Isolation and concentration of acute myeloid leukemia blasts in minimal residual disease using a microfluidic system

Alexandra Teixeira[a,b,c]
Maria Sousa-Silva[a,d], Alexandre Chícharo[a], Kevin Oliveira[a], Adriana Carneiro[a], Paulina Piairo[a], Belém Sampaio-Marques[b,c], Paula Ludovico[b,c], Sara Abalde Cela[a] and Lorena Diéguez[a]
[a.] *International Iberian Nanotechnology Laboratory (INL), Avda. Mestre José Veiga, 4715-310 Braga, Portugal*
[b.] *Life and Health Sciences Research Institute (ICVS), Escola de Medicina, Universidade do Minho, Campus Gualtar, 4710-057 Braga, Portugal*
[c.] *ICVS/3B's - PT Government Associate Laboratory, Braga/Guimarães, Portugal*
[d.] *Escola de Ciências, Universidade do Minho, Campus Gualtar, 4710-057 Braga, Portugal*
alexandra.teixeira@inl.int

Acute myeloid leukemia (AML) is characterised by the accumulation of immature myeloid progenitors in the bone marrow, interfering with the normal production of blood cells. This type of leukemia is the most common in adults and is frequently associated with poor outcomes and response to conventional therapies, particularly in older individuals[1,2]. Unfortunately, the majority of the patients that can achieve clinical complete remission after the conventional treatment ultimately relapse due to the persistence of some residual cells that remains undetectable, condition called minimal residual disease (MRD)[3]. Thus, an earlier and accurate diagnosis of MRD would allow for a better prognosis and also better follow up of the patients. Over the last years, microfluidics has demonstrated to be one of the technologies with potential to overpass the limitations of the conventional technologies. This technology is a powerful tool for the isolation and concentrations of rare cells from biological fluids towards earlier cancer diagnosis[4,5]. Thus, this work aims to develop a microfluidic system for the isolation of leukemic blasts based on positive selection. First, in order to maximise cell-to-surface interaction and consequent attachment, distinct microfluidic devices composed by micropillars with different geometries and also a herringbone were designed and fabricated. Then, for the optimisation of the microfluidic devices, some parameters were tested, including different functionalisation strategies for the immobilisation of the antibody in the surface and flow rates. AML cell lines with known concentrations were spiked peripheral blood mononuclear cells obtained from healthy donors and run through the devices. Once the optimal conditions are found and the best isolation efficiency obtained, we expect to perform a validation of this microfluidic system in a cohort of AML patients at different stages of the disease.

REFERENCES

[1] D. Fu, B. Zhang, S. Wu, Y. Zhang, J. Xie, W. Ning, H. Jiang, *Front. Immunol.* **2021**, *12*, 2010.
[2] A. M. Almeida, F. Ramos, *Leuk. Res. reports* **2016**, *6*, 1.
[3] N. J. Short, F. Ravandi, *Haematologica* **2019**, *104*, 1532.
[4] S. Ribeiro-Samy, M. I. Oliveira, T. Pereira-Veiga, L. Muinelo-Romay, S. Carvalho, J. Gaspar, P. P. Freitas, R. López-López, C. Costa, L. Diéguez, *Sci. Rep.* **2019**, *9*, 8032.
[5] H.-Y. Cho, J.-H. Choi, J. Lim, S.-N. Lee, J.-W. Choi, *Cancers (Basel).* **2021**, *13*, 1385.

FIGURES

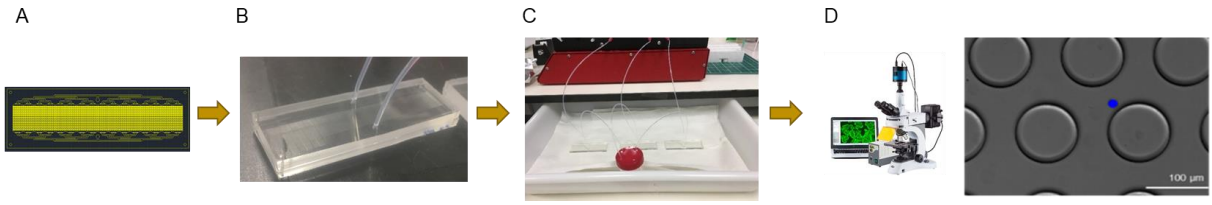

Figure 1 Overview of all process from the design to the analysis of the microfluidic devices. Design of the devices composed by pillars in the AutoCAD (A); Fabrication of the devices using a polymer (PDMS) (B); setup of the experiment during the running of the samples (cells+PBMCs) in the devices and analysis in the fluorescence microscope (D).