MICROBIAL BIODIVERSITY & SYNTHETIC BIOTECHNOLOGY TO IDENTIFY AND DEVELOP ANTI-INFECTIVES

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Key words: myxobacteria, antimicrobials, biosynthetic engineering

Introduction. For decades microbial secondary metabolite research has yielded numerous compounds representing novel chemical space and exhibiting unprecedented mechanisms of action. This is especially true for medically used antibacterials, almost all of which are natural products themselves or natural product derived. Despite the successes in this field we face numerous challenges because of microbial and viral resistance as well as new and re-occurring infectious diseases; in addition, the number of new anti-infectives approved for the market is on a constant decline, which also holds true for the number of pharmaceutical companies active in this field. Consequently we aim to contribute to the identification and development of novel natural products for application.

Methods. Using our microbiological expertise in the area of unique microorganisms we continuously isolate and prioritize promising producer species based on phylogenetic reasons for our research (1). From these species novel basic structures exhibiting useful activities are identified (2), structurally elucidated and production is subsequently optimized using genetic engineering and synthetic biotechnology efforts. Mode of action is studied in depth using various biochemical and molecular biological tools.

Results. Recent progress in the identification of novel myxobacterial species, genera and even families will be summarized as well as our dereplication concept based on a novel database system to use myxobacteria for the identification of new natural products exhibiting promising anti-infective activities. At this stage we have screened approximately 1500 extracts to prioritize 300 active strains from which less than 100 were dereplicated in depth to give 30 promising strains from which at least four new basic structures exhibiting intriguing activities were identified. In addition, results from synthetic biotechnology studies to optimize production and structure (3,4) of compounds will be presented together with data on mode of action of novel scaffolds (5).

Conclusions. Microbial natural products from selected organisms continue to be a rich source of novel and evolutionary optimized compounds. These represent unexploited chemical space with tremendous potential for application as chemical biology tools or even pharmaceuticals.

Acknowledgements. Financial support by the German Research Society (DFG) and the German Ministry of Science and Technology (BMBF) is highly appreciated.

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