

## Biocompatible chitosan nanoparticles encapsulating iron oxide with a MRI high-relaxivity

H-Y. Kuo<sup>1,2</sup>, J-J. Wang<sup>2,3</sup>, R-T. Tsai<sup>2</sup>, I-R. Chang<sup>1</sup>, K. Ng<sup>2</sup>, C-L. Liu<sup>4</sup>, and C-R. Shen<sup>1,2</sup>

<sup>1</sup>Graduate Institute and Department of Medical Biotechnology and Laboratory Science, Chang Gung University, Kweishan, Taoyuan, Taiwan, <sup>2</sup>Molecular Imaging Center, Chang Gung Memorial Hospital, Kweishan, Taoyuan, Taiwan, <sup>3</sup>Department of Medical Imaging and Radiological Sciences, Chang Gung University, <sup>4</sup>Graduate School of Biochemical Engineering, Min Chi University of Technology, Taishan, Taipei, Taiwan

Chitosan has been used to encapsulate both CdSe/ZnS quantum dots or gadolinium-diethylenetriaminepentaacetate, forming functional nanoparticles that can be used in *in vitro* or *in vivo* studies as fluorescent biological labels as well as magnetic resonance imaging (MRI) contrast agents, respectively. In this study, we have developed and demonstrate chitosan encapsulating iron oxide with potential as a MRI T2 contrast agent, and it showed that the biocompatible chitosan coating superparamagnetic iron oxide (C-SPIO) nanoparticles maintained their desirable high relaxivity. C-SPIO nanoparticles were synthesized via in situ hybridization in the magnetic field. Magnetic resonance images of samples containing differing concentrations of mouse macrophages embedded in 1% agarose show a number of dark regions due to the superparamagnetic iron oxide particles, consistent with the number predicted by transmission electron microscopy. Colabeling of cell samples with a fluorescent dye leads to strong correlations between magnetic resonance and fluorescence microscopic images, showing the presence of the superparamagnetic iron oxide particles at the cell site. Most importantly, some toxicity occurring *in vitro* in the presence of high concentrations of dextrane coating superparamagnetic iron oxide (D-SPIO) were not found in the same or even higher doses of C-SPIO. It again reveals the excellent biocompatibility in combination with low toxicity of chitosan available as an undisputed biomolecule of great potential. Also, this result lays the foundation for our approach to tracking the movement of cells in live animals and human.

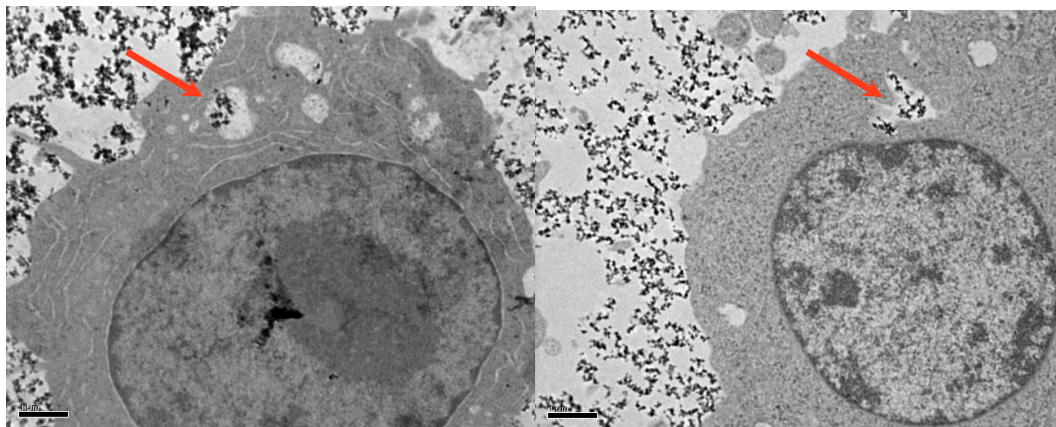


Figure 1. Transmission electron micrographs of a 100-nm slice of macrophages labeled *in vitro* using 72.9nm D-SPIO(left) and 132nm C-SPIOs (right).