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Review Article

Investigation Into the Potential Prospects of Induced Pluripotent Stem Cells

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Abstract

Cell cultures and stem cell studies have revolutionized the field of biotechnology and regenerative medicine by opening various medicine sectors that were once closed due to lack of information and technology. The potent ability of stem cells has proven to be really significant in the field of medical research for treating degenerative diseases and disorders, thus developing novel therapeutics. Induced pluripotent stem cells are created by reprogramming adult cells to behave like an embryonic-like pluripotent state cell. The reprogramming of cells is done by introducing specific combinations or sets of genes into the cells using viral vectors. This in turn resets the genetic program and reprograms the cells in a way that the cells can differentiate into any type of cell in the human body. Induced pluripotent stem cells have the ability to self-renew and differentiate into all cell types, also including gametes. This type of stem cell can be cultured in lab, and have been proven to renew themselves indefinitely. These cells can be reprogrammed from cells obtained from any healthy person or patient. Stem cells are considered as a valuable resource in the field of medicine but pluripotent stem cells in nature are embryonic stem cells, so their study and isolation posed multiple ethical barriers to be overcome, and inducing pluripotent nature in adult cells has proven to be a solution to overcome those barriers. Induced pluripotent stem cells are considered to be the key for regenerative medicine as their potent ability can be manipulated to replace any diseased or damaged tissues. The authors have discussed the current status of induced pluripotent stem cells and their potential future prospects in this paper. There are also a lot of ethical and legal challenges and opportunities that must be overcome to fully exploit the potential of stem cells. Overall, the aim of this paper is to shed light on the significance of the study and development of stem cells and its research in the field of medicine, and its potential to formulate newer therapies and therapeutics. The authors tend to provide an overview of stem cell research and hope to inspire further research and development in this area to generate significant results in novel and effective stem-cell based therapies.

Keywords: Induced pluripotent stem cell; Potency; Stem cell therapy; Vectors; Reprogramming technology.

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Introduction

Induced pluripotent stem cells (iPSCs) are normal adult cells that have been reprogrammed to return to an embryonic-like pluripotent state. This reprogramming is done by conventional rDNA technology methods using vectors. The genetic make-up of adult cells is typically altered in order to reprogram an adult cell to achieve pluripotency. iPSCs were discovered in 2006 by Shinya Yamanaka and his colleagues [1].

This discovery revolutionized the field of regenerative medicine, as it provided a source of pluripotent stem cells that did not require the use of embryos or involve the ethical concerns associated with such use. iPSCs have a very wide potential; this includes the development of patient-specific (personalized medicine) cell therapies, drug discovery, disease modelling, and tissue engineering. However, challenges remain in ensuring the safety and efficacy of iPSC-based therapies and addressing issues such as immune rejection and tumor formation.

Research on iPSCs is a rapidly growing medical field, as many researchers hope to explore and exploit the potential applications in regenerative medicine, disease modelling, drug development, and more. iPSCs have been used to model a wide range of diseases, including neurodegenerative disorders like Parkinson's disease and Alzheimer's disease and genetic disorders like cystic fibrosis and sickle cell anemia.

iPSCs can be used to study the cellular and genetic mechanisms involved in these diseases and to develop potential therapies [2,3]. iPSCs also have the potential to revolutionize the drug development process, as they allow for more accurate and personalized testing of drugs on the isolated cells of the patient to be treated.

iPSCs can differentiate into any cell in the human body and eventually develop into any type of tissue that is required, such as heart tissue, liver tissue, and more. These tissues can be used for drug testing and for transplantation into patients with damaged or diseased tissue.

iPSCs can be used as models to study the effects of gene editing technologies such as CRISPR-Cas9, which can be used to correct genetic mutations associated with diseases. iPSCs are currently being used to create patient-specific cell therapies, which have the potential to treat a range of diseases and injuries, such as spinal cord injuries, diabetes, and heart disease.

iPSC research holds great promise for advancing the understanding of human development and disease progression, as well as for developing new therapies and treatments.

Stem cells

Stem cells are the type of cell that have unique ability of all different types of cells of a body. They are unspecialized cells that can renew into any type of cell in the body such as muscle cells, nerve cells, blood cells etc.

Potency of stem cells

Stem cells have a special ability to differentiate into different cell types. This ability of the stem cell to differentiate into many types of cells is referred as potency of stem cells [4]. Stem cells are classified based

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on their potency to differentiate into different types of cells (Table 1).

Totipotent stem cell

Totipotent stem cells have the ability to differentiate into any type of cell in the body of the organism. These cells are also called as early-embryonic as they are found in the later zygotic stages of an organism, which later differentiates and give rise to any type of cells that forms the organs, organ systems and the entire organism. Totipotent cells contain the ability to proliferate and divide until it forms a complete organism. Fertilized egg is the best example for totipotent stem cell.

Pluripotent stem cell

Pluripotent stem cells are known for their ability to differentiate and divide into almost any type of cell except it can't form an entire organism. It forms all embryonic germ layer that make up the human body, which includes Ectoderm: which gives rise to skin and nervous system, Endoderm: which forms the gastrointestinal and respiratory tracks, Mesoderm: which gives rise to musculoskeletal system and cardiovascular system.

These stem cells are capable of self-renewing themselves by dividing and differentiating into the three primary types of cells that generally make up the entire human body. Embryonic stem cells which can differentiate and give rise to any cell type that can help to make up the entire body is a great example for pluripotent stem cell.

Multipotent stem cell

Multipotent stem cells are different from pluripotent stem cells as their ability to differentiate into different cell types that makes up the body of an entire organism is limited to a very small number of cell types. This kind of stem cell is limited to differentiate within a specific tissue or an organ. Multipotent stem cells usually found in organs that can regenerate damaged tissue. These cells are commonly found in the body throughout life, and they play a major role in the body's capability to repair and regenerate damaged tissues. Multipotent stem cells are highly important in the development, protection and tissue repair of an organism. The best example for this is the Hematopoietic stem cell which is localized to the bone marrow, which has the ability to differentiate into every type of blood cell such as red blood cells, white blood cells and platelets.

Unipotent stem cell

Unipotent stem cells possess the ability to differentiate into just only one type of cell but it has its own self-renewal property which helps one to distinguish it from non-stem cells. Unipotent stem cells are derived from multipotent cells. They are more stable and has a low chance of mutations compared to pluripotent and multipotent cells as they are more specialized. Even with only differentiating into only one type of cell they are important for maintenance and repair of various tissues in our body. The best example for unipotent stem cell is epidermal stem cell that produces cells in skin which takes place throughout our life.

Oligopotent stem cell

These stem cells can only differentiate into a limited number of cell types, which makes

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them less specialized than unipotent stem cells but more specialized than pluripotent and multipotent stem cells. They differentiate into very few types of cells, but they are important for tissue maintenance and repair. The best example for this is the lymphoid cell which can give rise to variety of blood cells like B and T cells but not to a different blood cell type like red blood cell.

Classification of stem cells based on potency and site of origin		
S.no.	**Potency**	**Site of Origin**
1	Totipotent	Early embryonic stem cells
2	Pluripotent	Embryonic stem cells
3	Multipotent	Hematopoietic stem cells
4	Oligopotent	Myeloid stem cells
5	Unipotent	Adult tissue specific stem cells

Table 1: Classification of stem cells based on potency and site of origin.

Cell reprogramming technology

Cell reprogramming technology is a novel approach that allows us to alter the nature of a cell and produce the desired type of cells. This approach alters the gene expression patterns of a cell, thus converting one type of cell into another type of cell [5]. The principle of this approach is based on the idea that all cells in the body contain the same genetic information except gametes, and by altering the gene expression patterns in a cell, it is possible to convert one cell type into another. The most well-known form of cell reprogramming is induced pluripotent stem cell (iPSC) technology, which involves reprogramming adult cells into a pluripotent state similar to that of embryonic stem cells.

This technology was first developed in 2006 and has since revolutionized the field of regenerative medicine. Cell reprogramming also involves the direct lineage conversion of cells, which means one type of cell is directly converted into another without first reverting to a pluripotent state. One type of cell is entirely converted into a completely different cell type. Induced pluripotent stem cells provided the backbone for the research and development of cell reprogramming technology, which allows us to decide and change the fate of cells by manipulating gene expression [6,7].

Another major application of this technology is the development of neuronal cells by inducing gene expression changes in somatic cells. There are speculations among researchers as to whether neuronal cell development can be either induced by gene expression and transcriptional factor alteration or by inducing changes with chemical compounds from endogenous astroglia and other cells.

Recent trends in the induced neuronal cells majorly deal with the application of cell transplantation therapy for neurodegenerative disorders. Cell reprogramming technology has many

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potential applications in medicine, including the development of patient-specific therapies for a wide range of diseases and conditions [8]. It also has the potential to revolutionize drug discovery and development by allowing scientists to study the effects of new drugs on different types of cells without the need for animal testing.

Methods and mechanisms involved in cell reprogramming

Cell reprogramming technology makes use of various methods and mechanisms to bring forth results. The methods can be summarized as somatic cell nuclear transfer technology, induced PSC technology, direct reprogramming technology, trans-differentiation, and small-molecule induced reprogramming. SCNT technology is used to produce totipotent cells. This is done by injecting a nucleus isolated from a differentiated adult cell into an enucleated oocyte. This process results in the creation of a new cell, known as a cloned embryo, which can develop into a genetically identical organism to the donor of the somatic cell.

In the context of cell reprogramming, nuclear transfer can be used to create induced pluripotent stem cells, which are cells that have been reprogrammed to an embryonic-like state where they can differentiate into many different cell types. The process involves taking a somatic cell, such as a skin cell, and transferring its nucleus into an oocyte that has had its own nucleus removed [9]. This oocyte is then stimulated to divide and develop into a blastocyst, which contains a mass of cells that can be harvested and used to derive iPSCs. The cells isolated from the blastocyst have the ability to differentiate into all three germ layers and also show indefinite cell division. This gave researchers various cell study models but raised ethical concerns about using oocytes. Nuclear transfer is a complex and technically challenging procedure that requires specialized expertise and equipment; even then, the success rate is relatively low. It is also a controversial technique due to ethical concerns surrounding the use of human embryos and the potential for reproductive cloning. However, it still remains an important tool for research into cell reprogramming and regenerative medicine.

Inducing pluripotency in normal cells to make them differentiate into different types of cells in the body can also be done using recombinant DNA technology. This reprogramming process is typically achieved by the introduction of a set of genes called pluripotency factors into adult cells. Some of the most commonly used pluripotency factors are Oct4, Sox2, Klf4, and c-Myc, which are introduced into adult cells using viral vectors or electroporation.

These factors work together to activate a set of genes that are normally expressed in embryonic stem cells, which leads to the reprogramming of adult cells to a pluripotent state [10].

This is the method to produce pluripotent stem cells, but this is still under careful study as these genetic changes can lead to cancerous modifications in cells. The major problem to be overcome in this method is avoiding the tumor or cancer-based transcriptional markers that are inactive in the genome. Using epigenetic modifications, cell fate is altered in this method. This

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involves histone modifications, which are necessary to induce pluripotency but can also lead to cancerous mutations. Direct reprogramming and trans-differentiation are two related concepts in the field of stem cell biology and regenerative medicine. Direct reprogramming can be defined as the process by which one type of cell is converted directly into another type of cell without going through an intermediate pluripotent stage. This is achieved by introducing specific transcriptional factors or other molecular cues that promote the desired cell fate using vectors or other methods. Trans-differentiation, on the other hand, is the process by which a fully differentiated cell is converted into a different type of cell without going through a pluripotent intermediate stage. This process occurs naturally in certain organisms, such as during limb regeneration in salamanders, but researchers believe that this can also be induced experimentally by introducing specific molecular cues. Somatic cells obtained from humans and mice have been converted into different types of cells like myoblasts, neurons, etc. Direct reprogramming and trans-differentiation are based on the theoretical belief in their ability to reduce the preparation time for transplantation and other therapies, but in practice they are still less efficient, tedious, and time-consuming processes. Both direct reprogramming and trans-differentiation hold great promise for regenerative medicine, as they offer the potential to generate specific types of cells for use in tissue repair and regeneration. The major benefit of these technologies is that they don't raise any ethical concerns like those that arise with the use of embryonic stem cells [11]. These technologies are still in the early stages of development, but they have already shown great potential for treating a variety of diseases and injuries, including heart disease, diabetes, and spinal cord injuries. Small molecule-induced cell reprogramming is a technique that is being used to convert one type of cell into another type by using small molecules that have the ability to mimic the effects of transcriptional factors, which are proteins that regulate gene expression. This method avoids the use of genetic manipulation and can be more efficient and precise than traditional cell reprogramming techniques. Selection of such small molecules is done based on their ability to activate or inhibit specific signaling pathways or transcription factors that are involved in the differentiation of the target cell type. When the cells are exposed to these molecules, they trigger a series of molecular events that lead to the conversion of one cell type into another.

Small molecule-induced cell reprogramming has been used to generate various different cell types, such as neurons, cardiomyocytes, and hematopoietic cells. This technique has potential applications in regenerative medicine, drug discovery, and disease modelling. As this technology is still under careful observation and study, more optimized and successful results are needed to fully exploit its potential.

Factors and genes affecting pluripotency

Induced pluripotent stem cells are generated under the methods of cell reprogramming technology which is done by the combined state of the factors and the conditions. By the discovery of induced pluripotent stem cells,

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many factors undergo several critical plays in the reprogramming with the ectopic expression of OCT3/4, SOX2, KLF4, c-MYC (OSKM) called as the most robust method.

Even though the somatic cells reprogramming in pluripotent condition is dependent on the ectopic expression of OSKM genes, it is still ineffective and only few numbers of cells proceed the complete reprogramming stages [12,13].

The efficiency of the reprogramming technology is dependent on many factors and the inclusion of cells' pluripotency and proliferation or on the epigenetics. Activation and the inhibition which provide effective reprogramming have been identified by many processes, hence found the activators and the inhibitors.

OCT3/4, SOX2 and KLF4 are the important activators of the pluripotency genes and the differentiation is helped by inhibitors to the genes. NANOG is also a key regulator of pluripotency and it came into the action along with the OCT3/4 and SOX2 for the reprogramming process. Some transcription factors (NR5A2, UTF1, FOXH1, SALL4, GLIS1) are also help in promotion and regulation along with the major factors of reprogramming process. In addition to the factors like c-MYC, cyclin D1 and suppressors of p53 also contribute in the development of efficiency of reprogramming process by the methods- cell proliferation and apoptosis.

The changes like presence and absence of disease associated mutations are accidentally help in the increase of robust in colonies of generated iPSC [14]. GBX2, NANOGP8, SP8, ZIC1, PEG3 are possibly involved as the transcription factors which improves the reprogramming process and it is found by the screening of genes expressed differentially.

Hence, these factors are major critical one in enhancing pluripotency and promoting self-renewal positions and therefore these are confirmed as transcription factors in pluripotency for the generation of iPSC.

Cells that can and cannot be reprogrammed into iPSCs

The reprogramming of cells using iPSCs includes some criteria like selection of the source cell, ethical consideration, reprogramming methods, reprogramming factors, reprogramming efficiency, pluripotency variation and genetic stability. Under these criteria certain cells fall such as fibroblast, blood cells, adipocytes, neural cells, liver cells, pancreatic cells and dermal cells.

Selection of donor cells

The first step is to choose the type of somatic cells that will serve as the donor cells for reprogramming. These cells are usually obtained from a patient's own body, making them autologous and reducing the risk of immune rejection.

Selection of reprogramming factors

To reprogram the donor cells, a set of transcription factors called "Yamanaka factors" are introduced into the cells. The Yamanaka factors were discovered by Shinya Yamanaka and his team in 2006 and have been widely used in iPSC generation. These factors are Oct4 (Pou5f1), Sox2, Klf4, and c-Myc. Sometimes, other factors may be used or

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substituted to improve efficiency or reduce potential risks associated with c-Myc.

Delivery of reprogramming factors

The reprogramming factors are delivered into the donor cells using various methods, such as viral vectors, plasmids, or modified mRNA [15].

Viral vectors are commonly used because they efficiently integrate the reprogramming factors into the cell's DNA. Once inside the cell, the reprogramming factors begin to exert their effects on gene expression.

Induction of pluripotency

The introduced reprogramming factors activate or suppress specific genes in the donor cells, leading to a profound change in their cellular identity. The cells begin to undergo a series of molecular and epigenetic changes that transform them into pluripotent stem cells.

Selection and expansion of iPSC colonies

After introducing the reprogramming factors, not all cells will successfully undergo reprogramming. The process is highly inefficient, and only a small fraction of the cells will be reprogrammed into iPSCs. These reprogrammed cells form colonies that can be identified and isolated.

Characterization of iPSCs

The isolated iPSC colonies are further characterized to ensure they possess the defining characteristics of pluripotent stem cells [16,17].

These characteristics include the expression of pluripotency-associated markers, the ability to differentiate into cells from all three embryonic germ layers (ectoderm, mesoderm, and endoderm), and the ability to form teratomas (tumors containing tissues from all three germ layers) when injected into immunocompromised mice.

Expansion and maintenance of iPSCs

Once verified, iPSC colonies can be expanded and maintained in culture. They can be stored frozen for future use or differentiated into specific cell types for research or therapeutic applications.

Fibroblast

Fibroblasts are connective tissue cells found in the skin and other organs. They are the first cell types that were successfully reprogrammed into iPSCs. First fibroblasts are extracted from a patient or donor through a simple skin biopsy or other methods depending on the tissue source. The isolated fibroblasts are then exposed to specific reprogramming factors.

These factors are typically a set of transcription factors, which are genes that play a key role in regulating the expression of other genes. The most commonly used reprogramming factors are Oct4, Sox2, Klf4, and c-Myc [18,19]. These factors are usually delivered into the fibroblasts using viral vectors or other methods, such as plasmid transfection or mRNA transfection. The fibroblasts, now carrying the reprogramming factors, are cultured in a specialized growth medium that supports their transformation into pluripotent stem cells. During this process, some cells may fail to reprogram, while others may only partially reprogram. Therefore, specific techniques and conditions are used to select and isolate fully

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reprogrammed iPSC colonies. The selected iPSC colonies are carefully examined to confirm their pluripotency [20]. This includes testing their ability to express pluripotency markers, the potential to differentiate into various cell types of the three germ layers and the maintenance of a normal karyotype. Once confirmed, the iPSC colonies are expanded in culture. They can be frozen and preserved for future use or differentiated into specific cell types for therapeutic purposes or research applications.

