LICENSING OPPORTUNITY

A Liquid Biopsy based PCR Assay to Predict Drug Resistance in Prostate Cancer

Here we present a diagnostic assay to predict clinical outcome to AR signaling inhibitors in metastatic castration-resistant prostate cancer (mCRPC) patients. A well-known genomic alteration is amplification of the AR gene in nearly half of mCRPC cases. Presence of somatic AR amplification and mutations as well as AR-V7 have shown strong association with shorter progression-free survival and overall survival with abiraterone or enzalutamide in mCRPC patients.

COMMERCIAL OPPORTUNITY

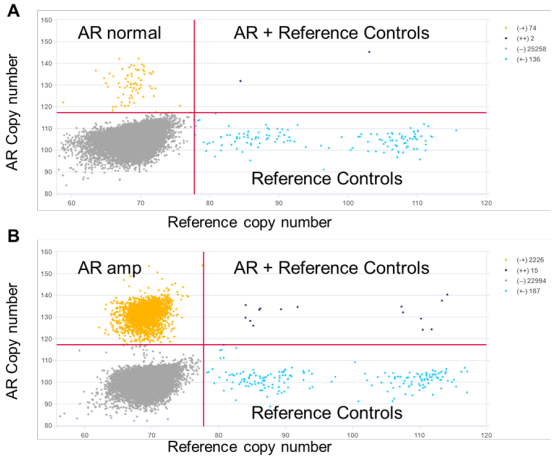
- Prostate cancer is one of the leading causes of cancer death in males in the western world, which occurs typically in the advanced mCRPC state. The American Cancer Society estimates 248,530 new cases of prostate cancer in the US in 2021. In patients with mCRPC, cancer grows and metastasizes despite treatment with androgen-deprivation therapy.

- To date, there are no approved biomarker to personalize therapy in clinical practice for mCRPC. However, AR aberrations, including gain and splice variant 7, represent the most specific and reliable predictive biomarkers to guide treatment decisions in mCRPC. Moffitt's diagnostic provides a screening platform to detect both AR gain and AR-V7 to predict clinical outcome to AR inhibitors in chemotherapy-naive mCRPC patients.

- Liquid biopsies using circulating cell-free DNA (cfDNA) in blood allows for detection of genetic alterations, treatment response and overall survival. Current genetic testing assays using NGS or q-PCR are designed to detect genetic variations at either DNA or RNA level albeit separately. Moffitt's assay tests both DNA and RNA simultaneously in single a PCR tube within a day. For mutations and AR-V7 detection, our assay is over 10 times more sensitive than NGS (0.01% vs 0.1%). For AR copy number change, our assay is over 2x more sensitive than similarly described procedures. (1.5% vs 3-5%).

TECHNOLOGY

Androgen receptor (AR) signaling inhibitors such as abiraterone or enzalutamide represent the standard treatment in mCRPC patients. However, some mCRPC patients display a primary resistance to AR signaling inhibitors. Three milliliters of plasma samples from patients before initiating treatment with abiraterone or enzalutamide will be used to isolate total nucleic acids including both cell-free DNA and RNA. Following reverse transcription, a bimodal and multiplex digital PCR assay will be used for the simultaneous detection of AR amplification, mutations and AR-V7. This assay combines detection of both circulating DNA and RNA into one streamline PCR reaction. The detected targets of alterations include: **(1)** AR amplification at its enhancer region and gene body; **(2)** AR somatic mutations; and **(3)** AR-V7 and AR-full length gene. Using the novel methodology, preliminary proof-of-concept *in vitro* studies using a human prostate carcinoma epithelial cell line (22Rv-1 cells) showed AR amplification compared to controls (See Figure).



PUBLICATION/PATENT

Provisional application was filed for Dr. Liang Wang in 2021

CONTACT

The Innovation Office
813.745.6828
InnovationMarketing@Moffitt.org

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