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CONCISE REVIEW: A PLURIPOTENT STEM CELL

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ABSTRACT

Regenerative medicine is a multidisciplinary field concerned with the replacement, repair or restoration of injured tissues. This field emerged from the need for reconstruction in children and adults in whom tissue has been damaged by diseases, trauma and congenital anomalies. Stem cell research is a promising field with an alluring potential for therapeutic intervention, and thus begs a critical understanding of the long-term consequences of stem cell replacement. Stem cells are basic cells of all multicellular organisms having the potency to differentiate into wide range of adult cells. Self renewal and totipotency are characteristic of stem cells. Though totipotency is shown by very early embryonic stem cells, the adult stem cells possess multipotency and differential plasticity which can be exploited for future generation of therapeutic options. There are several types of pluripotent stem cells. The identification of stem cells in an adult have been a challenge to scientists.

KEYWORDS: Stem Cell, Totipotency, Trauma.

What exactly are Pluripotent Stem Cells?

Pluripotent stem cells are also known as 'true' stem cells because they have the ability to differentiate into almost any cell in the body. In other words, under the right circumstances, a stem cell that is isolated from an embryo can produce almost all of the cells in the body. Yet after this embryonic development stage is over, the stem cells no longer have this unlimited potential to develop into all cell types.[1] Their pluripotency is thus lost and they can only become certain typesofcells.

One of the "cells that are self-replicating, are derived from human embryos or human fetal tissue, and are known to develop into cells and tissues of the three primary germ layers. Although human pluripotent stem cells may be derived from embryos or fetal tissue, such stem cells are not themselves embryos." (From the National Institutes of Health Guidelines for Research Using Human Pluripotent Stem Cells.)[2]

"Self-replicating" means the cell can divide and to form cells indistinguishable from it. The "three primary germ layers" -- called the ectoderm, mesoderm, and endoderm -- are the primary layers of cells in the embryo from which all tissues and organs develop.[3]

Human pluripotent stem cells can also be known as human embryonic stem cells.

The availability of human pluripotent stem cells (PSCs), which are capable of self-renewal and have the potential to differentiate into virtually any cell type, can now help to overcome the limitations of animal models for certain disorders. The ability to model human diseases using cultured PSCs has revolutionized the ways in which we study monogenic, complex and epigenetic disorders, as well as early- and late-onset diseases. Several strategies are used to generate such disease models using either embryonic stem cells (ES cells) or patient-specific induced PSCs (iPSCs), creating new possibilities for the establishment of models and their use in drug screening.[4]

What makes a Stem Cell Pluripotent?

To understand how a cell becomes pluripotent, it helps to consider the human body in the very early stages of development. After an egg is fertilised by a sperm, a single cell results. This cell - the fertilised egg that is totipotent - has the potential to create an entire organism. In the initial hours and days following fertilisation, this single totipotent cell divides into more totipotent cells that are exact copies of the original.[5]

Approximately four days after fertilisation, the totipotent cells start to specialise and form a cluster of cells known as a blastocyst. The blastocyst has yet another smaller group of cells known as the inner cell mass and it is these inner pluripotent stem cells that will go on to create most of the cells and tissues in the human body. These pluripotent stem cells are therefore different than totipotent stem cells because they don't develop into a complete organism. As such, a pluripotent cell won't give rise to the placenta or other tissues that are vital for foetaldevelopment. It will still develop into the other specialised cell types in the human body, such as nerve or heart cells.[6]

You may have also heard the term 'stem cell line.' Stem cells from embryos can be used to create these pluripotent stem cell 'lines,' which are grown in the laboratory or cultured from foetal tissue.[7]

Classification of Pluripotent Stem Cells

There are several types of pluripotent stem cells:

- Embryonic stem cells are isolated from the inner cell mass of the blastocyst. The embryos are excess ones produced from in vitro fertilisation, but the practice is still controversial because it does destroy the embryo, which could have been implanted to create a baby.
- Embryonic germ cells are taken from aborted foetuses and these pluripotent cells are derived from very early cells. These early cells are those that can become sperm and eggs.
- Embryonic carcinoma or cancer cells are isolated from a type of tumour that sometimes occurs in a foetus.[8]

Benefits and Future of Pluripotent Stem Cells

Pluripotent stem cells provide a chance to obtain a renewable source of healthy cells and tissues to treat a wide array of diseases such as heart disease and diabetes. Burn victims and those who suffer from autoimmune diseases such as Parkinson's can all potentially benefit from the use of pluripotent stem cells.

