Superparamagnetic Nanoparticles for Imaging and Therapeutics

Awarded: Nathan Kohler
Mentors: M. Zhang – UW; Glen E. Fryxell – PNNL

Project Summary:

Superparamagnetic nanoparticles have many biomedical applications (e.g. cell separation, contrast enhancement in magnetic resonance imaging (MRI), drug delivery, hypothermic therapies at the cellular level, and magnetic-field-assisted radionuclide therapy). The goal of this research is to develop novel liposome/nanoparticles-conjugate/drug systems with combined cancer diagnostic and therapeutic functions. These "smart" nanoparticle conjugates or liposome's are designed to recognize tumorspecific markers and target only individual tumor cells. These particles will enable doctors to detect tumors with MRI at the cellular level in very early stages and measure the therapeutic efficiency of hyperthermia simultaneously.

Superparmagnetic nanoparticle drug delivery systems have been developed by modifying the nanoparticle surface with methotrexate (MTX), a common chemotherapeutic drug used extensively in cancer therapies for leukemia, breast, and several other forms of cancer. MTX was grafted onto the nanoparticle surface via a peptide bond enabling the drug to be released only under intracellular conditions. In vitro results of MTX modified nanoparticles grown in culture with human breast cancer cells have demonstrated: (1) a lowered cellular viability indicating the MTX has been cleaved from the nanoparticle and is released into the cellular cytoplasm and (2) the existence of the magnetite nanoparticles in the lysozomal compartments where the MTX would be cleaved from the particle surface.

To improve circulation time in vivo, PEG amine and carboxylate terminal self assembled monolayers capable of targeted drug delivery are being synthesized. Currently, a PEG molecular weight 600 carboxylate silane has been demonstrated via NMR and FTIR and is being tested on the superparamagnetic nanoparticle system.

Publications, Presentations and Proposals:

1. Zhang Y, Kohler N, Sun Conroy, Zhang M. Self-assembled coatings on individual monodisperse magnetite nanoparticles for efficient intracellular uptake. In preparation.
2. 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).

3. 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)
4. 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.
5. Kohler N, Zhang Y, Busche B, Zhang M. Superparamagnetic Nanoparticles for Imaging. International Symposium on Optical Science and Technology. SPIE Annual Meeting, July 2002.

Selected Figures:

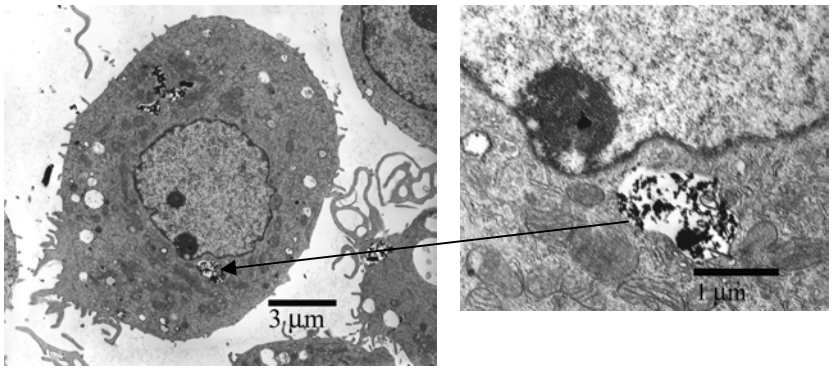

Figure 1: MTX modified nanoparticles have been visualized via TEM in human breast cancer cells. Nanoparticles are in lysozomal compartments where the MTX molecule is cleaved from the particle surface.

