Camouflaging lipid particles with cell membranes for effective gene delivery to cancer cells

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The low tumor targeting of lipid nanoparticles (LNPs) limits their clinical applications in oncology as nonviral RNA delivery systems. We functionally integrated LNPs with cancer cell membrane components to enhance their targeting capabilities, exploiting cancer cell self-recognition and interactions with stromal cells in the tumor microenvironment. The biomimetic nanocarrier was developed by cloaking RNA-loaded LNPs with nanoghosts obtained from the membrane of triple negative breast cancer cells. RNA-LNPs were fabricated by microfluidics and were incorporated into nanoghosts using ultrasound-assisted fusion, yielding stable biomimetic LNPs [1]. The structure is well defined, characterized by an RNA-LNP core, preserving the internal arrangement of lipids and RNA, enveloped by a nanoghost shell, as assessed by physicochemical analyses and Small-Angle X-ray Scattering. Biomimetic LNPs displayed strong affinity for both cancer-associated fibroblasts and homotypic cancer cells, resulting in significantly improved biological activity compared to uncoated LNPs. This work provides proof of concept that RNA-LNPs can be effectively integrated into self-assembled biomimetic carriers to enable dual targeting of tumor and stromal cells. The enhanced selectivity and delivery performance of biomimetic LNPs highlight their therapeutic potential for overcoming stromal barriers in tumors such as triple negative breast cancer.

Keywords:
Lipid nanoparticles, RNA delivery, Camouflaging nanoparticles, SAXS, Heterotypic targeting

References:

[1] S. Garbujo et al. Journal of Colloid And Interface Science, 709, 139972. 2026.