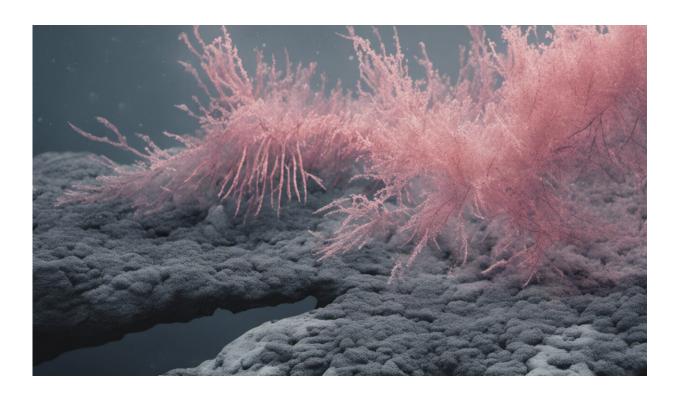


Research into use of diabetes medication for treatment of metastatic prostate cancer

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Credit: AI-generated image (disclaimer)

Patients with localized prostate cancer have a good chance of survival, but mortality rates among those with advanced, metastatic forms of the condition remain high. Until now, the precise mechanism behind the spread of the tumor has not been fully explained.



But an international research team headed by MedUni Vienna has succeeded in decoding the underlying cellular signal pathway and has carried out research using a common diabetes medication that could provide a new treatment option. The study has just been published in the journal *Molecular Cancer*.

Using a complex mouse model, the research team under Lukas Kenner (MedUni Vienna Department of Pathology, Department of Laboratory Animal Pathology at Vetmeduni Vienna) examined prostate cancer cells and identified the key factors in the regulation of tumor cell growth and the way they interact with each other. The protein signal transducer and activator of transcription 3 (STAT3) plays the leading role—its activation by another protein called interleukin 6 (IL6) has been a focus for cancer researchers in connection with tumor progression for some time now.

"Interestingly, our study showed for the first time that permanent activation of STAT3 prevents the development of <u>prostate</u> cancer as well as the development and spread of metastases. Conversely, we discovered that the loss of the signal pathway between STAT3 and IL6 in the prostate can lead to massive tumor growth and metastasis, which significantly increases the aggressiveness of the cancer and the mortality rate," explained principal investigator Lukas Kenner, summarizing the core findings.

Potential medication already available

In the course of the study, the researchers also found that activation of STAT3 in the prostate leads to increased levels of cell components (LKB1/pAMPK) that are responsible for the regulation of glucose metabolism and are linked to type 2 <u>diabetes mellitus</u>. The proteins LKB1/pAMPK block certain cancer molecules (mTOR and CREB) and as a result also stop the tumor growing.



"In light of this finding, we used a common diabetes drug in our research," said Kenner. Kenner and his team discovered that the active ingredient metformin, which is used in the treatment of type 2 diabetes to regulate glucose levels, can significantly slow the progression of STAT3-positive prostate cancer, a condition with a metabolism that is very similar to type 2 diabetes.

"As metformin is already available, our research findings could be useful in developing new treatment options for patients with STAT3-positive prostate cancer in the foreseeable future," Kenner pointed out, looking ahead to further research into the newly discovered approach.

Most common form of cancer in men

Prostate cancer has been the most common type of cancer in men in Austria since 1994, followed by lung cancer (Statistics Austria, 2022). In 2019, 6,039 new cases and 1,352 deaths due to prostate cancer were recorded. In the vast majority of cases, tumors in the prostate gland remain localized, meaning that they can be treated effectively. However, about 20% of patients develop metastatic <u>prostate cancer</u>, which is still incurable. Malignant prostate tumors are the second most common cause of cancer-related death in men worldwide (after lung cancer).

More information: Jan Pencik et al, STAT3/LKB1 controls metastatic prostate cancer by regulating mTORC1/CREB pathway, *Molecular Cancer* (2023). DOI: 10.1186/s12943-023-01825-8

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