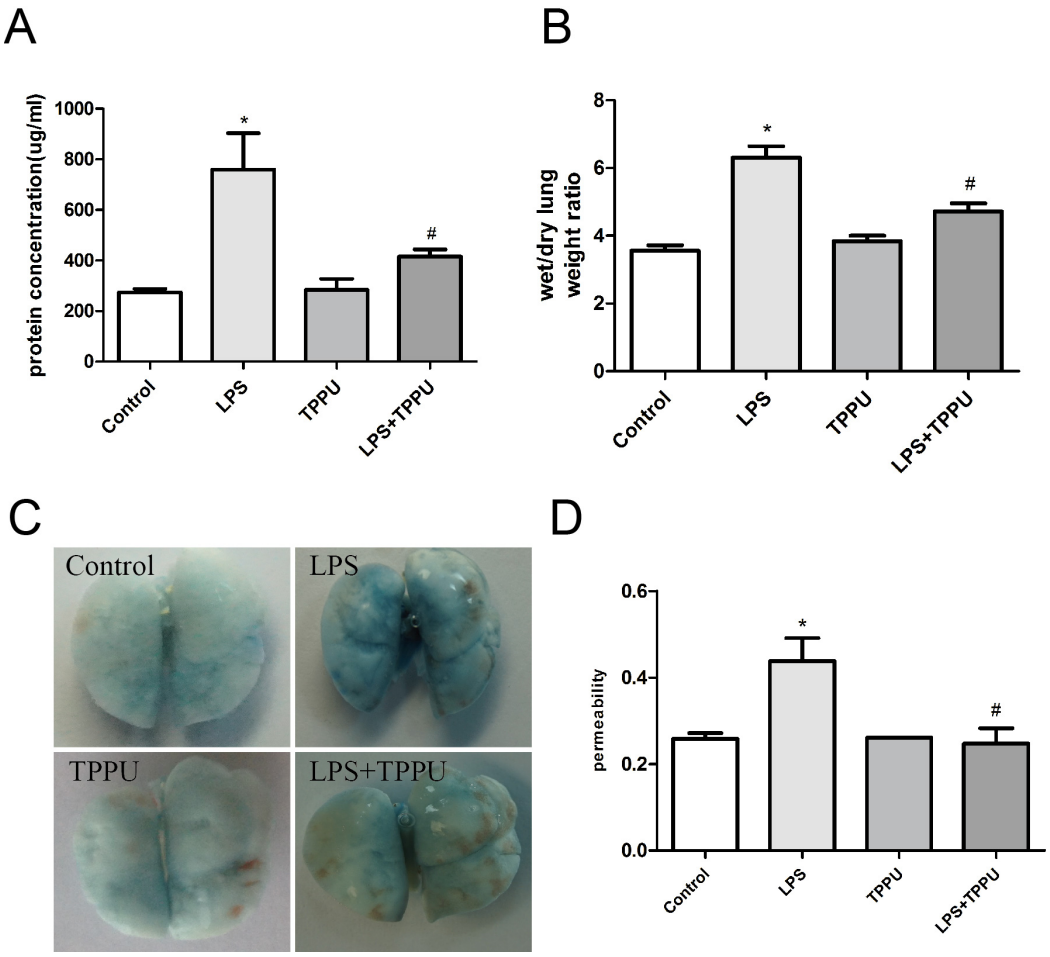
EETs reduces LPS-induced hyperpermeability by targeting GRP78 mediated Src activation and subsequent Rho/ROCK signaling pathway

