Functionalized biomimetic magnetite nanoparticles as smart nanocarriers

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Introduction

Magnetite nanoparticles are interesting in biotechnology as they can be manipulated by a magnetic field and functionalized with different molecules. Although magnetotactic bacteria biomineralize magnetosomes (the ideal magnetic nanoparticle), scaling-up magnetosome production is still challenging, thus promoting the research on biomimetic, meaning inorganic magnetite synthesis by magnetosome-asociated proteins. MamC protein from *Magnetococcus marinus* MC-1 is a strong candidate since controls the morphology and size of the crystals, producing BMNPs with novel surface properties that are superparamagnetic at body temperature while having a large magnetic moment per particle under an external magnetic field.

Methods

These BMNPs were functionalized with the DO-24 monoclonal antibody (mAb) directed against the ectodomain of the human Met/HGF receptor (overexpressed in many cancers) and the chemotherapy drug doxorubicin (DOXO). The stability, immunocompetence and release of the molecules absorbed were assayed. Real-time cytotoxicity and cellular interaction of the functionalized nanoparticles were evaluated with cell lines expressing or not Met/HGF. Breast tumors were induced in BALB/c mice to check the cytocompatibility, biodistribution and toxicity of the unfunctionalized BMNPs and DOXO-BMNPs in the absence/presence of a magnetic field. The hyperthermia response of the different BMPs was also analyzed.

Results

Non-functionalized BMNPs were cytocompatible while the functionalized complexes became cytotoxic and showed good stability at physiological pH (DOXO release is pH dependent). DOXO-mAb-BMNPs present hyperthermia and discharge DOXO within the nuclei. The *in vivo* BMNPs administration did not show any morphological alterations and the DOXO-BMNPs under a magnetic field showed BMNPs accumulation in the tumor site and growth decrease of the tumor.

Discussion

The mAb and DOXO coupling to the BMNPs does not alter their magnetic properties. The DOXO internalization from DOXO-mAb-BMNPs was more efficiently in the presence of a magnetic field and in the Met^+ cells, suggesting the selective recognition of DO-24 and the magnetic properties of the BMNPs enhance DOXO internalization. DOXO release in the tumor site was comparable to soluble DOXO. Therefore, these nanocarriers could represent an effective targeted drug delivery, which might be combined with hyperthermia to increase efficiency, resulting in a targeted local treatment of localized tumors with a decrease in the systemic side effects.