Engineered Human Neural Stem Cells for Treating Spinal Cord Gliomas: A Neurobiology-based Approach

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Abstract

There are currently no experimental models showing autonomic dysfunction for intramedullary spinal cord gliomas (ISCG), a lethal disease with no effective treatment. We have developed a rat model of ISCG and determined whether genetically engineered human neural stem cells (hNSC) could be developed into potent therapies for ISCG. ISCG rats received injection of hNSC.CD-TK, hNSC.CD or hNSC.CD-TK debris adjacent to the tumor epicenter 7 days after glioma cell implantation, followed with daily prodrug administration (5-FC and GCV; i.p. throughout the study). Post-tumor survival was assessed by time lasted before loss of body weight-bearing stepping in the hindlimb. Also evaluated were autonomic functions and tumor growth rate in vivo. ISCG rats with hNSC.CD-TK treatment showed significantly improved survival than controls that received hNSC.CD or hNSC.CD-TK debris (P < 0.05, median rank test), with better maintained autonomic function and reduced tumor growth rate. hNSC.CD-TK cells migrated diffusively into ISCG clusters to mediate targeted oncolytic effect in manners that spared spinal cord projection pathways. Through impeding glioma growth and preserving spinal cord neurobiology, dual gene-engineered hNSC regimen significantly prolonged survival in a rat model that emulated sensorimotor and autonomic dysfunctions of human cervical ISCG. Our findings may provide a stem cell-based multimodal approach to treating ISCG and help formulate a recovery neurobiology-based therapeutic strategy for gliomas.

Biography

After receiving his Medical and Master of Science Degrees in Beijing University, Prof. Teng obtained his Ph.D. in Cell Biology/Neuroscience at Georgetown University, USA. For his postdoctoral training, he studied respiratory neurobiology, and stem cell biology and neurodegeneration at Georgetown University and Harvard Medical School, respectively. He investigates Functional Multipotency of Stem Cells and Recovery Neurobiology of the Spinal Cord via multimodal approaches that integrate stem cell biology, neural oncology, chemical engineering, and molecular pharmacology. Work of his team received the prestigious 2011 Apple Award of the American Spinal Injury Association (ASIA), the ERF New Investigator Award
from the Foundation of Physical Medicine & Rehabilitation (2004), the Annual CNS Research Award from the Congress of Neurological Surgeons (2001), and the Mayfield Award (2012 and 2015) and Larson Research Award (2015) from the American Association of Neurological Surgeons/Congress of Neurological Surgeons (AANS/CNS) Joint Section on Disorders of the Spine and Peripheral Nerves. He is presently Professor and Director, Laboratory of Spinal Cord Injury, Stem Cell Biology and Neurofacilitation Research, Departments of Physical Medicine & Rehabilitation (PM&R) and Neurosurgery, Harvard Medical School/Spaulding Rehabilitation Hospital/Brigham & Women’s Hospital. Prof. Teng was elected President (2013-2014) of the American Society for Neural Therapy and Repair.