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Introduction

Annual grand meetings in the Uzbekistan Palace of International Forum son the occasion of the anniversary of the Constitution of Uzbekistan have become a good tradition. President Islam Karimov sums up the development of state and social reforms, and determines the title of the next year.

Addressing the participants in a report entitled 'Our objective is to decisively move toward the development, democratic renewal and modernization of the country', the President of Uzbekistan emphasized, "The Day our Constitution was adopted, December 8, 1992, will remain a milestone in our history, a holiday that laid the groundwork for building an independent democratic state with a socially oriented market economy, and shaping a civil society with the key objective of ensuring human interests, rights and freedoms, with the rule of law, and equality of all the country's citizens under the law."

Traditionally, the meeting focused on the past stage of development and the progress achieved. In due time, the country completely drew the line at various forms of the so-called 'shocking therapy' unacceptable for local people, which offered all former Soviet republics to rush into a raging whirlpool of a market economy, hoping for its self-regulation, without well-thought programs and not taking into account the historical, national and traditional peculiarities. With such a policy it would be difficult to predict our future. The correctness of the way we have chosen, which is based on five principles, is primarily proved by the heights we have achieved in a historically short period of time on our way toward democratization and liberalization of the political, economic and humanitarian spheres of society, in the process of sustainable economic development and increasing the quality of life for the population.[2]

Since gaining its independence, Uzbekistan's economy has grown by almost five times, the income per capita by 8.7 times, while the country's population has increased by 1.5 times and on January 1, 2015 is expected to make up 31.5 million people. It is noteworthy that the country's external debt does not exceed 15

percent, and internal debt, namely the government's debt to the population, stands at zero. Exports and foreign exchange reserves grow steadily.

Analyzing the progress achieved, President Karimov touched upon the law on the openness of state authorities and administration, which was adopted in 2014 following an extensive legal experiment, and which caused big international response and appreciation of the expert community. The act has undoubtedly increased the responsibility of governing bodies for quality decision making.

Under the implementation of the 'Concept of intensifying democratic reforms and forming the civil society in the country', special attention has been paid to the issues of democratization and liberalization of the economy, creation of effective mechanisms of supporting small business and private entrepreneurship. More than 160, or 44% of licensing procedures, 19 or 25% of activities subject to licensing have been canceled in recent years under the laws on licensing procedures in business, on the competition, on guarantees of freedom of entrepreneurship (in new edition) and other legislative acts. The form and frequency of the statistical, tax and financial reports submitted by business entities to state authorities have been reduced 1.5 - 2 times. There is a favorable environment for extensive development of family business - a new form of business, which is fully consistent with the traditions of the Uzbek people.

The speech highlighted the issues of national security in the face of growing geopolitical opposition, the escalating struggle for spheres of influence, radicalism, terrorism and extremism, the financial and economic crisis. In the context of the current situation, the President emphasized as follows: "... all of us need to soberly assess the situation, to mobilize all our forces and capabilities to face the challenges and make the appropriate changes and additions to our programs, especially the 'Concept of intensifying democratic reforms and forming the civil society in the country".

Uzbekistan has achieved a significant progress in this field. The country has built absolutely new industries and high-tech manufactures from scratch. Our finished goods rank decent in the global market. Uzbekistan is proud of its car

industry, including the manufacture of cars, trucks and specialized machinery, manufacture of engines and major component parts, as well as up-to-date agricultural machine engineering based on global designs, petrochemical and oil and gas industry, railway car engineering, consumer electronics, and pharmaceuticals.

President of Uzbekistan also drew attention to the most critical problem, the solution of which predetermines the prospects and the future of our country, the increase of the level and quality of life and well-being of our people. There is a need to remove all the obstacles and limitations, and provide a complete freedom for the development of private property and enterprise.

The country has achieved a significant progress in this direction. More than 31 thousand state owned companies in various sectors of the economy were transferred to private owners and shareholders. Many industries, such as agriculture, trade, all kinds of services, have been transferred into private property almost completely. The share of state ownership was minimized in the industries related to the consumer goods production like textiles, knitwear, leather and footwear, food, pharmaceuticals, furniture, as well as in the residential sector. The manufacture and service sectors take the lead in the performance and service growth rates.

