

STRONG CHILDREN'S RESEARCH CENTER

Summer 2012 Research Scholar

Name: Paul Carlson
School: University of Minnesota
Mentor: Kate Ackerman, MD

ABSTRACT

Title: *Analysis of the role of Zfp201 (Fog2) in early Lung Morphogenesis*

Congenital Diaphragmatic Hernia (CDH) is a severe defect occurring in approximately 1 in 3000 live births. Newborns with CDH often suffer from pulmonary hypoplasia, and as a result the mortality rate associated with this condition is very high. To date, relatively little is known about the underlying molecular basis of CDH or the mechanism of development of pulmonary hypoplasia. A mouse model of CDH has been developed with a mutation in the zinc finger protein gene *Zfp201 (Fog2)*. The mutation causes both abnormal diaphragm development and bilateral pulmonary hypoplasia in mice and in humans. Interestingly, mutant mouse lungs have a specific lobar patterning defect and fail to develop an accessory lobe. Expression array and *in situ* hybridization experiments show downregulated expression of Fibroblast growth factor 10 (*Fgf10*), a critical factor in lung branching morphogenesis. Experiments were designed to determine whether localized delivery of FGF10 protein is sufficient to rescue accessory lung bud formation in the mutant. Embryonic mouse lungs were harvested at E10.5 and cultured on porous polystyrene membranes. Heparin-coated agarose beads were then soaked in recombinant mouse FGF10 and were placed at the site of absent accessory lung bud outgrowth. It was found that the presence of FGF10 induced budding of lung epithelium toward the bead. Furthermore, several mutant lungs demonstrated the formation of branches at the site where accessory lobe formation should take place. This result demonstrates that FGF10 rescues major bronchial branching in this important genetic model and plays a role in the mechanism of diaphragm defect associated pulmonary hypoplasia.