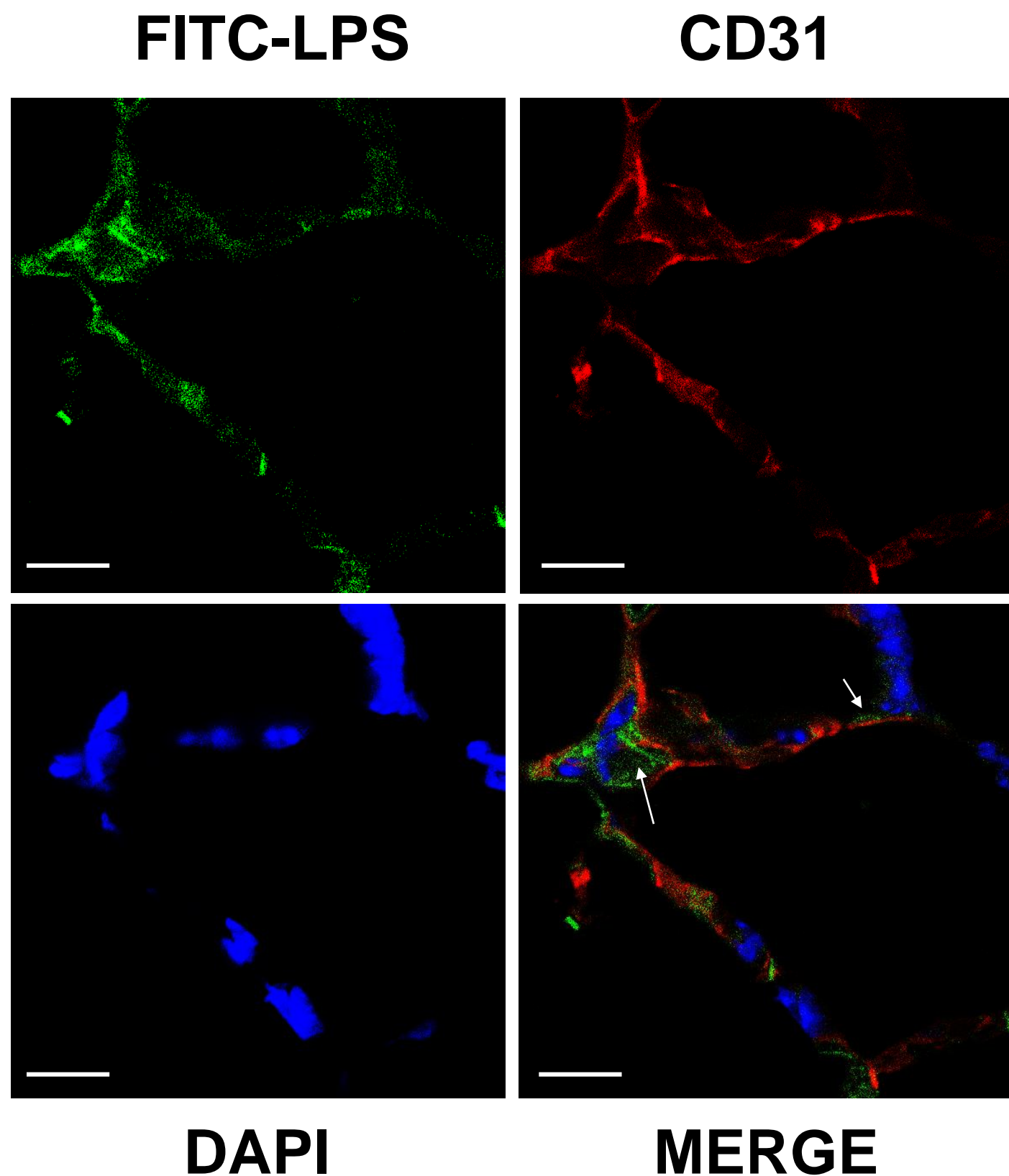
