Club cell protein 16 (CC16): a novel protective protein during aging-related emphysema and small airways remodeling

ORAL COMMUNICATION

Authors

M. Laucho-Contreras a,b, F. Polverino b,c,d, H. Aslam b, B. R. Celli b,c, C. A. Owen b,d

a University Hospital of Caracas. Caracas, Venezuela
b Division of Pulmonary and Critical Care Medicine, Brigham and Women’s Hospital and Harvard Medical School. Boston, USA
c The Lovelace Respiratory Research Institute. Albuquerque, USA
d University of Parma. Parma, Italy

Correspondence

Caroline A. Owen
Division of Pulmonary and Critical Care Medicine, Brigham and Women’s Hospital Room 855B, Harvard Institutes of Medicine Building, 77 Avenue Louis Pasteur, Boston, MA 02115, USA.
E-mail: cowen@rics.bwh.harvard.edu

GOALS

CC16 deficiency is linked to human COPD and exaggerated pulmonary inflammation and COPD-like chronic lung pathologies in cigarette smoke (CS)-exposed mice. Moreover, plasma CC16 levels are inversely related to lung function decline in the general population independent of smoking status or pack-years. COPD is a disease of accelerated aging, and aging is associated with low-grade tissue inflammation, however the factors that contribute to these processes are not known. Thus, we tested the hypothesis that CC16 deficiency alone leads to low-grade pulmonary inflammation followed by the development of COPD-like lung pathologies in mice as they age.

METHODS

We measured pulmonary inflammation, lung function, emphysema, and small airway fibrosis in air-exposed WT vs. CC16−/− mice at intervals up to 18 months of age. We also measured lung levels of proteinases, cytokines, and oxidative stress.

RESULTS

CC16−/− mice had greater pulmonary inflammation (total leukocytes and macrophages), emphysema, and small airway fibrosis, and left shifts in their pressure-volume flow loops than WT mice at 12 and 18 months of age. These changes were associated with increased lung levels of metalloproteinase 9 (MMP-9) but not cytokines or oxidative stress in CC16-deficient aging lungs.

CONCLUSIONS

Our results show a novel association between CC16 deficiency and aging-related chronic pulmonary inflammation and chronic lung pathologies that contribute to lung function decline. These changes may be linked to increased lung levels of MMP-9 and increased extracellular matrix protein turnover in CC16-deficient lungs.