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IMMORTALITY THROUGH STEM CELLS

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ABSTRACT
Stem cell engineering is a rapidly emerging field of applied biology in modern era which aims to deliver high quality life to man kind with overall aim to enhance the health of global population. This upcoming field of medical science has led to many new innovations and inventions, right from Embryonic Stem cell to Adult stem cell therapy treating sickle cell anaemia and many other diseases. Some very new phases are coming in path as we proceed towards advancement of stem cell engineering. Such a new phase is Induced Pluripotent Stem Cell Therapy and its quite interesting to think that if this technology can lead us to immortality or not.

INTRODUCTION

Till now Immortality is one of those abilities whose attainment for human being is only possible in mythological stories but some scientists believe that it will become a possibility in upcoming years by 2025 or 2030. Throughout years biotechnology has focused on technical fronts like improving mechanics of machines and GMO's but moving ahead, manipulation of genes has made this a cutting edge science with no subset as much as stem cell engineering. Eventually, biotechnology is trying to cure aging and this will allow one to turn back the body clocks. Manipulating the potency of stem cells is becoming game changer. A biological immortality does not claim total immunity from death. A living being can still die from means other than senescence, such as through injury or disease.

It is interesting to think that whether stem cell engineering along with technical advancements will lead us to immortality or biological immortality? What will be the consequences of it? If one can design such a stem cell with potential to regenerate into any type of tissue or organ at will of patients, then no injury would be too severe, no disease would be too lethal and would be replaceable.

Biological Immortality

Biological immortality refers to a stable or decreasing rate of mortality from senescence thus decoupling it from chronological age. Biologist uses this word to designate those cells which are not subjected to Hay flick Limit that is the point at which cells can no longer divide due to DNA damage or shorter length of telomeres.

The best examples are cancer cells as they express the telomere lengthening enzyme telomerase. The immortal cell can be created by induction of oncogenes or loss of tumour suppressor genes. Normal stem cells and germ cells can also be said to immortal regarding cell line. According to Theory of Extreme Lifespans through perpetual -equalising interventions (ELPIs) by Biontologist Marian Kyriazis, the ability to attain biological immortality is inherent in human biology and there will be a time when human continue to develop their intelligence by living indefinitely, rather than through evolution by natural selection.

Embryonic Stem Cells

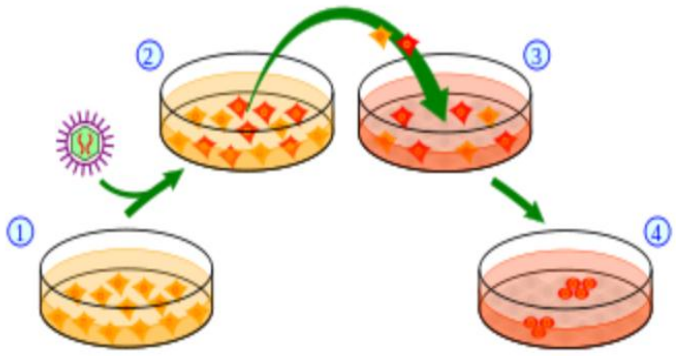
Embryonic Stem cells is the category of stem cells derived from very early embryos at the blastocyst stage development prior to implantation in the uterine wall. These are creators of every cell in the body and are known to be omnipotent specialized cell in the body. Thomson's article clearly demonstrated that "the human ES cell lines that he had derived were immortal and pluripotent i.e., they could form derivatives of the three primary germ layers and in principle all tissue of the human body.

The cost for this research however is destruction of human embryos and this placed it in ethically sensitive arena. Many societies and religion don't adopt this idea as they believe that life begins at fertilization and consider it as "murder" (Christine Mummery, 2004) After isolation from the embryo, there cell grow indefinitely in culture labs in primitive state provided with feeder cells. Apart from ethical issues these Embryonic Stem cell supplied with feeder cells presents a xenorisk to patients and therefore unlikely to be approved for clinical use.

Reversing the Process: Induced Pluripotent Stem Cells (iPSC's)

Induced Pluripotent Stem Cells are a type of stem cell generated directly from adult stem cell. Shinaya Yamanaka's lab showed that introduction of four specific gene encoding transcription factors could convert adult cells into Pluripotent stem cells (Christine Mummery, 2004). These Pluripotent stem cells can propagate into every other type of cell of body and thus a great stand in field of regenerative medicine.Since, as discussed earlier the generation of Embryonic Stem cells involves ethical barriers, so, the best way to get out of this issue is induced Pluripotent stem cell. There are many medically beneficial qualities in iPSC for example, a patient can have its own iPSC line.

Production of iPSC involves certain steps, starting from isolation to generating colonies (Fig:1). First donor cells are isolated and cultured (Step1) than stem cell associated genes are transduced into cell by viral vector (Step 2). After transduction, using mitotically inactivated feeder cells, these donor cells are harvested (Step 3). A small subset of transfect cells become iPSC and generate Embryonic Stem cell like colonies (Step 4). It was first generated by Shinaya Yamanaka's team at Kyoto University in 2006, they hypothesized that genes important to embryonic stem cell function might be able to induce an embryonic state in adult cells, experimented in mouse fibroblasts into pluripotent stem cells using the same four pivotal genes. Every technology flourishes along with its challenge counterpart. Low efficiency, risk of mutations and potential tumour risk carried out by some reprogramming factors are same of the major challenges faced by this technology.