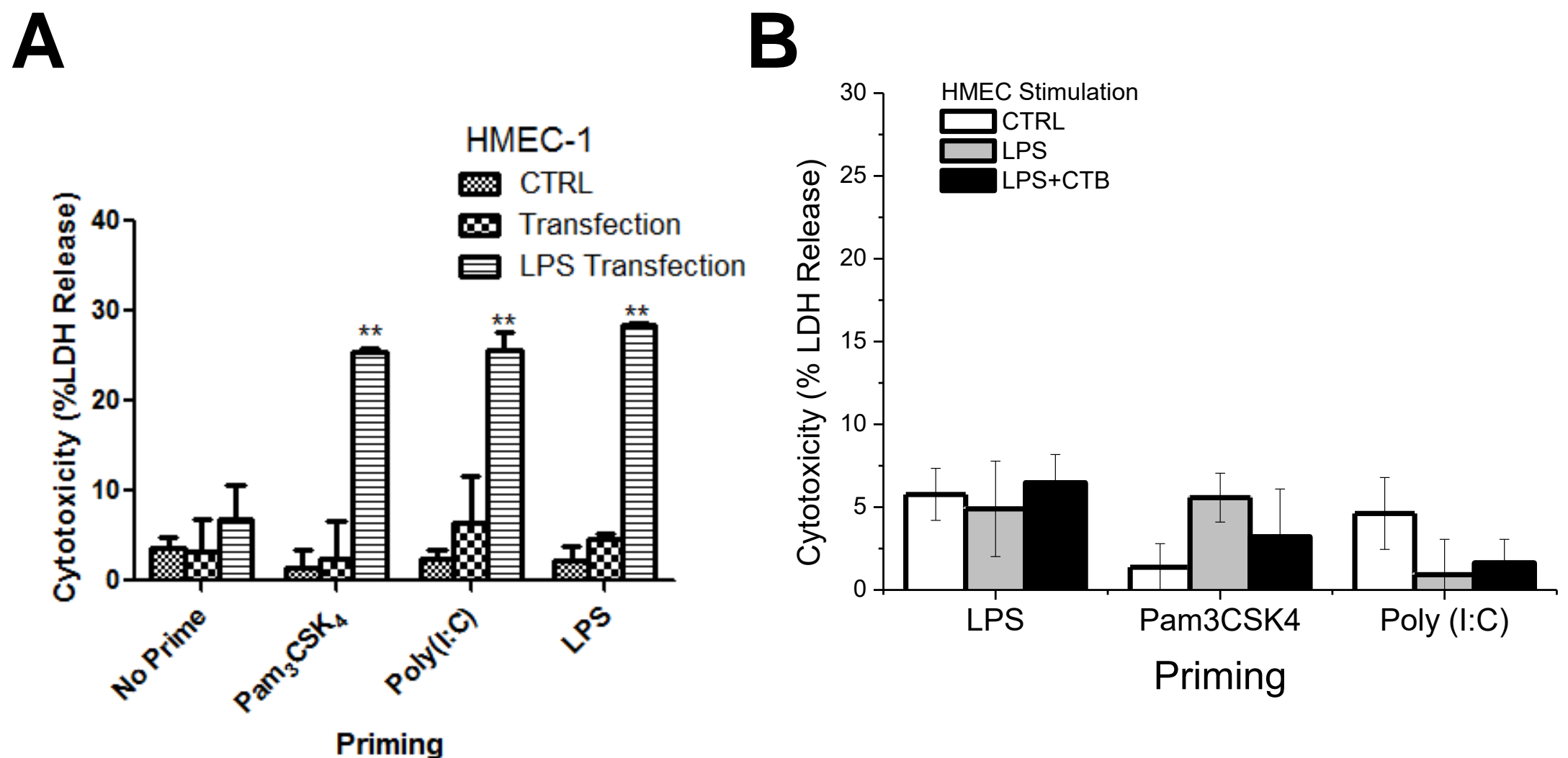


