

PubMed

**Format:** Abstract**Full text links**

Am J Pathol. 2019 Dec 12. pii: S0002-9440(19)30851-X. doi: 10.1016/j.ajpath.2019.10.014. [Epub ahead of print]

Collagen VI Deficiency Results in Structural Abnormalities in the Mouse Lung.

Mereness JA¹, Bhattacharya S², Ren Y², Wang Q², Anderson CS², Donlon K², Dylag AM², Haak J², Angelin A³, Bonaldo P⁴, Mariani T⁵.

Author information

Abstract

Collagen 6 (COL6) is known for its role in a spectrum of congenital muscular dystrophies, which are often accompanied by respiratory dysfunction. However, little is known regarding the function of COL6 in the lung. We confirmed the presence of COL6 throughout the basement membrane region of mouse lung tissue. Lung structure and organization was studied in a previously described Col6a1^{-/-} mouse, which do not produce detectable COL6 in the lung. The Col6a1^{-/-} mouse displayed multiple histopathological alveolar and airway abnormalities. The airspaces of Col6a1^{-/-} lungs appeared simplified, with larger (29%, $P < 0.01$) and fewer (31%, $P < 0.001$) alveoli. These airspace abnormalities included a reduction in IsolectinB4⁺ alveolar capillaries and Sftpc⁺ ATII cells. Alterations in lung function consistent with these histopathological changes were evident. Col6a1^{-/-} mice also displayed multiple airway changes including increased branching (59%, $P < 0.001$), increased mucosal thickness (34%, $P < 0.001$), and increased epithelial cell density (13%, $P < 0.001$). Comprehensive transcriptome analysis revealed that the loss of COL6 is associated with reductions in integrin-paxillin-PI3K signaling in vivo. In vitro, COL6 promoted steady-state phospho-paxillin levels and reduced cell density (16% to 28%, $P < 0.05$) at confluence. Inhibition of PI3K, or its downstream effectors, resulted in increased cell density to a level similar to that seen on matrices lacking COL6.

Copyright © 2019. Published by Elsevier Inc.

PMID: 31837950 DOI: [10.1016/j.ajpath.2019.10.014](https://doi.org/10.1016/j.ajpath.2019.10.014)

LinkOut - more resources

