and in mice treated with bleomycin in combination with the peptide. Further, to differentiate the crosslinking activity of LOX from other potential effects, primary human fibroblasts were cultured with rLOX in the presence of the inhibitor, beta-aminopropionitrile. The expression levels of ECM (collagen and fibronectin), pro-fibrotic factors (IL-6 and TGF-beta), and transcription factor (c-Fos) were examined by real-time PCR, ELISA, immunoblotting, or hydroxyproline assay. RESULTS/ANTICIPATED RESULTS: LOX mRNA was increased in lung tissues and matching fibroblasts of SSc patients. rLOX-induced ECM production in vitro and ex vivo in lung fibroblasts and in human lung tissues maintained in organ culture, respectively. Additionally, TGF-beta and bleomycin induced ECM production, LOX mRNA expression and activity. Endostatin peptide abrogated these effects. In vivo, rLOX synergistically exacerbated pulmonary fibrosis in bleomycin-treated mice. The inhibition of LOX catalytic activity by beta-aminopropionitrile failed to abrogate LOX-induced ECM production. LOX increased the production of IL-6, IL-8, and c-Fos neutralization blocked the effects of LOX. Further, LOX induced c-Fos expression and its nuclear localization. DISCUSSION/SIGNIFICANCE OF IMPACT: LOX expression and activity were increased with fibrosis in vitro, ex vivo, and in vivo. LOX induced fibrosis via increasing ECM, IL-6 and c-Fos translocation to the nucleus. These effects were independent of the crosslinking activity of LOX and mediated by IL-6. Our findings suggest that inhibition of LOX may be a viable option for the treatment of lung fibrosis. Further, the use of human lung in organ culture establishes the relevance of our findings to human disease.

The role of TGFβ in driving early cystic fibrosis lung disease
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OBJECTIVES/SPECIFIC AIMS: Transforming growth factor-beta (TGFβ) is a genetic modifier of cystic fibrosis (CF) lung disease. TGFβ’s pulmonary levels in young CF patients and its mechanism of action in CF are unknown. We examined TGFβ levels in sputum from CF and investigated the effects of hyperplasia, and decreased CFTR expression. CF mice had higher bronchoalveolar lavage fluid from CF patients (n = 15) and non-CF control patients (n = 21) < 6 years old were determined by ELISA. CF mice and non-CF mice were intratracheally treated with an adenoviral TGFβ1 vector or PBS; lungs were collected for analysis at day 7. Human CF and non-CF AECs were treated with TGFβ or PBS for 24 hours then collected for analysis. RESULTS/ANTICIPATED RESULTS: Young CF patients had higher bronchoalveolar lavage fluid TGFβ than non-CF controls (p = 0.03). Mouse lungs exposed to TGFβ demonstrated inflammation, goblet cell hyperplasia, and decreased CFTR expression. CF mice had greater TGFβ-induced lung mechanics abnormalities than controls; both CF human AECs and CF mice showed higher TGFβ-induced MAPK and PI3K signaling compared with controls. DISCUSSION/SIGNIFICANCE OF IMPACT: For the first time, we show increased TGFβ levels very early in CF. TGFβ drives CF lung abnormalities in mouse and human models; CF models are more sensitive to TGFβ’s effects. Understanding the role of TGFβ in promoting CF lung disease is critical to developing patient specific treatments.

Trauma-related acute respiratory distress syndrome (ARDS) in India: Current incidence and management strategies
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OBJECTIVES/SPECIFIC AIMS: Aim 1: To determine the true incidence of trauma-related acute respiratory distress syndrome (ARDS) in India. We propose to perform a prospective observational study to determine the incidence of ARDS in India. Aim 2: To perform a preliminary assessment of risk factors for ARDS in the Indian trauma population. We will leverage these findings against the global ARDS data to provide a foundation for further interventional studies. Aim 3: To evaluate the current management strategies and patient outcomes from ARDS in trauma subjects admitted to the Jai Prakash Narayan Apex Trauma Center (JPNATC). These findings will identify areas in need of practice-based performance improvement in ARDS therapies in India. METHODS/STUDY POPULATION: This section proposes an observational study of trauma patients with ARDS in the Indian trauma population. We will leverage these findings against the global ARDS data to provide a foundation for further interventional studies. Outcome data will include discharge location, ICU and hospital length of stay and improvement in ARDS therapies in India. METHODS/STUDY POPULATION: This section proposes an observational study of trauma patients with ARDS in the Indian trauma population. We will leverage these findings against the global ARDS data to provide a foundation for further interventional studies. Outcome data will include discharge location, ICU and hospital length of stay and