

Fructose Fuels Cancer Growth Indirectly, Lab Study Finds

Diets containing excess fructose—which is found in high-fructose corn syrup and table sugar—can help tumors grow, studies suggest.

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Feeding fructose to lab animals with cancer made their tumors grow faster, a new study has shown. But the tumors didn't directly consume fructose, the researchers found. Instead, the liver converted it into a type of fat that cancer cells gobbled up.

Studies have suggested that diets containing excess fructose—which is found in high-fructose corn syrup and table sugar—can help tumors grow. But how this common dietary sweetener might do so has been a bit of a mystery. The researchers believe their study provides some important answers.

The NIH-funded study, published December 4 in *Nature*, showed that several types of cancer cells lacked the [enzyme](#) needed to use fructose directly. However, liver cells have the necessary enzyme, called KHK, [and used it to convert fructose into fats called lipids](#).

The findings could open up a new avenue for potential cancer treatments, said the study's senior researcher, Gary Patti, Ph.D., of Washington University in St. Louis. A drug that blocks the KHK enzyme slowed fructose-fueled tumor growth in mice, the scientists showed.

According to Kristine Willis, Ph.D., of NCI's [Division of Cancer Biology](#), the study also addresses a topic of great interest to both researchers and the public.

"It's starting to get at a very important question ... [of] how the food we eat may provide [nutrients](#) that contribute to tumor growth and progression," said Dr. Willis, who wasn't involved in the new study.

However, she said, "people should not take this as a reason to attempt to eliminate all fructose from their diets."

"The sugars in whole fruits and vegetables, which include fructose, are metabolized differently by the body than the high-fructose corn syrup in ultra-processed foods," continued Dr. Willis. "Apples are still healthy; junk food still isn't."

Do tumors use fructose?

Look at the back of that box of cookies in your pantry and you're likely to find high-fructose corn syrup listed as an ingredient. The same goes for many sodas, sauces, and cereals. As ultra-processed foods have become more common over the last 50 years, [fructose consumption has risen dramatically](#).

High-fructose corn syrup is made of [glucose](#) and fructose. It's well known that cancer cells consume a lot of glucose to fuel their relentless growth. But less is known about how cancer cells use fructose.

That's in part because, until relatively recently, scientists lacked the tools needed to detect and track all the nutrients used by cells or whole animals, Dr. Willis said.

New advances in the field of [metabolomics](#), Dr. Patti said, allowed them to differentiate fructose from glucose—which has the same chemical formula but a different structure—and track its fate.

Most dietary fructose is broken down in the small intestine, liver, and kidneys, with very little fructose entering the bloodstream, said the study's lead author, Ronald Fowle-Grider, Ph.D., of Washington University in St. Louis. With the new tools in hand, the research team wanted to understand whether and how tumors outside of those organs use fructose.

First, they showed that both fructose and high-fructose corn syrup accelerated the growth of skin, breast, and cervical tumors in mouse and [zebrafish models of human cancers](#).

High-fructose corn syrup has been linked with weight gain and [metabolic syndrome](#). But mice fed a high-fructose diet for several weeks didn't gain any weight, nor did they have changes in their [blood sugar](#) levels.

"I think that is a really key point," Dr. Patti said. "High-fructose corn syrup has been associated with obesity, and [obesity has been associated with certain cancers](#). So, you could connect the dots [between fructose and cancer] that way. But in our studies, that wasn't the case," he explained.

The researchers then tracked how cancer cells in lab dishes used fructose. They were baffled to find that the cells weren't using it at all. It turned out that these cancer cells lacked KHK, the main enzyme needed to break down fructose.

The team suspected that the liver, which has KHK, might be converting fructose into nutrients cancer cells can use, such as glucose or fats.

The liver converts fructose to fat

To test that idea, the scientists mixed human cancer and mouse liver cells in the same lab dish and fed them fructose. The liver cells readily used fructose as energy; and although the cancer

cells didn't, their growth increased dramatically.

The researchers then tracked how liver cells used fructose, finding that it was indeed converted into many kinds of fats, called [lipids](#). The cancer cells, in turn, absorbed one particular group of lipids called LPCs.

Additional experiments revealed that cancer cells used LPCs to build new [membranes](#), which form the outer coating of cells and encase many of their inner structures. All cells need lipids to build new membranes when they grow and divide, Dr. Patti explained. But because cancer cells divide so quickly, they require a lot of these lipids.

The researchers also found that mice had a surge of LPCs in their blood after eating high-fructose corn syrup. When they fed LPCs to mice with skin, breast, or cervical tumors, the tumors took off.

But there is some potential good news. In mice fed high-fructose corn syrup, an [experimental drug](#) that blocks the KHK enzyme substantially slowed tumor growth. The drug, called PF-06835919, has been tested as a treatment for [fatty liver disease](#), a condition that [may be triggered by eating too much high-fructose corn syrup](#).

These findings shed “light on complex metabolic interactions between normal organs and cancer cells,” noted Hyllana Medeiros, Ph.D., and Sophia Lunt, Ph.D., of Michigan State University, in [a commentary on the new study](#).

Similar kinds of sly cooperation between cancer cells and healthy tissues—a phenomenon called “metabolic cross talk”—have been reported before, they added. For instance, a study showed that some pancreatic cancer cells grow by [instructing neighboring cells to provide them with specific nutrients](#).

Does the same cycle happen in humans?

“Obviously this is the beginning of a story, not the end,” said Dr. Willis. Among the many parts of the story left to fill in is whether the same cycle of fructose metabolism occurs in people with cancer.

There are some hints that it might. For instance, a small study found that women eating [diets high in fructose had increased blood levels of LPCs](#), the same lipids that Dr. Patti and his colleagues observed in the blood of mice fed fructose.

But Drs. Medeiros and Lunt noted that some types of cancer can use fructose directly as an energy source. There may even be some tumors that use fructose directly as energy and use fructose-derived LPCs to build new membranes, Dr. Patti pointed out. Those two scenarios aren't mutually exclusive, he said.

He and his colleagues at Washington University's Center for Human Nutrition are in the early

stages of following up on this study, he said, including working to design human studies. Their hope is to test whether PF-06835919 or another KHK inhibitor can slow cancer growth in people, even without changing their diets, he explained.

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