FUNGAL PHYSIOLOGY

Reaching the right location

“the sporulation-specific transcription factor BrIA was essential for the production of FqC”

Fungi produce an impressive array of secondary metabolites. In many cases, the biosynthetic pathways that are required to produce these complex bioactive compounds are known, but little information is available on their localization *in vivo*. Lim *et al.* now report on the localization of fumiquinazolines in *Aspergillus fumigatus*.

The fumiquinazolines are a family of cytotoxic peptidyl alkaloids that are generated sequentially. The biosynthetic pathway for fumiquinazolines is predicted to involve the non-ribosomal peptide synthases (NRPSs) FmqA and FmqC, the FAD-dependent monooxygenase FmqB and the FAD-dependent oxidoreductase FmqD. Using a series of single-deletion mutants, Lim *et al.* confirmed that the *fmqA–fmqD* gene cluster encodes the enzymes that are necessary for the biosynthesis of fumiquinazolines.

A. fumigatus sporulates well in solid culture but not in liquid culture, and liquid chromatography–mass spectrometry (LC–MS) analysis

indicated that the levels of fumiquinazoline C (FqC) were higher in extracts from solid cultures than in extracts from liquid cultures. Solid cultures of *A. fumigatus* were fractionated to separate the conidia and conidiophores from the vegetative and invasive hyphae, and LC–MS analysis confirmed that FqC was enriched in the conidial fraction, whereas the other fumiquinazolines, FqA and FqF, were not. To further probe the potential link between the production of FqC and sporulation, metabolic profiling of mutant strains in which conidiophore development was disrupted revealed that the sporulation-specific transcription factor BrIA was essential for the production of FqC and the preceding metabolite in the biosynthetic sequence, FqA.

The oxidoreductase FmqD is the final enzyme in the FqC biosynthesis pathway and converts FqA to FqC. To visualize the location of FmqD *in vivo*, an FmqD–GFP fusion protein was overexpressed and was shown to localize to the cell wall, mainly in conidia. In addition, the amino-terminal signal peptide of FmqD was essential for cell wall localization. Cell wall localization was also lost if cells were treated with the inhibitors brefeldin A or

cytochalasin A, which indicates that cell wall localization of FmqD requires transport through the classic ER–Golgi secretory pathway in an actin-dependent manner. In *Aspergillus* spp., many secreted proteins are passed through the secretory pathway to the cell wall and then released into the environment, and these data suggest that FqC may follow a similar pathway.

This study reveals that *A. fumigatus* FqC is specifically targeted to the conidial cell wall by a dual strategy that involves the use of a sporulation-specific transcription factor and cell wall localization of the final enzyme in the biosynthetic pathway. Filamentous fungi develop multimorphic forms, from asexual conidia to vegetative hyphae, and it is possible that these distinct structures may harbour distinct secondary metabolites. This, and the implications of the conidial location of FqC for *A. fumigatus* virulence, will be interesting avenues for future research.

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ORIGINAL RESEARCH PAPER Lim, F.Y. *et al.* Coordination between BrIA regulation and secretion of the oxidoreductase FmqD directs selective accumulation of fumiquinazoline C to conidial tissues in *Aspergillus fumigatus*. *Cell. Microbiol.* <http://dx.doi.org/10.1111/cmi.12284> (2014)