Medical Xpress

Researchers identify genomic and immune indicators that predict lethal outcomes in prostate cancer

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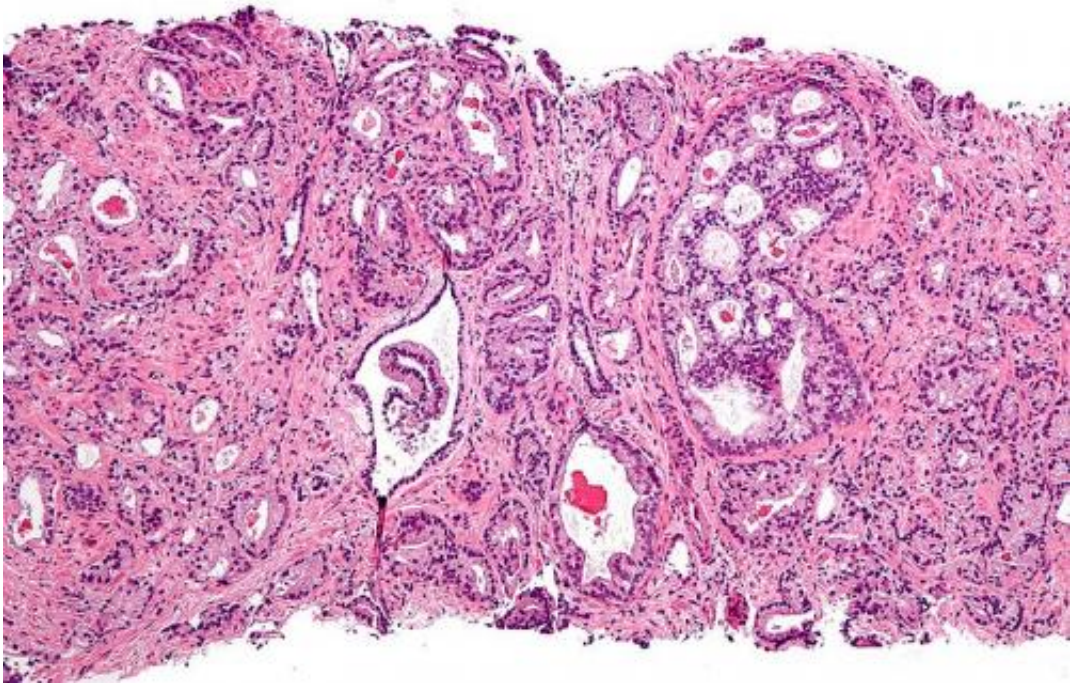

Micrograph showing prostatic acinar adenocarcinoma (the most common form of prostate cancer) Credit: Wikipedia, CC BY-SA 3.0

Prostate cancer is one of the most common cancers among men in the United States. One in nine men will be diagnosed during his lifetime. When diagnosed, a patient's disease is graded from 1 to 5 based on how aggressive it is, with 5 being the most aggressive. Those with grades 4/5

disease are at the highest risk of poor outcomes or death from the disease; however, there are no immunologic or genomic indicators that can help physicians determine the best course of treatment for this group of patients.

Moffitt Cancer Center researchers, led by Kosj Yamoah, M.D., Ph.D., associate member and director of cancer disparities research in the departments of Radiation Oncology and Cancer Epidemiology, are hoping to change that. The team conducted studies to determine if genomic heterogeneity in tumors from grade 4/5 prostate cancer patients can be exploited to identify patient subsets that are at higher risk for lethal outcomes and that may benefit from targeted treatment strategies. Their results were published in the journal *European Urology*.

Their studies focused on transcriptomic interactions between the tumor immune content score and the Decipher score, a 22-gene classifier that provides a score predicting the probability that cancer will spread. The researchers analyzed data from 8,071 prostate cancer patient samples of any disease grade (6,071 prostatectomy and 2,000 treatment naïve) in the Decipher Genomics Resource Information Database (GRID) registry. Each patient sample was also given an immune content score (ICS) that was derived using the mean expression of 264 immune cell-specific genes.

The samples were separated into four distinct immunogenomic subsets based on their results: ICS high/Decipher high, ICS low/Decipher high, ICS high/Decipher low and ICS low/Decipher low. The researchers discovered that approximately 25% of all grade 4/5 patient samples were in the ICS high/Decipher high subset.

The ICS high/Decipher high patient samples were further evaluated for the association between immunogenomic subtypes and radiation response signatures. They found that the ICS high/Decipher high subset

were genomically more radiosensitive, meaning these tumors would respond well to radiation therapy. This subset also had a higher abundance of T cells and monocyte/macrophages. However, the research team says further research is needed to unravel the biologic mechanisms of this association.

"Our results will aid in the subtyping of aggressive prostate cancer patients who may benefit from combined immune-radiotherapy modalities," said Yamoah.

Although the findings may not be applicable to other tumor genomic platforms at this time, he said the Decipher GRID platform is used routinely in clinical care throughout the country and the results can be readily validated in various ongoing clinical trials and promises to be practice changing in the near future.

More information: Kosj Yamoah et al, Novel Transcriptomic Interactions Between Immune Content and Genomic Classifier Predict Lethal Outcomes in High-grade Prostate Cancer, *European Urology* (2020). DOI: 10.1016/j.eururo.2020.11.038

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