MSc project

Understanding & Designing Antibiotics

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The alarming rise of drug resistant bacteria urgently calls for novel Antibiotics. To date, resistance has been observed against all clinically used antibiotics, which is soon expected to cause more human deaths than cancer. To make things worse, the industry's drug-discovery pipeline for antibiotics is almost empty. It is hence of pressing need to develop novel antibiotics that operate via unexploited mechanisms and that are robust to resistance development.

Ideal templates for such magic bullets could be **peptide-antibiotics** that specifically target the membrane-anchored cell wall precursor *lipid II, also known as the Achilles' heel of bacteria*. These peptides kill even the most refractory pathogens without detectable resistance and without showing cytotoxicity. However, due to the challenge of studying small drug–receptor complexes in membranes, structural data on peptide–lipid II binding are scarce and totally absent in native-like media. In consequence, the physiological binding modes could never be visualized. This lack of knowledge critically limits the use of lipid II binding peptides as templates for antibiotic design.

In Utrecht, in the Bijvoet Center for Biomolecular research, we work with several highly promising antibiotics (i.e., **Plectasin** [Schneider et al., Science 2010]) in native cell membranes in order to develop novel and improved antibiotics. **We offer MSc projects on the functional and structural characterisation of these promising antibiotics; and also on the design of improved antibiotics.**

MSc projects could involve:

- **Molecular Biology** (Antibiotics expression/purification with bacteria)
- **Drug Binding Studies** with Biophysical methods (i.e., Fluorescence, ITC)
- **Drug Design** (using structural & computational insights)
- **Structural Studies** (solid-state NMR in bacterial cell membranes)
- **Study of Drug Activity** studies against bacterial pathogens