The grand meeting spotlighted the development of social infrastructure. Annually, the name of the next year is declared in the hall of O'zbekiston Palace. This is a pivotal moment, because it paves the way to the adoption of the national program, which, in turn, vectors the further growth of living standards, enhancement of authority of our motherland in the international arena. As a rule, such documents address a wide range of relevant issues, which somehow affect the interests of each citizen.

500-600 thousand children are annually born in Uzbekistan. The care for their health, upbringing and education predetermines the future. The comprehension of this axiom makes it clear how important it was to name 2014 The Year of the Healthy Child in this grand hall a year ago. 4.7 trillion sums and

$260 million have been invested from different sources to meet the tasks of the program.

Throughout the year, great importance has been attached to the improvement of reproductive health system, development of pediatric services. The national program on further strengthening of reproductive health, maternal health, children and adolescent health for 2014 - 2018 years has been approved.[3]

Its implementation would contribute to growing our children physically healthy and spiritually mature, and generally bring the state youth policy to a higher level. The program has incorporated a wide range of different activities aimed at prevention of child morbidity and improvement of his health. For instance, it envisages the development of mother and child screening service. This year alone, owing to the timely identification of pathologies in screening centers, and appropriate treatment, more than 20 thousand children under risk were born healthy.

Certain steps have been taken in the current year to improve the efficiency of education and training. Particular attention was given to pre-school and primary education, since these stages are crucial in terms of child's pursuit to knowledge, his willingness to learn and advance. The intensified introduction of advanced information and communication technologies, Internet, promotion of physical culture and sports among children, especially girls, has tangibly contributed to the progress.

Uzbekistan is a country of young people. People under 30 make up more than 60% of the population. That is why social programs of the previous years were mainly focused on children and youth. There is a century-old tradition of respect for elders, especially elderly people. So, it was decided to call the forthcoming 2015 the Year of Care for the Senior Generation. Coming up with the initiative, Islam Karimov said as follows: "It is the duty of each of us to constantly revere and care of our fathers, grandfathers, mothers, who are making an invaluable contribution to the establishment of peace, harmony and happiness in every family and stability in the society through their life experience, and by their

own example, who are actively involved in the transformations in all spheres, especially in nurturing of a healthy generation in the spirit of our historical population, cultural values and good traditions."[3]

The trend is obviously important. Presently, there are more than 2.8 million people aged over 60 years, 225 thousand people - over 80 years, 44 thousand - older than 90 years in the country. 8,700 people have stepped over a 100-year threshold. Most importantly, the number of elderly people is increasing. In the years of independence, the average age of the population increased from 67 years in 1990 to 73.5 in men and 75.8 in women. A new social program is about to be approved. Talking about its aims and objectives, the head of state said: "When developing the program, we have to aim at addressing the existing problems concerning the life of the elderly, strengthening of material and moral support, in a word, we should practically meet the name we have given to the coming year.

Today, when we are establishing a working group to develop a new social program, it seems relevant to look back and review what has been done in recent years again. The currently functioning system should be the starting point for the further creation of better conditions for the full-fledged life of our mothers and fathers."

A large-scale work is underway across the country to fully support the older generation. The government budget has allocated more than 11.6 trillion sums for state pensions, and more than 105 billion sums for allowances this year alone.

The President drew attention to the fact that currently the country's pension exceeds 41% of the average wage. The President stressed that such a concern of the elderly is observed in quite few countries.

Representatives of the older generation are financially and morally supported by non-governmental organizations, social structures, and the scale of the support is constantly expanding. For instance, in 2013, the Nuroniy Foundation allocated 610 million sums for these purposes, and in the first nine months of 2014 - more than 553 million sums. The Mahalla Charity Fund supported veterans with

over 1.5 billion sums in 2013, and with 1.6 billion sums in the first nine months of 2014.[3]

Special needs of certain categories of elderly people are taken into account as well. For instance, this October a presidential decree introduced a regulation, which envisages granting 3,109 participants in the Second World War and 69,994 compatriot veterans of the labor front line with the opportunity to undergo free health rehabilitation in preventive and treatment institutions of the republic once a year at a time suitable for them.