Pluripotent stem cells have a vast potential for the treatment of disease, namely because they give rise to the majority of cell types in the human body. These include muscle, blood, heart and nerve cells. Another potential use for pluripotent stem cells involves the generation of cells and tissues for use in transplantation.[9]

Pluripotent stem cells can evolve into specialised cells that ultimately can replace diseased cells and tissues. Drug research is another area that pluripotent stem cells may benefit. Animals are a commonly used model to assess the safety and use of drugs. Instead of initially testing drugs on animals, they can be evaluated through testing on cells grown from pluripotent stem cells. Those drugs that appear tolerated and safe can then progress to testing on animals and finally, humans.[10]

Challenges for Pluripotent Stem Cells

It is often seen that, the discoveries with the greatest therapeutic benefits present the most difficult challenges; this is particularly true for pluripotent stem cells. Researchers have been working on ways for the controlling the development process of pluripotent stem cells into the many different cell types in the human body. Another obstacle that contributes to the research, is that the cells used in treatment are rejected from a person's body due to their immune system. More controversial is the fact that many scientists and members of the public have ethical issues with the use of pluripotent stem cells from human embryos or foetal tissues.

Though the positive uses of pluripotent stem cells are enormous, new research and ethical challenges must be taken into account before the public can reap it’s benefits entirely. It is hoped that the additional research and perseverance in this field of study can yield to the treatment of diseases that can be cured using pluripotent stem cells.[11]

Stem cell therapy consists of advanced technologies and therapies that aim to replace damaged cells with healthy new ones. Cells may be dysfunctional due to many numbers of reasons, which include, genetics, disease, injury or aging. Presently, stem cells have aided to treat cancer, Parkinson's disease, spinal cord injuries and diabetes, among other serious diseases. Unfortunately, there are several drawbacks faced by researchers that must be overcome before stem cell therapies can become a successful reality for those suffering from disease. Researchers do expect to eventually move beyond these challenges but the unfortunate reality is that those suffering from disease often have little time to wait for treatment.

Identifying Stem Cells in Adult Tissues

The identification of stem cells in an adult have been a challenge to scientists. Tissues that contain stem cells are found only in scarce amounts amongst many number of cells, thus it is a tedious process to extract these cells from the tissue. The research involved is complex and even after cells are isolated, the process to successfully trigger differentiation into the desired cell type is another challenge for researchers. The limited understanding of stem cell control and regulation bringsabout a lag in fully utilizing these cells to its maximum potential. In addition, researchers must also use the correct laboratory medium, or solution, to persuade the growth and this has proven to be difficult.[12]

Stem Cell Integration

If scientists do manage to identify, isolate and trigger the appropriate differentiate of stem cells, the cells still must be implanted into the patient and accepted among the native body cells. This success is therefore dependent on effective integration into the patient's body systems and other cells. For example, if cardiac cells are implanted, they must be able to beat in sync with the patient's own heart cells. For a patient who suffers from a neural based disease, any neural cells must integrate into the complicated network of natural neural cells if they are to effectively function and replace damaged cells.[13]

Immunological Rejection
Immunological rejection is a major barrier to successful stem cell transplants. When a patient's immune system views the transplanted cells as 'foreign' rather than 'self,' it wages an attack on the newly transplanted cells. Recipients of the transplant usually have to take strong immunosuppressive drugs to reduce the chances of rejection but these drugs then leave the patient vulnerable to infection by any other viruses or microbes in the environment.

