BEIKE BIOTECHNOLOGY Beike Stem Cells for Multiple Sclerosis (MS)

What is the disease and how does it affect the body?

Multiple sclerosis (MS) is a common neurological disease and a major cause of disability, particularly affecting young adults. It is characterized by patches of damage occurring throughout the brain and spinal cord, with loss of myelin sheaths – the insulating material around nerve fibres that allows normal conduction of nerve impulses terial around nerve fibre cells that make myelin (oligodendrocytes)[1].MS affects over two million people worldwide and shows a clear gender bias, with women being affected twice as frequently as men[2].Etiology of MS is still unknown; it is generally thought that the disease will develop in genetically susceptible individuals as a result of an autoimmune response directed against components of myelin[2]. An environmental agent or event (virus, bacteria, chemicals, lack of sun exposure) has been hypothesized to act in concert with a specific genetic predisposition to result in immune dysfunction[3].

What happens to the body if the disease remains untreated?

MS affects principally young adults and leads to severe physical and cognitive impairment. MS follows a relapsing-remitting (RR) course in 85% and a primary progressive (PP) course in 15% of patients. In the majority of RR patients, secondary progression (SP) occurs after a median interval of 19 years, with persisting relapses in 40% of cases. Overall,MS patients loose the ability to walk independently at a median age of 63 years, but 1–3% of patients suffer from the malignant form of MS and reach this level of disability only in a few weeks or months[4,5].MS also leads to visual disturbances, loss of sensation, speech and swallowing dysfunction, bowel and bladder incontinence, erectile penile dysfunction.

What are the current treatments and its efficiencies?

MS is, at present, incurable. We do not know the cause of the disease.

We do not know the cause of genetic factors culminating in autoimmune attack within the brain and spinal cord (central nervous system, CNS) is generally the accepted synthesis, but what such environmental factors may be remains obscure. Immune treatments are therefore routinely used, and these can reduce individual relapses both in severity (steroids, given acutely) and in frequency (interferons, glatiramer, and more recently various monoclonal antibodies, taken regularly). However, immune treatments have no impact on patients with progressive disability pact on taken regale deficits continue relentlessly, to accumulate[1].

How stem cells help relieve the disease's symptoms?

Some published papers showed that Mesenchymal stem cell is potentially good for MS [1,6,-11].

Improvement:

Most MS patients Beike have treated, utilizing the combination of mesenchymal stem cell therapy and rehabilitation, showed visible signs of improvement: increasing muscle strength, decreasing muscle tone of spasticity, improving swallow ability, regaining eyesight, regaining motor development and coordination etc.

However, when discussing improvements, it is important to remember that improvements might greatly differ from one patient to another due to many factors, such as patient's medical duration, severity, complication, physical condition, age and so on. Therefore, improvement cannot be guaranteed.

Mechanism:

The mechanisms of mesenchymal stem cell for MS are probably based on the following aspects: (1)MSCs exert their immunomodulatory functions on numerous immune cells including T cells, B cell, NK cells and dendritic cells (DCs)[12],MSC on one side induced peripheral T cell tolerance to myelin proteins thus reducing migration of pathogenic T cells to the CNS and, on the other side, homed themselves to the CNS where they preserved axons and reduced demyelination [6].(2) MSC can protect axons and improve neuronal survival[13-15], possibly via anti-apoptotic effects[16], anti-oxidant effects[17], or the release of trophic factors[18]. (3)MSC can induce endogenous neurogenesis[19] and oligodendrogenesis[20-22].(4)MSC can decrease production of proinflammatory cytokines and chemokines[23] (5)MSCs also appear to reduce gliotic scar formation – gliosis representing a major barrier to spontaneous repair[20,24].

References

1. Scolding N, Adult stem cells and multiple sclerosis.Cell Prolif. 2011 Apr;44 Suppl 1:35-8. 2. Payne N, Siatskas C, Bernard CC. The promise of stem cell and regenerative therapies for multiple sclerosis. J Autoimmun. 2008 Nov; 31(3):288-94.

3. Dyment DA, Willer CJ, Scott B, Armstrong H et al. Genetic susceptibility to MS: a second stage analysis in Canadian MS families. Neurogenetics. 2001 Jul; 3(3):145-51. 4. Confavreux C, Vukusic S. Age at disability milestones in multiple sclerosis. Brain. 2006 Mar;129(Pt 3):595-605.

