Induced Pluripotent stem (iPS) cells

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Abstract: All animal cells come from stem cells. Stem cell pluripotency means a stem cell having the potential to differentiate into any of the three germ layers: endoderm, mesoderm or ectoderm. Induced pluripotent stem (iPS) cells can be differentiated to any fetal or adult cell type. However, the pluripotent stem cells cannot develop into a fetal or adult organism alone because they are lack of the potential to contribute to extraembryonic tissue, such as the placenta.
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1. Introduction

Stem cells describe all of the cells that can give rise to the different cells found in tissues. Under a right condition, a stem cell can become all type of the cells in the body. Cell pluripotency means a stem cell having the potential to differentiate into any of the three germ layers: ectoderm (epidermal tissues and nervous system, etc), endoderm (interior stomach lining, gastrointestinal tract and lungs, etc) or mesoderm (muscle, bone, blood and urogenital, etc). Pluripotent stem cells can be differentiated to any fetal or adult cell type. However, the Pluripotent stem cells cannot develop into a fetal or adult organism alone because they are lack of the potential to contribute to extraembryonic tissue, such as the placenta. After the embryonic development stage is over, the stem cells no longer have this unlimited potential to develop into all cell types, the pluripotency is lost and they can only become certain types of cells.

Induced pluripotent stem cells (iPSCs) are genetically reprogrammed adult cells that exhibit a pluripotent stem cell-like state similar to embryonic stem cells.[1] While these artificially generated cells are not known to exist in the human body, they show qualities remarkably similar to those of embryonic stem cells (ESCs); thus, iPSCs are an invaluable resource for drug discovery, cell therapy, and basic research.

After an egg is fertilized by a sperm, a single cell comes out. This fertilized egg is totipotent which has the potential ability to create an entire organism. However, the totipotent cells change to pluripotent cells that lost the ability of totipotent – the pluripotent cannot differentiate to an entire body.

There are several key types of pluripotent stem cells: (1) Embryonic stem cells are isolated from the inner cell mass of the blastocyst. (2) Embryonic germ cells are taken from aborted foetuses and these pluripotent cells are derived from very early cells. (3) Embryonic carcinoma or cancer cells are isolated from a type of tumour that sometimes occurs in a foetus.

Yamanaka and colleagues first demonstrated that retrovirus-mediated delivery and expression of Oct4, Sox2, c-Myc and Klf4 is capable of inducing the pluripotent state in mouse fibroblasts, and they also reported the successful reprogramming of human somatic cells intoiPS cells using human versions of the same transcription factors delivered by retroviral vectors. The generation of patient-specific iPS cells circumvents an important roadblock to personalized regenerative medicine therapies by eliminating the potential for immune rejection of non-autologous transplanted cells. (Wu, Hamilton et al. 2009).

Mouse and human fibroblasts have been transformed into iPS cells by retroviral transduction or plasmid transfection with four genes. Tumor formation has been found in offspring of mice generated from blastocysts made mosaic with iPS cells. The adenoviral vectors can reprogram human fibroblasts to pluripotent stem cells for use in individualized cell therapy without the risk for viral or oncogene incorporation (Zhou and Freed 2009).

Domesticated ungulate pluripotent embryonic stem (ES) cell lines would be useful for generating precise gene-modified animals. Many efforts have been made to establish domesticated ungulate pluripotent ES cells from early embryos without success. Wu, et al, reported that properties of porcine pluripotent stem cells that may facilitate the eventual establishment of porcine ES cells (Wu, Chen et al. 2009).

Pluripotent stem cells have the potential for treatment of many diseases. Pluripotent stem cells can

evolve into specialized cells that ultimately can replace diseased cells and tissues. The positive uses of pluripotent stem cells are enormous but new research and ethical challenges must be taken into account before the public can reap the full benefits. For those who suffer from the many diseases that may be treated by pluripotent stem cells, additional knowledge and research will hopefully come sooner rather than later. The positive uses of pluripotent stem cells are enormous but new research and ethical challenges must be taken into account before the public can reap the full benefits.

