Stem Cell Therapy: A Whole World of New Era

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It was in late 19th century when the term 'Stem Cell' was coined by Theodor Boveri and Valentin Haecker where as the key properties of a stem cell were first defined by Ernest McCulloch and James Till in the early 1960s but no one had predicted that by 2021 Stem cell therapy (SCT) will be seen as a panacea for all ills.[1,2] Stem cells hold immense potential in treatment of diseases that were considered traditionally as "degenerative, chronic, incurable, irreversible and diseases with genetic predisposition" such as Duchenne muscular dystrophy, diabetes, heart disease, spinal cord injuries, Parkinson's, Multiple Sclerosis, Alzheimer's disease etc.

The two characteristic feature of a stem cell that has aroused unlimited possibilities in stem cell therapy are **Self-renewal** and **Potency.**

Self-renewal is the ability to go through numerous cycles of cell growth and cell division, known as cell proliferation, while maintaining the undifferentiated state whereas Potency means - the capacity to differentiate into specialized cell types.[3,4] Pluripotent stem cells that are being used in research today mainly come from embryos, hence the name, "embryonic stem cells". These were first isolated by American biologist James Thomson in 1998.[5] Because of the above two properties, embryonic stem cells (ESC) remain a theoretically potential source for regenerative medicine. At present there are no approved treatments using ESC. Several developed and developing countries have several restrictions on carrying out research of either human ES cell or the production of new human ES cell lines as there are ethical considerations regarding the use of unborn human tissue using ESC. Adult stem cells, unlike ESCs, do not have the ability to differentiate into cells from all three germ layers. However, in 2006, scientists Shinya Yamanaka, along with Kazutoshi Takahashi, discovered that it is possible to reprogram multipotent adult stem cells to the pluripotent state (Induced Pluripotent stem cell – iPSCs).[6] This was a turning point in the research arena of stem cells as this process prevented endangering the fetal life.To be useful in therapy, stem cells must be converted into desired cell types as necessary or else the whole regenerative medicine process will be pointless besides the possibility of teratoma formation *in vivo* by the undifferentiated ESCs. In directed differentiation, the extracellular microenvironment plays a significant role in controlling cell behavior. By manipulating the culture conditions, it is possible to restrict specific differentiation pathways and generate cultures that are enriched in certain precursors *in vitro*.[7] However, achieving a similar effect *in vivo* is a challenge.

Currently the most popular stem cell therapy is multipotent haematopoietic stem cell (HSC) transplantation. At this point of time according to ICMR (Indian Council of Medical Research) only the blood forming (hematopoietic) stem cells from bone marrow or umbilical cord blood are routinely used to treat blood cancers and different blood disorders.[8] Worldwide several promising clinical trials are going on in several degenerative/ chronic incurable diseases. Recently, In August 2018, Shinya Yamanka initiated the first approved clinical trial to treat PD (Parkinson's Disease) using iPSCs.[9] Strategy behind the trial involved the generation of dopaminergic progenitors from donor matched allogeneic cells followed by transplantation into the patient's brain by a special device. Japan had recently gave approval to stem-cell treatment for spinal-cord injuries. They discovered that injection of stem cells isolated from the patients' bone marrow resulted in regaining some sensory loss and

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mobility. This is the first government approved stem cell-based therapy targeting spinal-cord injuries.[10]

In Diabetes mellitus, Pluripotent stem cells (PSCs) are considered the cells of choice for beta cell replacement strategies.[11] Pancreatic grafts producing insulin have been successfully generated but converting them into true functioning cells of the pancreas *in vivo* while protecting them from the attack of immune system in the greatest challenge. To elude the immune system, researchers are working on the solution. This consists of a capsule in a polyethylene net that is filled with approximately 40 million immature cells of the pancreas. The capsules block the T cells of the immune system, which are too large to pass through the thick net and at the same time allow the transplanted cells to receive nourishment from the blood flow, as well as sensing and regulating the blood sugar level.[12]

In coming decades, stem cell therapy is going to be a major game changer in all the fields of medicine. Researches are being done from every corner of the world exploring the limitless possibilities of stem cells besides several obstacles in the way. Currently, untreatable neurodegenerative diseases, spinal cord injuries, osteoarthritis, retinitis pigmentosa have the possibility of becoming treatable with SCT. Induced pluripotency enables the use of a patient's own cells. Cord and tissue banks are becoming increasingly popular, as they gather cells that are the source of regenerative medicine in a struggle against present and future diseases. With SCT and all its regenerative benefits, we certainly hope to reduce human sufferings and prolong human life.

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