Researchers find key developmental pathway activates lung stem cells

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Researchers from the University of Pennsylvania School of Medicine found that the activation of a molecular pathway important in stem cell and developmental biology leads to an increase in lung stem cells. Harnessing this knowledge could help develop therapies for lung-tissue repair after injury or disease. The investigators published their findings online last week in advance of print publication in *Nature Genetics*.

"The current findings show that increased activity of the Wnt pathway leads to expansion of a type of lung stem cell called bronchioalveolar stem cells," says senior author Edward Morrisey, Ph.D., Associate Professor of Medicine and Cell and Developmental Biology.

"This information will give us a more extensive basic understanding of Wnt signaling in adult tissue repair in the lung and other tissues and also start to help us determine whether pharmacological activation or inhibition of this pathway can be utilized for treatments," explains Morrisey, who is also the Scientific Director of the Penn Institute for Regenerative Medicine.

Activation of the Wnt signaling pathway leads to expansion, or increase in number, of bronchioalveolar stem cells in the lung. A protein called GATA6 inhibits Wnt signaling by directly regulating the expression of another protein in the Wnt pathway called frizzled 2 (Fzd2).

Wnt signaling is a major pathway in stem cell biology. The finding that GATA6 negatively regulates Wnt signaling and that GATA6 has been shown to play important roles in embryonic stem cell replication and differentiation suggests that these two pathways are linked not only in lung stem cells but in other tissues where they play important roles including the heart, gut, and pancreas.

"We were surprised by the robust activation of Wnt signaling after loss of GATA6 expression in the lung," says Morrisey. "Such a robust activation is rarely observed."

Wnt signaling can be pharmacologically modulated with compounds, including lithium, already approved by the FDA. Use of such compounds, both known and newly identified through ongoing screens, could allow for forced expansion and differentiation of key stem cell populations in the lung and other tissues for adult tissue repair after injury or disease.

Future directions of the Morrisey lab include not only a more extensive basic understanding of Wnt signaling in adult-tissue repair in the lung and other tissues, but also starting to determine whether pharmacological activation or inhibition of this pathway can really be utilized for treatments.

Source: University of Pennsylvania

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