5. Confavreux C, Vukusic S. Natural history of multiple sclerosis: a unifying concept. Brain. 2006 Mar;129(Pt 3):606-16. 6. Uccelli A, Benvenuto F, Laroni A, Giunti D.Neuroprotective features of mesenchymal stem cells.Best Pract Res Clin Haematol. 2011 Mar;24(1):59-64.

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9. Slavin S, Kurkalli BG, Karussis D.The potential use of adult stem cells for the treatment of multiple sclerosis and other neurodegenerative disorders.Clin Neurol Neurosurg. 2008 Nov;110(9): 943-6.

10. Karussis D, Kassis I. The potential use of stem cells in multiple sclerosis: an overview of the preclinical experience. Clin Neurol Neurosurg. 2008 Nov; 110(9):889-96.

11. Uccelli A, Mancardi G. Stem cell transplantation in multiple sclerosis. -Curr Opin Neurol. 2010 Jun; 23(3):218-25.

modulate pathogenic immune response in experimental autoimmune encephalomyelitis.

16. Crigler L, Robey RC, Asawachaicharn A, Gaupp D, Phinney DG. Human mesenchymal stem cell subpopulations express a variety of neuro-regulatory molecules and promote neuronal cell survival and neuritogenesis. Exp Neurol 2006; 198(1): 54–64.

18. Wilkins A, Kemp K, Ginty M, Hares K, Mallam E, Scolding N. Human bone marrowderived mesenchymal stem cells secrete brain-derived neurotrophic factor which promotes neuronal survival in vitro. Stem Cell Res 2009; 3(1): 63–70. 19. Munoz JR, Stoutenger BR, Robinson AP, Spees JL, Prockop DJ. Human stem/ progenitor cells from bone marrow promote neurogenesis of endogenous neural

12. Payne N, Siatskas C, Bernard CC. The promise of stem cell and regenerative therapies for multiple sclerosis: J Autoimmun. 2008 Nov;31(3):288-94.

13. Gerdoni E, Gallo B, Casazza S, Musio S, Bonanni I, Pedemonte E, Mantegazza R, Frassoni F, Mancardi G, Pedotti R, Uccelli A.Mesenchymal stem cells effectively Ann Neurol 2007; 61(3): 219–227.

14. Kassis I, Grigoriadis N, Gowda-Kurkalli B, Mizrachi-Kol R, Ben-Hur T, Slavin S, Abramsky O, Karussis D. Neuroprotection and immunomodulation with mesenchymal stem cells in chronic experimental autoimmune encephalomyelitis. Arch Neurol 2008; 65(6): 753–761.

15. Zhang J, Li Y, Lu M, Cui Y, Chen J, Noffsinger L, Elias SB, Chopp M. Bone marrow stromal cells reduce axonal loss in experimental autoimmune encephalomyelitis mice. J Neurosci Res 2006; 84(3): 587–595.

17. Lanza C, Morando S, Voci A, Canesi L, Principato MC, Serpero LD, Mancardi G, Uccelli A, Vergani L.Neuroprotective mesenchymal stem cells are endowed with a potent antioxidant effect in vivo. J Neurochem 2009; 110(5):1674–1684.

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20. Bai L, Lennon DP, Eaton V, Maier K, Caplan AI, Miller SD, Miller RH.Human bone marrow-derived mesenchymal stem cells induce Th2-polarized immune response and promote endogenous repair in animal models of multiple sclerosis. Glia 2009; 57(11): 1192–1203.

21. Akiyama Y, Radtke C, Kocsis J. Remyelination of the rat spinal cord by transplantation of identified bone marrow stromal cells. J Neurosci 2002; 22(15): 6623–6630.

22. Rivera FJ, Couillard-Despres S, Pedre X, Ploetz S, Caioni M, Lois C, Bogdahn U, Aigner L.Mesenchymal stem cells instruct oligodendrogenic fate decision on adult neural stem cells. Stem Cells 2006; 24(10): 2209–2219.

23. Uccelli A, Prockop DJ.Why should mesenchymal stem cells (MSCs) cure autoimmune diseases?Curr Opin Immunol. 2010 Dec;22(6):768-74.

24. Li Y, Chen J, Zhang CL, Wang L, Lu D, Katakowski M, Gao Q, Shen LH, Zhang J, Lu M, Chopp M.Gliosis and brain remodeling after treatment of stroke in rats with marrow stromal cells. Glia 49, 407–417.Glia. 2005 Feb;49(3):407-17.

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