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## Targeting metabolism to develop new prostate cancer treatments

**Date:** February 27, 2014

**Source:** University of Houston

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**Summary:** The next generation of prostate cancer therapies is targeted at metabolism. A cascade of biochemical reactions inside the cell is being observed and reviewed by scientists, with a focus on an enzyme considered a master regulator of metabolism. By doing so, scientists hope that new research will unlock more effective and less harmful treatments. With approximately one out of six American men being diagnosed and nearly a quarter of a million new cases expected this year, prostate cancer is the most common malignancy among men in the U.S.

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Daniel Frigo is looking at a cascade of biochemical reactions inside the cell, focusing on an enzyme considered a master regulator of metabolism. Frigo hopes this research will unlock more effective and less harmful prostate cancer treatments.

*Credit: Jessie Villarreal*
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**A** University of Houston (UH) scientist and his team are working to develop the next generation of prostate cancer therapies, which are targeted at metabolism.

With approximately one out of six American men being diagnosed and nearly a quarter of a million new cases expected this year, prostate cancer is the most common malignancy among men in the U.S. Since prostate cancer relies on androgens for growth and survival, androgen ablation therapies are the standard of care for late-stage disease. While patients initially respond favorably to this course of treatment, most experience a relapse within two years, at which time limited treatment options exist. At this stage, known as castration-resistant prostate cancer, androgen-deprivation therapies are no longer effective, but interestingly, androgen receptor signaling is still active and plays a large role in the progression of the cancer. Because of this, both androgen receptors and the processes downstream of the receptor remain viable targets for therapeutic intervention. Unfortunately, it is unclear which specific downstream processes actually drive the disease and, therefore, what should be targeted.

Daniel Frigo, an assistant professor with the UH Center for Nuclear Receptors and Cell Signaling (CNRCS), has set his sights on a particular cascade of biochemical reactions inside the cell. Focusing specifically on an enzyme known as AMPK, which

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is considered a master regulator of metabolism, Frigo and his team have demonstrated that androgens have the capacity to take control of this enzyme's molecular signals.

"The androgen signaling cascade is important for understanding early and late-stage prostate cancer progression," Frigo said. "We found that when androgens activated this signaling pathway, it hijacked normal conditions, allowing the tumor to use diverse nutrients to the detriment of the patient. These results emphasize the potential utility of developing metabolic-targeted therapies directed toward this signaling cascade for the treatment of prostate cancer, and we look forward to exploring this and other metabolic pathways further in order to develop the next generation of cancer therapies."

In their studies, Frigo's team showed that prostate cancer cells respond to androgens not only by increasing the breakdown of sugars, a process known as glycolysis that is commonly seen in many cancers, but also escalating the metabolism of fats. While much of the research on cancer metabolism has historically focused on glycolysis, the researchers say it's now becoming apparent that not all cancers depend solely on sugars.

Their findings further indicate that the metabolic changes brought about by the AMPK enzyme result in distinct growth advantages to prostate cancer cells. They say, however, that our understanding of how androgen receptor signaling impacts cellular metabolism and what role this has in disease progression remains incomplete.

The Frigo lab is one of several within the CNRCS concentrated on the role of nuclear receptors in cancer prevention and treatment, and his team has long studied the androgen receptor, which turns on or off various signaling pathways. Frigo believes these pathways hold the potential for better cancer treatments. Targeting these underexplored metabolic pathways for the development of novel therapeutics, Frigo's ultimate goal is to unlock more effective and less harmful cancer treatment alternatives.

With funding from the Department of Defense, National Institutes of Health, Texas Emerging Technology Fund and Golfers Against Cancer, Frigo's latest research appears in *Nature's Oncogene*. One of the world's leading cancer journals, *Oncogene* covers all aspects of the structure and function of genes that have the potential to cause cancer and are often mutated or expressed at high levels in tumor cells.

#### Story Source:

The above story is based on materials provided by [University of Houston](#). The original article was written by Lisa Merkl. *Note: Materials may be edited for content and length.*

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1. J B Tennakoon, Y Shi, J J Han, E Tsouko, M A White, A R Burns, A Zhang, X Xia, O R Ilkayeva, L Xin, M M Ittmann, F G Rick, A V Schally, D E Frigo. **Androgens regulate prostate cancer cell growth via an AMPK-PGC-1 $\alpha$ -mediated metabolic switch.** *Oncogene*, 2013; DOI: [10.1038/ncr.2013.463](#)

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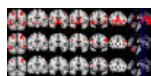


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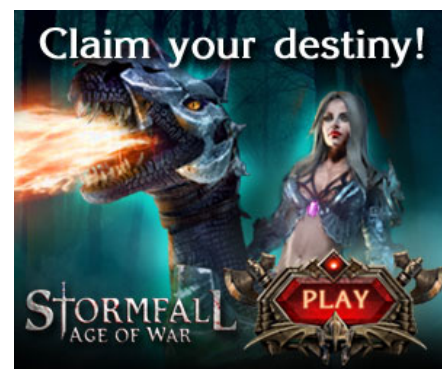
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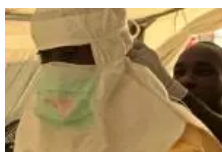
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