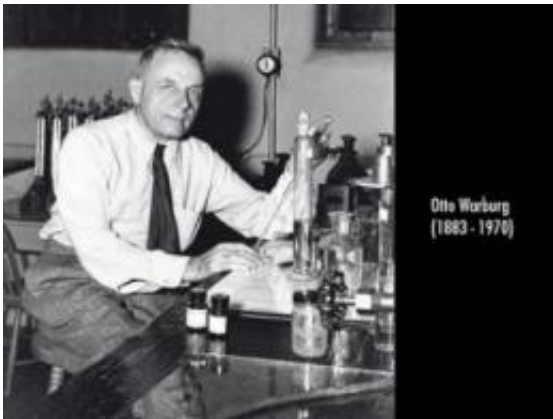


Enzyme that flips switch on cells' sugar cravings could be anti-cancer target

December 22 2011



Cancer cells' metabolic preference is known as the "Warburg effect," after 1931 Nobel Prize winner Otto Warburg. Credit: Wikipedia commons

Cancer cells tend to take up more glucose than healthy cells, and researchers are increasingly interested in exploiting this tendency with drugs that target cancer cells' altered metabolism.

Cancer cells' sugar cravings arise partly because they turn off their mitochondria, power sources that burn glucose efficiently, in favor of a more inefficient mode of using glucose. They benefit because the byproducts can be used as building blocks for fast-growing cells.

Scientists at Winship Cancer Institute of Emory University have shown that many types of [cancer cells](#) flip a switch that diverts glucose away

from mitochondria. Their findings suggest that [tyrosine kinases](#), enzymes that drive the growth of several types of cancer, play a greater role in mitochondria than previously recognized.

The results also highlight the enzyme PDHK (pyruvate dehydrogenase kinase) as an important point of control for cancer [cell metabolism](#).

The results were published online Thursday by the journal *Molecular Cell*.

"We and others have shown that PDHK is upregulated in several types of human cancer, and our findings demonstrate a new way that PDHK activity is enhanced in cancer cells," says Jing Chen, PhD, associate professor of hematology and [medical oncology](#) at Emory University School of Medicine and Winship Cancer Institute. "PDHK is a very attractive target for anticancer therapy because of its role in regulating cancer metabolism."

Chen and Sumin Kang, PhD, assistant professor of hematology and medical oncology at Emory University School of Medicine, are co-corresponding authors. Postdoctoral fellows Taro Hitosugi, Jun Fan and Tae-Wook Chung are co-first authors of the paper. Co-authors at Emory include Georgia Chen, PhD, Sagar Lonial, MD, Haiyan Fu, PhD, and Fadlo Khuri, MD. Collaborators at Yale University, Novartis and Cell Signaling Technology contributed to the paper.

Chen and his colleagues started out studying the tyrosine kinase FGFR1, which is activated in several types of cancer. Tyrosine kinases attach a phosphate to other proteins, making them more or less active. They found that FGFR1 activates the enzyme PDHK, which has a gatekeeper function for mitochondria.

"We used FGFR1 as a platform to look at how metabolic enzymes are

modified by oncogenic tyrosine kinases," Chen says. "We discovered that several oncogenic tyrosine kinases activate PDHK, and we found that many of those tyrosine kinases are found within mitochondria."

This was a surprise because tyrosine kinases are usually thought to drive growth by being active next to the cell membrane, Chen says.

Introducing a form of PDHK that is insensitive to [tyrosine](#) kinases into [human cancer](#) cells forces the cells to grow more slowly and form smaller tumors in mice, they found. This indicates that PDHK could be a target for drugs that specifically target cancer cells' altered metabolism.

The experimental drug dichloroacetate (DCA), which inactivates PDHK, is being used in new clinical trials for cancer. Chen is collaborating with Haian Fu, professor of pharmacology and director of the Emory Chemical Biology Discovery Center, to find other, more potent inhibitors of PDHK.

More information: T. Hitosugi et al. Tyrosine Phosphorylation of Mitochondrial Pyruvate Dehydrogenase Kinase 1 Is Important for Cancer Metabolism. *Mol Cell* (2011). www.cell.com/molecular-cell/

Provided by Emory University

Citation: Enzyme that flips switch on cells' sugar cravings could be anti-cancer target (2011, December 22) retrieved 26 April 2024 from <https://medicalxpress.com/news/2011-12-enzyme-flips-cells-sugar-cravings.html>

<p>This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.</p>
--