Detection of clinically informative circulating mRNA biomarkers for Prostate Cancer Prognosis Using an ISFET Lab-On-Chip Platform

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Background

Prostate cancer (PCa) is the second most common cause of male cancer-related death worldwide. The gold standard of treatment for advanced PCa is androgen deprivation therapy (ADT). However, eventual failure of ADT is common and leads to lethal metastatic castration-resistant PCa. As such, the detection of relevant biomarkers in the blood for drug resistance in metastatic castration-resistant PCa patients could lead to personalized treatment options. mRNA detection is often limited by the low specificity and high cost of qPCR assays which are restricted to specialized laboratories.

Methods

Loop-mediated isothermal amplification (LAMP) is an amplification technique that can be performed at one temperature (60 - 65oC). Ion-sensitive field-effect transistors (ISFETs) can detect the rate of pH change, when protons are released during an amplification event. In combination, these techniques can be utilised as a handheld device where the biosensor output can be recorded using, e.g., a mobile phone.

Results

Here, we present a novel reverse-transcription loop-mediated isothermal amplification assay and demonstrated its capability for sensitive detection of PCa relevant mRNA targets including androgen receptor (AR) and YAP1, to 3×10^1 RNA copies per reaction. We demonstrate correlation with the gold standard for mRNA quantitation, qRT-PCR. Validation of this technique was conducted with rapid detection (<15 min) of extracted RNA from prostate cancer cell lines 22Rv1s and DU145s. We also demonstrate its utility in plasma from a cohort of men with locally advanced and metastatic disease. Finally, we demonstrate the ability to combine both assays on a single Lab-on-Chip platform.

Conclusions

This work presents a foundation for the detection of diagnostic, prognostic, predictive and monitoring circulating mRNA biomarkers in PCa on a minimally-invasive lab-on-chip device for use at the point-of-care.

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