EDITORIAL
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Carbon dots: multifunctional nanoplatforms for advanced tumor immunotherapy

Hong-Xin Liu[1], **Min Zheng**[1*]

[1]College of Chemistry and Life Science, Advanced Institute of Materials Science, Changchun University of Technology, Changchun 130022, China.

[*]**Correspondence to:** Min Zheng, College of Chemistry and Life Science, Advanced Institute of Materials Science, Changchun University of Technology, No. 2055 Yanan Street, Changchun 130022, China. E-mail: zhengm@ciac.ac.cn.

Tumor immunotherapy has revolutionized cancer treatment, yet critical challenges persist, including inefficient antigen delivery, immunosuppressive tumor microenvironment (TME), and poor targeting precision. Carbon dots (CDs), as versatile carbon-based nanomaterials, have emerged as transformative tools in this field, leveraging their exceptional biocompatibility, tunable surface functionality, unique optical properties, and efficient cargo-loading capacity [1–8]. This editorial provides a comprehensive overview of the latest advancements in carbon dots (CDs)-based strategies for tumor immunotherapy, emphasizing their diverse roles in enhancing antitumor immunity.

CDs as antigen-delivery platforms

CDs function as versatile and efficient nanocarriers for delivering antigens. Through rational design, CDs can be tailored to achieve precise immune targeting and activation. For example, chiral CDs conjugated with ovalbumin (OVA) form L/D-OVA nanovaccines that promote dendritic cell (DC) maturation, enhance antigen cross-presentation, and suppress B16-OVA melanoma growth. Notably, D-type isomers elicit superior immune activation due to enantioselective interactions with immune cells [9]. Further refining this approach, lactobionic-acid-modified chiral CDs (LLAO/DLAO) leverage receptor-mediated recognition to improve DC targeting, upregulating CD80/CD86 expression and boosting cytokine secretion [10] (Figure 1a). In a distinct strategy, CDs conjugated with tumor-cell-derived antigens (e.g., GMal + B16F10-Ag, GMal + CT26-Ag) retain native antigenic profiles, enabling specific tumor targeting and when combined with Anti-Programmed death receptor 1 (αPD-1) inducing durable, personalized immune responses [11] (Figure 1b). Expanding beyond passive and receptor-mediated targeting, spleen-directed amphiphilic CDs (O_{12}-Tta-CDs) have been engineered to overcome the liver-dominant accumulation typical of conventional mRNA vectors. These systems facilitate efficient mRNA delivery, promote DC maturation and antigen presentation, and thereby inhibit Mouse T-cell lymphoma cells (E.G7OVA) tumor growth, prevent recurrence, and exert prophylactic immunity [12].

Metal doped CDs as immune adjuvants

Doping CDs with metal ions (e.g., Cu^{2+}, Zn^{2+}, Mn^{2+}) confers potent immuneadjuvant functionality, enabling them to remodel the tumor microenvironment through ion-mediated catalytic reactions or direct activation of signaling pathways. This approach offers distinct advantages in reversing immunosuppression and treating immunologically “cold” tumors. Copper-doped CDs (e.g., FG-CDs@Cu [13], Copper-doped CDs [14], synthesized by modifying the surface of luteolin-derived CDts with copper ions, generate reactive oxygen species via Fenton-like reactions. This triggers immunogenic cell death (ICD) and repolarizes M2 to M1 macrophages, thereby reversing TME immunosuppression.) deplete glutathione (GSH), inhibit Glutathione Peroxidase 4 (GPX4), and generate reactive oxygen species via Fenton-like reactions to induce ferroptosis. This triggers immunogenic cell death (ICD) and repolarizes M2 to M1 macrophages, thereby reversing TME immunosuppression. Zinc-doped CDs (ZnM) functionalized with mannan achieve TME modulation and depletion of regulatory T cells (Tregs) and myeloid-derived suppressor cells (MDSCs). By leveraging Zn^{2+}-mediated immune activation and lymphatic targeting, they achieve 96.38% tumor suppression and complete inhibition of lung metastasis [15] (Figure 1c). Other innovative designs include CD-based honeycomb nanoassemblies responsive to cancer-associated fibroblasts. These systems surface-immobilize doxorubicin (DOX) and an immunotherapy enhancer (Fe^{2+}), while encapsulating the TME modulator losartan within a mesoporous structure, thereby enhancing tumor penetration and immune activation [16] (Figure 1d).

