IMBA International MARINE BIOTECHNOLOGY Association Established 1989

IMBA symposium

Drugs from the *Sea*

Thursday, March 31 2022

Via Zoom

8:00am-10:00am EST

8:00-8:30am
Drugs from the Sea: Successes and Opportunities, Russell Hill, Ph.D., IMET-UMCES

8:30-9:00am
Marine Natural Products as Antimicrobials, Alan Dobson, Ph.D., UCC

9:00-9:30am
Breakthroughs in Marine Natural Products Chemistry, Liva Rakotondraibe, Ph.D., OSU

9:30-10:00am
Four Flash Talks by Graduate Students & Junior Scientists

Register Here

Submit Abstracts Here

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Agenda

Intro and Main Speakers

8:00-8:25 Russell Hill

8:25-8:30 Q&A

8:30-8:55 Alan Dobson

8:55-9:00 Q&A

9:00-9:25 Liva Rakotondraibe

9:25-9:30 Q&A

Flash Talks by Graduate Students/Junior Scientists

9:30-9:35 Shahad Abbas

9:35-9:40 Dr. Maysoon Nedham Awadh

9:40-9:45 Jabal R. Haedar

9:45-9:50 Masato Kogawa

9:50-9:55 Jéssyca de Freitas Silva

9:55-10:00 Daniela Tizabi

See abstracts below.

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Drugs from the Sea: Successes and Opportunities

Russell T. Hill

Institute of Marine and Environmental Technology, University of Maryland Biotechnology Institute, Baltimore, Maryland, USA

Many promising bioactive compounds have been found in marine invertebrates, including sponges. Sponges and other marine invertebrates generally harbor complex and abundant communities of symbiotic microbes. This raises the question, whenever bioactive compounds are found in the holobiont (the marine invertebrate plus its associated microbial communities), whether the compounds of interest are being produced by the invertebrate or by its associated bacteria. Compounds derived from marine invertebrates that have been developed as pharmaceuticals will be reviewed. Several specific examples will be considered of cases in which the true sources of the bioactive compounds are bacterial symbionts rather than the marine invertebrates, including the recent example in which the kahalalides were found to be produced by a highly-specialized bacterial symbiont that is present in the algal diet of the sacoglossan from which the kahalalides were originally identified. In addition to being implicated in the production of some important compounds first found in marine invertebrates, many interesting and novel bacterial can be isolated from marine invertebrates that can serve as a resource for screening programs.

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Marine Natural Products as Antimicrobials

Alan D.W. Dobson

School of Microbiology and Environmental Research Institute, University College Cork, Cork, Ireland.

The oceans are home to marine microorganisms that produce a broad spectrum of novel secondary metabolites with unique and diverse chemical structures, that are likely to hold the key to the development of novel antimicrobial drugs or drug leads. The unique physiological, biochemical and molecular properties that marine bacteria possess means that they are highly likely to produce different compounds than their terrestrial counterparts.A large number of antibacterial Marine Natural Products and derivatives have to date been isolated from marine microorganisms. In this respect marine *Streptomyces* have in particular emerged as an important resource for bioactive natural products with genome mining based approaches gaining traction in the search for biosynthetic gene clusters (BGC) encoding novel bioactive natural products (NP). A major problem with these NP is that they are typically produced in low yields or are encoded in cryptic or silent BGC. Different strategies that have been employed to overcome these problems include optimization of culture conditions, ribosome engineering, heterologous expression, regulatory network control and combinatorial biosynthesis. Examples of how these approaches have been successfully employed in the context of the discovery of novel secondary metabolites from marine *Streptomyces* will be explored.

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Breakthroughs in Marine Natural Products Chemistry

Liva Rakotondraibe

Dept. Of Medical Chemistry and Pharmacognosy, The Ohio State University, Columbus, Ohio, USA

Natural products have been known to be the sources of many FDA approved drugs. For instance, 38.6% of the small molecules approved for antitumor agent in Western medicine from 1946 to 2019 were either natural products or their synthetic derivatives. Due to costs, re-isolation and the long process, many major pharmaceutical companies have lost interest of exploring drug discovery from natural products. While most plants have been already explored, only countable species of marine organisms and their derived microbes have been investigated although they have been reported to produce knew and bioactive compounds. As part of ongoing natural product projects, Dr. Rakotondraibe's research group is interested in discovering bioactive compounds from marine sources. In this presentation he will discuss his breakthroughs NMR-based dereplication strategy to avoid re-isolation of known bioactive compounds from natural products. In addition, updates on marine bioactive compound isolation and structure elucidation work as well as challenges and opportunities in the exploration of marine organisms and their microbial associates will be also discussed.

