

**Supplementary Figure 1**. SIRT3 is diminished in the lungs of mice subjected to *P. aeruginosa*induced pneumonia. (**A**, **B**, **C**) Representative Western blots and optical band densitometry of SIRT3, Ac(K68)-SOD2 and total amounts of SOD2 from lung homogenates of control or mice subjected to *P. aeruginosa* (strain K; i.t.) for 4 hours. Means ± s.e.m., n = 3-4, \**P* < 0.05. (**D**) Colony forming units (CFU) of *P. aeruginosa* in the lung homogenates of control and infected mice. Means ± s.e.m., n = 6-7 mice per group; \**P* < 0.05.



**Supplementary Figure 2**. SIRT3 deficiency is associated with enhanced production of IL-1 $\beta$ . (**A**,**B**) Representative western blots and optical band densitometry of IL-1 $\beta$  in lysates from wild-type and SIRT3 deficient peritoneal macrophages. Cells were treated with LPS (0 or 3 ng/ml) for 4 hours. Means ± s.d., *n* = 3; \**P* < 0.05 (ANOVA). (**C**) Representative immunoblots of cleaved caspase 1 (Cl-casp.1) and  $\beta$ -actin from wild-type or SIRT3 deficient peritoneal macrophages. Cells were treated with or without LPS, as indicated.



**Supplementary Figure 3.** Lung protective and anti-inflammatory effects of viniferin are absent in SIRT3<sup>-/-</sup> mice. (A) *SIRT3<sup>-/-</sup>* mice subjected to saline, LPS (3 mg/kg; i.t.) for 24 hours. Mice were also treated with/without viniferin (0 or 120 mg/kg, i.p.) once a day for 3 consecutive days prior to LPS exposure. Representative images show H&E staining of lung sections. Scale bar: 20  $\mu$ m. (B,C) neutrophil content (B), protein amounts (C), and TNF- $\alpha$  (C) and MIP-2 (D) cytokine levels were determined in bronchoalveolar lavage (BAL) fluids from SIRT3<sup>-/-</sup> mice subjected to LPS with/without viniferin treatment. Data presented as means ± s.e.m., *n* = 3-5 mice per group; *ns* = not significant.

## **Supplementary Figure 4**



**Supplementary Figure 4**. Viniferin increases TFAM accumulation in macrophages. Representative western blots and optical band densitometry for TFAM and  $\beta$ -actin from macrophages treated with viniferin (0 or 1  $\mu$ M) for 24 hours. Means ± s.e.m., *n* = 3, \**P* < 0.05.