Whole lung image-based quantification of alveolar airspace histological parameters identifies diffuse emphysematous phenotype in a mouse model of obstructive lung diseases

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Background

Pulmonary emphysema is a pathophysiological characteristic of severe obstructive lung diseases including chronic obstructive pulmonary disease (COPD) and cystic fibrosis (CF). Recently, a murine model of COPD/CF that exhibits pulmonary emphysema has been uniquely established by inducing airway-specific overexpression of the epithelial Na⁺ channel β subunit (β ENaC-Tg mice) (Shuto T., et al., *Sci Rep*, 2016). However, little is known about the biochemical and histological differences between β ENaC-Tg mice and the existing emphysematous mouse model, for example, elastase-induced mouse model.

Method

We analyzed the biochemical parameters by quantitative RT-PCR using mouse lung tissue RNA samples. The histological assessment was performed employing a new method to evaluate emphysema in lung tissue section using whole lung image-based auto-measure parameters (area, perimeter, (major axis + minor axis)/2, feret diameter) by fluorescence microscope BZ-X710 (Keyence). We compared the parameters between β ENaC-Tg mice and elastase-induced model mice, a general model of emphysema in COPD.

Results

Expression analysis revealed that elastase-induced model mice exhibited transient up-regulation of inflammatory and senescence-like markers (KC, IL-6, p21, Sirt1) at disease induction period (1 day after elastase administration), which did not last until onset of disease (after 3 weeks); while these up-regulations were stable and constant during the whole disease process in β ENaC-Tg mice. Histological analyses revealed that even though the extent of emphysema was similar in both models, the coefficient of variation (CV) of all alveolar airspace histological parameters was smaller in β ENaC-Tg mice.

Conclusions

These assessments demonstrate that β ENaC-Tg mice exhibit not only inflammatory and senescence-like but also diffuse-type emphysematous phenotypes. The study also provides novel and useful image-based quantification method that covers whole lung tissue.