In this research project we plan to unravel an exciting new discovery linking the transcriptional regulator OmpR and sRNA OmrA with iron acquisition in a Gram-negative human enteropathogen *Yersinia enterocolitica*. *Y. enterocolitica*, the causative agent of yersiniosis – an acute or chronic zoonotic disease is a heterogeneous species that comprises many biotypes with varying degrees of virulence: low-virulence biotypes 2–5, mainly identified in Europe and high-virulence biotype 1B that is prevalent in North America. Interestingly, in the past ten years, the prevalence of strains of biotype 1B has dramatically increased in Poland which raises concerns epidemiologists. *Y. enterocolitica* is found free-living in the environment or in association with a host. Residing in these different ecological niches *Y. enterocolitica* has to adapt to large environmental fluctuations. Mechanisms of iron acquisition contribute greatly to the pathogenic power of *Y. enterocolitica.* It has been shown previously that unique to *Y. enterocolitica* high-pathogenicity strains of biotype 1B, iron chelator yersiniabactin (Ybt) and the FyuA receptor for Fe-Ybt determine high pathogenicity of this biotype. Furthemore, Hfq protein (chaperone of small non-coding RNAs (sRNAs) represses production of FyuA and Ybt. Working with *Y. enterocolitica* of low pathogenic biotype, we have identified a correlation between the functioning of transcriptional regulator OmpR of EnvZ/OmpR signaling pathway, and several cellular responses. Recently, proteomic analysis revealed the influence of OmpR on the production of proteins involved in iron acquisition; the haem receptor HemR and the siderophore receptors FepA and FecA uncovering so far unknown link between OmpR regulator and iron acquisition. In the past decade many bacterial sRNAs together with their chaperone Hfq were shown to be involved in many cellular processes including outer membrane biogenesis. sRNAs changing the translation and stability of the mRNA regulate gene expression at the post-transcriptional level. In *E. coli* sRNA OmrA and OmrB negatively regulate iron-regulated receptors present in the outer membrane. In *Y. enterocolitica* only OmrA exists and the targets of its posttranscriptional regulation are not yet know.

The primary scientific objective of this project is to reveal the molecular mechanisms explaining/underlying the impact of OmpR regulator on the outer membrane iron-regulated proteins involved in iron acquisition in *Y. enterocolitica* of low and high pathogenicity. Based on the proteomic data and the results of the *in silico* analysis we hypothesize that OmpR might directly and/or indirectly influence the expression of: (i) the iron homeostasis global regulator Fur; (ii) the outer membrane receptors for haem (HemR) and iron-bound siderophores); (iii) the conserved small RNA OmrA that in turn (with Hfq) might control the stability and/or translation of transcripts encoding the receptors.

To achieve the aims we are planning to carry out detailed studies on the expression of selected genes at the transcriptional and posttranscriptional level and on the interactions of the OmpR and sRNA OmrA with their targets.

Identification of *Y. enterocolitica* iron-regulated receptors, whose expression is dependent on OmpR and/or sRNA OmrA will broaden our knowledge on the role of these regulators in the physiology not only *Y. enterocolitica*. Our findings are likely to have implication for the regulation of similar iron acquisition in other pathogens which cause life-threatening infections like plaque bacilli *Yersinia pestis*. The results obtained during the planned studies will also have important practical applications. New antimicrobial drug targets are constantly sought due to the spread of antibiotic resistance. Compounds that block the synthesis of bacterial virulence factors are now being considered for use in antimicrobial therapy. This study may, therefore, be a starting point in the search for inhibitors of iron acquisition. Effective inhibition of the iron transport, could replace or complement classical antibiotic therapy and contribute to the successful treatment of *Yersinia* infections.