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MIT researchers see alternative to common colorectal cancer drug

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A compound that accumulates in cells more readily than a commonly used colorectal cancer drug may be just as useful in treating colorectal tumors, but with fewer side effects, MIT researchers have found.

Both compounds are analogues of cisplatin, a potent anticancer agent, but the newly investigated compound, known as cDPCP, may better target colorectal cells, potentially sparing other body tissues from damage.

"This compound, the antitumor properties of which were established in mice over 20 years ago, emerged in our search for platinum anticancer drug candidates with cellular uptake properties analogous or superior to those of oxaliplatin," said Stephen Lippard, the Arthur Amos Noyes Professor of Chemistry at MIT and senior author of a paper on the work appearing in the June 16 online edition of the *Proceedings of the National Academy of Sciences.*

cDPCP could become an alternative to oxaliplatin, which was approved by the FDA in 2004 and is usually the first therapeutic line of defense against colorectal cancer. More than 100,000 Americans are diagnosed with colorectal cancer every year, making it the fifth most common cancer in the United States, according to the National Cancer Institute.

Oxaliplatin and cisplatin fight tumors by entering the cell nucleus and binding to DNA, damaging it and inducing cell death, said Ryan Todd, a graduate student in chemistry and co-lead author of the paper.

cDPCP kills cells in a similar way. However, the key difference is that while oxaliplatin and cisplatin can enter almost any cell, causing harmful side effects, cDPCP requires the assistance of organic cation transporters (OCTs) embedded in the cell membrane.

That help is required because cDPCP is a positively charged molecule. Working with cultured human cells, the researchers found that cDPCP engages the assistance of OCT1 and OCT2, which are present in the colon. Thus, cDPCP could be specifically targeted to colorectal tumors.

"cDPCP may affect other cells in the body, but there could be greater targeting of colorectal cancer cells because of uptake by the transporters," said graduate student Katherine Lovejoy, co-lead author of the paper.

cDPCP's anticancer activity was first observed in mice 20 years ago, but it was never tested in humans, in part because it was not expected to readily cross cell membranes.

Researchers in Lippard's lab, working with other cancer researchers at MIT, have started studying the effectiveness of cDPCP in mice expressing human colorectal tumors, and they also hope to launch clinical trials in humans.

Source: Massachusetts Institute of Technology

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