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Therapeutic potential of naive and genetically modified mesenchymal stem cells for traumatic brain injury

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There is increasing evidence that bone marrow-derived mesenchymal stem cells (BMSC) hold potential for stimulating recovery of the damaged brain tissue after traumatic brain injury (TBI). In a rat TBI model, we have tested the effects of BMSC, genetically modified with the intracellular domain of Notch1 gene (NICD) and the neo-resistant gene, which display properties of neuroprogenitorlike cells. After selection for G418 resistance, resultant BMSC-NICD were transduced with a GFP lentivirus and grown in non-adherent conditions to generate neurospheres. Rats received a unilateral, controlled cortical impact (CCI) over the forelimb sensorimotor cortex and were grafted with neurospheres into the cortex or striatum one week later. Control rats received vehicle or injured sham surgery only. Short and long term studies demonstrated that BMSC-NICD neurospheres evoke behavioral recovery in rats that received either striatal or cortical grafts. Survival of grafted cells was better in those rats that received striatal grafts suggesting that striatum is a better transplant site.

Currently, we are developing mechanically damaged organotypic hippocampal slice cultures as an in vitro TBI model. Cell death caused by mechanical injury is analyzed by propidium iodide (PI) uptake. Immediately after the injury, some of the damaged slices received MSC isolated from rat adipose tissue. Preliminary data of PI uptake suggest that transplanted MSC decrease cell death in this in vitro TBI model. We will further explore mechanisms underlying these apparent MSC neuroprotective effects. Our studies suggest that MSC could be developed as a novel therapy for TBI.

Biography

Glavaski-Joksimovic is an Assistant Professor at the Department of Neurosurgery, Medical College of Wisconsin. She received her Ph.D degree in Neuroscience and Veterinary Anatomy at the Iowa State University. Following graduation, she conducted a postdoctoral training at the Iowa State University, Karolinska Institute, and Northwestern University. From 2009 to 2011, Dr. Glavaski-Joksimovic worked as a Research Assistant Professor at the Department of Pediatrics, Feinberg School of Medicine, Northwestern University. In May 2011, she joined the Medical College of Wisconsin. Dr. Glavaski-Joksimovic's studies are focused on the therapeutic potential of adult stem cells in a brain injury and disease.

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