A novel biomarker panel for active surveillance of prostate cancer patients

- Bachelor's Thesis -

Bachelor's Degree in Biochemistry and Molecular Biology

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"Nothing in life is to be feared, it is only to be understood.
Now is the time to understand more, so that we may fear less."

Marie Curie

Abstract

Prostate cancer (PCa) is the second most detected cancer in men, and the eighth leading cause of cancer death worldwide. Active surveillance is a viable option PCa management and, according to recent studies, positively impacts patient quality of life without worsening treatment outcomes. However, conventional clinical biomarkers are insufficient for accurately differentiating between indolent and aggressive PCa, with tissue biopsies being an invasive and costly requirement.

Due to its non-invasive and affordable nature, liquid biopsy has the power to improve PCa patients' monitoring, reducing the number of repeated biopsies and the total costs of active surveillance. Recent findings from the DIBIOMEC group have demonstrated that levels of sTWEAK and exomiR-X in semen can be potential biomarkers for PCa prognosis.

Hence, this project aims to determine whether a biomarker panel composed of the cytokine sTWEAK and the exomiR-X measured in semen, can be used as a prognostic tool for PCa patients under active surveillance. For that, a retrospective study including 51 PCa patients was designed, where participants were re-classified into two groups: *Upgrading* and *No Upgrading* according to the result obtained from their confirmation biopsy. Semen levels of sTWEAK were determined by ELISA technique and exomiR-X was quantified by RT real-time qPCR.

Preliminary results indicate that a biomarker panel including PSA density, Percentage of positive biopsy cores, sTWEAK levels in semen, exomiR-X expression levels in semen, and tumour detection by nuclear magnetic resonance (NMR) can accurately classify 87.2% of PCa patients in *Upgrading* / *No upgrading*. It outperforms classical biomarkers such as total PSA, thus improving the clinical management of PCa patients under active surveillance. These findings indicate that molecular markers (sTWEAK and exomiR-X) have great potential to boost the model's stratification power, improving its sensitivity. Further studies with larger cohorts will be necessary to validate the proposed panel utility.

In addition, we also identified potential target genes under the control of exomiR-X. These in silico targets include argonaute RISC component 1 (*AGO1*), argonaute RISC catalytic component 3 (*AGO3*), calmodulin 1 (*CALM1*), calmodulin 2 (*CALM2*), and ubiquitin A-52 residue ribosomal protein fusion product 1 (*UBA52*), all involved in cellular processes such as Wnt signalling, Rho GTPases signalling, and gene expression control. Further experiments are needed to experimentally validate the involvement of exomiR-X in PCa progression.

Keywords: prostate cancer, active surveillance, liquid biopsy, sTWEAK