Neutrophil Extracellular Traps (NETs) are web-like structures built up of sticky threads of DNA decorated with antimicrobial proteins. They are released from the cell, neutrophil, to entrap microbes, prevent from their spread out through the organism and lastly, to annihilate the invader. NETs release can be triggered by many stimuli including bacteria, viruses or fungi. The structure of NETs and its functions has not been thoroughly investigated. According to the latest findings, NETs incorporate metallic elements such as zinc, iron, copper and calcium, as well as contain calprotectin and lactoferrin (zinc and iron binding proteins, respectively). Zinc and iron are microelements which play a crucial role in regulation of the immune system. Iron is a well-known component of antimicrobial proteins, but also is necessary for bacteria replication. Therefore, during infection, a battle between the host and invader occurs for resources of this element. Zinc is an important component of calprotectin, necessary for its antibacterial and antifungal activity. Although we know about the presence of iron and zinc in the structure of NETs, we do not know their exact impact on the mechanism of NET's formation and efficiency. Our preliminary studies indicate, that zinc and iron inhibit NETs release. Moreover, neutrophils isolated from patients with iron deficient anemia (IDA), exhibit a decreased capacity to reduced spontaneous release of NETs.

The aim of the project is to investigate how microelements, essentially iron and zinc affect the capacity of neutrophils to release NETs. Moreover, we will investigate the capability to release NETs by cells isolated from patients suffering from microelement disorders, specifically IDA and hemochromatosis. Lastly, we will introduce a mice model with iron and zinc disorders caused by inappropriate nutrition, whereby we will be able to determine if microelement supplementation could be harmful for the organism by influencing its immune system.

IDA is the most frequently diagnosed type of anemia. Appropriate diagnosis and treatment of this disorder is necessary, since patients suffer from weakness and decreased immunity. Zinc deficiency also results in disorders of the immune system. Until now, the precise cause of immunity changes in patients with these deficiencies has not been truthfully described. Therefore, further comprehensive research whether microelements homeostasis disorders affect the function of neutrophils, specifically NETs release, is of critical importance. The results obtained in the mouse model study will help answer the important question - does uncontrolled and excessive iron and zinc supplementation cause more harm than good to the natural response against body-borne pathogens?