Washington University in St. Louis
Office of Technology Management

LIQUID BIOPSY ASSAY FOR PERSONALIZED PROSTATE CANCER TREATMENT

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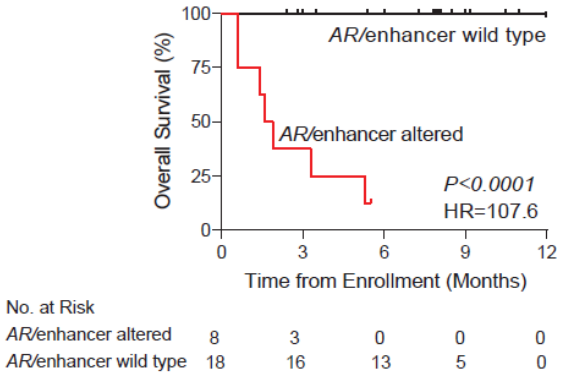
T-019287

Technology Description

A team of researchers at Washington University has developed “EnhanceAR-Seq”, a circulating tumor DNA (ctDNA) assay that predicts which patients are at high risk for developing resistance to androgen receptor (AR)-directed treatment for metastatic prostate cancer. This non-invasive liquid biopsy can stratify patients for personalized therapy before any treatment has begun and is much more sensitive than the current circulating tumor cell assay (AR-V7).

Patients who are resistant to AR-directed prostate cancer therapy have a very poor prognosis with median survival of only 5.5 months. The current test for resistance (AR-V7) has low sensitivity (3-30%) and does not identify resistance until multiple lines of therapy have failed. EnhanceAR-Seq (Enhancer and neighboring loci of Androgen Receptor Sequencing) offers an alternative for earlier and more sensitive detection. The EnhanceAR-Seq assay includes a customized gene panel and bioinformatics pipeline that can be performed on plasma cell-free DNA to robustly track genomic alterations involving the *AR* enhancer, *AR* gene body, and 84 other important genes. These biomarkers could reliably and sensitively identify patients with resistant disease, thereby enabling clinicians to consider alternate therapeutic regimens (e.g., chemotherapy or immunotherapy). EnhanceAR-Seq has the potential to significantly improve the management of metastatic prostate cancer by enhancing clinical decision-making and opening the door to more personalized treatment strategies.



Wild type vs. altered AR/enhancer predicts survival in patients undergoing AR-directed treatment for prostate cancer.

Stage of Research

The inventors performed EnhanceAR-Seq prospectively on 40 patients that received AR-directed therapy for prostate cancer. The assay effectively stratified patients based on progression-free survival and overall survival, identifying 78% of patients that developed treatment resistance and 89% of patients with primary resistance (compared to AR-V7 analysis which had only an 8% positivity rate).

Publications: Maher, C., Dang, H. X., Chauhan, P. S., Ellis, H., Feng, W., Harris, P., ... & Atkocius, A. (2020). AR enhancer and locus genomic alterations as cell-free DNA biomarkers of primary resistance to AR-directed treatment of metastatic

prostate cancer. *Journal of Clinical Oncology* 38, no. 15_suppl 5529-5529.

Applications

- **Personalized medicine with liquid biopsy**:
  - identify high-risk metastatic prostate cancer patients early and help select appropriate therapy (e.g., olaparib for a patient with DNA damage response gene mutation identified in our panel)
  - patient risk stratification for clinical trials
  - clinical decision-making regarding AR-directed treatment vs. other types of systemic therapy
  - secondary trial endpoint to identify resistance to AR-directed therapy
  - monitor genomic events relevant to the solid tumor

Key Advantages

- **Early, sensitive, personalized identification:**
  - EnhanceAR-Seq detects 78% of patients that are resistant to AR-directed therapy, including 89% of those with primary therapeutic resistance, compared to 3-30% detection with the AR-V7 assay currently used in practice
  - could identify resistant patients and tailor the therapeutic regimen early when more options are available (unlike AR-V7 assay which cannot identify patients until after they have received multiple lines of treatment)
  - includes 85 genes in an optimized gene panel which can help guide further treatment decision-making such as the decision to offer targeted inhibitors or agents that target DNA damage response pathways
- **Non-invasive -** EnhanceAR-Seq analysis can be performed on plasma cell-free DNA with no biopsy needed

Patents: Application pending

Related Web Links: Chaudhuri Lab; Chaudhuri Profile; Maher Profile; Pachynski Profile