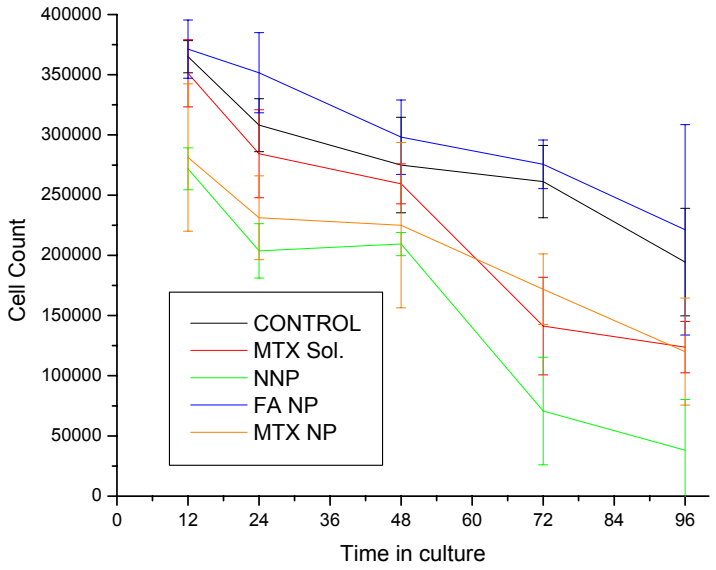

Figure 2: In vitro cell culture results have demonstrated the MTX grafted nanoparticles show a similar reduction in cellular viability compared to soluble (unmodified) MTX at blood plasma concentrations.

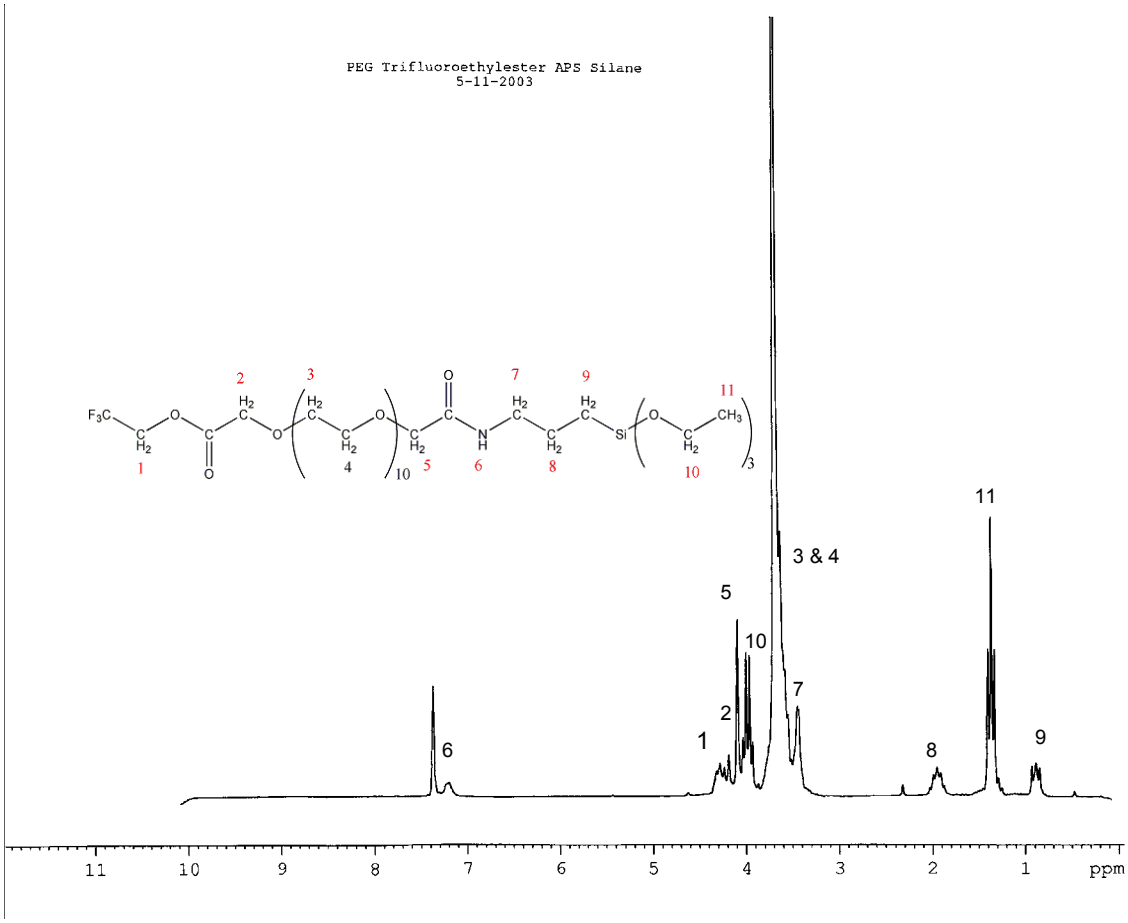

Figure 3: **H**NMR analysis of Trifluoroethylester (Carboxylate Terminal) PEG silane. Peak analysis demonstrates the self assembled monolayer structure which can be immobilized on the nanoparticle surface.