Supplemental Figure 1



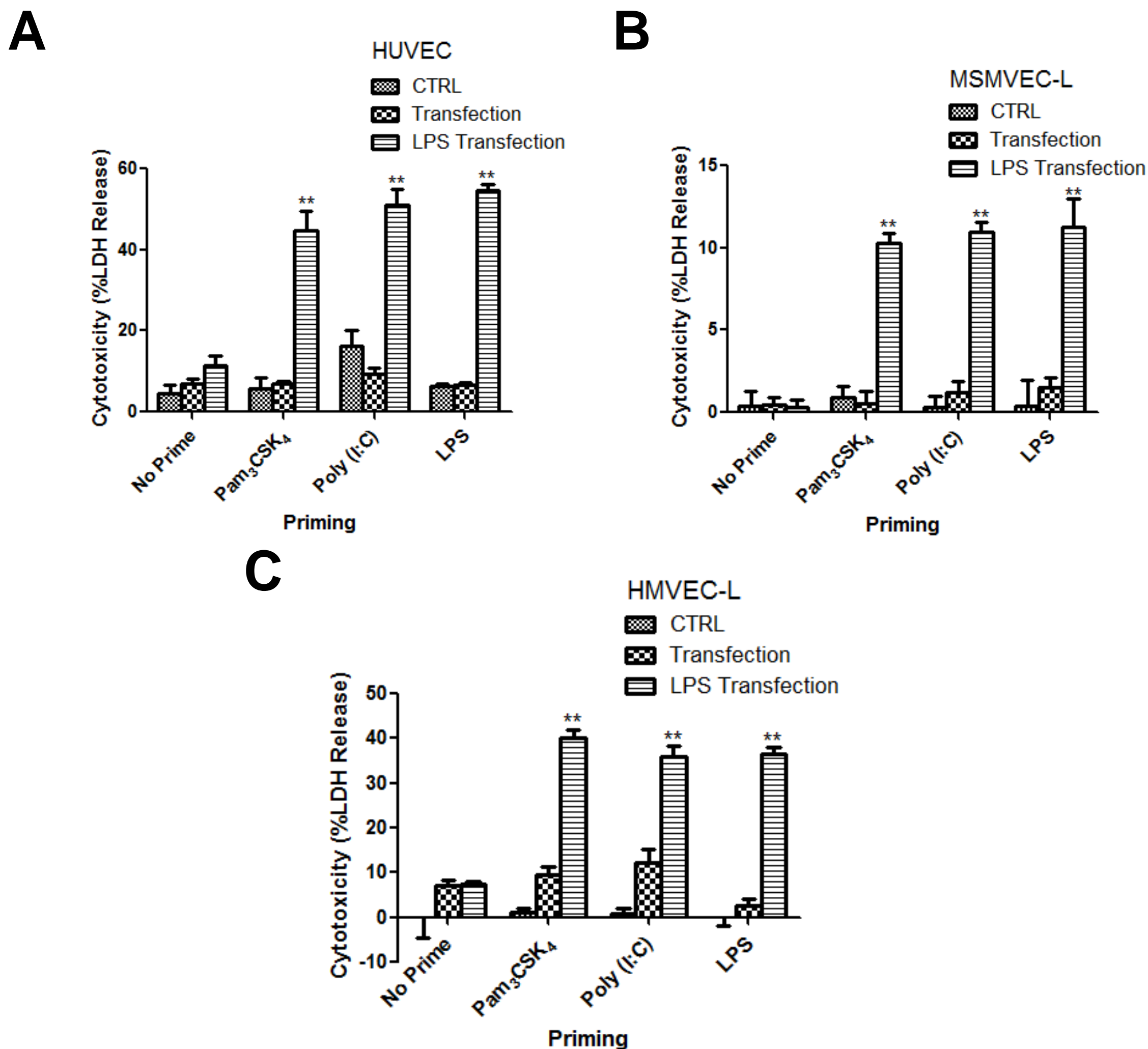
Supplemental Figure 1. Internalization of LPS *in vivo*. C57BL/6 mice were injected i.p. with 10 mg/kg FITC-LPS (Green) for 16 hours. Lungs were harvested post a cardiac perfusion with PBS. OCT-embedded cryosections were immunostained with anti-CD31 antibodies (Red). Nuclear DNA was labeled by DAPI (Blue). Confocal image results show LPS internalization in lung microvascular endothelial cells following LPS treatment. Scale bar, 10 μ m. Please also see the Supplemental video.

