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Title: LSC 2013 abstract - The role of inducible nitric oxide synthase (iNOS) for the remodeling of alveolar septa in surfactant protein D deficient mice

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Body: Chronic obstructive pulmonary disease (COPD) is a major source of morbidity and mortality worldwide. iNOS expressed by alveolar macrophages (AM) mediates lung remodeling in COPD-models. Surfactant Protein D (SP-D) modulates the immune system. SP-D deficient mice (DKO) develop an emphysematous phenotype with a fibrotic component with age and hyperplasia of alveolar epithelial type II cells. AM produce high amounts of iNOS. Thus, we hypothesize that iNOS mediates interstitial remodeling in SP-D knockout mice. Using unbiased stereology, we compared DKO, SP-D/iNOS double-knockout mice (DiNOS) and wild type mice (wt) aged 29 weeks at light and electron microscopic level to quantitatively assess morphometric changes in the different components of the blood-gas barrier (alveolar epithelium, interstitial tissue and endothelium). Septal wall thickness was significantly reduced in DiNOS compared to DKO (4.2+/-0.6µm vs. 6.8+/-1.0µm). We found a significant decrease in the absolute volume of the blood-gas barrier in DiNOS (121.8 vs. 77.4 vs. 66.9 mm^3 in DKO, DiNOS and wt respectively). This effect can be attributed to a decrease in volumes of amorphous extracellular matrix (ECM) (22.2 vs. 14.5 vs. 16.0 mm^3), interstitial cells (20.8 vs. 15.5 vs. 12.4 mm^3) and alveolar epithelium (53.8 vs. 29.6 vs. 20.2 mm^3). Volumes of collagen and elastin fibrils as well as endothelia remained virtually unchanged. iNOS mediates remodeling of septal walls e.g. deposition of amorphous ECM in DKO. Our results underscore the hypothesis that iNOS plays an important role in the development of the phenotypic alterations in old SP-D deficient mice.