Detection of minimal residual disease in acute myeloid leukemia using microfluidics

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Background & objectives

Acute myeloid leukemia (AML) is the most common form of leukemia in adults and characterised by the accumulation of immature myeloid progenitors in the bone marrow, interfering with the normal production of blood cells. Unfortunately, disease relapse is very frequent (~80%) in older patients who had achieved complete remission after treatment, due to the persistence of residual malignant cells that remain undetectable, a condition called minimal residual disease (MRD). An earlier and accurate diagnosis of MRD would allow for a more accurate assessment of prognosis and a better follow-up of the patients. Nevertheless, conventional technologies used for the diagnosis of AML present several limitations in an MRD scenario, including poor sensitivity. Recently, microfluidics has demonstrated to be a powerful tool for rare cell isolation, hence potentially capable to overcome the sensitivity limitations of conventional diagnostic tools.

The main goal of this work was to develop a microfluidic system for the enrichment of leukemic blasts from different body fluids based on positive immune-selection.

Methods

The protocol for blast enrichment was developed and optimised testing different parameters, including different geometries, functionalisation strategies, antibodies, and flow rates. Experiments were performed spiking 200 AML cells in suspensions containing 3 million peripheral blood mononuclear cells, obtained from healthy donors, to mimic the real scenario. Once the optimal conditions were found, and the best isolation efficiency obtained, a validation of this microfluidic system was performed using clinical samples (bone marrow and peripheral blood) from AML patients. Results were benchmarked against standard analysis using flow cytometry.

Results

The best combination of parameters resulted in an average capture efficiency of 57% of the spiked AML cells. Results obtained were similar the analysis by flow cytometry.

Conclusion

The microfluidic devices developed demonstrated the ability to isolate cells at low density and small size, such as AML cells. Dowstream genetic analysis of the isolated cells can be done to obtain molecular information about the patients, and to demonstrate the utility of this system for MRD assessment and patient stratification.