Blood cells

Different types of blood cells, such as T cells, B cells, and myeloid cells, can be reprogrammed into iPSCs. Blood cells, such as skin cells, can be isolated from an individual by a simple blood draw or a skin biopsy. Specific transcription factors, usually delivered through viral vectors or other methods, are introduced into these somatic cells. These factors play a crucial role in turning on or off specific genes responsible for maintaining the cell's specialized state. The introduced reprogramming factors work together to reprogram the adult blood cells, resetting them to a pluripotent state, similar to embryonic stem cells [21].

Once the cells are successfully reprogrammed into iPSCs, they can be expanded and maintained in culture. These iPSCs can now differentiate into various cell types, including blood cells, as needed. We can guide iPSCs through specific differentiation pathways to produce the desired blood cell types.

Neural Cells from the brain and nervous system can be reprogrammed into iPSCs, allowing the study of neurological disorders and potential therapeutic application. Hepatocytes, the main functional cells of the liver, have also been successfully reprogrammed into pluripotent stem cells. Certain pancreatic cells have been reprogrammed into iPSCs, showing potential for diabetes research and regenerative medicine. The reprogramming process involves introducing specific transcription factors or other reprogramming factors that can reset the cell's identity and turn it into a pluripotent state [22]. Some cells such as germ cells, mature red blood cell, neurons, mature muscle cell and certain immune cells are more resistant to the reprogramming process due to their specific characteristics, gene expression patterns, and epigenetic modifications.

Cell type-specific epigenetic barriers

Different cell types in the body have distinct epigenetic profiles, including DNA methylation and chromatin structure, which play a crucial role in gene regulation. These epigenetic barriers can prevent the successful reprogramming of certain cell types. Some cells might have more tightly regulated chromatin structures or specific gene expression patterns that make them resistant to reprogramming.

Cellular age and senescence

Cells from older individuals may have accumulated more genetic and epigenetic changes over time, making them less amenable to reprogramming. Senescent cells, which are aged or damaged cells, might have altered gene expression patterns that hinder the reprogramming process.

Lineage-specific transcription factors

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The transcription factors used for reprogramming may not be sufficient to fully reprogram cells of certain lineages. The combination of factors required to reprogram one cell type may differ from what is necessary for another cell type.

Genetic mutations

Cells with significant genetic mutations or abnormalities might be less likely to reprogram successfully. These mutations could interfere with the proper function of essential genes required for reprogramming.

Reprogramming efficiency

Reprogramming efficiency varies between cell types. Some cell types are naturally more amenable to the reprogramming process, while others require more optimization and fine-tuning of the reprogramming factors. Germ cells are reproductive cells that undergo specialized processes during gametogenesis [23,24]. These cells have unique epigenetic characteristics that make their reprogramming into iPSCs more difficult. Mature red blood cells lack a nucleus and essential cellular machinery, which limits their potential for reprogramming into pluripotent stem cells. Certain neural cells and neural progenitor cells can be reprogrammed into iPSCs, fully matured neurons in the brain have proven more challenging to reprogram [25].

Muscle cells have specialized structures and gene expression patterns that make reprogramming into pluripotent stem cells more difficult. Immune cells like mature T cells, have unique gene expression patterns and epigenetic marks that pose obstacles to reprogramming.

Induced pluripotent stem cells vs other stem cells

Stem cells are those cells that can transform into numerous other cells and are substantially present in various regions of the body, for instance, the bone marrow. iPSCs are artificial stem cells that are made from discernible somatic cells by genetic manipulation. They're deduced from the skin or blood cells, which are antithetical to other stem cells. Though iPSCs are genetically reprogrammed to an embryonic stem cell-like state, they're largely more profitable than adult stem cells and embryonic stem cells [26,27].

The former is also known as somatic stem cells, which are undifferentiated cells that multiply to replenish dying cells. These cells are set up in a wide range of tissues, including the skin, heart, brain, liver, and bone marrow, but they're generally confined to becoming any cells in the part where they live, therefore being known as multipotent.

On the other hand, the iPSCs can be differentiated into any type of cell, including neural cells, which the adult stem cells aren't able to do. The method used to acquire iPSCs and adult stem cells is another significant distinction. While adult stem cells are taken from living tissue, iPSCs are created in a laboratory through a process called cellular reprogramming [28].

As a result, iPSCs can be produced in vast quantities, while adult stem cells could be harder to come b.

On the other hand, iPSCs (induced pluripotent stem cells) and embryonic stem cells (ESCs) have numerous parallels, but

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there are also some important differences between them. One key similarity between iPSCs and ESCs is their pluripotency, which means that they have the ability to differentiate into any type of cell in the body. This makes both types of stem cells potentially useful for regenerative medicine and tissue engineering. However, there are some differences in the way that iPSCs and ESCs are generated. iPSCs are generated by reprogramming adult cells, such as skin cells, back into an embryonic-like state using genetic manipulation methods. ESCs, on the other hand, are deduced from the inner cell mass of embryos that are generally discarded after in vitro fertilization procedures. Because iPSCs can be generated from a patient's own cells, they have the potential to reduce the risk of immune rejection when used for transplantation or other curative procedures.

In discrepancy, ESCs are more likely to be rejected by a patient's immune system because they aren't genetically identical to the patient. Still, there are also some challenges associated with iPSCs [29]. For illustration, there's a threat of inheritable mutations and instability during the reprogramming process, which could affect their safety and efficacy. The cell reprogramming technology used to generate iPSCs is highly time-consuming and expensive.

Other than the major types of stem cells, we can also consider other cells such as mesenchymal stem cells (MSCs) and hematopoietic stem cells (HSCs). MSCs are a type of stem cell that is present in many tissues throughout the body, like bone marrow, umbilical cord tissue, and fat tissues. They have the ability to differentiate into cells of bone, cartilage, and other such cells. They also have immunomodulatory properties, which means they have the ability to influence the activity of immune cells, by marking its significance in the treatment of inflammatory and autoimmune diseases [30]. MSCs are advantageous over iPSCs in terms of lowering the risk of tumorigenicity and genetic abnormalities and being easier to obtain. Whereas HSCs are a type of adult stem cell that can give rise to blood cells such as red blood cells, white blood cells, and platelets. They are basically used to treat leukemia, lymphoma, and other blood disorders through bone marrow transplantation. Unlike iPSCs, HSCs are naturally occurring stem cells found in bone marrow and cord blood and are less advantageous than the latter.

iPSCs in the treatment of neurodegenerative disorders

Neurodegenerative disorders can be categorized as a group of conditions that affect the nerve cells in the brain and spinal cord and lead to their degeneration and death over time. As the name suggests, these disorders are slowly progressive and continue to worsen with time. These disorders can have a significant impact on a person's cognitive, motor, and sensory functions. Neurodegenerative disorders include Alzheimer's disease, Parkinson's disease, etc. These two neurodegenerative disorders are highly common and affect the majority of the population throughout the world, but so far there is no permanent cure for them. Induced pluripotent stem cells are said to be a possible remedy, or at least a temporary fix, for these

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conditions, as they can provide a source to replace the lost neurons [31].

iPSCs can renew and divide into any type of cell, so they can be useful as a source of neurons to replace the degenerating neurons in a patient. Induced pluripotent stem cells hold a lot of promise as an effective tool for the treatment of neurodegenerative disorders.

The biggest advantage of using iPSCs in neurodegenerative disorder treatment is that they can be used to generate and divide into neurons by reprogramming the patient's own cells, which entirely reduces the risk of immune rejection. iPSCs can also be genetically modified to contain disease-causing mutations, allowing researchers to study the disease in a laboratory setting and test potential treatments without violating any ethical regulations [32,33].

These stem cells can be made to divide into any kind of nerve cell that was lost or degenerated by these disorders. These neurons can be used to study disease mechanisms, screen for potential drugs, and ultimately be transplanted into patients to replace lost or damaged neurons. So far in the clinical trials, stem cell therapy for neurodegenerative disorders has shown both promising and negative results. iPSC-generated neurons have proven to be effective in replacing the lost neurons, but there are still concerns over oncogenic mutations and immune rejection, so the complete development and acceptance of these therapies still have a long way ahead.

iPSCs in the treatment of Parkinson's disease

Parkinson's disease is a progressive neurodegenerative disorder that is associated with loss of body movement. This is caused by the loss of dopamine-producing neurons in the brain. Dopamine is a neurotransmitter that is highly essential for controlling movement of the body, and due to this condition, patients suffer from a lack of dopamine, which directly affects the physical movements of the body [34].

The symptoms of Parkinson's disease always develop gradually over time and include tremors, stiffness, slowness of movement, and difficulty with balance and coordination. As the disease continues to progress, patients also begin to experience cognitive changes, such as memory loss and difficulty with thinking and reasoning, but this can vary from patient to patient. PD has been found to have mutations in various genes, like parkin, LRRK2, SNCA, etc. There are also cases where many other types of mutations have led to PD. For the treatment of PD, iPSCs were used to create nerve cell lines from patients with the disease [35].

The primary studies using these iPSC-generated neurons were done on primates, such as monkeys. Dopaminergic neurons that were generated from adult cells were then transplanted into Parkinsonian cygnus monkeys; this showed positive results to a certain extent as the dopaminergic neurons helped to improve their motor functions. Multiple other methods of testing continued to be done on primates before the human trials began. The beginning of human trials was done by using iPSC-generated neurons as a study model for testing various therapies. Multiple scientists began to research PD

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using iPSCs. Dermal fibroblasts obtained from a PD patient were used to develop iPSC cell lines by using plasmid vectors that expressed genes such as OCT3/4 and L-MYC.

These genes are regulatory elements for pluripotency [36]. Multiple cell lines of neurons were developed using iPSCs obtained from cells such as fibroblasts using viral or retroviral vectors. The obtained cell lines of neurons from iPSCs were made in such a way that they contain similar mutations as those of the PD patient from whom they were generated. Enhanced activities and other suppressed gene activities were reported to be found in those neurons.

The generated cell lines of neurons with mutations were used as human-like study models as they can respond to different treatments and drugs that have to be tested. This reduced the risk of direct human trials; however, the mutations in genes such as parkin or PINK1 showed a direct reduction in dopaminergic neurons obtained from cell lines [37].

Several mechanisms that lead to PD were confirmed using these generated cell lines. Pharmacogenomics, dynamics, and kinetics of various drugs that were designed for PD were tested on these cells to confirm their safety and efficacy.

Further studies showed relationships between the calcium pathway of physical movements and dopaminergic neurons that directly affect movements in PD patients. In 2020, a researcher named Schweitzer and his team showed autologous transplantation of iPSC-derived dopaminergic progenitor cells in a PD patient. This implantation was done to the midbrain of the patient. Primary tests were conducted on humanized mouse models to confirm the safety of immune rejection and other factors. The iPSC-generated neurons were given clinical-grade safety and were transplanted into the putamen of the patient [38,39]. Grafting success was later confirmed using positron emission tomography, and the grafting was done without any immunosuppression. All these are still clinical trials, and there is still no perfected treatment for PD using iPSCs, as there are still several challenges that need to be addressed before iPSC-based therapies can be used in human patients with Parkinson's disease. For example, the safety and efficacy of iPSC-derived neurons need to be carefully evaluated in preclinical studies and clinical trials. There are also concerns about the potential risk of tumor formation, as iPSCs have the ability to form tumors if they are not fully differentiated.

iPSCs in the treatment of Alzheimer's disease

Alzheimer's disease is a progressive neurodegenerative disorder. This disorder is associated with the loss of memory, the ability to think, etc. This has been regarded as the most common cause of dementia. Alzheimer's disease also starts out very slowly and gradually worsens over time. The exact cause of Alzheimer's disease is still not known, but among researchers it is speculated to be caused by multiple factors, including genetic mutations and lifestyle. Symptoms of Alzheimer's disease are memory loss, difficulty with problem-solving and reasoning, confusion, and changes in personality and behavior [40]. As the disease

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progresses, patients have trouble speaking, walking, and performing simple tasks. There is still no cure for Alzheimer's disease, but there are a lot of drugs and therapies that are still going through clinical trials. Some medicines are available to deal with the symptoms and progression of the disease.

iPSCs are considered to have the potential to be used in the treatment of AD. AD is a neurodegenerative disorder that is caused by the cytotoxic buildup of certain proteins, amyloid plaques, and tau tangles in the brain. This gradually leads to the loss of neurons and cognitive decline in the patient. iPSCs can be used to generate neurons to replace the damaged ones and counter the loss of neurons due to cytotoxicity [41].

These transplanted neurons have the potential to integrate with the patient's nervous system and reduce the risk of AD while improving cognitive health. The major aim of this is to repair the damaged regions of the brain and restore their functional ability. iPSCs can also be used to generate brain tissues and neurons to study the accumulation of cytotoxic substances that leads to AD by serving as study models for researchers. The primary clinical trials for the treatment of AD using iPSC were done in primates and mammalian animal study models such as mice [42,43]. Transplantation of homogenous progenitor cells in animal models has proven to be effective, as in the case of AD study model mice that have shown differentiation into glial cells. Study models of human neurons are made using adult cells, such as peripheral blood cells obtained from AD patients, by converting them into iPSCs using viral vectors such as the Sendai virus that can encode for OCT4, c-MYC, etc. These study models that are made using cells obtained from AD patients have been useful in determining the type of AD and the cytotoxic elements that can or have caused AD. However, there is still no definitive treatment for AD using iPSCs, as there are still several challenges that need to be overcome before iPSC-based therapies for AD can become a reality [44]. These include improving the efficiency and safety of iPSC generation and transplantation, ensuring the transplanted cells survive and function properly in the brain, and avoiding the formation of tumors.

iPSCs in the treatment of blood disorders

Sickle cell anemia is a very famous blood disorder. This has been found to be a genetic blood disorder that directly affects the production of hemoglobin. This in turn affects the ability of red blood cells to carry oxygen throughout the body. Sickle cell anemia is characterized by the weird sickle like shape observed in the hemoglobin molecules in red blood cells that leads to their easy breakdown. This will eventually lead to the gradual loss of RBCs in patients and might eventually lead to the death of patients [45]. Symptoms of sickle cell anemia include pain, fatigue, jaundice, retarded growth and development in children. It has also shown an increased risk of infections. Treatment for sickle cell anemia may include medications to manage pain and prevent complications, blood transfusions, and bone marrow transplants for severe cases. Management and treatment of sickle cell anemia is ongoing, and patients require lifelong care to manage the condition effectively. Thalassemia is

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another blood disorder and is classified into two types, α-thalassemia and β-thalassemia. α-thalassemia is characterized by gene aberrations such as deletions that leads to defects in the α-globin chain and β-thalassemia is also caused by point mutations that leads to the defects in β-globin synthesis [46]. Both these defects are caused by mutations that affects molecular processes like transcription and translation of mRNA and splicing errors. Treatments that are currently available for thalassemia includes regular blood transfusions, bone marrow transplants, and some drugs and medications to alleviate the symptoms.

iPSCs in the treatment of sickle cell anemia and thalassemia

Finding a permanent cure for these disorders has been a huge challenge, but the primary treatments are bone marrow transplantation and regular blood transfusions for patients. These methods have produced positive results in their treatment, but they have also shown severe cases of graft rejection and immune rejection for both bone marrow transplantation and blood transfusion. Histocompatibility between transplants and patients over long intervals has proven to be a difficult challenge to overcome for the complete success of this treatment [47,48]. Gene therapy is also being considered as an option to treat these diseases, but it still has a very long way to go before it is implemented due to unsure results and ethical issues. Technologies like antisense and knockout mechanisms are currently being tested for their efficacy and safety in treating these disorders. Such therapies have shown positive results in mouse-like animal study models. Prenatal diagnosis of these disorders has proven to be very helpful in the detection and treatment of these disorders at very early stages [49].

iPSCs are now being tested for their efficacy and safety in treating these disorders. Developing study cell models of patients using iPSC has been a major advantage of this technique, as it reduces the risk of ethical backlash from society. Somatic cells are being used to produce study models to understand the underlying mechanisms involved in the progression and fatal nature of these disorders. Sickle cell anemia and thalassemia study models generated using iPSCs and the cells prepared for transplantation therapy using iPSCs have proven to cure these disorders in a mouse study model [50].

Sickle cell anemia and β-thalassemia were cured in mouse study models by combining hematopoietic cells generated using iPSCs and gene therapy to target and silence the mutations that lead to these disorders.

This kind of therapy might be useful in curing human patients, as iPSCs can provide an amazing source of hematopoietic cells and can be used to generate cells using the patient's own cells, thus avoiding the risks of immune rejection.

Human study models are currently being generated using iPSCs and fibroblasts [51]. Viral vectors carrying certain transcriptional factor genes like OCT4 help in generating these study models. However, there is still a long way to go before these therapies can actually come into human usage, as their efficacy and ethical nature are still being questioned.

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iPSC in the treatment of rheumatoid arthritis

Rheumatoid arthritis is one of the autoimmune diseases that initially affect the joints. It is characterized by inflammation of the synovium and it will lead to swelling, loss of body stiffness and joint deformity. In this case rheumatoid affect the other organs in the human body.

Rheumatoid is the genetic linked disease and also environmental factors. Certain genes may increase the risk of developing rheumatoid [52]. Factors like smoking and hormonal changes may trigger the disease in (RA) individuals. The symptoms usually occur symmetrically which means they affect both sides of the body Pain. Fatigue, loss of appetite, and low-grade may also accompany RA. Rheumatoid arthritis is a chronic condition, can vary from one person to another. Some individuals may experience mild symptoms that come and go, while others may have more severe and progressive disease. (RA) individuals have anti-cyclic citrullinated peptides and specific antibodies like the rheumatoid factor. Imaging tests such as x-ray, ultrasound or MRI used to assess joint damage and disease progression [53]. RA often requires a multidisciplinary approach involving rheumatology, primary care physicians and treatment strategies as needed.

iPSc in the treatment of T Cells

Regulatory T cells (tregs) are the specialized type of immune cells that play a critical role in maintaining immune tolerance and also preventing autoimmunity. PSCs are a type of stem cell that can differentiate into any cell type in the body.

