

WHITEPAPER

# Cyanobacteria, Cancer, and Renewable Fuel



**LESSONS FROM THE FIELD:  
THE VALUE OF INTERDISCIPLINARY RESEARCH**

Multidisciplinary research means scientists can reach into one field, pull a technology or concept, and apply it in a new and unique way in another area of science.

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GERWICK LABORATORY

William H. Gerwick, Ph.D. heads the Gerwick Laboratory ([www.gerwick.org](http://www.gerwick.org)), a multidisciplinary marine biomedical research facility that is part of the Center for Marine Biotechnology and Biomedicine at the University of California at San Diego’s Scripps Institution of Oceanography. At the Gerwick Lab, researchers in the pharmaceutical sciences, chemistry, biochemistry, molecular biology, microbiology and other fields collaborate in discovering useful compounds produced by marine algae, especially blue-green algae (cyanobacteria). The lab sends diving teams around the world to gather algae samples and bring them to the lab for analysis.

One of the most promising compounds is curacin A, which was discovered in cyanobacteria found by divers off the coast of the Caribbean island of Curacao. To date, more than 200 papers have been written on curacin A’s properties, uses and potential methods of synthesis in journals covering chemistry, biology, pharmacology and medicine.

“Curacin A has, on the one hand, a deceptively simple looking structure,” explains Gerwick, “but it has many, many things to teach us about how molecules are put together by nature.”

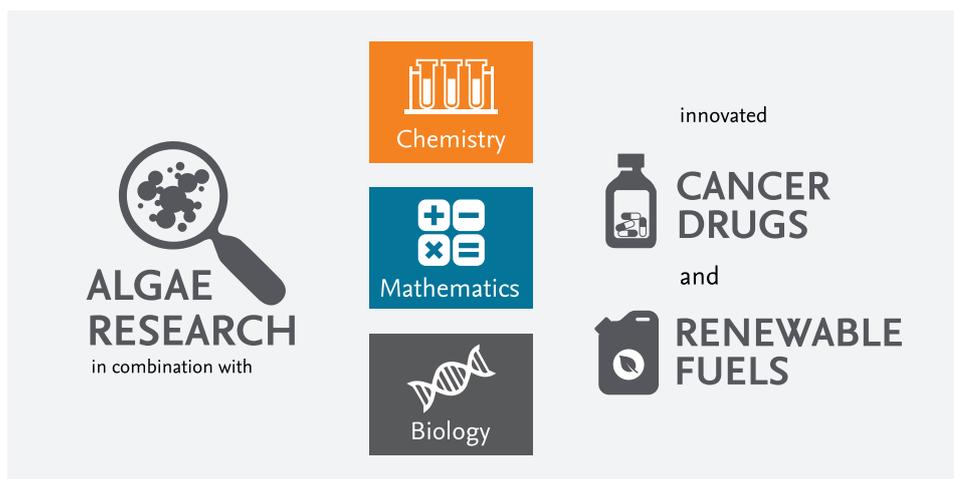
For example, they have learned that, although the curacin A molecule has no chlorine or halogen atom in it, during its biosynthesis it gets chlorinated and that the chlorine activates a particular carbon atom so that a very unique cyclopropyl, or three-membered ring, forms. “That was a tremendous surprise,” he says.

Then, at the terminus of the curacin A molecule opposite the cyclopropyl is a carbon-carbon double bond, something which is unusual in a molecule that is put

together from acetate units. As a result of several studies they came to realize that this molecule was undergoing a terminal decarboxylation to introduce a double bond. So he worked with his colleague David Sherman from the University of Michigan Medical School Department of Microbiology and Immunology and some x-ray crystallographers at the University of Michigan to figure out the details of that mechanism. While the mechanism was interesting in its own right, it also led to advances in the biofuels arena, where they learned a way to make hydrocarbons from cyanobacteria that more closely resemble petroleum-based diesel fuel.

“People in the field of biofuels looked at this and said, ‘Ah, that’s how it is done,’” says Gerwick.

As Gerwick explains, it had long been recognized that cyanobacteria produces long-chain hydrocarbons that are very similar to diesel. One type of biodiesel comes from breaking apart the ester bond in vegetable oils and then methylating it to produce fatty acid methyl ester (FAME). The other type of biodiesel is one where



that carboxyl group is completely missing, so there is no oxygen in the molecule to begin with, the organism decarboxylated it. This type of biodiesel more closely mimics the fuels we actually use in combustion engines. The discoveries from curacin A led to identifying the gene cluster that results in such terminal decarboxylation. Identifying this led to a new way to make hydrocarbons with a terminal double bond.

