Researchers Find Promising Cancer-Fighting Power of Synthetic Cell-Signalling Molecule

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Novel anti-cancer compounds called Enigmols suppress the growth of human cell lines representing cancers of the prostate, breast, colon, ovary, pancreas, brain and blood, and reduce tumors in three animal studies, new research shows.

In addition, Enigmols did not show side effects at effective doses, according to the research conducted at the Georgia Institute of Technology, Emory University and Wayne State University. The studies were funded by the National Cancer Institute.

"Many agents suppress cancer cells in a Petri dish and then not in the whole animal, or have unacceptably high toxicity for normal tissues," said Georgia Tech Professor of Biology Al Merrill. "Finding that Enigmols are effective in three animal models leads us to hope these may be a new approach to treat cancer." However, human trials must still be done to determine safety and efficacy in people, the researchers cautioned.

The findings were presented by Georgia Tech postdoctoral researcher Qiong Peng on April 19 in a "late-breaking" poster at the American Association for Cancer Research 96th Annual Meeting in Anaheim, Calif. After considering comments from other scientists at the meeting, the researchers plan to submit the results to a scientific journal in coming weeks.

Enigmols are synthetic analogs of sphingolipids, a group of cell-signaling

molecules that help cells decide whether to grow or die via a controlled process called apoptosis. Cancer cells are usually defective in these regulatory pathways, so researchers hypothesized that structurally modified sphingolipid analogs might be even better at making cancer cells behave more normally.

Merrill and his collaborators have been studying sphingolipids for more than a decade, having first shown that sphingolipids in food, such as low-fat dairy products and soybeans, suppress tumors in mouse models for colon cancer.

Encouraged by these findings, Emory University Professor of Chemistry Dennis Liotta and his colleagues at Emory prepared almost 100 sphingolipid-based analogs that led to the discovery that the Enigmols were the most potent. The lead compounds were named "Enigmols" because sphingolipids were named after the sphinx for their enigmatic properties. Emory University holds the patent on compounds of this type.

In addition to being more potent than naturally occurring sphingolipids, the researchers have also found that Enigmols can be administered orally and appear in often-difficult-to reach organs such as the prostate. "This is what suggested to us that Enigmols should be tested against other cancer types," Merrill explained.

Subsequently, the researchers found that Enigmols suppress the growth of human prostate tumors implanted in mice, which is a commonly used model to test new anti-cancer drugs. They were also effective in two other mouse models for colon cancer.

"We do not know why Enigmols affect such a wide range of tumor cell types," Merrill said. "But it may be due to the involvement of sphingolipids in multiple cell-signaling pathways. This means a

compound may affect several different targets, rather than just one."

In essence, Enigmols may act like a multi-drug combination therapy, the investigators speculate.

Enigmols are also being tested in combination with other cancer chemotherapeutic drugs using funds from EmTech Bio -- a life sciences technology business incubator operated by Georgia Tech and Emory. This research is coordinated with Slainte Bioceuticals, a start-up biotechnology company in metro Atlanta that is helping to bring this potential drug to market.

"Even if Enigmols are effective in humans, the greatest success is likely to come from the right combination of drugs that interact in a synergistic way," Merrill noted. So information from the EmTech Bio study may be particularly useful if Enigmols enter human clinical trials because the patients will have undergone, and will probably be undergoing, other treatments anyway, he added.

In addition to Merrill, Peng and Liotta, the research team is also comprised of: researcher Cameron Sullards of Georgia Tech and Emory researchers Dirck Dillehay, David Pallas, Selwyn Hurwitz and Anatoliy Bushnev; graduate students Holly Symolon and Sarah Pruett of Emory and Jeremy Allegood of Georgia Tech; post-doctoral fellow Steve Moody; and Georgia Tech research technicians Carrie Pack, Samuel Kelly and Elaine Wang. Additional collaborators at Wayne State University are Professors Eva Schmelz and Paul Roberts.

Source: Georgia Institute of Technology