Multiple Sclerosis (MS) is one of the most common neurodegenerative diseases and is responsible for the majority of neurological disability among young adults. Data from the World Health Organization (WHO) indicate that currently the number of people with MS on the world is estimated approximately 2.3 million. The disease usually has a multiphase course with numerous periods of exacerbation and remission. The pathological basis of MS is demyelination of white matter fibers caused by the myelin sheaths breakdown of neurons, as a result of the damage of soluble myelin protein. MS is an autoimmune disease characterized by a variable clinical picture and diversified pathophysiological course. Apart from neuronal damage, it is characterized by a loss of blood-brain barrier (BBB) integrity, as well as leukocytic infiltration to the central nervous system (CNS), leading to a chronic inflammation and neurotransmission disorders. The heterogeneous course of these processes makes it difficult to predict the progression of the disease and to implement appropriate therapeutic management.

Blood platelets are multitasking circulatory cells that are involved in the pathophysiology of many neurodegenerative diseases. Platelets possess a large variety of compounds stored in α-granules, such as membrane receptors, immunomodulatory mediators and cell adhesion molecules. These compounds affect the permeability of BBB and support the infiltration of autoreactive T-cells, which may lead to formation of new neuroinflammatory lesions in CNS. There are epidemiological reports, including the publications of the team of my scientific supervisor, confirming the disordered function of blood platelets in MS patients, which may be leading to an increased risk of ischemic episodes, such as stroke and myocardial infarction, especially in the SPMS phase.

The aim of the latest scientific research carried out by the team of my scientific supervisor, was to understand the molecular mechanisms of increased platelet prothrombotic activity in SPMS. Preliminary studies have shown elevated concentration of β-tubulin in blood platelets from SPMS patients, in comparison to healthy volunteers.

The hemostatic function of blood platelets is conditioned by their activation, that leads to a reconstruction of cytoskeleton and consequently changes the shape of platelets, adhesion, aggregation and degranulation of intracellular granules and an inflammatory mediators. Microtubules consist of globular proteins – α-tubulin and β-tubulin that along with the other filaments form a platelet cytoskeleton. Cytoskeleton proteins play a significant role in the reorganization of cell architecture. Quantitative and/or structural changes in cytoskeletal proteins may directly induce changes in the biological response of blood platelets, e.g. supporting the formation of a blood clot at the site of damaged blood vessel, which leads to the occlusion of the vessel and consequently to ischemia.

In this project, comparative analysis are planned with intention to explain the cause and consequences of the observed differences in platelet β-tubulin concentration. This research is aimed at determining at what stage of formation and the lifetime of blood platelet, the β-tubulin synthesis is disturbed.

In the first step of the study, the level of β-tubulin in megakaryocytes will be determined by the ELISA method in the SPMS and control group. This experiment will allow to establish whether increased β-tubulin synthesis in SPMS occurs in the megakaryocytes, or in the platelets. Despite the lack of the nucleus, platelets are able to synthesize proteins based on own mRNA molecules, which are derived from their precursor cells – megakaryocytes. In addition, the expression of β-tubulin at mRNA level will be determined in megakaryocytes and platelets by Real-Time PCR method.

Subsequent analysis will be focused on identifying potential differences in the β-tubulin structure present in SPMS platelets, including posttranslational modifications assessed with tandem mass spectrometry. Moreover, comparative analysis of the sequence of platelet-derived transcripts from SPMS and healthy controls, will be carried out using sequencing system. The study material was previously obtained (based on the consent of the relevant Bioethics Commission), isolated, purified and collected as a "banked" cDNA library, as well as protein fraction derived from platelets and megakaryocytes from SPMS patients and healthy volunteers.

Determination of the molecular basis of the increased β-tubulin concentration may in the contribute to the elucidation of the mechanism of increased prothrombotic activity of platelets, particularly context of their enhanced adhesion and aggregation properties observed in patients with SPMS. This can contribute to the establishment of new therapeutic targets and the development of new antiplatelet therapies in MS.