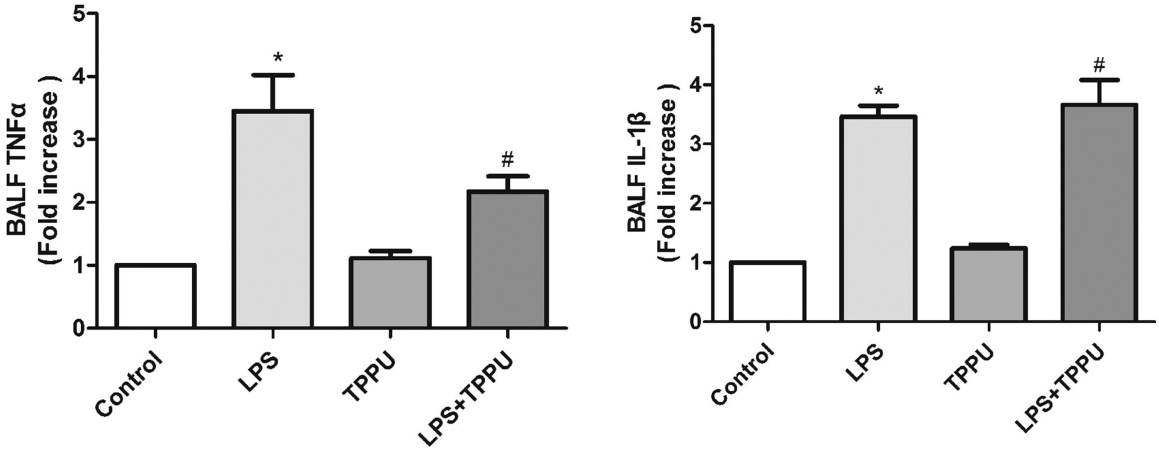
Supplementary Materials



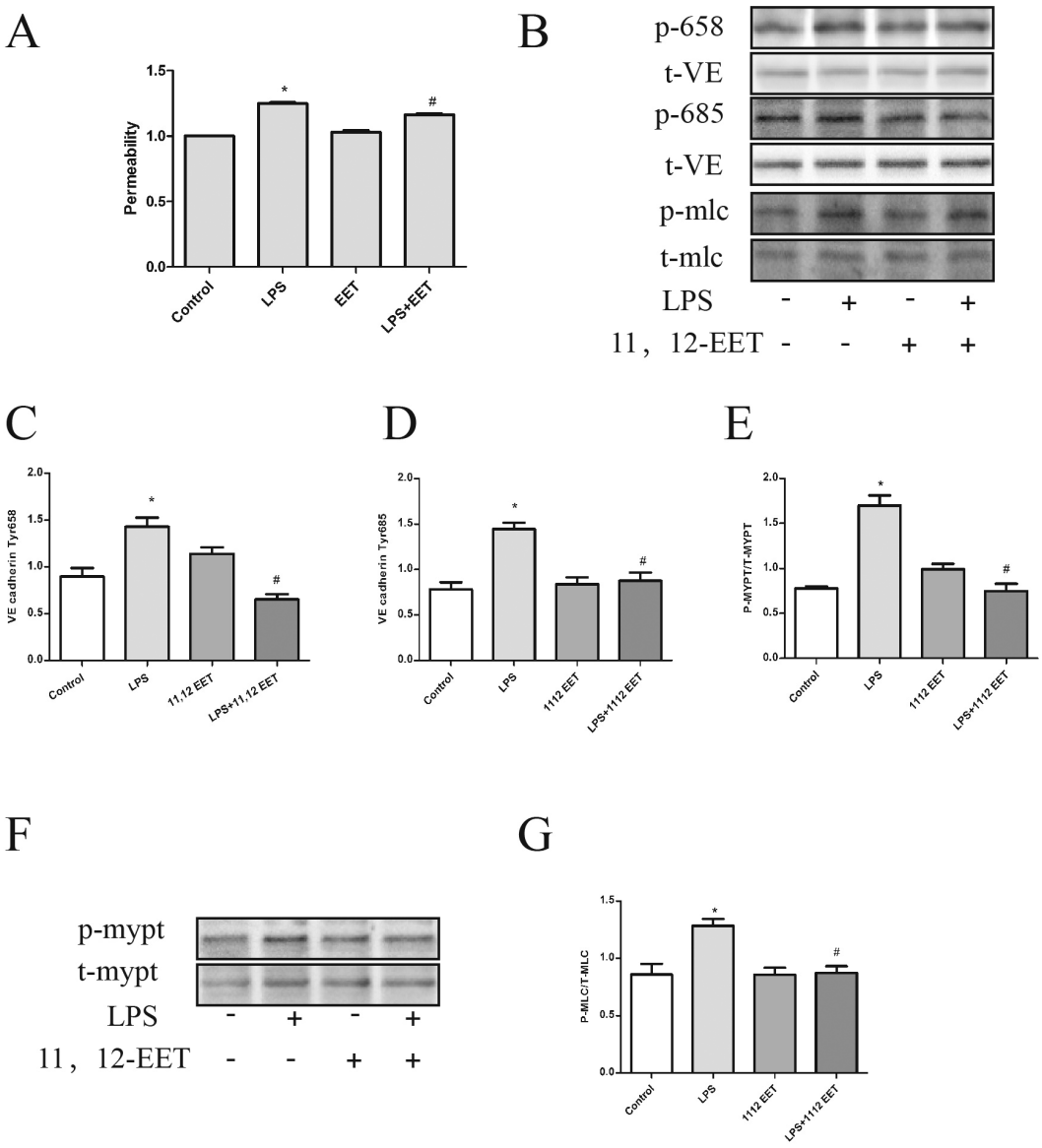
Supplementary Figure 1: sEH inhibitor TPPU reduced sepsis induced mortality. (**A**) survival curve of mice in 96 hours after LPS treatment; (**B**) HE staining of lungs that indicates leukocytes infiltration; (**C**) Determination of MPO activity in lung tissues; (**D**) immunohistochemistry staining of lung tissue MPO expression that indicates neutrophils infiltration. In survival curve test, we use 10 mice in each group, while for other test, $n = 5$. $^{*}P < 0.05$ versus WT; $^{\#}P < 0.05$ versus WT+LPS.



