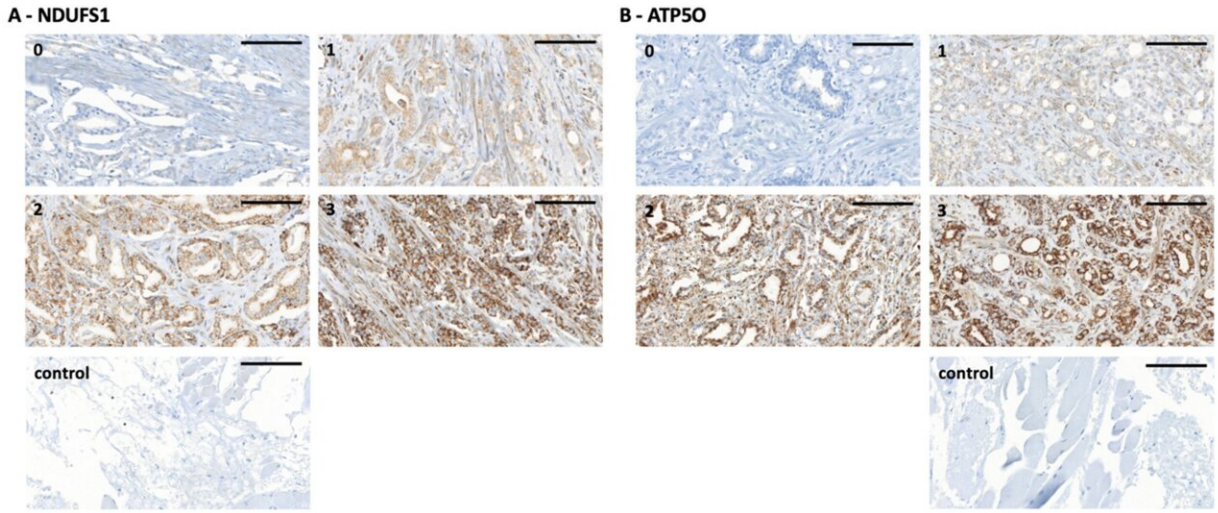
Two proteins identified as novel markers of greater prostate cancer aggressiveness

December 22 2021, by Johannes Angerer



(A) NDUFS1 immunohistochemistry staining of PCa tissue microarray (TMA) samples. (0) staining intensity of 0 to 0.5, (1) staining intensity of 1, (2) staining intensity of 2, (3) staining intensity of 3, (control) technical negative control staining (left). Scale bar = 100 µm. (B) ATP5O immunohistochemistry staining of PCa TMA samples. (0) staining intensity of 0 to 0.5, (1) staining intensity of 1, (2) staining intensity of 2, (3) staining intensity of 3, (control) technical negative control staining (right). Scale bar = 100 µm. Credit: DOI: 10.3390/cancers13236036

Prostate cancer is the most commonly diagnosed cancer in men and is among the top five causes of cancer-related death. In most cases, prostate cancer can be successfully treated, but there is a group of

patients who suffer an aggressive course and often fatal outcome. The joint study conducted by a research team led by Robert Wiebringhaus and supervised by Lukas Kenner from MedUni Vienna's Department of Pathology and the Department of Laboratory Animal Pathology at Vetmeduni, member of the Executive Board of the Comprehensive Cancer Center of MedUni Vienna and University Hospital Vienna, has identified novel cancer markers in patients with aggressive prostate cancer that indicate poorer survival and can therefore be used in future to help assess risk. The study was published in the highly regarded journal *Cancers*.

In Austria, 1 in 9 deaths among male cancer patients is due to prostate cancer. According to Statistics Austria, around 6,000 men are diagnosed with the disease every year. While some prostate cancers develop slowly and require minimal treatment, there are more aggressive forms that progress very quickly. In order to be able to treat prostate cancer more efficiently, it is necessary to understand the complex processes in the tumor at the molecular level.

In 2015, a research team led by experimental pathologist Lukas Kenner from MedUni Vienna's Department of Pathology and the Department of Laboratory Animal Pathology at Vetmeduni recognized, using a mouse model, that the protein STAT3 has a surprising tumor-suppressing role in prostate cancer. It was shown at that time that patients with low levels of STAT3 in cancer cells experience significantly worse disease progression than patients with high levels. A follow-up study showed that there was a higher metabolic rate in prostate cancer tissue as against healthy prostate tissue. This provides the tumor with extra energy to grow and metastasize.

The latest study by Ph.D. student Robert Wiebringhaus from Lukas Kenner's team and molecular biologist Brigitte Hantusch builds on these findings. For the recent study, prostate cancer tissue was separated from

healthy tissue using a laser microscope and the proteome, i.e., the totality of the proteins present, was then analyzed using mass spectrometry (proteomics analysis). This facilitated the analysis of thousands of peptides and proteins. There was found to be a higher concentration of proteins of the intracellular mitochondrial respiratory chain in the more aggressive cancer tissue.

Mitochondria are organelles, i.e., structurally delimited cell areas with a specific biological function, and are also referred to as the "powerhouses of the cells." In a machinery consisting of enzyme complexes, the so-called respiratory chain or "oxidative phosphorylation" produces energy-rich degradation products via the breakdown of sugar and, in a final step, these generate the universal energy carrier adenosine triphosphate (ATP). This is an important regulator of cellular energy-producing processes. Those cells with a particularly high energy requirement, such as cancer cells, can cover this demand via oxidative phosphorylation.

Two proteins of interest from proteomics analysis—NDUFS1 and ATP5O—were studied in more depth in a collection of samples from patients with associated clinical data. Using immunohistochemical staining and data analysis, these two proteins were shown to be associated with a lower probability of survival in more aggressive forms of prostate cancer.

Further analyses of the transcriptome, which comprises all genes that are transcribed in the cell at a certain point in time, also showed a rectified shift in the concentration of mRNA (messenger ribonucleic acid). This means that there is a direct correlation between the genetic transcripts and the proteins produced. The current study by Wiebringhaus et al. represents an important step in establishing a link between NDUFS, ATP5O and cancer aggressiveness. NDUFS1 and ATP5O could therefore serve as additional immunohistochemical markers for aggressive prostate tumors and, at the same time, as new targets for

cancer treatment.

More information: Robert Wiebringhaus et al, Proteomic Analysis Identifies NDUFS1 and ATP5O as Novel Markers for Survival Outcome in Prostate Cancer, *Cancers* (2021). DOI: 10.3390/cancers13236036

Provided by Medical University of Vienna