

Compound discovered in Florida Keys shows early promise as colon cancer treatment

September 29 2010

A chemical compound made from a type of bacteria discovered in the Florida Keys by a University of Florida pharmacy researcher has shown effectiveness in fighting colon cancer in preclinical experiments.

Writing online in the Journal of Pharmacology and Experimental Therapeutics, scientists say the compound — known as largazole because it was first found near Key Largo — inhibits human [cancer](#) cell growth in cultures and rodent models by attacking a class of enzymes involved in the packaging and structure of DNA.

More study is needed, but scientists hope that the discovery will lead to new treatments for the roughly 50,000 people struck with colorectal cancer each year in the United States. Researchers are enthusiastic because in addition to having the marine [bacteria](#) as a natural source of the chemical, they have been able to synthetically produce the active chemical compound extracted from the bacteria.

“It is challenging to develop natural marine products into [drug therapies](#) due to what is termed the ‘the supply problem,’” said Hendrik Luesch, an associate professor of [medicinal chemistry](#) in the UF College of Pharmacy. “We have solved the supply problem for largazole because it has a relatively simple structure, which has made it easy to reproduce in the lab.”

The Luesch lab discovered largazole while investigating samples of bacteria from the Florida Keys, publishing the finding in 2008.

Known as cyanobacteria, the microbes have evolved to fend off predators or cope with harsh conditions in a marine environment, employing toxins to aid their own survival. The toxins are the compounds chemists such as Luesch wish to isolate and understand in a quest to create drugs that similarly fend off invading cancers in the body.

Since the discovery, Luesch's lab determined the compound inhibits enzymes known as histone deacetylases, or HDACs, which are linked to many diseases and are increasingly viewed as promising for [cancer therapy](#).

Jiyong Hong, an assistant professor of chemistry at Duke University, teamed with the UF researchers to chemically reproduce the compound for further preclinical testing, which indicates it is a potent inhibitor of cancer cells that has the right properties to reach its intended target without the toxic side effects of many cancer drugs.

“Knowing HDAC is the target that makes largazole effective means we can predict good drug properties because there are already two anticancer products on the market that work this way,” said Luesch, who is a member of the UF Shands Cancer Center.

Three important aspects make this marine compound more promising than other natural products as an effective cancer-fighting drug, Luesch said — availability of supply, knowing its mode of action and the fact that its cellular target is already a proven anticancer target known to result in the necessary selectivity for cancer cells over normal cells.

Luesch presented the findings Sept. 9 at the Marine Drug Discovery Symposium in Pohang, South Korea, and is scheduled in mid-October to present data at the Marine Natural Products Symposium in Phuket, Thailand. The research will be featured on the cover of November's Journal of Pharmacology and Experimental Therapeutics.

He completed his initial preclinical studies that demonstrated largazole's effectiveness in inhibiting the growth of more than one type of [colon cancer](#) cell through the 2009 American Recovery and Reinvestment Act stimulus funding from the National Cancer Institute.

Provided by University of Florida

Citation: Compound discovered in Florida Keys shows early promise as colon cancer treatment (2010, September 29) retrieved 9 April 2024 from <https://phys.org/news/2010-09-compound-florida-keys-early-colon.html>

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