Pluripotent stem cells: benefits, properties and uses

INTRODUCTION

Pluripotent stem cells give rise to nearly all cells types of the body, like, muscle, nerve, heart, and blood. They hold huge promise for both research & health care. The advance in human biology continues to generate interest among scientists, patients suffering from a wide range of diseases, including cancer, heart disease and diabetes, their families. Embryonic stem (ES) cells, is derived from inner cell mass of mammalian blastocysts they have the ability to grow for an indefinite period while maintaining pluripotency. These properties have led to hope that human Embryonic Stem cells might be useful to understand the disease mechanisms, to monitor effective and safe drugs, to treat patients of various diseases and injuries, such as juvenile diabetes and spinal cord injury. Cell culture is the one of the most important basic biomedical research.

From many decades, many innumerable insights into both normal & pathologic cellular processes have been gleaned by the study of human cells explanted in vitro. Primary human cells have a small life span in culture, there is a regulation of tissue formation, regeneration, and repair. Many human cell types have never closely been adapted for the expansion in vitro, and the lack of available models of normal & pathologic tissue structure has render many new important questions in human growth and disease pathogenesis and it is hard to find. At present three types of methods have been reported to induce pluripotency artificially in mouse somatic cells. Embryonic stem like cells can also be recognized by long-term culture of bone marrow cells, and pluripotent stem cells can be generate adult germ cells, either by vitro culture of spermatogonial cells or by the

parthenogenesis of unfertilized eggs. The capability to reprogram cells from the human blood will let the generation of patient-specific stem cells for the diseases. In this disease-causing somatic mutations are then restricted to the cells of the hematopoietic lineage. Depending on methods used, reprogramming of the adult cells to gain iPSCs may pose significant risk those could limit their use in humans. Many scientists around the world, announced the discovery of the method that could eliminate oncogenes after the induction of pluripotency, which will increase the potential use of iPSC in human disease. In April 2009, it was verified that generation of iPS cells is feasible without any genetic modification of the adult cell: a repetitive treatment of cells by means of certain proteins channelled into the cells viapoly-arginine anchorswas sufficient to induce pluripotency. Pluripotent stem cells are a unique scientific and medical source. The pluripotent stem cells are derived using non-Federal funds 8yat the beginning, embryos donated voluntarily by couples who are undergo fertility treatment in an vitro fertilization clinic. Human embryonic stem cells isolated from more surplus embryos from in vitro fertilization clinics represent an immortal circulation of pluripotent cells that can theoretically generate any cell type inside the human body.

PLURIPOTENT STEM CELLS

PLURIPOTENT STEM CELLS are generated from adults cells where induced pluripotent stem cells is the part of pluripotent stem cells and it is also called as iPS cells or iPSC’s.

Pluripotent stem cells give rise to nearly all of the cells types of body, like muscle, nerve, heart, and blood.

Pluripotent stem cells are called master cells because they are able to make cells from all three body layers, so they can produce any cells or body needs to repair itself, it is called pluripotency. Pluripotent stem have promising future in the area of regenerative medicine because it it is different in effect on the cells of the body which are neurons, heart, pancreatic liver cells. It can help in the representation of single cell which can remain to lost the damage or diseased cells. IPSC they are similar to natural pluripotent stem cells, like embryonic stem cells in many ways, like the appearance of certain stem cell genes & proteins, chromatin methylationpatterns, doubling time, embryoid bodyformation, teratomaformation, viablechimeraformation, and potency and differentiability.

Pluripotent stem cells

EMBRYONIC STEM CELLS

Embryonic stem cells is the most important type of pluripotent cells. Embryonic stem cells(ES cells) arepluripotentstem cellsthat are derived from theinner cell massof ablastocyst an early-stage preimplantationembryo. Humanembryos reach theblastocyststage 4–5 days postfertilization, at which time they consist of 50–150 cells. From adult tissue iPSC has been derived. They cannot by pass the need of embryos but they can be matched in the patients which mean that pluripotent stem cells line will be present in the each individual. Without any risk of immune rejection autologous cells can be used for recognising the basic behaviour of disease present in the patients

therapeutic transplants are not safe in iPSC technology. ESC that are appeared which have large domains of the genome that have a specific histone code, that are not found in more mature cells, which allows very fast inactivation or activation of gene expression. Embryonic stem cells arepluripotent that are able todifferentiatein all derivatives of the three germ layers: ectoderm, endoderm, andmesoderm. It includes more than 220 cell types in the adultbody. Pluripotency distinguishes embryonic stem cells fromadult stem cellsfound inadults; while embryonic stem cells can produce all cell types in body, adult stem cells they aremultipotentand they can create only limited number of cell type.

