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Title: LSC 2013 abstract - NADPH oxidase isoform 2 (NOX2) is expressed in alveolar macrophages of emphysematous patients and prevents elastase-induced emphysema through the involvement of MMP9/TIMP1 gene expression

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Body: Reactive oxygen species (ROS), which are mainly generated by NADPH oxidase, are known to participate in the pathogenesis of emphysema. There is evidence that NOX2, an isoform expressed in inflammatory cells and NOX1, detected in alveolar epithelial cells, contribute in the development of emphysema, but their specific role needs to be elucidated. To determine whether NOX2 and NOX1 are involved in human emphysema, their expressions were studied by immunohistochemistry in lungs of emphysematous patients. In addition, we investigated the contribution of NOX2 and NOX1 in elastase-induced emphysema using NOX2- and NOX1-deficient mice.NOX2 was mainly detected in alveolar macrophages of healthy and emphysematous lungs and NOX1 was present in alveolar epithelium and bronchial cells. Furthermore, elastase exposure increased NOX2 and NOX1 mRNA expression in mouse lungs. In parallel, elastase-induced alveolar airspace enlargement was prevented in NOX2-deficient mice but not in NOX1-deficient mice. NOX2 deficiency led to accumulation of apoptotic neutrophils in bronchoalveolar lavage after elastase instillation and the level of Il-6 and TNFa levels was identical between NOX2-deficient and WT mice under elastase; suggesting impaired clearance by macrophages. Furthermore, NOX2 deficiency reduced elastase-induced ROS production in particular in macrophages and matrix metalloproteinase (MMP)-9 and tissue inhibitor of metalloproteinase (TIMP)-1 gene expression but not MMP-2. Finally, these results demonstrate that NOX2 is involved in elastase-induced emphysema through the involvement of MMP9/TIMP1 gene expression.