



The Potential of exosomal RNAs as biomarkers for Prostate Cancer

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Abstract

Prostate cancer (PCa) is currently the most diagnosed cancer of Australian men, and the incidence is likely to keep increasing given our ageing population. Compounding this issue is the fact that the available tests are either discouragingly invasive, or lacking in specificity/sensitivity and offer no prognostic information. To overcome these issues we have been profiling the RNA content of exosomes isolated from PCa cell lines and patient body fluid samples including urine, plasma and saliva and have developed a miRNA signature for the diagnosis of early PCa. The large bodies of data also afforded an opportunity to probe the functional potential of exosomal RNAs. This was done using *in silico* methodologies as well as some experiments regarding the role of PCa exosomal RNAs in the tumour microenvironment.

Urine exosomal miRNAs (exomiRs) provided the most robust diagnostic signature found during this project. They also hold some potential as prognostic and treatment response markers for PCa. Furthermore, urinary exomiRs can be harvested from patients in a non-invasive manner which is a significant step forward in the clinical care of PCa. The expression profile of urine exomiRs will be investigated in future experiments on much larger sample sizes to confirm the diagnostic and prognostic potential highlighted by this project. ExomiRs may also have roles in PCa immune evasion with the potential to inhibit the tumour killing and proliferative abilities of cells within the immune system, most likely natural killer cells and dendritic cells. This work needs further biological validation in future experiments. PCa exosomes were also shown to be potent inducers of myofibroblast transdifferentiation which suggests that PCa exosomes are in part responsible for metastatic progression of the disease. However, PCa exomiRs do not appear to be absorbed by recipient cells and do not impact the process of myofibroblast transdifferentiation.