Sea Grant California

Probing the Medical Potential of Microbial Marine Life

// Paul Jensen and Bradley Moore,
Scripps Institution of Oceanography

BACKGROUND

If you compost your kitchen waste, you may know that certain kinds of bacteria are responsible for transforming your discarded peels and rinds into new soil. You may be less aware that, in the process of rotting this organic debris, some bacteria produce chemicals (called secondary metabolites) that kill other bacteria. In other words, they are antibiotics. Indeed, the majority of antibiotics on the market today — streptomycin, actinomycin and erythromycin, to name just a few — were inspired by terrestrial microbes.

Because the sea — particularly the deep sea — is relatively unexplored, there is hope that marine microbes may similarly contribute to drug discovery.

Sea Grant Trainee Kelley Gallagher warms up in a hot tub after collecting sediment samples in the bracing waters off Santa Barbara.
Image: P. Jensen/SIO

"It is so rare for bacteria to make these compounds," says the project's leader Paul Jensen of Scripps Institution of Oceanography, UC San Diego.

PROJECT

The purpose of this project was to explore the biomedical potential of a group of marine bacteria closely related to the medically prolific group of soil bacteria known as actinomycetes.

The first step in this effort was to begin the process of documenting the diversity of these bacteria in existing and new sediment cores collected off California. To do this, bacteria in the cores were cultured and assayed for their antibiotic and anti-inflammatory activity; molecules of interest were then isolated and structurally characterized. The complete genomes of two marine actinomycetes (both with unique genomic structures) were sequenced and compared, speeding the process of mining for new biosynthetic genes and their products.

The work has led to the discovery of a new group of marine actinomycetes, dubbed MAR4, that produce a rare class of secondary metabolites, called hybrid isoprenoids, with strong antibiotic and other biomedically relevant properties.

Molecular techniques are now being used to identify the genes in the MAR4 bacteria that code for the enzymes responsible for hybrid isoprenoid production. These genes are then cloned, sequenced and experimentally characterized.

"It is so rare for bacteria to make these compounds," says the project's leader Paul Jensen of Scripps Institution of Oceanography, UC San Diego. "Here off California, we've found a whole group of bacteria that make them. We are so enthused and confident of their medical potential that we are investigating the whole class."

OUTCOMES

Significant progress has been made in understanding the evolution of secondary metabolite genes, and the mechanisms by which bacteria adapt to the marine environment. Scientists have also been able to describe the biosynthesis of hybrid isoprenoids (including the promising anti-inflammatory compound cyclomarin) and have characterized the novel biosynthetic enzymes associated with producing them.

Ongoing experiments are shedding light on the molecular basis of this biosynthetic pathway. Such work opens the door to being able to engineer, literally build, new antibiotics or anticancer therapies. Any new medicines or drug leads have the potential to offer societal benefits.

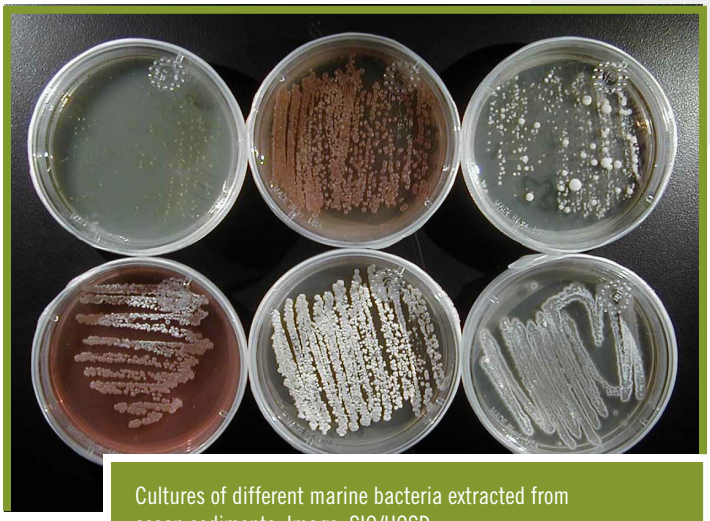
Further work on halogenated meroterpenoids (enzymes that add chlorine to molecules) has led to the discovery of three unique chloroperoxidases, of interest because of their ability to enhance the bioactivity of molecules, meaning they can make drugs more effective. Current efforts are centering on their in vivo and in vitro characterizations, with the goal being to apply novel marine enzymes as biocatalysts.

IMPACTS

This research offers valuable new insights into the diversity of actinomycetes in marine sediments off California and has led to a large collection of strains that will continue to be explored as a source of new medicines. Cataloging these strains provides a tangible framework for assessing biodiversity and its value to marine biotechnology.

It has also highlighted the importance of microbial diversity (in the local marine environment) as a source of novel compounds and novel genes with tremendous medical potential.

All sequence data, including that from the biodiversity and biosynthesis studies, as well as the two genomic sequences, have been deposited in public databases, accessible to the scientific community.



Cultures of different marine bacteria extracted from ocean sediments. Image: SIO/UCSD

Sea Grant researcher Paul Jensen of UCSD's Scripps Institution of Oceanography Image: SIO/UCSD

PUBLICATIONS

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STUDENTS: Kelley Gallagher, Ph.D; Kevin Penn, Ph.D; Taylor Stratton, Ph.D.

CONTACT: Paul Jensen, Scripps Institution of Oceanography, UC San Diego
858-534-7322 | pjensen@ucsd.edu

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