

Imaging MSCs Applied to the Mouse Model of GVHD

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Graft-versus-host disease (GVHD), a fatal complication caused by allogeneic hematopoietic stem cell transplantation, has been traditionally treated with immunosuppressive agents that disrupt the T-cell activation and proliferation. The side effects of these therapeutic drugs and presence of drug resistance necessitate the development of novel ways of therapies. Mesenchymal stem cells (MSCs) have shown to suppress the alloreactivity of T-cells, thereby possessing great potential in treating GVHD. In this study, therapeutic efficacy of human MSCs (hMSCs) was tested in the intestine GVHD mice models, and in the meantime, hMSCs were transduced with a triple fusion reporter gene carrying luc (luciferase) –mrfp (mimeric red fluorescence protein)-ttk (truncated thymidine kinase) to study the stem cell distribution in the disease model by means of bioluminescence (BLI) imaging technique. Despite the similar weight loss patterns of the allogeneic disease animals, 100% of the allogeneic animals without hMSCs injection died, and only 30% with hMSCs injection died within 6 weeks. BLI imaging only showed transient migration of stem cells to the intestines, while the majority were entrapped in the lung and then disappeared after 1 week. However, a strong BLI signal was observed in the allogeneic animals after 1 month transplantation, which persisted until the sacrifice of the animals after week 7. Ex-vivo imaging confirmed that the signals were from the abdominal areas, and quantitative RT-PCR proved the existence of more transduced cells in the intestines and lungs of the allogeneic animals than in the syngeneic animals. Immunohistochemistry shows that hMSCs were fused in the large intestine without engraftment, but engrafted in the lungs. In summary, MSCs are effective in the treatment of GVHD, and molecular imaging technique has revealed the distribution patterns of stem cells in the GVHD animals. The mechanisms behind the MSC treatment and the BLI signal return need to be further elucidated.