Signaling pathway is 'executive software' of airway stem cells

June 17 2011

Researchers at Duke University Medical Center have found out how mouse basal cells that line airways "decide" to become one of two types of cells that assist in airway-clearing duties. The findings could help provide new therapies for either blocked or thinned airways.

“Our work has identified the Notch signaling pathway as a central regulatory ‘switch’ that controls the differentiation of airway basal stem cells,” said Jason Rock, Ph.D., lead author and postdoctoral researcher in Brigid Hogan's cell biology laboratory. “Studies like ours will enhance efforts to develop effective genetic, cellular, and molecular therapies for airway diseases - a leading cause of death worldwide.”

The work was published in *Cell Stem Cell* on June 3.

Together with the current findings, recent studies suggest that the Notch signaling pathway represents a potential therapeutic target for airway remodeling and lung disease, he said. “Notch is like an executive software package that helps to maintain the delicate balance of the epithelium, the lining of the airway,” said senior author Brigid Hogan, Ph.D., chair of the Duke Department of Cell Biology. “The Notch pathway plays a role in other parts of the body, including neural stem cells, and this is the first time we have seen the results of the Notch pathway in airways. We have also found that the function of Notch signaling is conserved in basal cells from human airways.”

Notch signaling dictates whether the daughters of basal stem cells

assume one of two different fates, Hogan said. Sustained, high levels of Notch pathway activation result in more secretory cells. These make the needed amount of mucus to move out particles that need to be cleared. Low levels of Notch signal lead to ciliated cells, which act as brushes to move the mucus along toward clearance. Notch, however, isn't required for basal stem cells to proliferate and make additional basal cell daughters.

Airway disease, including chronic obstructive pulmonary disease, cystic fibrosis, asthma, acute allergies, and transplant complications, can range from fatal to debilitating, so understanding the secrets of how healthy cells can grow, and in the proper amounts, after injury is important. Fifty-five percent of deaths from lung disease result from changes in the small airways, Hogan said.

The researchers also demonstrated in this work that the smallest airway branches in humans are the same size and are organized like the largest (tracheal) airway tubes in mice. The next step for the team is to investigate the behavior of the daughters of basal cells to learn what machinery is involved in making them commit to various lineages, and how this system is coordinated to help restore lung function, Hogan said.

Provided by Duke University