



MagPure chip: a microfluidic device for the purification of Circulating tumor cells and the integration in liquid biopsy workflow

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Circulating tumor cells (CTCs) have received significant attention over years for their potential clinical significance in assessing cancer diagnosis and prognosis earlier, as well as in tailoring anti-cancer therapies. Nevertheless, challenges raised by CTC rarity and heterogeneity within patient blood samples have hampered their wider use in clinical studies. To address these challenges, we report the development of an immunomagnetic-based microfluidic device, the MagPure chip [1], for the isolation and characterization of CTCs. In particular, the strategy relies on the depletion of background white blood cells (WBCs) and enrichment of CTCs (negative selection) via the integration into the MagPure chip of magnetic microstructures acting as WBC capture spots. The strength of this device relies on the fabrication and integration of permanent magnetic microstructures using the magnetic composite polymer approach [2], a straightforward and cost-effective fabrication process, which led to magnetic traps generating magnetic forces as high as several nanoNewtons. In the context of CTC sorting, the performances and biocompatibility of the MagPure chip were studied on model blood samples with spiked cancer cell lines. The MagPure chip achieved an average WBC depletion efficiency of 87% (corresponding to the average ratio of labeled WBCs) and an average CTC recovery rate of 81%. Furthermore, the MagPure chip showed compatibility with routine biological studies, including 2D and 3D cell culture, as well as phenotypic and genotypic analyses (Figure 1). Finally, aiming for a clinical context implementation, we successfully developed a two-step separation workflow for whole blood processing by combining a size-based pre-enrichment system (commercialized ClearCell FX1® system) with the MagPure chip as a subsequent purification step, thus benefitting from the advantages of both separation methods. The designed two-step workflow led to high throughput (7.5 mL blood processed in less than 4 h) and high purity, with a WBC depletion rate as high as 99.99% (947 WBCs/mL) and a CTC recovery rate of 70%. The highly purified sample thus obtained enabled downstream analysis such as long-term cell culture and phenotypic analysis, while preserving short processing time to ensure compatibility with clinical follow-up.

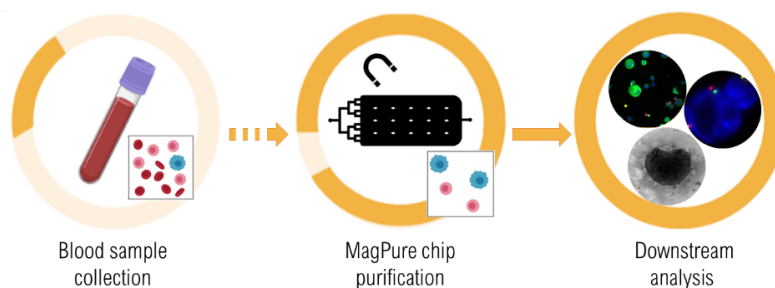


Figure 1: Liquid biopsy-based workflow for CTC isolation and analysis through MagPure chip purification

References

- [1] L. Descamps, J. Garcia, D. Barthelemy, E. Laurenceau, L. Payen, et al, *MagPure chip: an immunomagnetic-based microfluidic device for high purification of circulating tumor cells from liquid biopsies*. *Lab Chip* **22**, 4151–4166 (2022).
- [2] L. Descamps, M.-C. Audry, J. Howard, S. Mekkaoui, C. Albin, D. Barthelemy, et al., *Self-Assembled Permanent Micro-Magnets in a Polymer-Based Microfluidic Device for Magnetic Cell Sorting*. *Cells* **10**, 1734 (2021).