Drug-resistant bacteria are big challenge for modern medicine. One of the most common hospital-acquired infections is caused by methicillin-resistant *Staphylococcus aureus* (MRSA). Despite of progress in field of *Staphylococcus* treatment, every year new MRSA strains appear which reveal resistance even for newest antibiotics. Most of antimicrobial therapeutics targets a single cellular protein by a single compound. For example, methicillin interacts with proteins that are involved in the synthesis of peptidoglycan – one of the essential substances of the cell wall. Since bacteria are able to adapt quickly to changes in their external environment by mutational changes or horizontal gene transfer, gaining resistance for single-targeted therapeutics is rapid process.

Alternative targets for antimicrobial therapeutics are regulatory RNAs which modulate gene expression. Riboswitches are common regulatory RNA structures in bacteria, which in response to binding of small metabolites modulate gene expression. Family of riboswitches binding same ligand can control multiple genes spread among the genome, which are part of multiple metabolic pathways. Thus, application of the analogs of natural ligands can lead to dysregulation of multiple metabolic processes, hindering the gain of resistance.

The main goal of this project is identification of the RNA regulatory networks of methicillin-resistant *Staphylococcus* aureus which could be targeted by antimicrobial compounds. RNA regulators will be identified by application of novel bioinformatics methods and software for synergistic analysis of high throughput transcriptomic data derived from multiple experimental approaches on level of transcription, translation and RNA structure.

Identified RNA regulators will be used for reconstruction of regulatory networks in MRSA. Next, we will analyze and predict how metabolic pathways are affected by identified regulatory mechanism. RNA regulators with strongest potential for antimicrobial targeting will be examined by experimental methods based on *in vivo* assays with reporter gene constructs.

The main output of the project will be list of reliable targets for development of novel classes of antibiotics. Additionally, we will provide set of novel RNA regulators and present new mechanisms of gene expression in MRSA in response to infection and antibiotic treatment. All those data will be released to public via publications and deposition in scientific databases, thus facilitating further development of antimicrobial therapies of drug resistant *Staphylococcus aureus*.