Warburg Effect-Driven Photothermal Therapy of Tumors using Glycosylated β-C_3N_4 Carbon Nanodots

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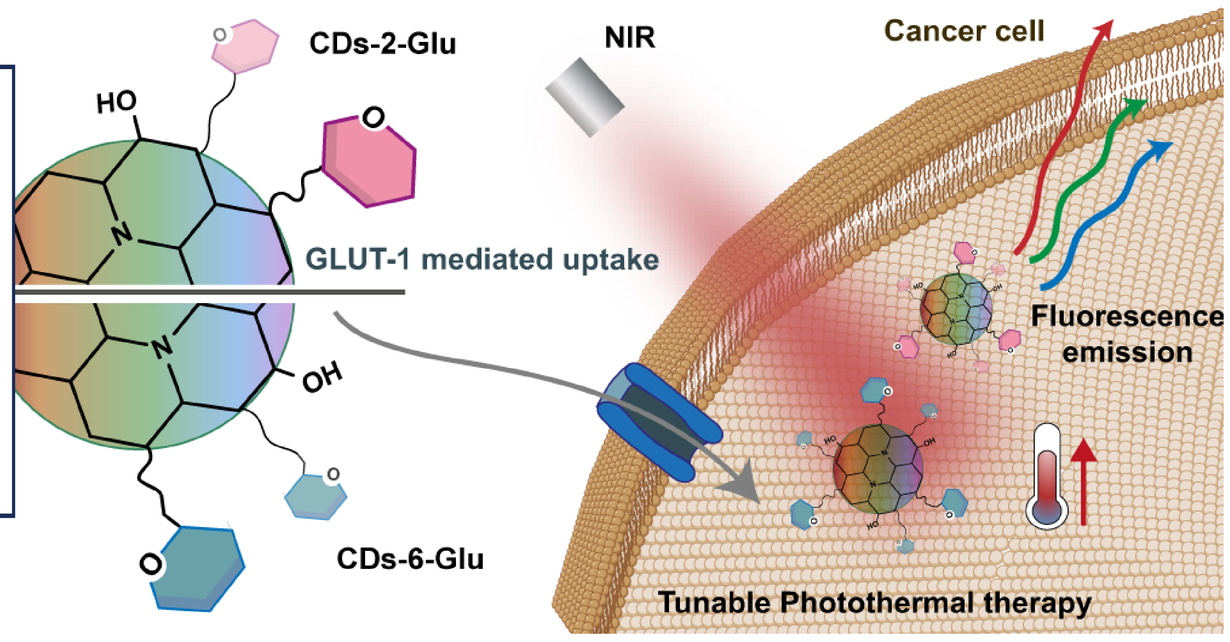
Introduction

Photothermal therapy (PTT) based on light-to-heat converting nanomaterials represents a promising non-invasive strategy for cancer treatment. Carbon nanodots (CDs) combine efficient photothermal conversion, biocompatibility, and intrinsic fluorescence, enabling theranostic applications.

In this study, glucose-functionalized CDs are explored as selective and tunable PTT agents for triple-negative breast cancer, exploiting tumor-specific glucose metabolism (Warburg effect) to enhance targeting and therapeutic efficacy.



Methods

Carbon nanodots (CDs) were obtained by solvothermal decomposition of citric acid and urea in dimethyl sulfoxide (DMSO), and subsequently their surface was functionalized with eiher 2-deoxy- or 6-deoxy- (D)-glucose, conjugated through a PEG spacer via click-chemistry.