Therefore, programming Tregs from PSCs could be a promising approach for preventing or treating autoimmune diseases. The stages of PSCs are generated from different sources, such as embryonic stem cells or induced pluripotent stem cells and it can also be generated from somatic cells such as skin cells by reprogramming them back to a pluripotent state. PSCs can be differentiated into hematopoietic progenitor cells (HPCs), which are the precursor cells for Tregs [54]. HPCs can be further differentiated into Tregs by exposing them to specific growth factors and cytokines, this process involves the activation of specific transcription factors such as Foxp3, which are critical for Treg development. Programmed Tregs can be combined with other immunomodulatory therapies, such as immune checkpoint inhibitors or antigen-specific tolerance induction to achieve a synergistic effect. Tregs, it evaluates their long-term safety and efficiency in clinical programs. Since their discovery in 2006, iPSCs have shown great potential in various areas of research and medicine [55].

iPSCs are generated by reprogramming adult cells, such as skin cells, into a pluripotent state, similar to embryonic stem cells. Which means they can give rise to different types of cells in the body.

Areas where iPSC research has shown progress

Disease modeling

iPSCs have been used to create cell models of various diseases, allowing researchers to study the underlying mechanisms and

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develop potential treatments. By reprogramming cells from patients with specific diseases, researchers can generate disease-specific iPSC lines and differentiate them into the affected cell types. This approach has been used to study diseases like Parkinson's, Alzheimer's, heart disease, and many others.

Drug discovery and toxicity testing

iPSCs have the potential to revolutionize drug development by providing more accurate models for testing drug efficacy and safety. Researchers can generate iPSC-derived cells representing different organs or tissues and test the response to various drugs or toxic substances. This approach may help identify potential drug candidates earlier in the development process and reduce the reliance on animal testing.

Regenerative medicine

iPSCs have opened new avenues for regenerative medicine. Researchers are exploring their potential for developing personalized cell-based therapies. iPSCs can be differentiated into various cell types, including neurons, heart cells, and pancreatic cells, which could be used to replace damaged or diseased tissues in patients.

Transplantation

Researchers are investigating the potential of iPSCs to overcome the limitations of organ transplantation. By generating patient-specific iPSCs and differentiating them into the required cell types, it may be possible to transplant tissues or organs without the risk of rejection by the immune system.

Basic biological research

iPSCs have provided valuable tools for studying developmental biology and basic cellular processes. By reprogramming cells, researchers can investigate early embryonic development and the differentiation of cells into different lineages.

iPSCs also offer opportunities to study rare diseases that are difficult to access or replicate in animal models.

Ongoing clinical trials in iPSCs

X-linked chronic granulomatous disease

X-linked chronic granulomatous disease is a human immunodeficiency disease that suppresses the activities of white blood cells (WBC), protecting them from bacteria, fungi, and other disease-causing organisms. Here, by using G1XCGD-modified autologous BM CD34 cells that possess the human CGD gene, autologous CD34+ hematopoietic stem cells (HSC) have been altered in the process of ex vivo transduction [56]. The bone marrow was being regulated by the chemotherapy, and it was grafted to gain an effective gene therapy for X-linked chronic granulomatous disease (X-CGD). The toxicity can be removed because of the synthesis of white blood cells (WBC) with the help of transplanting the gene-modified stem cells. In some cases, the evolution of the myelodysplasia and leukaemia complex involved mouse-derived retroviral vectors. A new lentiviral vector was assessed by this trail, which provided a possible way to pinpoint the fault, but the risk of difficulties had been reduced. The safety, practicability, and effectiveness of cellular gene therapy in patients with chronic granulomatous disease using autologous CD34+ cells that were transplanted from ex

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vivo transduced bone marrow were evaluated in two parts. The first and most important part of this trail is the examination of the offspring of grafted cells' efficacy and safety, which was conducted by biochemical and functional regeneration [57]. The second important part is the examining the clinical effectiveness, longitudinal study of clinical effect in the condition of increase in immunity against the fungal and the bacterial infection, transduction of hematopoietic cells in the infected person by ex vivo lentiviral-mediated gene transfer and the appraisal of engraftment kinetics and firmness. It is a prospective, non-controlled, randomized phase I/II clinical study with the G1XCGD lentiviral vector containing the human CGD gene. Roughly 3-6 infected persons were rehabilitated with the G1XCGD lentiviral vector who around the target total of 16 patients.

Geographic atrophy with age-related macular degeneration

The disease that causes blurred central vision is the most common disease for elderly or elderly people. It is known as age-related macular degeneration (AMD), and in the later stage of dry AMD, it is also called geographic atrophy (GA). No treatment has been introduced for geographic atrophy until now. In the geographic atrophy stage, the neurosensory retinal cells and the retinal pigment epithelium (RPE) can be destroyed and die. Stem cell biology advancements improve pluripotent cells' differentiation in RPE in vitro, which is used in potential treatment of AMD. Blooming cell-based related techniques are vital here [58,59]. Induced pluripotent stem cell (iPSC) development provides a free hand for individualized autologous therapy. Here, the somatic cells of the GA-affected persons have been generated by iPSC. Participants in this phase I/IIa prospective single-arm, single-centre clinical trial will undergo an autologous RPE subretinal transplant from iPSCs in one eye, and they will be followed up for five years after the procedure. Technique, and the differentiated iPSC is induced with RPE. Then it is cultured into a monolayer through a thin layer of scaffold under in vitro conditions. RPE transplantation should be developed in a small portion of the patient's subretinal area. This transplantation was done with the idea of protecting the neurosensory retina from degenerating again. A biodegradable polylactic-co-glycolic acid (PLGA) is used to check the safety and feasibility of the transplanted iPSC-derived RPE from the monolayer scaffold because the potential autologous cell-based therapy for GA is related to AMD. Five people will get an RPE transplant in one eye [60]. GA, best-corrected visual acuity (BCVA) between 20/100 and inclusive of counting fingers (CF), and a companion eye with the same or greater BCVA are all requirements for eligibility. A second cohort of up to seven additional participants with GA and BCVA between 20/80 and CF (inclusive) in the eye being considered for RPE transplantation and the same or better visual acuity in the other eye may undergo the procedure to collect additional safety and potential efficacy data useful for organizing future studies. If the National Eye Institute (NEI) Data and Safety Monitoring Committee (DSMC) gives clearance to proceed based on a review of data from the first cohort, to account for screening

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errors, a maximum of 20 individuals may be registered. Participants in this phase I/IIa prospective single-arm, single-centre clinical trial will undergo an autologous RPE subretinal transplant from iPSCs in one eye, and they will be followed up for five years after the procedure [61].

The key end measure is the safety of the RPE/PLGA transplantation, which is assessed by looking at how the patient's visual acuity changed and compiling a list of unfavourable events that occurred 12 months after the transplant. Secondary outcome measures include changes in the following parameters at 12, 24, and 60 months relative to baseline, assessed in the transplanted region and, where appropriate, compared with responses from other regions of the macula and/or with corresponding regions in the fellow eye: retinal sensitivity and fixation parameters measured by microperimetry; multifocal electroretinography (mfERG) responses; macular structure [62]. A few NEI participants are involves in photoreceptor imaging or RPE methods like adaptive optics-assisted macular imaging.

Applications of iPSCs

iPSCs are widely used in many fields as they are highly advantageous over the techniques that have been used before. Some of the applications include:

1. Disease modelling: iPSCs are used in disease modelling to study the principle of genetic disorder and diseases by following methods:
    - Patient-specific models: Patients with particular genetic disorders or complicated features may be used to create iPSCs. Researchers can create pluripotent cells with the same genetic mutations as the patients by reprogramming adult cells, including skin or blood cells, into iPSCs.
    - Recapitulating disease phenotypes: Patient-specific cells with disease-relevant phenotypes are available from an accessible and renewable source in the form of iPSCs. Researchers can see and examine the illness characteristics, such as altered cellular behaviour, diminished functionality, or molecular alterations, by developing iPSCs into the cell types impacted by the disease. This makes it possible to identify prospective therapy targets and gain a better knowledge of how a disease develops.
    - Testing gene editing and gene therapy methods: iPSCs can be used to evaluate the effectiveness and security of gene editing methods like CRISPR-Cas9 for treating genetic alterations that cause disease. iPSCs offer a platform for evaluating gene therapy strategies that transfer therapeutic genes into cells produced from patients.

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2. Drug discovery and toxicity testing: The use of induced pluripotent stem cells (iPSCs) in drug discovery and toxicity assessment is crucial. How iPSC technology is applied in these fields is as follows:

    - Disease modelling for drug screening: By differentiating iPSCs from patients with certain diseases into cell types that are relevant to those disorders, researchers can produce in vitro disease models. These models make it possible to evaluate potential treatment candidates for their effectiveness against a given condition. In comparison to conventional cell culture models, iPSC-based illness models offer a more accurate picture of human physiology, improving the predictive power of drug screening assays.
    - Testing for toxicity and safety: iPSC-derived cells can be utilised to assess the potential toxicity and safety of proposed medications. Researchers can evaluate the effects of various medication candidates on cellular viability, functionality, and negative effects by exposing iPSC-derived cells to them. With less need for animal testing and an improved safety profile before clinical trials, this method makes it possible to identify drug candidates with potential toxicities early on.

