Exploring Brazilian Cyanobacteria for the Identification of New Bioactive Natural Products

Márcio Barczyszyn Weiss[1]*, Jaewon Yoon[1], João P. B. Domingues[1], Samuel C. Amaral[1], Vítor F. Freire[2], Fernanda Rios Jacinavicius[1], Helori Vanni Forastieri[3], Leticia Veras Costa Lotufo[3], Ricardo M. Borges[4], Roberto G. S. Berlinck[2], Camila Manoel Crnkovic[1]

marciobweiss@gmail.com

1-Lab.azul, Departamento de Tecnologia Bioquímico-farmacêutica, FCF, USP, Av. Prof. Lineu Prestes, 580, São Paulo, SP, 05508-000, Brazil. 2- Organic Cchemistry of Biological Systems, IQSC, USP, Av. Trab. São Carlense, 400, São Carlos, SP, 13566-590, Brazil. 3- LAFARMAR, ICB I, USP, Av. Prof. Lineu Prestes, 1524, 05508-000, São Paulo, SP, Brazil. 4- laabioippn, IPPN, UFRJ, Av. Carlos Chagas Filho, 373, 21941-902, Rio de Janeiro, RJ, Brazil.

Cyanobacteria are among the earliest life forms on Earth. These photoautotrophic prokaryotes inhabit diverse ecosystems, including rivers, forests, permafrost, and deserts, employing several strategies that include the production of a wide variety of natural products. Developing efficient strategies to optimize the screening of potentially novel and bioactive compounds is essential for discovering molecules of biotechnological interest. In this study, we present a pipeline to identify promising bioactive features from fractions of freshwater cyanobacterial strains isolated from Brazilian environments (Atlantic Rain Forest, Pantanal, and Cerrado). Samples were evaluated for their bioactivities and were analyzed using high-resolution mass spectrometry. Metabolomics was performed via GNPS molecular networking, while DAFdiscovery was used to highlight features potentially correlated with biological activity. SIRIUS supported annotation and chemical classification of metabolites. Dereplication revealed several potentially novel peptides and polyketides associated with bioactivity against mammalian melanoma (MCF-7) and colorectal cancer (HCT-116) cell lines. This study demonstrates the utility of metabolomics tools for the rapid prioritization of bioactive features, streamlining subsequent isolation and structural elucidation efforts. Our findings highlight the effectiveness of integrating computational tools with bioassays to accelerate the discovery of bioactive natural products.

Keywords: Cyanobacteria, metabolomics, dereplication, molecular networking, mass spectrometry