SORTING OF EXTRACELLULAR VESICLES BY USING OPTICALLY-INDUCED DIELECTROPHORESIS ON AN INTEGRATED MICROFLUIDIC CHIP

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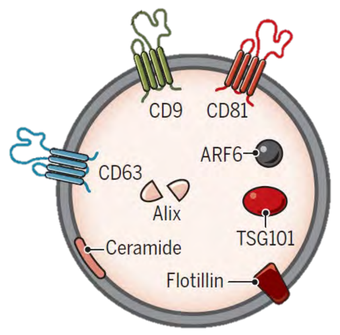
ABSTRACT

This study presents a new method to automatically sort nano-scaled extracellular vesicles (EVs) by using optically-induced dielectrophoresis (ODEP) techniques. An optimal intensity of green light at an optimal moving velocity (10 μm/sec) of the moving light patterns on an integrated microfluidic chip was explored. It successfully sorted EVs with three different sizes (small: 150 to 175 nm, middle: 175 to 200 nm, and large: 200 to 250 nm) within 30 mins. It may be useful for the diagnosis and risk assessment of cancer in the clinical applications. Moreover, the ODEP technique can provide an efficient separation method, which may be useful for understanding the bioactive roles of the EV cargos, and immunomodulatory pathways for therapeutic treatments.



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INTRODUCTION

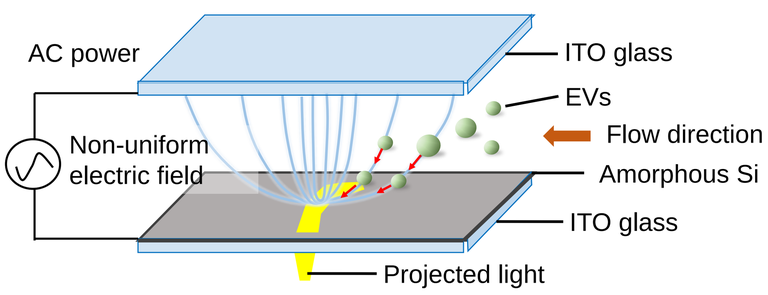


Fig.1 An illustration of EVs manipulation and separation via optically-induced dielectrophoresis (ODEP).

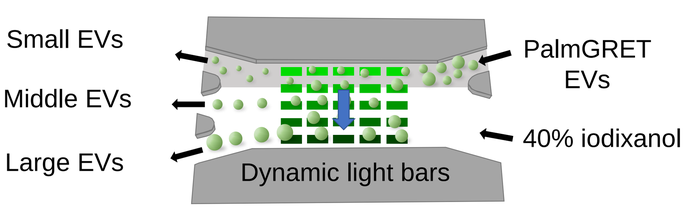


Fig. 2 An schematic diagram of size-based sorting on a microfluidic chip.

$$F_{ODEP} = 2\pi r^3 \varepsilon_m Re(f_{CM}) \nabla E^2$$

$$\underline{F}_{drag} = -6\pi\mu r \underline{v}$$

- ∇E^2 decrease ∝ intensity of light pattern
- Drag force constant ∝ velocity of light pattern
- Different size of particle

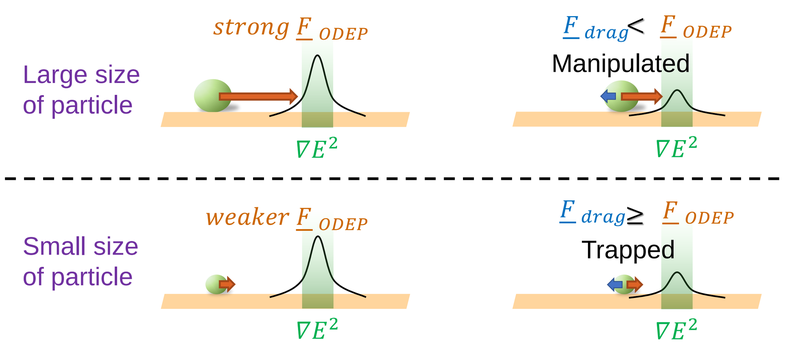
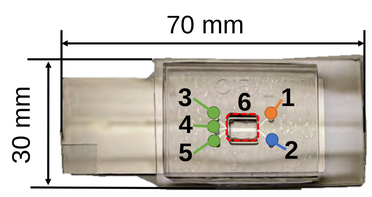


Fig. 3 Working principle of EVs size-based sorting.