Multifunctional integration for synergistic

The real potential of CDs in immunotherapy lies in its multifunctional integration ability, which enables a single platform to realize antigen delivery, adjuvant activity and multimodal therapy simultaneously, thus coordinating the anti-tumor immune response. Based on this antigen delivery core, the advanced design also incorporates additional treatment modules. For example, manganese-coordinated polyphenol CDs can not only mediate photothermal therapy to induce immunogenic cell death and antigen release, but also activate STING pathway with released manganese ions [17]. Photothermal CDs-incorporated hydrogels (iCD@Gel) induce ICD under NIR irradiation, releasing damage-associated molecular patterns (DAMPs) that synergize with CpG oligonucleotides (CpG ODNs) to enhance DC maturation and $CD8^+$ T cell infiltration [18] (Figure 1e). Further expanding this paradigm, photocatalytic CDs can trigger tumor cell pyroptosis to generate in situ whole cancer cell vaccines, which preserve complete antigen repertoires to elicit broad-spectrum immune responses [19]. Boron-doped CDs (^{10}B-CDs) not only utilize thermal neutron irradiation to kill prostate cancer cells via DNA damage but also leverage RM-1 cells’ dual function as tumor cell antigens and ^{10}B-CDs delivery vehicles. This transforms the immune state from “cold” to “hot”, thereby enhancing antitumor efficacy [20]. Similarly, red CDs (RCD)-doped copper metal-organic framework nanoparticles (Cu-MOF@RCD) utilize their tumor microenvironment-responsive and NIR-responsive properties to catalyze the decomposition of tumor endogenous H_2O_2 through a Fenton-like reaction. Combined with immune checkpoint blockade (ICB) therapy, this strategy effectively suppresses tumor metastasis [21]. Additionally, deformable honeycomb-like nanoassemblies enable the regulated and sequential delivery of therapeutic agents to different components of the tumor microenvironment, enhancing the efficacy of chemoimmunotherapy [16]. Moreover, CDs have the potential to directly modulate immune checkpoints by degrading PD-L1, and activating the cGAS-STING pathway, thereby reversing immunosuppressive signaling and restoring the immune system's ability to target cancer cells [22]. Therefore, by integrating targeting [23], immune activation [24, 25], and microenvironment modulation into a unified system, CDs-based platforms exemplify a powerful and versatile strategy for next-generation cancer immunotherapy [26].

Challenges and translational prospects

Despite their immense potential, the clinical translation of CDs-based immunotherapies faces several interconnected challenges. These

