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Droplet microfluidic platform for extracellular vesicle isolation and handling

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Extracellular vesicles (EVs) are double-layered phospholipid vesicles having nanometric size that are rapidly gaining in popularity as biomarkers of various diseases, acting as cargoes of valuable information from the cell of origin [1]. Despite their value, their current use in clinical practice is still limited. Among the limiting factors, one of the most critical is their isolation. In fact, conventional approaches are characterized by low purity and throughput, or poor reproducibility [2]. Here, we propose a droplet microfluidic platform developed for EV isolation by affinity capture with magnetic beads [3]. This platform is capable of processing large sample volumes in a relatively short time. Systematic comparison with commercial methods proves that the platform leads to an improved EV capture efficiency of 2.5-fold. This is due to the fact that EVs and magnetic beads are co-encapsulated within the same droplet, which acts promoting their mixing [4]. The beads are extracted within the microfluidic system and collected for EV analysis. At first, the platform has been validated from the microfluidics point of view: throughput, automation and magnetic beads handling have been investigated. Then, the EV isolation capability has been performed by the most used techniques: confocal microscopy and flow-cytometry prove the presence of EVs captured on the beads, while scattering techniques and protein assays allow defining a capture efficiency. Finally, the miRNAs cargo has been quantified to verify the EV integrity. The remarkable improvements compare with monophasic microfluidic indicate how droplet microfluidics represent a suitable technology for EV isolation especially in case of clinical applications [5], where a few mL of starting sample is considered. To achieve this aim, preliminary validation using human plasma samples will be presented.
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