Characterization of novel metabolites originating from *Streptomyces albus* ssp. *chlorinus*

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Natural products are a prime source of agents displaying biological activitiy over the whole spectrum of therapeutically relevant indications, including anticancer, antibacterial, antifungal, antiparasitic, antiviral and many further treatment options that are indispensable in modern medical care. The structural and chemical diversity of natural products is enormous and evolutionarily optimized to exert “drug-like” properties, which can hardly be matched by any synthetic library of small molecules. Although the discovery rate of new natural products remained stably high over the last two decades, the majority of natural products being published today bear structural similarity to previously published compounds. This raises the concern if the top-down investigation of natural products will yield a sufficient number of new chemotypes in the future. Recent vast sequencing efforts, where entire genomes of secondary metabolite producing organisms have been assessed, revealed a very rich source of biosynthetic gene clusters (BGC), whose secondary metabolites still remain to be identified. Hence, a large number of novel chemical scaffolds stay “hidden” in the numerous publicly available bacterial genomes. Therefore, there is a strong need in innovative methods to exploit this biosynthetic potential.

Our strategy to discover novel compounds combines three well-established tools. In a first step, *in-silico* genome mining using modern databases gives us an overview on all the potential BGCs of a *Streptomyces* sp. Through cultivation and LC MS characterization of the metabolic profile, the main metabolites of the strain can be allocated in a second step. After correlation of known metabolites to the respective BGCs, a manageable number of uncharacterized BGCs remains. Those promising BGCs are captured and in a third step expressed in selected advanced host organisms.

The high potential of this combined approach is confirmed by the discovery of several new natural products. In this poster we present novel structures whose biosyntheses are governed by BGCs of the wild type strain *Streptomyces albus* ssp. *chlorinus,* including the following new compounds:

NRP-2O18 is a novel NRPS molecule produced by the host organism after heterologous expression of a BGC. Its structure is a small cyclic peptide consisting of five amino acids only, among them an unusual amino threonine.

NRP-4E8 is produced after expression of the corresponding NRPS gene in the heterologous host organism and comprises a set of eight peptide derivatives. The central element of the structures is a core lysine. Three amino acid based fatty acid units are condensed to this core by the NRPS to build the NRP-4E8 structure.