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Email: icamm26@hcmus.edu.vn
Website : https://icamm26.hcmus.edu.vn/

Surface-Engineered Mesoporous Silica Nanoparticles as Dual-Function Nanomedicines

Author(s): Peilin Chen[1,2,*]

Institution: [1]Reseach Center for Applied Sciences, Academia Sinica, Taiwan
[2]Institute of Physics, Academia Sinica, Taiwan

E-mail: ***peilin@as.edu.tw**

Abstract: Mesoporous silica nanoparticles (MSNs) offer a uniquely tunable materials platform for therapeutic delivery because their size, pore chemistry, and surface charge can be engineered independently to control circulation, biodistribution, and cargo stability. Here we present a ligand-free MSN design built on ~25 nm PEGylated, quaternary-amine–modified MSNs that achieves targeted delivery without receptor ligands, while enabling added biofunction through surface engineering. In a brain-tumor model, ligand-free MSN25-PEG-TA exhibits prolonged circulation and enhanced penetration across the blood–brain barrier, leading to markedly increased accumulation of doxorubicin cargo in orthotopic glioma and improved survival in vivo, consistent with a protein-corona–assisted transport mechanism and efficient tumor access enabled by small particle size.

Beyond delivery, we further demonstrate that "drug-free" MSN-PEG/TA directly suppresses metastatic progression by modulating focal-adhesion signaling and angiogenic processes, reducing the burden of lung metastasis, and improving survival in xenograft models when combined with chemotherapy. Building on these materials, we introduce a pore-functionalized sulfonate MSN formulation designed to stabilize labile chemotherapeutics and to add intrinsic antimetastatic activity. Sulfonate-functionalized MSNs enable high irinotecan loading and preserve the active lactone form during storage and under physiological conditions, while providing sustained release, prolonged systemic exposure, and strong antitumor/antimetastatic efficacy with reduced systemic toxicity in metastatic colorectal cancer models.

Keywords: *Mesoporous silica nanoparticle, Nanomaterials, Advanced Biomaterials*