3. Cell replacement therapy: iPSCs have the capacity to differentiate into a range of cell types, including pancreatic, cardiomyocyte, and neuronal types. These cells can be employed in cell replacement therapies, which involve replacing sick or damaged cells in patients with new, healthy ones created from iPSCs. The treatment of ailments like Parkinson's disease, heart disease, diabetes, and spinal cord injuries has potential with this strategy.

4. Personalized medicine: iPSCs can be produced from specific individuals, giving researchers the opportunity to construct patient-specific disease models and individualised treatment plans. This method considers the patient's genetic history as well as the unique disease characteristics, resulting in more effective and focused treatments.

5. Regenerative medicine and tissue engineering: iPSCs can be used in tissue engineering methods to create transplantable, functional tissues and organs. Researchers want to develop tissues and organs that may be utilized for transplantation by encouraging iPSCs to differentiate into particular cell types and organizing them into three-dimensional structures, overcoming the obstacles of immunological

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rejection and a lack of available organs.

6. Understanding developmental biology: iPSCs are a useful resource for researching the mechanisms of early human development and differentiation. Researchers can restore adult cells' pluripotency by reprogramming them.

Ethical issues

Some rules and regulations were brought into the research and development process to ensure the disciplines were conducted ethically. These guidelines measure the safety of the scientists' scientific works to ensure that they do not pose a danger to human lives. Lots of guidelines for experiments using humans as the testing host, like the Nuremberg Code of 1947 and the Belmont Report of 1978, have been proposed to avoid unethical research and treatments. Even though these guidelines are being followed nowadays, many new ideas have emerged, and the usage has also changed [63].

The renovations of the ethics and the guidelines should be changed accordingly, as the world is now experiencing changes and the newer research must be useful and safe for livelihoods. However, ethical terms and conditions that are being regulated globally by international organizations are important, but the most challenging part is the acceptance and tolerance of following the rules by the individual countries, which vary according to their own needs and their own lives. New and modified guidelines of rules and ethics should be proposed for the development of induced pluripotent stem cell research, genomics, and biomedicine, and the new advancements of these bio-related technologies will be beneficial in promoting the area of regenerative medicine.

Here, specific rules and regulations are provided for the usage of the particular cells in the stem cell therapy. This regulates and is being used in introducing the cells into the patients to examine their functioning and the results of the work of the project.

Now there are various disciplines that are principled for these kinds of works that are undergone to determine the proper method of using the cells, stem cells, and tissues for the treatment of the patients [64].

The guidelines given by the ISSCR (International Society for Stem Cell Research) provide an upgraded and enhanced ethic, particularly for the use of stem cells under the supervision of experts all around the world. Even though it has been updated on some minor issues, the guidelines differ among individuals.

The major guidelines of ethical, regulatory terms and conditions of society of the cell therapy are:

- Conditions of production.
- The properties of the clinical graded cells.
- Genetic material.
- Genetic manipulation.
- Intellectual property rights and patents.
- Protected and secured personal information.
- Informed consent.

Future prospects of iPSC

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Pluripotency can separate into all the types of cells by expression of specific recap factor and has wide range of operations. The cell is an abecedarian unit of all living organisms. The mortal body consists of further than 200 cell types, some of which work singly (blood cell) and some work together in network (synapses). In embryogenesis, the first experimental stage is zygote. They're discerned into morula and blastocyst before implantation. The inner cell mass can separate into all types of cells (ectoderm, endoderm and mesoderm).

The eventuality of mortal embryonic stem cells (ESCs) and convinced pluripotent stem cells (iPSCs) in regenerative drug. ESCs, first reported in 1998, were anticipated to be pivotal in treating conditions like Parkinson's complaint and spinal cord injuries. The use of ESCs faced ethical enterprises and vulnerable rejection.

The iPSCs were introduced in 2007 and they showed implicit in treating inheritable diseases by correcting inheritable blights in case-specific iPSCs. As iPSCs are being deduced from the case's own cells, barring the threat of vulnerable rejection. The first clinical trial using autologous iPSCs for the treatment of wet age-related macular degeneration (AMD) was initiated in 2014 in Japan. Although autologous iPSC remedy has benefits, similar as avoiding vulnerable rejection, it has limitations [65].

The process is expensive and time-consuming. Allogenic iPSCs, deduced from benefactors, offer the advantage of iPSC technology lies in the inflexibility to establish iPSC lines from benefactors of different periods and the capability to estimate patron characteristics before generating clinical-grade iPSC duplicates. To minimize vulnerable rejection, matching the mortal leukocyte antigen (HLA) types between patron and philanthropist is important. The iPSCs offer implicit advantages in regenerative drug, and allogenic iPSC remedy grounded on HLA matching can give a more doable and accessible approach to treat colorful conditions. The operations of convinced pluripotent stem cells (iPSCs) in complaint modeling and medicine webbing.

The limitations of beast models in directly representing mortal conditions and emphasize the necessity of complaint models using mortal cells. The complaint-specific iPSC lines were first reported in 2008, and since also, there have been successful reconstructions of complaint countries using iPSCs.

For illustration, iPSCs deduced from cases with spinal muscular atrophy, Rett pattern, and domestic dysautonomia have been used for medicine confirmation and studying complaint mechanisms.

The study of iPSCs deduced from cases with thanatophoric dysplasia type I and achondroplasia were used to test the effectiveness of a medicine called statin in correcting demoralized cartilage.

The eventuality of iPSCs in medicine webbing, including medicine displacing, which involves testing being medicines for new remedial operations. The use of case-specific iPSCs can replicate complaint phenotypes and aid in the development of individualized drug. numerous case-specific iPSC lines have been established, which is

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anticipated to grease exploration on rare conditions [66].

The issue of control in case-deduced iPSC exploration. While healthy benefactors' cells are readily available, the inheritable differences among individualities can be contestation. Healthy family members, similar as maters and sisters, may be better control benefactors. The progress in inheritable editing technologies, similar as custom made nucleases, can further enhance the use of case-specific iPSCs. The mortal embryonic stem cells (ESCs) and convinced pluripotent stem cells (iPSCs) are applied in clinical and artificial operations.

The shift towards large scale suspense cell culture systems, similar as incentive steins with dynamic shifting, to achieve scaling- up, invariant quality, and low cost in the product of pluripotent cells. The use of iPSC generation as a technology for genome-wide epigenetic resetting in cancer exploration. While the accumulation of inheritable mutations is well established in cancer inauguration and progression, the donation of epigenetic abnormalities, similar as aberrant methylation, isn't understood.

The cancer-specific epigenomes in glioblastoma-deduced iPSCs didn't help the re-established neural grandfathers from flaunting nasty geste upon transplantation. This states that the shifted genome of glioblastoma is a definitive cause of nasty geste rather than epigenetic changes.

Still, the epigenetic insecurity convinced during the reprogramming process can be employed to study cancer development and explore common molecular mechanisms involved in both processes [67].

Directed isolation styles from ESCs and iPSCs have been established as models for in vivo isolation from the embryo. The capability of pluripotent stem cells to abstract the experimental process in vitro makes them precious in the study of experimental biology and iPSCs generated from physical cells of rare creatures facing extermination enable access to their experimental processes, contributing to species-specific molecular biology exploration.

This can prop in the conservation of risked creatures, artificial use of precious bioresources, and the study of species-specification. Non-mortal primate iPSCs have been established from a range of primates and evolutionary analysis. These iPSCs deduced from easy to gain fibroblasts or blood cells allow for the analysis and comparison of interspecies cells in vitro. By comparing humans and hams, experimenters have linked mortal-specific traits in the regulation mechanisms of LINE-1 transposons.

The study of elaboration and development using iPSCs is still in its early stages but offers significant implicit for understanding the processes by which living effects have achieved diversity and complexity. The technology of factor intermediated convinced pluripotency, particularly iPSCs, has had a significant impact on drug, transplantation remedy, complaint modeling, and medicine discovery.

Ongoing clinical studies, enhancement of clinical grade iPSC banks, medicine webbing, and displacing are anticipated to accelerate

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the progress of iPSC grounded curatives. In the field of life lores, iPSC ways have also made advancements in stem cell biology, cancer exploration, and evolutionary analysis.

Conclusion

In conclusion, authors intend to highlight the tremendous potential of induced pluripotent stem cells (iPSCs) as a transformative technology in regenerative medicine and disease modeling through this review.

Through reprogramming somatic cells into a pluripotent state, iPSCs offer remarkable advantages over traditional stem cell sources, such as ethical considerations and reduced immune rejection risks. Their ability to differentiate into various cell types has opened up new avenues for personalized therapies and drug development, promising to revolutionize the medical landscape. While iPSCs have shown great promise, several challenges remain to be addressed. The safety concerns regarding genomic stability, tumorigenicity, and off-target effects must be thoroughly investigated and mitigated before widespread clinical applications can be realized. Additionally, the standardization of protocols, optimization of reprogramming methods, and development of efficient differentiation strategies are crucial for enhancing the reliability and reproducibility of iPSC-based therapies. It is evident from this review that iPSC research is evolving rapidly, driven by ongoing scientific advancements and collaborative efforts across multiple disciplines. As our understanding deepens, iPSCs hold the potential to transform how we approach and treat various diseases, providing hope for patients with currently untreatable conditions.

