

Project Title: Aptamer-based urinary biosensor for bladder cancer detection and surveillance
Principal Investigator: Jaime Landman

Bladder cancer is an aggressive and heterogeneous disease associated with substantial morbidity, mortality, and cost. It is highly prevalent being the tenth most diagnosed cancer and the thirteenth leading cause of cancer deaths in the world. The gold standard for bladder cancer diagnosis and surveillance remains highly invasive and expensive, and currently, noninvasive urinary tests have yet to match the sensitivity and specificity of an expensive surgical procedure. Therefore, a simple-to-use and reliable assay is still needed for bladder cancer detection and surveillance. Our approach focuses on defining and profiling the molecular biomarkers of bladder cancer in urine by utilizing directed molecular evolution to generate confirmation-switching DNA aptamers-single-stranded DNA-based biorecognition agents-that recognize disease states. We have developed and validated a molecular evolution platform that can generate aptamers using biological fluids without prior knowledge of the biological markers. Our method yielded promising aptamers that can detect cancerous urine samples. Eight aptamer candidates were identified with the capability of distinguishing between cancer and non-cancer clinical urine samples with statistical significance. Ongoing efforts are focused on identifying the urinary biomarkers' identities (transcriptomics, proteins, or metabolites) recognized by the selected aptamers. To achieve the proposed work, we have designed a fluorescence assay to measure the activities, or "switching" functionalities, of the conformational-switching aptamers under differing conditions (buffer, synthetic urine, and clinical urine samples) in a high-throughput screening manner. Molecular assays (protease/nuclease treatment and size filtration assays) along with our high-throughput assay will be used to help elucidate the urinary biomarker entity, and analytical techniques (mass spectrometry and next-generation sequencing) will be used to further identify the biomarkers. Independent analytical techniques (Western blots, ELISA, and qPCR) will be used to validate the identified biomarkers for clinical significance. The proposed work aims to better understand the urinary composition associated with bladder cancer and ultimately translate the cancer-specific aptamers into a convenient at-home dipstick assay for bladder cancer surveillance, thus increasing the accessibility of point-of-care diagnostics for bladder cancer.