Cancer
As scientists learn more and more about stem cells, they hope one day to develop effective cancer treatments based on stem cell research. However, stem cells also have the ability to foster tumour growth and caution must be taken before stem cell therapy becomes commonplace. Cancer is generally a consequence that occurs when cells abnormally divide. The challenge for scientists is to find a balance between directing cell growth into specialized tissues that can replace damaged ones, and also ensuring that cells don't excessively grow and become cancer cells.

Despite the numerous challenges facing researchers, stem cells still hold promise for treating many diseases. Continued research should yield more information to ensure that stem cells treat disease with safety and success.

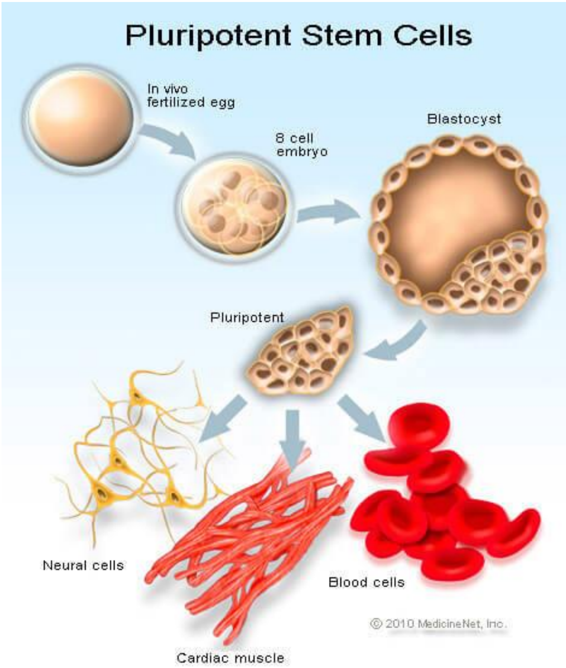
What is Stem Cell Therapy?
Stem cell therapy is a set of techniques that aim to replace cells damaged or destroyed by disease with healthy functioning ones.[14] The techniques themselves are still relatively new but their applications and benefits are broad. Some of the diseases they can help include:

- Cancer.
- Parkinson's disease.
- Diabetes.
- Various injuries (e.g. spinal cord).
- Eye diseases.

Types of Stem Cell Therapy
There are a number of stem cell therapies that are currently being investigated or used to treat a range of diseases. These are:

- Adult stem cell transplants using bone marrow stem cells.
- Adult stem cell transplants using peripheral stem cells.
- Stem cell transplants using umbilical cord blood.
- Therapeutic cloning.

Benefits of Current Stem Cell Therapy
Stem cell therapy is still experimental, but researchers have found the treatments worthwhile for many diseases. Bone marrow stem cells, for example, are used to replace blood cells in people suffering from leukaemia and other cancers. Burn victims are also benefiting from stem cell therapy, which allows for new skin cells to be grafted as a replacement for damaged ones. Furthermore, new healthy cells can also be grown to treat eye diseases as well as replace dysfunctional tissues. The ultimate goal of stem cell therapy is to replace unhealthy or damaged cells with healthy ones and to do so efficiently, allowing the human body to go back to its normal functioning.



The Indian Perspective
When ethical jingoism dominated the scenario in the west, eastern countries like India and Singapore were taking rapid strides to reap the benefits of this science to the maximum possible extent. Unlike the public opinion in the west, which is against researches in this field, the public opinion in many eastern countries including India is far more supportive. This may be partly due to the scientific temper inculcated by the epics and in numerous religious texts which are in fact acclaimed worldwide for their scientific value. This openness is reflected in the Indian Department of Biotechnology [DBT]'s statement that India is open to stem Cell research; and it promptly made regulatory provisions to control unethical practices and in fact pioneered in bringing up a widely acceptable legal framework for research.[15]

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