Development of an effective tumor-targeted contrast agent for Magnetic Resonance Imaging based on Mn/H-Ferritin nanocomplexes

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Abstract:
Magnetic resonance imaging (MRI) is a non-invasive diagnostic technique routinely used in clinical practice. Contrast agents (CAs) are commonly exploited to facilitate the recognition of abnormal regions and decrease the risk of misdiagnosis caused by limited MRI sensitivity. Nowadays, only a few gadolinium-based CAs are clinically approved. Concerns about their toxicity persist and their administration is approved only under strict controls. On this basis, the aim of this project was to develop and validate a novel manganese-based CA. Manganese is a an essential paramagnetic metal able to generate a positive contrast like gadolinium, but eventually less toxicity for the human body. Mn ions were loaded in the core of a recombinant nanocarrier H-Ferritin, which is selectively recognized by the majority of human cancer cells by means of transferrin receptor 1. The obtained preparation (Mn@HFn-RT) was characterized, showing superior relaxivity, optimal colloidal stability, and a good safety profile. In vitro experiments validate the hypothesis that Mn@HFn-RT efficiently and selectively target breast cancer cells. Mn@HFn-RT administration in vivo enabled the direct detection of tumors by positive contrast enhancement in a breast cancer murine model, using very low metal dosages and exhibiting rapid clearance after diagnosis. Hence, Mn@HFn-RT could be proposed as a promising CA candidate for the improvement of MRI performance.