

Genome mining reveals endopyrroles from a nonribosomal peptide assembly line triggered in fungal-bacterial symbiosis.

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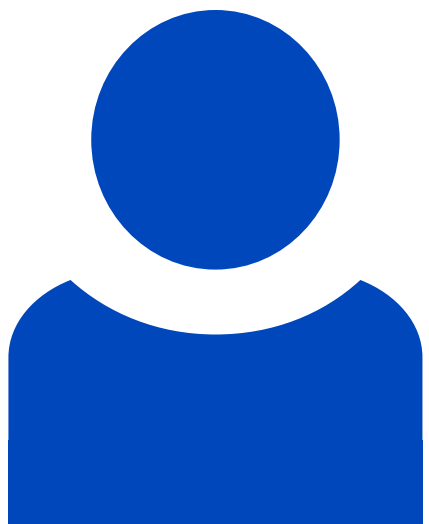
Abstract

The bacterial endosymbiont (*Burkholderia rhizoxinica*) of the rice seedling blight fungus (*Rhizopus microsporus*) harbors a large number of cryptic biosynthesis gene clusters. Genome mining and sequence similarity networks based on an encoded nonribosomal peptide assembly line and the associated pyrrole-forming enzymes in the symbiont indicated that the encoded metabolites are unique among a large number of tentative pyrrole natural products in diverse and unrelated bacterial phyla. By performing comparative metabolic profiling using a mutant generated with an improved pheS *Burkholderia* counterselection marker, we found that the symbionts' biosynthetic pathway is mainly activated under salt stress and exclusively in symbiosis with the fungal host. The cryptic metabolites were fully characterized as novel pyrrole-substituted depsipeptides (endopyrroles). A broader survey showed that endopyrrole production is a hallmark of geographically distant endofungal bacteria, which produce the peptides solely under symbiotic conditions.

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