The aim of the proposed project is to investigate the role of bacterial *saoABC* operon in regulation of gene expression, particularly in the context of common significant interactions between bacterial and host cells such as bacterial cells' internalisation to endosomes, which occur during invasive infections caused by *Staphylococcus aureus* and may contribute to their chronic character and therefore to their clinical relevance. The research on *saoABC* operon, operon of three genes *saoA*, *saoB* and *saoC*, which occur across all known genomes of species belonging to *Staphylococcus* genus, originated from the study on class II toxin-antitoxin system *pemIK*$_{Sa}$ toxin-antitoxin system. Bacterial toxin-antitoxin systems play an important role in bacterial metabolism in response to stress conditions. Preliminary results convincingly suggest the existence of functional links among toxin-antitoxin system *pemIK*$_{Sa}$, alternative RNA polymerase σ^B subunit and *saoABC* operon in the context of the response of the bacterial cell to stress stimuli, particularly those related to internalisation. Internalisation is a process of penetration of bacteriall cells into the host cells. Within endosomes of host cells bacteria may form persisters, which are a metabolically dormant fraction of bacterial cells resistant to adverse conditions related to host immune system activity or drug treatment, even if they do not possess genes providing antibiotic resistance. This further points to the likely possibility of these three systems playing together a significant role in pathogenesis of clinically relevant chronic and recurrent infections caused by *S. aureus* strains, the role which is the subject of this research project. The aim is a detailed analysis of interdependencies between functions of *saoABC* operon, toxin-antitoxin system *pemIK*$_{Sa}$ and subunit σ^B. Such interdependencies are of significant importance when referred to bacterial cells internalisation to eukaryotic host cells, phenomenon which is common in the context of host-pathogen interactions during staphylococcal pathogenesis. The aim is expected to be achieved firstly by focusing on the consequences of DNA-binding properties of SaoC protein. Additionally, by thorough analysis of expression of *saoABC* operon's genes, in the wild type strains as well as in deletion mutants, in the context of well-characterised staphylococcal transcription regulation systems and their engagement in intracellular survival of staphylococci, such as the aforementioned alternative σ^B subunit of RNA polymerase and *pemIK*$_{Sa}$ toxin-antitoxin (TA) system in particular.

The research will be among all focused on detailed analysis of changes in gene expression of *saoABC* operon in stress conditions as well as changes in gene expression of *saoABC*, *pemIK*$_{Sa}$ operon and *sigB* genes upon internalisation of bacterial cells to endosomes of eukaryotic cells. This will be the first attempt to assess how tightly integrated these three systems are in the context of staphylococcal pathogenesis, which will undoubtedly open up completely new paths of research into the phenomena of internalisation and intracellular survival of staphylococci as well as into the formation of intracellular persister cells. Other research paths aim at identification of functional partners of SaoC protein and factors interacting with uncharacterised regulatory sequences which were found upstream *saoC* gene. Both paths are meant to preliminarily validate the hypothesis of SaoC being a novel, uncharacterised staphylococcal alternative σ factor as well as point out novel staphylococcal transcription factors.

The results obtained in the course of the proposed research project will cast new light on synergistic interactions among *saoABC* operon, well-described stress response system related to the subunit σ^B and recently characterised toxin-antitoxin system *pemIK*$_{Sa}$ in *S. aureus*, an opportunistic pathogen of human and animals. The knowledge of the role of *saoABC* operon in regulation of the response to stress conditions, its relevance in pathogenesis, as well as the level of integration with known regulatory systems will be expanded. In the course of thorough investigation the obtained results point out that the role of *saoABC* operon may be relevant in the process of pathogenesis of *S. aureus* and undoubtedly deserve more insightful research. Undertaking the proposed research tasks offers a chance for the identification of further unknown and uncharacterised factors and regulatory systems, particularly those linked to turning the metabolism of the bacterial cell being internalised to a host cell towards persister phenotype formation.