Summing up the implementation of the national program The Year of the Healthy Child, President Islam Karimov emphasized that district medical associations, the Republican Specialized Center of Cardiology, cancer clinics and regional hospitals have been equipped with modern medical equipment by means of $28.5 million of credit and grant funds of foreign financial institutions. It is worth noting that 2014 has marked the beginning of large-scale projects to be continued next year. The projects are equally important for improving medical services for children and elderly people. For instance, up-to-date X-ray machines and ultrasound scanners will enable doctors in district health institutions to diagnose and prescribe treatment for many diseases in the place of residence.

Reconstruction and overhaul of medical institutions will continue to contribute to improving the quality of care in the communities. This year, such work, worth nearly 410 billion sums, has been carried out in 137 district and regional medical institutions.[3]

Thus, the meeting has paved the way for new social initiatives aimed at further improving the quality of life and prosperity in Uzbekistan.

The aim of the qualification work:

To define the importance of stem cells to organism regeneration.

The task of the qualification work:

To collect information about stem cells and to get knowledge. To direct stem cells to wound organism with artificial way and define character of regeneration.

The object of the qualification work:

The hemopaetic stem cells of red blood bone marrow of mammalia.

The importance of the qualification work:

to strengthen regeneration process of weak organisms with artificial biological way and increase living organism.

The structure of the qualification work:

The theme of "Stem cells" consists of introduction, two chapters (the first chapter is about information of stem cell, the second one is the importance stem cells to organism regeneration), 4 parts which are belonged to chapter, experiments, conclusion, recommendation and literature.

Information about the stem cells

The term "stem cell" was proposed for scientific use by the Russian histologist Alexander Maksimov (1874–1928) at congress of hematologic society in 1908 Berlin. It postulated existence of haematopoietic stem cells. Stem cells have the remarkable potential to develop into many different cell types in the body during early life and growth. In addition, in many tissues they serve as a sort of internal repair system, dividing essentially without limit to replenish other cells as long as the person or animal is still alive. When a stem cell divides, each new cell has the potential either to remain a stem cell or become another type of cell with a more specialized function, such as a muscle cell, a red blood cell, or a brain cell. Stem cells are distinguished from other cell types by two important characteristics. First, they are unspecialized cells capable of renewing themselves through cell division, sometimes after long periods of inactivity. Second, under certain physiologic or experimental conditions, they can be induced to become tissue- or organ-specific cells with special functions. In some organs, such as the gut and bone marrow, stem cells regularly divide to repair and replace worn out or damaged tissues. In other organs, however, such as the pancreas and the heart, stem cells only divide under special conditions. Stem cells can become cells of the blood, heart, bones, skin, muscles, brain etc. There are different sources of stem cells but all types of stem cells have the same capacity to develop into multiple types of cells.[26]

Stem cells (center ones) can develop into any cell type. They are valuable as research tools and might, in the future, be used to treat a wide range of diseases. Stem cells are different from other cells in the body. There are three unique properties of all stem cells regardless of their source. These include:

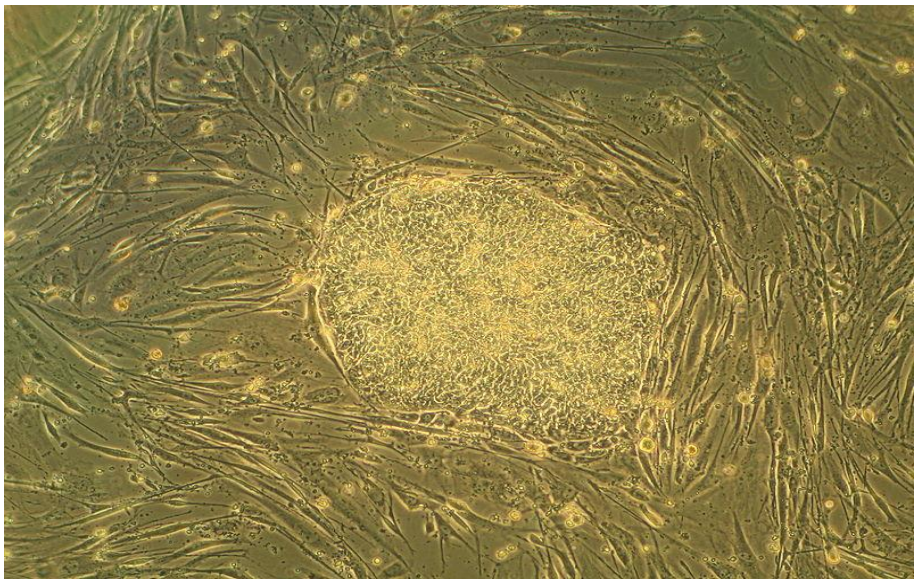
- capability of dividing and renewing themselves for long periods
- being unspecialized and basic cells
- they can give rise to any type of specialized cell because they are unspecialized.

