

Intimate bacterial-fungal interaction triggers biosynthesis of archetypal polyketides in *Aspergillus nidulans*.

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Abstract

Fungi produce numerous low molecular weight molecules endowed with a multitude of biological activities. However, mining the full-genome sequences of fungi indicates that their potential to produce secondary metabolites is greatly underestimated. Because most of the biosynthesis gene clusters are silent under laboratory conditions, one of the major challenges is to understand the physiological conditions under which these genes are activated. Thus, we cocultivated the important model fungus *Aspergillus nidulans* with a collection of 58 soil-dwelling actinomycetes. By microarray analyses of both *Aspergillus* secondary metabolism and full-genome arrays and Northern blot and quantitative RT-PCR analyses, we demonstrate at the molecular level that a distinct fungal-bacterial interaction leads to the specific activation of fungal secondary metabolism genes. Most surprisingly, dialysis experiments and electron microscopy indicated that an intimate physical interaction of the bacterial and fungal mycelia is required to elicit the specific response. Gene knockout experiments provided evidence that one induced gene cluster codes for the long-sought after polyketide synthase (PKS) required for the biosynthesis of the archetypal polyketide

orsellinic acid, the typical lichen metabolite lecanoric acid, and the cathepsin K inhibitors F-9775A and F-9775B. A phylogenetic analysis demonstrates that orthologs of this PKS are widespread in nature in all major fungal groups, including mycobionts of lichens. These results provide evidence of specific interaction among microorganisms belonging to different domains and support the hypothesis that not only diffusible signals but intimate physical interactions contribute to the communication among microorganisms and induction of otherwise silent biosynthesis genes.

Involved units

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