

Supplementary Text: Secondary Metabolites

Assignment of function to the putative secondary metabolite genes and clusters remains tentative but there are some clues. Gliotoxin is an epipolythiodioxopiperazine (ETP) derived from serine and phenylalanine, and thus is most likely product of a 2-module NRPS, of which five are present in the *A. fumigatus* genome. The putative gliotoxin gene cluster 17 comprises 12 genes (GenBank Accession Accession AY838877) and was identified by a comparative genomics approach based on homology to genes from the sirodesmin (another ETP) biosynthetic gene cluster of *Leptosphaeria maculans*¹. Comparisons between the putative gliotoxin and sirodesmin gene clusters have enabled steps in the gliotoxin biosynthetic pathway to be deduced². Three-module NRPS found in a cluster that includes a prenyl transferase related gene, a methylase, and several P450 hydroxylases may account for the diketopiperazine-derived toxins such as the fumitremorgins and tryprostatins. A potential alkaloid cluster could be the source of fumigaclavines, whose biosynthetic pathway is related to the lysergic acid (ergotamine) pathway of *Claviceps*. *A. fumigatus* genes with moderate similarity to a sesquiterpene cyclase resembling the trichodiene synthase Tri5 of *Fusarium/Gibberella/Stachybotris* may be involved in the synthesis of monoterpene-like compounds such as fumagillin. Phthioic acid, a methyl-branched chain fatty acid produced by *A. fumigatus*, could be the product of one of the three homologs of a family of PKS genes from *Mycobacterium* spp. that also produce this compound³.

References:

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2. Gardiner, D. M., Waring, P. & Howlett, B. J. The epipolythiodioxopiperazine (ETP) class of fungal toxins: distribution, mode of action, functions and biosynthesis. *Microbiology* 151, 1021-32 (2005).
3. Minnikin, D. E., Kremer, L., Dover, L. G. & Besra, G. S. The methyl-branched fortifications of *Mycobacterium tuberculosis*. *Chem Biol* 9, 545-53 (2002).