"Cancer driver gene" reduces metastasis in prostate cancer

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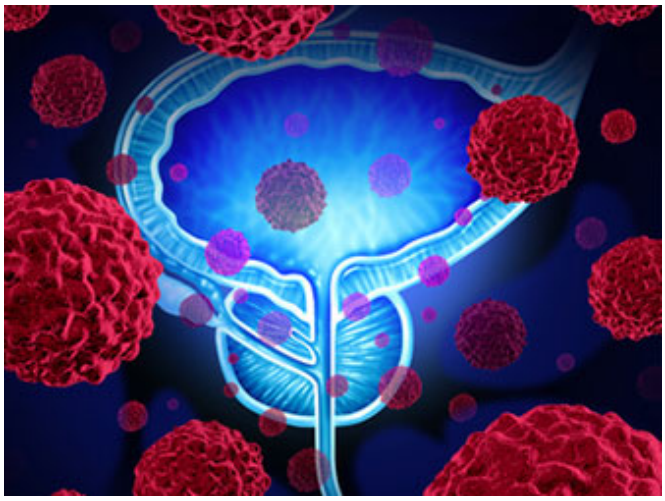

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A gene that is responsible for cancer growth plays a totally unexpected role in prostate cancer. The gene Stat3 is controlled by the immune modulator interleukin 6 and normally supports the growth of cancer cells. The international research team led by Prof. Lukas Kenner from the Medical University of Vienna, the Veterinary University of Vienna, and the Ludwig Boltzmann Instituite for Cancer Research (LBI-CR) discovered a missing link for an essential role of Stat3 and IL-6 signalling in prostate cancer progression.

Interleukin 6 (IL-6) is an important cytokine that controls the cell survival and tumor growth. Hyperactive IL-6 may support cancer growth, particularly as it controls STAT3, which was shown to have an oncogenic role in most tumours. Many therapies are therefore designed to suppress IL-6 or STAT3.

But the situation is different in prostate cancer. Lukas Kenner's research group has shown that, contrary to expectations; active STAT3 suppresses cell growth in prostate tumours. It activates the gene p14ARF, which blocks cell division and thus inhibits tumour growth.

"Using knockout mice, which are preclinical model organisms, we can link IL-6/Stat3 signalling to ARF, an important gene for cell cycle control and decisions to grow or to arrest. These findings have consequences for prostate cancer metastasis," explained Jan Pencik, a PhD fellow in the lab, headed by Lukas Kenner.

For this reason, STAT3 and p14ARF are ideally suited to act as biomarkers for the prognosis of this disease. If these two factors are missing in tissue samples, the risk is massively increased that the tumour grows and forms metastases. According to Lukas Kenner, this is important, as the predictive power of these proteins as biomarkers is twice as good as the previous gold standard. As only about 10 % of patients with prostate cancer die from the disease, this can help to prevent unnecessary therapeutic interventions with severe side effects such as incontinence and impotence. A non-invasive nuclear medical test based on these findings might soon be able to replace the painful removal of tissue samples to be examined.

Receptor blockers can enhance prostate cancer

The reversed role of interleukin 6 as an inhibitor of prostate cancer has an additional significance. Blockade of interleukin 6 is used to treat other diseases, such as rheumatoid arthritis. According to Kenner, this means that therapies that block the IL-6 pathway may enhance the growth of prostate cancer. Thus, the drug that is used to treat inflammatory disease may exacerbate malignancies. "Applying IL-6/Stat3 blockers to clinical practice might be dangerous for patients with cancerous lesions, further studies are mandatory to assess the possibility of increased cancer risk right now", says coauthor of this study,

Helmut Dolznig, also from the Medical University of Vienna. The study was financed mainly by the LBI-CR and the FWF. These results have just been published in the distinguished scientific journal *Nature Communications*.

More information: "STAT3 regulated ARF expression suppresses prostate cancer metastasis." *Nature Communications* DOI: 10.1038/ncomms8736