

**Adiponectin deficiency induces mitochondrial dysfunction and promotes endothelial activation and pulmonary vascular injury**

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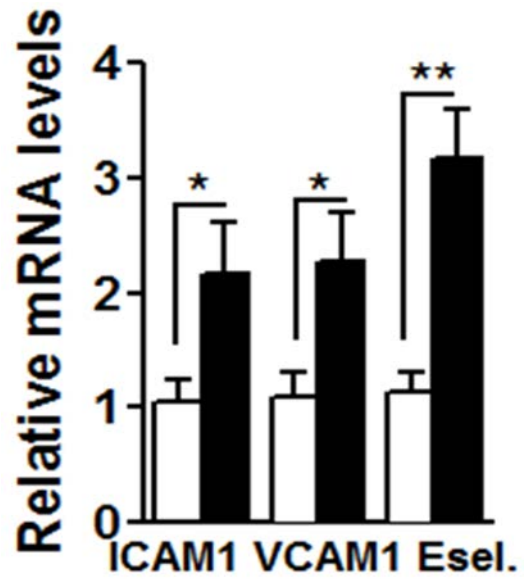
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Author Contributions: Conceived and designed—D.S.; performed experiments—D.S.; analyzed the data—D.S., C.T., V.B.; wrote the manuscript—D.S.; edited the manuscript— D.S., C.T., V.B.; All authors have approved the version of the submitted manuscript.

**Running title:** *Adiponectin-PGC-1 $\alpha$  Axis Regulates Endothelial Activation and Lung Injury*

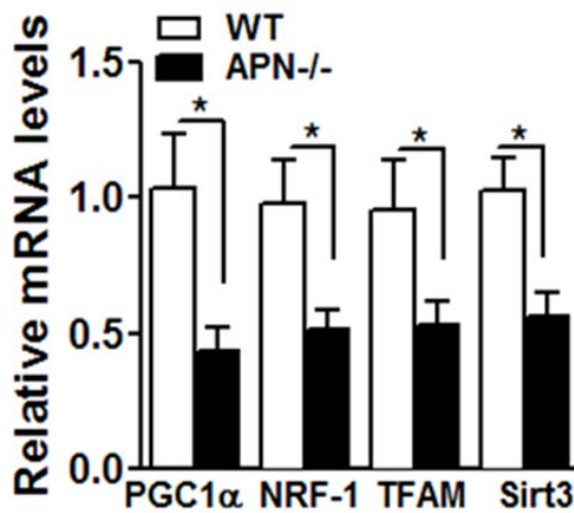
**Supplementary Information**

Supplementary Figure 1



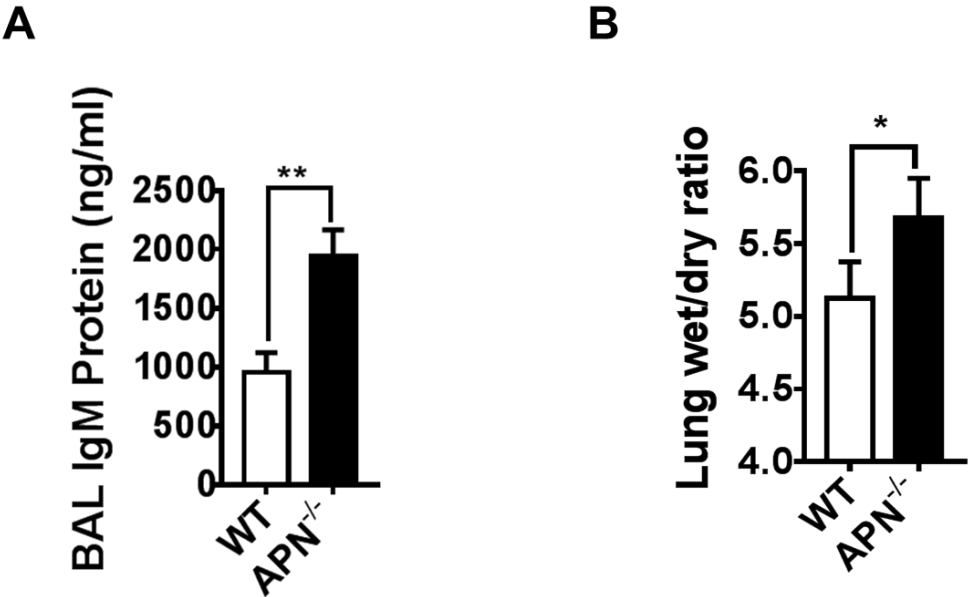
**Figure S1.** APN<sup>-/-</sup> mice show upregulated mRNA expression of endothelial adhesion markers ICAM-1, VCAM-1 and E-selectin in the lungs of APN<sup>-/-</sup> mice as compared to wild type control mice at baseline (BSL). HPRT1 was used as control gene. (n = 4 in each group, \*p<0.05 and \*\*p<0.01).

