Specific gene predicts higher chance of surviving prostate cancer

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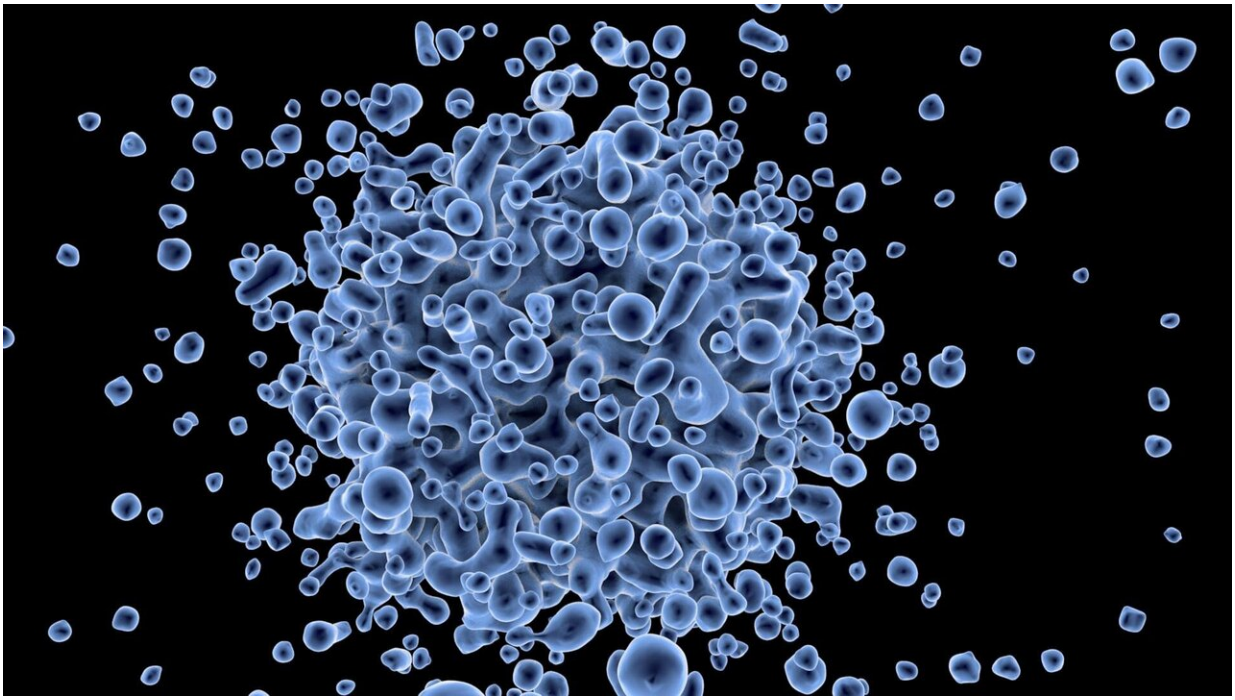

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According to *Statistics Austria* about 5,600 men are diagnosed with prostate cancer in Austria every year, meaning it accounts for roughly a quarter of all cancers in men. For some the cancer develops slowly and requires minimal treatment, but others have aggressive forms of the disease which progress very quickly. In order to be able to treat prostate cancer more effectively, better understanding of the complex

mechanisms that occur at the molecular level within the tumor is needed. In 2015, a team led by molecular pathologist Lukas Kenner of MedUni Vienna made the unexpected discovery that the protein STAT3 plays a tumor-suppressing role in prostate cancer using a mouse model. They showed that the progression of the disease was significantly worse in patients with low STAT3 levels in cancer cells, compared to patients with high levels.

These findings served as the starting point for a recent study conducted by Monika Oberhuber, a doctoral candidate in Kenner's team at MedUni Vienna's Department of Pathology, together with the Center for Biomarker Research in Medicine, a COMET Competence Center with funding from the Austrian Research Promotion Agency (FFG). The study analyzed numerous large patient data sets and compared patients with high and low expression of STAT3 in tissue.

This led to the identification of correlations between the expression characteristics of different gene clusters. The researchers discovered that patients with low STAT3 have a highly active metabolism. Metabolism—especially cellular respiration—is much more active in prostate tumors than in healthy prostate tissue. This gives the tumor additional energy to grow. Patients with low STAT3 exhibit higher cellular respiration and more active tumors, in which many new proteins form.

Oberhuber also investigated the relationship between low STAT3 and an active metabolism using paraffin-embedded tissue sections. The tumor tissue was separated from the healthy tissue with a laser microscope and then analyzed using mass spectrometry.

Intriguingly, the results showed a direct correlation between STAT3 and PDK4, which slows down cellular respiration. By showing that patients with low STAT3 also had low PDK4, it was possible to prove that PDK4

is directly regulated by STAT3. This means that PDK4 levels are a good predictor of the course of the disease. In other words, prostate cancer patients with low PDK4 have a worse prognosis than patients with high PDK4. The PDK4 gene also plays an important role in the development of other tumors and diseases, such as diabetes. A follow-up study into PDK4 is now planned to investigate its potential applications in prostate cancer treatment.

More information: Monika Oberhuber et al. STAT 3 -dependent analysis reveals PDK 4 as independent predictor of recurrence in prostate cancer, *Molecular Systems Biology* (2020). DOI: 10.15252/msb.20199247

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