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A Microfluidic-Based Approach to Generate Cell-Derived Nanovesicles for In Vivo Transport and Delivery of Therapeutic Materials

Different drug delivery agents, including synthetic polymers, virus-based vectors, lipid-based vectors, and extracellular vesicles (EVs), have been explored previously. EVs are promising nanovesicles to deliver therapeutic drugs, vaccines and therapeutic nucleic acids such as microRNAs because these vesicles can be functionalized using targeted ligands to selectively deliver to a particular cell type in the body. However, to date, their clinical translation is limited by insufficient quantities production, size heterogeneity, and poor drug or small RNA loading efficiency.

To address these issues, Stanford researchers have developed a scalable microfluidic platform that can load therapeutic materials while controlling the size of microfluidically-processed EVs (mpEVs) using a pressure-based disruption and reconstitution process.

Stage of Development
Pre-clinical: in vivo validation in mice

Applications

- MicroRNA delivery
- Dendritic cell vaccine delivery
- Small molecule drug delivery
- Contrast Imaging: reconstructed microbubbles for targeted vascular contrast imaging

- Cancer
- Infectious Diseases
- Inflammation
- Brain diseases beyond blood-brain barrier (BBB crossing)

Advantages

- Uniform Size EVs
- Biocompatible
- Non-toxic
- Simple and reproducible technique
- Can generate a wide variety of biomimetic cell membrane vesicles
- Customized vesicles for personalized therapy
- Easy to use
- types of cargo: DNA, RNA, protein, drugs, imaging probe

Publications

- Jugniot, N., Dahl, J. J., et al. (2022). Immunotheranostic microbubbles (iMBs)-a modular platform for dendritic cell vaccine delivery applied to breast cancer immunotherapy. Journal of Experimental & Clinical Cancer Research, 41(1), 299.
- Jugniot, N., Massoud, et al. (2022). Biomimetic nanobubbles for triple-negative breast cancer targeted ultrasound molecular imaging. Journal of Nanobiotechnology, 20(1), 267.
- Liu, Y., Sukumar, et al. (2021). Camouflaged Hybrid Cancer Cell?Platelet Fusion Membrane Nanovesicles Deliver Therapeutic MicroRNAs to Presensitize Triple?Negative Breast Cancer to Doxorubicin. Advanced functional materials, 31(41), 2103600.
- Bose, R. J., Kumar, U. S., et al. (2022). Engineered Cell?Derived Vesicles Displaying Targeting Peptide and Functionalized with Nanocarriers for Therapeutic microRNA Delivery to Triple?Negative Breast Cancer in Mice. Advanced healthcare materials, 11(5), 2101387.
- Wang, K., Kumar, U. S., et al. (2021). A microfluidics-based scalable approach to generate extracellular vesicles with enhanced therapeutic microRNA loading for intranasal delivery to mouse glioblastomas. ACS nano, 15(11), 18327-18346.

Patents

- Published Application: WO2023064555
- Published Application: 20240408033

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