Supplementary Figure 2



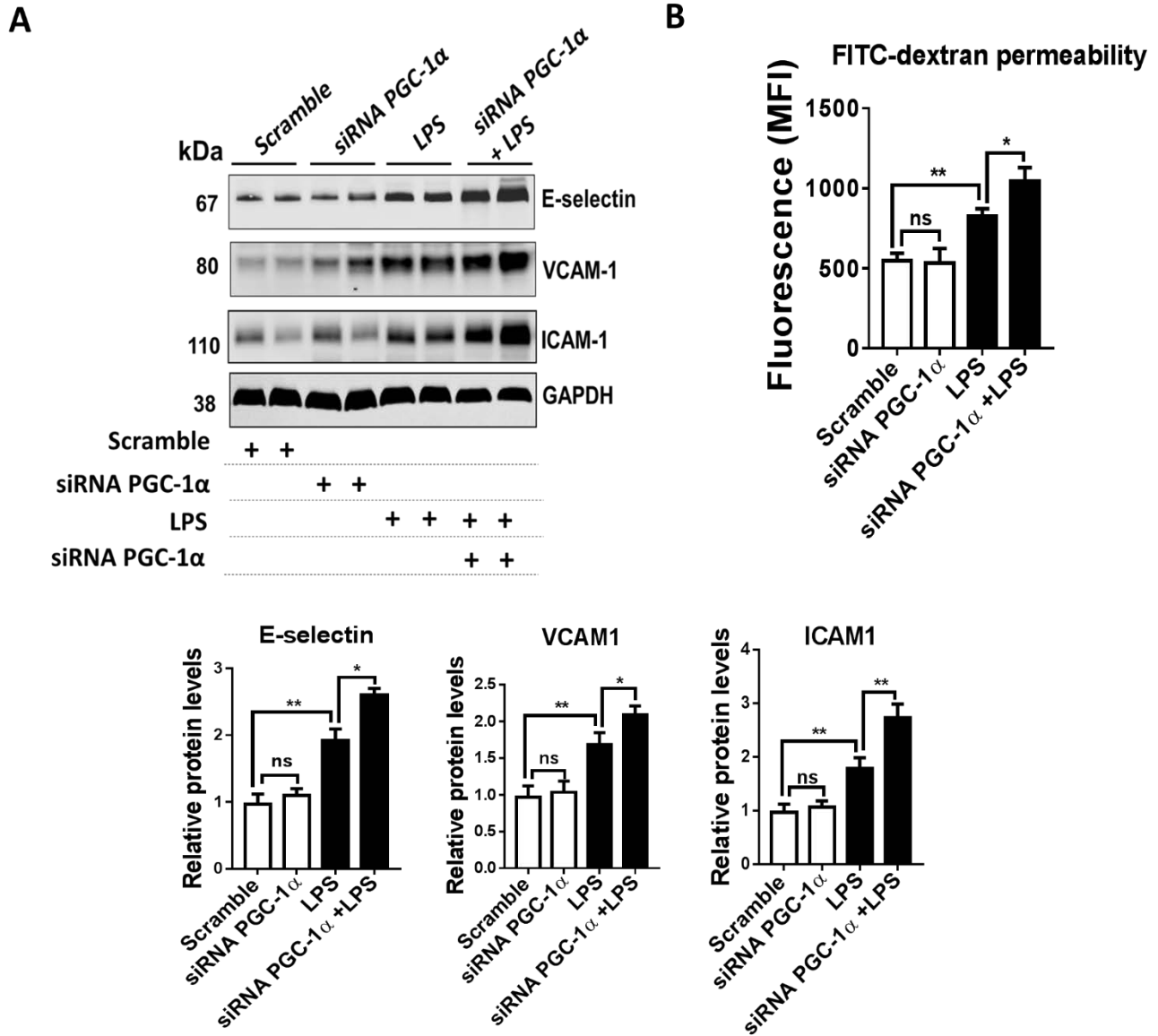
**Figure S2.** APN<sup>-/-</sup> mice show downregulated mRNA expression of mitochondrial biogenesis regulating genes PGC-1 $\alpha$ , NRF-1, TFAM and sirt3 in the lungs of APN<sup>-/-</sup> mice as compared to wild type control mice at baseline (BSL). HPRT1 was used as control gene. (n = 4 in each group, \*p<0.05).

