New study says molecule can starve cancer cells

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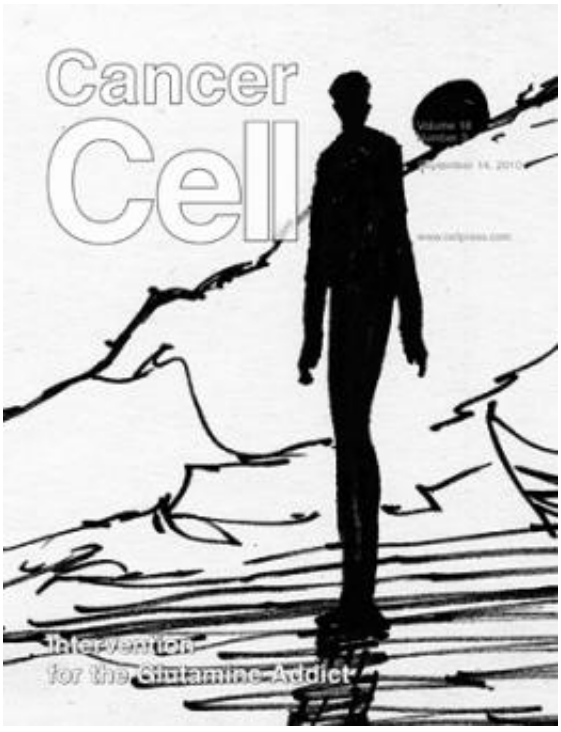

This sketch (by Efraim Racker, the late Albert Einstein Professor of Biochemistry at Cornell) depicts a glutamine addict (symbolizing a cancer cell). Cornell researchers report on a molecule that can "block the addiction" and thus intervene against cancer.

While overcoming an addiction is usually the healthy choice, cancer cells' addiction to the amino acid glutamine is key to their vitality and growth. But Cornell researchers have discovered a molecule that can

block cancer cells from using glutamine, thereby inhibiting their growth.

Researchers have long believed that starving cancer cells, little turbo-charged engines capable of metastasizing in even the most difficult of conditions, would break the glutamine addiction and help fight some cancers. But they have struggled for decades with how to accomplish this feat.

Now, they have discovered a molecule that does the job. Dubbed 968 by investigators, the molecule binds to the enzyme glutaminase, which inhibits cancer growth by blocking the cancer cells' utilization of glutamine.

"Cancer cells demand a tremendous amount of energy," said Richard Cerione, the Goldwin Smith Professor of Pharmacology and Chemical Biology in the Colleges of Veterinary Medicine and Arts and Sciences at Cornell and senior author of the research, which is the cover story in the Sept. 14 issue (Vol. 18:3) of *Cancer Cell*. "One of the key enzymes that fuels the process is glutaminase, whose activation in cancer cells can be blocked by the small molecule 968."

The finding could lead to a new class of drugs, capable of halting cancer progression without harming normal cell growth, he said.

"This is the rebirth of a century-old empirical observation -- that cancer cells have altered metabolisms -- and further development of the discovery in the 1970s and '80s that growth factor receptors and other signaling proteins are also altered in cancer cells," said Cerione. "This new information now offers exciting possibilities for designing strategies to stop tumor growth, to effectively reverse cellular transformation."

After discovering that 968 inhibited glutaminase and effectively shrunk tumor cells in mice, Cerione and his research team tested the molecule

to understand its effects on non-cancerous cells. Because the energy needs of normal cells are different than those of cancer cells, normal cellular functions are much less reliant on elevated glutamine metabolism, which means that 968 only impacts cancerous cells, Cerione said.

"We have effectively stopped the growth of breast cancer cells in the lab without affecting normal mammary cells," said Cerione, who is now investigating the impact of 968 on other forms of cancer, including prostate, ovarian and pancreatic cell lines. "We've validated our target. The next step will be to commercialize a small class of molecules capable of stopping cancer cell growth in humans."

Cerione and colleagues are currently working with the KensaGroup, of Ithaca, N.Y., to do just that, although he is quick to add that his work is not done. He will continue to explore the effects of 968 and glutaminase on cancer cells to obtain detailed information on how cancer cells re-program their metabolism to sustain their malignant characteristics.

"Our research has highlighted a previously unrecognized connection between the cell's metabolic machinery and the signaling pathways and growth factor receptors that regulate cell growth," said Cerione. "However, I believe that it is reasonable to suspect there is a broader role for these connections between metabolism and cell signaling that may well impact other areas in biology and biomedicine."

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