P48 – **Bacterial inhabitants of the human not-tumoral, peri-tumoral, and tumoral prostate tissue**

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According to previous demonstrations in different inflammatory and tumor conditions,[1-7] it is conceivable that modifications in terms of bacterial populations could be observed also in prostate cancer (PCa), where they may contribute to cancer development by enhancing pro-inflammatory responses, by modifying the prostate extracellular microenvironment,[9-10] or through diverse unknown mechanisms. To date, very little information is available on the prokaryotic ecosystem of the tumoral prostate gland[11].

In order to characterize the prostate tumor tissue-specific microbial communities, we assessed the microbiome profile of matched tumor, peri-tumor, and non-tumor tissues on 16 human radical-prostatectomy specimens by massive ultra-deep pyrosequencing.

We observed significant differences in specific microbial populations among the different areas. In particular, Staphylococcus and *Streptococcus spp* were more represented, respectively, in the tumor/peri-tumor tissues and in the non-tumor tissues ($p<0.05$), whereas *Propionibacterium spp.* were the most abundant.[12] To assess potentiality of specific bacteria to be exploited as new biomarkers, we also characterized the urine microbiome from the same PCa patients. As expected, alpha-diversity demonstrated a richer microbiome in urine samples when compared to the prostate samples ($p<0.05$). The beta-diversity could also distinguish urine from prostate samples. Interestingly, the two kinds of PCa matrices presented a completely different microbiome profile with some of the microorganisms being represented exclusively in the tumor lesions and vice versa. Finally, when comparing the urine *Phylum* and *Genus* profiles from PCa patients to the urine profiles from benign prostate hyperplasia patients, as control, we did not find any statistically significant difference.

From this pilot study, we conclude that the prostate contains a plethora of bacteria, which set themselves within the gland with a distribution dependent on the nature of the tissue, thus suggesting a possible pathophysiological correlation between the composition of the local microbial niche and the presence of the tumor itself. Interestingly, some rarely-identified species were uniquely present in tumor lesions, as they have been also observed in colon cancer patients.[6,13] Biological fluids such as semen or expressed prostatic secretions could be more informative than urine and deserve to be analysed in new, prospective studies.

Despite the descriptive nature of this study and the limitations due to the restricted number of specimens and the lack of comparison with the gut-microbioma, these findings are relevant as they pave the way for future investigations aimed to discover whether the specific prokaryotic neighbours of PCa cells and/or their metabolites can be exploited as novel biomarkers and/or therapeutic targets.

References

1. Belkaid Y, Hand TW. *Role of the microbiota in immunity and inflammation*. Cell 2014;157:121-41
2. Cox AJ, West NP, Cripps AW. *Obesity, inflammation, and the gut microbiota*. Lancet Diabetes Endocrinol 2015;3:207-15
3. Ohkusa T, Koido S. *Intestinal microbiota and ulcerative colitis*. J Infect Chemother 2015;21:761-68
4. Hullar MA, Burnett-Hartman AN, Lampe JW. *Gut microbes, diet, and cancer*. Cancer Treat Res 2014;159:377-99
5. Zitvogel L, Galluzzi L, Viaud S; *Cancer and the gut microbiota: an unexpected link*. Sci Transl Med 2015;7:271ps271
6. Cipe G, Idiz UO, Firat D, et al. *Relationship between intestinal microbiota and colorectal cancer*. World J Gastrointest Oncol 2015;7:233-40
7. Alfano M, Canducci F, Nebuloni M, et al. *The interplay of extracellular matrix and microbiome in urothelial bladder cancer*. Nat Rev Urol 2016;13:77-90
8. Sfanos KS, Isaacs WB, De Marzo AM. *Infections and inflammation in prostate cancer*. Am J Clin Exp Urol 2013;1:3-11
9. De Marzo AM, Platz EA, Sutcliffe S, et al. *Inflammation in prostate carcinogenesis*. Nat Rev Cancer 2007;7:256-69.
10. Cohen RJ, Shannon BA, McNeal JE, et al. *Propionibacterium acnes associated with inflammation in radical prostatectomy specimens: a possible link to cancer evolution?* J Urol 2005;173:1969-74
11. Sfanos KS, Sauvageot J, Fedor HL, et al. *A molecular analysis of prokaryotic and viral DNA sequences in prostate tissue from patients with prostate cancer indicates the presence of multiple and diverse microorganisms*. Prostate 2008;68:306-20
12. Cavarretta I, Ferrarese R, Cazzaniga W, et al. *The Microbiome of the Prostate Tumor Microenvironment*. Eur Urol 2017;72:625-631
13. Nistal, E, Fernandez-Fernandez, N, Vivas JL, et al. *Factors Determining Colorectal Cancer: The Role of the Intestinal Microbiota*. Front Oncol 2015;5, 220