

Multimodal Imaging of MSCs into Animal Models of GVHD - Route of Transplantation

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Mesenchymal stem cells (MSCs) have shown promise in the treatment of graft-versus-host disease (GVHD), a fatal complication caused by allogeneic bone marrow transplantation. However, its underlying mechanisms remain poorly understood. In particular, it is unknown whether stem cell distribution pattern is correlated with the treatment efficacy. In this study, we injected human MSCs (hMSCs) into the GVHD animals via either carotid artery or tail vein. The distribution patterns of hMSCs were imaged with the bioluminescence imaging technique (BLI) after stem cell transduction with a triple fusion reporter gene carrying luc (luciferase) –mrfp (mimeric red fluorescence protein)-ttk (truncated thymidine kinase). Meanwhile, a mixed population of transduced hMSCs and Tc-99m-labeled hMSCs were transplanted for combined planar imaging, single-photon emission computed tomography imaging (SPECT) and BLI. It was found that these combined imaging modalities correlated well with each other, revealing the initial distribution of the cells *in vivo*. Artery injection led to a strong, whole-body distribution of the cells that persisted about two weeks in the allogeneic models, while cells were cleared in the syngeneic animals within one week. Although some cells were accumulated in the lungs, a much higher dose migrated to other tissues or organs including the intestines, as confirmed by *in vivo* BLI imaging, *ex-vivo* BLI imaging, immunohistochemistry and quantitative RT-PCR. In contrast, due to the first pass effect as well as the large size of hMSCs, stem cells injected i.v. into the animal models are mainly entrapped in the lung and quickly cleared within 1 week from the lung, with only a small fraction of cells transiently traveling to the target intestines on day 1. Survivals, clinical scores and weight loss of the animals along with time were also compared. This study may show the potential of artery injection in the treatment of diseases by altering the drug distribution patterns.