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Research Project:

Towards Catalytic Antibiotics: Rational Design, Synthesis and Biological Evaluation

The emergence of multidrug-resistant pathogens has triggered an on-going intensive search for novel antibiotics. While our lab has a long-standing experience in the development of new antibiotics, the proposed research focuses on the development of *catalytic antibiotics as a new paradigm in antibiotics research*. In its initial step, the project aims to chemically modify the existing antibacterial drugs to act on their targets in a catalytic manner. Currently the group is focused on rationally redesigning aminoglycoside class of antibiotics to act in a catalytic manner.

The possible benefits include: i) activity at lower dosages and subsequent elimination of side effects, ii) activity against drug-resistant bacteria, and iii) reduced potential for generating new resistance. *The main motivation of this project is that no such drugs are currently available and, if successful, this new paradigm will pave a way to new era in antibiotics development.*

Students are performing the rational design, chemical synthesis, and biological evaluation of synthetic molecules for their antibacterial activity, including catalytic activity on their target-bacterial ribosome and/or ribosomal particles. The lead compounds will be evaluated by means of cryo-EM and MD simulations to extract potential mechanisms of catalytic action. The lead compound will be tested *in vivo* for the development of potential new antibiotics with novel mechanisms of action.