Seminal Plasma Metabolomics Reveals Lysine and Serine Dysregulation as Unique Features Distinguishing Between Prostate Cancer Tumors of Gleason Grade 6 and Gleason Grade 7

**Oluyemi Falegan**, Author, **Biochemistry and Molecular Biology, Cumming School of Medicine, University of Calgary, Calgary, Alberta, T2N 4N1**

Presenting Author

**Keith Jarvi**, Coauthor, **Division of Urology, Department of Surgery,, University of Toronto, Toronto, Ontario, M5T 1P5**

**Hans Vogel**, Coauthor, **Department of Biological Sciences, University of Calgary, Calgary, Alberta, T2N 1N4**

**Eric Hyndman**, Coauthor, **Department of Surgery, Cumming School of Medicine, University of Calgary, Calgary, Alberta, T2N 4N1**

Background Prostate cancer (PCa) is a metabolic disease and the fifth leading cause of cancer-related deaths worldwide in men. Most men are diagnosed with low grade indolent disease and differentiating these men from those who have life threatening cancer is a challenging but important clinical dilemma. There are currently limited biomarkers that can distinguish between the indolent Gleason grade 6 and higher-grade disease. Moreover, some individuals initially diagnosed with low grade disease progress to higher grade disease. Currently prostate biopsies are the only reliable methods of stratifying risk, but biopsies can cause significant morbidity, sample only a small portion of the gland and are costly. Therefore, biomarkers distinguishing between indolent and aggressive patterns of PCa are urgently required to minimize biopsy-associated morbidity, prevent over-treatment of indolent PCa and to better stratify patients for appropriate treatment.

Methods Seminal fluid samples were collected from normal individuals (n=13) prior to infertility treatment and histologically confirmed prostate cancer patients (n=51). The metabolomics technique, 1H Nuclear Magnetic Resonance spectroscopy and Orthogonal Partial Least Square Discriminant Analysis multivariate statistical analysis were used to compare the populations.

Results Alterations in amino acids levels, specifically lysine and serine and changes in glycolytic intermediates were the most significant metabolic features associated with differences between healthy controls and prostate cancer and between Gleason grade 6 (GS6) and Gleason Grade 7 (GS7) samples. OPLS plots discriminated healthy controls from prostate cancer samples (R² = 0.54, Q² = 0.31; AUC= 0.96), and GS6 from GS7 samples (R² = 0.62, Q² = 0.49; AUC= 0.98) based on lysine and serine content.

Conclusions This study suggests that seminal plasma metabolomics profiling of seminal fluid is a promising means of differentiating indolent from aggressive disease. Particularly, lysine and serine levels may be able to differentiate Gleason grade 6 from Gleason grade 7 disease.

Funding This study was supported by the Johnson & Johnson Alberta Health Innovation Partnership (JAHIP).