A widespread bacterial phenazine forms conjugates with biogenic thiols and crosslinks proteins.

Heine D, Sundaram S, Beudert M, Martin K, Hertweck C (2016) A widespread bacterial phenazine forms conjugates with biogenic thiols and crosslinks proteins. *Chem Sci* 7, 4848-4855.

Details

PAPER

Abstract

Phenazines are redox-active compounds produced by a range of bacteria, including many pathogens.
Endowed with various biological activities, these ubiquitous N-heterocycles are well known for their
ability to generate reactive oxygen species by redox cycling. Phenazines may lead to an irreversible
depletion of glutathione, but a detailed mechanism has remained elusive. Furthermore, it is not understood why phenazines have so many protein targets and cause protein misfolding as well as their
aggregation. Here we report the discovery of unprecedented conjugates (panphenazines A, B) of panthetheine and phenazine-1-carboxylic (PCA) acid from a Kitasatospora sp., which prompted us to
investigate their biogenesis. We found that PCA reacts with diverse biogenic thiols under radical-

forming
conditions, which provides a plausible model for irreversible glutathione depletion. To evaluate the scope of the reaction in cells we designed biotin and rhodamine conjugates for protein labelling and
examined their covalent fusion with model proteins (ketosynthase, carbonic anhydrase III, albumin). Our
results reveal important, yet overlooked biological roles of phenazines and show for the first time their
function in protein conjugation and crosslinking.

Beteiligte Forschungseinheiten

Biomolekulare Chemie Christian Hertweck Mehr erfahren

Biotechnikum Miriam Agler-Rosenbaum Mehr erfahren

Leibniz-HKI-Autor*innen



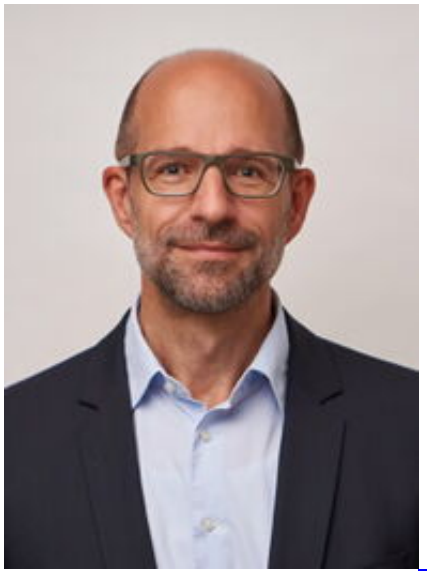
Matthias Beudert

Details



Daniel Heine

Details



Christian Hertweck

Details



Karin Martin

Details



Srividhya Sundaram

Details

Identifier

doi: DOI: 10.1039/C6SC00503A