Signaling pathways involved in lung fibrosis and in postnatal lung development

We are interested in exploring the consequences of Hedgehog signaling in the lung in two contexts: postnatal lung development, and lung injury and scarring. Hedgehog expression is high within the lung during embryonic development, and declines after birth. During postnatal lung development, new alveoli are formed through the formation of new alveolar septa, and these new septa undergo a maturation process involving loss of stromal cells and alterations of the capillaries within the septal walls. We are testing the hypothesis that reduction in Hedgehog signaling is necessary for this maturation process. In addition, we are testing the hypothesis that under certain conditions of lung injury, Hedgehog signaling is re-expressed, driving proliferation of stromal cells and worsening fibrosis (scarring).

During a concentration, a student would examine the effects of activating or inhibiting Hedgehog signaling in mice at specific time periods during neonatal life or in relation to a fibrosis-inducing lung injury. Hedgehog signaling can be modified using an inhibitory antibody, small molecule inhibitors, genetically modified mice, and an adenovirus that directs expression of Sonic Hedgehog in the lung. Mouse tissues are used for morphological analysis, immunostaining, physiological measurements, and quantification of fibrosis.

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