The Miyamoto laboratory focuses on the discovery and development of novel biomarkers to guide the personalized treatment of patients with prostate and bladder cancer. We focus on two general classes of biomarkers, namely those based on the molecular profiles of tumor biopsies, and those based on circulating tumors cells (CTCs) in the blood that can be sampled non-invasively and repeatedly. By analyzing these patient-derived specimens, we have identified new molecular predictors of response to therapy and potential mechanisms of treatment resistance. Our overall aim is to develop tools for “real-time precision medicine” to probe the molecular signatures of cancers as they evolve over time, and to guide the precise and rational selection of appropriate therapies for each individual patient with prostate or bladder cancer.

Prostate cancer is the most common cancer in men and the second leading cause of cancer-related death in men. There is a critical unmet need for predictive biomarkers to guide prostate cancer therapy in settings ranging from localized to metastatic disease. In localized prostate cancer, reliable biomarkers are sorely needed to guide the rational selection of appropriate management options tailored to each patient’s tumor, including active surveillance, radical prostatectomy, or radiation therapy. In metastatic prostate cancer, multiple FDA-approved therapeutic options that increase survival are now available, including androgen receptor (AR) targeted therapies, cytotoxic chemotherapy, and PARP inhibitors. However, we lack non-invasive biomarkers that can reliably predict treatment responses and precisely guide selection of the most appropriate therapy for each individual patient. A major focus of our laboratory is the investigation of circulating tumors cells (CTCs), which are rare cancer cells shed from primary and metastatic tumors into the peripheral blood. CTCs represent a type of “liquid biopsy” that may be performed repeatedly and non-invasively to monitor treatment efficacy and study tumor evolution during therapy. In collaboration with a multidisciplinary team at MGH, we have developed novel molecular assays using microfluidic technologies to isolate and analyze CTCs from the blood of cancer patients. Our recent studies include the interrogation of androgen receptor (AR) signaling status to predict therapeutic response in patients receiving AR-targeted therapies, and the use of single cell RNA-seq to nominate noncanonical Wnt signaling as a contributor to enzalutamide resistance. Most recently, we derived CTC RNA signatures that predict resistance to AR-targeted therapy in metastatic cancer.
and early dissemination in localized cancer. Ongoing projects include the development of CTC molecular signatures for the prediction of clinical outcomes after radiation therapy, and for the early detection of clinically significant prostate cancer. Another focus of the laboratory is the development of novel tissue-based biomarkers. We utilize technologies including microfluidic real-time PCR, next-generation sequencing, and RNA in situ hybridization [RNA-ISH] to evaluate molecular signatures in limited quantities of tumor biopsy tissues. Our past and ongoing efforts are directed at correlating molecular findings with clinical outcomes in order to identify novel biomarkers predictive of treatment response.

Bladder cancer is the fifth most common cancer in the US, causing 18,000 deaths per year. Muscle-invasive bladder cancer is aggressive and has a high propensity for metastasis, but can often be treated effectively with either radical cystectomy or bladder-sparing trimodality therapy (transurethral tumor resection followed by chemoradiation). However, the decision regarding which treatment to pursue is often based on arbitrary factors including patient or physician preference. There is an urgent unmet need for molecular biomarkers to guide patients towards the most appropriate therapy based on the biology of their tumor. We recently performed gene expression profiling of bladder tumors from patients treated with bladder preservation therapy, and identified immune and stromal molecular signatures predictive of outcomes after chemoradiation therapy. We are currently evaluating these and other candidate biomarkers as predictors of treatment response in prospective clinical trials and carefully defined retrospective clinical cohorts.

Selected Publications:


* Co-first authors