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The Identification of sponge-associated bacteria from coast of Kuwait and their potential biotechnological applications

Shahad Abbas and Huda Mahmoud

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Sponges-associated microbes could be a rich source for biomolecules with potential roles in biotechnology. In this study, we combined both 16S rRNA next generation sequencing gene amplicon and cultivation techniques to explore the abundance and diversity of microbiomes associated with several novel sponge species thriving in the Arabian Gulf. Seven sponge samples were collected from two different locations from Kuwait marine environment and the majority of their associated bacteria were affiliated to more than 25 bacterial phyla. In the case of cultivable bacteria, a total of 315 bacterial isolates associated with *Haliclona* sp. sponge were cultivated, identified molecularly and screened for their biotechnological potentials. The cultivated isolates were affiliated to phyla Proteobacteria and Firmicutes and were distributed among 6 bacterial genera. Out of the 315 bacterial isolates, selected strains of *Bacillus*, *Ferrimonas*, *Pseudovibrio*, *Shewanella*, *Spongiobacter*, and *Vibrio* were chosen to determine their antimicrobial activity, protease activity and their biomineralization ability. Tested against Gram-positive, Gram-negative bacteria and yeast, a total of seven *Bacillus* strains exhibited weak to moderate growth inhibition against indicator microorganisms. In addition, a total of 29 strains of *Bacillus* sp., *Ferrimonas* sp., *Shewanella* sp., and *Vibrio* showed different ranges of positive protease activity. Furthermore, the cultivated strains chosen for the biomineralization test proved their ability to produce different shapes of calcium carbonate crystals. Our knowledge of sponge-associated bacteria in the Arabian Gulf is scarce and our observations highlights the importance of studying sponge-associated bacteria living in a stressed environment in order to enhance their isolation and evaluate their potentials in biotechnology.

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An Assessment Of Biosurfactant Production By A Mixed Microbial Culture Enriched From Marine Sediment

Dr. Maysoon Nedham Awadh

Assistant Professor, Environmental Biotechnology, Department of Biology, College of Science, University of Bahrain, Kingdom of Bahrain

Biological surfactants (Biosurfactants) are bioactive secondary and amphiphilic metabolites produced by microorganisms and exhibit several biotechnological and pharmaceutical applications. Most of previous research has focused on the deployment of terrestrial isolated microbes for biosurfactants production. However, marine microorganisms are considered as a promising source for low molecular weight biosurfactants which act as foaming, emulsifying, DNA transferring and antimicrobial agents. Thereof, a mixed microbial culture designated as MTB was enriched from marine sediment in Bahrain and its ability to produce biosurfactants was assessed. The MTB culture was enriched in a biphasic chemically defined medium containing 2% v/v of NaCl and 10% v/v of waste engine oil as a sole source of carbon and sulfur. As compared to the uninoculated controls, the enriched cultures exhibited changes in color and turbidity as well as the texture of oil with time. The oil displacement test and Wilhelmy-plate method were utilized to assess the production of biosurfactants in the cell-free culture supernatants. The average dimeter of the formed clear zone of cultures was measured to be 1.43 cm ± 0.1 and synchronized by surface tension reduction from 73.7 mN/m ± 0.03 to a minimum of 42.2 mN/m ± 0.17 after 7 days of incubation. Surface tension reduction verifies that MTB has used engine oil waste as a carbon and sulfur source for growth and biosurfactants production. The results of this study improve our understanding of surface-active compounds production under high salinity medium (mimicking seawater), which enables the future optimization and development efforts in related fields.

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Characterization of New Members of Theonellapeptolide-type Compounds from Marine Sponge *Theonella swinhoei*

Jabal R. Haedar, Agustinus R. Uria, Subehan, Dya Fita Dibwe, & Toshiyuki Wakimoto

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In the effort to discover novel pharmacologically active secondary metabolites from marine environments, we successfully identified three new (1-3) and three known (4-6) cyclic-tridecapeptides that are belonged to theonellapeptolide-type compounds from marine sponge *Theonella swinhoei*. These compounds were purified through several steps of chromatographic techniques from an ethyl-acetate extract of *T. swinhoei*. Their structures were determined by combinations of 2D NMR and mass spectrometric analyses as well as chemical derivatization with Maryef's reagent. In addition, all the isolated compounds displayed anti-austerity activities, a strategic to eradicate cancer cells that are able to survive under nutrition starvation condition, with the most potent activity was observed from compound 5 with PC50 of 3.5 µM against pancreatic cancer cell line Mia-PACA-2. Study activity relationship suggested the importance of N-methyl b-alanine and N-methyl L-isoleucine at amino acid residue position 4 and 6 to their anti-austerity activity. Finally, this study demonstrated the first peptide compounds that showed anti-austerity activity by preferring to kill pancreatic cancer cell in nutrition starvation condition.

