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Heat induced radiocation sequestration with magnetic iron oxide nanoparticles

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Heat Induced Radiocation Sequestration (HIRS) is a chelate free method that employs heat to induce tight bonds between radiocations and magnetic nanoparticles (NPs). HIRS employs three steps: (i) "Loading," that is heating to induce bonding between a magnetic NP and a radiocation, (ii) stripping, incubating the now radioactive magnetic NP with a chelator to remove loosely bound radiocations and, (iii) purification, separating high molecular weight, now radioactive NPs from low molecular weight radioactive-chelate complexes. To demonstrate HIRS for medical imaging, we employed Feraheme (FH), an FDA approved, heat stable, magnetic iron oxide NP indicated for treating iron anemia. As shown in the figure, a FH NP consists of a core of magnetic iron oxide (blue ball) and a thick polymer shell (gray). HIRS employed Loading (2h @ 120C), Stripping, a desferoxamine chelator (15 min @ 25C) and Purification (G-25 size exclusion chromatography). (Purification of magnetic FH NP was most rapidly accomplished with chromatography, rather than magnetic extraction.) HIRS labeled FH NPs with $^{89}Zr^{4+}$ or $^{64}Cu^{2+}$ (for PET imaging) or $^{111}In^{3+}$ for SPECT imaging. HIRSS NP labeling was highly stable to chelate challenge (incubation with chelate) and protein challenge (incubation with serum). After an intravenous injection in mice, 89Zr-FH was internalized by blood monocytes. Using PET/CT imaging, monocyte trafficking to normal lymph nodes and to an abnormal limb inflammation was imaged. With appropriate selection of magnetic NPs, Loading and Stripping conditions, HIRS might find application beyond medical imaging, in areas such as the magnetic radiometal extraction for radiocation analyses, or the magnetic extraction and sequestration of radiocations for long-term storage.

Biography

Lee Josephson is a Chemist and Chemical Biologist who designs radioactive and fluorescent and magnetic materials for biological applications. He is an Associate Professor at Harvard Medical School. He is a co-author of over 100 peer-reviewed Pubmed articles and a co-inventor on more than 30 issued US patents. He is a co-founder of AMAG Pharmaceuticals (AMAG, AMEX) and T2 Biosystems (NASDAQ, TTOO), and is partner in MedChem Imaging (MCI) LLC.

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