

Regenerative Medicine and stem cell research

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Cite this as:
BMCJ 2017;3(2): 1-2

Received April 5, 2017;
Accepted May 12, 2017

Tissue engineering and regenerative medicine are fundamentally based on principles of cell transplantation, cell culture, stem cell function and materials science and engineering toward the development of functional substitutes. Definitely the most physiological substitutes are from autologous cells. A tissue from the host is dissociated and expanded in culture, and the expanded cells are implanted into the same host.¹

The expanded cells are seeded onto a scaffold synthesized with the appropriate biocompatible, biodegradable and bioresorbable biomaterial. In case of collection of autologous cells from the diseased organ of the host a tissue biopsy may not yield enough normal cells for expansion and transplantation. In these situations, pluripotent human embryonic stem cells are considered to be a viable source of cells because they can serve as an alternative source of cells from which the desired tissue can be derived.

There are two types of stem cells one is Embryonic Stem Cells which are totipotent and can develop into all cell types and can self-renew indefinitely. The second type of stem cells are Adult Stem Cells which are multipotent and can develop into a few cell types but not all. They are located in few organs or may be unidentified and hard to find.

Embryonic stem cells (ESCs), derived from the inner cell mass of the blastocyst². They have the ability to proliferate in an undifferentiated but pluripotent state and the ability to differentiate into cells from all three embryonic germ layers *in vitro* and *transplantation of these autologous cells* would not need postoperative immunosuppression. However the use of human ES cells (hESCs), involves significant ethical limitations since it entails sacrifice of an embryo at blastocyst stage to harvest these

cells. In addition there are risk of potential allogeneic immune rejection and teratoma formation of hESC-derived cells by recipients after cell transplantation.^{3,4}

These limitations were addressed adequately by discovery of induced pluripotent stem cells (iPSCs), generated from adult somatic cells by forced expression of a specific set of four transcription factors (Yamanaka factors), Oct4, Sox2, cMyc, and Klf4 by Takahashi and Yamanaka in 2006.⁵

Induced hPSCs capable of self-renewal indefinitely while retaining the capability to differentiate into cells of all three germ layers, both *in vivo* and *in vitro*. These cells are very effective cell sources for many biomedical procedures in tissue engineering and regenerative medicine in spite of several safety concerns in regards to genetic and epigenetic aberrations and tumorigenesis.⁶

The ability of Induced hPSCs to restore pluripotency to somatic cells through the expression of reprogramming factors has led to fantastic achievements in manipulating human diseases at genetic and epigenetic level and offers infinite hope for regenerative medicine. However, in spite of rapid development in this field, scientists are highly concerned about the ethical limitations and potential side effects of application of stem cells in the regenerative medicine which might affect their research applications and therapeutic potential.

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