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IN VIVO STEM CELL TRACKING USING MULTIMODALITY MOLECULAR IMAGING

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Introduction: Determining the fate and function of stem cells after implantation plays a pivotal role in the development of new therapeutic applications in regenerative medicine. In the current study we used lentiviral vectors encoding for various reporter genes and micron-sized iron oxide particles (MPIOs) to label mesenchymal stem cells (MSCs). Labeled cells were implanted in rodents and monitored for survival and osteogenic differentiation using bioluminescence imaging (BLI), micro single photon emission computed tomography/CT (SPECT/CT), or micromagnetic resonance imaging (MRI). We demonstrate that we are able to track tissue-specific differentiation of MSCs using optical, nuclear, and MR-based imaging modalities in various implantation models.

Methods: MSCs were labeled with MPIOs and injected into rat degenerated coccygeal intervertebral discs (IVD). In addition, MSCs were transduced with a lentivector encoding for GFP and Luciferase. The cells were injected into NOD/SCID mice via the tail vein and BLI was used to track the cells. MSCs were transduced as well with a lentivector encoding for the human sodium iodide symporter (hNIS) gene and implanted subcutaneously in mice. We used SPECT/CT to detect uptake of 99mTc-pertechnetate by the implanted cells. MSCs were also transduced with lentivectors encoding for either Luc or hNIS genes driven by the human osteocalcin (hOc) promoter. Expression of the reporter gene was evaluated in vitro in conditions of osteogenic induction. MSCs transduced with lenti-hOC-Luc were further infected with adeno- BMP2 vector and implanted in mice. BLI was performed to quantify osteogenic activity in this model.

Results: MPIO-labeled cells were tracked in the rat IVD up to 25 days post-implantation. In mice injected systemically with Lenti-GFP-Luc labeled cells, the bioluminescent image was seen in the lungs 1 hour after injection and lasted for 48 hours. Lenti-hNIS labeling was verified using immunostaining. The graft of lenti-hNIS labeled cells demonstrated radioisotope uptake in vivo. In vitro, cells labeled with lenti-hOC-hNIS stained positively. Luciferase expression was detected only in lenti-hOC-Luc labeled cells that also expressed BMP2.

Conclusions: We were able to monitor implanted stem cells in a minimally invasive, longitudinal, and quantifiable manner. The use of functional reporter vectors allows us to monitor cell function as well as cell fate using different imaging modalities, at various implantation sites.

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