



Medical Education and Research Grant Outcome Report

Name: Molecular Mechanisms of Lung Organogenesis, Tumorigenesis, and Asthma

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Department: Medical Genetics

Program: New Investigator Program

Grant Duration: 08-01-05 to 07-31-08 (36 months)

Expenditures: \$100,000 (100% expended)

Use of Funds (Taxonomy): Basic research

Research Keywords: Lung, organogenesis, disease, genetics, gene expression

► **Description:** The goal of this project is to better understand the molecular and genetic mechanisms involved in lung formation and lung diseases such as cancer and asthma. Using a mouse model, the investigators focused on a large category of proteins termed transcription factors. There were two aims: (1) to compile a database of transcription factor expression patterns in the embryonic lung, and (2) to investigate one transcription factor, SOX2, a prominent stem cell factor, regarding its involvement in lung cell differentiation.

► **Results:** Regarding Aim 1, investigators examined approximately 1,100 genes and identified over 70 transcription factors expressed in the embryonic lung. They then examined the regulation of these transcription factors to determine involvement in lung disease.

Regarding Aim 2, the researchers discovered that SOX2 is required for formation of the trachea and esophagus. Mutations in this gene have recently been identified in human patients with anophthalmia-esophageal syndrome. One particular signaling pathway, fibroblast growth factor pathway, was found to regulate SOX2 expression in the developing lung.

In addition, a specific transcription factor, β -Catenin, was found to be essential in lung progenitor cells. It's expected that further research on this pathway may lead to the use of stem cell-based therapy for lung diseases.

These findings offer a wealth of information to all lung researchers and also serve as a foundation for this team's future research into treatment of lung diseases. National Institutes of Health (NIH) funding has been requested to study possible predictors and drug targets for asthma.

► **Met Objectives:** Project completed

► **Timeline for Application of Results:** 5-7 years

► **New Partnerships or Collaborations:**

- Collaborations with researchers at UW School of Medicine and Public Health Department of Asthma, Allergy, and Pulmonary Research (NIH proposal under review)
- Collaborations with European researchers working on SOX2 research

► **Matched Dollars (cash or in-kind):** \$0

► **Dissemination:**

- Published journal article: *Developmental Dynamics*
- Other articles submitted for publication

► **Additional Funding:** From the American Heart Association—2 years at \$60,000 per year. An application has been submitted for consideration by the NIH.