The role of airway interferon response and its impact on the activation of immune system in antisynthetase syndrome

Over 6000 distinct rare diseases, which are diseases affecting less than 1 person in 2000, have been distinguished. In Poland, even 2.3-3 million people in total suffer from rare diseases, affecting about 7% of the population. One of the rare diseases is antisynthetase syndrome, classified among idiopathic inflammatory myopathies (IIM). In the course of antisynthetase syndrome, typical clinical symptoms occur such as muscle weakness and myalgia, arthritis, interstitial lung disease, Raynaud's phenomenon and skin lesions resembling scaling and thickening of the skin on hands (so called mechanic's hands symptom). The disease is usually progressive and can lead to deterioration of the quality of life or even disability. The immunological hallmark of antisynthetase syndrome is the presence of specific autoantibodies, so called antisynthetase antibodies. Although advances have been made in the understanding of this disease, triggering factors of antisynthtase syndrome remain unknown. It is well established that in the course of this syndrome, the immune system is disturbed and immune cells, which normally protect our organism against infections, begin to attack their own tissues.

Many studies suggest that autoimmune process in antisynthetase syndrome initiates within airways. Upper airways are the first-line defence in interaction between organism and the environment. Every day they are exposed to bacteria and viruses, allergens or air pollution and within the respiratory tract numerous processes defending us against harmful factors are constantly occurring. Epidemiological observations have shown that prior to IIM patients more often had past medical history of upper and lower respiratory tract infections. Interestingly, the seasonality in incidence of antisynthetase syndrome is observed with the peak in March-April, suggesting a possible relation between the disease and exposure to seasonal pathogens. In addition, observations indicate that before the onset of antisynthetase syndrome, patients are often exposed to harmful airborne agents such as for example dust, what supports the possible relation of the disease with the injury of the respiratory tract epithelium. Interferons are proteins, released by our cells to enhance antiviral defence and regulate the functioning of the immune system.

In the project we will assess the response of the immune system within the airway epithelium of patients with antisynthetase syndrome, following the activation of viral-sensing receptors. We will evaluate whether the secretion of interferons in response to activation of these receptors is similar to that observed in healthy volunteers, or is rather excessive or impaired. We will compare phenotypes and activation of peripheral blood immune cells in patients with antisynthetase syndrome and healthy controls. Furthermore we will evaluate how the infection within the airways affects the functioning of blood immune cells.

Nasal epithelial cells will be collected from study participants for subsequent primary epithelial cells culturing. In in vitro experiments we will evaluate the immune response towards activation of RIG-I/MDA5 and TLR9 receptors, that are capable of recognizing viruses. From peripheral blood samples we will isolate immune cells, evaluate their activity and subsequently we will stimulate them with interferons and supernatants from nasal epithelial cells cultures, assessing how stimulation impacts their functionality and secretion of substances, necessary for the body's defence. In the project we will use the latest technologies including polymerase chain reaction (PCR) and flow cytometry.

We hope that the results of our study would bring scientific society of immunologists and rheumatologists closer to understanding the processes leading to the onset of antisynthetase syndrome. We hope that they will enable a breakthrough in understanding idiopathic inflammatory myopathies and antisynthetase syndrome and unravel the possibilities for more effective treatment of this disease.