Genomics-driven discovery and synthetic biology of specialized metabolites from bacteria

Our main research focus:

- Functional genomics of cryptic biosynthetic gene clusters
- Comparative metabolomics using mass spectrometry
- Microbial physiology of specialized metabolites
- Biosynthesis of natural products (enzymes, cofactors, toxins)
- Synthetic biology of natural products (“Pathway Engineering”)

Bacteria are incredibly resourceful organisms. They produce natural products like enzymes, signaling molecules, cofactors or toxins. These molecules are extremely valuable for humans. Enzymes drive biotechnological applications in diagnostics or food processing. Cofactors serve as vitamins. Toxins can act as antibiotics or insecticides. Our aim is the discovery of novel biosynthetic routes useful for biotechnology, pharmacology or agriculture. Therefore, we investigate cryptic biosynthetic pathways, i.e. pathways with as-yet unknown products found encoded in microbial genomes. We combine functional genomics and comparative metabolomics to link biosynthetic gene clusters to their corresponding natural products. Functional genomics comprises techniques to perform targeted activation or inactivation of genes or to transfer and “re-factor” whole gene clusters for expression in an “optimized” host organism (Synthetic Biology). Comparative metabolomics refers to the systematic comparison of “as many
metabolites as possible” found in an organism. We employ high-resolution mass spectrometry and computational analyses to find novel specialized metabolites. In addition, we investigate the physiological role of the metabolites we discovered and study single biochemical steps in detail. Finally, we use synthetic biology to “engineer” biosynthetic pathways: By channeling biomass into the biosynthetic route the yield of the natural product can be increased. Recombining pathways can lead to the production of novel metabolites with enhanced properties for various applications.

Our current focus is on rare cofactors produced by bacteria of the genus Mycobacterium. Rare cofactors are involved in various intriguing physiological processes like breakdown of organic molecules, defense against various stresses, antibiotic resistance or antibiotic biosynthesis. Therefore, we make rare cofactors available for biotechnology and study their biosynthesis and physiology in the natural producers.