Precision systems medicine in urological Tumors: Molecular profiling and functional testing

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Background: Most precision cancer medicine efforts are based on the identification of oncogenic driver mutations by genome sequencing. We believe and have emerging evidence that this will miss therapeutic opportunities and additional technologies, such as cell-based functional testing should be included. Pioneering studies in leukemia indicate the value of ex-vivo drug testing to identify novel, clinically actionable therapeutic opportunities.\(^3\)

Methods: Using conditional re-programming technology, we established patient-derived cells (PDCs) from castration-resistant prostate cancer (CRPC)\(^3\) and renal cell cancer (RCC) in order to pilot precision systems medicine in solid tumours. The PDCs were compared with primary tumour tissue by genomic profiling and then subjected to drug sensitivity profiling with >306 approved and investigational oncology drugs.

Results: Here, we generated both benign and malignant PDCs from prostate tissue, including six benign PDCs that were androgen receptor (AR)-negative, basal/transit-amplifying phenotype, but could re-express AR in 3D-culture. The PDCs from a CRPC patient displayed multiple CNAs, some of which were shared with the parental tumor.\(^2\) The cancer-selective drug profile for these PDCs showed sensitivity to taxanes, navitoclax, bexarotene, oxaiplatinum and mepacrine.\(^3\)

Our aim is to generate molecular profiles and drug testing data using representative PDCs from each patient to help clinicians in treatment decision and to facilitate the early selection of the best drug candidates for clinical development. We believe this approach will help to personalize treatment, prioritize drugs for clinical testing, provide for intelligent selection of drug combinations and improve treatment outcomes.

Legal entity responsible for the study: University of Helsinki

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Reference: