# MBG FOCUS TALK

hosted by Ditlev E. Brodersen, Structural Biology


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Dept. of Mathematics, Aud. D1


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## Structure-Based Engineering of Antibiotic Biosynthesis Enzymes


Streptomyces soil bacteria are competent chemists that are able to produce thousands of chemically complex natural products. Key to the development of this rich source of metabolites appears to be an evolutionary pressure that promotes chemical diversity; new biosynthetic pathways are continuously being formed in these bacteria, which may result in the appearance of a novel bioactive compound that provides significant competitive advantage to the producing organism. This is reflected in the biosynthetic enzymes that have been able to evolve relatively freely and, as a consequence, have resulted in a situation where the functions of even similar proteins may greatly differ. In recent years, our work has focused on understanding the details of this process in the so-called tailoring steps in the biosynthetic pathways of anthracyclines and angucyclines. We have demonstrated how insertion of a single amino acid is sufficient to convert a SAM-dependent methyltransferase into a mono-oxygenase [1], elucidated how allosteric effects influence the activity of FAD-dependent mono-oxygenases [2,3] and what determines the stereochemistry of angucycline 6-ketoreduction [4,5]. The work provides an opportunity for further protein engineering efforts for generation of improved bioactive natural products.



[1] T. Grocholski et al., Proc Natl Acad Sci U S A 112, 9866–9871 (2015).
[2] P. Kallio et al., Biochemistry 52, 4507–4516 (2013).
[3] P. Kallio et al., Biochemistry 50, 5535–5543 (2011).
[4] P. Patrikainen et al., Chem Biol 21, 1381–1391 (2014).
[5] P. Paananen et al., Biochemistry 52, 5304–5314 (2013).