Insights into the lifestyle of uncultured bacterial natural product factories associated with marine sponges.

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Abstract

The as-yet uncultured filamentous bacteria "*Candidatus* Entotheonella factor" and "*Candidatus* Entotheonella gemina" live associatedwith the marine sponge *Theonella swinhoei* Y, the source of numerous unusual bioactive natural products. Belonging to the proposed candidate phylum "Tectomicrobia," Candidatus Entotheonella members are only distantly related to any cultivated organism. The *Ca.* E. factor has been identified as the source of almost all polyketide and modified peptides families reported from the sponge host, and both *Ca.* Entotheonella phylotypes contain numerous additional genes for as-yet unknown metabolites. Here, we provide insights into the biology of these remarkable bacteria using genomic, (meta)proteomic, and chemical methods. The data suggest a metabolic model of *Ca.* Entotheonella as facultative anaerobic, organotrophic organisms with the ability to use methanol as an energy source. The symbionts appear to be auxotrophic for some vitamins, but have the potential to produce most amino acids as well as rare cofactors like coenzyme F_{420} The latter likely accounts for the strong autofluorescence of *Ca.* Entotheonella filaments. A large expansion of protein families involved in regulation and conversion

of organic molecules indicates roles in host-bacterial interaction. In addition, a massive overrepresentation of members of the luciferase-like monooxygenase superfamily points toward an important role of these proteins in *Ca.* Entotheonella. Furthermore, we performed mass spectrometric imaging combined with fluorescence in situ hybridization to localize *Ca.* Entotheonella and some of the bioactive natural products in the sponge tissue. These metabolic insights into a new candidate phylum offer hints on the targeted cultivation of the chemically most prolific microorganisms known from microbial dark matter.

Beteiligte Forschungseinheiten

Synthetische Mikrobiologie Gerald Lackner Mehr erfahren

Leibniz-HKI-Autor*innen

Gerald Lackner

Details

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