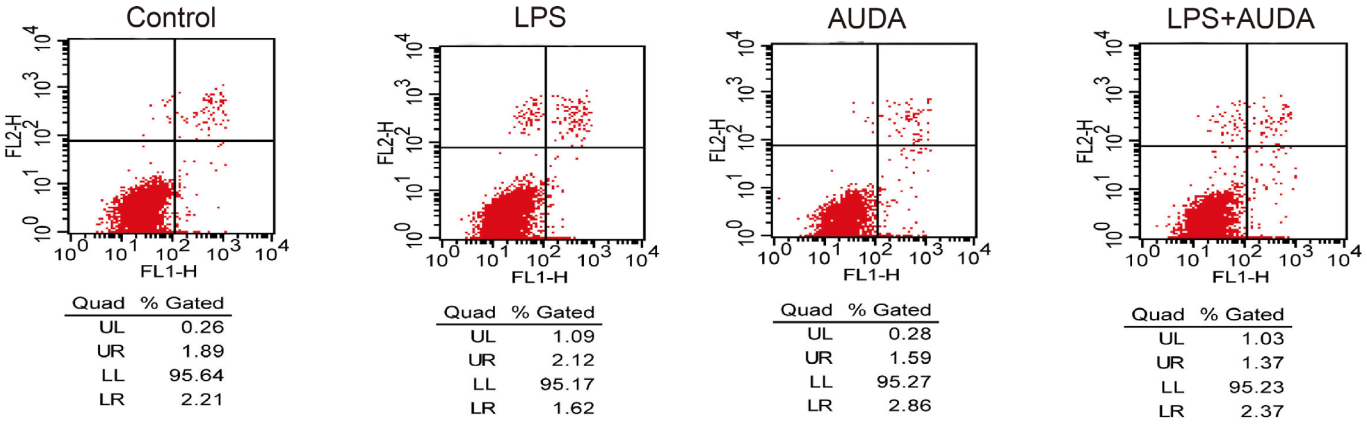
Supplementary Figure 2: sEH inhibitor TPPU reduced LPS induced mortality by attenuation of permeability increase. (**A** and **B**) pulmonary transvascular albumin permeability in BALF and wet-to-dry lung weight ratios were measured. (**C**) lung vascular permeability was assessed by accumulation of Evans Blue dye in the lungs. Lungs were excised after perfusion and imaged. (**D**) Spectrophotometric analysis of Evans Blue stained albumin content in the lung tissues was quantified. Data are expressed as means ± SEM. $n = 5$ per group. $^{*}P < 0.05$ versus WT; $^{\#}P < 0.05$ versus WT + LPS.



Supplementary Figure 3: ELISA of TNF-α and IL-1β in BALF. (**A**) The level of TNF-α in BALF; (**B**) The level of IL-1β in BALF; Data are expressed as means ± SEM. $n = 5$ per group. $^{*}P < 0.05$ versus WT; $^{\#}P < 0.05$ versus WT + LPS.



Supplementary Figure 4: 11,12-EET suppressed LPS-induced hyperpermeability by targeting Adherens Junction Components. (**A**) *in vitro* permeability assay that showing the effect of 11,12-EET on vascular barrier function; (**B**) the effect of 11,12-EET pretreatment on VE cadherin 658 and 685 tyrosine as well as MLC phosphorylation. (**C**) LPS-induced MYPT phosphorylation was attenuated by 11,12-EET treatment. Each tests was repeated for at least three times. Data are expressed as means ± SEM. $^{*}P < 0.05$ versus LPS; $^{\#}P < 0.05$ versus LPS + AUDA.



Supplementary Figure 5: Role of endothelial apoptosis in LPS-induced hyperpermeability. LPS treatment did not induce endothelial apoptosis, and moreover, AUDA had no obvious effects on endothelial cells treated with LPS.