

Within an Antarctic sea squirt, scientists discover a bacterial species with promising anti-melanoma properties

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Synoicum adareanum lives on the Antarctic sea floor and gets its nutrition from microorganisms and organic carbon in the seawater. This type grows in colonies with many individual lobes that are connected at their base. Its microbiome hosts a suite of different microorganisms, including a bacterium in the phylum, *Verrucomicrobium*, that produces a compound with anti-melanoma properties. Credit: Bill J. Baker, University of South Florida

There are few places farther from your medicine cabinet than the tissues of an ascidian, or "sea squirt," on the icy Antarctic sea floor—but this is precisely where scientists are looking to find a new treatment for melanoma, one of the most dangerous types of skin cancer.

In a new paper that was published today in *mSphere*, a research team from DRI, Los Alamos National Laboratory (LANL), and the University of South Florida (USF) made strides toward their goal, successfully tracing a naturally-produced melanoma-fighting compound called "palmerolide A" to its source: A microbe that resides within *Synoicum adareanum*, a species of ascidian common to the waters of Antarctica's Anvers Island archipelago.

"We have long suspected that palmerolide A was produced by one of the many types of bacteria that live within this ascidian host species, *S. adareanum*," explained lead author Alison Murray, Ph.D., research professor of biology at DRI. "Now, we have actually been able to identify the specific microbe that produces this compound, which is a huge step forward toward developing a naturally-derived treatment for [melanoma](#)."



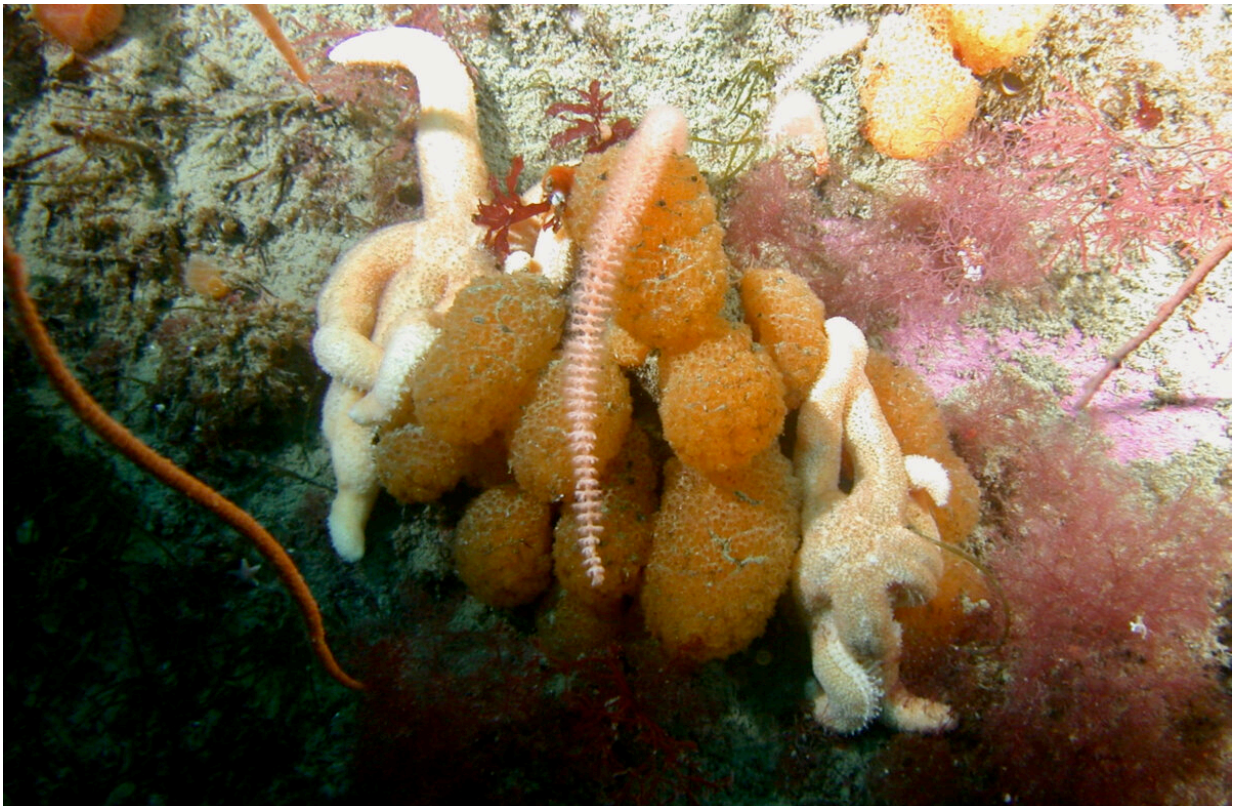
Late spring at Arthur Harbor. The waters surrounding Anvers Island, Antarctica, are home to a species of sea squirt called *Synoicum adareanum*. New research has traced the production of palmerolide A, a key compound with anti-melanoma properties, to a member of this sea squirt's microbiome. Credit: Alison E. Murray, DRI

