Circulating Platelets
A Novel Liquid Biopsy Source for Cancer Diagnostics and Therapy Stratification

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Akademisk avhandling

som med vederbörligt tillstånd av Rektor vid Umeå universitet för avläggande av filosofie doktorsexamen framläggs till offentligt förvar i Sal 933, 9 trp, byggnad 3A,
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Avhandlingen kommer att försvaras på engelska.

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Abstract

As conventional tissue biopsies have several drawbacks, much effort has been directed toward the development of minimal-invasive liquid biopsy platforms for detecting and profiling cancer. Platelets are the second most abundant cells in blood and have very versatile functions both in physiological and pathophysiological conditions. When exposed to tumors and their environment, platelets exchange biomolecules with tumor cells changing the platelets' RNA profile, resulting in tumor-mediated education of the platelets. Our research group and collaborators have previously shown that platelets sequester material while in circulation and with that ability accumulate cancer specific information. Platelet RNA profiles or detection of tumor-derived biomarkers within them may provide insight into ongoing cancer-related processes in a patient, allowing for implementation of personalized therapy strategies.

This thesis evaluates whether circulating platelets could have a potential role (as a liquid biopsy source) in cancer diagnostics, therapy stratification, and monitoring of the disease. Gene expression analysis using digital droplet PCR and RNA-sequencing were the main methods used to address this. Prostate Cancer is the main model used in this thesis but this platform is applicable to other tumor types such as colorectal-, breast-, and lung cancer.

We found platelets of cancer patients to contain tumor-derived information enabling selection of biomarker panels discriminating early stage cancer patients from healthy individuals as well as therapy responders from non-responders with high accuracy. The RNA transcript within the platelets was more informative in regards to therapy stratification compared to circulating free DNA of matched patient samples, in which genomic changes were analyzed. Combining both increased the accuracy in predicting therapy outcome.

Platelets show usefulness as a novel liquid biopsy source for early detection and individualizing patient therapy decisions (for personalized medicine). The techniques used are promising but large-scale validation is necessary.

Keywords
platelets, biomarkers, liquid biopsy, therapy stratification, PCa, tumor educated platelets, RNA, companion diagnostics, personalized medicine