

Bacteria-induced production of the antibacterial sesquiterpene lagopodin B in *Coprinopsis cinerea*.

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Abstract

Fungi defend their ecological niche against antagonists by producing antibiosis molecules. Some of these molecules are only produced upon confrontation with the antagonist. The basidiomycete *Coprinopsis cinerea* induces the expression of the sesquiterpene synthase-encoding gene *cop6* and its two neighboring genes coding for cytochrome P450 monooxygenases in response to bacteria. We further investigated this regulation of *cop6* and examined if the gene product is involved in the production of antibacterials. Cell-free supernatants of axenic cultures of the Gram-positive bacterium *Bacillus subtilis* were sufficient to induce *cop6* transcription assessed using a fluorescent reporter strain. Use of this strain in a microfluidic device revealed that the *cop6* gene was induced in all hyphae directly exposed to the supernatant and that induction occurred within less than one hour. Targeted replacement of the *cop6* gene demonstrated the requirement of the encoded synthase for the biosynthesis of the sesquiterpene lagopodin B, a previously reported antibacterial compound from related species. Accordingly, lagopodin B from *C. cinerea* inhibited the growth of several Gram-positive bacteria including *B. subtilis* but not Gram-negative

bacteria. Our results demonstrate that the *C. cinerea* vegetative mycelium responds to soluble compounds of a bacterial culture supernatant by local production of an antibacterial secondary metabolite.

Leibniz-HKI-Autor*innen



Gerald Lackner

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