Genetically functionalized magnetosomes as MRI contrast agent for molecular imaging: in vitro proof of binding and in vivo proof of contrast

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Abstract

Molecular imaging aims at detecting molecular markers in a preserved environment using non-invasive imaging modalities. Specific contrast agents are dedicated to one imaging modality and functionalized to target pathological biomarkers, in order to reveal preliminary stages of disease. Combining high magnetic field scanners and innovative contrast agents, Magnetic Resonance Imaging (MRI) might achieve the high sensitivity and specificity requested by molecular imaging applications.
Magnetosomes are iron-oxide nanoparticles of interest for MR-based molecular imaging. These regular crystals of magnetite embedded in a lipid bilayer are produced by magnetotactic bacteria and can be functionalized for biomarkers targeting using genetic tools [1]. Furthermore, they present promising MR contrasting properties [2].

Here, translational gene fusion was used to successfully produce from AMB1 strain magnetosomes expressing RGD peptides at their membrane. We obtained in vitro proof of specific binding of these RGD-magnetosomes with U87 cell line (human model of glioblastoma), known for expressing 3 integrins targeted by RGD. The genetic fusion of RGD peptide with Venus (Venus-RGD), a variant of GFP, enabled to demonstrate by fluorescence imaging both binding and internalization of Venus-RGD-functionalized magnetosomes, assessing the specificity. The MR contrasting properties of these nanoplatforms were then measured using relaxometry which demonstrates their great sensitivity for MR imaging.

As a first proof of contrast, we validated the ability to acquire mouse brain angiogram [3] combining intravenous injection of wild type magnetosomes with high field MRI on a mouse model of glioblastoma developed for future molecular imaging studies.

This work demonstrates the feasibility of producing functionalized magnetosomes along with the ability to use them in vivo as contrast agent for MRI, opening the way for their use in further molecular imaging studies.

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