

Genome mining and heterologous expression reveal two distinct families of lasso peptides highly conserved in endofungal bacteria.

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Abstract

Genome mining identified the fungal-bacterial endosymbiosis *Rhizopus microsporus*-*Mycetohabitans* (previously: *Burkholderia*) *rhizoxinica* as a rich source of novel natural products. Yet, most of the predicted compounds have remained cryptic. In this study we employed heterologous expression to isolate and characterize three ribosomally-synthesized and post-translationally modified peptides (RiPPs) with lariat topology (lasso peptides) from the endosymbiont *M. rhizoxinica*: burhizin-23, mycetohabin-16 and mycetohabin-15. Through coexpression experiments it was shown that an orphan gene product results in mature mycetohabin-15, albeit encoded remotely from the core biosynthetic gene cluster. Comparative genomics revealed that mycetohabins are highly conserved trait among *M. rhizoxinica* and related endosymbiotic bacteria. Gene knockout and reinfection experiments indicated that the lasso peptides are not crucial for establishing the symbiosis; instead, the peptides are exported into the environment during endosymbiosis. This is the first report on lasso peptides from endosymbiotic

bacteria.

Beteiligte Forschungseinheiten

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