Supplementary Figure 1. Effect of SOD overexpression on ceramide-induced reactive oxygen species. a. Hydrogen peroxide (H_2O_2) levels in the bronchoalveolar (BAL) lavage of wild type (wt) or transgenic mice (Cu/Zn SOD Tg) after i-t. instillation of ceramide (Cer) (levels normalized by number of cells in the BAL, mean + SEM; $p<0.001$ Kruskal-Wallis ANOVA; # $p<0.05$ versus control; * $p<0.05$ versus wt cer). **b.** Genotyping of Cu/Zn SOD mice. Microphotograph of DNA agarose gel. Lanes marked with IL-2 show internal control. Lanes marked SOD show expression in the mouse DNA of human Cu/Zn SOD gene as a 236 bp transcript.

Supplementary Figure 2. Lung MMP-9 activity following ceramide instillation. Densitometric measurements of MMP-9 activity in mice receiving intra-tracheal vehicle (lanes 1-4) compared to those receiving ceramide (lanes 5-10; C12:0 1 mg/kg; 48h), using gelatin zymography (shown as digested white bands on the dark background of the Coomasie-stained gel). Mean + SD ($p=0.007$)

Supplementary Figure 3. Schematic of the putative crosstalk of ceramide-induced oxidative stress and apoptosis causing alveolar destruction in the lung. Cigarette smoke, like VEGF receptor inhibition, upregulated lung ceramides. Ceramide augmentation increased reactive oxygen species in the lung, coupled with an inhibition of anti-oxidant enzyme activity, such as superoxide dismutase (SOD). Ceramide triggered ROS-dependent caspase-3 and ASMase activation, the latter causing further increases in lung ceramides. While caspase inhibition augmented the mitochondrial superoxide dismutase activity, overexpression of Cu/Zn SOD decreased ceramide-induced ASMase and caspase-3 activation and protected the lung

against ceramide-induced alveolar destruction, as it protected against cigarette smoke-induced emphysema.