**Induced Pluripotent Stem Cells (iPSC): Promise and Progress in Disease Modeling and Regenerative Medicine.**

**A critical viewpoint.**

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One of the major challenge in the biomedical contemporary research is the development and clinical implementation of Regenerative Medicine, which deals with the "process of replacing, engineering or regenerating human cells, tissues or organs to restore or establish normal function". Regenerative medicine refers to a group of biomedical approaches to clinical therapies that, in particular, includes the use of stem cells.

“The field of stem cell research has continued to advance at a terrific pace over the past year, with continued improvements in technology allowing us to interrogate the pathways underpinning development, injury, and repair of our cells, tissues, and organs. We have seen leaps forward in the translation of these advances into preclinical and clinical research.”

As a new research frontier stand the accomplishments in Induced Pluripotent Stem Cell (iPSC or simply iPS) technology that provided previously unanticipated chances to study and model human disease in the culture dish and the long-term may lead to new medical treatments.

Induced pluripotent stem cells are pluripotent stem cells that can be generated directly from adult cells. When properly activated by transcription factors, skin cells from mice could be reprogrammed to immature stem cells, which, in turn, can grow into all types of cells within the body.

The iPSC technology was first reported by Shinya Yamanaka, from Kyoto, Japan, who showed in 2006 that the introduction of four specific transcription factors, could convert adult cells into pluripotent stem cells. He was awarded the 2012 Nobel Prize along with Sir John Gurdon "for the discovery that mature cells can be reprogrammed to become pluripotent”.

Indeed Yamanaka conducted in 2006 a series of amazing experiments, showing that when introduced into mouse skin cells can reprogrammed into Embrionic Stem-like induced pluripotent stem (iPS) cells, capable of generating cells of ectodermal, endodermal and mesodermal lineages. It was soon shown that these four factors can also convert human fibroblasts to iPS cells. Shortly thereafter, many laboratories reproduced this finding, including the generation of iPS cells from patients. This discovery has also solved a critical political and ethical problem, as it reduces the need to use human oocytes for stem-cell research. Although the therapeutic potential of Yamanaka’s discovery has not yet been realized, his work has spurred many scientists worldwide to work in the area of regenerative medicine.

Immediately after the 2006 publication of the iPS cell experiments by Yamanaka, in 2007, Rudolf Jaenisch at Whitehead Institute for Biomedical Research, Cambridge, USA, showed that iPS cells derived from a mouse with sickle cell anemia could be converted to hematopoietic progenitors. Following the correction of the defective gene by homologous recombination, autologous iPS cells were converted to hematopoietic progenitors and transplanted back into the mouse, ameliorating the disease. These experiments unequivocally demonstrated the therapeutic potential of iPS cell technology, offering hope and confidence that this technology will have a major impact on human health. Collectively, the groundbreaking contributions by Yamanka and Jaenisch form the basis for work on regenerative medicine currently performed in hundreds of laboratories around the world.

Pluripotent stem cells hold great promise in the field of regenerative medicine. Because they can propagate indefinitely, as well as give rise to every other cell type in the body (such as neurons, heart, retinal, pancreatic, liver cells, and others), they represent a single source of cells that could be used to replace those lost to damage or disease.

Scientists are now trying to treat patients suffering from various diseases and injuries, such as Parkinson diseases, macular degenerations, cardiac failure, spinal cord injury, and platelet deficiency, in Japan and other countries, pre-clinical studies are actively going on to test the efficacy and safety of these treatments using animal models.

While the iPSC technology has not yet advanced to a stage where therapeutic transplants have been deemed safe, iPSCs are readily being used in personalized drug discovery efforts and understanding the patient-specific basis of disease.

Indeed different approaches to disease modelling are undertaken. Primary cells of patients can be used for disease modelling, but they are not easily available and cannot be expanded in culture. Adult stem cells or induced pluripotent stem cells (iPSCs) can be expanded in culture and differentiated into the disease-affected cells that can be used to recapitulate disease pathogenesis *in vitro*. Patient-specific disease models can be used to identify new biomarkers for improved diagnostic procedures, such as earlier detection of disease onset. These disease models can also be used to identify compounds that alleviate disease pathology *in vitro*, which can be further developed into novel drugs. Stem-cell-derived cells can also form the basis for cell replacement therapies.

However, beyond the enthusiasm over this “disease-in-a-dish” approach, many limitations need to be addressed and solutions found for ensuring that the future of iPSC technology lives up to at least some of its therapeutic promise.