Drugs used to treat diabetes could be used to reduce pancreatic and prostate tumor growth

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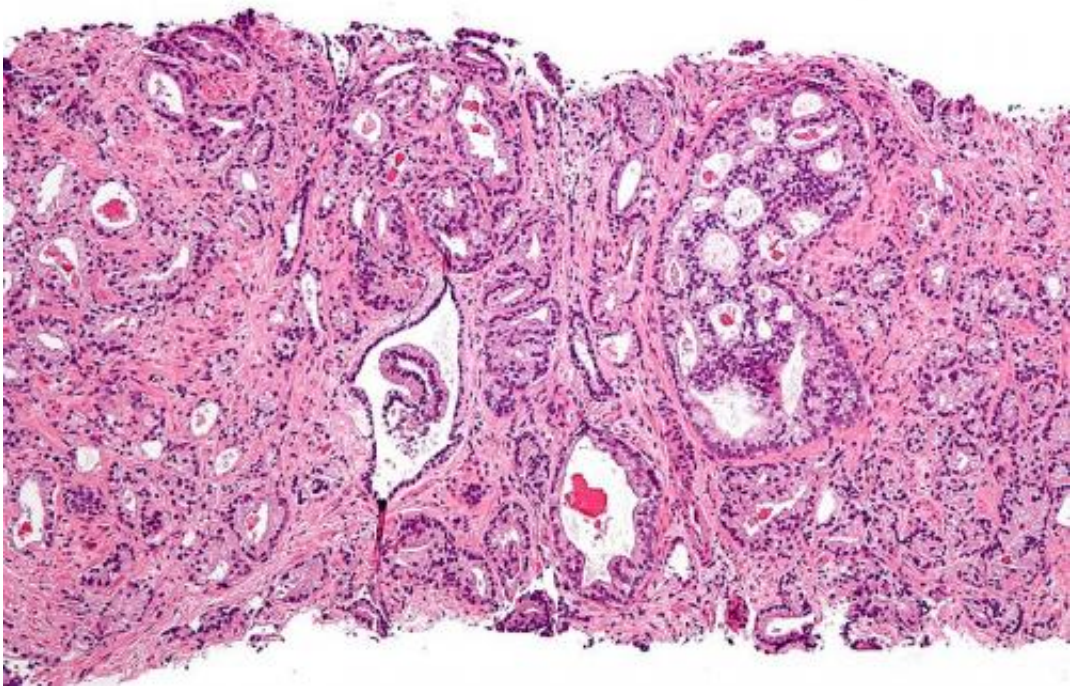

Micrograph showing prostatic acinar adenocarcinoma (the most common form of prostate cancer) Credit: Wikipedia, CC BY-SA 3.0

UCLA scientists have identified a new mechanism that delivers a key substance that fuels the growth of pancreatic and prostate cancer cells, a finding that offers new hope in the fight against two of the deadliest forms of the disease.

Cancer cells require high amounts of the sugar glucose to survive and

grow, and long-standing research has established passive glucose transporters, known as GLUTS, as the primary method the body uses to deliver glucose to tumors.

But the results of a three-year study by UCLA researchers, demonstrated that pancreatic and prostate cancer cells also utilize glucose from sodium-dependent glucose transporters known as SGLTs, specifically SGLT2.

The findings in the study, which was published online today in the journal *PNAS*, provide the first promising evidence that positron emission tomography (PET) imaging techniques and SGLT2 inhibitors could be used to better diagnose and treat pancreatic and prostate cancers , said Ernest Wright, professor of physiology in the David Geffen School of Medicine at UCLA and lead author of the three-year study.

"This is exciting because it provides strong evidence that SGLT2 inhibitors, such as those currently approved by the FDA to treat diabetes, could potentially block glucose uptake and reduce tumor growth and increase survival in pancreatic and prostate cancers," said Wright, who is also a member of the UCLA Jonsson Comprehensive Cancer Center.

Wright, Jorge Barrio, Dr. Claudio Scafoglio and colleagues first mapped the distribution of sodium-dependent glucose transporters in human cancer tumors, then measured glucose uptake in fresh tumors using a glucose analog specifically transported by SGLTs. They observed that SGLT2 was present in pancreatic and prostate andenocarcinomas and that it assisted in delivering the glucose that is vital to cancer growth and survival, Wright said.

The team then measured sodium-dependent glucose transporter activity in a mouse cancer model using a radioactive imaging probe for sodium-dependent glucose transporters. This measuring procedure is based on

PET imaging techniques pioneered at UCLA. The results confirmed that SGLT2 is actively involved in glucose uptake and the growth of these tumors.

Passive glucose transporters serve as the basis for current clinical methods to detect and stage cancer tumors using PET imaging techniques, but this type of imaging is not effective for pancreatic and prostate cancers, Barrio noted.

"The specific radioactive imaging probe we have developed for SGLTs on these tumors holds tremendous promise to diagnose, stage and monitor SGLT-based therapeutic interventions in pancreatic and prostate cancers, and potentially other cancers," said Barrio, a distinguished professor of molecular and medical pharmacology.

Pancreatic cancer is the fourth-leading cause of cancer-related death in the United States behind only lung, colon and breast cancers, and overall five-year survival rates hover at 7 percent. Prostate cancer, though generally more treatable and with improved survival rates is still the second-leading cause of cancer-related deaths in men.

Wright and Barrio will next begin a clinical study to further investigate the importance of sodium-dependent glucose transporters in glucose delivery. They hope that these findings will lead to the potential use of current Food and Drug Administration-approved SGLT2 inhibitors to reduce the viability of pancreatic and prostate cancer cells and increase patient survival.

More information: "Functional expression of sodium-glucose transporters in cancer." *PNAS* 2015 ; published ahead of print July 13, 2015, DOI: 10.1073/pnas.1511698112