The bacterium that the team identified is a member of a new and previously unstudied genus, *Candidatus Synoicohabitans palmerolidicus*. This advance in knowledge builds on what Murray and her colleagues have learned across more than a decade of research on palmerolide A and its association with the [microbiome](#) (collective suite of microbes and their genomes) of the host ascidian, *S. adareanum*.

In 2008, Murray worked with Bill Baker, Ph.D., professor of chemistry

at USF and Christian Riesenfeld, Ph.D., postdoctoral researcher at DRI to publish a study on the microbial diversity of a single *S. adareanum* organism. In 2020, the team expanded to include additional researchers from LANL, USF, and the Université de Nantes, and published new work identifying the "core microbiome" of *S. adareanum*—a common suite of 21 bacterial species that were present across 63 different samples of *S. adareanum* collected from around the Anvers Island archipelago.

In the team's latest research, they looked more closely at the core microbiome members identified in their 2020 paper to determine which of the 21 types of bacteria were responsible for the production of palmerolide A. They conducted several rounds of environmental genome sequencing, followed by automated and manual assembly, gene mining, and phylogenomic analyses, which resulted in the identification of the biosynthetic gene cluster and palmerolide A-producing organism.



Sycoicum adareanum in 80 feet of water at Bonaparte Point, Antarctica. New research has traced the production of palmerolide A, a key compound with anti-melanoma properties, to a suite of genes coded in the genome by a member of this sea squirt's microbiome. Credit: Bill J. Baker, University of South Florida

"This is the first time that we've matched an Antarctic natural product to the genetic machinery that is responsible for its biosynthesis," Murray said. "As an anti-cancer therapeutic, we can't just go to Antarctica and harvest these [sea squirts](#) en masse, but now that we understand the underlying genetic machinery, it opens the door for us to find a biotechnological solution to produce this compound."

"Knowing the producer of palmerolide A enables cultivation, which will finally provide sufficient quantity of the compound for needed studies of its pharmacological properties," added Baker.

Many additional questions remain, such as how *S. adareanum* and its palmerolide-producing symbiont are distributed across the landscape in Antarctic Oceans, or what role palmerolide A plays in the ecology of this species of ascidian. Likewise, a detailed investigation into how the genes code for the enzymes that make palmerolide A is the subject of a new report soon to be published.



Andrew Schilling (University of South Florida) dives in 100 feet of water at Cormorant Wall, Antarctica. Samples for microbiome characterization were collected by SCUBA divers working in the chilly subzero seas off Anvers Island, in the Antarctic Peninsula. Credit: Bill J. Baker, University of South Florida

To survive in the harsh and unusual environment of the Antarctic sea floor, ascidians and other invertebrates such as sponges and corals have developed symbiotic relationships with diverse microbes that play a role in the production of features such as photoprotective pigments, bioluminescence, and chemical defense agents. The compounds produced by these microbes may have medicinal and biotechnological applications useful to humans in science, health and industry. Palmerolide A is one of many examples yet to be discovered.

"Throughout the course of disentangling the many genomic fragments of the various species in the microbiome, we discovered that this novel microbe's genome appears to harbor multiple copies of the genes responsible for palmerolide production," said Patrick Chain, Ph.D., senior scientist and Laboratory Fellow with LANL. "However the role of each copy, and regulation, for example, are unknown. This suggests palmerolide is likely quite important to the bacterium or the host, though we have yet to understand it's biological or ecological role within this Antarctic setting."

"This is a beautiful example of how nature is the best chemist out there," Murray added. "The fact that microbes can make these bioactive and sometimes toxic compounds that can help the hosts to facilitate their survival is exemplary of the evolutionary intricacies found between hosts and their microbial partners and the chemical handshakes that are going on under our feet on all corners of the planet."

More information: Alison E. Murray et al, Discovery of an Antarctic Ascidian-Associated Uncultivated Verrucomicrobia with Antimelanoma Palmerolide Biosynthetic Potential, *mSphere* (2021). [DOI: 10.1128/mSphere.00759-21](https://doi.org/10.1128/mSphere.00759-21)

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