Madonna R Peter et al., Hereditary Genet Curr Res 2018, Volume 7
DOI: 10.4172/2161-1041-C1-002

Detection of tumor-related DNA methylation biomarkers in liquid biopsies from metastatic castration resistant prostate cancer patients to improve treatment decisions

Madonna R Peter[1, 2], Misha Bilenky[3], Ruth Isserlin[4], Anthony M Joshua[5], Aaron R Hansen[5], Gary Bader[4], Neil E Fleshner[6], Martin Hirst[3] and **Bharati Bapat[1,2,6]**

[1]Lunenfeld-Tanenbaum Research Institute, Canada
[2]University of Toronto, Canada
[3]Canada's Michael Smith Genome Sciences Centre - British Columbia Cancer Agency, Canada
[4]The Donnelly Centre for Cellular and Biomolecular Research - University of Toronto, Canada
[5]Princess Margaret Cancer Centre, Canada
[6]University Health Network, Canada

Background: Liquid biopsies are emerging as an important source of minimally invasive biomarkers, especially in metastatic castration resistant prostate cancer (mCRPC), where tumors are often inaccessible for biopsy based strategies. In particular, circulating cell free nucleic acids, such as cfDNA, can harbor tumor specific genomic and epigenomic changes. Tumor related DNA methylation markers are detectable in circulation of mCRPC patients; however, genome wide changes in the cfDNA methylome of mCPRC patients undergoing current androgen targeting therapies have not been extensively investigated.

Methods/Results: In collaboration with the University Health Network Genitourinary Biobank (Toronto, Canada), we prospectively collected a cohort of mCRPC patients that received treatment with either enzalutamide or abiraterone acetate. Plasma cfDNA was isolated at baseline (prior to starting treatment), week-12 and clinical progression. As cfDNA methylation detection can be challenging due to low yield and quality, we optimized a protocol that involves methylated DNA immuno precipitation (MeDIP) followed by next generation sequencing (NGS). Overall, we are able to obtain good quality NGS data with high mappability to the genome as well as >5x coverage of 46-51% CpGs in the genome. We applied this MeDIP-seq protocol to cfDNA samples from 11 enzalutamide treated and 5 abiraterone treated patients that completed all study visits. We performed within patient analysis to identify differentially methylated regions (DMRs) associated with treatment and clinical progression. Overall, there were a number of DMRs identified through our established pipeline, with known mCRPC genes implicated, such as members of the HOX family of transcription factors and Wnt pathway members.

Conclusions: Overall, we are able to detect methylation signals from low yields of cfDNA and potentially tumor specific methylation markers. We are currently performing pathway analysis and correlation with clinical parameters. Validation of these methylation markers in mCRPC could further shed light on underlying disease mechanisms and novel biomarkers.

Biography

Madonna R Peter is currently a PhD student at the University of Toronto, Department of Laboratory Medicine & Pathobiology and under the Supervision of Dr. Bharati Bapat (Lunenfeld-Tanenbaum Research Institute, Mount Sinai Hospital, Toronto, Canada). Previously, she completed her MSc in the Department of Immunology (University of Toronto).