Jena School for Microbial Communication
Graduate School of Excellence

PhD project title:
Non-canonical diversification strategies of nonribosomal peptides in bacteria

PhD Student: Friedrich J. Ehinger
Supervisors: Prof. Dr. C. Hertweck, Dr. H. Kries

Abstract:

Nonribosomal peptides (NRP) are a large and diverse group of biomolecules characterized by their peptide bonds despite a nonribosomal origin. Usually, NRP are biosynthesized by multimodular assembly lines – nonribosomal peptide synthetases (NRPS). Different NRP act as chemical mediators in microbial communication and, vice versa, the NRPS-based generation of NRP can be influenced by intra- and intercellular signaling. NRP constitute a main compound source for several pharmaceutical classes such as antibiotics or cancer chemotherapy and anti-inflammatory agents. Although most NRPS-relying biosynthesis routes follow a well-understood process, several non-canonical thiotemplated process steps were discovered during the last years. This is exemplified by the surprising potential of bacterial enzymes to transform amide bonds into thioamides or by the discovery of novel non-proteinogenic amino acids incorporated into NRP.

During the doctoral studies, the natural scope of the recently discovered non-canonical biosynthesis reactions will be determined by investigating further gene clusters showing similar unusual biosynthetic potential. It will be assessed if the uncommon reactions could be applied to tailor pharmaceutically and biotechnologically relevant compounds. In addition, the yet cryptic biosynthetic pathway leading to the formation of certain non-proteinogenic amino acid building blocks will be dissected. Overall, these works will advance the understanding of structural diversity in NRP – immediately relating to the comprehension of information exchange between microorganisms.