By overcoming the existing challenges and harnessing the full potential of iPSCs, we can unlock a new era in regenerative medicine, ultimately improving the lives of countless individuals worldwide.

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Competing interests

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Author contributions

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References

1. Alison MR, Poulsom R, Forbes S, Wright NA. An Introduction to Stem Cells. J Pathol. 2002;197(4):419-23. PubMed | CrossRef

Citation: Jhoshitha D, Divyadharshini P, Padmini D, Joe AJV, Prapanjan KK, Prabahar AA. Investigation Into the Potential Prospects of Induced Pluripotent Stem Cells. J Regen Biol Med. 2023;5(4):251-77.
DOI: https://doi.org/10.37191/Mapsci-2582-385X-5(4)-136

2. Zakrzewski W, Dobrzyński M, Szymonowicz M, Rybak Z. Stem Cells: Past, Present, and Future. Stem Cell Res Ther. 2019;10(1):68. PubMed | CrossRef
3. Potten, C. (Ed.). Stem cells. Elsevier. 1996.
4. Gardner RL. Stem Cells: Potency, Plasticity and Public Perception. J Anat. 2002;200(3):277-82. PubMed | CrossRef
5. Wang H, Yang Y, Liu J, Qian L. Direct Cell Reprogramming: Approaches, Mechanisms and Progress. Nat Rev Mol Cell Biol. 2021;22(6):410-24. PubMed | CrossRef
6. Buganim Y, Faddah DA, Jaenisch R. Mechanisms and Models of Somatic Cell Reprogramming. Nat Rev Genet. 2013;14(6):427-39. PubMed | CrossRef
7. Srivastava D, DeWitt N. In Vivo Cellular Reprogramming: The Next Generation. Cell. 2016;166(6):1386-96. PubMed | CrossRef
8. Vierbuchen T, Wernig M. Molecular Roadblocks for Cellular Reprogramming. Mol Cell. 2012;47(6):827-38. PubMed | CrossRef
9. Yu C, Liu K, Tang S, Ding S. Chemical Approaches to Cell Reprogramming. Curr Opin Genet Dev. 2014;28:50-56. PubMed | CrossRef
10. Li H, Collado M, Villasante A, Strati K, Ortega S, Cañamero M, et al. The Ink4/Arf Locus is a Barrier for Ips Cell Reprogramming. Nature. 2009;460(7259):1136-9. PubMed | CrossRef
11. De Carvalho DD, You JS, Jones PA. DNA Methylation and Cellular Reprogramming. Trends Cell Biol. 2010;20(10):609-17. PubMed | CrossRef
12. Smith ZD, Sindhu C, Meissner A. Molecular Features of Cellular Reprogramming and Development. Nat Rev Mol Cell Biol. 2016;17(3):139-54. PubMed | CrossRef
13. Aydin B, Mazzoni EO. Cell Reprogramming: The Many Roads to Success. Annu Rev Cell Dev Biol. 2019;35:433-52. PubMed | CrossRef
14. González F, Boué S, Izpisúa Belmonte JC. Methods for Making Induced Pluripotent Stem Cells: Reprogramming a la Carte. Nat Rev Genet. 2011;12(4):231-42. PubMed | CrossRef
15. Buganim Y, Faddah DA, Cheng AW, Itskovich E, Markoulaki S, Ganz K, et al. Single-Cell Expression Analyses During Cellular Reprogramming Reveal an Early Stochastic and a Late Hierarchic Phase. Cell. 2012;150(6):1209-22. PubMed | CrossRef
16. Li Z, Sun C, Qin Z. Metabolic Reprogramming of Cancer-Associated Fibroblasts and its Effect on Cancer Cell Reprogramming. Theranostics. 2021;11(17):8322-8336. PubMed | CrossRef
17. Apostolou E, Hochedlinger K. Chromatin Dynamics During Cellular Reprogramming. Nature. 2013;502(7472):462-71. PubMed | CrossRef
18. Hanna J, Saha K, Pando B, van Zon J, Lengner CJ, Creyghton MP, et al. Direct Cell Reprogramming is a Stochastic Process Amenable to Acceleration. Nature. 2009;462(7273):595-601. PubMed | CrossRef
19. Iwafuchi-Doi M, Zaret KS. Pioneer Transcription Factors in Cell Reprogramming. Genes Dev. 2014;28(24):2679-92. PubMed | CrossRef
20. Utikal J, Polo JM, Stadtfeld M, Maherali N, Kulalert W, Walsh RM, et al. Immortalization Eliminates a Roadblock During Cellular Reprogramming into Ips Cells. Nature. 2009;460(7259):1145-8. PubMed | CrossRef
21. Mertens J, Marchetto MC, Bardy C, Gage FH. Evaluating Cell Reprogramming, Differentiation and Conversion Technologies in Neuroscience. Nat Rev Neurosci. 2016;17(7):424-37. PubMed | CrossRef
22. Stadtfeld M, Maherali N, Breault DT, Hochedlinger K. Defining Molecular Cornerstones During Fibroblast to Ips Cell Reprogramming in Mouse. Cell Stem Cell. 2008;2(3):230-40. PubMed | CrossRef
23. Downing TL, Soto J, Morez C, Houssin T, Fritz A, Yuan F, et al. Biophysical Regulation of Epigenetic State and Cell Reprogramming. Nat Mater. 2013;12(12):1154-62. PubMed | CrossRef
24. Macarthur BD, Ma'ayan A, Lemischka IR. Systems Biology of Stem Cell Fate and Cellular Reprogramming. Nat Rev Mol Cell Biol. 2009;10(10):672-81. PubMed | CrossRef
25. Hanna JH, Saha K, Jaenisch R. Pluripotency and Cellular Reprogramming: Facts, Hypotheses, Unresolved Issues. Cell. 2010;143(4):508-25. PubMed | CrossRef

Citation: Jhoshitha D, Divyadharshini P, Padmini D, Joe AJV, Prapanjan KK, Prabahar AA. Investigation Into the Potential Prospects of Induced Pluripotent Stem Cells. J Regen Biol Med. 2023;5(4):251-77.
DOI: https://doi.org/10.37191/Mapsci-2582-385X-5(4)-136

26. Shi Y, Inoue H, Wu JC, Yamanaka S. Induced Pluripotent Stem Cell Technology: A Decade of Progress. Nat Rev Drug Discov. 2017;16(2):115-130. PubMed | CrossRef
27. Hu K. All Roads Lead to Induced Pluripotent Stem Cells: The Technologies of Ipsc Generation. Stem Cells Dev. 2014;23(12):1285-300. PubMed | CrossRef
28. Malik N, Rao MS. A Review of the Methods for Human Ipsc Derivation. Methods Mol Biol. 2013;997:23-33. PubMed | CrossRef
29. Guzzo RM, Gibson J, Xu RH, Lee FY, Drissi H. Efficient Differentiation of Human Ipsc-Derived Mesenchymal Stem Cells to Chondroprogenitor Cells. J Cell Biochem. 2013;114(2):480-90. PubMed | CrossRef
30. Zhao Y, Yin X, Qin H, Zhu F, Liu H, Yang W, et al. Two Supporting Factors Greatly Improve the Efficiency of Human Ipsc Generation. Cell Stem Cell. 2008;3(5):475-9. PubMed | CrossRef
31. Okano H, Morimoto S. iPSC-based Disease Modeling and Drug Discovery in Cardinal Neurodegenerative Disorders. Cell Stem Cell. 2022;29(2):189-208. PubMed | CrossRef
32. Valadez-Barba V, Cota-Coronado A, Hernández-Pérez OR, Lugo-Fabres PH, Padilla-Camberos E, Díaz NF, Díaz-Martínez NE. iPSC for Modeling Neurodegenerative Disorders. Regen Ther. 2020;15:332-39. PubMed | CrossRef
33. Katt ME, Mayo LN, Ellis SE, Mahairaki V, Rothstein JD, Cheng L, et al. The Role of Mutations Associated with Familial Neurodegenerative Disorders on Blood-Brain Barrier Function in An Ipsc Model. Fluids Barriers CNS. 2019;16(1):20. PubMed | CrossRef
34. Rõlova T, Lehtonen Š, Goldsteins G, Kettunen P, Koistinaho J. Metabolic and Immune Dysfunction of Glia in Neurodegenerative Disorders: Focus on iPSC Models. Stem Cells. 2021;39(3):256-65. PubMed | CrossRef
35. Fernández-Santiago R, Ezquerra M. Epigenetic Research of Neurodegenerative Disorders Using Patient iPSC-based Models. Stem Cells Int. 2016;2016:9464591. PubMed | CrossRef
36. Ahani-Nahayati M, Shariati A, Mahmoodi M, Olegovna Zekiy A, Javidi K, Shamlou S, et al. Stem Cell in Neurodegenerative Disorders; an Emerging Strategy. Int J Dev Neurosci. 2021;81(4):291-311. PubMed | CrossRef
37. Fanizza F, Campanile M, Forloni G, Giordano C, Albani D. Induced Pluripotent Stem Cell-Based Organ-On-A-Chip as Personalized Drug Screening Tools: A Focus on Neurodegenerative Disorders. J Tissue Eng. 2022;13:20417314221095339. PubMed | CrossRef
38. Han C, Chaineau M, Chen CX, Beitel LK, Durcan TM. Open Science Meets Stem Cells: A New Drug Discovery Approach for Neurodegenerative Disorders. Front Neurosci. 2018;12:47. PubMed | CrossRef
39. Murtaza N, Uy J, Singh KK. Emerging Proteomic Approaches to Identify the Underlying Pathophysiology of Neurodevelopmental and Neurodegenerative Disorders. Mol Autism. 2020;11(1):27. PubMed | CrossRef
40. de Rus Jacquet A, Denis HL, Cicchetti F, Alpaugh M. Current and Future Applications of Induced Pluripotent Stem Cell-Based Models to Study Pathological Proteins in Neurodegenerative Disorders. Mol Psychiatry. 2021;26(7):2685-2706. PubMed | CrossRef
41. Valadez-Barba V, Cota-Coronado A, Barragán-Álvarez CP, Padilla-Camberos E, Díaz-Martínez NE. iPSC for Modeling of Metabolic and Neurodegenerative Disorders. In Novel Concepts in iPSC Disease Modeling. Acad Press. 2022(59-84). CrossRef
42. Lee CT, Bendriem RM, Wu WW, Shen RF. 3D Brain Organoids Derived From Pluripotent Stem Cells: Promising Experimental Models for Brain Development and Neurodegenerative Disorders. J Biomed Sci. 2017;24(1):59. PubMed | CrossRef
43. Liu GH, Ding Z, Izpisua Belmonte JC. iPSC Technology to Study Human Aging and Aging-Related Disorders. Curr Opin Cell Biol. 2012;24(6):765-74. PubMed | CrossRef
44. Tcw J. Human iPSC Application in Alzheimer's Disease and Tau-Related Neurodegenerative Diseases. Neuro sci Lett. 2019;699:31-40. PubMed | CrossRef
45. Rao I, Crisafulli L, Paulis M, Ficara F. Hematopoietic Cells from Pluripotent Stem Cells: Hope and Promise for the Treatment of Inherited Blood Disorders. Cells. 2022;11(3):557. PubMed | CrossRef
46. Kim C. Disease Modeling and Cell Based Therapy with iPSC: Future Therapeutic Option with Fast and Safe Application. Blood Res. 2014;49(1):7-14. PubMed | CrossRef

