

Multiomics examinations of metabolic consequences in tick-borne diseases

Tick-borne diseases are an important and growing epidemiological and clinical problem in the world and in Poland. The most common diseases in Poland are Lyme borreliosis and tick-borne encephalitis. These diseases may take severe course, often with the risk of neurological and psychiatric complications and death, especially in the case of tick-borne encephalitis. Human anaplasmosis and human babesiosis are less frequent tick-borne diseases with diverse clinical course (the differences in the severity of the course between European and American patients, the higher rate of complications and deaths in the American population than in Europe), and possible serious and long lasting complications. All of the above described infections can occur as mono-infections and co-infections (infection with multiple pathogens) that cause many diagnostic and therapeutic problems.

In order to identify the causes of these problems, research is conducted worldwide to analyze the pathomechanisms of the development of these infections. The results of the planned studies will help explain the consequences of metabolic changes in the course of these diseases and their effect on the effectiveness of antibiotic therapy. No specific biomarkers have been identified for tick-borne diseases so far. Identifying biomarkers of individual diseases or biomarkers that differentiate tick-borne diseases of different etiology but with similar clinical symptoms is very important because the antigenic composition of the available serological tests (both ELISA and Western blot) is diverse and the results are often incomparable and difficult to interpret. It leads to delay of proper diagnosis and implementation of targeted treatment. The consequence of this is a significant increase in the cost of diagnosis and treatment of these patients. This is also one of the main reasons for the increasing number of people treated with many different antibiotics for a long time (cocktail of antibiotics used for several months) which may have long-term metabolic and health consequences. Potential biomarker of these diseases can be one of the products of metabolic processes at the level of lipidome or proteome.

Because no research has yet been conducted to assess the effects of co-infection with pathogens on the metabolism of phospholipids and proteins the proposed research may be a breakthrough in the assessment of metabolic changes in the human body during infection with one or more pathogens. Faster and more specific diagnostics would allow early diagnosis and would allow for targeted and personalized pharmacotherapy. The results of the planned study will help answer the question whether non-standard Lyme borreliosis treatment regimens, including long-term treatment with multiple antibiotics, cause metabolic changes that are dangerous for patients.

The research hypothesis is a consequence of successful research showing that Lyme borreliosis and tick-borne encephalitis influence on some lipid mediators in plasma and cerebrospinal fluid. These results emphasize that there is a real possibility of determining, based on extensive studies of the lipid and proteome changes in the metabolism of phospholipids and proteins in patients infected with various pathogens. Because lipid structure and protein structure modifications affect their functions in the body, they can also lead to cellular signaling pathway disturbances and may be responsible for either adaptation or cell death.

Research will be conducted in biological fluids [blood, csf, urine] of patients with Lyme borreliosis, tick-borne encephalitis, human anaplasmosis, babesiosis, skin cells of patients with erythema migrans and healthy volunteers. An important goal of the study will be to identify potential metabolites as biomarkers of individual diseases or biomarkers differentiating diseases with similar symptoms but different etiologies. The results of these studies will also help to determine the proper and personalized treatment.

New modern analytical and biochemical methods will be used to assess lipid and proteomic changes, including the combination of mass spectrometers with liquid and gas chromatography. The results obtained during the project may radically change the diagnosis and pharmacotherapy of tick-borne diseases. This will enable faster diagnosis of these diseases and targeted medical activities for the public health. In addition, the creation of a model based on the consolidated actions of representatives of different research groups, including physicians, medical analysts, chemists and biologists will create the possibility of further interdisciplinary biomedical research on other infectious diseases.