Supplemental Figure 2



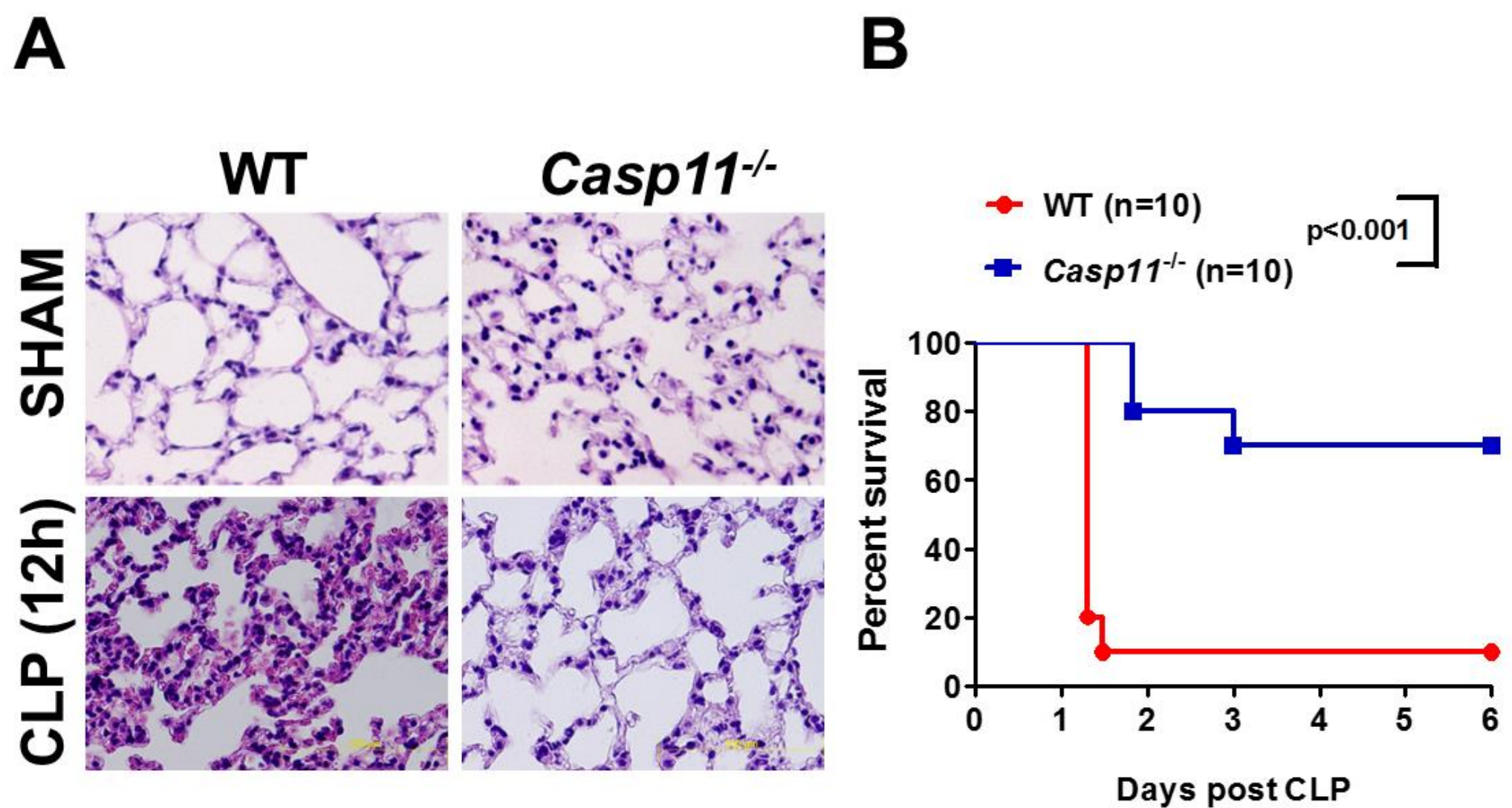
Supplemental Figure 2. Evaluation of LDH release in HMEC-1. (A) LDH release by human dermal microvascular endothelial cell (HMEC-1). Cells were primed for 6 h with 1 $\mu\text{g}/\text{ml}$ LPS, Pam3CSK4, or 5 $\mu\text{g}/\text{ml}$ poly(I:C). Primed cells were either untreated (CTRL); Mock transfection (transfection); or transfected with 2 $\mu\text{g}/\text{ml}$ LPS for 16 h (LPS transfection). (B) LDH release in primed HMEC-1 after culture in medium alone (CTRL), 2 $\mu\text{g}/\text{ml}$ LPS or 2 $\mu\text{g}/\text{ml}$ LPS together with 20 $\mu\text{g}/\text{ml}$ cholera toxin B (CTB) for 16 h.