Stem cells have an interesting history that has been somewhat tainted with debate and controversy. In the mid 1800s it was discovered that cells were basically the building blocks of life and that some cells had the ability to produce other cells. Attempts were made to fertilise mammalian eggs outside of the human body and in the early 1900s, it was discovered that some cells had the ability to generate blood cells.

In 1968, the first bone marrow transplant was performed to successfully treat two siblings with severe combined immunodeficiency. Other key events in stem cell research include:

- 1978: Stem cells were discovered in human cord blood
- 1981: First in vitro stem cell line developed from mice
- 1988: Embryonic stem cell lines created from a hamster
- 1995: First embryonic stem cell line derived from a primate
- 1997: Cloned lamb from stem cells
- 1997: Leukaemia origin found as haematopoietic stem cell, indicating possible proof of cancer stem cells

In 1998, Thompson, from the University of Wisconsin, isolated cells from the inner cell mass of early embryos and developed the first embryonic stem cell lines. During that exact same year, Gearhart, from Johns Hopkins University, derived germ cells from cells in fetal gonad tissue; pluripotent stem cell lines were developed from both sources. Then, in 1999 and 2000, scientists discovered that manipulating adult mouse tissues could produce different cell types. This meant that cells from bone marrow could produce nerve or liver cells and cells in the brain could also yield other cell types. These discoveries were exciting for the field of stem cell research, with the promise of greater scientific control over stem cell differentiation and proliferation.[26]



Stem cells are undifferentiated biological cells that can differentiate into specialized cells and can divide (through mitosis) to produce more stem cells. They are found in multi cellular organisms. In mammals, there are two broad types of stem cells: embryonic stem cells, which are isolated from the inner cell mass of blastocysts, and adult stem cells, which are found in various tissues. In adult organisms, stem cells and progenitor cells act as a repair system for the body, replenishing adult tissues. In a developing embryo, stem cells can differentiate into all the specialized cells—ectoderm, endoderm and mesoderm (see induced pluripotent stem cells)—but also maintain the normal turnover of regenerative organs, such as blood, skin, or intestinal tissues.

There are three known accessible sources of autologous adult stem cells in humans:

