DESCRIPTION FOR THE GENERAL PUBLIC

According to the estimates of the World Health Organization, approximately 1/3 of the human population is infected with *Mycobacterium tuberculosis* (M.tb). The infections are latent but in approximately 10% of people they can progress into active tuberculosis (TB). Each year the disease affects about 10 million people and is a cause of 2 million deaths. The pandemic of HIV infection and an increasing frequency of isolation of multi drug resistant (MDR) and extremely drug resistant (XDR) *M.tb* strains worsen the epidemiological situation of TB in the world. The incidence of drug-resistant TB is about 500.000 cases per year. The treatment of MDR-TB and XDR-TB is extremely costly, prolonged and often impossible. In this way, despite almost century-long prophylactic vaccination of humans with antituberculosis vaccine - BCG, TB is registered on the list of incurable infectious diseases. Despite intensive research, interactions between mycobacteria and human body occurring at the molecular, cellular and tissue level are still poorly understood. To gain novel insights into the mechanisms underlying TB, this project will focus attention on interleukin-18 (IL-18), a cytokine that has been implicated in both protective and pathological processes associated with active and latent *M.tb* infection. The results of this study will allow us to verify a hypothesis that IL-18 and IL-18BP (IL-18 binding protein), which inhibits the activity of IL-18, are important components of the mechanisms of immune responses to mycobacteria, which are initiated at the level of macrophage signal transduction receptors leading to the secretion of pro-inflammatory and regulatory cytokines in humans with active or latent *M.tb* infection. IL-18, belonging to the family of IL-1, has a strong ability to stimulate the production of IFN-gamma by T cells and NK cells, thereby increases the mycobactericidal activity of macrophages that kill the intracellularly growing mycobacteria. The project studies planned in the constructed research groups: patients with active pulmonary TB, individuals with latent *M.tb* infection and healthy volunteers not infected with *M.tb*, including the evaluation of the promoter polymorphism of the IL-18 encoding gene, assessment of the expression of the gene and determination of IL-18 concentration in serum and cultures of whole blood stimulated with specific *M.tb* antigens, will allow the multiparameter analysis of IL-18 involvement in *M.tb* driven reactions. The simultaneous examination of both IL-18 and IL-18BP in our research will be the first to demonstrate the participation of free IL-18 in the immune and pathological processes in TB. Regarding the demand for rapid and accurate TB diagnostic tests we want to check if IL-18 and IL-18BP reflects the immune status of humans with active or latent *M.tb* infections. Taking into consideration the role of IL-18 binding receptor (IL-18R) in the initiation of the signal transduction cascade leading to IFN-gamma production, the assessment of IL-18R gene expression is also planned. The combined analysis of the results for the serum levels of IL-18 and IL-18BP and mycobacterial antigens driven IL-18, IL-18BP and IFN-gamma production with IL-18, IL-18BP and IL-18R genes expression levels will shed new light on the mechanisms that make the immune system capable of destroying *M.tb* that may be useful in designing new vaccines and TB treatment regiments.