

Research aims to starve breast cancer cells

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The most common breast cancer uses the most efficient, powerful food delivery system known in human cells and blocking that system kills it, researchers report.

This method of starving <u>cancer cells</u> could provide new options for patients, particularly those resistant to standard therapies such as tamoxifen, Georgia Health Sciences University researchers said.

Human estrogen receptor-positive <u>breast cancer cells</u> thriving in a <u>Petri dish</u> or transplanted onto mice die when exposed to a drug that blocks the transporter, called SLC6A14, said Dr. Vadivel Ganapathy, Chairman of GHSU's Department of Biochemistry and Molecular Biology.

"It basically starves the cancer cell," said Ganapathy, corresponding author of the study published in the <u>Journal of Biological Chemistry</u>. The transporter can carry 18 of the known 20 amino acids, fuel all cells need in some combination. Amino acids enable cells to make proteins, which they need to function and survive. The cell type determines its amino acid needs and delivery system. Rapidly growing, dividing estrogen receptor-positive breast cancer needs nearly every amino acid so it makes the smart choice of utilizing the transporter that can deliver the biggest load, Ganapathy said.

SLC6A14 is the only transporter known to carry all 10 <u>essential amino</u> <u>acids</u>, essential because the body can't make them so they have to be delivered via the bloodstream from food. The transporter also takes eight of the nonessential amino acids along for the ride, Ganapathy said.



And it is a fast ride. The transporter has three energy sources instead of the usual one or two, he said.

Interestingly, SLC6A14 is expressed at low levels in most of the body. "There are specialized features of this transport system which could be used by every cell to its advantage but they do not seem to do that. It's expressed only at low levels in normal tissues," Ganapathy noted. While that may seem like a loss for healthy cells, it bolsters the cancer-fighting potential for drugs that block SLC6A14 by making it a more specific cancer target. "Since the normal cells do not depend on this transporter, you can use a drug that selectively blocks it to target cancer cells" Ganapathy said.

The compound they used is alpha-methyl-DL-tryptophan, already used in humans for short periods when they are getting a PET scan in certain areas of the brain. When the researchers treated estrogen receptor-positive breast cancer cells with it or put it in the drinking water of the mice with the cells, rapid growth stopped and the cancer cells died. Further studies showed alpha-methyl-DL-tryptophan seemed to impact only cells expressing the SLC6A14 transport system. Even another type of breast cancer, estrogen receptor-negative, wasn't impacted.

Provided by Georgia Health Sciences University

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