Amyotrophic Lateral Sclerosis Research Program

U.S. Army Medical Research and Materiel Command
Overcoming the Practical Barriers to Spinal Cord Cell Transplantation for ALS
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The promise of stem cell regeneration has been the hope of many ALS patients, as well as others suffering from neurological disorders. Although multiple clinical trials are currently testing different stem cell therapies as treatment alternatives for neurodegenerative diseases and spinal cord injury, optimal injection parameters have not yet been defined nor are there sufficient data to effectively minimize post-surgery complications such as graft rejection. With support from an FY10 ALSRP TDA, Dr. Nicholas Boulis from Emory University is pursuing two aims in order to generate needed data to help guide clinical practice. The first part of his project entails determining the tolerance and toxicity of cell dosing, and numbers of permissible spinal cord injections in order to establish basic safety and injection parameters. The second part deals with optimizing immunosuppression following surgical spinal cord stem cell transplantation in order to minimize graft rejection. Taken together, the data generated from this project will significantly help translate stem cell therapy to patients with ALS.

For the first aim, Dr. Boulis injected minipigs with human neural progenitor cells and then assessed the pig’s gait and motor function, as well as general morbidity. All animals, despite increases in the volume and number of injections, returned to their preoperative baseline within 14 days, showing complete motor function recovery. However, swelling of the spinal cord with escalating volume doses prevented complete healing of the spinal cord in some cases. Dr. Boulis also was able to safely increase the number of injections to 40 in the swine model, as long as the volume of each injection was kept low. Ultimately, Dr. Boulis concluded that 25 micro liters is likely the ideal injection volume in order to maximize stem cell delivery and minimize tissue damage. These experiments support the functional safety of various injection volumes and numbers in the spinal cord, and provide critical insight to consider when developing safety thresholds for other studies.

The second part of Dr. Boulis’ project, focusing on the immune response to intraspinal stem cell therapy, is still ongoing. Graft rejection remains a significant risk for intraspinal stem cell therapies, and an assay to non-invasively monitor the immune response to transplanted intraspinal cell grafts is essential in order to move the field forward. Dr. Boulis hypothesized that graft-specific host antibodies generated after stem cell transplantation may be detected in the peripheral blood and can be used as a diagnostic marker of cellular graft rejection. To test this hypothesis, levels of graft-specific antibodies were measured in the peripheral blood of ALS patients and minipigs following either no immunosuppression or treatment with tacrolimus. Preliminary results provide evidence for a decreased immune response to transplanted intraspinal stem cell grafts with tacrolimus immunosuppression. In future studies, Dr. Boulis plans to correlate the peripheral blood findings to immunohistological analysis of transplanted grafts. Taken together, Dr. Boulis’ quest to overcome the barriers to spinal cord cell transplantation could significantly advance the treatment of ALS.