Supplemental Figure 3



Supplemental Figure 3. Measurement of LDH release. LDH release by Human Umbilical Vein Endothelial Cells (HUVEC) (A); Mouse lung microvascular endothelial cell (MsMVEC-L) (B); and human lung microvascular endothelial cell (hMVEC) (C). Cells were primed for 6 h with 1 μ g/ml LPS, Pam3CSK4, or 5 μ g/ml poly(I:C). Primed cells were transfected with 2 μ g/ml LPS (LPS transfection) or without LPS (transfection) for 16 h.

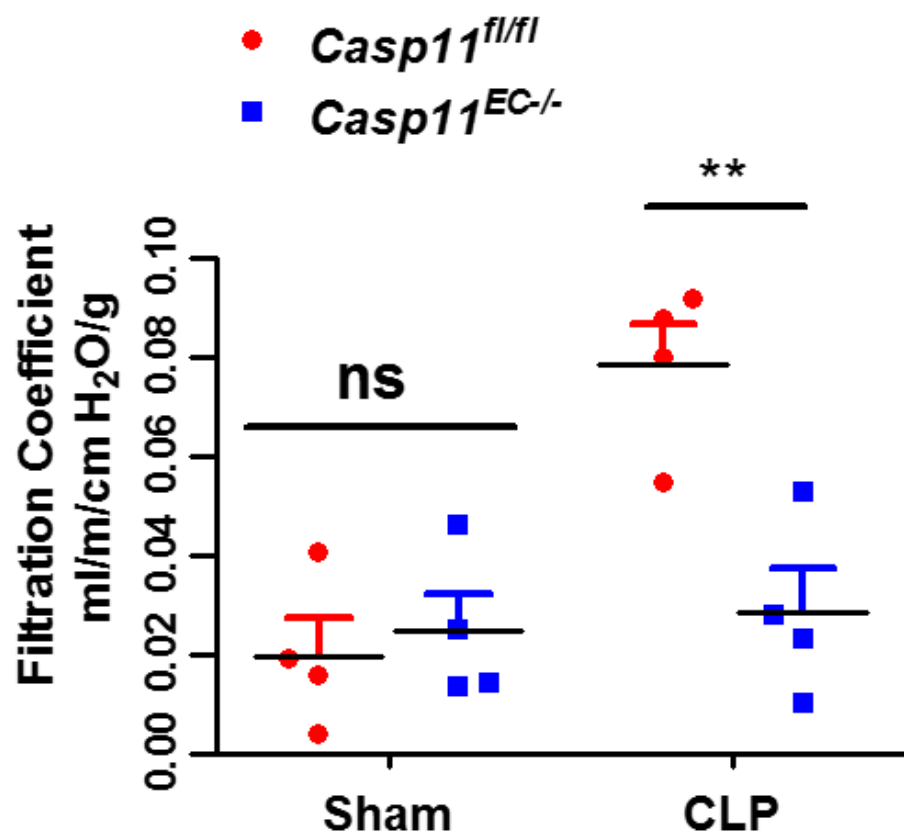
