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Imaging neural stem cell graft-induced structural repair in stroke

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Cell therapy is a promising approach for human neurological disorders. Clinically relevant, is the development of multimodal, non-invasive molecular neuroimaging approaches to monitor the survival and function of grafted cells.

In the present study, we used magnetic resonance imaging (MRI) and positron emission tomography (PET) to track the infarct evolution, tissue repair and the fate of grafted neural stem cells. We genetically engineered embryonic stem cell–derived neural stem cells (NSCs) with a triple fusion reporter gene to express monomeric red fluorescence protein and herpes simplex virus truncated thymidine kinase for multimodal molecular imaging and SPIO labeled for MRI. The infarct size, as well as fate and function of grafted cells were tracked in real time for 3 months using MRI and PET. We report that grafted NSCs reduced the infarct size in animals with less then 1 cm3 initial infarct in a dose-dependent manner, while larger stroke was not amenable to such beneficial effects. PET imaging revealed increased metabolic activity in grafted animals and visualized functioning grafted cells in vivo. Immunohistopathological analysis demonstrated that, after 3-month survival period grafted NSCs dispersed in the stroke-lesioned parenchyma and differentiated into neurons, astrocytes and oligodendrocytes. Longitudinal multimodal imaging provides insights into time course dose-dependant interactions between NSC grafts and structural changes in infracted tissue.

Biography

Dr Marcel Daadi is a Senior Investigator and Director of The Regenerative Medicine Department at the Molecular Medicine Research Institute, a Consultant Assistant Professor, Director, Stem Cell Research, CIRM Disease Team Stroke Neural Transplant Program, at Stanford University School of Medicine. Dr. Daadi received his Ph.D. in Neuroscience at the National Centre for Scientific Research, Universite de la Mediterranee, Aix-Marseille II, Marseille, France. He is one of the leading research experts in translational neural stem cell research and product development for Parkinson's disease and stroke. He serves on various Editorial boards and grant review committees including NIH and the Maryland Stem Cell Research Fund.

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