Microbiome profiling and molecular alterations to explain gender related urothelial bladder cancer diversities

Bladder cancer (BC) remains the most common malignancy of the urinary tract. The great majority of BC are urothelial cell cancers (UBC). At presentation, about 75% of UBC are confined to the mucosa (NMIBC – non-muscle invasive bladder cancer), while in the remaining 25% cancers infiltrate muscle layer of the bladder wall (MIBC - muscle invasive bladder cancer) or already formed metastases. Sex related differences are observed in the epidemiology of BC. The incidence of disease is 3-4 fold higher in men compared to women but at the same time women are diagnosed with more advanced disease. However regardless of the stage of UBC at diagnosis female gender is related – albeit not constantly - with higher risk of disease recurrence and progression. Number of causes were introduced to explain gender UBC diversities including delayed diagnosis, inequality in health care and disparate tumor biology.

Although molecular profiling of bladder cancer has been recently performed, there is lack of investigations showing possible explanations of gender gap at molecular level. A microbiota is an "ecological community of commensal, symbiotic and pathogenic microorganisms". The synonymous term microbiome describes either the collective genomes of the microorganisms. Researchers are increasingly interested in the link between cancer and the microbiome. There are no investigations on the impact of sex differences in the urinary microbiome and bladder cancer biology. Using 220 tissue samples (110 female/110 male) from patients subjected to bladder tumor resection (including 20 patients without cancer at final pathological examination as control group) we plan to perform comprehensive characterization of microbiome and molecular alterations that could be responsible for gender gap in bladder cancer. Our project aims to fill the knowledge gap by implementing the state-of-the-art molecular technologies to uncover sex-related differences in bladder cancer microbiome variability and accompanying molecular alterations. Thus, we may expect that this project will also bring new information on relationship between BC occurrence and bladder microbiota as well as molecular alterations that would explain gender disparities. In conclusion, this project will open new perspectives not only in basic research, but will also create the tenet for future pre-clinical and, possibly, clinical modes studies.