MULTI-MODALITY IMAGING-VISIBLE REPORTER GENE LABELED HUMAN MESENCHYMAL STEM CELLS FOR TREATING ISCHEMIC ARTERIAL DISEASES

ACC Poster Contributions
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Background: Stem cell therapies, although promising for treating ischemic arterial diseases in preclinical and clinical studies, have been hampered by low cell survival rate, poor cell retention and the inability to monitor and track cell fate. Recently, we have shown that cell microencapsulation coupling with a multifunctional imaging contrast agent, perfluorooctylbromide (PFOB), offer a means to improve cell survival and enable capsule tracking with multiple imaging modalities. However, cell viability within the capsule cannot be assessed in vivo. Stem cell labeling with reporter genes may offer the ability to assess cell viability within microcapsules. Here, we are evaluating the potential of an imaging-visible, perfluorinated, microcapsule containing human mesenchymal stem cells (hMSCs) that are transfected with the triple-fusion reporter gene (TFR).

Methods: Bone marrow-derived hMSCs were transiently transfected with a plasmid construct containing firefly luciferase (bioluminescence imaging reporter, BLI), red fluorescence protein, and herpes simplex truncated thymidine kinase (positron emission tomography reporter, PET). Microencapsulation of transfected hMSCs was performed using a modified cell encapsulation method with the addition of PFOB. BLI was acquired to assess cell transfection efficiency and viability after encapsulation. In vitro hMSC uptake of [18F]-labeled 9-[4-fluoro-3-(hydroxymethy)butyl] guaninderivatives ([18F]-FHBG) was performed at 37°C for 60 min to determine radioisotope incorporation. All data were normalized and compared to empty microcapsules.

Results: BLI indicated that hMSCs can be transfected with TFR gene. The viability of hMSCs remained high (84%) after transfection and microencapsulation. Compared to empty microcapsules, PFOB-encapsulated TFR-hMSCs demonstrated the highest [18F]-FHBG uptake (169.4%), followed by naked TFR-hMSCs (108.3%) and non-transfected hMSCs (-2.3%).

Conclusion: PFOB microencapsulation of TFR-hMSCs maintains cell viability in vitro. Importantly, encapsulated TFR-hMSCs showed a higher affinity and retention of FHBG which offers the ability to use PET imaging for monitoring cell delivery.