

Editorial

Regenerative Medicine in Neurological Disorders: The Present Situation and Future Issues with Stem Cell Therapy

Feifei Wang*

Center for Innovative and Translational Medicine, Kochi University Medical School, Kohasu, Oko-cho, Nankoku, Kochi 783-8505, Japan

EDITORIAL

The repair of injured neuronal tissue in the central nervous system (CNS) has been considered to be impossible. Stem cell transplantation, however, has provided hope that the damaged neurons may be repaired. Expectations for the regenerative capacity represented by human induced pluripotent stem (iPS) cells have increased, not only for clinical application but also as potential tools to develop new pharmaceutical agents. In this chapter, the potential stem cell sources for neurological disorders and future issues will be described.

Embryonic stem cells and iPS cells

Embryonic stem (ES) cells are pluripotent stem cells and can be isolated from the blastocyst, an early-stage embryo. In 1998, researchers at the University of Wisconsin were the first to successfully isolate and cultivate human ES cells [1]. ES cells represented a promising source for cell transplantation because of their ability to differentiate into all somatic cell lineages, but the clinical applications for these cells has remained somewhat hampered by the ethical implications of using human embryos. However, use of human iPS cells rather than stem cells from human embryos begun to help overcome these issues. iPS cells were developed by Dr. Shinya Yamanaka, a professor at Kyoto University who was awarded the Nobel Prize in Physiology or Medicine in 2012 [2]. In Japan, the world's first clinical research using human iPS cells will soon begin and will test their effect in treating age-related macular degeneration. The competition between researchers to approach clinical applications for iPS cells is increasing. Despite the genetic analysis of iPS cells that has been conducted, the mechanisms of cellular reprogramming have yet to be fully elucidated [3]. Recent reports reveal that the genomes of iPS cell lines exhibit chromosome abnormalities, residual epigenetic markers from the parent somatic cell type, and a higher than normal number of coding sequence mutations [4]. In addition, the tumorigenic potential of iPS cells remains a great concern; these cells have been shown to form teratomas. Although new approaches to improve the safety and efficiency of iPS cells have been suggested, patients and their families need to be informed of the potential risks.

*Corresponding author

Feifei Wang, Center for Innovative and Translational Medicine, Kochi University Medical School, Kohasu, Oko-cho, Nankoku, Kochi 783-8505, Japan, Tel: +81-88-880-2561; Fax: +81-88-880-2435; E-mail: f-wang@kochi-u.ac.jp

Submitted: 02 July 2013

Accepted: 22 July 2013

Published: 24 July 2013

Copyright

© 2013 Wang.

OPEN ACCESS

Neural stem cells

Neural stem cells (NSCs) are thought to be an optimal cell source for the treatment of neurological disorders because of their potential to differentiate into cells of glial and neuronal lineage. Intraparenchymal transplantation of NSCs into the injured brain region induced functional improvement in the animal models of stroke [5]. NSC transplantation is also shown to be highly effective for treating spinal cord injury in primates [6]. The host microenvironment is an important element in defining the success of NSC grafting, and as such, some scaffolds have been developed to provide an appropriate cellular microenvironment that promotes neurite regeneration and synaptic reconstruction in the host brain [7]. However, there are ethical problems surrounding the use of fetal tissues associated with abortion, but these issues do not exist for autologous NSCs obtained from patient brain biopsies. Additionally, NSCs are relatively difficult to isolate and prepare. These points represent major obstacles to the advancement of NSC clinical applications.

Mesenchymal stem cells

Mesenchymal stem cells (MSCs) are non-hematopoietic stem cells that are found in the bone marrow and contribute to hematopoietic stem cells' niche homeostasis. MSCs have many advantages for cell transplantation therapy because they are easily available and pluripotent, but they don't have any associated ethical issues. Currently, MSC-based clinical trials are being conducted for CNS disease throughout the world. In stroke patients, Honmou *et al.* reported the feasibility and safety of autologous transplantation of human MSCs that had been expanded in autologous human serum [8]. Mean lesion volume was reduced by 20% at 1 week after MSC infusion. The excellent ability of MSCs to reduce the size of stroke lesions is a result of trophic factor secretion that promotes neural survival, angiogenesis, anti-inflammation and neurogenesis [9]. However, isolated MSCs are a heterogeneous population that frequently contains contaminating cells. The biological properties of MSCs cultured *in vitro* are significantly different from those *in vivo* [10]. Concerns over the MSC's safety and quality have been debated.

Umbilical cord blood cells

Human umbilical cord blood (HUCB) serves as a source of nutrients and oxygen between a mother and fetus, and can be collected at birth using non-invasive procedures. It has been recently reported that the use of HUCB may not be limited to the treatment of hematological disorders, and that HUCB transplantation could induce regeneration in CNS disorders [11]. HUCB cells, unlike embryonic stem cells, avoid ethical issues, can be collected easily, and have a history of clinical use in patients with cancer, sickle-cell anemia, immunodeficiency, marrow failure and genetic diseases [12]. Recently, HUCB transplantation for neurological diseases has been performed. Dr. Kurtzberg, director of the Carolinas Cord Blood Bank at Duke University, has initiated studies of autologous cord blood in children with neonatal brain injury and cerebral palsy [13]. We are also proceeding with a project that aims to develop HUCB for use in treating patients with cerebral palsy and other refractive disorders through clinical and basic research [14]. Since several private and public cord blood banks exist throughout the world, an application for treating a variety of human disorders would be relatively simple. HUCB transplantation doesn't require a perfect match. The HUCB therapeutic mechanisms might occur mostly via trophic factor secretion in the local environment. Moreover, the population of pluripotent stem cells in HUCB is being identified, and some studies demonstrated that HUCB has the potential to differentiate into neuronal cells [15,16]. It is important to assess the properties of HUCB that are suitable for such an application.

