Red Light-Assisted Heterogeneous Tumor Microenvironment-Responsive Carbon Monoxide Release for Cancer Therapy

*Jian Cheng, and Jinming Hu**

No.96, JinZhai Road Baohe District, Hefei, Anhui, 230026, P.R.China.
Department of Polymer Science and Engineering, School of Chemistry and Materials Science, University of Science and Technology of China
Hefei, Anhui, P.R.China
cjivn@ustc.edu.cn,* jmhu@ustc.edu.cn

A tumor microenvironment-responsive carbon monoxide (CO) delivery system shows great promise for cancer therapy but faces two key challenges: (i) achieving controlled CO release at the tumor site and (ii) improving carrier penetration into tumor tissue[1]. This study introduces a red light-assisted, tumor microenvironment-responsive CO-releasing carrier that adapts to tumor heterogeneity, such as pH and redox variations. The system undergoes charge conversion to enhance tissue penetration. Under red light, it generates reactive oxygen species (ROS) via photodynamics, working with glutathione (GSH) to release CO and ferrous ions. Elevated hydrogen peroxide (H_2O_2) in tumor cells triggers a Fenton reaction, enabling sustained CO release coordinated with GSH[2]. This approach ensures precise, controllable CO release and effective tumor accumulation, significantly boosting antitumor efficacy and offering a novel strategy for low-toxicity, efficient CO delivery systems.

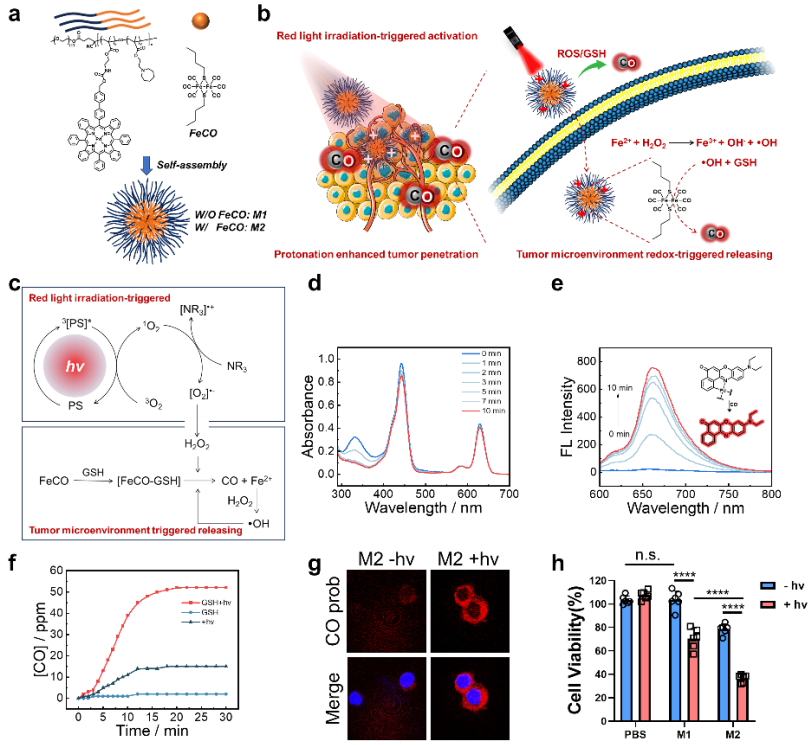

Figure 1: (a) Preparation of CO-releasing micelles. (b) Red light-activated tumor microenvironment-responsive CO release for cancer therapy. (c) Proposed mechanism of CO releasing. (d, e, f) Detection of CO Release Under red light irradiation in the presence of 10 mM GSH, (d) UV-Vis spectroscopy, (e) Fluorescence spectroscopy, (f) CO Sensor. (g) Visualization of intracellular CO release in cells. (h) Cytotoxic effect of micelles on 4T1 cells with and without red light irradiation.

References:

[1] Zhou, Y.; et al. *Biomaterials* **2020**, *255*, 120193.
[2] Song, C. Z.; et al. *J. Am. Chem. Soc.* **2023**, *145*, 17755–17766.