

Exploiting the natural diversity of microviridin gene clusters for discovery of novel tricyclic depsipeptides.

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Abstract

Microviridins are ribosomally synthesized tricyclic depsipeptides produced by different genera of cyanobacteria. The prevalence of the microviridin gene clusters and the natural diversity of microviridin precursor sequences are currently unknown. Screening of laboratory strains and field samples of the bloom-forming freshwater cyanobacterium *Microcystis* via PCR revealed global occurrence of the microviridin pathway and an unexpected natural variety. We could detect 15 new variants of the precursor gene *mdnA* encoding microviridin backbones that differ in up to 4 amino acid positions from known isoforms of the peptide. The survey not only provides insights into the versatility of the biosynthetic enzymes in a closely related group of cyanobacteria, but also facilitates the discovery and characterization of cryptic microviridin variants. This is demonstrated for microviridin L in *Microcystis aeruginosa* strain NIES843 and heterologously produced variants.

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