Development of a Magneto-sonoporation-Enhanced Stem Cell Labeling Technique

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PURPOSE: Monitoring of stem cells migrating or homing to the targets is essential for the success of stem cell-based therapies. For non-invasive magnetic resonance imaging (MRI) to serially track cell migration, recent efforts have focused on labeling cells with MR contrast agents, such as superparamagnetic iron oxide (SPIO) particles. The currently-available MR cell labeling techniques include simple incubation and magneto-electroporation. We attempted to develop an alternative instant cell labeling technique, using ultrasound to facilitate MR-labeling of cells, called magneto-sonoporation (MSP), which is based on the fact that ultrasound can increase cell membrane permeability to external molecules.

METHODS: We tested the MSP approach using mouse LacZ-neural stem cells, C17.2. In vitro study, the cells were suspended in PBS at a density of 1-5x10^6 cells/mL and mixed with Feridex (Berlex Imaging, Wayne, NY) at 2mg Fe/mL. Then, the Feridex-cell mixture was transferred to the sterilized cell labeling container and subjected to 1-MHz ultrasound at 0.3W/cm^2 intensity, 50% duty cycle, and 5-mins exposure time. After the MSP treatment, we performed Prussian blue stain and immnocytochemistry to confirm the success of Feridex-labeling. Then, we evaluated the cell viabilities and metabolic assimilation rate using trypan blue exclusion and MTS (3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2H-tetrazolium) assay (CellTiter 96 AQueous, Promega). The viability of MSP-labeled cells was 0.938 ± 0.045. Both in vivo T2-weighted and T2*-weighted MR imaging showed MR signal void at the brains injected with Feridex-labeled cells, which was not seen at the control brains injected with control cells. The Prussian blue stain and anti-dextran/β-gal double-staining confirmed that the cells were successfully localized in the target brains and consistent with the MR signal changes of MR labeling (Figure 2).

RESULTS: Of the in vitro study, both Prussian blue staining and immnocytochemistry demonstrated successful labeling of cells with Feridex- or dextran-positive cells (Figure 1). The viability of MSP-labeled cells was 0.938 ± 0.03, which was close to the metabolic assimilation rate, 0.935 ± 0.045. Both in vivo T2-weighted and T2*-weighted MR imaging showed MR signal void at the brains injected with Feridex-labeled cells, which was not seen at the control brains injected with control cells. The Prussian blue staining and anti-dextran/β-gal double-staining confirmed that the cells were successfully localized in the target brains and consistent with the MR signal changes of MR imaging (Figure 2).

Conclusion: This technical development demonstrates the potential of using magneto-sonoporation to facilitate MR labeling of stem cells, which may become a safe and efficient MR labeling approach to instantly label large amounts of stem cells for preclinical and clinical applications.

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Reference: