Circulating EVs for AML minimal residual disease biomarkers detection

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Aim: We propose to evaluate the feasibility of a peripheral blood EV-based liquid biopsy method for AML disease monitoring in real time with molecular precision.

Introduction: Acute myeloid leukemia (AML) is a hematopoietic stem cell disorder with high mortality rate mainly due to the high frequency of post-treatment relapse. Minimal residual disease (MRD) determination in AML patients receiving treatment is useful to assess chemotherapy response and predict relapse. One approach to upgrade the current invasive MRD monitoring (traditionally based on bone marrow aspirates/biopsies) is to use methods that identify cancer-associated biomarkers in patients' blood. Recently, extracellular vesicles (EVs) have been increasingly recognized as a potential source of biomarkers, since the levels of EVs are markedly increased in cancer patients' blood and those EVs potentially carry molecular signatures associated with specific cancer phenotypes.

Methods: The profile of EVs isolated from AML patients' blood plasma collected from paired AML diagnostic and complete remission samples is being compared and correlated with clinical data. A size-exclusion chromatography (SEC) method was optimized to isolate the plasmatic EVs. The EVs profile is then characterized according to their size, plasmatic concentration, morphology and protein content.

Results: EVs with decreasing size were successfully isolated between SEC fractions 3 to 6, with a size ranging from 300 nm to 30 nm, respectively. Fraction 7 presented the smaller EVs, although mixed with some plasmatic protein contaminants. The expression of EV markers such as CD63, HSP70 or Syntenin-1 was confirmed and allow to distinguish EV subpopulations between fractions 3 to 7. The expression of leukemia-specific markers is currently being studied in the EVs isolated from the paired AML blood samples.

Conclusion: The presented EV-based liquid biopsy proposed method for AML monitoring could unravel biomarkers for diagnostic and prognostic purposes in AML patients.

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