1. Sample inlet
2. 40% iodixanol
3. Small EV outlet
4. Middle EV outlet
5. Large EV outlet
6. ODEP operation area

Fig. 4 A photograph of a prototyped chip (70 mm x 30 mm)

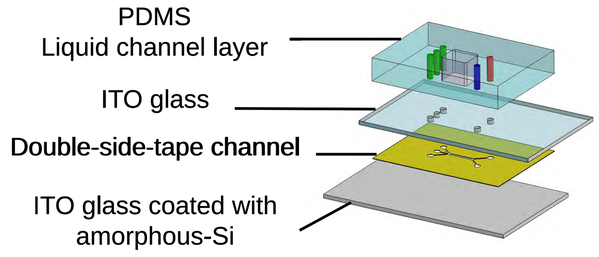


Fig. 5 Exploded view of the OIES platform.

RESULTS

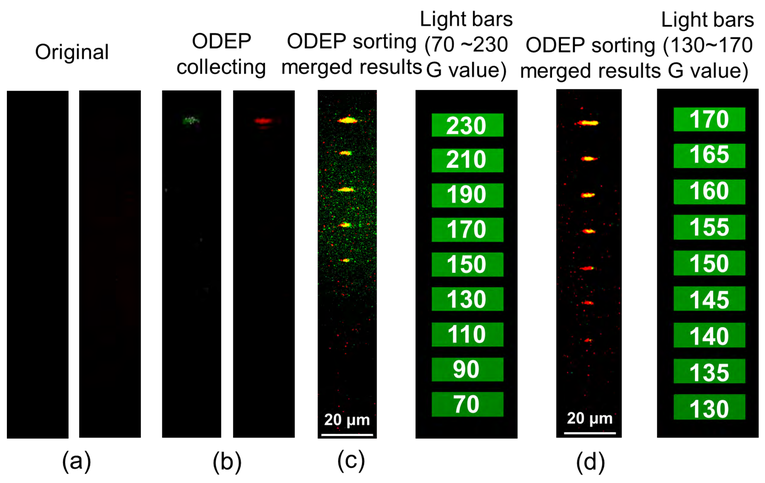


Fig. 6 Optimal light intensity for EVs sorting.

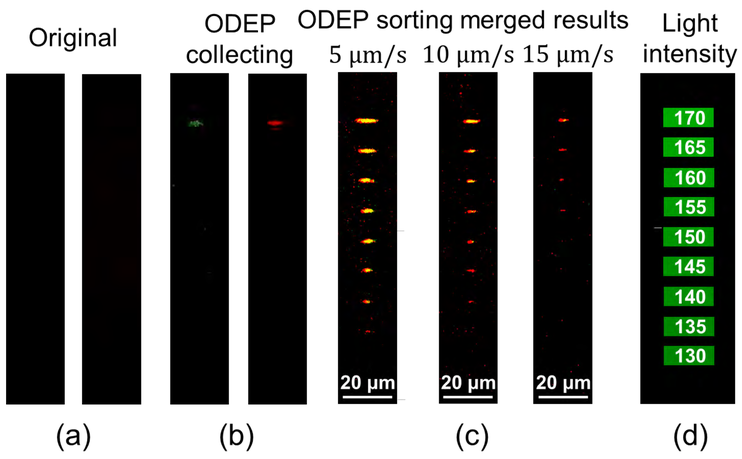
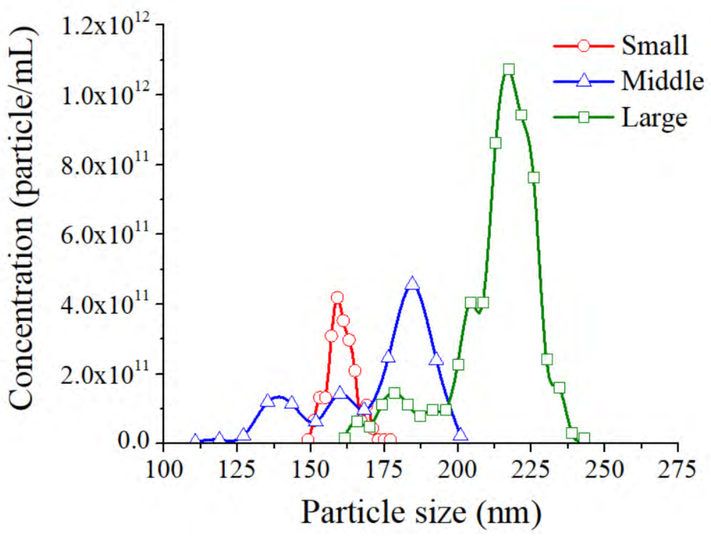


