Smart Magnetic Nanoparticle Imaging Probes –

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Project Summary:

Superparamagnetic magnetite nanoparticles have many good potentials in biomedical applications. However, the use of these magnetite nanoparticles in medicine is generally hindered by the tendency of agglomeration of nanoparticles, short circulation time in plasma, non-specific targeting, and low efficiency of nanoparticle uptake to target cells. One of effective approaches to solving these problems is to coat nanoparticles with biocompatible polymers and targeting agents. The protein-resistive, nonantigenic and biocompatible polyethylene glycol (PEG) has been coated on nanoparticle surfaces, to disperse the nanoparticles and reduce nonspecific protein adsorption and further clearance by macrophages. Moreover, research has been performed to attach PEG-FA conjugates to the surfaces of nanoparticles to combine the advantages of both PEG and folic acid. The current challenge is to prevent the agglomeration during both the nanoparticle synthesis and the following surface modification processes, and make self-assembled coating on individual nanoparticles.

In this work, we developed an effective synthetic route to produce stable, well-dispersed magnetic nanoparticles, and a novel method was proposed to produce self-assembled PEG and PEG conjugates on individual nanoparticle surfaces for efficient nanoparticle targeting and intracellular uptake to cancer cells. Stable monodisperse magnetite nanoparticles were produced using our circulating system through a well-controlled synthesis process. A novel dialysis method was developed to change the solvent of the nanoparticle solution during the coating process, to avoid nanoparticle agglomeration due to centrifugation, which can be used universally for the surface modification of nanoparticles. AFM, FTIR and XPS techniques were used to demonstrate that monodisperse nanoparticles were obtained using our synthetic route, and the individual nanoparticles were coated with self-assembled PEG and PEG-FA conjugates via chemical bonding. It was seen that cells took up much more FA-PEG coated nanoparticles than PEG coated nanoparticles over the whole cell culture period. These methods can also be used to prepare magnetic nanoparticles-polyethylene glycol) (PEG) conjugates coupled with fluorescent tags to enable subcellular targeting. The resultant nanoparticles conjugates are uniquely suited for cellular analysis using the combined confocal and magnetic resonance microscopy (CM-MRM) at PNNL. The magnetic reagents provide enhanced contrast for MRM analysis, while the fluorescent tags provide subcellular targeting and rapid detection via simultaneous confocal microscopy.

Publications, Presentations and Proposals:

1. Y. Zhang, N. Kohler, and M. Zhang "High-Efficiency Intracellular Uptake of Superparamagnetic Magnetite Nanoparticles for Biomedical Applications" in Nanoscience and Nanotechnology in Perspective", G. Liu, et al. (eds), pp 282, Frontiers of Science and Technology for the 21st Century,Tshinghua University Press (2002).
2. Kohler N, Zhang Y, Zhang M. Characterization of methotrexate modified superparamagnetic nanoparticles and their uptake into human chronic myologenous leukemia cells. 2003 Nanotech Conference and Tradeshow, San Francisco, CA, February 23-27, 2003. (Submitted September, 2002)
3. Kohler N, Zhang Y, Zhang M. Synthesis of methotrexate modified superparamagnetic nanoparticles and their uptake into Breast Cancer Cells. MRS Fall Meeting, Boston, MA. December 2-6, 2002.

4. Kohler N, Zhang Y, Busche B, Zhang M. Superparamagnetic Nanoparticles for Imaging. International Symposium on Optical Science and Technology. SPIE Annual Meeting, July 2002.
5. Zhang Y, Kohler N, Sun Conroy, Zhang M. Self-assembled coatings on individual monodisperse magnetite nanoparticles for efficient intracellular uptake. In preparation.

Figures:

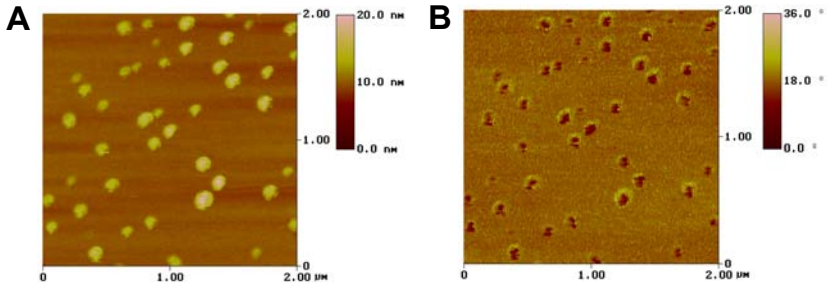

Figure 1, AFM images of the nanoparticles after PEG modification under height (A) and phase (B) mode. These self-assembled nanoparticles remained monodisperse and PEG was coated on individual nanoparticles to form a core-shell structure.

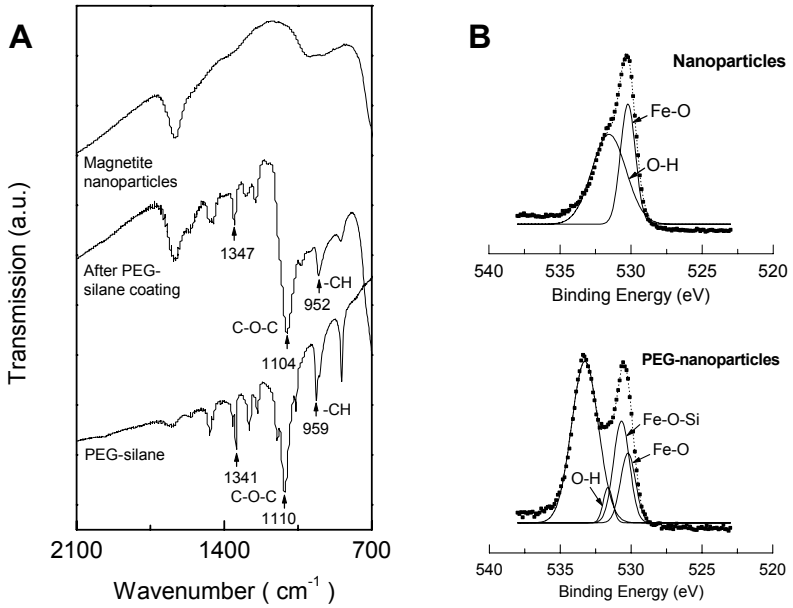

Figure 2, FTIR (A) and XPS O_{1s} (B) spectra of the PEG coated nanoparticles. PEG was chemically bonded to the nanoparticles.