

## Evaluation of immunological, microbiological and metabolomic profiles of patients with chronic obstructive pulmonary disease in selected clinical phenotypes

Chronic obstructive pulmonary disease (COPD) is a common disease with a high mortality rate and no effective treatment to date. It is characterized by persistent symptoms from the respiratory tract and irreversible and progressive limitation of the airflow. The reason for that is a chronic and excessive inflammatory response to toxic substances and gases. The main risk factor for COPD is cigarette smoking which is responsible for most cases of COPD.

COPD has very diverse manifestations and several phenotypes, that is observable physical properties, have been distinguished: chronic bronchitis and emphysema. Chronic bronchitis is characterized by a chronic cough with sputum expectoration, whereas emphysema is caused by destruction of lung tissue and is associated with a progressive shortness of breath on exertion. Both phenotypes can be present either separately or can co-exist in one person. The presence of chronic bronchitis or emphysema impacts the presence of symptoms, the disease course and its treatment. However, it is unknown why some patients develop chronic bronchitis and other emphysema. It appears that inflammatory changes in the airways characteristic for COPD could be present already in long-term smokers without airflow limitation. Differences in structural changes of the respiratory tract are probably associated with the impact of different inflammatory cells and cytokines (substances secreted by these cells) which have been extensively studied by scientists from around the world. However, these relationships remain still uncertain.

The authors of this study decided to use the latest methods of assessment of the airway inflammation: metabolomic and microbial analyses. Recent studies have suggested that some of the molecules from the metabolic pathways could be important in COPD development and it is suggested that they could be involved in phenotype development as well.

Moreover, in recent years it has emerged that microbiome could play a role in COPD development. It is suggested that some species of bacteria and viruses colonising the airways could modify the inflammation in COPD patients and in the long-term smokers.

The aim of this study is to analyse the associations between inflammatory pathways and structural phenotypes of COPD. The study group will comprise of 50 COPD patients, 50 smokers without COPD and 20 control subjects (never smokers) matched by age and sex. To assess the airway inflammation we plan to use induced sputum as a recognized and standardized method which can be acquired safely, easily and non-invasively. We will use standard methods which assess cellular and cytokine composition as well as a novel method which analyses changes on a molecular level: liquid chromatography and mass spectrometry to assess the presence of metabolomic molecules. Moreover, in our project we will study the impact of the airway microbiome (bacteria and viruses) on the inflammation type and structural changes of the airways and lungs. To assess these structural changes we will use high resolution computed tomography (HRCT) which will allow for assessment of the bronchial wall thickness and the extent of emphysema. Next, we will assess the associations between the studied inflammatory markers and structural changes in the airways and lungs. We expect that for a specific phenotype we will identify specific inflammatory markers which are already present in smokers without airflow limitation. Results of our study might help in our understanding of how emphysema and chronic bronchitis develop, what is the relationship between inflammation and structural changes and finally, if specific changes in the airways are present before we detect airflow limitation.