Five types of bacteria linked to aggressive prostate cancer

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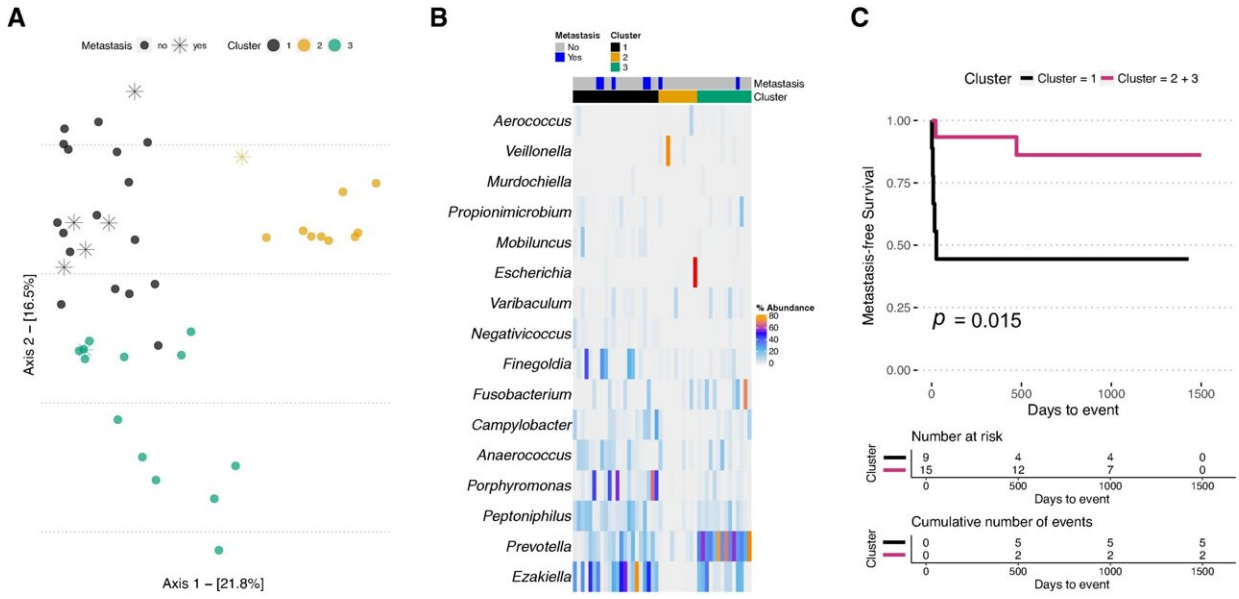

Presence and composition of urine microbiota identify participants with a poorer prognosis. The figure presents an analysis of 16S OTU sequence from urine sediments. (A) Principal coordinate analysis (Manhattan distance) of family-level OTU data from urine sediments from 46 patients undergoing assessment for prostate cancer. Clustering with k-means suggested three clusters: cluster 1 (black), cluster 2 (yellow), and cluster 3 (green). Samples from patients who developed skeletal metastases are indicated with diamonds. (B) Heatmap demonstrating a variety of bacterial genera selected to demonstrate differences across the three family-level clusters. (C) Kaplan-Meier analysis investigating metastasis-free survival: cluster 1 (black); clusters 2 plus 3 (pink). OTU = operational taxonomic unit. Credit: *European Urology Oncology* (2022). DOI: 10.1016/j.euo.2022.03.006

Researchers at the University of East Anglia have found a link between bacteria and aggressive forms of prostate cancer.

They identified five types of bacteria which were common in urine and tissue samples from men with aggressive prostate cancer.

It is hoped that these findings could help pave the way for treatments that could target these particular bacteria and slow or prevent the development of aggressive disease.

Project lead Prof Colin Cooper from UEA's Norwich Medical School, said: "We already know of some strong associations between infections and cancer. For example, the presence of Helicobacter pylori bacteria in the digestive tract can lead to stomach ulcers and is associated with stomach cancer, and some types of the HPV virus can cause cervical cancer.

"We wanted to find out whether bacteria could be linked to the way prostate cancer grows and spreads."

Dr. Jeremy Clark, also from UEA's Norwich Medical School, said: "While prostate cancer is responsible for a large proportion of all male cancer deaths, it is more commonly a disease men die with rather than from.

