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Modular synthetic approaches towards natural sphingoid base-type signaling molecules

Sphingoid bases and sphingolipids are essential multifunctional cellular compounds, which serve not only as integral components of cell membranes, but also as essential regulatory signals for fundamental cellular processes. They were first thought to exist exclusively in eukaryotes, but have now been repeatedly identified and isolated from important bacterial and viral sources. Despite being abundant signaling molecules, the biological function of many sphingolipid derivatives remains elusive.

Prominent examples of fungal origin are sphingofungins and myriocin (ISP-1), which exhibit antifungal activity in the picomolar to nanomolar range. Their discovery has led to the development of many pharmaceutical drug leads (e.g. FTY720 and safinol). But the intrinsic biological role of sphingofungins is unknown until to date. In another study bacterial sulfonolipids, such as **RIF-1** and **RIF-2**, regulate an onset of development in one of the closest living relatives of animals, the choanoflagellate *Salpingoeca rosetta*. A structural analog IOR-1 inhibits partially the activity of RIF molecules.

Due to their intrinsic biological function of these types of molecules, this research project will focus on efficient and new synthetic strategies towards of rare microbial sphingoid base-type signaling molecules to allow their detailed functional analysis.

Publications

Bissell AU, Rautschek J, Hoefgen S, Raguž L, Mattern DJ, Saeed N, Janevska S, Jojić K, Huang Y, Kufs JE, Herboeck B, Guo H, Hillmann F, Beemelmanns C, Valiante V (2022) Biosynthesis of the Sphingolipid Inhibitors Sphingofungins in Filamentous Fungi Requires Aminomalonate as a Metabolic Precursor. *ACS Chem Biol* , [Details PubMed](#)

Leichnitz D, Peng CC, Raguz L, Rutaganira F, Jautzus T, Regestein L, King N, Beemelmanns C (2021) Structural and functional analysis of bacterial sulfonosphingolipids and rosette-inducing factor 2 (RIF-2) by mass spectrometry-guided isolation and total synthesis. *Chemistry* , [Details PubMed](#)

Raguž L, Peng CC, Kaiser M, Görls H, Beemelmanns C (2021) A Modular Approach to the Antifungal Sphingofungin Family: Concise Total Synthesis of Sphingofungin A and C. *Angew Chem Int Ed Engl* , [Details PubMed](#)

Roman D, Raguž L, Keiff F, Meyer F, Barthels F, Schirmeister T, Kloss F, Beemelmanns C (2020) Modular Solid-Phase Synthesis of Antiprotozoal Barnesin Derivatives. *Org Lett* , [Details PubMed](#)

Guo H, Schmidt A, Stephan P, Raguž L, Daniel Braga D, Kaiser M, Dahse HM, Weigel C, Lackner G, Beemelmanns C (2018) Precursor-directed Diversification of Cyclic Tetrapeptidic Pseudoxylallemycins. *Chembiochem* 19(21), 2307-2311. [Details PubMed](#)

Rischer M, Raguž L, Guo H, Keiff F, Diekert G, Goris T, Beemelmanns C (2018) Biosynthesis, Synthesis, and Activities of Barnesin A, a NRPS-PKS Hybrid Produced by an Anaerobic Epsilonproteobacterium. *ACS Chem Biol* 13(8), 1990-1995. [Details PubMed](#)

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Start of PhD

August 1, 2016

Doctoral Disputation

February 3, 2023