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Research elucidates way lungs fight bacteria and prevent infection

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Actor and pancreatic cancer patient Patrick Swayze's recent hospitalization with pneumonia as a result of his compromised immune system underscores the sensitivity of the lungs: many patients die from lung complications of a disease, rather than the disease itself.

Lungs are delicate and exposed to the environment, almost like an open wound. Consequently, the body has developed an elaborate immuno-defense system to combat inhaled pathogens and bacteria - in a healthy individual, this system effectively blocks hundreds of potentially sickening assaults daily.

It works like this: airway epithelial cells initiate an immune response to inhaled bacteria by signaling for white blood cells to move from the bloodstream into the lungs and airway to fight potential infection.

For the first time, researchers at Columbia University Medical Center have demonstrated that this signaling cascade includes the activation of epithelial proteases, a type of enzyme capable of opening the junctions between the cells in the airway mucosa, to enable the white blood cells to get through to the site of the infection. The opening of these junctions is initiated by a change in calcium levels.

The work by Drs. Jarin Chun and Alice Prince in the Departments of Pharmacology and Pediatrics at Columbia's College of Physicians and Surgeons was published Jan. 22, 2009 in the journal *Cell Host & Microbe*.

Getting white blood cells to the site of an infection, however, is often a double-edged sword. On the one hand, having as many white blood cells as possible at the site of an infection is beneficial, but on the other hand too many white blood cells can lead to excessive inflammation, interfering with breathing and damaging the airways.

Cystic fibrosis is one disease where this work might have particular import, Dr. Chun says. People with cystic fibrosis possess an abnormal gene that causes normal mucus to become thick and sticky, leaving the lung more prone to infection and inflammation, while still killing infection-causing bacteria.

The findings, in mice, demonstrate a way to inhibit proteases and restrict the junctions between cells in the airway mucosa, meaning that fewer white blood cells can get into the airway - causing less inflammation.

Thus, epithelial proteases could be an important target to control inflammation in the lung, and could serve as the basis for the development of novel drugs to help the human body get the optimal number of white blood cells to an infection site without letting inflammation spiral out of control.

Source: Columbia University