Supplemental Figure 4



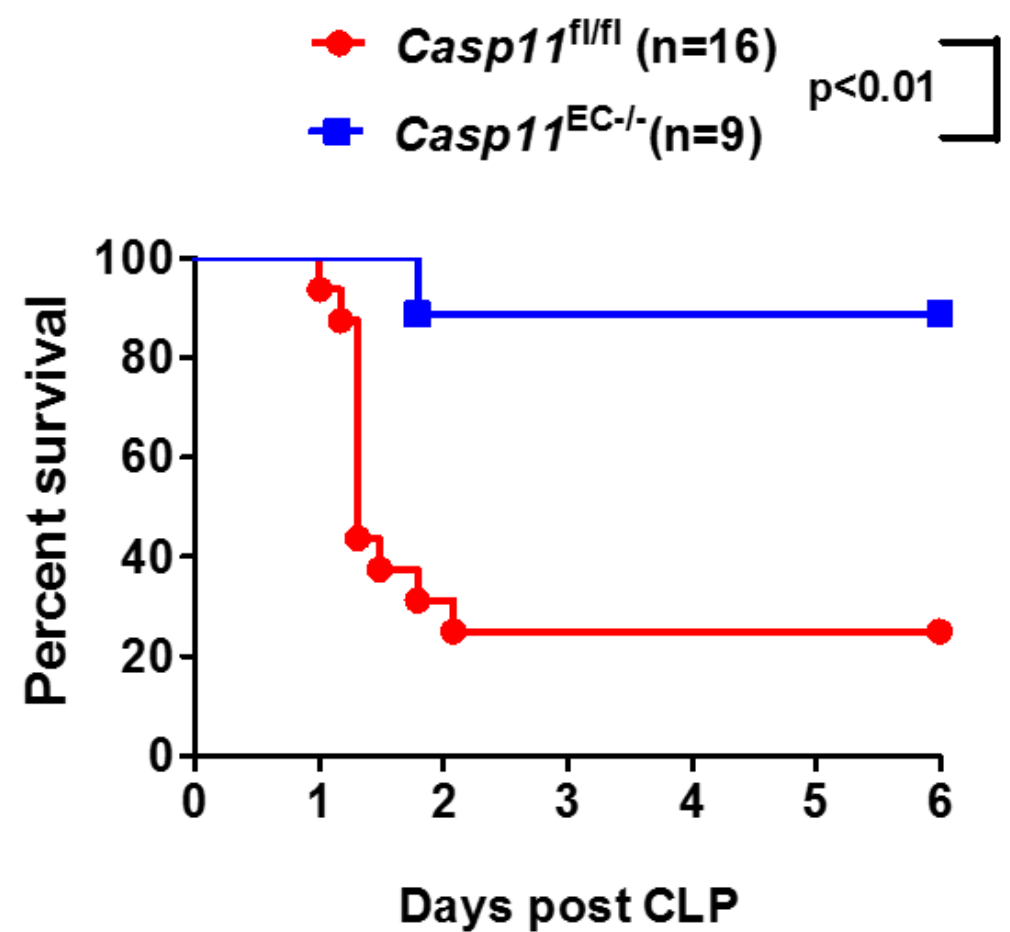
Supplemental Figure 4. Disruption of Caspase-11 protects against CLP-induced lung injury and mortality. (A) Representative H&E staining of lung sections from *Casp11*^{-/-} and control mice post CLP surgery for 12 hours (scale bar, 100 μ m). (B) CLP surgery was performed and survival analyzed using Kaplan-Meier log-rank test to compare *Casp11*^{-/-} (n=10) and control wild type mice (n=10).

