Despite modern intensive care and antibiotic treatment, the mortality of sepsis is high, reaching about 50%. Current theories suggest that the sepsis is associated with an early immune response, characterized by continuous activation and release of pro-inflammatory mediators. This response may subsequently become inadequate, leading to systemic inflammatory response, which results in organs failure. On the other hand, its counterbalancing by sustained expression of potent anti-inflammatory mediators may suppress immune response overmuch.

Neutrophils and macrophages are the crucial populations of cells involved in the immune response. Neutrophils have the ability to absorb microorganisms, release the content of their granules with bactericidal properties (reactive oxygen species), but also are capable of releasing neutrophil extracellular traps (NETs). These structures are traps that are intended to immobilize the pathogen and create favorable conditions for its neutralization. Although scientists have done a lot of research to better understand the essence of this phenomenon, our knowledge on this subject still remains incomplete. One of the blood cells type essential for immune response are macrophages. Macrophages are type of white blood cell, that engulfs and digests cellular debris, foreign substances and microbes. They are highly specialized in removal of bacteria, dying or dead cells and cellular debris and called professional phagocytes. When a macrophage ingests a pathogen, the pathogen becomes trapped in a phagosome, which then fuses with a lysosome. Within the phagolysosome, enzymes and toxic peroxides digest the pathogen. The efficiency of phagocytosis is highly dependent of physiological conditions of host.

The main aim of the project is to identify the impact of different mediators profiles observed during a course of sepsis on phagocytosis. We will test how sera obtained in different time points during the course of sepsis from patients affects phagocytosis performed by neutrophils and macrophages. The concept of changing mediator profile affecting phagocytosis will be investigated through evaluation of main phases of phagocytosis e.g. the uptake of pathogen, phagosomal reactive oxygen species generation, pH of phago- and lysosomes, fusion of phago- and lysosomes and degradation of phagolysosomes, as well as the secretion of neutrophil extracellular traps (NETs).

The proposed project will try to find an answer on the question: how the immune system can control an infection and what happens when the immune system fails. If the changing mediator profile modulate the efficiency of phagocytosis?

Results obtained with current proposal should provide novel data on the influence of changing protein mediators profile on phagocytosis. In the future obtained results may help to identify new therapeutic targets to enhance efficacy of treatment.