DOE/ER/63477-3

Human hepatic stem cell imaging for both MRI and PET have been accomplished within SCID/nod mice, and succeeded in cell specificity labeling with *in vitro, ex vivo*, and *in vivo* image tracking. For MRI, stem cell labeling was accomplished by two methods: 1.) *in vitro* labeling the stem cells just prior to in vivo transplantation, and/or 2.) transplanting the stem cells into SCID/nod mice and in vivo specificity labeling the cells just prior to MRI. For labeling techniques 1 & 2, multiple image controls were utilized and include: A.) stem cells(-) and contrast label(-), B.) stem cells(+) and contrast label(-), and C) stem cells(-) and contrast label(+) help to confirm signal noise background interference, which is a result of slight nonspecific cell labeling. Contrast labeled stem cells are directly transplanted into liver tissues, the tissues excised, and immediately MR imaged to determine cell dispersion dynamics. In this method, the contrast labeled cells appear as void foci throughout the organs. The images are imported into Metamorph imaging software and analyzed for foci radii, diameter, and to discern spheroid volumes. Then, cell numbers are extrapolated to understand "imaged" cell aggregate requirements using this technique. For this ex vivo method, a cell aggregate of ~100 stem cells is required to MRI monitor signal activities. For in vivo imaging, contrast labeled human stem cells within SCID/nod mice are also confirmed as small foci voids and are evident within liver tissues. Initially, these short-term studies where accomplished by in vitro labeling stem cells, transplanting the cells, then in vivo imaging the tissues between days 3-15. Next and to avoid imaged time limitations of detaching contrast agents, the proliferative stem cells were labeled after transplantation, and before MR imaging. This was accomplished to confirm the ability to specifically label unique cell subsets after the human stem cells integrated into foreign host tissues.

Stem cell labeling for PET was accomplished by utilizing a Lenti Viral Vector to modify the stem cells DNA such that the cells either: 1) have overexpression of thymidine kinase (TK) for FHBG (F18) labeling, or 2) expression of green fluorescent protein (GFP) for fluorescence imaging. *In vitro* controls were utilized for both TK and GFP. *In vitro* TK labeled cells were imaged after the cells were exposed to varying amounts of FHBG (and F18 construct). For petri dish cultures, it was determined that 10 μCi was an adequate amount to visualize stem cell labeling activities. FHBG labeling using 1mCi showed nonspecific labeling to the petri dish walls and bottom surfaces. For in vivo monitoring of stem cells that were previously transplanted into SCID/nod mice – with a mouse weight of ~30g, it was determined that 100uCi within a 0.3ml bolus was adequate for stem cell labeling and monitoring for up to 14 hours. The FHBG label was tail vein injected in the mice to generate contrast image labeling of the transplanted stem cells. At the end study, a concurrent Phospher imaging technique was accomplished on excised tissues, to include lung, kidney, liver, and spleen. This technique is used as a secondary confirmation of FHBG activity within specific tissues, and contrasted against PET imaging analysis.

Refereed Articles

McClelland R, Wauthier E, Schmelzer E, Reid L* and Hsu, E*(*co-senior authors). : Specificity Cell Labeling using 7.1T microMRI: in vivo Long Term Tracking of Transplanted Human Hepatic Stem Cells. Manuscript in final stages of editing for submission.

McClelland R, Wauthier E, Reid L* and Hsu E* [co-senior authors]. *In Vivo* microPET Tracking of Contrast Labeled Human Hepatic Stem Cells: FHBG & Lenti Viral Vectors. Final stages of editing prior to submission of manuscript.
McClelland R, Wauthier E and Reid LM. Biological effects of extracellular matrix from stem cell compartment versus mature liver on human hepatic stem cells. In preparation
McClelland R, Schmelzer E, Wauthier E and Reid LM. Type III collagen substratum elicit self-replication of human hepatic stem cells. In preparation.

Conferences

McClelland R, Wauthier E, Reid LM*, and Hsu E*. *In vivo* imaging of transplanted human hepatic stem cells: negative contrast labeling and micro-MRI tracking. ***24th Army Science Conference (Transformational Science and Technology for the Current and Future Force).*** 2004
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