Idiopathic pulmonary fibrosis: disease presentation, clinical course and potential biomarkers

THESIS FOR DOCTORAL DEGREE (Ph.D.)

By

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ABSTRACT

The interest and research within the area of the fatal lung disease idiopathic pulmonary fibrosis (IPF) has increased exponentially over the past decades. This has resulted in important insights into the nature and pathogenesis of the disease, which ultimately constitute the knowledge base upon which diagnostic, management, treatment decisions and guidelines are shaped. With a prognosis worse than many cancers and a complete absence of curative treatments apart from lung transplantation, the introduction of the first approved treatments, although not curative but disease modifying, has been a major leap forward for patients and the research community.

Despite the increasing interest, many questions still remain unanswered. Observational studies based on registry data can provide important complementary information to data generated in clinical trials about the patient population, disease behavior and treatment. Combining clinical data with biological samples such as serum and lung tissue from patients with IPF, enables studies where associations between biological processes and the clinical behavior can be explored.

This thesis attempts to address open questions in IPF by using data from patients enrolled in the Swedish IPF registry and samples from its biobank. The studies can be divided in two parts: In the first part, we have explored potential gender differences. Further, we have taken a comprehensive look into the patient population and explored patient characteristics, disease severity, evaluated antifibrotic treatment and discerned potential disease phenotypes with distinct disease trajectories. The second part comprises studies where we have leveraged register data with results generated from analyzes of serum samples. In these studies, we have taken different approaches in order to profile the repertoire of autoantibodies and proteins present. We demonstrate, both in an *in vitro* cell culture model and in patient serum, how proteins related to remodeling, inflammation and cell recruitment are upregulated in IPF and we describe their associations to disease severity and progression. Investigating the presence of antibodies related to rheumatoid arthritis in IPF revealed how autoimmune mechanisms are active and might play a role in a subgroup of IPF patients. Taken together, these discoveries contribute to the field by expanding established observations while also generating results and hypotheses that warrants further studies to refine and improve our understanding of IPF.