The immune system protects our body against bacterial, fungal and viral infections. When the infection starts, the defense mechanisms related to the activation of leukocytes and fever are activated. Due to the high energy expenditure, such an intense involvement of the immune system must be time-limited. If the organism cannot defeat the infectious factor in a short time, it takes a different line of defense and a program of tolerance of this factor is activated. This phenomenon is best known in research on bacterial endotoxin that initially induces a strong reaction of the immune system and then this endotoxin begins to be tolerated. Consequently, the dose of endotoxin that has stimulated the leukocytes and has induced fever does not work anymore. It is not known exactly how long such a state (called endotoxin tolerance) remains in the body, and above all it is not known what the consequences are.

It has been shown many times that the immune system, apart from fighting infection, is involved in fighting with cancer. For many years, researchers have emphasized the fact that cancer patients for a few years before diagnosis display a reduced tendency to get fever during infection. Indeed, this phenomenon has been confirmed by us in a survey on cancer patients. Due to the fact that during endotoxin tolerance both the reactivity of the immune system and the fever are weakened, we suppose that endotoxin tolerance will contribute to the progression of the neoplastic disease. For this reason, we believe that prolonged endotoxin tolerance in a body should be counteracted. Therefore, the main aim of the project is **to determine whether endotoxin tolerance promotes the development of cancer**. We expect that the occurrence of endotoxin tolerance will accelerate cancer growth. Furthermore, since there is evidence to suggest that supplementation with some probiotic bacteria may decrease endotoxin level in the body, we are going to check whether it can affect endotoxin tolerance.

The research will be carried out in vitro using cell lines (2D and 3D cultures) and in vivo on a mouse cancer model and endotoxin tolerance model. We will use methods such as flow cytometry, biotelemetry, biochemical and immunoemzymatic methods, analysis of gene expression and methods for assessing the reactivity of immune cells. The knowledge obtained in this project will explain why immune system tolerate cancer cells. Furthermore, the understanding the interaction between probiotic bacteria and ET will extend a list of probiotic applications to prevent ET-induced immunosuppression in cancer. Although the studies will be carried out on the model of endotoxin tolerance, which may occur during gram-negative bacteria infection or leaky gut syndrome, it cannot be ruled out that similar effects will be observed during prolonged exposure to agents of other origin. We hope this research will indicate a new strategy for cancer immunotherapies.