



Universität Potsdam · Am Neuen Palais 10 · 14469 Potsdam

**Mathematisch-Naturwissenschaftliche
Fakultät**

University of South Bohemia
České Budejovice
Faculty of Science

Department of Students Affairs
Dr. Jana Jersakova

Prof. Elke Dittmann-Thünemann
Institute of Biochemistry and Biology
Department of Microbiology
Telefon: 0331-9775120
Telefax: 0331-9775062

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Review on the Doctoral Dissertation of Tomáš Galica: “Diversity and Ecological Role of Cyanobacterial Lipopeptides”

Tomáš Galica presents a dissertation paper outlining his scientific contributions to understanding the genetic and structural diversity of cyanobacterial lipopeptides and discussing ecological functions of the metabolites. Cyanobacteria are well recognized as prolific producers of complex secondary metabolites, yet the knowledge on the diversity of secondary metabolites is still limited and the exploitation of the metabolites is in its infancy. Amphiphilic lipopeptides are of great importance in other bacterial phyla where they play important roles e.g. in biofilm formation, interspecies interactions and as antibiotics. There were already isolated studies on individual cyanobacterial lipopeptides and their biosynthesis before the work that have highlighted the therapeutic potential of the metabolite group as antifungal agents. Tomas Galicia has now approached the diversity of cyanobacterial lipopeptides in a more systematic way, at the genomic, metabolomic as well as the physiological level.

His thesis includes five manuscripts of which four are already published, a fifth study is in revision. In one of his two first-author studies Tomáš Galica has comprehensively analyzed available genome sequences for the presence of lipopeptide biosynthetic gene clusters (BGCs). Using the fatty acid-AMP-ligase (FAAL)-encoding gene as signature, he could mine a significant number of new lipopeptide BGCs and categorize them into three distinct groups based on biosynthetic features. He has found evidence for several independent evolutionary lineages in the cyanobacterial phylum and dissected a number of putative recombination events. His systematic analysis points towards a more frequent occurrence of lipopeptide BGCs in cyanobacteria featuring complex morphologies and a predominance in strains with a substrate-associated lifestyle. These findings indicate a possible role of such lipopeptides in biofilm development and surface colonization, similar as described for lipopeptides of other phyla. The study provided the basis for prioritization of strains for analytical, structural and ecological studies. With this study, Tomáš Galica has laid foundations for the subsequent functional studies on lipopeptides.

Bankverbindung:
Landeszentralbank, Filiale Potsdam
Kontonummer: 160 015 00
BLZ: 160 000 00

Dienstgebäude: Karl-Liebknecht-
Str. 24/25, Haus 25, R. B1.11-12

E-mail: editt@uni-potsdam.de
Internet: <http://www.bio.uni-potsdam.de/professuren/mikrobiologie/mikrobiologie>

Tomáš Galica also contributed to a methodological study where high-resolution mass spectrometry and collision-induced dissociation was used to optimize the detection of lipopeptides in cyanobacteria. As part of this study, a dual technique was developed for the detection of β -amino-acid containing lipopeptides. The advanced analytical method together with the phylogenomic analysis led to the discovery of novel and widespread cyanobacterial siderophores, the cyanochelins. Two new types of β -amino-acid containing lipopeptides could be uncovered in the strains *Rivularia* sp. PCC 7116 and *Rubidibacter*, respectively. Tomas Galica and colleagues could not only isolate and elucidate the new compounds but also provide evidence for iron-lipopeptide complexes and the photoreduction of Fe^{3+} to Fe^{2+} . The cyanochelin study represents one of only few functional studies on the ecological role of cyanobacterial secondary metabolites and represents an important contribution within its research field.

Tomáš Galica was also involved in further studies highlighting the specificity and promiscuity of cyanobacterial FAALs where he contributed to the bioinformatic dissection of the domains and a biosynthetic study of the lipopeptide muscotoxin where he participated in isotopic labeling, feedings experiments and interpretation of data. Overall, he presents a methodologically very versatile dissertation that is very well focused on the topic of lipopeptides and makes an original contribution to the field.

Tomáš Galica presents an extensive introduction into the field covering the ecology and evolution of cyanobacteria, the diversity of lifestyles, the ecological significance as well as the current knowledge on lipopeptides, their BGCs and physiological roles. This section prepares exceptionally well for the individual studies and gives a good overview of the current state of knowledge on lipopeptides. The chapter is also well illustrated. In the results and discussion section, Tomáš Galica summarizes the most important findings in the individual manuscripts that are included in the dissertation. The final summary and future perspective chapter is relatively short and could have opened a view on a broader context. The work is raising a number of questions. Does the proposed siderophore function of lipopeptides exclude an influence in biofilm formation? How can the work contribute to the development of general concepts for the genomic mining of specialized metabolites in cyanobacteria? How can work described in the thesis add to the exploitation of cyanobacterial lipopeptides?

The thesis clearly merits acceptance as doctoral dissertation without further corrections.



Elke Dittmann-Thünemann