A scheme of the generation of induced pluripotent stem

Fig: 1 A scheme of generation of Induced pluripotent stem cell

The cells are not quite omnipotent, meaning they can differentiate into almost all of the different types of cell, but not all. Much like adult stem cells, immune rejection would not be a concern become the cells would be taken from the person's own body in the first place. Scientists are not sure of exact process of reverse engineering in iPSC's.

Now concluding , we cannot go ahead with embryonic stem cell research as it sounds ethically sensitive, so the best way to move ahead is by inducing pluripotency to adult stem cells and transforming them into Induced pluripotent stem cells.

Production of Induced Pluripotent Stem Cells

In 2007, Yamanaka had successfully transformed human fibroblasts into pluripotent stem cells using the same four pivotal genes (Christine Mummery, 2012).

In 2007,Yamanaka had successfully transformed human fibroblasts into pluripotent stem cells using the same four pivotal genes (Christine Mummery , 2012).(Fig.2).

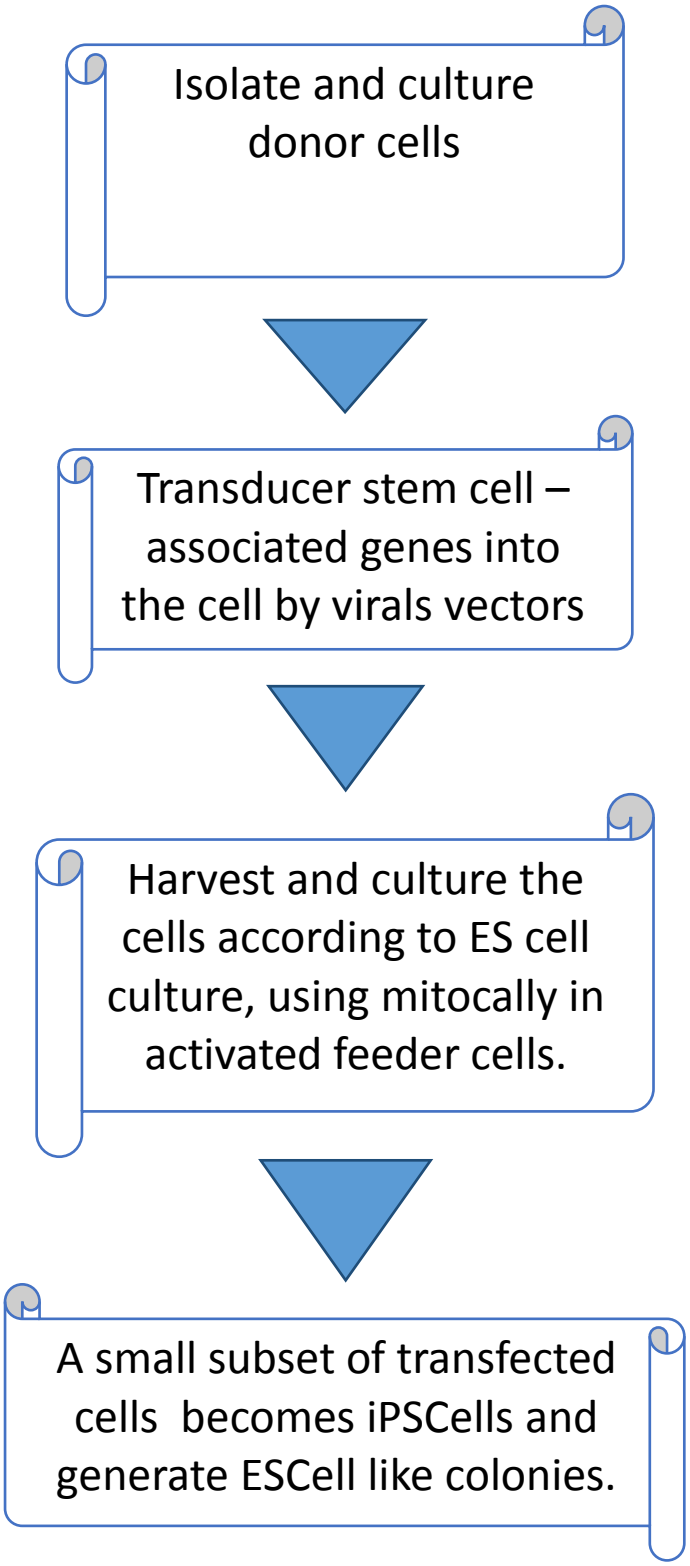


Fig: 2 Schematic diagram of production of induced pluripotent stem cell

Reprogramming Factors

The core reprogramming cocktail consist of transcription factors Oct4 ,Sox2, Klf4 (Fig.3)and can be augmented by addition of factors that enhance the efficiency of iPSC cell generation. Each of them contains a highly conserved domain which is responsible for its special function. Reproductive factors are likely to effect changes in transcription through their interaction recruiting the RNA polymerase machinery or modify the local chromatin structure (Schmidt et al, 2012).

