Application of stem cell technology for the treatment of Malignant glioma of spinal cord

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Glioma is the most malignant type of primary central nervous system tumors, and has an extremely poor prognosis. One potential therapeutic approach is to induce the terminal differentiation of glioma through the forced expression of pro-neural factors. Our goal is to show the proof of concept of the neuronal conversion of C6 glioma through the combined action of small molecules. We investigated the various changes in gene expression, cell-specific marker expression, signaling pathways, physiological characteristics, and morphology in glioma after combination treatment with two small molecules (CHIR99021, a glycogen synthase kinase 3 [GSK3] inhibitor and forskolin, a cyclic adenosine monophosphate [cAMP] activator). Here, we show that the combined action of CHIR99021 and forskolin converted malignant glioma into fully differentiated neurons with no malignant characteristics; inhibited the proliferation of malignant glioma; and significantly down-regulated gene ontology and gene expression profiles related to cell division, gliogenesis, and angiogenesis in small molecule-induced neurons. In vivo, the combined action of CHIR99021 and forskolin markedly delayed neurological deficits and significantly reduced the tumor volume. We suggest that reprogramming technology may be a potential treatment strategy replacing the therapeutic paradigm of traditional treatment of malignant glioma, and a combination molecule comprising a GSK3 inhibitor and a cAMP inducer could be the next generation of anticancer drugs.

CURICULUM VITAE

Yoon Ha, MD, PhD received his medical degree and PhD from Yonsei University. He completed his internship and neurosurgery residency at Severance hospital, Yonsei University in 1999.
In 2015, Dr. Ha was appointed Professor of Neurological Surgery in Yonsei Univ. Dr. Ha is board certified in the fields of Neurological Surgery.
Dr. Ha has an active research interest in spinal surgery and basic research, particularly in numerous multicenter outcome research studies of spinal deformities, cervical OPLL, spinal cord injury, spinal trauma and tumors involving the spinal column.
He has served as an Editor in Chief of *"The Neurospine"* and editor on the Editorial Boards of Neurosurgery (2016), Neurosurgery Focus (2017), and Asian spine journal (2017～).
During his career in medicine, Dr. Ha has won numerous awards for medicine. He has won the Synthes Award for Research in Spinal cord injury and spinal column injury at Congress of Neuyrological Surgeons in 2004 (San Francisco). He received basic science research award in Cervical Spine Research Societies in 2004 (Boston) and 2009 (Salt Lake City).
Dr.Ha's clinical fields of interest are Adult Spinal Deformity Surgery, Cervical Deformity and Correction Surgery, Cervical OPLL and spondylotic myelopathy, Endoscopic spine surgery for lumbar degenerative disease, Robotic spinal surgery for spine tumor resection and Biologic therapy for Malignant Spinal cord tumor.