University of Prince Edward Island

Faculty of Veterinary Medicine
Summary of Dissertation

Submitted in Partial Fulfilment
of the Requirements for the

DEGREE OF DOCTOR OF PHILOSOPHY

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Development of a Surface-Active Chemical Elicitor Method for the Activation and Characterization of New Natural Products in Marine Streptomyces

This thesis presents an integrated approach to marine natural product discovery by combining chemical elicitation with untargeted metabolomics to unlock the biosynthetic potential of marine-derived Streptomyces and curated microbial extract libraries. A key challenge in the field, re-isolation of known compounds and difficulty activating silent biosynthetic gene clusters, is addressed through a high-throughput surfactant screen (Chapter 2), in which nine surfactants were tested across 31 marine Streptomyces strains. Biologically relevant surfactants were shown to modulate developmental pathways, activating silent gene clusters and upregulating cryptic metabolites. A novel dereplication pipeline, incorporating GNPS molecular networking and metadata-informed filtering, was developed to distinguish biosynthetic products from media- or surfactant-derived artifacts.

Chapter 3 details the use of rhamnolipid elicitation in S. albidoflavus RKJM0023, resulting in the discovery of a new family of lipopeptides, albubactins A–H and their acids (A–C). Albubactin A was synthesized to confirm its structure and absolute configuration. Chapter 4 describes the identification of acyl-surugamide A2, a new cyclic peptide bearing a rare N-ε-acetyl-L-lysine residue, discovered via molecular network clustering and genome mining.

Chapter 5 explores the antiviral screening of a marine microbial fraction library against HCoV-229E. Viability and cytotoxicity assays identified active fractions, which were then clustered by metabolomic similarity and annotated, revealing known antiviral scaffolds. Mild antiviral activity was confirmed for several annotated molecules and the isolated chartarutine B.

Together, this work provides a scalable framework for activating silent biosynthetic pathways using surfactant-based chemical elicitation in marine Streptomyces. The integrated analytical pipeline developed here advances natural product discovery by expanding access to cryptic metabolites and highlights the untapped potential of marine microbes for bioactive compound discovery.

Publications

LeClair, M.M., Maw, Z.A., Grunwald, A.L., Kelly, J.R., Haltli, B.A., Kerr, R.G., and Cartmell, C. (2022) Discovery of Levesquamide B through Global Natural Product Social Molecular Networking. Molecules 27: 7794.

Maw, Z.A., Grunwald, A.L., Haltli, B.A., Cartmell, C., and Kerr, R.G. (2024) Discovery of the Lipopeptides Albubactins A–H from Streptomyces albidoflavus RKJM0023 via Chemical Elicitation with Rhamnolipids and Synthesis of Albubactin A. J Nat Prod 87: 1682–1693.

Maw, Z.A., Haltli, B., Guo, J.J., Baldisseri, D.M., Cartmell, C., and Kerr, R.G. (2024) Discovery of Acyl-Surugamide A2 from Marine Streptomyces albidoflavus RKJM-0023—A New Cyclic Nonribosomal Peptide Containing an N-ε-acetyl-L-lysine Residue. Molecules 29: 1482.

Presentations

Annual Meeting of American Society of Pharmagnosy, Poster Presenter: Discovery, Upregulation, and Synthesis of Cryptic Albubactin A-F using Rhamnolipid's as a Chemical Elicitor on Solid Fermentation of Marine Streptomyces albus RKJM-0023, Rockville, MN, US. (July 2023)

Graduate Studies & Research Days, Oral Presentation: Discovery of new natural products from a surfactant chemical elicitor study in marine Streptomyces, Charlottetown, PEI, Canada. (Oct 2022)

Annual Meeting of American Society of Pharmagnosy, Poster Presenter: Molecular network driven discovery of new natural products from complex metabolite mixtures from a surfactant chmeical elicior sudy in marine Streptomyces, Charlston, SC, US. (July 2022)

American Society of Pharmagnosy Younger Member Symposium, Poster Presentation: Using molecular networking to dereplicate complex biotransformation from a surfactant chemical elicitor study with marine Streptomyces, Virtual. (2021)

Gordon Research Conference in Marine Natural Products, Poster Presentation: Surfactants as chemical elicitors for marine Streptomyces and metabolomic strategies to dereplicate biotransformations, Ventura, CA, US. (Feb, 2020)

Maritime Natural Product Conference, Oral Presentation: Molecular networking as a dereplication tool for silent natural product discovery using surface-active chemical elicitors in marine Streptomyces, University of New-Brunswick, Saint-John NB (July 2019)

Graduate Studies & Research Days, Oral Presentation: Chemical elicitation of natural product biosynthesis with surfactant molecules in marine Streptomyces, University of Prince Edward Island PEI, Canada (May 2019)

UPEI Multi-Diciplinary Conference, Oral Presentation: Surface-active molecules as chemical elicitors for activation of silent natural product biosynthesis in marine Streptomyces, University of Prince Edward Island PEI, Canada (Aug 2018)

Maritime Natural Product Conference, Oral Presentation: Stimulation of silent natural product biosynthesis using surface active molecules in marine Streptomyces, University of Prince Edward Island PEI, Canada (Jul 2018)

Graduate Studies & Research Days, Oral Presentation: Stimulation of silent natural product biosynthesis using surface-active molecules in marine Streptomyces, University of Prince Edward Island PEI, Canada (May 2018)

Maritime Natural Product Conference, Poster Presentation: The lipopeptide cystargamide stimulates the production of silent natural products in some Streptomyces species, University of Prince Edward Island PEI, Canada (Aug 2017)

Awards

Lévesque Graduate Fellowship in Nutrisciences and Health (2018)
Bruce James Dewar Memorial Scholarship (2018)

Biographical Data –

Born in Halifax, NS.