Citation: Jhoshitha D, Divyadharshini P, Padmini D, Joe AJV, Prapanjan KK, Prabahar AA. Investigation Into the Potential Prospects of Induced Pluripotent Stem Cells. J Regen Biol Med. 2023;5(4):251-77.
DOI: https://doi.org/10.37191/Mapsci-2582-385X-5(4)-136

47. Ye Z, Zhan H, Mali P, Dowey S, Williams DM, Jang YY, et al. Human-induced Pluripotent Stem Cells From Blood Cells of Healthy Donors and Patients with Acquired Blood Disorders. Blood. 2009;114(27):5473-80. PubMed | CrossRef
48. Georgomanoli M, Papapetrou EP. Modeling Blood Diseases with Human Induced Pluripotent Stem Cells. Dis Model Mech. 2019;12(6):dmm039321. PubMed | CrossRef
49. Kim JY, Nam Y, Rim YA, Ju JH. Review of the Current Trends in Clinical Trials Involving Induced Pluripotent Stem Cells. Stem Cell Rev Rep. 2022;18(1):142-154. PubMed | CrossRef
50. Wattanapanitch M. Recent Updates on Induced Pluripotent Stem Cells in Hematological Disorders. Stem Cells Int. 2019;2019:5171032. PubMed | CrossRef
51. Maali A, Atashi A, Ghaffari S, Kouchaki R, Abdolmaleki F, Azad M. A Review on Leukemia and iPSC Technology: Application in Novel Treatment and Future. Curr Stem Cell Res Ther. 2018;13(8):665-75. PubMed | CrossRef
52. Lee J, Kim Y, Yi H, Diecke S, Kim J, Jung H, et al. Generation of Disease-Specific Induced Pluripotent Stem Cells from Patients with Rheumatoid Arthritis and Osteoarthritis. Arthritis Res Ther. 2014;16(1):R41. PubMed | CrossRef
53. Kim J, Kang SC, Yoon NE, Kim Y, Choi J, Park N, et al. Metabolomic Profiles of Induced Pluripotent Stem Cells Derived from Patients with Rheumatoid Arthritis and Osteoarthritis. Stem Cell Res Ther. 2019;10(1):319. PubMed | CrossRef
54. Kim J, Kim Y, Choi J, Jung H, Lee K, Kang J, et al. Recapitulation of Methotrexate Hepatotoxicity with Induced Pluripotent Stem Cell-Derived Hepatocytes from Patients with Rheumatoid Arthritis. Stem Cell Res Ther. 2018;9(1):357. PubMed | CrossRef
55. Rim YA, Park N, Nam Y, Ju JH. Generation of Induced-Pluripotent Stem Cells Using Fibroblast-Like Synoviocytes Isolated from Joints of Rheumatoid Arthritis Patients. J Vis Exp. 2016;(116):54072. PubMed | CrossRef
56. Rae J, Newburger PE, Dinauer MC, Noack D, Hopkins PJ, Kuruto R, et al. X-Linked Chronic Granulomatous Disease: Mutations in the CYBB Gene Encoding the Gp91-Phox Component of Respiratory-Burst Oxidase. Am J Hum Genet. 1998;62(6):1320-31. PubMed | CrossRef
57. Cale CM, Morton L, Goldblatt D. Cutaneous and Other Lupus-Like Symptoms in Carriers of X-Linked Chronic Granulomatous Disease: Incidence and Autoimmune Serology. Clin Exp Immunol. 2007;148(1):79-84. PubMed | CrossRef
58. Holz FG, Bellman C, Staudt S, Schütt F, Völcker HE. Fundus Autofluorescence and Development of Geographic Atrophy in Age-Related Macular Degeneration. Invest Ophthalmol Vis Sci. 2001;42(5):1051-6. PubMed | CrossRef
59. Klein ML, Ferris FL 3rd, Armstrong J, Hwang TS, Chew EY, Bressler SB, et al. Retinal Precursors and the Development of Geographic Atrophy in Age-Related Macular Degeneration. Ophthalmol. 2008;115(6):1026-31. PubMed | CrossRef
60. Sunness JS, Margalit E, Srikumaran D, Applegate CA, Tian Y, Perry D,et al. The Long-Term Natural History of Geographic Atrophy from Age-Related Macular Degeneration: Enlargement of Atrophy and Implications for Interventional Clinical Trials. Ophthalmol. 2007;114(2):271-7. PubMed | CrossRef
61. Keenan TD, Agrón E, Domalpally A, Clemons TE, van Asten F, Wong WT, et al. Progression of Geographic Atrophy in Age-related Macular Degeneration: AREDS2 Report Number 16. Ophthalmology. 2018;125(12):1913-1928. PubMed | CrossRef
62. Jaffe GJ, Chakravarthy U, Freund KB, Guymer RH, Holz FG, Liakopoulos S, et al. Imaging Features Associated with Progression to Geographic Atrophy in Age-Related Macular Degeneration: Classification of Atrophy Meeting Report 5. Ophthalmol Retina. 2021;5(9):855-67. PubMed | CrossRef
63. Volarevic V, Markovic BS, Gazdic M, Volarevic A, Jovicic N, Arsenijevic N, et al. Ethical and Safety Issues of Stem Cell-Based Therapy. Int J Med Sci. 2018;15(1):36-45. PubMed | CrossRef
64. King NM, Perrin J. Ethical Issues in Stem Cell Research and Therapy. Stem Cell Res Ther. 2014;5(4):85. PubMed | CrossRef
65. Wang Z, Zheng J, Pan R, Chen Y. Current Status and Future Prospects of Patient-Derived Induced Pluripotent Stem Cells. Hum Cell. 2021;34(6):1601-1616. PubMed | CrossRef

Citation: Jhoshitha D, Divyadharshini P, Padmini D, Joe AJV, Prapanjan KK, Prabahar AA. Investigation Into the Potential Prospects of Induced Pluripotent Stem Cells. J Regen Biol Med. 2023;5(4):251-77.
DOI: https://doi.org/10.37191/Mapsci-2582-385X-5(4)-136

66. Fukushima S, Miyashita A, Kuriyama H, Kimura T, Mizuhashi S, Kubo Y, et al. Future Prospects for Cancer Immunotherapy Using Induced Pluripotent Stem Cell-Derived Dendritic Cells or Macrophages. Exp Dermatol. 2023;32(3):290-96. PubMed | CrossRef
67. Fujita J, Fukuda K. Future Prospects for Regenerated Heart Using Induced Pluripotent Stem Cells. J Pharmacol Sci. 2014;125(1):1-5. PubMed | CrossRef

Citation: Jhoshitha D, Divyadharshini P, Padmini D, Joe AJV, Prapanjan KK, Prabahar AA. Investigation Into the Potential Prospects of Induced Pluripotent Stem Cells. J Regen Biol Med. 2023;5(4):251-77.
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