Functional analysis of environmental DNA-derived microviridins provides new insights into the diversity of the tricyclic peptide family.

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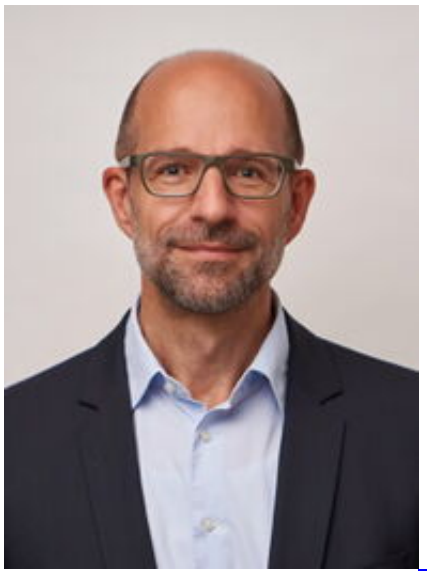
Abstract

Microviridins represent a unique family of ribosomally synthesized cage-like depsipeptides from cyanobacteria with potent protease-inhibitory activities. The natural diversity of these peptides is largely unexplored. Here, we describe two methodologies that were developed to functionally characterize cryptic microviridin gene clusters from metagenomic DNA. Environmental samples were collected and enriched from cyanobacterial freshwater blooms of different geographical origins containing predominantly Microcystis sp. Microviridins were produced either directly from fosmid clones or after insertion of environmental DNA-derived gene cassettes into a minimal expression platform in Escherichia coli. Three novel microviridin variants were isolated and tested against different serine-type proteases. The comparison of the bioactivity profiles of the new congeners allows deduction of further structure-function relationships for microviridins. Moreover, this study provides new insights into microviridin processing and gene cluster organization.

Beteiligte Forschungseinheiten

Biomolekulare Chemie Christian Hertweck Mehr erfahren

Leibniz-HKI-Autor*innen



Christian Hertweck

Details



Keishi Ishida

Details

Identifier

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