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# Monitoring sugar metabolism in liver may be a key to cancer diagnosis

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Scientists may have discovered a significant new diagnostic marker for liver cancer, according to a paper published in the April 18 online issue of *Nature Cell Biology*.

A study led by The University of Texas MD Anderson Cancer Center found that a gene known as KHK (ketohexokinase or fructokinase) is expressed differently in normal liver tissues versus liver tumors. The findings reveal that liver cancer cells had a much reduced level of fructose metabolism versus healthy cells.

"Normal liver cells catalyze both glucose and fructose for energy, amino acid and lipid production," said Zhimin Lu, M.D., Ph.D., professor of Neuro-Oncology. "However, we found that liver tumors stopped using fructose. Thus, monitoring fructose metabolism could potentially be used for liver cancer diagnosis."

Lu's team discovered that reduced fructose metabolism in liver tumor cells is caused by aberrant alternative splicing of the KHK gene. This resulted in expression of a variety of the gene product called KHK-A, which lost the ability to process fructose.

"KHK-A has two enzymatic activities, sugar kinase and protein kinase," said Lu. "We discovered that KHK-A was not only a sugar kinase but also a protein kinase."

The team showed that KHK-A's protein kinase activity enhanced tumor

cell DNA and RNA synthesis and newly identified KHK-A as essential for liver tumor formation. Kinases are enzymes that allow cells to transfer phosphate, crucial for energy production and protein regulation.

"It is this protein kinase activity that we believe can be targeted to treat the liver tumor," he said. "Our study revealed a pivotal mechanism underlying how liver and liver tumor cells use fructose and highlight the instrumental role of the KHK-A protein in promoting tumor development."

**More information:** A splicing switch from ketohexokinase-C to ketohexokinase-A drives hepatocellular carcinoma formation, DOI: 10.1038/ncb3338

Provided by University of Texas M. D. Anderson Cancer Center