

## Prostate cancer (PCa) candidate biomarkers identified by proteome profiling of formalin-fixed and paraffin-embedded PCa tissue sections

<sup>1</sup>Sofia Lage Vickers, <sup>1</sup>Alejandra Paez, <sup>1</sup>Juan Bizzotto, <sup>1</sup>Maria Pia Valacco,<sup>2</sup>Nora Navone, <sup>1</sup>Elba Vazquez, <sup>1</sup>[Geraldine Gueron](#)

<sup>1</sup>Department of Biological Chemistry, FCEN, University of Buenos Aires, IQUIBICEN-CONICET, Buenos Aires, Argentina; <sup>2</sup>Department of Genitourinary Medical Oncology, The University of Texas, M.D. Anderson Cancer Center, Houston, TX

**Background:** Although it is well known that prostate cancer (PCa) is a progressive disease involving multiple gene alterations, little is known at the proteome level. Most of the functional information of the cancer-associated genes relies in the proteome, an exceptionally complex biological system involving several proteins that function through dynamic protein-protein interactions and post-translational modifications.

**Methods:** To identify potential PCa protein biomarkers, we carried out an in depth proteomic analysis (ESI-MS/MS) using human PCa and BPH tissue. Samples were obtained using phase-transfer surfactant-aided extraction/tryptic digestion of formalin-fixed and paraffin-embedded sections mounted on microscope slides. Data analysis was based on label-free spectral counting.

**Results:** We identified, 1331 and 1239 proteins in PCa and BPH tissue proteomes respectively. 71 proteins were present in at least 50% of PCa samples and not in BPH samples, while 122 proteins were present in at least 50% of BPH samples and not in carcinoma samples. To identify gene ontology classifications, we utilized DAVID database. The top cellular localization annotations of proteins identified within PCa tissue samples were cell surface, extracellular, or membrane-bound. The majority of proteins were functionally annotated as either being protein binding or as having catalytic activity. Finally, the top biological processes of the proteins were metabolic processes, regulation of biological processes and RNA processing. In order to prioritize candidate markers for PCa, we compared the differential protein expression based on normalized spectral counts between tissue samples. We set as cut-offs proteins that were found with a minimum of three peptides within our PCa proteomes. This filter resulted in the selection of 11 proteins. The list contained proteins that were previously studied in the context of prostate cancer progression, including SSBP1, GDF15, NDRG1, C4A & APOE, thus providing further confirmation for the robustness of our quantification method. We next subjected our candidate list to bioinformatics analysis (*OncoPrint*). Accordingly, the 5 proteins aforementioned were significant up-regulated (fold change >1.5, P<0.05) in prostate adenocarcinoma vs. normal prostate gland. Whole exome analysis (*cBioportal*), revealed amplification as the most frequent genetic alteration and RNASeq data also confirmed a significant up-regulation for these proteins (P<0.05).

**Conclusion:** We hereby report and offer a new set of biomarkers in addition to the existing diagnostic tests that could significantly improve sensitivity and specificity in PCa diagnosis.

Conflict of Interest: none

Funding Acknowledgements: Prostate Cancer Foundation, University of Buenos Aires, National Scientific and Technology Agency (Argentina), CONICET.