Enzyme-mimicking catalytic Activity in Tumoral Microenvironment: Towards Glutathione-Glucose Depletion for Cancer Therapy

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New strategies in cancer therapy focus on the degradation of key metabolites, such as Glutathione (GSH) [(1)] or Glucose [(2),(3)]. GSH is a natural antioxidant which maintains the cytosol concentration of Reactive Oxygen Species (ROS) (e.g. H_2O_2, O_2^- or $^{\cdot}OH$) below cytotoxic levels. Since glucose is the major source of energy in cells, particularly under neoplasia, large amounts of this metabolite are required to ensure ATP levels. Thus, new nanomaterials showing the ability to alter these molecules levels (Figure 1) may have an effect on controlling cancer growth. In this work, synthesis and characterization of a nanoplatform based on Cu(II) and Fe(III) with outstanding enzyme-like activity mimicking towards GSH-oxidation are presented. As cytosol GSH levels decrease, more H_2O_2 is available to increase ·OH hydroxyl levels via Fenton-process. High reactivity of ·OH radicals is responsible for oxidizing glucose, DNA, amino acids or membrane-lipids, causing critical cell damage entailing cell apoptosis. In this way, the catalytic peroxidation of organic molecules is enhanced in the presence of GSH.

A spinel-like Cu(II)Fe(III) mixed nanoxide with additional NIR response has been synthesized. Its catalytic activity in tumoral-like conditions (i.e. high GSH/H_2O_2 levels and mildly-acidic pH) was higher in comparison with non-GSH conditions. Moreover, their metabolic cytotoxicity and its internalization mechanism within two different cell lines (U-251MG and hpMSC) were evaluated in order to achieve a deeper understanding in their interaction with different cells.

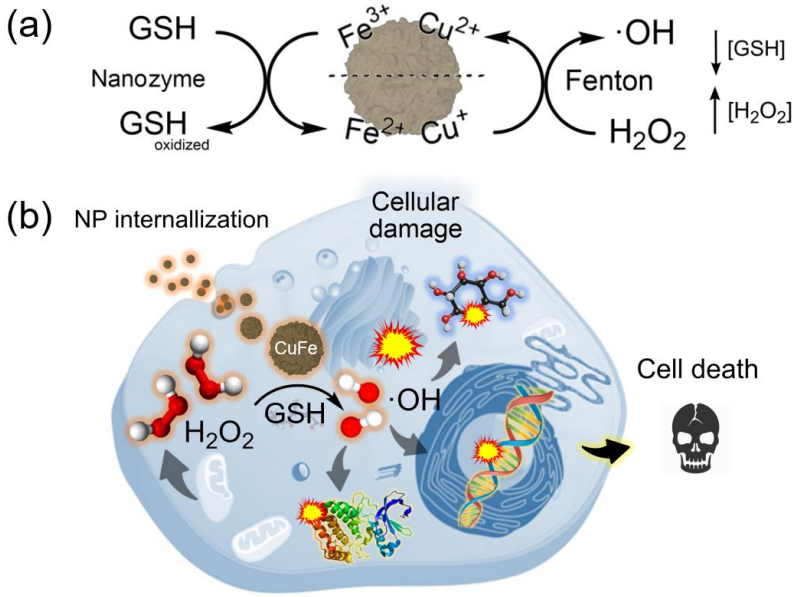

Figure 1. Schematic view of CuFe action mechanism. (a) Dual activity of CuFe catalyst: its interaction with tumour-abundant GSH enhances the generation of toxic ·OH radicals, which (b) can damage key compounds in cells such as glucose, DNA and proteins, entailing cell death.

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