Fraunhofer IZI

Fraunhofer Institute for Cell Therapy and Immunology IZI

Liquid Biopsy

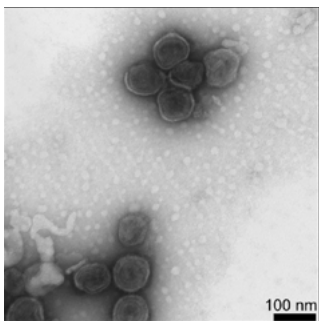
Project group

Liquid biopsy is a diagnostic method in which circulating biological material is extracted from bodily fluids to be analysed for molecular biomarkers. It is a non- to minimally invasive method, requiring only a few millilitres of fluids to be collected, and it can be frequently repeated to obtain continuous information. Conventional solid tissue biopsies are nonetheless regarded as the current gold standard. However, due to its inherent invasiveness and associated risks, its execution is limited to a few time points and it does not allow for a full evaluation of the pathological tissue.

These issues can be overcome by liquid biopsy. The informative source can range from single molecules such as cell free DNA to complex entities such as circulating tumour cells or extracellular vesicles. Liquid biopsy can be advantageous for early diagnostic and patient stratification. But it also enables a more frequent assessment of patient status and therapy response, thereby allowing therapy efficacy evaluation and appropriate adjustments.

Our group focuses on liquid biopsy for extracellular vesicles (EVs) and its application on a point-of-care microfluidic device. EVs are cell-derived, membraneous particles of sub-micron diameter present in virtually all bodily fluids. They are ideal candidates for diagnostics based on their ability to carry numerous biomarkers related to the state of the cell at the point of secretion. Additionally, the molecular information is protected by the lipid bilayer of the vesicle. To obtain disease- or tissue relevant information, it is, however, necessary to specifically isolate disease-derived EVs from complex samples, such as urine or blood plasma, to probe them for markers of

Transmission electron microscopic image of EVs.



interest, whether by functionalised beads, liquid phase assays or lateral flow immunochromatographic assays.

Next to the diagnostic approach by the use of EVs, another goal is the early detection of the cytokine release syndrome (CRS). It is a systemic life-threatening process characterised by elevated levels of circulating pro-inflammatory cytokines and immune effector cells due to an overreaction of the immune system caused by infections (COVID-19, sepsis, e.g.), cancer or treatments such as CAR-T cell transplants. CRS is frequently correlated with poor prognosis and requires fast diagnosis and therapy to circumvent permanent damages.

Pathologies associated with higher longevity such as oncological or neurodegenerative diseases are an increasing societal burden. Liquid biopsies' earlier detection potential and ease of follow-up for targeting therapies can play an important role in diminishing this load while improving the quality of life of patients, which is the ultimate goal of our group.

We share our expertise with partners in the following areas

- General and specific EV isolation from cell culture medium and bodily fluids (ultracentrifugation, size exclusion chromatography, density gradient centrifugation, immunoaffinity)
- Characterisation of EVs (western blot, nanoparticle tracking analysis, electron microscopy)
- Spotting and analysis of molecules on planar surfaces
- Antibody microarray analysis of surface molecules on EVs
- Assay integration in microfluidic devices
- Lateral flow immunochromatographic assay development

Our completed and recent projects in Liquid Biopsy

- NanoCapture – Selective capture and multiplex analysis of prostate cancer-derived EVs
- BrainLab – Automated, targeted isolation of neural EVs with magnetic beads for protein and RNA analysis from Alzheimer's disease patient samples
- KODIAK – Microfluidic assay integration for early detection and monitoring of cytokine release syndrome in a sensitive point-of-care optical reader

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