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Challenges of stem cell therapy in developing country

Abstract

Stem cell therapy comprises a modern technology aimed to replace damaged cells with healthy new ones. Cells are rendered dysfunctional due to any number of reasons such aging, disease, genetic modification, injury. Nowadays, Stem cell therapies are providing substantial benefit to patients suffering a wide range of diseases such as cancer, non-cancer, neuronal disease, diabetes and injuries such as brain trauma and spinal cord injuries. It is well established and rapidly growing in developed country however in developing country, there are several challenges which is shielding the booming of this therapy. Therefore we do expect to eventually remove these challenges to create the fresh environment of modern stem cell therapeutic medicine.

Keywords: stem cell, stem cell therapy, cell differentiation, neuronal disease, brain trauma

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Jay Prakash Sah[1,2]

[1]Soonchunhyang Institute of Medi-bio Science, Soonchunhyang University, South Korea

[2]Department of Medical Laboratory Science, Pokhara University, India

Correspondence: Jay Prakash Sah, Soonchunhyang Institute of Medi-bio Science, Soonchunhyang University, SIMS-25, Bongjeong-ro, Dongnam-gu, Cheonan-si, Chungcheongnam-do, South Korea, Tel +82 010 2768 1729, Email shahjayprakash1@gmail.com

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Introduction

Stem cells are undifferentiated cells having capacity to self-renew.[1] They are without specific function but under given conditions will differentiate to become any one of the body's many cell types.[2] They serve as the basis for the development of the fetus, as well as a resource cells for repair of damaged tissue.[3,4] On the basis of potency, these can be categorized as toti-potent, pluripotent and multipotent.[5] They mainly include embryonic stem cells (ESC), pluripotent stem cells (iPS), Epiblast-derived stem cells (Epi-SC), and adult tissue stem cells. Such cells can differentiate into wide and diverse range of specialized cell types like fibroblasts, neurons, myocytes, blood cell, bone cell etc.[6] Thomson et al.[7] developed the first ESCs line in 1998 and this research gave a burning flint to treat the disease as a separate branch of therapy as regenerative medicine.[7] Considering these marvelous work and their finding, scientists have been attracted since past few decades towards the advancement of stem cell research to provide new era in modern therapeutic medicine because of their high potential to treat many diseases. Stem cell treatments include new technologies and therapies that aim to replace damaged tissues and cells in order to treat disease or injury.[8] One of the stem cell properties is to congregate in these damaged areas and generate new cells and tissues by performing a repair and renewal process, restoring functionality. ESC, iPS, and adult stem cell therapies, which include bone marrow stem cells and peripheral stem cells are currently being investigated or used to treat a wide range of diseases. Bone marrow stem cells are used to replace blood cells in people suffering from leukemia and other cancers.[9] Burn victims are also benefiting from stem cell therapy, which allows for new skin cells to be grafted as a replacement for those that have been damaged.[10]

There is extensive works and trials in area of stem cells research in developed countries but in most of the developing countries including Nepal, this area is still neglected and growing very slowly. In comparison to Nepal, neighboring countries like India, China has huge advancement in the area of stem cells research.[10] Therefore the present Review has been confined to publish reports of major challenges related to full blown functioning of stem cell therapy in the developing country. In this young field with considerable promise, there are many exciting prospects that are hampering from the early establishment.

There are many challenges that are necessary to explore to fasten the growth of stem cell therapy. I have tried to explain in two parts. One is the challenges facing the scientist globally which requires better understanding of technical and research advancement. Next one is the major problem far apart along with global challenges in developing country.

Manufacturing issues

This is the major emerging issue facing globally. Before introduction of stem cell to a human subject, fruitful consideration of manufacturing process as well as the characterization and formal safety assessment of the product is necessary. Manufacturing Consistency must be addressed by the manufacturing process. Similarly establishing a dialog with the International Conference as well as improving communications with health authorities, preclinical testing specialists is sophisticated way to ensure streamline safety evaluation regarding stem cells and their products.[11] Nevertheless, early interaction between regulatory agencies, therapy developers, and drug safety scientists is also important in this field.

