



# Engineering cell/ECM interactions in lung disease

Patrick Link, PhD  
Postdoctoral Research Fellow  
Department of Physiology and Biomedical Engineering  
Mayo Clinic



Cell characteristics are regulated through a variety of mechanisms, such as cytokines, the mechanical environment, or epigenetics. In lung diseases, abnormal regulation of multiple mechanisms combine to determine a shift from a healthy state toward a disease state. In lung diseases such as pulmonary fibrosis or pulmonary hypertension, cells become activated, which results in increased extracellular matrix deposition, increased cellular contractility, and increased tissue stiffness. I present work here, which is essential to defining the extracellular matrix as an important driver of diseased cell states.

Using models of lung disease, I quantified changes to baseline cellular phenotype. I questioned whether a disease state could modulate cellular contraction. I found fibroblasts isolated from patients with pulmonary fibrosis had an increased baseline contractile state which could only be significantly changed through combined silencing of transcriptional co-factors YAP and TAZ. These data show disease state can reprogram cellular contractile phenotype.

Then, I wanted to identify if the extracellular matrix could regulate cellular phenotype independent of substrate stiffness. Using hydrogels of healthy and diseased stiffnesses, I coated the gels with decellularized extracellular matrix from healthy and diseased tissue. I identified significant changes in cellular phenotype for healthy cells coated on normal stiffness-diseased extracellular matrix. Combined, these research works show that early changes in extracellular matrix composition shift cell state toward propagating disease.

## ABOUT the SPEAKER

*Dr. Patrick Link took a non-traditional path to becoming a post-doctoral research fellow. Before finishing college, Dr. Link joined the U.S. Army and became a Special Forces Medical Sergeant. As a Green Beret, Dr. Link cared for and treated many people with various lung diseases, sparking his interest. After leaving the military, Dr. Link got bachelor's degrees in Biology and Emergency Medical Care before getting his M.S. and Ph.D. in BME. Currently, Dr. Link is a post-doctoral research fellow in Dr. Daniel Tschumperlin's Tissue Repair and Mechanobiology Lab at Mayo Clinic. His research focuses on understanding what starts mechanobiology and how mechanobiology shapes the microenvironment. A special emphasis of his research is on understanding what regulates different aspects of mechanobiology during disease initiation, progression, and persistence. Dr. Link is specifically interested in engineering extracellular matrix/cell interactions for a therapeutic benefit. Dr. Link's research has earned fellowships through both the NIH and the NSF. Dr. Link currently has 16 peer-reviewed publications and has earned many awards, including awards in service and BME excellence.*

**Monday, February 6 at noon**  
**1003 Engineering Centers (Tong Auditorium)**