Regulating the cell shift of endothelial cell-like myofibroblasts in pulmonary fibrosis

Xiuju Wu[1,5], Daoqin Zhang[2,5], Xiaojing Qiao[1], Li Zhang[1], Xinjiang Cai[1], Jaden Ji[1], Jocelyn A. Ma[1], Yan Zhao[1], John A. Belperio[3], Kristina I. Boström[1,4] and Yucheng Yao[1]

[1]Division of Cardiology, David Geffen School of Medicine at UCLA, Los Angeles, CA, USA. [2]Department of Pediatrics, Stanford University, Stanford, CA, USA. [3]Division of Pulmonary and Critical Care Medicine, Clinical Immunology, and Allergy, David Geffen School of Medicine, University of California, Los Angeles, CA, USA. [4]The Molecular Biology Institute at UCLA, Los Angeles, CA, USA. [5]These authors contributed equally to this work.

Corresponding author: Yucheng Yao (yyao@mednet.ucla.edu)

Shareable abstract (@ERSpublications)
New mouse models of pulmonary fibrosis are created to identify a previously unknown cell population that contributes myofibroblasts to pulmonary fibrosis. A small molecule is identified to redirect myofibroblasts and reduces pulmonary fibrosis. https://bit.ly/3DF6XjH

Cite this article as: Wu X, Zhang D, Qiao X, *et al*. Regulating the cell shift of endothelial cell-like myofibroblasts in pulmonary fibrosis. *Eur Respir J* 2023; 61: 2201799 [DOI: 10.1183/13993003.01799-2022].

This single-page version can be shared freely online.

This article has an editorial commentary: https://doi.org/10.1183/13993003.00407-2023

Received: 15 Sept 2022
Accepted: 25 Jan 2023

Abstract

Pulmonary fibrosis is a common and severe fibrotic lung disease with high morbidity and mortality. Recent studies have reported a large number of unwanted myofibroblasts appearing in pulmonary fibrosis, and shown that the sustained activation of myofibroblasts is essential for unremitting interstitial fibrogenesis. However, the origin of these myofibroblasts remains poorly understood. Here, we create new mouse models of pulmonary fibrosis and identify a previously unknown population of endothelial cell (EC)-like myofibroblasts in normal lung tissue. We show that these EC-like myofibroblasts significantly contribute myofibroblasts to pulmonary fibrosis, which is confirmed by single-cell RNA sequencing of human pulmonary fibrosis. Using the transcriptional profiles, we identified a small molecule that redirects the differentiation of EC-like myofibroblasts and reduces pulmonary fibrosis in our mouse models. Our study reveals the mechanistic underpinnings of the differentiation of EC-like myofibroblasts in pulmonary fibrosis and may provide new strategies for therapeutic interventions.