Lineage-Negative Progenitor Cells Mobilize To Regenerate Lung Epithelium After Major Injury

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Technology description

Scientists at the University of California, San Francisco have identified and characterized a rare LNEP cell population in mice that is capable of regenerating tissue in damaged lungs. In normal lungs, LNEPs remain inactive until triggered by lung damage. Injury-activated cells proliferate and migrate to damaged areas and subsequently differentiate into mature epithelia. By identifying a novel set of biomarkers, including the expression of B4, CD14, and CD200, the inventors further enriched this LNEP population. The investigators successfully isolated and grafted enriched cells into mice with lungs damaged by influenza, ultimately resulting in lung tissue regeneration. This is the first successful demonstration stem cell engraftment in lungs.

The inventors further demonstrated that Notch signaling plays a significant role in the regeneration process in these mice; elevated Notch signaling resulted in the failure of tissue regeneration. Notch signaling was similarly elevated in lung tissue samples from human patients suffering from idiopathic pulmonary fibrosis or sclerdoma, suggesting that this technique has promise in humans as well as mice. Once validated in human samples, this invention could allow for the autologous transplantation of lung stem cells in patients with chronic lung illnesses such as idiopathic pulmonary fibrosis.

This invention is a novel method of isolating a rare lineage-negative epithelial progenitor (LNEP) cell population and introducing it into the lungs of patients suffering from chronic fibrosis or acute injury. Chronic respiratory diseases are a major cause of mortality and account for over four million deaths yearly worldwide. Existing treatments merely reduce symptoms without offering a cure. Moreover, treating symptoms is a significant financial burden, with global costs predicted to double to $800 billion by 2021. In the US, Medicare alone spent $8 billion in 2006 on the treatment of chronic lung diseases.

Previous attempts to regenerate lung tissue have focused on mature epithelial cells, which fail to proliferate in patients with chronic lung diseases. This method instead relies on a rare sub-population of stem cells that has successfully repaired damaged lungs in mice. Once validated in human samples, this method could pave the way for stem cell therapies for chronic lung illnesses

Data Availability

Published manuscript

Related Materials

Lineage-negative progenitors mobilize to regenerate lung epithelium after major injury. Vaughan AE, Brumwell AN, Xi Y, Gotts JE, Brownfield DG, Treutlein B, Tan K, Tan V, Liu FC, Looney MR, Matthay MA, Rock JR, Chapman HA. Lineage-negative progenitors mobilize to regenerate lung epithelium after major injury. Nature. 2015 Jan 29;517(7536):621-5. doi: 10.1038/nature14112. Epub 2014 Dec 24.

Application area

Markers for the identification and isolation of lung epithelial progenitor cells
Autologous stem cell therapy for lung tissue
Disease applications
Idiopathic pulmonary fibrosis and other chronic fibrotic lung diseases
Lung injury caused by smoking
Lung injury caused by viral or bacterial infection

Advantages

Addresses the cause of lung disease rather than merely ameliorating symptoms
First successful method of engrafting stem cells in lungs
Isolated cells have the ability to differentiate into multiple lung epithelial cell types
No risk of immune rejection

Institution

University of California, San Francisco

Inventors

Andrew Vaughan
Harold Chapman

联系我们

叶先生

电 话：021-65679356

手 机：13414935137

邮 箱：yeyingsheng@zf-ym.com