

Characterization of the urinary microbiota in bladder cancer patients

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Introduction & objectives: Mounting evidence indicates that the microbiota plays an important role in carcinogenesis and response to treatments. The dogma that urine is sterile has been overturned and dysbiosis of the urinary microbiota has been linked to numerous urological disorders. We tested the hypothesis that alteration in urinary microbial community composition may be associated to bladder cancer development and progression. Therefore, we performed a study to characterize the urinary microbiota associated with non-muscle invasive and muscle invasive bladder cancer (NMIBC, MIBC).

Materials & methods: Urines were collected with a catheter from BC patients before transurethral resection or cystectomy, and age-matched non-neoplastic subjects. Subjects with prior history of sexually transmitted infection, chronic intestinal inflammation, urinary tract infection and recent usage of antibiotic or immunomodulatory agents were excluded. Bacterial DNA was extracted and amplified for 16S rDNA sequencing. The analyses were done using custom scripts developed for the Qiime software suite and the Silva v. 128 database.

Results: We isolated bacterial DNA from urine samples of 12 non-neoplastic control subjects and 27 BC patients. Metrics to assess differences in microbial alpha diversity were statistically similar between cancerous and healthy samples. However, higher Chao1 index was observed when considering exclusively MIBC compared to controls, indicating that bacterial richness increases with tumor invasiveness. The most abundant phyla in both groups were *Actinobacteria*, *Bacteroidetes*, *Firmicutes* and *Proteobacteria*. Interestingly, at the family level we found that NMIBC displayed a reduction in the abundance of *Sphingobacteriaceae*, *Bifidobacteriaceae* and *Enterobacteriaceae*. High grade NMIBC and MIBC showed decreased *Bifidobacterium* and *Ruminococcus* genera, which are known to protect from inflammation, and increased *Corynebacterium*, a potential opportunistic bacteria.

Conclusion: The urinary microbiota of BC patients displayed a significantly different pattern relative to control group, suggesting that the tumor microenvironment can influence dysbiosis. In particular, we found specific bacteria to associate with aggressive tumors. A better understanding of the urinary microbiota could pave the way for exploring new therapeutic options based on the manipulation of the microbial community. Analysis of additional samples is ongoing.