Human embryonic stem cell structure

SOMATIC CELL NUCLEAR TRANSFER

The somatic cell nuclear transfer (SCNT) means, transferring the nucleus from a somatic cell, any cell of the body, to an other cell, in this case it’s an egg cell. This kind of pluripotent stem cell called ntES cell, which has only been made successfully in the inferior animals. To make ntES cells in the human patients, an egg donor, would be needed.

The process of transferring a differentnucleusinto the egg “ reprograms” it to a pluripotent condition, reactivating full set of genes for creating all the tissues of the body.

PRODUCTION OF INDUCED PLURIPOTENT STEM CELLS

iPSCs are introduced in a set of pluripotency associated genes or reprogramming factors in to a given cell kind. The original set of

reprogramming factor are genes Oct4 (Pou5f1), Sox2, cMyc, and Klf4. It is a slow and unsufficient process which takes 1-2 weeks in mouse cells & 3-4 weeks in human. It has efficiency of 0. 01%- 0. 1%. For improving the efficiency and time taken to get ipsc considerable changes have been done. In reprogramming factor, cell start to make colonies that look like pluripotent stem cells.

Pluripotency is maintained by a combination of epigenetic, transcriptional and posttranscriptional mechanisms.

PRODUCTION OF Ipsc CELLS

GENERATION OF INDUCED PLURIPOTENT STEM cells.

1. They divide & culture donor cells.
2. Transfect the stem cell-associated genes into cells by viral vectors.
3. Harvest and culture the cells according to the Embryoic Stem cell culture by the use of mitotically in feeder cells.
4. A small set of transfected cells become iPS cells & generate ES-like colonies

Generation of IPS cells

Types of Pluripotent Stem Cells

There are several types of pluripotent stem cells are –

- Embryonic stem cells which are joined from the inner cell mass of blastocyst & the embryos are produced from in vitro fertilisation,

although this is important cause it eliminates the embryo, which could have been implanted for the formation of a baby.

- Embryonic germ cells which are obtained from the aborted foetuses and these pluripotent cells are copied from past cells. These past cells are those which can form sperm & eggs.
- Embryonic carcinoma or the cancer cells which are cosset from tumour that sometimes are prevalent in a a foetus.

DIFFERENCE BETWEEN TOTIPOTENT, PLURIPOTENT, AND MULTIPOTENT

Totipotent cellscan form all the kind of cell in a body, in addition the extraembryonic, or the placental cells. Embryonic cells, the 1 st couple of cell divisions following fertilization are the only cells that are totipotent cells.

- Pluripotent cellscan also give rise to all of the type of cells that make up the body. Embryonic stem cells are called pluripotent.
- Multipotent cellscan expand into more than 1 cell type, but they are more limited than the pluripotent cells, adult stem cells & cord blood stem cells are often considered as multipotent.

BENEFITS OF PLURIPOTENT STEM CELLS

1. Pluripotent stem cells give a renewable basis of healthy cells & tissues to treat many type of diseases similar to heart disease and diabetes.
2. People who are burn & those patients who suffer from autoimmune diseases like Parkinson’s can give advantage from the usage of pluripotent stem cells.

3. Pluripotent stem cells have large potential for treatment of diseases, because they give rise to majority of cell types in human body, which include muscle, blood, heart & nerve cells.
4. The use for pluripotent stem cells include the generation of cells & tissues that are use in transplantation.
5. Drug study & research next method that pluripotent stem cells are beneficial. Animals are mostly used to measure the safety and use of drugs. Those drugs which are secure and used in development for testing on animals.

TURNING PLURIPOTENT CELL INTO TREATMENT

Over time, many techniques are developed, pluripotent stem cells could any one of the day allow doctors to create & form, rejection-proof transplant to patch a scarred heart, revitalize damaged nerves or reboot an immune system which is not able of fighting infection.

Doctors have first obtainedpluripotentstem cells that match the patient genetically through geneticreprogramming, nuclear transfer, orparthenogenesis.

There are four critical steps:

- To growpluripotentstem cellsthat create a large quantity of healthy cells.
- Restore faulty genes, this would be needed if the cells are carrying a genetic disorder, such as sickle cell anemia which turn the stem cells into a specific cell kind or a tissue. A genetically healthy line

ofpluripotentcells is recognized, they must be creating specialized kinds of cells and this process is called asdifferentiation.

- To transplant cells or tissue to the diseased or damaged organ or tissue, the cells will require to reach right part of the body, take hold and start to function.
- Scientists know how to deliver blood to the stem cells, but they still need to develop some effective delivery method for other cell types.

