

Bacteria in small sea life yield new way to make potential cancer drugs

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Researchers led by a University of Utah medicinal chemist have developed a novel method to make drugs for cancer and other diseases from bacteria found in sponges and other small ocean creatures.

In a study published Sunday, Nov. 5, in *Nature Chemical Biology* online, researchers examined symbiotic bacteria that live only in sea squirts and other marine life. These bacteria are responsible for making a wealth of chemicals, which accumulate in the tissues of sea squirts and may help to defend them against predators. Many of these chemicals have anticancer properties, but harvesting them in quantities for large-scale testing and production has been impractical.

The new method uses genetic pathways in the bacteria to produce the small chemicals and to manipulate them to invent new potential drugs. The ability to make these chemicals in the laboratory opens myriad possibilities for developing drugs to fight cancer, HIV, and other diseases, according to Eric W. Schmidt, Ph.D., assistant professor of medicinal chemistry at the University of Utah College of Pharmacy and senior author on the study.

"This represents a new way of attacking the problem," Schmidt said. "We're hoping we can use this to find a way to make natural molecules of compounds through single mutations in DNA."

To synthesize natural compounds, researchers have traditionally made them in the lab using labor-intensive routes. More recently, researchers

have begun to use genes to make small molecules within laboratory strains of bacteria. This genetic synthesis method is complicated because it's still difficult to understand how changing genes can lead to changes in small drug molecules.

"The promise of genes is that you can access the tremendous natural diversity of the world's organisms to find new natural compounds for human health," Schmidt said. "You can also use genetic engineering to modify these compounds and invent new drugs to target human diseases."

Sea squirts live with diverse bacteria that synthesize many small molecules. By examining the natural chemical and genetic diversity found in sea squirts and their symbionts, Schmidt and his colleagues from around the country identified individual mutations responsible for changing from one compound to another. By mimicking this natural process, the researchers synthesized a completely new compound. This paves the way to the genetic creation of large chemical libraries for testing against human diseases.

"This proves the concept works," Schmidt said. "We can extract bacteria from animals, take DNA from the bacteria, and produce compounds."

Now that they've shown compounds can be synthesized from DNA, the researchers want to figure out how to produce greater quantities of compounds for testing and drug development. *E. coli* is a good producer of compounds, but yields are not yet practical.

Source: University of Utah Health Sciences Center

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