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The roles of secondary metabolites in *Dictyostelium discoideum* – bacteria interactions

This project will focus on both the identification of novel natural products as well as on the elucidation of their roles in eukaryote-prokaryote interactions. The social soil amoeba *Dictyostelium discoideum* will serve as the model eukaryote, whose secondary metabolome will be explored in a systematic fashion. *D. discoideum* is a voracious and ubiquitous predator of bacteria causing the depletion of large bacterial reservoirs. This puts both organisms under strong evolutionary selection pressure: consequently, the bacteria have evolved mechanisms to prevent grazing, and the amoeba must counteract or surmount these mechanisms in order to survive, for instance by the secretion of antibacterial metabolites. In particular, we are interested in a group of small molecules known as polyketides, of which only very few have been investigated. The structures and physiological roles of most of them, however, remain unknown.

Specifically, we will examine their roles as signals or defense weapons in interspecies interactions when in contact with amoeba-pathogenic soil bacteria using a toolset of bioassays and methods that have been established in our lab. Emphasis will be put on the design of conditions that enable the expression of otherwise silent biosynthetic gene clusters of both the amoeba and bacteria. Thus, secondary metabolites will be accessible that would otherwise not be produced under standard laboratory conditions. Subsequent bioassay-guided fractionation of bioactive extracts from amoebal or bacterial cultures eventually allows for identification of natural products that orchestrate the coexistence and chemical warfare of the competitors

in nature through their antibacterial, amoebicidal or cytotoxic properties. Thus, this project may give rise to new leads for anti-infective or anticancer drugs.

Publications

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Supervisor

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