

Larriba S.¹, Barceló M.¹, Castells M.², Mercadal M.¹, López O.³, Bassas L.³, Vigués F.²

¹Bellvitge Biomedical Research Institute (IDIBELL), Human Molecular Genetics Group; Genes, Disease and Therapy Program, Barcelona, Spain,

²Bellvitge University Hospital-ICS, Dept. of Urology, Barcelona, Spain, ³Fundació Puigvert, Laboratory of Seminology and Embryology, Andrology Service, Barcelona, Spain

Introduction & Objectives: Prostate cancer (PCa) is the second most common cancer in men. Current biomarkers for early diagnosis and prognosis of PCa are insufficient and diagnosis is mainly based on the practice of tissue biopsies. Some molecular studies showed altered expression levels of miRNAs in prostate tumour tissue compared with normal controls. Interestingly, seminal plasma (SP) contains an extraordinary concentration of miRNAs, some of them specific to the reproductive glands that originate it, such as the prostate.

Objective: To determine if the quantification of miRNA expression levels in the seminal plasma would help to identify patients with cancer as a predictive test.

Materials & Methods: Seminal specimens from 29 individuals who presented moderately elevated PSA levels (4-18ng/ml): 24 were diagnosed with PCa and 5 with benign prostatic hyperplasia (BPH) (biopsy-proven). Fertile normozoospermic individuals were included as control group and vasectomy was taken into account given the growing number of individuals undergoing this contraceptive technique: five men were vasectomised individuals (Hct-V), and 9 were non-vasectomised normozoospermic individuals (Hct-noV). The semen was centrifuged to remove the cells and cell debris. The RNA was isolated from the total SP (miRCURY RNA Isolation kit-cell & plant). The expression of 9 miRNAs was analyzed (one of them was used as a normalizer) by RT-qPCR using the miRCURY LNATM Universal RT miRNA kit (Exiqon) and the Lightcycler 96 (Roche). The relative expression values were determined by the 2^{ddCq} strategy. For the statistical analysis of evaluation of differences between groups, the nonparametric Mann-Whitney test was used. Multivariate binary logistic regression and receiver operating characteristic (ROC) curve analysis of normalized data was used to distinguish the samples showing malignancy of prostate tumour.

Results: Our results evidenced that altered miRNA expression in PCa tissue can be also detected in seminal fluid. Six out of the 8 miRNAs analyzed in this study presented statistical differences between Hct and PCa samples. Additionally, the expression values of 4 out of the 8 miRNAs resulted in good predictive accuracy to discriminate the presence of malignant tumour in the prostate from the absence of the tumour. A multivariate model could be helpful to improve the non-invasive diagnosis of PCa, saving unnecessary biopsies.

Conclusions: We propose that single or multivariate models based on differentially expressed miRNAs in the semen may be suitable non-invasive biomarkers for predicting PCa or associated complications.