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## Title: Monodispersed Copper(I)- Based Nano Metal–Organic Framework as a Biodegradable Drug Carrier with Enhanced Photodynamic Therapy Efficacy

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### **Abstract:**

Photodynamic therapy (PDT) has emerged as an alternative treatment of cancers. However, the therapeutic efficiency of PDT is severely limited by the microenvironment of insufficient oxygen ( $O_2$ ) supply and overexpression of glutathione (GSH) in the tumor. Herein, a biodegradable  $O_2$ - loaded CuTz- 1@F127 (denoted as CuTz- 1-  $O_2$ @F127) metal–organic framework (MOF) therapeutic platform is presented for enhanced PDT by simultaneously overcoming intracellular hypoxia and reducing GSH levels in the tumor. The Cu(I)- based MOF is capable of a Fenton- like reaction to generate  $\cdot OH$  and  $O_2$  in the presence of  $H_2O_2$  under NIR irradiation. Meanwhile, the CuTz- 1-  $O_2$ @F127 nanoparticles (NPs) can release adsorbed  $O_2$ , which further alleviates intracellular hypoxia. In addition, the  $Cu^I$  in CuTz- 1@F127 can react with intracellular GSH to reduce the excess GSH. In this way, the efficiency of PDT is greatly enhanced. After tail intravenous injection, the NPs show high antitumor efficacy through a synergistic effect under 808 nm laser irradiation. More importantly, the NPs are biodegradable. In vivo biodistribution and excretion experiments demonstrate that a total of nearly 90% of the NPs can be excreted via feces and urine within 30 d, which indicates significant prospects in the clinical treatment of cancers.