# Microfluidic production of biomimetic liposomes for personalized therapy of metastatic melanoma

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Nanoparticles (NPs) modified by cell membranes represent an emerging biomimetic platform that can mimic the innate biological functions resulting from the various cell membranes in biological systems. Many research investigations have demonstrated the potential utility of biomimetic NPs in the treatment of cancer. As a simple and effective approach, delivery vehicles consisting of cell membranes are extensively researched and found to have various merits, such as prolonging the circulation time, alleviating immunogenicity, and accomplishing active targeting [1].
In this study, we investigated the use of microfluidic technology to produce biomimetic liposomes (hybrid liposomes) by fusing synthetic lipids directly with cell membranes (CM) obtained from a metastatic melanoma cell line (MM) extracted from a patient biopsy material. Here, a microfluidic sonication strategy for one-step and continuous generation of liposomes and hybrid liposomes is proposed to address the challenge of breaking the CM by purely hydrodynamic forces in microchannels. (Fig. 1). Two polypropylene microfluidic devices fabricated using 3D printing technology with different geometries were tested. Due to their complex internal structures, both geometries produced high-quality monodisperse hybrid liposomes by passively mixing the two phases containing lipids and CM, respectively. [2,3].
To evaluate the best hybridization conditions, we produced three hybrid liposomes formulations starting by three different amounts of CM. First, we demonstrated the effective fusion of the CM with liposomes through dynamic light scattering, nanoparticle tracking analysis, fluorescence resonance energy transfer (FRET) and flow cytometry characterizations. To explore the homotypic targeting strategy, 2D and 3D *in vitro* uptake studies were performed, showing that the hybrid liposomes had a stronger affinity for its source MM cancer cells than for hepatocellular carcinoma cancer cell line, with an 8- fold higher cellular uptake compared with liposomes. Moreover, to candidate this biomimetic nanosystem as a potential therapeutic tool for the personalized treatment of metastatic melanoma, cobimetinib and lenvatinib, were efficiently loaded, demonstrating an in vitro higher antitumor efficacy referred to the free drugs administration.

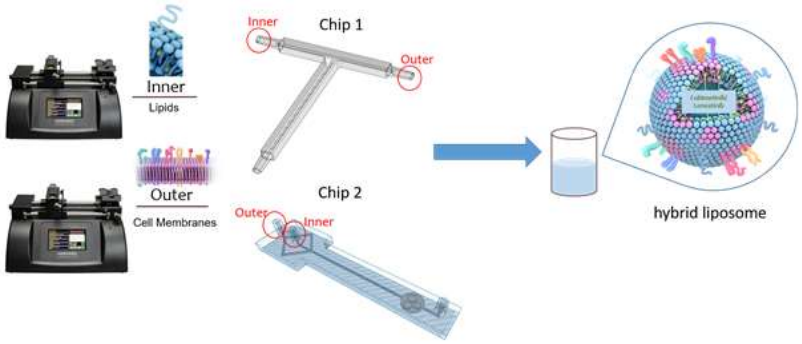


**Figure 1:** Schematic representation of setup producing hybrid liposome through microfluidics.

## References

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[2] Sommonte, F. et al., Pharmaceutics 14, 2484 (2022)
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