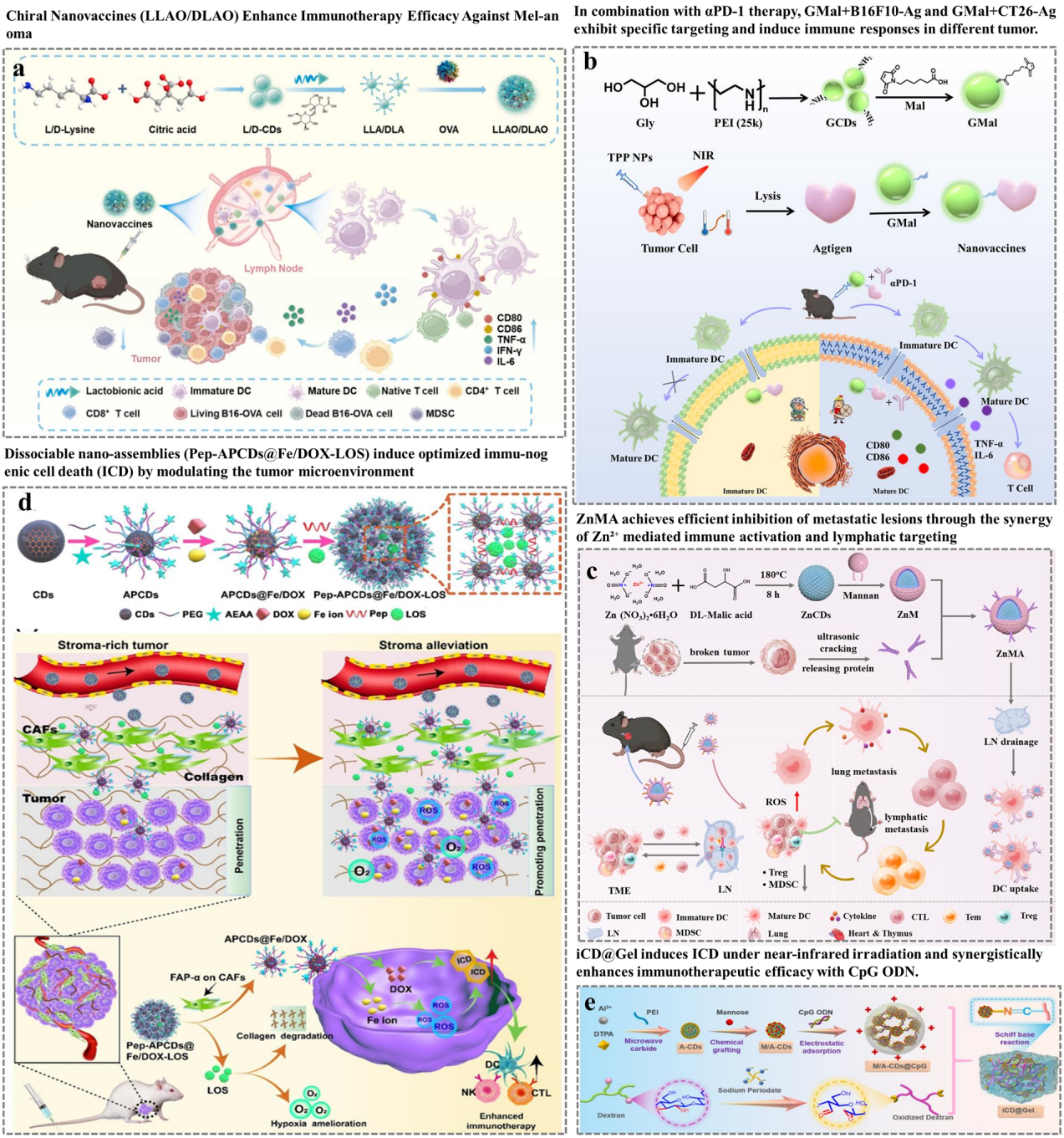

Figure 1 Applications of CDs in cancer immunotherapy. (a) Targeting chiral carbon dots to enhance melanoma immunotherapy. Reproduced with permission. Zhao R, Liu H, Xie Z, Zheng M. Targeting chiral carbon dots to enhance melanoma immunotherapy. *J Colloid Interface Sci*. 2026;703(Pt 1):139093. Copyright 2026, Elsvier. (b) Carbon dots and tumor antigen conjugates as nanovaccines for elevated cancer immunotherapy. Reproduced with permission. Liu H, Xie Z, Zheng M. Carbon dots and tumor antigen conjugates as nanovaccines for elevated cancer immunotherapy. *Small*. 2023;19(31):2206683. Copyright 2023, Wiley. (c) Engineering an effective carbon dot nanovaccine for synergistic immune activation and metastasis inhibition. Reproduced with permission. Liu H, Zhao R, Yang Z, Xie Z, Zheng M. Engineering an effective carbon dot nanovaccine for synergistic immune activation and metastasis inhibition. *Chem Eng J*. 2025; 522: 167801. Copyright 2025, Elsvier. (d) Transformable honeycomb-like nanoassemblies of carbon dots for regulated multisite delivery and enhanced antitumor chemoimmunotherapy. Reproduced with permission. Hou L, Chen D, Wang R, et al. Transformable honeycomb-like nanoassemblies of carbon dots for regulated multisite delivery and enhanced antitumor chemoimmunotherapy. *Angew Chem Int Ed*. 2021;60(12):6581–6592. Copyright 2021, Wiley. (e) Immunoinducible carbon dot-incorporated hydrogels as a photothermal-derived antigen depot to trigger a robust antitumor immune response. Reproduced with permission. Liu S, Zhang M, Yu H, et al. Immunoinducible carbon dot-incorporated hydrogels as a photothermal-derived antigen depot to trigger a robust antitumor immune response. *ACS Appl Mater Interfaces*. 2023;15(6):7700–7712. Copyright 2023, ACS. CDs, Carbon dots; OVA, ovalbumin; DC, dendritic cell; MDSC, myeloid-derived suppressor cell; αPD-1, Anti-Programmed death receptor 1; TNF-α, Tumor Necrosis Factor-alpha; IL-6, Interleukin-6; NIR, Near Infrared; TPP NPs, 5,10,15,20-Tetraphenylporphyrin Nanoparticles; PEG, Polyethylene Glycol; AEAA, Aminoethyl anisamide; DOX, doxorubicin; Pep, Phosphoenolpyruvate; LOS, Losartan; TME, tumor microenvironment; LN, Lymph node; ROS, Reactive oxygen species; CTL, Cytotoxic T Lymphocyte; NK, Natural killer cell; DTPA, Diethylenetriaminepentaacetic acid; PEI, Polyethyleneimine.