Supplementary Figure 3



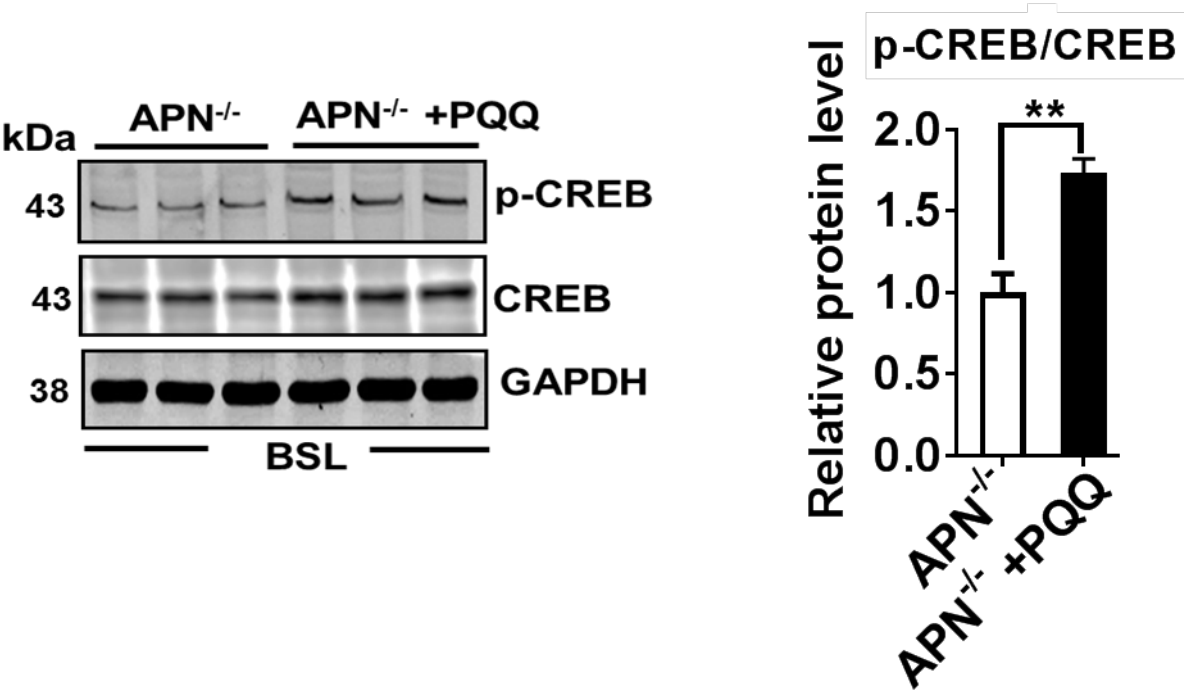
**Figure S3.** A) IgM protein level in the BAL fluid from APN<sup>-/-</sup> and wild type (WT) mice in response to LPS (24h). B) Wet/dry ratio of lungs from APN<sup>-/-</sup> and wild type (WT) mice in response to LPS. (n=8 in each group, \*p<0.05 and \*\*p<0.01).

Supplementary Figure 4



**Figure S4.** Suppression of PGC-1 $\alpha$  on lung endothelial cells aggravate LPS-induced pulmonary endothelial vascular leakage. A) Western blots for ICAM-1, VCAM-1 and E-selectin in lung endothelial cells treated with siRNA PGC-1 $\alpha$  (48h) and stimulated with LPS (1 $\mu$ g/ml, 24h). B) Endothelial permeability measured by Dextran-FITC permeability to lung ECs treated with siRNA PGC-1 $\alpha$  (48h) and stimulated with LPS (1 $\mu$ g/ml, 24h). (n=3 in each group, \*p<0.05 and \*\*p<0.01).

Supplementary Figure 5



**Figure S5.** PQQ treatment increases the expression of p-CREB in the lungs of APN deficient mice. (n=6 in each group, \*p<0.05 and \*\*p<0.01).