There are about 200 different kinds of cells in a human body. Stem cells can differentiate into any kind of cells Human iPS cells hold great promise for cardiovascular research and therapeutic applications, but the ability of human iPS cells to differentiate into functional cardiomyocytes has not yet been demonstrated (Zhang, Wilson et al. 2009). Reprogramming differentiated human cells to iPS cells has applications in basic biology, drug development, and transplantation. Human iPS cell derivation previously required vectors that integrate into the genome, which can create mutations and limit the utility of the cells in both research and clinical applications (Yu, Hu et al. 2009). Human iPS cells derived from somatic cells hold promise to develop novel patient-specific cell therapies and research models for inherited and acquired diseases (Ye, Zhan et al. 2009).

Pluripotent stem cells have the potential to differentiate into almost any cell in the animal body. Under certain condition, the pluripotent stem cells from and embryo can produce all of the cells in the body. However, after the embryonic development stage, the stem cells will lost the ability and differentiate to adult cells. Pluripotent stem cells can evolve into specialized cells that ultimately can replace diseased cells and tissues.

After an egg is fertilized by a sperm, the zygote is created. The zygote is a single cell that has the totipotent ability. In the early hours and days (4 days for human) following fertilization, this single totipotent cell divides into more totipotent cells that are exact copies of the original zygote.

About 4 days after fertilization, the totipotent stem cells start to specialize and form a cluster of cells called the blastocyst. The blastocyst has a smaller group of cells called inner cell mass that are inner pluripotent stem cells. These pluripotent stem cells can differentiate to different somatic cells to form the animal body but lost totipotent ability.

Embryonic germ cells are taken from aborted foetuses and these pluripotent cells are derived from very early cells. These early cells can become sperm and eggs. Embryonic stem cells are isolated from the inner cell mass of the blastocyst. Embryonic carcinoma or cancer cells are isolated from a type of tumour that sometimes occurs in a foetus.

We can recover the embryonic stem (ES) cells from embryos and manipulate them in vitro to study early development and use them. We can differentiate ES cells into most of the cell types that are useful for therapeutic and other purposes. However, this arouses ethical problems. People, especially the relegious group are against the usage of human embryonic cell as these cells from human embryos. Even some other people consider that the embryo is not a real person and does not hold the human right, it is under debate. To avoid the rebate, the usage of iduced pluripotent stem (iPS) cells from the somatic tissue is a good condidate for the stem cell application.

ES cells are originally come from the inner cell mass of embryos. The ES cells exhibit an almost unlimited proliferative ability in culture and maintain the pluripotent potential to differentiate into all cell lineages in the body. All the cells in the animal body come from the stem cells. To get ES cells, normally it needs to destroy preimplantation embryos at the blastocyst stage of 100–200 cells. Some people especially religious groups consider that life begins at stage and that performing research on ES cells derived from the destruction of human blastocysts is morally unacceptable. Also, transplanted ES cells for therapeutic purposes can trigger host immune rejection. As iPS stem cells come from same person to apply them, it will be avoid these problems.

Normally gene expression in differentiated cells is dynamic and reversible. However, introducing of certain transcription factors could convert specialized cell types from one lineage to another. When transfering the nuclei of the somatic cells into oocutes or make fusion the sotmatic cells with ES cells, they are reprogrammed, and genome-wide transcriptional activity and DNA methylation patterns are converted from the somatic state to an embryonic state.

In 2006, Kazutoshi Takahashi and Shinya Yamanaka established murine ES-like cell lines from mouse embryonic fibroblasts (MEFs) and skin fibroblasts by expressing four transcription factor genes encoding **Oct4, Sox2, Klf4, and c-Myc** (Takahashi & Yamanaka 2006). They called these somatic cell-derived cell lines induced pluripotent stem (iPS) cells. These iPS cell lines perform similar properties as ES cells and express ES cell-specific genes. In the years after Takahashi and Yamanaka's initial success in reprogramming mouse cells, several groups used the same strategy to generate human iPS cells. The set of transcription factors to reprogram is same in both mouse and human somatic cells, which means that the transcription factor networks are

conserved in these two species to control self-renewal and pluripotency.

iPS cell lines could be generated from different cell types, such as fibroblasts, progenitor cells, hepatocytes, B cells, neuronals kidneys, muscles, keratinocytes, and adrenal glands, etc. The efficiency of cell reprogramming varies among different cell types.