include synthetic difficulties in achieving precise size control and batch-to-batch uniformity, which are crucial for ensuring pharmacological reproducibility; uncertainties regarding long-term safety, including unresolved questions about the metabolic fate and potential immunogenicity upon prolonged exposure; limited tumor penetration, particularly in hypoxic and fibrotic regions, due to reliance on passive targeting mechanisms; and a lack of optimized protocols for combining CDs with radiotherapy, chemotherapy, or other immune-modulating agents. A tumor-immunophenotype-guided design paradigm is warranted moving forward. For "cold" tumors, which are less responsive to immune therapy, CDs can be engineered to deliver STING pathway agonists or chemokines to remodel the immunosuppressive microenvironment. For "hot" tumors, platforms that co-deliver tumor antigens with checkpoint inhibitors may help reverse T-cell exhaustion. In metastatic settings, organotropic or tissue-specific targeting via ligand engineering could enhance the accumulation of CDs in LNs or distant organs.

Advancing the clinical translation of CDs-based immunotherapies further requires robust, scalable synthesis protocols, validation of personalized designs in humanized models, and careful attention to regulatory aspects of long-term biosafety and immunotoxicity. Ultimately, bridging the gap from concept to clinic demands an integrated translational pathway that synergizes fundamental immunology, rational materials design, controlled manufacturing, and rigorous clinical evaluation. Thanks to these concerted efforts, CDs-based nanoplatforms show great promise as they evolve from laboratory concepts into tangible cancer immunotherapy solutions.

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tumor microenvironment to enhance the immune therapy response. *J Colloid Interface Sci.* 2026;703(Pt 2):139170. Available at: https://doi.org/10.1016/j.jcis.2025.139170

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Author contributions

Min Zheng and Hong-Xin Liu wrote the original draft. Min Zheng revised and edited the manuscript. All authors have reviewed and agreed to the final draft.

Competing interests

The authors declare no conflicts of interest.

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Abbreviations

TME, tumor microenvironment; CDs, Carbon dots; OVA, ovalbumin; DC, dendritic cell; ICD, immunogenic cell death.

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