Chimeric bio-hybrid liposomes for targeted therapy against Triple-Negative Breast Cancer

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Triple-negative breast cancer (TNBC) is an aggressive carcinoma driven by chemoresistant cancer stem cells (CSCs) responsible for relapse and metastasis. While cell membrane-coated nanoparticles offer a promising biomimetic strategy, their clinical translation is often hindered by low membrane yields and batch variability. To address these limitations, we developed Hybrid-MASLiN, a scalable core-shell nanoplatform featuring a bioactive solid lipid nanoparticle core composed of maslinic acid (MA). This core encapsulates the hydrophobic drug docetaxel (DTX) to enable a synergistic dual-therapy. This core serves as a versatile carrier that can encapsulate hydrophobic drugs such as docetaxel (DTX) to enable a synergistic dual-therapy (MASLiN). The MASLiN core is cloaked with a chimeric hybrid liposomal shell that co-assembles synthetic lipids with biological membrane fragments derived from CSCs and T-lymphocytes. This modular coating exploits homotypic recognition for precision targeting of aggressive tumor cells, while providing an immunomodulatory interface designed to counteract the immunosuppressive tumor microenvironment.
Successful assembly was validated via Dynamic Light Scattering (DLS) and TEM-EDX, which confirmed the presence of a phosphorus-rich lipid bilayer surrounding the electron-dense MASLiN core. Functional assays highlighted the selective profile on the nanoparticles. Hybrid-MASLiN increased cellular internalization and cytotoxicity in TNBC cells and CSCs compared to bare formulations, while exhibiting minimal uptake and no toxicity in healthy fibroblasts and T-lymphocytes. Furthermore, acute systemic toxicity studies in immunocompetent mice showed no adverse effects at high doses, supporting overall biocompatibility. By integrating the biophysical robustness of synthetic liposomes with the homing precision of biological membranes, this chimeric interface presents a promising, scalable approach to overcoming the translational barriers of biomimetic nanomedicine in refractory tumors.

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