Sox2 and Oct 4 bind to a complex called XPC, RAD23B and CENT2 to mediate the transactivation of NANOG which is further important for ES cell pluripotency.

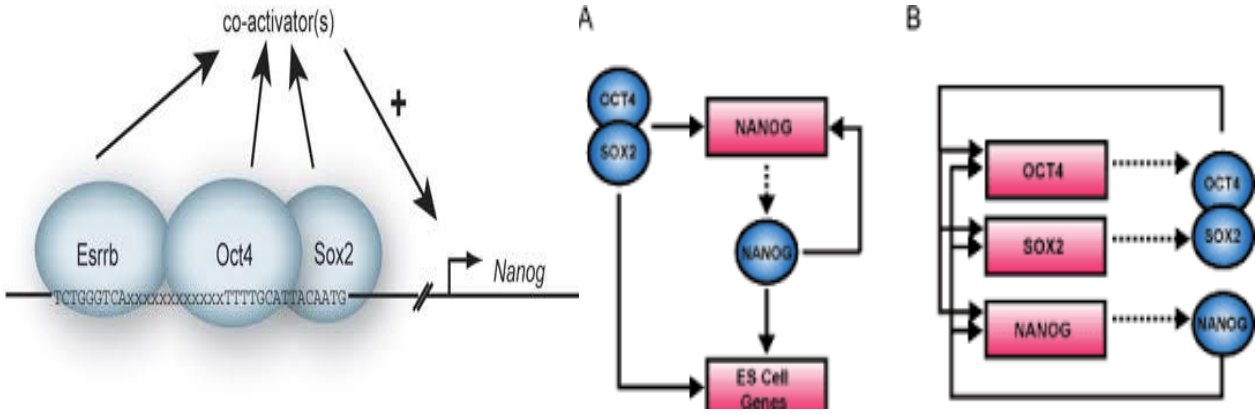


Fig: 3 Diagrammatic Representation of Reprogramming Factor

Nanog: Immortal One

- NANOG is a transcription factor critically involved with self renewal of stem undifferentiated embryonic stem cells, thought to function with other factor like Oct 4., in humans this protein is encoded by NANOG gene. They have ability to maintain pluripotency. Demonstrated embryos expressed pluripotency marker genes like NANOG, POU5F1.
- NANOG is a homeobox protein named after the land in Celthric myth called TriNANOG whose inhabitants remain forever young. Actually, Homeobox is a DNA sequence around 180 base pairs long that is invoved in the regulation of patterns of anatomical development in animals, fungi, plants.

Telomere and Telomerase Activity In Generation Of iPSC

- Telomere: Shortening of telomere to a critically short length in adult stem cells, something that is associated with organism aging is sufficient to impair stem cells mobilization and tissue regeneration and is proposed to be a key determination of organismal longevity. (Marion et al, 2010)Reprogramming increases telomerase activity and restores telomeres length leading to a rejuvenated status of telomeric chromatin is also reprogrammed to an ES cell – like status.
- Telomerase are necessary to sustain cell division unrestricted by the Hay flick limit of ~50 cell division. Human Embryonic Cells, hESCs express high telomerase activity to sustain self renewal and proliferation and iPSC also demonstrated high telomerase activity and express hTERT (human telomerase reverse transcriptase), a necessary component on the telomerase protein complex.

Immortal Examples

Immortal under edge of knife: Planarian Worm

Planarian worm is one of flatworms of turbellaria class. These exhibit an extraordinary ability to regenerate lost body part. Cut the worm into two pieces and each piece can regenerate into a complete organism. What happens inside is the cells at the wound site proliferate to form a blastema that will differentiate into new tissue and regenerate the missing parts of the piece of the cut planarian. New tissues can grow due to pluripotent stem cells that have ability to create all various cell types. These adult stem cells are called neoblasts and comprise 20% or more of cells in adult animal.

A planarian worm

Humans To Immortality: Would Be Results

- Female fertility covers a very limited span , and that would be really hard constrain to remove – a very small percentage of population would be of fertile females and this could even lead to extinction.
- Since the proportion of births in relation to the total population would be tiny ,genetic variability would suffer in the long run and so would the ability to react to changes in the environment.
- Current biological weapons are simple organisms that have been produced through natural growth and not genetically modified. But upcoming phase of bioweapons could feature genetically modified organisms with new pathogenic characteristics motivating Chimeras.

CONCLUSION

The quest for immortality continues with stem cell therapy, through one may achieve biological immortality but immortality is still under question mark. Pluripotency of induced pluripotent stem cell is useful in medical sector for treating ample of diseases and can further be used in many other areas as the research continues. The expectations from iPSC to immortalize human being is still under its infant stage but research in this area holds a promising future.

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