CANCER CELLS SELF-DESTRUCT
WHEN "SWEET TOOTH" IS THWARTED

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Johns Hopkins researchers have found evidence that some cancer cells are such incredible sugar junkies that they'll self-destruct when deprived of glucose, their biological sweet of choice.

"The change when we took away glucose was dramatic," says Chi Van Dang, M.D., Ph.D., director of hematology. "By the next day, we knew very quickly that the cells we had altered to resemble cancers were dying off in large numbers."

Scientists have long suspected that the cancer cell's heavy reliance on glucose, its main source of strength and vitality, also could be one of its great weaknesses, and Dang's new results are among the most direct proofs yet of the idea.

Results of the study, published in the February 17 issue of the Proceedings of the National Academy of Sciences, suggest that drugs which cut off the glucose supply may be a potent way of fighting cancer with few ill effects on healthy tissues.

With funding from the National Institutes of Health, Hyunsuk Shim, Ph.D., a postdoctoral fellow, Dang and others gave embryonic mouse cells an unusually active form of a gene known as c-Myc. Many cancer cells overuse this gene, mass-producing its protein to start chain reactions that help them switch from using oxygen for energy production to using glucose.

"When we bathed cells with high c-Myc levels in a cell medium with no glucose, they destroyed themselves by triggering a cell suicide process called apoptosis," says Dang. "Cells we hadn't altered stopped moving through the cellular life cycle, staying in the first two stages of cell development, and appeared fine in all other regards."

Dang produced similar results by exposing both types of cells to 2-deoxyglucose, a compound that resembles sugar but disrupts glycolysis, the process that produces energy from sugar, when cells absorb it.

When used with human tumor samples, 2-deoxyglucose killed some cell lines but spared others.

"The key factor appears to be a suicide-stopping gene, Bcl2, that prevents cells from entering apoptosis too easily," Dang says. "If this gene is active in the cancer cell, the cell is less sensitive to glucose deprivation."

One of the biggest obstacles to using a sugar-starvation treatment in cancer patients, according to Dang, is that central nervous system cells can't function properly without glucose.

"The brain is the only important organ that depends on glucose, so we need a drug that cuts off tumor cells' ability to get glucose but does not cross over into the brain," says Dang. "It might even be possible to alter 2-deoxyglucose so it behaves in this manner."

Dang and colleagues plan to begin testing 2-deoxyglucose and other sugar-stopping compounds in animal models of tumors soon.

Other authors on the paper were Yoon Chun and Brian Lewis.