Forming and transforming tubes in the mouse lung

Summary
The air passages in the mammalian lung are a tubular network with two compartments: the proximal tree-like airways and the distal honeycomb-like alveoli. Failure to form or maintain the airways and the alveoli causes serious illnesses including bronchopulmonary dysplasia, which is often seen in children born prematurely, and chronic obstructive pulmonary diseases, which is often seen in smokers. The epithelium surrounding the air passages arises from a group of foregut-derived epithelial progenitors. Early in development, these progenitors expand rapidly and undergo branching morphogenesis to form tubes of the airway compartment. Late in development, the progenitors continue to build tubes, which are subsequently transformed into the honeycomb-like alveoli. Work in our lab is revealing a hierarchical gene network controlling progenitor branching, which may underlie the evolution of the primitive amphibian lung. We have also found that the underpinning of the tube-to-alveolus transformation is the alveolar type 1 cell, a mysterious and arguably the thinnest cell in our body, which surprisingly has both a structural and signaling role. Elucidating such epithelial biology in the context of tube morphogenesis should facilitate functional integration of endogenous or engineered stem cells into tissue architecture in regenerative medicine.