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Synthetic molecule causes cancer cells to self-destruct

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Scientists have found a way to trick cancer cells into committing suicide. The novel technique potentially offers an effective method of providing personalized anti-cancer therapy. Most living cells contain a protein called procaspase-3, which, when activated, changes into the executioner enzyme caspase-3 and initiates programmed cell death, called apoptosis. In cancer cells, however, the signaling pathway to procaspase-3 is broken. As a result, cancer cells escape destruction and grow into tumors.

"We have identified a small, synthetic compound that directly activates procaspase-3 and induces apoptosis," said Paul J. Hergenrother, a professor of chemistry at the University of Illinois at Urbana-Champaign and corresponding author of a paper to be posted online this week ahead of regular publication by the journal Nature Chemical Biology. "By bypassing the broken pathway, we can use the cells' own machinery to destroy themselves."

To find the compound, called procaspase activating compound one (PAC-1), Hergenrother, with colleagues at the U. of I., Seoul National University, and the National Center for Toxicological Research, screened more than 20,000 structurally diverse compounds for the ability to change procaspase-3 into caspase-3.

The researchers tested the compound's efficacy in cell cultures and in three mouse models of cancer. The testing was performed in collaboration with William Helferich, a professor of food science and

human nutrition at the U. of I., and Myung-Haing Cho at Seoul National University. The researchers also showed that PAC-1 killed cancer cells in 23 tumors obtained from a local hospital.

Cell death was correlated with the level of procaspase-3 present in the cells, with more procaspase-3 resulting in cell death at lower concentrations of PAC-1.

"This is the first in what could be a host of organic compounds with the ability to directly activate executioner enzymes," said Hergenrother, who is also an affiliate of the Institute for Genomic Biology at the U. of I. "The potential effectiveness of compounds such as PAC-1 could be predicted in advance, and patients could be selected for treatment based on the amount of procaspase-3 found in their tumor cells."

Such personalized medicine strategies are preferential to therapies that rely on general cytotoxins, the researchers say, and could be the future of anti-cancer therapy.

Source: University of Illinois at Urbana-Champaign

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