

Journal club

Mouse lung regeneration after H1N1

This study demonstrates that following an ARDS-like syndrome in mice secondary to infection with a murine-adapted H1N1 virus, complete recovery follows the emergence of a population of stem cells bearing the differentiation markers of alveoli.

Contrary to the existing bleomycin-based models of pulmonary injury causing fibrosis, this murine H1N1 model sustains substantial airway damage and epithelial destruction, followed by viral clearing and histological recovery over several months. This represents a novel paradigm to investigate regenerative responses to infection.

Using molecular and immunohistochemical methods, the authors illustrate that following H1N1 infection, a cell population expressing p63, a known marker of stem cells in nasal and tracheal epithelia, emerges from distal bronchial epithelia in damaged lung and expands to form discrete 'pods' or islands of cells that concentrically surround distal airways. These pods assemble into novel alveoli-like structures bearing molecular markers and gene expression profiles of alveoli. Lineage tracing of these pods reveals a path originating in bronchiolar epithelium. Complete histological recovery including regeneration of alveoli–capillary networks follows over several months with no evidence of fibrosis. In parallel studies, the authors cultured comparable p63-positive stem cells derived from human distal airway epithelia, which similarly assembled into alveoli-like structures bearing specific molecular and genetic markers of alveolar and capillary development in vitro.

This work identifies a previously undescribed source of distal airway stem cells capable of regenerating damaged lung parenchyma following inflammation-induced lung injury, suggesting novel therapeutic approaches to currently non-reversible airway diseases. How the incipient alveoli-like structures integrate into existing airway structures remains to be seen.

► **Kumar PA**, Hu Y, Yamamoto Y, *et al*. Distal airway stem cells yield alveoli in vitro and during lung regeneration following H1N1 influenza infection. *Cell* 2011;**147**:525–38.

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