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Preparation and Multiscale Analytical Characterization of Nanoparticle-extracellular Vesicle Hybrids

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Despite the potentiality of nanoparticles (NPs), their effective clinical translation remains limited due to several drawbacks originating from their exogenous nature. Coating NPs with biological lipid membranes represents a promising strategy to bolster their performance in biomedical applications while preserving the properties of the core material. Current methods for achieving this coating often result in low efficiency and poor reproducibility. Here, we introduced an acoustic microfluidic device together with an analytical platform to prepare NP-lipid vesicle hybrids and characterize the hybridization. We demonstrated successful encapsulation of NPs within the lipid membrane of synthetic liposomes and natural vesicles (i.e. extracellular vesicles), improving yields and reproducibility compared to conventional encapsulation methods. The process of coating was investigated using fluorescence-based techniques at multiple levels of resolution (Förster Resonance Energy Transfer - FRET, Fluorescence Cross-Correlation Spectroscopy - FCCS, and Direct Stochastic Optical Reconstruction Microscopy - dSTORM).

Our approach has proven to be a flexible platform for producing NP-vesicle hybrids, enabling the identification of design rules to control encapsulation efficiency by tuning various parameters, such as buffer composition, NP/vesicle ratio, and vesicle rigidity