



Fibroblast growth factor 10 reverses cigarette smoke- and elastase-induced emphysema and pulmonary hypertension in mice

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Impaired FGF10 signalling is an integral part of the pathomechanism that leads to development of cigarette smoke-induced emphysema and PH. Restoration of FGF10 signalling reverses established cigarette smoke- and elastase-induced emphysema and PH in mice. <https://bit.ly/3PgqrBw>

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Abstract

Background COPD is an incurable disease and a leading cause of death worldwide. In mice, fibroblast growth factor (FGF)10 is essential for lung morphogenesis, and in humans, polymorphisms in the human *FGF10* gene correlate with an increased susceptibility to develop COPD.

Methods We analysed FGF10 signalling in human lung sections and isolated cells from healthy donor, smoker and COPD lungs. The development of emphysema and PH was investigated in *Fgf10*^{+/-} and *Fgfr2b*^{+/-} (FGF receptor 2b) mice upon chronic exposure to cigarette smoke. In addition, we overexpressed FGF10 in mice following elastase- or cigarette smoke-induced emphysema and pulmonary hypertension (PH).

Results We found impaired FGF10 expression in human lung alveolar walls and in primary interstitial COPD lung fibroblasts. In contrast, FGF10 expression was increased in large pulmonary vessels in COPD lungs. Consequently, we identified impaired FGF10 signalling in alveolar walls as an integral part of the pathomechanism that leads to emphysema and PH development: mice with impaired FGF10 signalling (*Fgf10*^{+/-} and *Fgfr2b*^{+/-}) spontaneously developed lung emphysema, PH and other typical pathomechanistic features that generally arise in response to cigarette smoke exposure.

Conclusion In a therapeutic approach, FGF10 overexpression successfully restored lung alveolar and vascular structure in mice with established cigarette smoke- and elastase-induced emphysema and PH. FGF10 treatment triggered an initial increase in the number of alveolar type 2 cells that gradually returned to the basal level when the FGF10-mediated repair process progressed. Therefore, the application of recombinant FGF10 or stimulation of the downstream signalling cascade might represent a novel therapeutic strategy in the future.

