

Study points to essential role of IL-22 in lung repair after the flu

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Once the initial episode of influenza has passed, the chronic effects tend to be overlooked. The results of a new study indicate that the cytokine interleukin-22 (IL-22) plays a critical role in normal lung repair following influenza infection. This study is published in the April 2013 issue of the *American Journal of Pathology*.

"With the increasing prevalence of more infective and/or [virulent strains](#) of influenza, understanding the impact of virus on the host epithelium and the processes involved in lung repair are of great importance," says John F. Alcorn, PhD, an [immunologist](#) affiliated with the department of pediatrics at the Children's Hospital of Pittsburgh of UPMC. He notes that the findings open up new possibilities for developing [therapeutic agents](#) that promote recovery of normal [lung function](#) and architecture after influenza infection and lessen the likelihood of secondary infections. "A key finding is that even after the resolution of infection, influenza results in lung parenchymal remodeling that may be critical to susceptibility to further injury," says Dr. Alcorn.

This series of experiments used 6- to 8-week-old wild-type (WT) mice (C57BL/6 strain) as well as IL-22-deficient mice, infected with influenza A PR/8/34 H1N1 or control vehicle. To determine the distribution of IL-22 in the lung, they used immunohistochemistry for the high affinity IL-22Ra1 receptor. Investigators found that in WT mice not infected with influenza, IL-22 receptors were distributed on epithelial cells of the large and small airways, but not within the parenchyma. They noted that this receptor distribution suggests that in

the absence of lung injury, IL-22 interacts mainly with the bronchial epithelial cells.

By 21 days post influenza infection, IL-22 receptors were observed in parenchymal tissue in injured areas, such as [alveoli](#) under repair. Researchers suggest that the IL-22 receptor can be upregulated at sites of influenza-associated injury.

The investigators also reported that 10 days after influenza infection, IL-22–deficient mice showed significantly more severe damage and greater lung edema than WT control mice, as indicated by higher lactate dehydrogenase levels and more total protein content in bronchoalveolar lavage. No differences were found in viral load. Another indication of more severe [lung injury](#) was an increase in the number of lymphocytes in the IL-22–deficient animals.

IL-22–deficient mice also showed functional impairments. For instance, those infected with influenza showed significantly decreased compliance (referring to lung distensibility) and increased hysteresis (referring to compliance differences during inspiration and expiration), indicating lung stiffness. Histological examination 21 days after influenza infection showed that IL-22–deficient mice displayed regions of diffuse inflammation and alveolar injury, few areas of metaplasia, higher intimal thickening, proteinaceous accumulation, and increased collagen deposition compared to WT mice. Gene expression analysis revealed aberrant expression of epithelial genes involved in repair processes in the mice lacking IL-22.

"The role of IL-22 in promoting epithelial repair is emerging. We demonstrate that IL-22 plays a critical role in regulating pulmonary epithelial repair responses during [influenza infection](#) and resolution," says Dr. Alcorn. IL-22 is currently under development as a potential therapeutic in human clinical trials.

More information: "IL-22 is essential for lung epithelial repair following influenza infection," by Derek A. Pociask, Erich V. Scheller, Sivanarayana Mandalapu, et al. (DOI: [dx.doi.org/10.1016/j.ajpath.2012.12.007](https://doi.org/10.1016/j.ajpath.2012.12.007)). It appears in the *American Journal of Pathology*, Volume 182, Issue 4 (April 2013)

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