Supplemental Figure 5

A

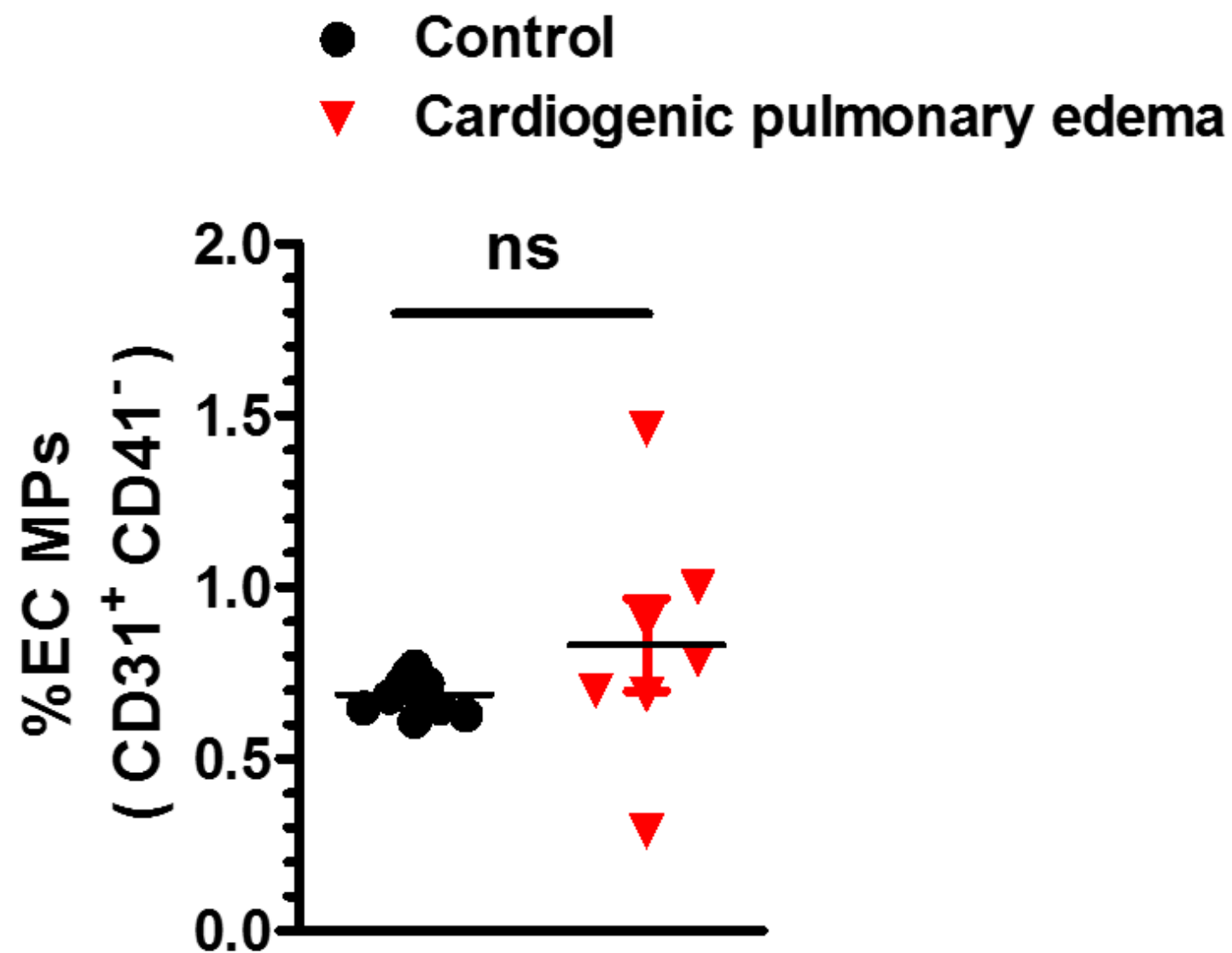


B



Supplemental Figure 5. Loss of endothelial Caspase-11 protects against CLP-induced lung injury and mortality. (A) The lung microvessel filtration coefficient was assessed in *Casp11^{fl/fl}* and *Casp11^{EC-/-}* mice following CLP surgery for 12 hours. (B) CLP surgery was performed and survival analyzed using Kaplan-Meier log-rank test to compare *Casp11^{EC-/-}* (n=9) and control *Casp11^{fl/fl}* mice (n=16).

Supplemental Figure 6



Supplemental Figure 6. Endothelial MPs levels in plasma of healthy volunteers and cardiogenic pulmonary patients. Assessment of endothelial derived MPs from plasma of healthy volunteers (Control, n=10) and cardiogenic pulmonary edema patients (n=7) (described in Supplement Table). No significant difference was observed for endothelial MPs production in plasma from cardiogenic pulmonary edema patients compared with healthy control.

Supplemental Table 1

	Healthy	ARDS	CPE
<i>Demographics</i>			
<i>Numbers</i>	10	7	7
<i>Male (n, %)</i>	(6, 66%)	(4, 57.1%)	(5, 71.4%)
<i>Age (years)</i>	57 ±10.7	60.7 ±19.2	60.5 ±17.6
<i>ARDS Etiology</i>			
<i>Sepsis</i>	NA	3(42.9)	NA
<i>Trauma</i>	NA	2(28.6)	NA
<i>Transfusion</i>	NA	1(14.3)	NA
<i>Pneumonia</i>	NA	4(57)	NA
<i>Edema</i>	NA	6(85.7)	7(100)
<i>MODS</i>	NA	3(42.9)	6(85.7)
<i>Severity of illness</i>			
<i>APACHE II</i>	NA	22.25 ±3.7	16.4 ±3.2
<i>Outcome</i>			
<i>Mortality (n, %)</i>	NA	3(42.9)	6(85.7)

Supplemental Table 1. Clinical characteristics of patients. Data are presented as mean ± SD or number (%), unless otherwise stated; Abbreviations: ARDS: Acute Respiratory Distress Syndrome; CPE: Cardiogenic Pulmonary Edema; MODS: Multiple Organ Dysfunction Syndrome; APACHE II: Acute Physiology and Chronic Health Evaluation II.