To get the patient-specific iPS cell lines is important in the clincal appliction. Reprogramming of fibroblasts from patients allows the establishment of disease-specific iPS cell lines. To study the disease mechanism, a key issue is whether the affected cell type derived from iPS cells can recapitulate the disease phenotype (Colman & Dreesen 2009).

Increase the expression of Sall4, Nanog, Esrrb, and Lin28 (SNEL) could generate higher-quality iPSCs. It is important and useful in scientific research and clinical medicine to apply the fact that somatic cells can be reprogrammed into iPS cells. However, there are many problems in the technology and theory (Saha & Jaenisch 2009). One of the problems is the use of retroviral and lentiviral vectors to introduce the 4 transcription factor genes into somatic cells for cell reprogramming. These viral vectors preferentially integrate into active genes and therefore have the potential to activate flanking cellular genes. And, the 4 introduced transcription factors may have oncogenic potentials. Although the iPS cells may be suitable for the study of disease mechanisms or for drug screening and validation, they have potentail danger for cell replacement therapy. Nuclear transfer to oocytes is an efficient way to transcriptionally reprogram somatic nuclei. The natural intervention triggering stem cell-based regeneration of an organ or system, and the fasting could play role to protect immune system regeneration then shifting stem cells from a dormant state to a state of self-renewal.

Bone marrow transplants have been done for more than 50 years and are widely used in many hospitals, providing a life saving treatment for cancer and other diseases including leukemia, anemia, and immune disorders. However, the stem cell at the end of the bone provide the useful opportunities to give these human blood stem cells their superior regenerative abilities. Artificial bone marrow may be used to reproduce hematopoietic stem cells.

We are all sentenced to be dealth just since we are born, and the aging is happening for all of us. Finally we will have the ability to grow a number of our own stem cell to make new young body parts to replace our old body parts what is young and for people who need them from their own stem cells. Nothing flashy (yet), but it shows where the tech could go. I we can replace all the body parts by the young ones, we will be as younger as we want.

Now, many companies are offering commercial iPS stem cells and the media.

According to Igawa, K., C. Kokubu, et al repoprt ("Removal of reprogramming transgenes improves the tissue reconstitution potential of keratinocytes generated from human induced pluripotent stem cells." Stem Cells Transl Med. 2014 Sep;3(9):992-1001. doi: 10.5966/sctm.2013-0179. Epub 2014 Jul 14), Human induced pluripotent stem cell (hiPSC) lines have a great potential for therapeutics because customized cells and organs can be induced from such cells. Assessment of the residual reprogramming factors after the generation of hiPSC lines is required, but an ideal system has been lacking. Here, we generated hiPSC lines from normal human dermal fibroblasts with piggyBac transposon bearing reprogramming transgenes followed by removal of the transposon by the transposase. Under this condition, we compared the phenotypes of transgene-residual and -free hiPSCs of the same genetic background. The transgene-residual hiPSCs, in which the transcription levels of the reprogramming transgenes were eventually suppressed, were quite similar to the transgene-free hiPSCs in a pluripotent state. However, after differentiation into keratinocytes, clear differences were observed. Morphological, functional, and molecular analyses including single-cell gene expression profiling revealed that keratinocytes from transgene-free hiPSC lines were more similar to normal human keratinocytes than those from transgene-residual hiPSC lines, which may be partly explained by reactivation of residual transgenes upon induction of keratinocyte differentiation. These results suggest that transgene-free hiPSC lines should be chosen for therapeutic purposes (Igawa, et al, 2014).

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