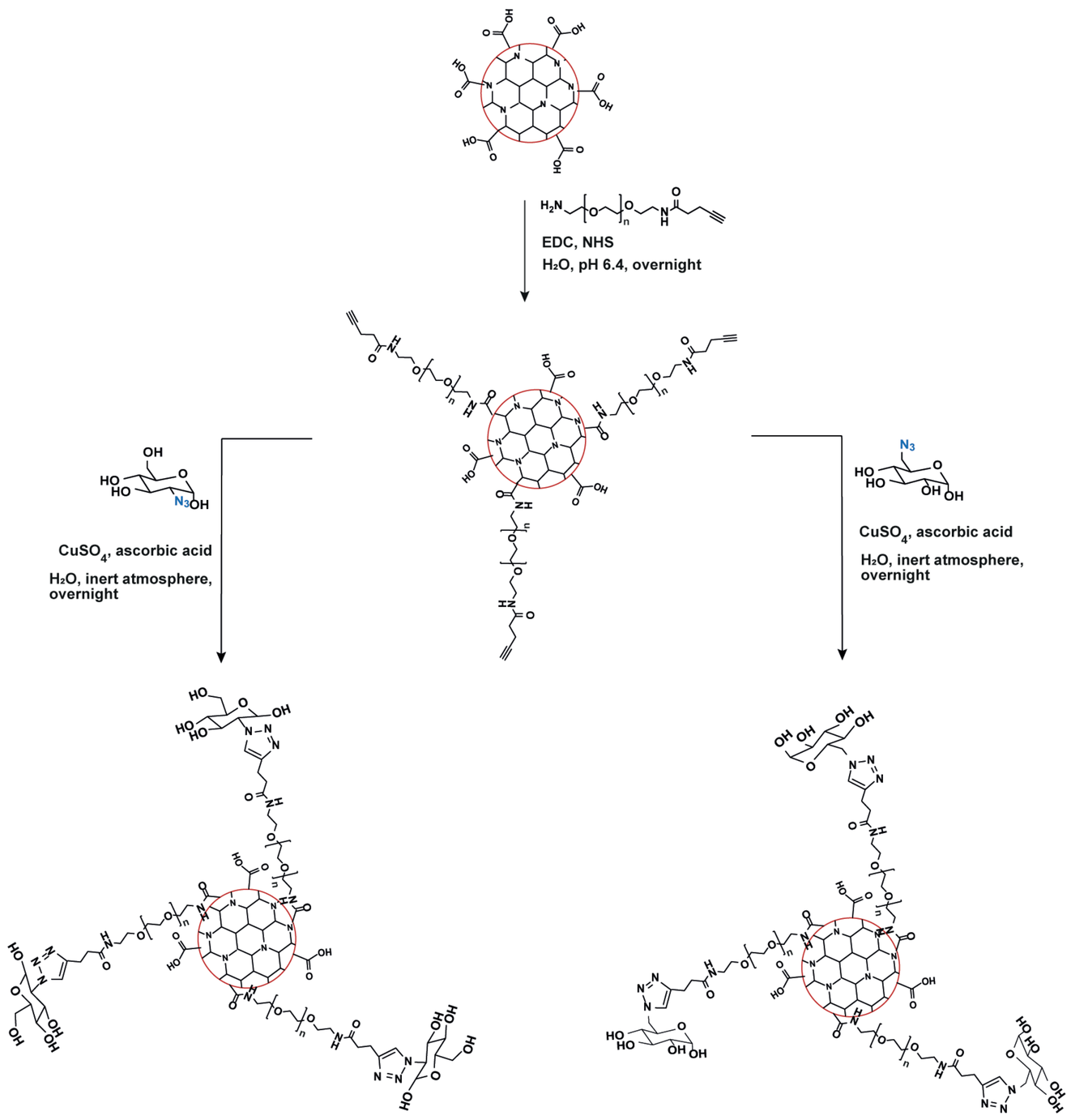


Figure 1. Scheme illustrating the synthetic pathwat adopted

The proficiency of the syntehtic pathway was demonstrated through FT-IR and ^{1}H-NMR studies.

Morphology

The reaction yieled colloidally stable β-C_3N_4 crystalline carbon nanodots (CDs) with ultrasmall size (~4.0 nm), that are retained as core structure in the final glycosilated CDs.

