Developmental Dynamics 2017

Ex vivo analysis of the contribution of FGF10^{+} cells to airway smooth muscle cell formation during early lung development

El Agha E., Kheirollahi V., Moiseenko A., Seeger W., Bellusci S.

Kazan Federal University, 420008, Kremlevskaya 18, Kazan, Russia

Abstract

© 2017 Wiley Periodicals, Inc.Background: Airway smooth muscle cells (ASMCs) have been widely studied during embryonic lung development. These cells have been shown to control epithelial bifurcation during branching morphogenesis. Fibroblast growth factor 10-positive (FGF10+) cells, originally residing in the submesothelial mesenchyme, contribute to ASMC formation in the distal lung. The reported work aims at monitoring the response of FGF10+ progenitors and differentiated ASMCs to growth factor treatment in real time using lineage tracing in the background of an air-liquid interface (ALI) culture system. Results: FGF ligands impose divergent effects on iterative lung branching in vitro. Moreover, time-lapse imaging and endpoint analysis show that FGF9 treatment leads to amplification of the FGF10+ lineage and represses its differentiation to ASMCs. Sonic hedgehog (SHH) treatment reduces the amplification of this lineage and leads to decreased lung branching. Finally, differentiated ASMCs in proximal regions fail to expand upon FGF9 treatment. Conclusions: Our data demonstrate, in real time, that FGF9 is an important regulator of amplification, migration, and subsequent differentiation of ASMC progenitors during early lung development. The attained results agree with previous findings regarding ASMC formation and highlight the complexity of growth factor signaling networks in controlling mesenchymal cell-fate decisions in the developing mouse lung.

http://dx.doi.org/10.1002/dvdy.24504

Keywords

Airway smooth muscle cell, FGF, Lineage tracing