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Fusion of Magnetic Liposomes with Model Membranes and Extracellular Vesicles

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Cytosolic delivery of biomolecules remains a major challenge for vaccine development as well as for the efficacy of treatments requiring specific intracellular targeting (e.g., nucleus, mitochondria). In the context of nanotechnologies, this challenge is particularly critical, as nanoparticles typically enter cells via endocytosis and consequently become trapped within endosomes. In the specific case of magnetic nanoparticles, this endosomal confinement has significant consequences: it drastically reduces their intracellular hyperthermia efficiency and prevents their magnetic manipulation in cellulo for targeting specific organelles.

We have developed fusogenic magnetic liposomes (MFLs) capable of fusion with biological membranes. The fusion of MFLs was first investigated using acceptor liposomes with well-defined charge (anionic or zwitterionic), size, and membrane composition. Fluorescence Resonance Energy Transfer (FRET), light scattering experiments, and isothermal titration calorimetry (ITC) demonstrated that fusion is initiated by electrostatic interactions and is strongly influenced by lipid composition [1]. The transfer of magnetic nanoparticles was assessed by magnetophoresis (Fig. 1)

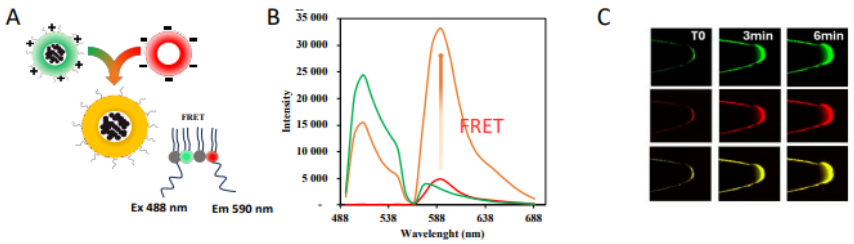

Figure 1: A) Sketch of the fusion between MFLs and acceptor liposomes. (B) FRET and (C) Magnetophoresis.

This lipid fusion strategy was also exploited to engineer extracellular vesicles (EVs), enabling the combination of the biological signature of EVs with the magnetic properties of nanoparticles within a single hybrid. Monitoring of both populations by nanoparticle tracking analysis (NTA), high-resolution flow cytometry, and transmission electron microscopy consistently revealed rapid association between EVs and liposomes, yielding hybrid structures of 100–200 nm with a Janus-like morphology. Protein assays and Western blot analysis demonstrated that the hybrids preserve canonical EV markers (CD63, CD81, syntenin) while maintaining vesicle integrity.

References

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