Fibroblast Growth Factor 18 (FGF-18) mRNA Expression Is Reduced in A Transgenic Mouse Model of Neonatal Lung Disease.

D. B. Pyles and T. D. Le Cras. Division of Pulmonary Biology, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio.

Background: Bronchopulmonary dysplasia (BPD) is a major problem in pediatrics as more and increasingly younger newborns survive premature birth. Disruption of postnatal alveolar and pulmonary vascular development plays a major role in the morbidity and mortality of BPD in premature newborns. While clinical studies have implicated increased TGF-alpha (TGF-α) and its receptor, the epidermal growth factor receptor (EGFR), in the pathogenesis of BPD, the precise role of TGF-α and downstream pathways involved are unclear. Studies from our group have shown that overexpression of TGF-α in the lungs of transgenic mice disrupts alveolar formation and causes chronic lung disease. **Objective:** The goal of this project was identify genes that play a role in the pathogenesis of TGF-α induced lung disease. **Methods:** TGF-α expression was induced in the lungs of transgenic mice from postnatal days 3 to 4 (1 day) and 3 to 5 (2 days). Microarray analysis was performed on lung RNA after 1 and 2 days of TGF-α expression. RT-PCR analysis was performed and to verify the microarray results for genes of interest. **Results:** Microarray analysis showed that 120 genes were significantly altered (increased or decreased; $P<0.05$) after TGF-α induction. Of particular interest was fibroblast growth factor-18 (FGF-18) which was reduced (33 & 60%), after 1 and 2 days of TGF-α expression compared to litter matched controls ($P<0.05$). RT-PCR analysis for FGF-18 mRNA confirmed the microarray results. **Conclusion:** Our studies showed that FGF-18 gene expression decreases early in the disruption of alveolar formation by TGF-α. FGF-18 has been shown to be critical for alveolar formation in knock-out mice and expression of FGF-18 surges during the alveolar phase of lung morphogenesis. Future studies will address the role of FGF-18 by using conditional FGF-18 transgenic mice to correct FGF-18 levels and determine whether this rescues alveolar formation and prevents neonatal lung disease.