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"MC-PATH: PATHWAY-CENTRIC ALGORITHM TO IDENTIFY BIOMARKERS OF PRIMARY ABIRATERONE RESISTANCE IN METASTATIC CASTRATION-RESISTANT PROSTATE CANCER"

By

Mayra Vendramini Tuiche
Molecular Biology, Genetics, and Cancer Program
Bachelor of Science 2015, Universidade de São Paulo, Brazil
Master of Science 2017, University of Florida

Thesis Advisor: Antonina Mitrofanova, Ph.D.
Rutgers School of Health Professions
Associate Professor, Department of Biomedical and Health Informatics
Associate Dean for Research at Rutgers School of Health Professions

Thursday, August 7th, 2025
MSB H-609B
11:30 A.M.

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ABSTRACT

Heterogeneous response to abiraterone is a significant challenge in metastatic castration-resistant prostate cancer (mCRPC). Mechanism-driven biomarkers of resistance may enable risk-based patient stratification to guide personalized therapy and improve clinical outcomes. In this thesis, we present MC-PATH, a novel algorithm that identifies groups of biological pathways associated with primary abiraterone resistance in mCRPC. Using transcriptomic data from metastatic tissues of mCRPC patients who did not receive any androgen receptor pathway inhibitors before biopsy, we associated pathway activity with abiraterone response and applied dimensionality reduction and clustering techniques to group multicollinear pathways that contribute to resistance. We identified six composite pathways associated with abiraterone failure and demonstrated their ability to predict risk of abiraterone resistance in two independent patient cohorts (Testing cohort 1: Wald test p-value=0·03, Testing cohort 2: Wald test p-value=0·02). A pathway-based risk score effectively stratified patients by risk of developing resistance (Testing Cohort 1: log-rank p<0·0001, Testing Cohort 2: log-rank p<0·0011) and outperformed existing biomarkers and other computational approaches. The identified composite pathways acted as clinically relevant tools for risk-based patient stratification and prioritization in two independent patient cohorts, thus enabling optimal treatment decisions and informing personalized therapeutic strategies in mCRPC.