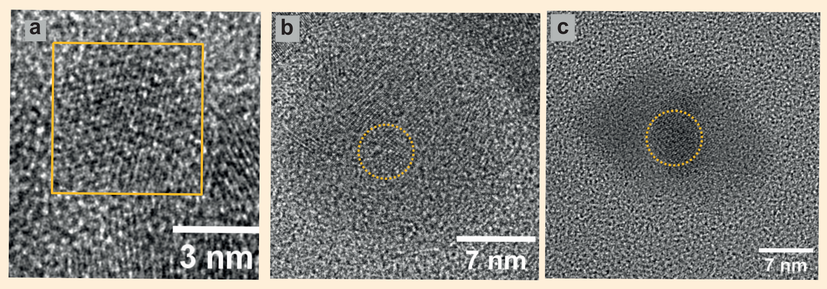


Figure 2. HR-TEM micrographs of CDs (a), CDs-2-Glu (b), and CDs-6-Glu (c).

Self-tracking properites

The multicolor fluorescence emission of CDs, retained after glycosilation, confers self-tracking properties to the nanostructures, which have been exploited to evaluate their cellular internalization. The study, performed in the presence of a GLUT-inhibitor (GLUTi), revealed a prevalent uptake in cancer cells through a glucose-mediated pathway.

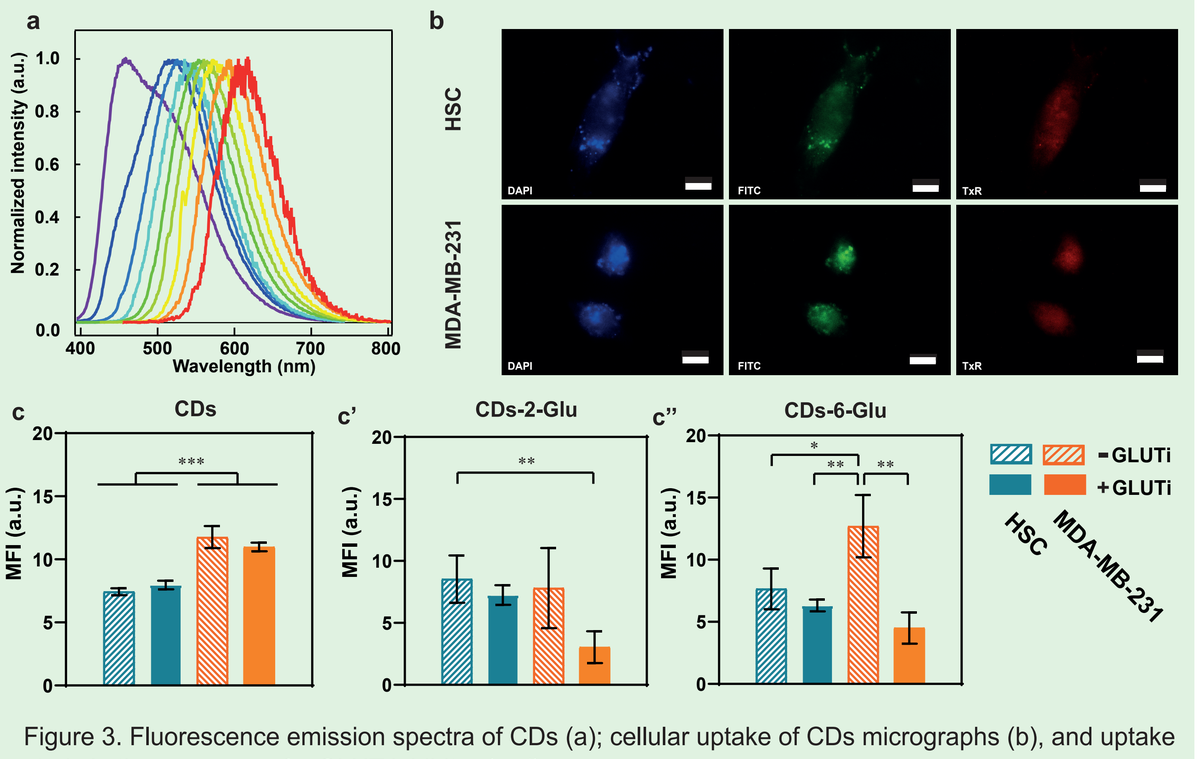


Figure 3. Fluorescence emission spectra of CDs (a); cellular uptake of CDs micrographs (b), and uptake study in the presence of a GLUT inhibitor (c-c').