Fig. 7 Optical light velocity for EVs sorting.



Sorting ratio

$$= \frac{\textbf{target EVs sorted}}{\textbf{total of target EVs detected}} \textbf{ x 100\%}$$

Small	150-175 nm	99.5%
Middle	175-200 nm	62.6%
Large	200-250 nm	82.9%

Fig. 8 qNano (TRPS) measurement results of the sorted EVs from three different outlets. The average sorting efficiency is 81.68%.

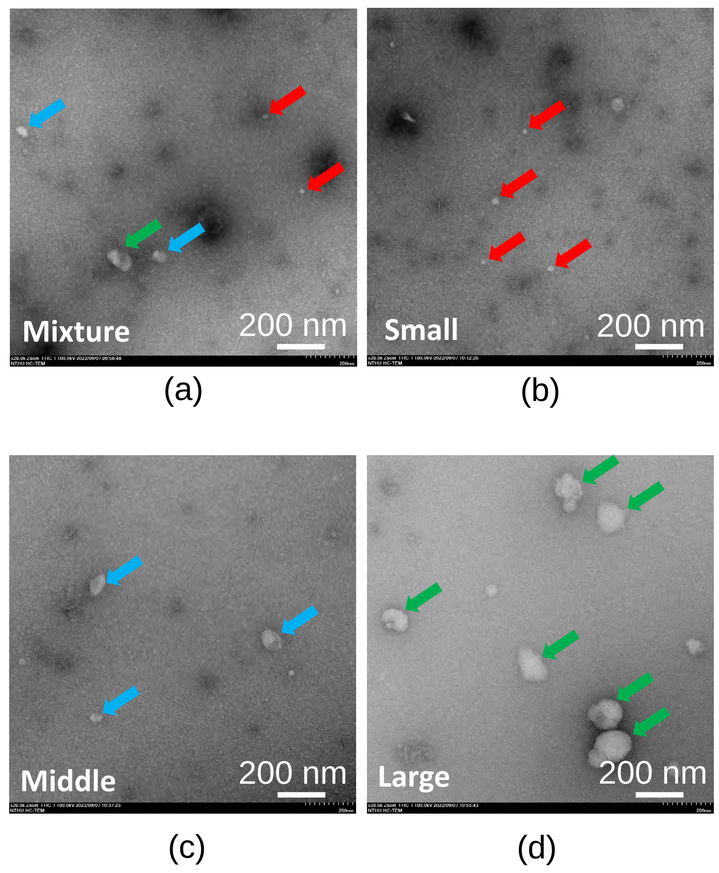


Fig. 9 TEM images of sorted EVs. The average diameters of small (b), middle (c) and large (d) sizes were around 43, 85, and 186 nm, respectively.

CONCLUSIONS

- ✓Automatically EVs sorting by an ODEP-based integrated microfluidic system.
- ✓Successfully sorted three sizes of nano-scaled EVs.
- ✓The entire process was finished within 30 min.
- ✓Sorting ratios were 99%, 63%, and 83% for small, middle and large Evs.

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