Getting the pluripotent stem cell

The cells can be made in one of several ways:

- Nuclear transfer— By using a patient’s skin cell and then transferring it into an egg (possibly the patient’s own, or of an egg donor).
- Geneticreprogramming— By transforming a skin cell or blood cell or other cell from the patient to apluripotentstem cell.
- Parthenogenesis— This is done by using unfertilized eggs. A woman may be able to give her own eggs to make stem cells that match her genetically, or draw on master banks of stem cells which are made from eggs.

WHY ARE PLURIPOTENT STEM CELLS IMPORTANT?

Pluripotent stem cells can be used to produce any cell or tissue the body might need to challenge a wide range of diseases, from diabetes to spinal cord injury, to childhood leukemia, or to heart disease.

Pluripotentstem cells can potentially be modified to provide a perfect genetic match for any patient. It means that the patient could get transplants of tissue and cells without matching tissue and tissue rejection problems. There

is also no need to take powerful immune-suppressing drugs for the rest of their lives. Although there is time in achieving this, researchers have treated mouse models of human disease by using this strategy and hope that same can be done with human patients.

Disease in a dish:

Pluripotent stem cells create excellent laboratory models for studying how a disease unfolds, which further helps scientists to locate and track, very earliest disease-causing actions in cells. Immune deficiencies like type1 diabetes, muscular dystrophy, and myriad other disorders which are embedded in fetaldevelopment. In the lab, researchers monitor from where the first muscle cell comes from, or the first blood cell, and how this is different when the patient has a genetic disease. By the use of this information, doctors are able to correct the genetic defect before the disease advances.

Applications:

Pluripotentstem cell has different characteristics that make it useful in different ways :

- Induced pluripotent cells(iPS cells) offer a unique chance to model many human disease and are already being used to make a lot of new discoveries about premature aging, disease, cancer, and more.
- They are made from a person’s own cells, they can be potentially manipulated to fix the defects that are causing disease and then used

to create healthy cells for transplant that won’t be rejected by the immune system.

- Embryonic stem cells(ES cells) are standard for the biological theory of pluripotency. Scientists are continuosly working with Embryonic Stem cells to study more about a cell with pluripotency and discover safe & better ways to create iPS cells.
- Each type of ES cell is important for different reasons:
    - ES cells made from donating early embryos are unique tools for the understanding of earliest stages of human development& specific tissues form, because they’re not modified to individual patients, their value is mainly in research.

MEDICAL RESEARCH

Disease modeling and drug development

An attractive feature of the human iPS cells is their ability to derive them from adult patients for the study of cellular basis of human diseases. Since iPS cells have property of self-renewing and are pluripotent, they stand for a theoretically unlimited source of patient-derived cells which further can be turned into any kind of cell in the body. This is important because many other types of human cells which are derived from patients tend to stop rising after a few passages in laboratory culture. iPS have been generated for a broad variety of human genetic diseases, including common disorders such as Down syndrome and polycystic kidney disease.

Organ synthesis

A proof-of-concept by induced pluripotent stem cells (iPSCs) to make human organ for thetransplantationwas reported by researchers of Japan. Human ‘ liverbuds’ (iPSC-LBs) were grown from a mixture of three different types of stem cells:

Hepatocytes(for liver function) coaxed from iPSCs

Endothelial stem cells(to form lining ofblood vessels) fromumbilical cord blood

Mesenchymal stem cells(to formconnective tissue).

This new approach allows different cell types to self-organize into complex organ, mimicking the process infetal development. After growing in vitro for few days, the liver buds were transplanted into mice where the ‘ liver’ quickly connected with host blood vessels and then continued to grow.

Tissue repair

Embryonic cord-blood cells were induced to pluripotent stem cells by the use of plasmid DNA. Using cell surface endothelial/pericytic markersCD31andCD146, researchers have identified ‘ vascular progenitor’, which is high-quality, multipotent vascular stem cells. After the iPS cells were directly injected into thevitreousof damagedretinaof mice, the stem cells then engrafted into retina, grow & repaired thevascular vessels.

Red blood cells

In 2014, type Ored blood cellswere synthesized at Scottish National Blood Transfusion Service from iPSC. The cells were induced to become

amesoderm& thenblood cells& then red blood cells. The final step was making them eject their nuclei & mature properly. Type O rbc’s can be transfused into all patients. Each pint of the blood contain about 2 trillion red blood cells, although some 107 million blood donations are collected globally each year. Human transfusions were not expected to begin until 2016.