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# "Gut Microbiome Association with Disease Severity and Treatment Responsiveness in NSIP"

The role of the gut microbiome in the modulation of the immune system and inflammation is an increasingly popular area of research, but little is known about its association with interstitial lung diseases (ILD), especially in the case of Non-Specific interstitial pneumonia (NSIP). There are many genetic, environmental, and molecular drivers for ILDs, and NSIP is a subset from ILDs which is characterized through clinical, histological, and radiological features. NSIP is often associated with specific conditions, such as connective tissue diseases and autoimmune diseases, or may be categorized as idiopathic (Kligerman et al., 2009). The unique cytokine profile of NSIP patients compared to patients with other ILDs indicates an inflammatory dysregulation; however, the treatment is primarily limited to non-targeted approaches to reduce inflammation such as steroids and other immunosuppressive medications (Flaherty & Martinez, 2006). While current treatment options are often, but not always, effective in reducing morbidity and mortality, they are associated with significant side effects. Since the gut microbiome is known to program immune and inflammatory responses, we **hypothesize that changes in the intestinal microbiota are associated with disease severity and treatment responsiveness in patients with NSIP.** Establishing these underlying associations can help develop new and personalized treatment strategies to reduce inflammation and immune system overactivation in patients with NSIP.

This project will perform 16s rDNA sequencing based phylogenetic analyses and metabolomic analyses of stool samples of patients with NSIP. Samples will be collected from NSIP patients when the patients will receive standard treatment and again after 3 months of treatment. Respiratory and health statuses will be assessed through K-BILD (ILD specific questionnaire), a EuroQuol-5D (quality-of-life questionnaire), ASA24 (dietary assessment tool), AUDIT-C (alcohol use questionnaire), and the MRC Dyspnea Score at each time point. Data will also be extracted from the patients' medical records including 6-minute walk, pulmonary function testing, radiographic findings on high resolution computed tomography, and histological results from samples of lung tissue. These findings will be used to characterize disease severity and assess response to therapy.

This work will identify the microbiota community characteristics, specific taxa, and the metabolites associated with NSIP disease status and response to therapy. The end goal is to use knowledge gleamed from our study to inspire the development of novel, specific, and targeted treatment options for NSIP patients that improve their quality of life and reduce harm from non-specific treatments.