Connecting Tissues and Investigators (Fibrosis in Pathology) ARC

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Aberrant fibrogensis or fibrosis is a common response to chronic tissue injury of almost every organ, contributing to about 45% of all deaths in the U.S. Fibrogenesis is also an essential process that contributes to the normal wound- healing response. Fibrosis at the phenotypic level shows remarkable similarities across different organ systems, but it is not understood whether cell populations or molecular mechanisms that contribute to the excessive deposition of extracellular matrix are conserved across organs.

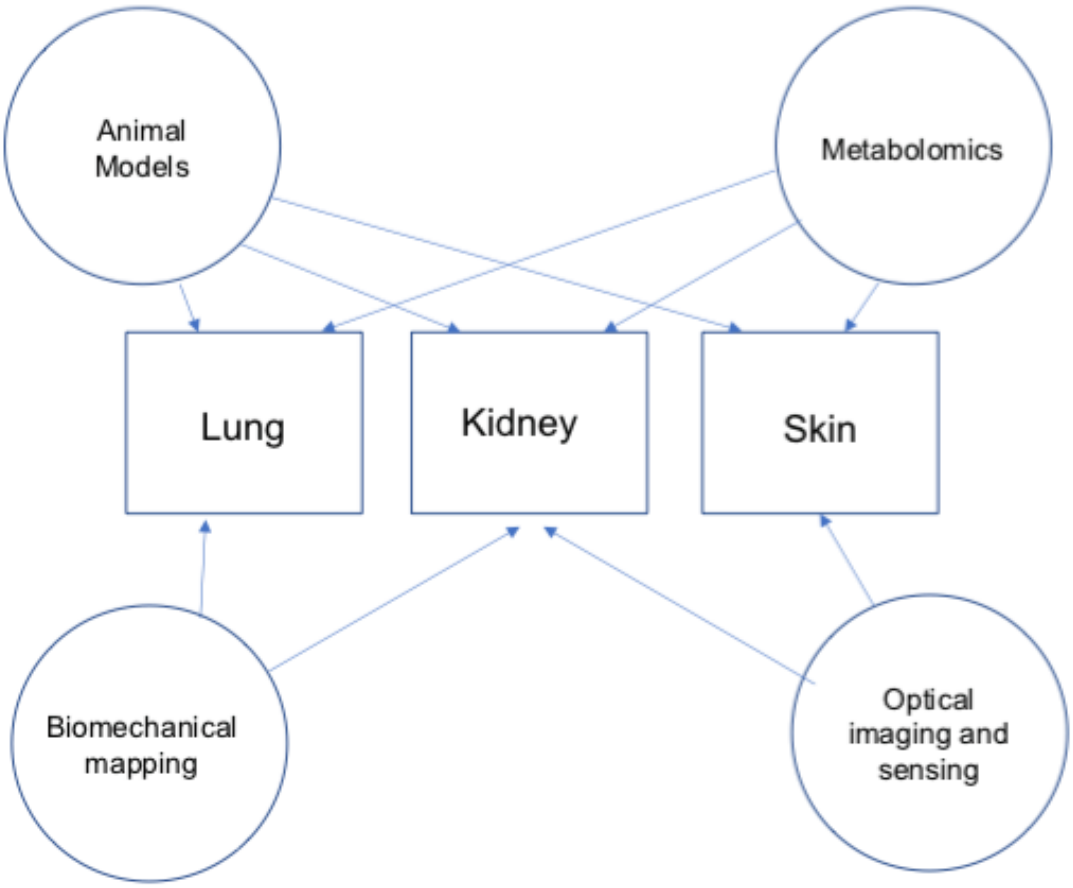
Our central hypothesis is that there are both shared and tissue-specific factors in organ fibrosis that can be utilized to develop improved and more-quantitative diagnostics and to identify either global and/or tissue-specific biomarkers and therapeutic targets. The proposed ARC will bring together basic researchers, clinicians, and bioengineers across the two campuses at Boston University to test this hypothesis, focusing on the following research areas:

Molecular phenotyping of profibrotic cells: one goal of this ARC is to identify similarities and differences in the cell types that contribute to organ fibrosis. Novel animal models available to our group along with state-of-the art single cell RNA-sequencing methods will be used to identify and characterize fibrosis-related stromal populations in organs such as the kidney, lung and skin. Biomechanical mapping will then be used to align these stromal cell types to matrix-related abnormalities, offering a unique picture of the diseased state.

Metabolomics: Emerging evidence in system biology implicates the alterations in small metabolites either in inducing fibrosis or as a consequence of fibrotic process. Leveraging two discrete clinically relevant models of organ fibrosis, in a set of well annotated plasma samples from two independent cohorts of scleroderma and renal transplant fibrosis, this proposal will perform an unbiased (non-targeted metabolomics) and targeted metabolomics analysis. The metabolomics fingerprint will be associated with scleroderma organ involvement and renal transplant fibrosis. Results obtained from such analysis will seed future mechanistic and sufficiently powered predictive clinical studies to probe their biomarker role.

Imaging of fibrosis: State-of-the-art optical methods for noninvasive sensing and imaging, will be exploited to generate quantitative measures of the degree of fibrosis, and assess important characteristics, such as structural anisotropy and alignment of the collagen.

Our intent is that knowledge gained from these collaborative studies will provide new directions for the development of targeted strategies for disease management and therapies, to lessen the severity of organ fibrosis.


Animal Models
Metabolomics
Lung
Kidney
Skin
Biomechanical mapping
Optical imaging and sensing

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