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Neurotrophin 3-expressing neural stem cells: A novel approach to remyelination and axon repair in animal model of multiple sclerosis

The therapeutic potential of bone marrow-derived neural stem cells (BM-NSCs) in experimental autoimmune encephalomyelitis (EAE), an animal model of multiple sclerosis (MS), has been recently suggested. However, current BM-NSCs therapy has resulted in only marginal improvement in clinical scores in EAE. To enhance the therapeutic effect, in the present study we transduced BM-NSCs with neurotrophin 3 (NT-3), a member of the neurotrophin family that has a strong capacity for neuroprotection and immunomodulation. We provide evidence that our approach has the following advantages compared to conventional NSC therapy: 1) NT-3 transduction enhanced BM-NSC proliferation and differentiation of oligodendrocytes and neurons, while inhibiting differentiation of astrocytes, thus promoting remyelination and neuronal repopulation, and reducing astrogliosis; 2) NT-3 transduction conferred a potent anti-inflammatory capacity to BM-NSCs, thus more effectively suppressing CNS inflammation and accelerating endogenous and exogenous remyelination, thereby significantly enhancing the therapeutic effects of BM-NSCs in CNS inflammatory demyelination. 3) The ready availability of BM-NSCs provides another advantage over brain-NSCs for MS therapy. 4) A Tet-on system can control NT-3 expression as desired. These advantages, together with the self-renewal property of NSCs, provide a novel approach to breaking the vicious inflammation-demyelination cycle, and this study should pave the way to an easily accessible, inducible and highly effective therapy for CNS inflammatory demyelination.

Biography

Guang-Xian Zhang earned his Ph.D. from Karolinska Institute, Stockholm, Sweden, in 1996 and began postdoctoral studies at the University of Pennsylvania School of Medicine in 2000. He is currently professor at the Department of Neurology, Thomas Jefferson University, and co-director of the Neuroimmunology Laboratories at this institution. He has published more than 80 peer-reviewed papers. He has also served as a reviewer for first-class journals, and as a reviewer on study section rosters in several funding agencies. His studies mainly focus on using neural stem cells as a novel approach for treatment of human multiple sclerosis, via mechanisms of immunomodulation, neural cell repopulation and neuroregeneration.

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