

Metabolic profiling in *Aspergillus flavus* to determine gene function

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Abstract

The *Aspergillus flavus* metabolome is of considerable interest because *A. flavus* produces the most toxic and carcinogenic compounds known from fungi and is a source of world-wide episodes of contamination of foods and animal feed with aflatoxins. Examination of the genes predicted to be involved in secondary metabolite biosynthesis suggests that *A. flavus* is capable of producing many more metabolites than have so far been discovered.

We have begun a collaborative project to examine some of these gene clusters to determine both their capability of producing known as well as unknown metabolites. To date, we have closely examined metabolite production by wild type *A. flavus* and mutants in biosynthetic genes in clusters 11, 23, 27 and 41. The backbone genes in clusters 27 and 41 are predicted to encode polyketide synthases (PKS). Cluster 11 contains a non-ribosomal peptide synthase (NRPS), while the backbone gene of cluster 23 encodes a hybrid PKS/NRPS. Using a comparative metabolomics approach based on UHPLC/orbitrap and microLC/triple TOF high resolution mass spectrometry (HRMS), we have been able to detect metabolites that are unique to each of the clusters under investigation. Our results show that clusters 11 and 27 produce the known *A. flavus* metabolites ditryptophenaline and asparasone, respectively. The PKS/NRPS of cluster 23 produces a tennellin-like metabolite, while the PKS of cluster 41, predicted to be a MSAS synthase, most likely produces a precursor that is converted to a meroterpenoid involved in developmental signaling. A related metabolite orcellinic acid has been characterized in *A. nidulans* and other species. The LC/MS and MSⁿ data are consistent not only with the products expected from these cluster backbone genes but also with the modifying enzymes encoded by decorating genes in each cluster.

Biography

José graduated as Pharmacist in 1997 at the University of Kinshasa (D.R. Congo). In 2005 he obtained his Ph.D. at the Katholieke Universiteit Leuven.

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