

2009 Abstracts



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Smooth Muscle Cell Related Vascular Remodeling in Pulmonary Hypertension in Congenital Diaphragmatic Hernia

Pulmonary hypertension in patients with congenital diaphragmatic hernia is highly lethal. Presently no definitive treatment exists for pulmonary hypertension because the pathogenic mechanisms are not fully understood. Pulmonary vascular remodeling is the central cause of pulmonary hypertension, and smooth muscle cells are a major participant in driving this process. My proposal will examine smooth muscle cell related mechanisms in pulmonary hypertension. I will explore the role of Slit3 in smooth muscle cell differentiation and migration, and I will use the Slit3 null mouse to examine the impact of Slit3 upon the developing pulmonary circulation and on pulmonary circulation physiology. The work will be accomplished through three aims.

Aim 1: Determine the molecular effects of Slit3 signaling on phenotype diversity, differentiation, and gene expression in pulmonary artery smooth muscle cells in vitro.

Aim 2: Characterization of the role of Slit3 upon pulmonary artery smooth muscle cell migration related to pulmonary vascular remodeling.

Aim 3: Determine the role of Slit 3 in physiologic function and structural development of the pulmonary circulation in a mouse model of congenital diaphragmatic hernia. Findings from this work may define direct therapeutic targets to treat pulmonary hypertension in patients with congenital diaphragmatic hernia. My results may also elucidate novel treatments for other forms of pulmonary hypertension.