Role of the interaction between HupA and HupS proteins during *Streptomyces* growth and stress response

Size of the typical bacterial cell equals about 2 μm. By contrast DNA strand forming bacterial chromosome can be 1000 longer than the cell. Because of that survival of bacteria requires DNA to be properly structured in order to be able to fit inside the cell without impairing its function. Various proteins called NAP are responsible for this process. They can bind DNA and through this lead to bending or bridging of DNA strands. In plant and animal cells similar role fulfill proteins called histones.

One the most abundant NAPs is a protein called HU. Two molecules of it bind together forming a dimer, which can interact with the DNA. Many bacterial species possess only one HU protein, but in some two slightly different versions of it were found. Apart from its role in maintaining DNA structure, HU protein can influence bacteria's response to changing environmental conditions. In order to properly react to stress i.e. high temperature, bacteria has to either begin or stop production of specific proteins. Special proteins called regulators participate in this process. Some of them can influence production of several other proteins and are considered to be global regulators. HU protein belongs to this group. In model organism *Escherichia coli* it is responsible for stress response like lack of oxygen, nutrients depletion or high temperature.

Phylum Actinomycetes includes, among others, pathogenic bacteria from genus *Mycobacterium* (*Mycobacterium tuberculosis* causes tuberculosis) or industrially important genus *Streptomyces.* Bacteria belonging to *Streptomyces* are usually not infectious, but are very important for the pharmaceutical industry. Around 2/3 of currently used antibiotics are produced by various species of *Streptomyces.* Many *Streptomyces* metabolites can be important clinically as agents against bacteria, fungi or immunosuppressants. However industrial production of *Streptomyces* metabolites involves exposing bacteria to various stress conditions such as shortage of oxygen or high salt concentration.

Other interesting feature of *Streptomyces* is their life cycle involving spore production, resembling more development of fungi than bacteria. During their life cycle changes occur in DNA compaction, which can require DNA binding by NAPs. Life cycle is also directly connected to production of useful metabolites. Interestingly *Streptomyces* possess to HU proteins with different structures. The first (HupA) is similar to most bacterial HU proteins, whereas the second (HupS) consists of two parts called: N-domain and C-domain. C-domain structure is unique for Actinomycetes and contains many positively charged amino acids. Possibly it can take part in DNA binding.

Proposed project aims to study the role of HU proteins in maintaining proper chromosome structure during *Streptomyces* growth and environmental stress response. Strains lacking one or both HU proteins will be used. This will allow for an assessment of HU influence upon the rate of growth in optimal and stress conditions. Afterwards analysis of chromosome structure and of changes in protein production will carried out in strains lacking HU proteins and/or in suboptimal conditions. Additionally purified HU proteins will be used to study the binding of HU to DNA, which could reveal the function of HupS unique C-terminal domain.