

## **FUNGI: THE PHARMACIST'S BEST FRIENDS**

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Filamentous fungi display many unique characteristics among them the biosynthesis of natural products which display a broad range of useful activities, in particular for pharmaceutical purposes. The bioactivities of fungal secondary metabolites range from, e.g., antibiotic or antifungal to immunosuppressant and lipid-lowering. These bioactivities have spurred efforts towards identifying genes involved in their biosynthesis. Accumulating data from studies of known secondary metabolite biosynthetic genes dispelled an original premise that fungal metabolic genes would be scattered throughout the genome. Rather the hallmark of secondary metabolite genes is that they are arranged in operon-like gene clusters, which is reminiscent to bacterial gene organization. Examples of secondary metabolite gene clusters include those encoding the biosynthetic machinery for pharmaceuticals of clinical use, such as the important  $\beta$ -lactam-antibiotics penicillin and cephalosporin, the antihypercholesterolaemic agent lovastatin, or the ergopeptines with their core structure D-lysergic acid amide. Beyond these "traditional" fungal metabolites the recent progress in fungal genome sequencing identified a plethora of genetic loci potentially dedicated to secondary metabolism. For example, *Aspergillus nidulans* harbors 40 or so gene clusters encoding putative polyketide or nonribosomal peptide pathways. However, their number is far higher than the number of known metabolites from this species. Pharmaceutical biotechnologists involved in lead discovery are now facing a new challenge: which of these often difficult-to-decipher clusters is active at all, and how does chemical and genetic knowledge correlate.

This talk will introduce into selected aspects of fungal secondary metabolism and also present approaches that help match chemical and genomic data in *Aspergilli* to explore hitherto cryptic metabolic pathways of the *Aspergillus* secondary metabolome.