

A LOW-COST AND EASY TO USE SORTING DEVICE FOR THE SEPARATION OF EXTRACELLULAR VESICLES FROM COMPLEX FLUIDS

Lyne Pillemont, Daniel Guneysu, Wilfrid Boireau, Celine Elie-Caille, Anne Marie Gué

► To cite this version:

Lyne Pillemont, Daniel Guneysu, Wilfrid Boireau, Celine Elie-Caille, Anne Marie Gué. A LOW-COST AND EASY TO USE SORTING DEVICE FOR THE SEPARATION OF EXTRACELLULAR VESICLES FROM COMPLEX FLUIDS. MicroTAS 2021, Oct 2021, Palm Spring, United States. , MicroTAS 2021, 2021, The 25th International Conference on Miniaturized Systems for Chemistry and Life Sciences. hal-03514467

HAL Id: hal-03514467 https://laas.hal.science/hal-03514467

Submitted on 6 Jan 2022

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers. L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



CONTEXT

Identifying and characterizing Extracellular vesicles (EVs) in biofluids could lead to unprecedented diagnosis/prognosis assays for a wide set of pathologies. Owe to their complexity in size, origin, membrane markers, there is currently no ideal technology available yet to sort, to quantify and characterize cell-derived microvesicles, and fully relate their structure and functions which have high potential in clinical diagnostics and early treatment of life threatening diseases such as cancer, cardio vascular diseases....

SEPARATION PRINCIPLE: HYDRODYNAMIC FILTRATION

At the channel crossing, a particle flowing next to the sidewall:

- radius $< R_c \rightarrow$ flow in **lateral channel**
- radius > $R_c \rightarrow$ stay in the main channel

Advantages and drawbacks:

- \checkmark Passive method \Leftrightarrow compatible with various applications
- \checkmark Robustness \Leftrightarrow less prone to clogging than filter-based geometries
- ✓ Reliability ⇔ independent of flow and pressure drop

LAB ON CHIP: DESIGN AND MANUFACTURING

Choosing the appropriate dimensions of the channels, we designed and fabricated chips enabling the separation of vesicles at tunable cutoff (150 - 900 nm).

W	7
(µn	ſ
10)

Fabrication process: successive lamination and photolithography

Dry Film: manufacturable process by laminating dry photosensible films

- Low cost
- Compatible with micronanotechnologies
- Biocompatible

Samples preparations

• Development of NP 140 / NP 480 / NP 920 calibrators: Biofunctionalization by proteins(OVA, CAS)

- Approx. 3500 CAS / NP 140 and 17000 OVA / NP 480
- Selective trapping verification by anti-CAS and anti-OVA

NPs	Diametre	Proteins	Immunocapture	SO
NP 140	140 nm	Casein	anti-CAS	
NP 480	480 nm	Ovalbumin	anti-OVA	Bl
NP 920	920 nm	_	_	











A LOW-COST AND EASY TO USE SORTING DEVICE FOR THE SEPARATION OF EXTRACELLULAR VESICLES FROM COMPLEX FLUIDS

Lyne PILLEMONT¹, Daniel GUNEYSU², Wilfrid BOIREAU², Céline ELIE-CAILLE², Anne-Marie GUE¹ ¹LAAS-CNRS, CNRS, Université de Toulouse, Toulouse, France ²FEMTO-ST, Université Bourgogne Franche-Comté, CNRS, Besançon, France

Approach

- bio-analytical system.

We propose to couple a microfluidic device (LOC) enabling to separate particles from a complex sample to a device allowing the capture of particles on specific spots and their analysis. These methods allow obtaining important information on a chip about nanoscale vesicles in terms of size, membrane

markers expression, and structure-function properties.

device in order to provide an integrated EVs sorting and capture





EVs characterization (AFM imaging, mass spectrometry)

Blood sample: Malassez cells characterization → Same filtration rate in

Sample "filtered"

Yamada, M., & Seki, M. (2005). Hydrodynamic filtration for utilizing microfluidics. Lab on a Chip, 5(11), 1233-1239. Fouet, M., et al. "Filter-less submicron hydrodynamic size Courson, R, et al. "Low-cost multilevel microchannel lab on promising enabler." RSC Advances 4,97 (2014): 54847-

Toulouse Cancer-Health foundation for funding this work. This work was supported by the micro and nanotechnology platform of LAAS-CNRS, member of the French network RENATECH