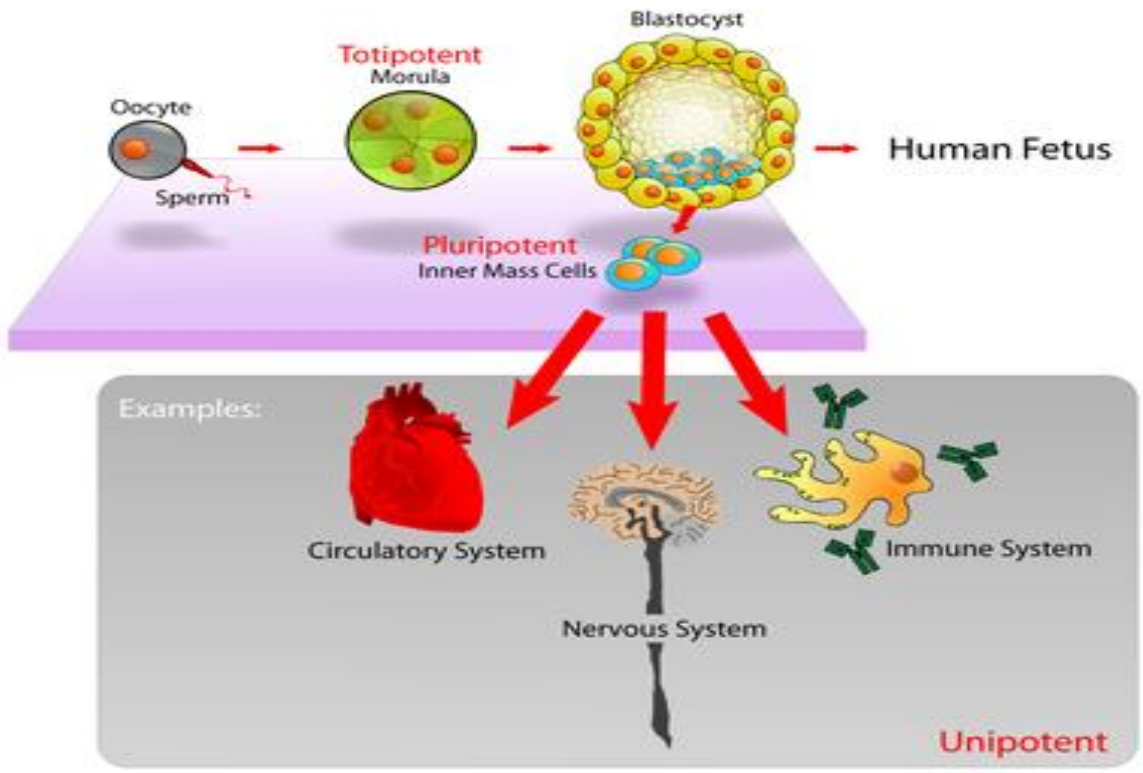
1. Bone marrow, which requires extraction by harvesting, that is, drilling into bone (typically the femur or iliac crest).

2. Adipose tissue (lipid cells), which requires extraction by liposuction.

3. Blood, which requires extraction through apheresis, wherein blood is drawn from the donor (similar to a blood donation), and passed through a machine that extracts the stem cells and returns other portions of the blood to the donor.

Stem cells can also be taken from umbilical cord blood just after birth. Of all stem cell types, autologous harvesting involves the least risk. By definition, autologous cells are obtained from one's own body, just as one may bank his or her own blood for elective surgical procedures.

Adult stem cells are frequently used in medical therapies, for example in bone marrow transplantation. Stem cells can now beartificially grown and transformed (differentiated) into specialized cell types with characteristics consistent with cells of various tissues such as muscles or nerves. Embryonic cell lines and autologous embryonic stem cells generated through Somatic-cell nuclear transfer or dedifferentiation have also been proposed as promising candidates for future therapies. Research into stem cells grew out of findings by Ernest A. McCulloch and James E. Till at the University of Toronto in the 1960s.



Pluripotent, embryonic stem cells originate as inner cell mass (ICM) cells within a blastocyst. These stem cells can become any tissue in the body, excluding a placenta. Only cells from an earlier stage of the embryo, known as the morula,

are totipotent, able to become all tissues in the body and the extra embryonic placenta.[30] Human embryonic stem cells

A: Stem cell colonies that are not yet differentiated.

B: Nerve cells, an example of a cell type after differentiation.

Potency specifies the differentiation potential (the potential to differentiate into different cell types) of the stem cell.

-Totipotent (a.k.a. omnipotent) stem cells can differentiate into embryonic and extraembryonic cell types. Such cells can construct a complete, viable organism. These cells are produced from the fusion of an egg and sperm cell. Cells produced by the first few divisions of the fertilized egg are also totipotent.

- Pluripotent stem cells are the descendants of totipotent cells and can differentiate into nearly all cells, i.e. cells derived from any of the three germ layers.

- Multipotent stem cells can differentiate into a number of cell types, but only those of a closely related family of cells.

- Oligopotent stem cells can differentiate into only a few cell types, such as lymphoid or myeloid stem cells.

