Understanding lung tissue heterogeneity in idiopathic pulmonary fibrosis (IPF)

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Idiopathic pulmonary fibrosis (IPF) is a chronic, progressive lung disease. IPF is consequence of fibrosis (irregular wound healing) and the microscopic appearance of fibrosis is heterogeneous. Identifying the causal associations between gene expression and histological structures will not only help understand molecular disease mechanisms involved, but it will also provide insights into potential therapeutic targets. The “lung DBP” (Driving Biomedical Problem), which is part of the Center for Causal Discovery (CCD), aims to study the causal genotype-phenotype mechanisms intrinsic to IPF by integrating and co-analyzing clinical variables reflecting disease progression, histopathological patterns in whole-slide H&E stained tissue images, and RNA-seq data collected from the same tissue.

Methods: Lung tissue from IPF patients and controls has been extracted and three slides were cut sequentially. The top and the bottom slides were stained with H&E and scanned, while the middle slide was used to collect RNA-seq data. We developed new computational pathology methods (i) to characterize fibrosis and other salient phenotypic features in IPF tissues, (ii) to quantify disease heterogeneity and (iii) to classify IPF samples from controls. We used a Mixed Graphical Model (MGM) causal algorithm to integrate these histopathological image features with the gene expression data from the same tissue and other clinical variables.

Results: In this poster, we present new computational pathology algorithms to characterize the heterogeneity in the microscopic appearance of fibrosis in IPF whole-slide H&E stained tissue images. Furthermore, we present the genes and gene networks that are causally related to these features and the clinical variables that are indicative of IPF severity. These results constitute a first step in our understanding of the dynamic changes that potentially occur in a progressive fibrotic lung disease.

Session to which submitted: Research highlights