Abstract:
Stem cell based therapies offer significant potential for the field of regenerative medicine. However, much remains to be understood regarding the in vivo kinetics of transplanted cells. A non-invasive method to repetitively monitor transplanted stem cells in vivo would allow investigators to directly monitor stem cell transplants and identify successful or unsuccessful engraftment outcomes. A wide range of stem cells continues to be investigated for countless applications. This protocol focuses on 3 different stem cell populations: human embryonic kidney 293 (HEK293) cells, human mesenchymal stem cells (hMSC) and induced pluripotent stem (iPS) cells. HEK 293 cells are derived from human embryonic kidney cells grown in culture with sheared adenovirus 5 DNA. These cells are widely used in research because they are easily cultured, grow quickly and are easily transfected. hMSCs are found in adult marrow. These cells can be replicated as undifferentiated cells while maintaining multipotency or the potential to differentiate into a limited number of cell fates. hMSCs can differentiate to lineages of mesenchymal tissues, including osteoblasts, adipocytes, chondrocytes, tendon, muscle, and marrow stroma. iPS cells are genetically reprogrammed adult cells that have been modified to express genes and factors similar to defining properties of embryonic stem cells. These cells are pluripotent meaning...
they have the capacity to differentiate into all cell lineages (1). Both hMSCs and iPS cells have demonstrated tissue regenerative capacity in-vivo. Magnetic resonance (MR) imaging together with the use of superparamagnetic iron oxide (SPIO) nanoparticle cell labels have proven effective for in vivo tracking of stem cells due to the near microscopic anatomical resolution, a longer blood half-life that permits longitudinal imaging and the high sensitivity for cell detection provided by MR imaging of SPIO nanoparticles (2-4). In addition, MR imaging with the use of SPIOs is clinically translatable. SPIOs are composed of an iron oxide core with a dextran, carboxydextran or starch surface coat that serves to contain the bioreactive iron core from plasma components. These agents create local magnetic field inhomogeneities that lead to a decreased signal on T2-weighted MR images (5). Unfortunately, SPIOs are no longer being manufactured. Second generation, ultrasmall SPIOs (USPIO), however, offer a viable alternative. Ferumoxytol (FerahemeTM) is one USPIO composed of a non-stoichiometric magnetite core surrounded by a polyglucose sorbitol carboxymethyl ether coat. The colloidal, particle size of ferumoxytol is 17-30 nm as determined by light scattering. The molecular weight is 750 kDa, and the relaxivity constant at 2T MRI field is 58.609 mM-1 sec-1 strength(4). Ferumoxytol was recently FDA-approved as an iron supplement for treatment of iron deficiency in patients with renal failure (6). Our group has applied this agent in an "off label" use for cell labeling applications. Our technique demonstrates efficient labeling of stem cells with ferumoxytol that leads to significant MR signal effects of labeled cells on MR images. This technique may be applied for non-invasive monitoring of stem cell therapies in pre-clinical and clinical settings.