Project description to the general public

Natural environment of most bacteria is dynamic and can change very quickly. To survive, bacterial cells have to adapt to the environment, notably to adjust their basic life processes to changing growth rate resulting from the availability of nutrients. Among these processes DNA replication, the key cell cycle step leading to the duplication of genetic material before division should be particularly taken into consideration. The way replication and growth are coordinated is still not fully explained, however the growing evidence suggests that multiple metabolic pathways are involved in regulation of replication according to the growth conditions.

The principal goal of this project is to elucidate molecular mechanisms linking replication and metabolism in *Escherichia coli*. The project focuses on main replication regulatory proteins including DnaA initiator and other factors influencing the initiation of replication. The research proposed here will lead to the identification of possible *in vivo*protein-metabolite interactions which may change the activity of replication regulators. Because the ability of binding ligands is often affected by post-translational modifications, the next research aspect will determine, whether proteins mentioned above can be post-translationally modified and whether potential protein-metabolite interactions depend on these modifications. Experiments will be conducted under different growth conditions to check if the replication control mechanisms vary depending on the metabolic status of bacterial cells The reliability of all identified interactions will be confirmed using *in vitro* methods. The results obtained in this project will serve as a starting point to conduct further research that will reveal the functional significance of discovered interactions and post-translational modifications and consequently, allowing us to better understand the connection between replication and metabolism. The approach is especially valuable because the *in vivo* protein-metabolite interactions analysis has been never performed in *Escherichia coli*.

All disturbances in fidelity and timing of replication may have serious consequences on the genome stability and integrity which can lead even to cell death. In higher organisms abnormalities in replication control are often connected with cancerogenesis. Because the replication is evolutionarily conserved, this project can contribute to the discovery of universal control mechanisms present in all domains of life which, if disturbed, may lead to various diseases. In turn, bacteria-specific pathways can be useful taking into account the targets for new antimicrobial drugs and antibiotic adjuvants.