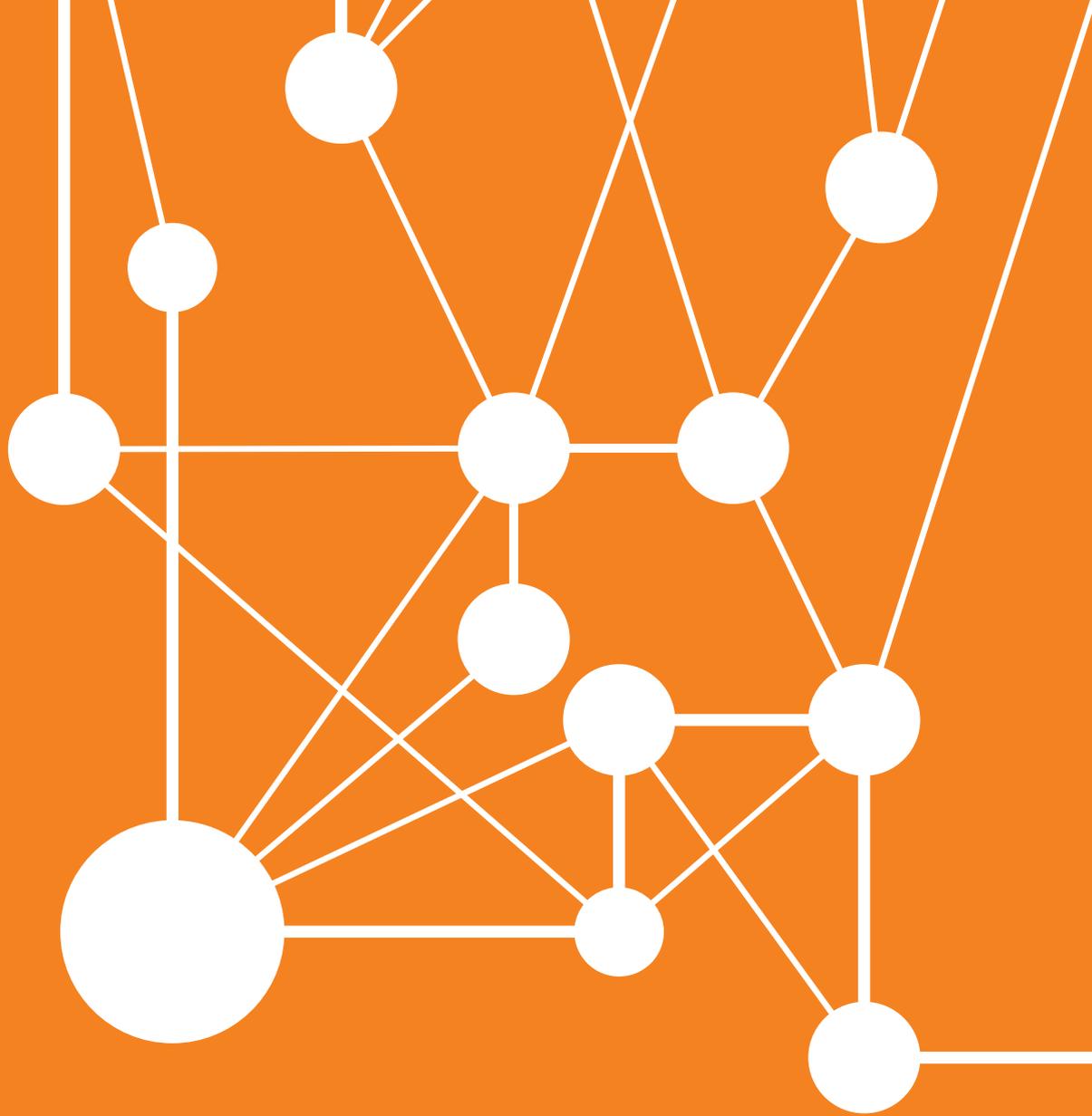
“There are quite a few patents on it, and companies have sprouted up around the whole notion of using this type of technology,” reports Gerwick. One of the more prominent is LS9, Inc., which was acquired by Renewable Energy Group, Inc. in January of 2014.

Among the most promising applications for curacin A is in the area of cancer treatment. The substance extracted directly from the cyanobacteria isn’t stable enough for treatment, but Peter Wipf, a medicinal chemist at the University of Pittsburgh, has synthesized curacin A analogues that were easier to synthesize and had improved properties.

“We look to nature for these inspirational substances that might be used to treat cancer or inflammation or other diseases, but usually there is no reason a compound from nature should be a good drug,” Gerwick points out. “A medicinal chemist will look at molecules like curacin A and get inspired to make molecules that are better behaved in the human body, such as being easily absorbed through the stomach and traveling to the right site in the body.”

Gerwick says that while there is a need for scientists who delve deeply into a single field, it is also important to be able to interact with scientists in other fields. In the case of curacin A, the Gerwick Laboratory brings together researchers from a variety of disciplines. David Sherman is a biochemist and Peter Wipf a medicinal chemist. Frank Kozusko, an Associate Professor in Hampton University’s Department of Mathematics, helped produce a mathematical model of in vitro cancer cell growth and treatment with the antimitotic agent curacin A. Gerwick advises proactively searching out and reading papers in adjacent fields as well as attending scientific conferences.

“I am a big proponent of multidisciplinary research,” he asserts. “By working at this juxtaposition of several fields, we can reach into one field, pull a technology or concept, and apply it in a new and unique way in another area of science. It is an opportunity for doing innovative, creative kinds of things that can really be game changing.”



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