DESCRIPTION FOR THE GENERAL PUBLIC

Bacteria from species *Helicobacter pylori* are present in the majority of human population. Infections caused by this pathogen are associated with an increased risk of development of gastric or duodenal ulcers, or even gastric carcinoma. Progress of tumorigenesis is, inter alia, correlated with cleavage of E-cadherin, one of the most crucial proteins responsible for maintenance of the intercellular junctions. Degradation of E-cadherin may be performed by several proteases; one of them is HtrA secreted by *H. pylori*. The use of chemical compounds that specifically inhibit the activity of HtrA is sufficient to preserve integrity of the epithelium infected by *H. pylori*. For this reason HtrA is regarded as a very attractive therapeutic target for development of novel drugs to cure *H. pylori* infections. However, the function of HtrA in the cell of this pathogen has been very poorly characterized so far, mainly due to a lack of *H. pylori* strains deprived of the functional *htrA* gene. In collaboration with Prof. Anna Pawlik from the Institute of Immunology and Experimental Therapy Polish Academy of Sciences in Wroclaw we successfully removed the *htrA* gene from *H. pylori* chromosome; this enables us to start a novel, previously infeasible research. To thoroughly investigate the physiological role of HtrA in *H. pylori* we plan to clarify two issues: (1) what kind of adaptations in the cell enable to delete the functional *htrA* gene (seeking the *htrA* suppressor mutations); (2) how the lack of HtrA or its proteolytic activity influences the profile of gene expression and proteome of this bacterium. Moreover, we attempt to isolate and identify the cellular substrates of HtrA. In our research we will apply advanced methodology, including the whole genome sequencing, analysis of gene expression using RNAseq, proteomic analysis by means of the two-dimensional fluorescence difference gel electrophoresis (DIGE) and subsequent protein identification by the mass spectrometry (MALDI-TOF) and techniques to study protein-protein interactions: “pull-down” and co-immunoprecipitation.

Knowledge gained as a result of this project should expand our understanding of the *H. pylori* physiology. Thorough exploration of functions played by HtrA in the cell of this pathogen should allow to develop strategy to circumvent the defence mechanisms of bacterial populations and formation of the resistant strains. Hence, it should lead to elaboration of an efficient treatment of the *H. pylori* infections.