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Anti-tumor activity of functionalized biomimetic magnetite nanoparticles produced in the presence of MamC protein of *Magnetococcus marinus* MC-1

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Magnetite Nanoparticles (MNPs) find many applications, including biotechnology, as they can be manipulated by an external magnetic field and functionalized with different molecules. Magnetotactic bacteria bio-mineralize magnetosomes (membrane-enveloped magnetites), which are the ideal magnetic particle. However, scaling-up magnetosome production is still challenging, so bio-mimetics, i.e. *in vitro* magnetite synthesis mediated by magnetosome-associated proteins is being explored. Our group is working with MamC from *Magnetococcus marinus* MC-1 that controls the morphology and size of the crystals, producing well faceted Biomimetic Magnetic Nanoparticles (BMNPs) of ~40 nm, which are paramagnetic at room and body temperature while having a large magnetic moment per particle under an external magnetic field. These BMNPs were cytocompatible and biocompatible in vivo. BMNPs were functionalized (isothermal adsorption) with a monoclonal antibody (mAb) recognizing the ectodomain of the human Met/HGF receptor (overexpressed in many cancers) and the chemotherapeutic Doxorubicin (DOXO). The functionalized BMNPs present hyperthermia and were stable at physiological pH, while releasing the adsorbed DOXO at acidic pH. mAb functionalization of BMNPs favored their interaction with cells expressing the Met/HGFR and cellular DOXO uptake and toxicity, which was enhanced upon cell exposition to a continuous magnetic field. Real-time cytotoxicity of the BMNPs showed that DOXO-mAb-BMNPs were significantly more toxic than DOXO-BMNPs on Met/HGFR expressing cells, while no differential toxicity was observed on cells not expressing this receptor. When DOXO-BMNPs were injected intravenously in tumor bearing mice and an external magnetic field was applied there, a higher amount of BMNPs accumulated in the tumor and tumor growth was decreased in comparison to mice in which no magnetic field was applied. These BMNPs could thus represent effective nano-carriers for targeted drug delivery and might be combined with hyperthermia to increase efficiency, resulting in a targeted local treatment of tumors with a decrease in the deleterious systemic side effects.

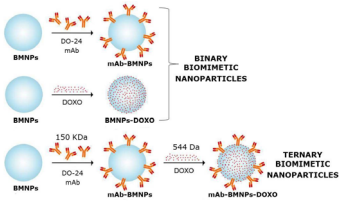

Figure 1. Functionalization of MamC biomimetic nanoparticles (BMNPs), with the DO-24 monoclonal antibody (mAb) and the chemotherapy drug doxorubicin (DOXO), for targeted anti-tumor treatment.

Biography

Ana Peigneux has his expertise in Molecular Biology focused on protein purification for biotechnological applications. Currently, she is pursuing PhD at the University of Granada, Spain. The main goal of her thesis is the study and the purification of magnetosome-associated proteins to synthesize magnetosome-like nanoparticles with improved magnetic properties. Moreover, she got two grants to do an Internship in Dr. Prat lab (Italy), where she applied these biomimetic magnetite nanoparticles as carriers for drug delivery.

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