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Study on Therapeutic Applications of induced Pluripotent Stem Cells

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ABSTRACT
Recent progress in therapeutic field induced Pluripotent Stem Cells (iPSCs) have opened up many gateways for the research. iPSCs possess unique properties of self renewal and differentiation to many types of cell lineage. Hence could replace the use of embryonic stem cells (ESC), and may overcome the various ethical issues regarding the use of embryos in research and clinics. The molecular mechanisms that play role in reprogramming to generate iPSCs from different types of somatic cell sources involves a plethora of molecules including miRNAs, DNA modifying agents (viz. DNA methyl transferases), NANOG, etc. While promising a number of important roles in various clinical/research studies, iPSCs could also be of great use in studying molecular mechanism of many diseases. Many toxic compounds (different chemical compounds, pharmaceutical drugs, other hazardous chemicals, or environmental conditions) which are encountered by humans and newly designed drugs may be evaluated for toxicity and effects by using iPSCs. Thus, the applications of iPSCs in regenerative medicine, disease modeling, and drug discovery are enormous and should be explored in a more comprehensive manner. Moreover, iPSC technology has been employed in various diseases for disease modeling and gene therapy.
Keywords : iPSCs, ESC,NANOG,Methyltransferases.

STEM CELLS BRAEK THROUGH

Till and McCulloch (1961) had an breakthrough of finding specialized cells called senescence which has been observed by them which were plays a major role in mice to survive at the time of research. Stem cells can be defined on the basis of their origin and potency into Adult Stem Cells and Embryonic Stem Cells (ESC), similarly, considering their potency as the base of classification, stem cells can be classified into unipotent, multipotent, oligopotent, pluripotent, and totipotent . Pluripotent stem cells are those which can differentiate into other cells of the adult body. This property exists for only a specific time period of pre-implantation development in the cells forming Inner Cell Mass (ICM).

However, the major breakthrough came in 2006 when Takahashi and Yamanaka introduced the concept of induced pluripotent stem cells (iPSCs) by generating stem cells that were having properties relating to ESCs. iPSCs were generated by using a combination of 4 reprogramming factors, including Oct4 (Octamer binding transcription factor-4), Sox2 (Sex determining region Y)-box 2, Klf4 (Kruppel Like Factor-4), and c-Myc and were demonstrated both self-renewing and differentiating like ESCs, and thus, could be used as an alternative for hESCs in various clinics/research. Since then, a number of different reprogramming factors/methods have been established.

Generation of iPSCs

Theoretically, iPSCs can be generated by using any somatic cell by employing appropriate reprogramming factors and most convenient method for their introduction to somatic cells. iPSC generation is reported by using cells from different sources such as fibroblasts, cord blood, peripheral blood. here are large numbers of reports showing the whole process in a detailed manner that can be summarized in three major steps—(i) establishment of initial cell culture, (ii) induction of iPSCs and, (iii) characterization and expansion of iPSCs