"And little is known about what causes some prostate cancers to become more aggressive than others. We now have evidence that certain bacteria are involved in this and are part of the puzzle."

The team worked with colleagues at the Norfolk and Norwich University Hospital, the Quadram Institute, and other collaborators to analyze urine or tissue samples from more than 600 patients with or without prostate cancer. And they developed methods of finding the bacteria associated

with aggressive prostate cancer.

Dr. Rachel Hurst, first author of this work and also from UEA's Norwich Medical School, said: "To detect the bacteria, we used many different approaches including whole genome sequencing of the tissue samples, a method which is being used increasingly as we transition into an era of genomic medicine.

"When tumor samples are sequenced, DNA from any pathogens present are also sequenced, making it possible to detect bacteria.

"We found several types of bacteria associated with aggressive prostate cancer, some of which are new types of bacteria never found before."

Two of the new bacteria species found by the team have been named after two of the study's funders—Porphyromonas bobii, after the The Bob Champion Cancer Trust and Varibaculum prostatecancerukia, after Prostate Cancer UK.

The set of bacteria found by the team include Anaerococcus, Peptoniphilus, Porphyromonas, Fenollaria and Fusobacterium. All of these are anaerobic, which means they like to grow without oxygen present.

Dr. Hurst said: "When any of these specific anaerobic bacteria were detected in the patient's samples, it was linked to the presence of higher grades of prostate cancer and more rapid progression to aggressive disease.

"We also identified potential biological mechanisms of how these bacteria may be linked to cancer.

"Among the things we don't yet know is how people pick up these

bacteria, whether they are causing the cancer, or whether a poor immune response permits the growth of the bacteria.

"But we hope that our findings and future work could lead to new treatment options, that could slow or prevent aggressive prostate cancer from developing. Our work could also lay the foundations for new tests that use bacteria to predict the most effective treatment for each man's cancer," she added.

The team also noted that many bacteria are beneficial to human life and it is not a simple matter to remove the harmful bacteria without removing the protection provided by the good bacteria.

Prof Daniel Brewer, from UEA's Norwich Medical School and a visiting worker at the Earlham Institute, said: "Knowing when we can watch and wait or whether we need to start treatment is a major challenge for people with prostate cancer. If we can target aggressive cancers while sparing others from unnecessary treatment it will dramatically improve the way we manage this disease.

"There seems to be a clear link between these bacteria and the way the cancer is behaving. We need to understand this relationship in more detail but it's a major step towards developing a cheap and quick test that could guide treatment decisions."

Robert Mills, Urology Consultant at the Norfolk and Norwich University Hospital, said: "This research has shown a potential link between more aggressive prostate cancer and the presence of certain bacteria in the prostate and in urine. Whether this is cause or effect is not clear and will be the subject of further research."

Collaborator Prof John Wain from the Quadram Institute said: "This research exemplifies the Norwich Research Park's multidisciplinary

approach to studying infection.

"The link between bacterial growth and cancer is not always straight forward and working with the cancer group at the Norwich Medical School has allowed us to demonstrate a possible link between bacteria living in the prostate and severe forms of prostate cancer.

"By combining advanced computational analysis of DNA sequence data from the urine of patients with an in depth understanding of cancer biology and the ability to characterize new species of bacteria we were able to show an association between the presence of several bacteria and progression to an aggressive form of prostate cancer.

"This will now enable further work to determine if there are causal relationships between microbes and cancer."

This research was led by the University of East Anglia in collaboration with the Quadram Institute and the Norfolk and Norwich University Hospital. Other collaborators included the Universities of Oxford, Cambridge, Manchester, St Andrews and Auckland, the Earlham Institute, the Institute of Cancer Research, the Royal Marsden NHS Foundation Trust, and Cancer Research UK.

"Microbiomes of Urine and the Prostate are Linked to Human Prostate Cancer Risk Groups' is published in the journal *European Urology Oncology*.

More information: Rachel Hurst et al, Microbiomes of Urine and the Prostate Are Linked to Human Prostate Cancer Risk Groups, *European Urology Oncology* (2022). DOI: 10.1016/j.euo.2022.03.006

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