Tracking the Resistance: Liquid biopsy monitoring of drug resistance in metastatic prostate cancer

Summary

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Supervisor:	PD Dr. Amin El-Heliebi
Availability:	This position is available.
Offered by:	Medical University of Graz
Application deadline:	Applications are accepted between February 04, 2019 00:00 and March 31, 2019 23:59 (Europe/Zurich)

Description

Background:

Prostate cancer (PC) remains one of the most common malignant cancer in men with a high mortality rate causing more than 90 000 deaths each year in Europe. Prostate cancer is linked to a dysregulation of the androgen receptor (AR) signaling pathways. Treatment involves androgen deprivation therapy (ADT) with drugs targeting the AR signaling pathways (1). Although promising results are obtained, virtually every patient develops a resistance to androgen deprivation therapy (2). The causes for therapy resistance are diverse and may include several molecular alterations of the tumor such as androgen receptor alterations. To improve individual treatment decision, tumor biopsies should be performed to investigate the underlying tumor biology. But this option remains clinically impracticable due to its invasive nature and potential burden for the patient. A promising possibility to obtain the molecular characteristics of a tumor in real-time is the analysis of liquid biopsies. Liquid biopsies include cell-free circulating tumor DNA (ctDNA) and circulating tumor cells (CTCs) which are released from the tumor sites into blood circulation (3-6). Both sample sources are potential surrogate markers for the tumor and may thereby inform of therapy resistance in real time.

Although promising, the dynamic changes of AR-alterations during the course of treatment are yet poorly understood. Without the knowledge of the dynamic changes there is no optimal treatment algorithm strategy for PC drugs available. There is a critical need to monitor the dynamic changes of the resistance causing AR-alterations over the course of treatment.

Hypothesis and Objectives:

Our overall hypothesis is that resistance mechanisms in prostate cancer are dynamically changing during the course of treatment and these changes predict sensitivity or resistance to androgen receptor targeting agents. We therefore aim to monitor these resistance mechanisms using liquid biopsy approaches. This may yield novel insights into how a tumor is able to evade cancer therapies.

Methodology:

- Isolation of circulating tumor cells and circulating nucleic acids from cancer patients
- Next generation sequencing (NGS)
- *In situ* padlock probe technology
- Multiplexed immunohistochemistry
- Image analysis (CellProfiler)
- Single cell analysis
- Real-Time qPCR approaches
- And many more

References:

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