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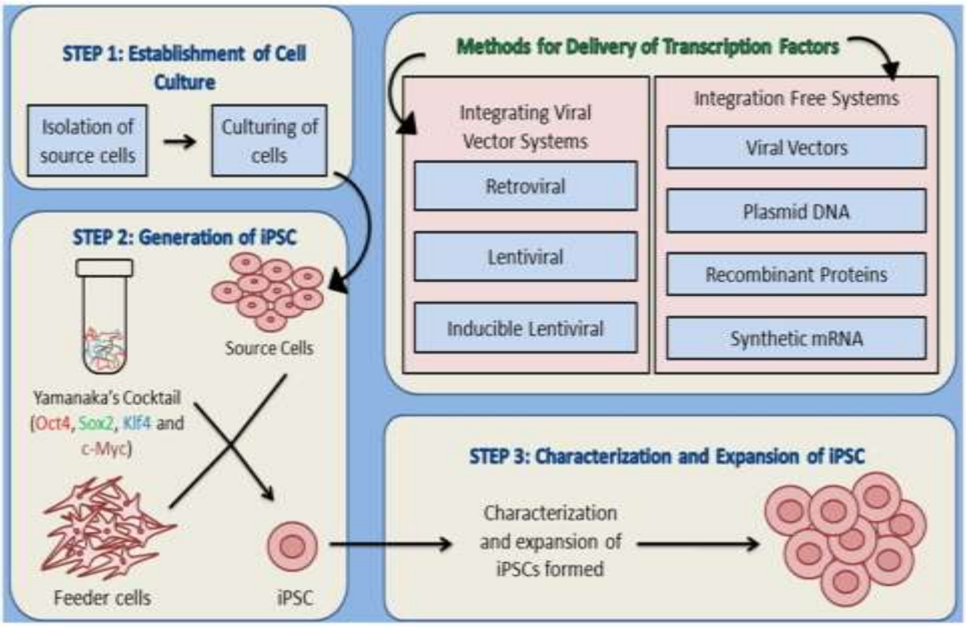
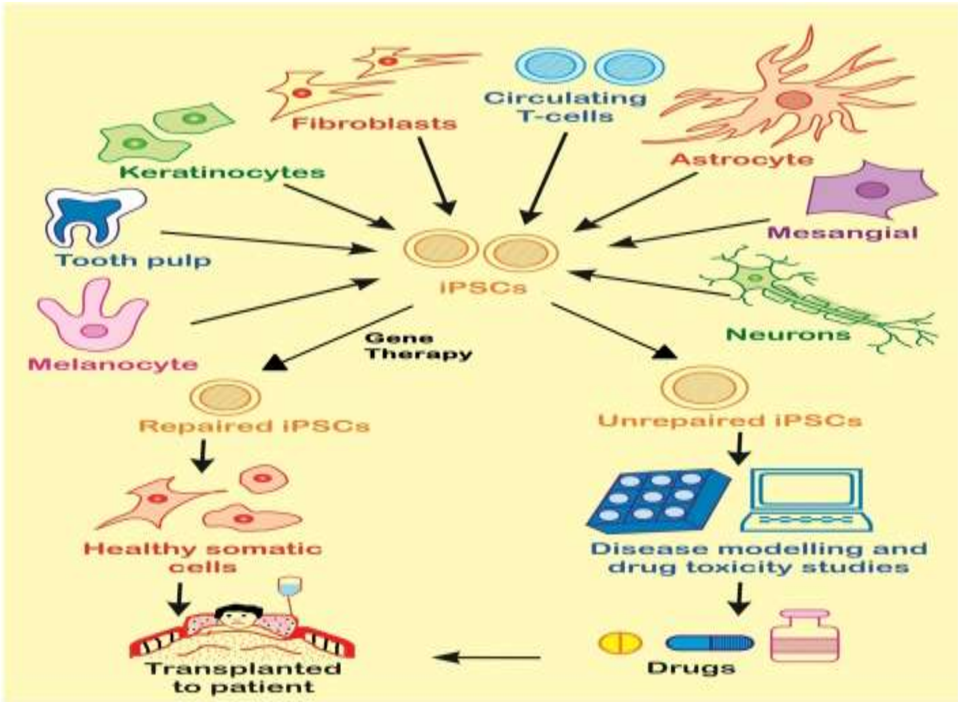


Applications of iPSCs



In disease modeling

The use of iPSCs for disease modeling is based on the fact that these cells are capable of self renewing and that these cells can differentiate into all types of cells of the human body which can be utilized for the preparation of different disease models to study those diseases.

Moad et al. used human prostate and urinary tract cells for the formation of iPSCs and further for studying the mechanisms that regulate the differentiation of prostate and urinary tract cells.

Devine et al. developed iPSCs from fibroblasts taken from a PD affected person possessing triplication of Synuclein gene by the transduction

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of four basic transcription factors. These iPSCs were then directed to differentiate into dopaminergic neurons in vitro for the study of PD

Regenerative medicine

A patient can only be transplated with the cells, tissues, or organs from the person who does not have any disease and whose physiological profile matches with the patient. Keeping these risks in mind, various tests are conducted before transplating tissues or organs into the patient's body. The use of iPSCs offers a good approach for these treatments as the cells that will be transplanted to patient's body will be differentiated from the repaired iPSCs generated from the somatic cells from patient's own body. iPSCs have been used in treating a number of injuries and degenerative diseases. Other than accidental injuries, diseases can also be treated with the help of iPSCs. iPSCS can also be used in cases of hepatocytes where loss of function of hepatocytes in culture and limited organ availability act as obstacles when fetal or adult progenitors are used for the development of hepatocytes. This lead to making use of iPScs for the generation of hepatocytes for various liver problems. Recently, there are accumulating data on the use of iPSC for ex-vivo blood expansion of various blood components. They can be used for the generation of Red Blood Cells (RBCs) which could be utilized for the generation of blood that is required over the globe for the purpose of treatment of various damages or diseases. iPSCs can also be used for the generation of various cells which can help in the repairmen of many tissues, for example, cardiovascular cells for the repairment of heart valves, vessels and ischemic tissues, but are limitations like safe delivery, post treatment adverse effects and standardization of protocols to generate large amounts of pure good quality cells.

CONCLUSION

Since the emergence of the field of iPSCs, it has highly developed and successfully expanded to different fields of regenerative medicine. Their application in clinical research will surely benefit the patients in future. At present there are few, but important applications of iPSCs but, if this field keeps on growing at the present pace, it wouldn't take long to expand the applications of iPSCs to more biological fields to aid research and treatments. iPSCs are important in disease modeling as they do not have ethical issues concerned as in case of ESCs and provide with the physiological conditions more close to humans which is not an advantage with the animal disease models. iPSCs also have a possibility of giving consistent phenotypes every time, which is an important issue for disease modeling.

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