CONCLUSIONS

An increasing number of hospitals and universities around the world are offering stem cell therapy to treat neurological disorders. However, it is necessary to remain cautious when using stem cells and where possible to anticipate unexpected and adverse results. Even so, stem cell therapy still has the potential to revolutionize the treatment of intractable disorders in the near future.

ACKNOWLEDGEMENTS

I would like to thank my colleagues in Kochi University Medical School, especially Profs. Yusuke Sagara, Assoc. Prof. Nagamasa Maeda and Assoc. Prof. Masayuki Tsuda for their assistance. This work was partly supported by a Grant-in-Aid for Young Scientists (B), The Ministry of Education, Culture, Sports, Science and Technology, Japan.

REFERENCES

- Thomson JA, Itskovitz-Eldor J, Shapiro SS, Waknitz MA, Swiergiel JJ, Marshall VS, et al. Embryonic stem cell lines derived from human blastocysts. *Science* 1998; 282: 1145-1147.
- Takahashi K, Tanabe K, Ohnuki M, Narita M, Ichisaka T, Tomoda K, et al. Induction of pluripotent stem cells from adult human fibroblasts by defined factors. *Cell* 2007; 131: 861-872.
- Pera MF. Stem cells: The dark side of induced pluripotency. *Nature* 2011; 471: 46-47.
- Hussein SM, Batada NN, Vuoristo S, Ching RW, Autio R, Närvä E, et al. Copy number variation and selection during reprogramming to pluripotency. *Nature* 2011; 471: 58-62.
- Takahashi K, Yasuhara T, Shingo T, Muraoka K, Kameda M, Takeuchi A, et al. Embryonic neural stem cells transplanted in middle cerebral artery occlusion model of rats demonstrated potent therapeutic effects, compared to adult neural stem cells. *Brain Res* 2008; 1234: 172-182.
- Iwanami A, Kaneko S, Nakamura M, Kanemura Y, Mori H, Kobayashi S, et al. Transplantation of human neural stem cells for spinal cord injury in primates. *J Neurosci Res* 2005; 80: 182-190.
- Kim BG, Kang YM, Phi JH, Kim YH, Hwang DH, Choi JY, et al. Implantation of polymer scaffolds seeded with neural stem cells in a canine spinal cord injury model. *Cytotherapy* 2010; 12: 841-845.
- Honmou O, Houkin K, Matsunaga T, Niitsu Y, Ishiai S, Onodera R, et al. Intravenous administration of auto serum-expanded autologous mesenchymal stem cells in stroke. *Brain* 2011; 134: 1790-1807.
- 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 neurogenesis. *Exp Neurol* 2006; 198: 54-64.
- Mabuchi Y, Houlihan DD, Akazawa C, Okano H, Matsuzaki Y. Prospective isolation of murine and human bone marrow mesenchymal stem cells based on surface markers. *Stem Cells Int* 2013; 2013: 507301.
- Harris DT, Badowski M, Ahmad N, Gaballa MA. The potential of cord blood stem cells for use in regenerative medicine. *Expert Opin Biol Ther* 2007; 7: 1311-1322.
- Kurtzberg J, Laughlin M, Graham ML, Smith C, Olson JF, Halperin EC, et al. Placental blood as a source of hematopoietic stem cells for transplantation into unrelated recipients. *N Engl J Med* 1996; 335: 157-166.
- Liao Y, Cotten M, Tan S, Kurtzberg J, Cairo MS. Rescuing the neonatal brain from hypoxic injury with autologous cord blood. *Bone Marrow Transplant* 2013; 48: 890-900.
- Wang F, Maeda N, Yasuhara T, Kameda M, Tsuru E, Yamashita T, et al. The therapeutic potential of human umbilical cord blood transplantation for neonatal hypoxic-ischemic brain injury and ischemic stroke. *Acta Med Okayama* 2012; 66: 429-434.
- Markiewicz I, Sypecka J, Domanska-Janik K, Wyszomirski T, Lukomska B. Cellular environment directs differentiation of human umbilical cord blood-derived neural stem cells in vitro. *J Histochem Cytochem* 2011; 59: 289-301.
- Kögler G, Sensken S, Airey JA, Trapp T, Müschen M, Feldhahn N, et al. A new human somatic stem cell from placental cord blood with intrinsic pluripotent differentiation potential. *J Exp Med.* 2004; 2002: 123-35.

Cite this article

Wang F (2013) Regenerative Medicine in Neurological Disorders: The Present Situation and Future Issues with Stem Cell Therapy. *J Neurol Disord Stroke* 1(1): 1005.