8th International Conference on
Neuroscience and Neurological Disorders

September 28, 2022 | Webinar

Received date: 20-06-2022 | Accepted date: 22-06-2022 | Published date: 10-10-2022

Thrombin preconditioning improves the therapeutic efficacy of mesenchymal stem cells in severe intraventricular hemorrhage induced neonatal rats

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Severe intraventricular hemorrhage (IVH) remains a major cause of high mortality and morbidity in extremely preterm infants. Mesenchymal stem cell (MSC) transplantation is a possible therapeutic option, and development of therapeutics with enhanced efficacy is necessary. This study investigated whether thrombin preconditioning improves the therapeutic efficacy of human Wharton's jelly-derived MSC transplantation for severe neonatal IVH, using a rat model. Severe neonatal IVH was induced by injecting 150 μL blood into each lateral ventricle on postnatal day (P) 4 in Sprague-Dawley rats. After 2 days (P6), naïve MSCs or thrombin-preconditioned MSCs (1 × 105/10 μL) were transplanted intraventricularly. After behavioral tests, brain tissues and cerebrospinal fluid of P35 rats were obtained for histological and biochemical analyses, respectively. Thrombin-preconditioned MSC transplantation significantly reduced IVH-induced ventricular dilatation on in vivo magnetic resonance imaging, which was coincident with attenuations of reactive gliosis, cell death, and the number of activated microglia and levels of inflammatory cytokines after IVH induction, compared to naïve MSC transplantation. In the behavioral tests, the sensorimotor and memory functions significantly improved after transplantation of thrombin-preconditioned MSCs, compared to naïve MSCs. Overall, thrombin preconditioning significantly improves the therapeutic potential and more effectively attenuates brain injury, including progressive ventricular dilatation, gliosis, cell death, inflammation, and neurobehavioral functional impairment, in newborn rats with induced severe IVH than does naïve MSC transplantation.

Recent Publications

1. So Yoon Ahn, et al. Intratracheal transplantation of mesenchymal stem cells attenuates hyperoxia-induced microbial dysbiosis in the lungs, brain, and gut in newborn rats International Journal of Molecular Sciences, 2022, 23 (12), 6601.
2. Ahn, S.Y.; Sung, D.K.; Chang, Y.S.; Sung, S.I.; Kim, Y.E.; Kim, H.-J.; Lee, S.M.; Park, W.S. BDNF-Overexpressing engineered mesenchymal stem cells enhances their therapeutic efficacy against severe neonatal hypoxic ischemic brain injury International Journal of Molecular Sciences, 2021, 22 (21), 11395.
3. So Yoon Ahn, Hyesoo Jie, Won-Beom Jung, Ji-Hyun Jeong, Sukjin Ko, Geun Ho Im, Won Soon Park, Jung Hee Lee, Yun Sil Chang, Seungsoo Chung. Stem cell restores thalamocortical plasticity to rescue cognitive deficit in neonatal intraventricular hemorrhage Experimental Neurology, Vol. 342, August 2021, 113736, ISSN 0014-4886.

Biography

So Yoon Ahn is currently working as a Clinical Associate Professor at Sungkyunkwan University School of Medicine, South Korea. She has an incredible experience in various fields of medicine. She has bagged various awards including the Academic Award, Korean Society of Perinatology (2019), Best Research Award, Pediatric Academic Societies and Asian Society for Pediatric Research Joint Meeting (2014) and more.

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