Title:	Smart Superparamagnetic Nanoparticle Imaging Probes for Brain Tumor Research
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Description:	The goal of this research is to develop novel magnetic nanoparticle conjugates that can serve as contrast enhancement agents in magnetic resonance imaging (MRI) and drug carriers in controlled drug delivery for cancer diagnostics and therapeutics, and to evaluate drug efficacy in vitro. Major challenges for in vivo applictions of magnetic nanoparticles include particle agglomeration causing short particle circulation time in blood, selective cell targeting, and efficiency of particle internalization by target cells. We propose to address these problems by developing an integrated system of nanoparticle-PEG-ligands. The first objective is to modify nanoparticles with PEG-linked PK11195 to give the nanoparticles highly specific targeting capability as well as to facilitate their internalization into the target cells. The short chains of PK11195 molecules allow the efficient internalization of the nanoparticles as opposite to the widely-used antibodies which are bulky and thus difficult to cross the cell membrane. The second objective is to develop nanoparticle-PEG-annexin V conjugates for detection of apoptosis in vitro. We will synthesize mutated annexin V with multiple amino groups to increase the immobilized amount of annexin V on nanoparticles and improve targeting efficiency. The third objective is to utilize the unique microscopy, magnetic resonance imaging (MRI) and optical confocal microscopy (CM) at PNNL, capable of carrying on magnetic resonance and optical confocal images simultaneously, to examine the kinetics of cellular uptake of nanoparticle conjugates and study efficacy of drugs to tumor cells. This study will provide insights to the mechanisms of the cell targeting by nanoparticle systems and nanoparticle internalization, and further our understanding in the interactions between material and biological systems at the cellular level.