Multiple Sclerosis (Latin: sclerosis multiplex, MS) is a chronic inflammatory disease of the central nervous system (CNS). Due to the fact that MS is a heterogeneous disease, with a variable clinical course and a diversified pathophysiological image, its etiology has not been clearly explained. In the course of MS are distinguished: the primary progressive phase (PP) constituting only 10% of cases, and the relapsing-remitting (RR) form, which in most cases changes to the secondary progressive (SP) phase after about ten years from the first symptoms. The development of the disease correlates with the progressive neurodegenerative process resulting from the demyelination of white matter fibers as a result of the breakdown of the myelin sheath of the nerve fibers. Pathomechanism is associated with autoimmunity directed against the myelin basic protein (MBP). In the case of MS, cells of the immune system, mainly autoreactive T cells, penetrate the CNS and release pro-inflammatory cytokines that activate macrophages leading to the formation of inflammatory demyelinating lesions in the white matter. The stimulation of T lymphocytes and the production of lymphokines affect the activation of B lymphocytes, which are transformed into plasma cells responsible for the production of autoantibodies. The activation of immune cells, the release of inflammatory mediators, immunomodulators and adhesion molecules increases the permeability of the blood-brain barrier (BBB). According to one of the main hypothesis of MS development, the interaction of blood platelets with lymphocytes and endothelial cells is the direct cause of BBB injury and is the first key step in the initiation of MS pathogenesis, leading to lymphocyte infiltration and the formation of CNS demyelination centers. Epidemiological studies confirm the occurrence of vascular lesions in MS resulting in an increased risk of cardiovascular diseases, mainly ischemic events such as myocardial infarction and ischemic stroke, whose pathogenic background is closely related to the excessive pro-thrombotic activity of platelets. Some reports, together with our previous publications, confirm abnormalities in platelet function in MS, including their increased activation, the presence in the active inflammatory demyelinating lesions and promotion of inflammatory reactions. Activation of platelets leads to the display of many receptors that are crucial for the interaction of platelets with endothelial cells and lymphocytes. Our previous reports on SPMS (a progressive form of MS with long-term demyelination and inflammation leading to permanent axonal damage and destruction of neurons, which correlates with the degree of progressive disability) confirm the high expression of platelet GPIIb/IIIa and selectin-P receptors responsible for intercellular platelet interaction.

Recent studies have shown that excessive activation of platelets and lymphocytes in autoimmune diseases is manifested by the formation of lymphocyte-platelet aggregates, which are characterized by unusually high adhesive abilities, and platelets are thought to be a key element mediating the adhesion of circulating lymphocytes to endothelial cells, which ensures their recruitment and initiates diapedesis. However, these mechanisms have never been studied in the course of MS. For this reason, the primary goal of the project is to determine the interaction of platelets and peripheral blood lymphocytes in SPMS, including their mutual activation and receptor connections. The main objective of the project is to determine the percentage of lymphocyte subpopulations involved in the formation of these aggregates. Considering the heterogeneity of lymphocytes involved in the development of autoimmunity and inflammatory processes and their key functions in the pathogenesis of MS, it seems important to determine the quantitative and qualitative ratio of lymphocytes interacting with platelets. The study will evaluate the level of markers of platelet and lymphocyte activity. The pathway activity (CD40/CD40L) responsible for the interaction of platelets with lymphocytes will also be determined. In addition, the functional consequences of platelet-lymphocyte interactions will be analyzed by assessing the ability of platelets to induce lymphocyte migration. By using a cell sorter to isolate lymphocyte-platelet aggregates, morphological evaluation of cell agglomerates isolated by using a confocal and an electron microscope will be possible.

The explanation of the molecular mechanisms of platelet-lymphocyte interactions in SPSM may be important for determining new therapeutic targets in MS and other autoimmune diseases.