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Detecting uncultivated talented producer with single-cell Raman analysis and genomics

Masato Kogawa, Franziska Hemmerling, Masahiro Ando, Kei Yura, Keigo Ide, Yohei Nishikawa, Masahito Hosokawa, Shigeki Matsunaga, Jörn Piel & Haruko Takeyama

Research Organization for Nano & Life Innovation, Waseda University, Tokyo, Japan ...
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Single cell technology is one of the most powerful tools for analyzing uncultured bacteria. In this presentation, we will introduce the analysis pipeline of uncultured bacteria by combining the technologies of in situ detection of intracellular molecules by Raman mictospectroscopy and single-cell genome analysis. This method enables efficient screening of uncultured producer of bioactive substances. We applied this method to the microbiome associated to *Theonella swinhoei*, the chemically rich sponge containing 'Entotheonella' symbionts producing multiple secondary metabolites. Filamentous bacteria containing aurantoside, the antifungal compound, was screened by Raman microscopy, and singe-cell genome analysis of each bacterial cell was conducted subsequently, and we found 'Candidatus Poriflexus aureus', a new sponge-associated Chloroflexi lineage as the unidentified aurantoside producer. In addition to the aurantoside biosynthetic gene cluster (BGC), numerous BGCs were detected on the exceptionally large 14 Mbp genome of 'P. aureus', suggesting that potential of this sponge holobiont as a chemical resource is higher than the previously assumed. This study identifying the owner of the aurantoside BGC of which the previous metagenomic study could not specify the bacteria highlights the importance of the single cell technologies to comprehensively study microbiomes, and expands the possibility of utilizing unknown useful microorganisms that are overlooked by conventional analysis methods.

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Sponge-associated *Bacillus* as potential reservoirs of novel antimicrobial substances

Jéssyca de Freitas Silva, Bruno Francesco R. de Oliveira & Marinella S. Laport

Institute of Microbiology, Federal University of Rio de Janeiro, Rio de Janeiro, Brazil... click to see more

The discovery of new antimicrobial substances is urgently necessary since the World Health Organization has reported a striking increase in multidrug-resistant bacteria (MDR). Sponge-associated bacteria stand out as versatile sources of biologically-active secondary metabolites. Two strains, previously isolated from marine sponges in our recent report, *Bacillus pumilus* 64-1 and *Bacillus subtilis* 84-5 were noteworthy. Both strains showed antibacterial activity against different bacteria, including MDR. In addition, strain 84-5 showed biosurfactant activity. Therefore, this study aimed to deepen our understanding on both activities of these two strains by an integrated strategy using guided-assays and genome mining. Chemical analysis, thin-layer chromatography and targeted-bioassays were performed for *B. pumilus* 64-1. The methanolic extract of strain 64-1 exhibited bacteriostatic activity on *Staphylococcus aureus* cells at a minimum inhibitory concentration of 29.6 µg/mL. At the genomic level, *B. pumilus* 64-1 (3.6 Mpb), it was identified 12 biosynthetic gene clusters (BGCs), including types I and III polyketide synthases (PKS), non-ribosomal peptide synthases (NRPS), bacteriocins, betalactones, sactipeptides, terpenes, and siderophores. In particular, an NRPS potential product showed 85% similarity with bacilysin, with high homology with the cluster present in other *Bacillus* strains. Eleven BGCs were predicted in the 84-5's genome (4.1 Mbp), including types I and III PKS, bacteriocins, terpenes, thiopeptides, and NRPS. Particularly, one of these BGC sequences showed 82% similarity with a surfactin from *Bacillus velezensis* FZB42. These results are promising for the employment of these sponge-associated *Bacillus* for the development of new treatments against antimicrobial-resistant bacteria and additional biomedical applications.

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Bioprospecting Novel Marine Actinomycetes for Anti-Tuberculosis Drugs

Daniela Tizabi, Liva Rakotondraibe ,Tsvetan Bachvaroff & Russell T. Hill

Institute of Marine and Environmental Technology, University of Maryland Center for Environmental Science, Baltimore, MD, USA... click to see more

Mycobacterium tuberculosis (M.tb), the causative agent of the infectious lung disease tuberculosis (TB) currently infects approximately 1.7 billion people and is responsible for over 1.4 million deaths annually. The rising threat of antibiotic resistance demands novel antibiotics with unique mechanisms of action to eradicate the disease. A novel collection of 101 marine actinomycetes previously isolated from the Caribbean giant barrel sponge *Xestospongia muta* were investigated for their ability to produce compounds that inhibit *M.tb*. Thirteen novel strain belonging to *Micrococcus*, *Micromonospora*, *Brevibacterium* and *Streptomyces* species were observed to consistently produce extracts that inhibit *M.tb* in a dose-dependent manner. Two particular isolates- *Micrococcus* sp. strain R8502A1 and *Micromonospora* sp. strain R45601– displayed greatest potency and were selected for further analysis through a dual genomics and chemistry-enabled approach. The complete genome of *Micrococcus* sp. strain R8502A1 sequenced with PacBio is 2.5 Mb, and lack of putative biosynthetic gene clusters (BGCs) identified through genome mining with antiSMASH suggests production of a novel anti-TB compound through a cryptic pathway. In contrast, the draft genome of *Micromonospora* sp. R45601 sequenced with Illumina MiSeq was 6.7 Mb and contains a putative BGC with 94% identity to the known anti-TB compound diazaquinomycin H/J, suggesting production of a chemical analog. HPLC has further isolated the active component of the *Micrococcus* extract and is currently being investigated with HPLC-MS and NMR. This analysis of novel sponge-associated marine actinomycetes has resulted in at least two potentially novel anti-TB compounds, supporting continued investigation into this group of bacteria for novel therapeutics.