Genetic instability

Another stem cell therapy issue faced globally is genetic instability in stem cell. The inherent genetic instability of hESCs and iPSCs in culture has been demonstrated.[12,13] Certain evidence for the instability of adult stem cells in culture is also shown by Sareen et al.[14] & Ueyama et al.[15] Therefore it is very important to perform a detailed genetic analysis like chromosomal aberration, karyotyping of the genome prior to any cell-based treatment. Acceptable degrees of genetic change must be established by a thorough examination. In the same way, cell surface markers and expression of transcription factors, as well as proliferation capacity and differentiation propensity, should also be evaluated.[16] Additionally, it is imperative to assess the heterogeneity of a culture because the engraftment of undifferentiated

or incorrectly differentiated cells may cause a substantial tumorigenic or immunogenic risk to the recipient.[16–18]

Stem cell culture condition

One of the concerns raised by the FDA is that the manufactured cell product must be fully characterized, predicted and free from contamination.[19] Meanwhile, another aspect related to stem cell therapy is to maintain the genotypic and phenotypic behavior of stem cell in proper condition *in vitro*. As the passage number of a stem cell lines increases, the potential for chromosomal aberrations also arise.[20,21] Therefore, minimizing the passage number might be required to decrease the chance of genetic variation. For this purpose, dosing and Pharmacokinetics considerations need to address that must be maximally feasible in the species chosen and the relevance to the intended human therapeutic dose. It is also important to consider the route of the administration of a product, whether it is administered systemically or locally.[22]

Pharmacological issue

Another aspect of problem facing globally during commitment of stem cell therapy is the challenges that cannot be addressed using standard analytical procedures developed for low-molecular-weight drugs or other biopharmaceuticals. Actually stem cells are highly sensitive to drugs. Sometime it's treatment during or after transplant for various common purposes like transplant rejection, decrease immunity at the time of transplant affects the administered stem cells.[23] Therefore actual pharmacokinetic behavior of stem cell must be considered by analyzing preclinical study in a large animal model.

Stem cell distribution after transplant

Pluripotent stem cells have capacity to form teratomas in immunocompromised animals.[24,25] A major problem is improper distribution and localization of stem cell after transplant. Therefore the ability to monitor cell distribution into the host after administration is necessary. Actually the stem cells may be essentially indistinguishable from host cells, therefore a suitable methodology must be required to monitor the behavior of transplanted cells, otherwise inappropriate ectopic tissue formation or tumorigenicity might be occurred. For this purpose, GFP-labeled cells can be administered to an animal model and the migration to organs other than the intended target can be monitored by qPCR, histological analysis and nuclear magnetic resonance (NMR) or magnetic resonance imaging (MRI) scans of either the whole animal or fixed slices of tissue.[26,27]

Immunological aspect- Before administration of stem cell into the host during stem cell therapy, cells are adequately characterized by analyzing their HLA antigen and other cell surface markers to prevent from immunological complication. Meanwhile, the host and graft cells should be monitored based on these immunological characteristics to get sufficient resolution in human subjects.[28] The risk of immunotoxicity is poorly characterized yet, so further investigation is necessary to explicate the interaction of graft with the host immunity.

Challenges in developing country

There are many challenges that are suppressing the growth of stem cell therapy in developing country. The first challenge is dominancy of peasant therapeutic methodology.[29] People still have a belief on primitive therapy due to lack of upgrading knowledge of modern medicine. Second challenge is lack of skilled human resources, poor transfusion services.[30] Third challenge is poor socioeconomic status, ethical issue and financial limitations when committed to treat the disease by stem cell, it requires the huge money which is in many cases impossible to spend. The fourth challenge is difficulty in keeping pace with technological advancement.[31] The fifth challenge is poor government support and policy even though lots of fund become freeze without doing research every year.[32] Therefore there should be the policy to take care of such artifact to strengthen the existing facilities and they should use such fund in the development of more centers for research and translational work. In addition, private sector should also be promoted along with government and private sector should also be forced by government to start research and clinical therapies in reasonable price in area of stem cells. International collaborations with advanced centers should be beneficial for this purpose.

Conclusion

Due to such drawback of stem cell therapy, the benefits of stem cell transplant are not reaching to common man. Beside research work, there is also need to improve social services in the country to educate the patients and their families to comply with treatment during the post-transplant period.[30] The goal of Stem Cell Treatments is to publish hurdle and challenges for establishment of stem cell therapy that will promote health and extend the human life span.

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Conflict of interest

The author declares no conflict of interest.

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