Designing novel antibiotics against *Staphylococcus aureus*

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Pathogenic infections represent a persistent threat to human health. The overuse of antibiotics in human, medicine and agriculture including food production contributes to the rise of antibiotic-resistant infections that are difficult to treat. The World Health Organization 2014 report states, "this serious threat is no longer a prediction for the future, it is happening right now in every region of the world and has the potential to affect anyone, of any age, in any country". Another major concern in this field is the phenomenon of bacterial persistence. Persistent cells are the small fraction of a bacterial population that tolerates antibiotics by entering a state of dormancy, thus creating a challenge to develop compounds that will target them. There is an urgent need to design novel antimicrobial agents

Staphylococcus aureus is one of the most important pathogens that cause complications ranging from minor to life-threatening infections. *Staphylococcus aureus* is worldwide problem. Our research goal is to **design peptide-like inhibitors for vital protein-protein interaction in bacteria.** We will design novel and selective antibiotic agents by studying the *Staphylococcus aureus* toxin-antitoxin (TA) system, an unexplored and novel basis for drug development. One of the types of TA systems consists of an antitoxin protein that binds to and inactivates a toxin protein. Upon degradation of the antitoxin, the toxin is released to induce bacterial cell death. TA systems play important role in the development of persistent cells, by inducing cell growth arrest that leads to antibiotic tolerance. Inhibiting TA interactions offers a good opportunity for development of novel antibacterial compounds because there are **no known mammalian homologs of TA pairs**.

We will discover and explore TA peptidic inhibitors using:**Phage Display** to identify short polypeptides.We will characterize their ability to penetrate bacterial cell and to induce bacterial cell death.

The novel techniques and concepts developed in the proposed interdisciplinary research program will shed light on the toxin antitoxin mode of action. These insights may reveal to the design of selective and effective antibiotic agents.