Microbiome — the ‘unforeseen organ’

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The advent of molecular methods for the identification and characterization of the microbiome has led researchers to understand the role of the microbiota in various clinical conditions. Research by Cavarretta and colleagues has revealed the presence of microbial dysbiosis and its potential relationship with pathophysiology in the prostate tumour microenvironment. This finding could potentially enable future investigations that clarify the role of the microbiota in the development of prostate cancer and its future management, from a different perspective.

The microbiota has tremendous potential to influence human physiology, both in health and in disease. The development of ‘omics’-based approaches has provided functional, quantitative, and mechanistic insights into the complex microorganism–host interactions that underlie various human diseases. The microbiota of the urinary tract is one such example and, relative to that of other organs, such as the gut, is a poorly investigated microbial niche. However, emerging evidence is beginning to indicate that the microbiota of the pelvic organs has important implications for urologists.

Prostate cancer is one of the most common cancers in men, with an estimated 161,360 new cases anticipated in the USA in 2017 (REF. 2). The lifetime risk of prostate cancer is estimated to be 16%3. Dietary, lifestyle and genetic factors are all established risk factors4. Furthermore, researchers have demonstrated that dysbiosis of the gastrointestinal microbiota confers an increased risk of prostate cancer5.

In a recently published paper, Cavarretta and colleagues6 reported the results of a detailed and comprehensive characterization of the microbiome of the tumour, peritumour, and nontumour tissues of men with prostate cancer. These researchers demonstrated that the prostate tissue taken from tumour, peritumour and nontumour locations contains specific microbial populations, with notable diversity in the prevalence of Staphylococcus spp in different tumour specimens6.

The authors analysed prostate specimens from 16 nondiabetic, nonobese white men with prostate cancer (Gleason score: 6 (n = 2), 7 (n = 10), 8 (n = 2), 9 (n = 2) and TNM Stage: pT2c (n = 1), pT3a (n = 11), pT3b (n = 4)) who underwent radical prostatectomy. Bacterial DNA was isolated from tissues followed by amplification of bacterial ribosomal RNA (rRNA) libraries (focused on variable regions 3–5 of the 16S rRNA gene). Extracted amplicons were purified and used for massive ultradeep pyrosequencing. The amplified bacterial rRNA gene sequences identified were then compared with those obtained from a standard database of bacterial DNA sequences using bioinformatics tools. Following quantification using real-time PCR, comparisons of total numbers of bacteria present in each sample, as defined by 16S copy number per μg of extracted DNA, intrasample (between tumour, peritumour, and nontumour samples from the same patient) and intersample differences in bacterial load were not statistically significant.

Analysis of the prostate microbiota revealed an abundance of Actinobacteria, Firmicutes and Proteobacteria: a total of 29 bacterial classes, 50 orders, 114 families, and 244 genera were detected from these three phyla. Significant differences in specific microbial populations among tumour or peritumour versus nontumour prostate specimens were observed.

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Staphylococcus spp. were more abundant in tumour/peritumour tissues than in nontumour tissues (P <0.05). Moreover, a significantly greater abundance of Lactobacillales was observed in the nontumoural, compared with tumoural samples (P <0.05) and the exclusive presence of Streptococcus spp. in nontumoural areas was reported. When investigated further, Propionibacterium spp. was found to be the most abundant genera. At each taxonomic level, certain microbial populations were found to be present exclusively in one or two..."
regions. Comparisons of β-diversity, defined as the ratio of regional to local species diversity were unable to differentiate between the three different areas of the prostate. Furthermore, the researchers did not observe any significant correlations between microbial burden at the taxonomic level and the extent of intra-prostatic inflammation, inflammatory cell density, serum PSA levels and Gleason score.

Owing to the unavailability of entirely nonmalignant prostate samples, the authors obtained biopsy samples from the non-tumoural areas of the prostate specimens. The gradual differences in the composition of the microbiota among different areas of these prostate tissues would suggest the presence of a noncausal correlation. However, these results could also reflect the presence of sampling artefacts. The team sampled the areas containing the highest-grade tumour within each tumour specimen, and recognized that this selection prohibits the identification of intraspecimen differences in composition of the microbiota between those with high-grade and low-grade disease. Thus, the study did not show any differences in correlation between the microbiota and the grade, or stage of disease. In addition, we must note that the sample size is very low (n = 16), which does not rule out the possibility that different tumour characteristics (such as stage and grade) might be associated with differences in the microbiota.

In addition to the limitations described by the authors, the influence of other limitations must also be considered. Firstly, further studies should aim to make the best use of ‘omics’ platforms to better understand the precise effects of colonization by certain strains of bacteria on tumour development and metastasis, and possibly the effects of recolonization of other organs. Interest in the role of the microbiota in tumour development and progression is warranted. Secondly, little is known about the molecular mechanisms by which oncogenic pathways bring about the switch from a nonmalignant to a malignant phenotype, thus detailed quantitative and qualitative proteomic and metabolomic analyses are warranted to study whether, and how, components of the microbiota can induce changes in global protein expression in various prostate tissues.

The authors conclude that the prostate contains a plethora of microorganisms, with a distribution that is dependent on the nature of the tissue, suggesting a possible pathophysiological correlation between the presence of a tumour and the composition of the microbiota. The authors also highlighted the need for a detailed study designed to establish whether the microbial profile described in their study is associated with, correlated with, or even responsible for, the onset of prostate cancer. The findings reveal the microbiota of the pathological prostate niche, albeit in a small number of patients, and confirm the presence of a localized prostate-specific microbial profile, thus supporting the previously held theory regarding the health benefits of a more diverse microbiota. These findings pave the way for future investigations designed to clarify the possible role of the microbiota in the progression of prostate cancer and to assess the potential for components of the prostate microbiota to be exploited as novel biomarkers and/or therapeutic targets, possibly enabling a very different approach to the future management of men with prostate cancer.

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