Project Title:	Development of coordination-driven supramolecular nanoplatforms for theranostic applications 配位驅動超分子納米平臺在治療學領域的應用
PI:	Prof Gigi LO

The team has developed a series of copper-assisted self-assembled nanoparticles for cancer therapy.

Mixing a glutathione (GSH)-responsive carboxy zinc(II) phthalocyanine (ZnPc*) and CuSO4·5H2O in water with or without the presence of the anticancer drug SN38 resulted in the formation of self-assembled nanotherapeutics labeled as ZnPc*/Cu/SN38@NP and ZnPc*/Cu@NP, respectively. The Cu^{2+} ions not only promoted the self-assembly of the carboxy phthalocyanine through metal complexation, but also catalysed the transformation of H_2O_2 to oxygen via a catalase-like reaction, rendering an oxygen-replenishing property to the nanosystems. Both nanosystems exhibited high stability in aqueous media, but the nanoparticles disassembled gradually in an acidic or GSH-enriched environment and inside human colorectal adenocarcinoma HT29 cells, releasing the encapsulated therapeutic components.

The disassembly process together with the activation by the intracellular GSH led to relaxation of the intrinsic quenching of the nanophotosensitisers and restoration of the photoactivities of ZnPc*. Under a hypoxic condition, ZnPc*/Cu/SN38@NP could attenuate the intracellular hypoxia level and maintain the photodynamic activity due to its Cu^{2+}-promoted oxygen-replenishing ability. The photodynamic effect of ZnPc* and the anticancer effect of SN38 worked cooperatively, causing substantial apoptotic cell death. The dual therapeutic actions could also effectively inhibit the tumor growth in HT29 tumor-bearing nude mice without initiating notable adverse effects to the mice. (*Acta Biomaterialia* 2023, 162, 57-71)