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Understanding secondary metabolite as key for unlocking new chemical diversity in fungi

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Filamentous fungi are prolific producers of bioactive small molecules known as secondary metabolites (SMs). The fungal SMs are Janus-faced: they are an important source for drug discovery and include important drugs like the antibiotic penicillin and the cholesterol-lowering lovastatin; yet many SMs are mycotoxins that are harmful to human, such as aflatoxins and fumonisins. Many SMs produced by pathogenic fungi also play an important role in infection and virulence, such as the T-toxins and HC-toxin. The advancement of genome sequencing technology has unlocked an unprecedented amount of microbial genomic information. These genome sequences also revealed a large number of secondary metabolite (SM) genes in fungi. For filamentous fungi in particular, the number of SM gene clusters encoded in the genome are often beyond the number of compounds that are reported for individual species. Continuous expanding our understanding of the relationship between SM compounds, the biosynthetic genes and microbial ecology will assist us in navigating the seas of genomic information in the search for new bioactive compounds. A specific

example is given here on how the investigation into the genes and enzymes involved in the biosynthesis of an interesting hexacyclic molecule, viridicatumtoxin, eventually leads to the discovery of a new immunosuppressive compound, neosartoricin, from the human pathogens *Aspergillus fumigatus* and *Neosartorya fischeri*. Future work on the application of the knowledge and techniques to the secondary metabolites of plant pathogens, in particular the wheat disease *Stagonospora nodorum*, will also be discussed.

Presented by

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