A potential catalytic therapy in oncology: Cu-Fe Nanoparticles responsive to tumor microenvironment

Jesús Santamaría
Javier Bonet-ALeta, María Sancho-Albero, Javier Calzada, Silvia Irusta, M.Pilar Martín-Duque, Jose L. Hueso,

1) Department of Chemical and Environmental Engineering, Institute of Nanoscience and Materials of Aragon (INMA), University of Zaragoza; 2) Networking Research Center in Biomaterials, Bioengineering and Nanomedicine, CIBER-BBN; 3) Instituto Aragonés de Ciencias de la Salud

jesus.santamaria@unizar.es

Heterogeneous catalysis has emerged as a promising alternative for the development of new cancer therapies. Also, regarding the tumor microenvironment as a reactor with very specific chemical features has provided a new perspective in the search for catalytic nanoarchitectures with specific action against chemical species playing a key role in tumor metabolism. One of these species is glutathione (GSH), whose depletion is the cornerstone of emerging strategies in oncology, since this metabolite plays a pivotal regulatory role as antioxidant agent, dampening the harmful effects of intracellular reactive oxidative species (ROS). Herein, we present copper-iron oxide spinel nanoparticles that exhibit a versatile and selective catalytic response to reduce GSH levels while generating ROS in a cascade reaction. We demonstrate a clear correlation between GSH depletion and apoptotic death in tumor cells in the presence of the copper-iron nanocatalyst. Furthermore, we also provide a novel analytical protocol, alternative to state-of-the-art commercial kits, to accurately monitoring the concentration of GSH intracellular levels in both tumor and healthy cells. We observe a selective action of the nanoparticles, with lower toxicity in healthy cell lines, whose intrinsic GSH levels are lower, and intense apoptosis in tumor cells accompanied by a fast reduction of GSH levels.

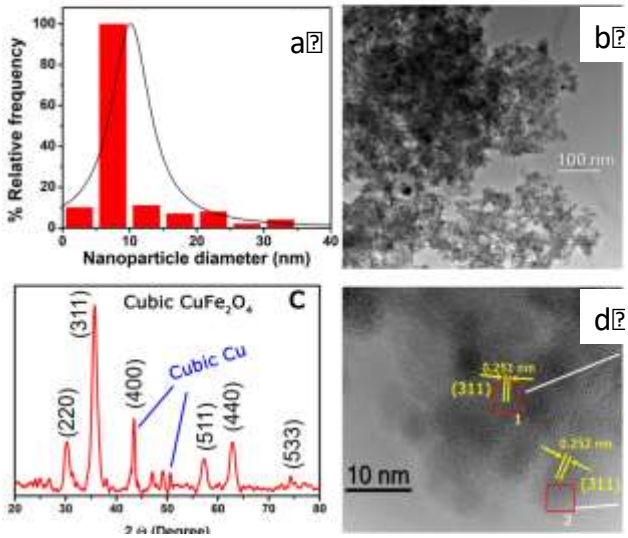

Figure 1: Characterization of Cu-Fe nanoparticles. a) Particle size distribution. b)Low magnification TEM image. c) XRD pattern showing a predominant cubic apinel phase of CuFe2O4 and a secondary phase of Cu. d) HRTEM images of CuFe nanoparticles

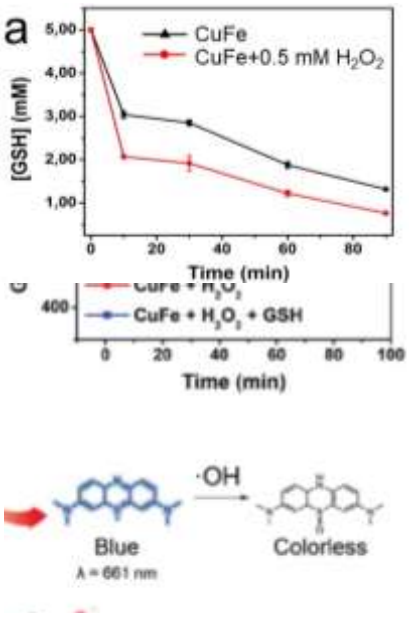

Figure 2: Starvation therapy: glutathione and glucose conversion under different reaction scenarios