Tunable NIR-Triggered photothermal therapy

A systematic study performed at increasing CD concentrations (0.10–0.50 mg mL^{-1}) and NIR power densities (1.25–6.25 W cm^{-2}) investigated the tunable photothermal conversion ability of the obtained CDs (Fig. 4a).

The results provided insights for the fine-tuning of irradiation conditions to achieve non-offensive, hyperthermic, or ablative regimes, resulting in coherent and modulable effects on cell viability *in vitro* (Fig. 4b-c).

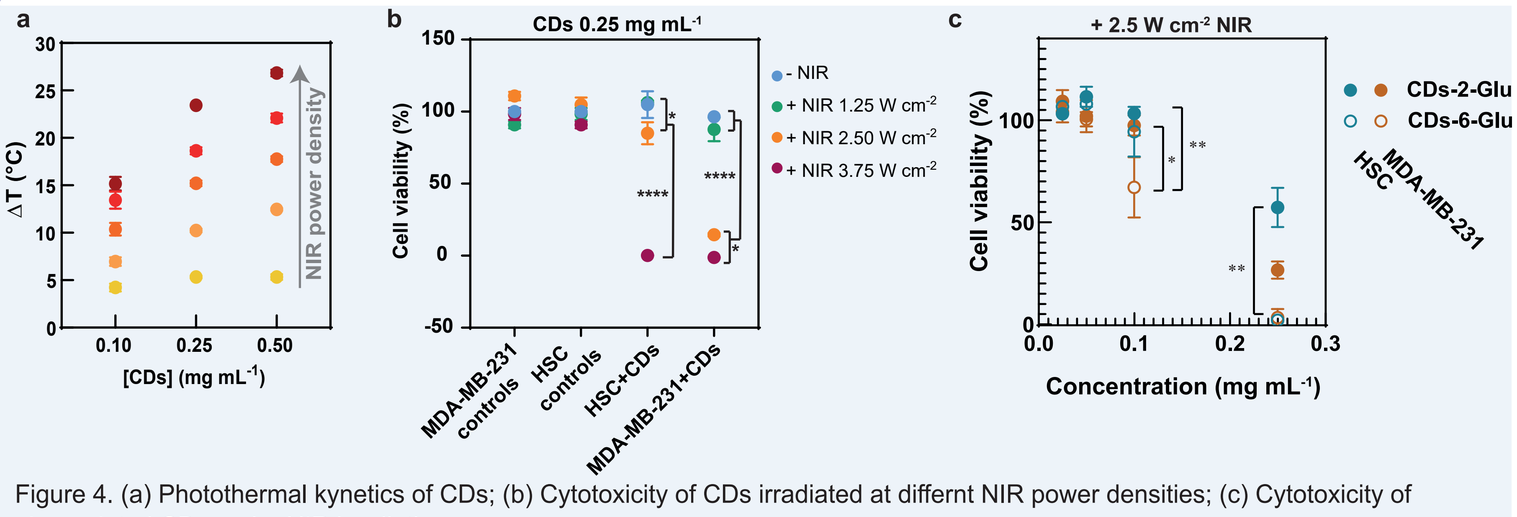


Figure 4. (a) Photothermal kynetics of CDs; (b) Cytotoxicity of CDs irradiated at differnt NIR power densities; (c) Cytotoxicity of glycosylated CDs under NIR irradiation.

Conclusions

Glycosylated CDs combine self-tracking multicolor fluorescence with finely tunable photothermal activity, resulting in inherent and highly controllable antitumoral effects. In addition, their surface engineering with glucose derivatives drives preferential tumor uptake via the Warburg effect, further enhancing treatment selectivity. The resulting theranostic nanoplatform demonstrates valuable potential in precise breast cancer therapy.

R.C. is supported with a post-doctoral fellowship by Fondazione VERONESI