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Scientists exploit cell metabolism to attack cancer

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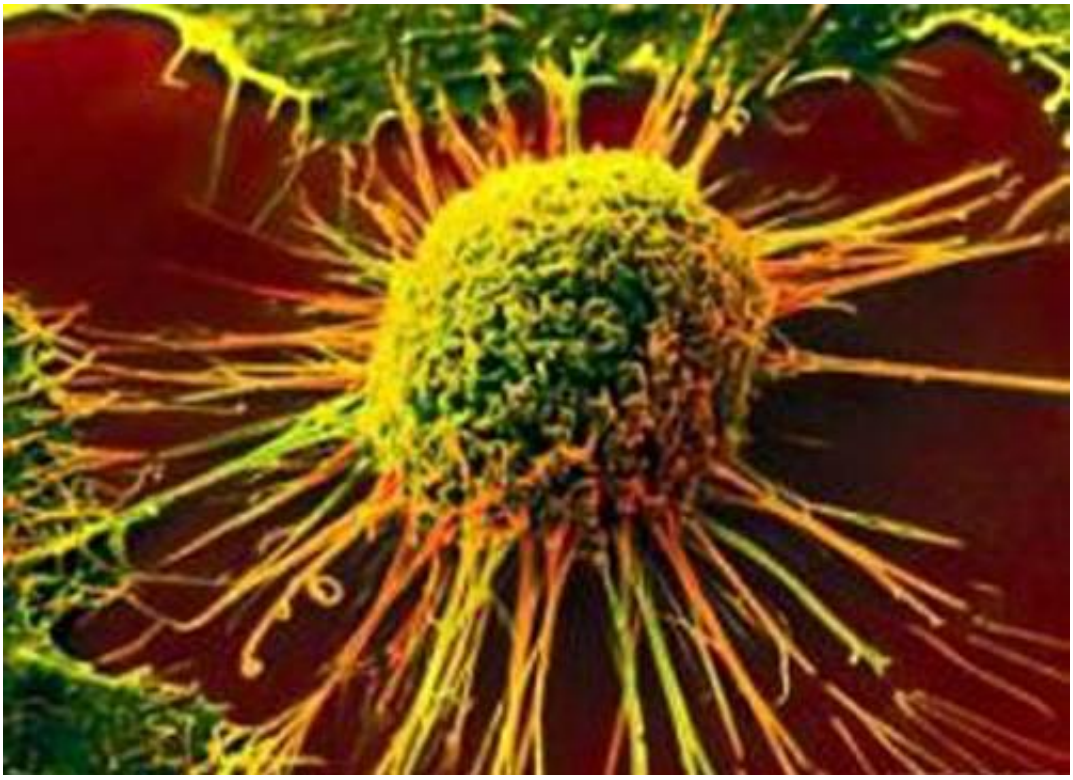

Cancer cells have their own unique way of reproducing, involving a shrewd metabolic reprograming that has been observed in virtually all types of cancer but not in normal cells. Now, University of Rochester Medical Center scientists have pinpointed one key source of the problem, which could lead to new treatment opportunities.

In an article published by *Cell Reports*, the scientific team shows for the first time how cancer-causing mutations control and alter the way cancer cells biosynthesize and replicate.

The discovery is the result of a close collaboration between the laboratories of Joshua Munger, Ph.D., associate professor of Biochemistry and Biophysics, and Hucky Land, Ph.D., the Robert and Dorothy Markin Professor and Chair of Biomedical Genetics and director of research at the URMC's Wilmot Cancer Institute.

"Every tissue or cell type in the body has different metabolic needs but as cells become cancerous their metabolism shifts in ways that are very different from normal cells," Munger said. "Being able to identify those differences is critical for developing treatment targets."

It's been known for decades that cancer cells siphon glucose from the bloodstream at alarming rates. But cancer's sugar addiction is only one part of the story, Land explained.

While sugar is the primary source of energy and fuel for biosynthesis of normal cells, in cancer cells sugar is metabolized differently. Cancer cells switch from burning to fermenting sugar, a process that the Land and Munger labs found is driven by cancer-causing mutations. Furthermore, they discovered that in cancer cells, sugar fermentation facilitates the consumption of glutamine, another nutrient source. Glutamine is abundantly available in the bloodstream, and cancer cells take in large amounts of it to support cell division.

"Our paper demonstrates that cancer cells, but not normal cells, depend on this link between sugar fermentation and glutamine consumption," Land said. "This suggests a novel way that we might be able to intervene with treatment."

Bradley Smith, Ph.D., a scientific staff member in the Land lab, led the laboratory experiments, which were conducted with colon cancer cells. Preclinical data show that by blocking enzymes that are specific to colon cancer cell metabolism, tumor growth is slowed or stopped.

This is a burgeoning area of research. Nationally, scientists have begun designing early-phase clinical trials to test experimental, targeted therapies aimed at the altered metabolism of cancer cells. Wilmot researchers are focusing on novel ways to apply this concept.

"Is it possible to apply this to other cancers? That's our next question," Munger said. "We're testing how this could be broadly applied in the clinic."

Provided by University of Rochester Medical Center