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Biomimetic Copper-Based Nanoplatform for Enhanced Tumor Targeting and Effective Melanoma Therapy

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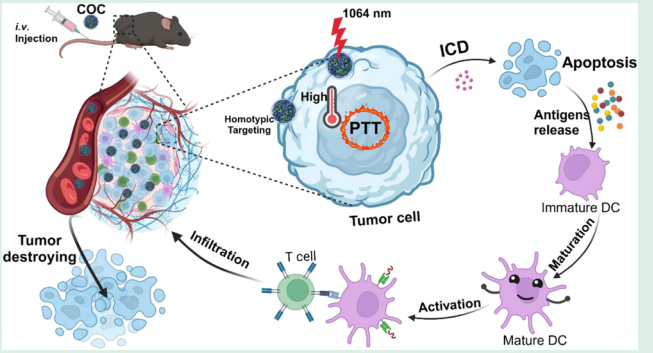
ABSTRACT: Designing advanced biomimetic nanoplatforms that combine photothermal therapy (PTT) and immune activation represents a modern approach to addressing the challenges of cancer therapy. This study presents a nanobiomimetic hollow copper-sulfide (HCuS) platform for precise homotypic tumor targeting and melanoma treatment. The HCuS@OVA@CM (COC) nanoplatform-encapsulated ovalbumin (OVA) antigen protein within HCuS nanoparticles and was coated with melanoma cell membranes (B16F10). Importantly, this design facilitates specific tumor accumulation and achieves 16.0% photothermal conversion efficiency under 1064 nm NIR-II irradiation, which is a key factor for therapeutic success. *In vitro* studies have demonstrated that this nanoplatform induces immunogenic cell death (ICD), enhances antigen presentation, and stimulates dendritic cell (DCs) maturation. *In vivo* experiments confirmed that COC-mediated NIR-II photothermal treatment significantly suppressed tumor growth without notable body weight loss. This biomimetic nanoplatform approach offers a targeted, enhanced, and effective immune response for tumor photothermal immunotherapy, making it a promising candidate for advanced melanoma treatment and anticancer therapy.



KEYWORDS: *cell membranes, hollow copper-sulfide nanoparticles, melanoma cancer, homotypic targeting, photothermal therapy, immunotherapy, combined therapy*

INTRODUCTION

Integrating photothermal therapy (PTT) and immunotherapy into multifunctional nanoplatforms is a promising strategy to overcome the limitations of conventional cancer therapies, enabling precise tumor ablation and sustained immune responses to address challenges in tumor eradication and recurrence prevention.[1] Traditional therapies like surgery, chemotherapy, and radiation often fail to achieve low toxicity and high specificity, underscoring the need for innovative, high-performance approaches.[2] Nanomedicine offers transformative potential through multifunctional nanoplatforms with adaptable features.[3] PTT, in particular, has emerged as a compelling option due to its noninvasiveness, high sensitivity, controllable laser power, and low toxicity.[4,5] It utilizes photothermal agents (PTAs) to convert light energy into localized hyperthermia, destroying intracellular biomolecules and effectively eliminating tumors.[6,7] Optimal PTT requires PTAs responsive to second near-infrared (NIR-II) lasers (1000−1700 nm), which penetrate deeply (∼10 cm) and induce localized heat under specific parameters (1064 nm, 1.0 W cm^{-2}), causing DNA damage, membrane disruption, and protein denaturation.[8,9] Inorganic NIR-II PTAs, including transition metals, noble alloys, and nonmetallic materials,[10−16] have shown therapeutic potential in inflammation reduction, tumor inhibition, and tissue repair.[17,18] Among these, hollow copper-sulfide nanoparticles (HCuS NPs) stand out due to their ease of synthesis, stable optical properties, high photothermal efficiency, biocompatibility, large drug-loading capacity, and postirradiation degradation.[19−21] These attributes make HCuS NPs ideal for multifunctional platforms combining PTT with other therapies like immunotherapy.

Cancer immunotherapy has advanced rapidly over the past decade, leveraging the immune system to initiate or boost antitumor responses. This approach offers several advantages over traditional therapeutic methods, including minimal side effects, establishment of immunological memory to inhibit recurrence, and improved efficacy in metastatic cancer.[22−25] When combined with PTT, immunotherapy benefits from PTT-induced ICD in tumors, resulting in the release of tumor-associated antigens (TAAs), heat shock proteins, endogenous adjuvants, and damage-associated molecular patterns. Antigen-

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