Impact of the pulmonary microbiome and host-gene interactions on respiratory function post-COVID19 infection

Recent clinical observations provide evidence that pulmonary fibrosis frequently develops after coronavirus disease 2019 (COVID-19). A substantial number of COVID-19 patients present with severe disease and Acute Respiratory Distress Syndrome (ARDS). ARDS itself has been shown to increase the risk for developing pulmonary fibrosis. Alterations in the lung microbiota of patients with pulmonary fibrosis correlate with important disease aspects including disease status, alveolar inflammation, host genotype, and the systemic host response. Moreover, bacterial burden (load) in the airways is predictive of disease progression and mortality in pulmonary fibrosis. Although there is convincing evidence that the microbiota is involved in disease progression, it remains to be determined whether the lung microbiota contributes to alterations in respiratory function post-COVID-19 infection.

In the current study, we aim to assess whether disturbance of the lung microbiome is associated with, or even precedes, the development of SARS-CoV-2-mediated impaired respiratory function, which would indicate a potential causal link. We hypothesize that disturbances of the microbiota in the lung post-SARS-CoV-2 infection will be different, depending on whether the patient recovers with or without the development of fibrosis. To study this, we aim to combine a longitudinal analysis of three time points with a comparison of two airway sites, which will provide information on both the temporal dynamics and the topography of the respiratory microbiota. Specifically, we have collect sputum and nasopharyngeal swabs from patients previously hospitalized (CHUV Lausanne) for COVID-19 at 3, 6 and 12 months post-infection. We will determine the composition of bacterial and fungal communities in these samples, based on 16S and ITS rRNA gene amplification and Illumina MiSeq sequencing. In addition, host-gene expression analysis will be determined using established multiplex qPCR panels for bacterial, fungal and viral recognition, associated defense mechanisms, inflammation and remodeling. Moreover, we will use statistical and computational approaches that allow us to integrate each individual analytical dataset (bacterial and fungal community composition, host gene expression, and clinical parameters to investigate associations between respiratory function (radiological and lung functional) and host-microbiota interactions.

Taken together, the work described in this application will provide the first insights on the impact of the lung microbiota on respiratory function post-COVID-19 infection and the underlying host gene expression signature. Utilizing lung microbiota analysis as a potential predictive measure for post-COVID19 impairment of respiratory function would not only allow us to personalize treatment regimens, but also significantly enhance our understanding of bacterial contribution to lung remodeling, a widespread pathophysiological process linked to high morbidity and mortality in respiratory disease.