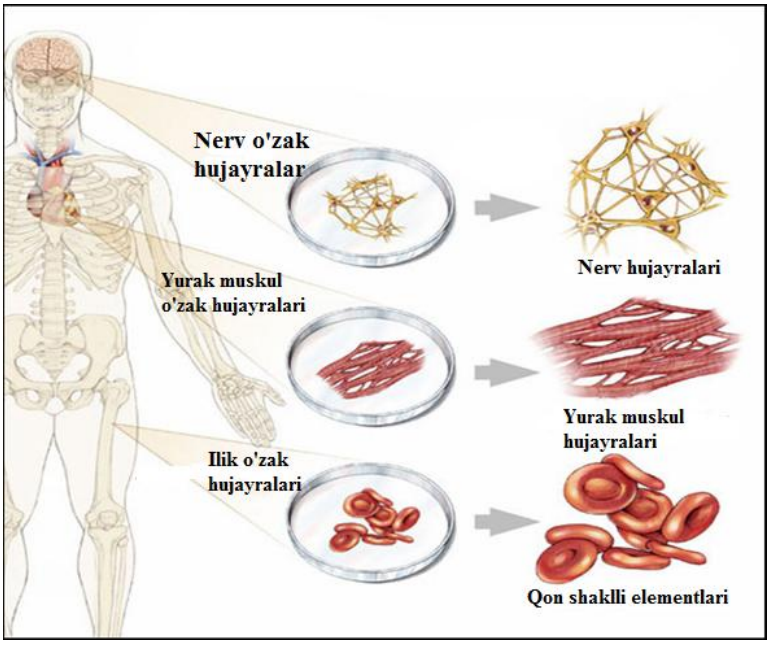
- Unipotent cells can produce only one cell type, their own, but have the property of self-renewal, which distinguishes them from non-stem cells (e.g. progenitor cells, muscle stem cells).

Totipotency is the ability of a single cell to divide and produce all of the differentiated cells in an organism. Spores and Zygotes are examples of totipotent cells. In the spectrum of cell potency, totipotency represents the cell with the greatest differentiation potential. Toti comes from the Latin totus which means "entirely."

It is possible for a fully differentiated cell to return to a state of totipotency. This conversion to totipotency is complex, not fully understood and the subject of recent

research. Research in 2011 has shown that cells may differentiate not into a fully totipotent cell, but instead into a "complex cellular variation" of totipotency.

The human development model is one which can be used to describe how totipotent cells arise. Human development begins when a sperm fertilizes an egg and the resulting fertilized egg creates a single totipotent cell, a zygote. In the first hours after fertilization, this zygote divides into identical totipotent cells, which can later develop into any of the three germ layers of a human (endoderm, mesoderm, or ectoderm), into cells of the cytotrophoblast layer or syncytiotrophoblast layer of the placenta. After reaching a 16-cell stage, the totipotent cells of the morula differentiate into cells that will eventually become either the blastocyst's Inner cell mass or the outer trophoblasts. Approximately four days after fertilization and after several cycles of cell division, these totipotent cells begin to specialize. The inner cell mass, the source of embryonic stem cells, becomes pluripotent.[32]



Research on Caenorhabditis elegans suggests that multiple mechanisms including RNA regulation may play a role in maintaining totipotency at different stages of development in some species. Work with zebra fish and mammals suggest a further interplay between miRNA and RNA binding proteins (RBPs) in determining development differences.

In September 2013, a team from the Spanish national Cancer Research Centre were able for the first time to make adult cells from mice retreat to the characteristics of embryonic stem cells thereby achieving totipotency.

A: Human embryonic stem cells (cell colonies that are not yet differentiated). B: Nerve cell biology, pluripotency (from the Latin plurimus, meaning very many, and potens, meaning having power) refers to a stem cell that has the potential to differentiate into any of the three germ layers: endoderm (interior stomach lining, gastrointestinal tract, the lungs), mesoderm (muscle, bone, blood, urogenital), or ectoderm (epidermal tissues and nervous system). However, cell pluripotency is a continuum, ranging from the completely pluripotent cell that can form every cell of the embryo proper, e.g., embyronic stem cells and iPSCs (see below), to the incompletely or partially pluripotent cell that can form cells of all three germ layers but that may not exhibit all the characteristics of completely pluripotent cells.

Hematopoietic stem cells are an example of multipotency. When they differentiate into myeloid or lymphoid progenitor cells, they lose potency and become oligopotent cells with the ability to give rise to all cells of its lineage.

Multipotency describes progenitor cells which have the gene activation potential to differentiate into multiple, but limited cell types. For example, a multipotent blood stem cell is a hematopoietic cell — and this cell type can differentiate itself into several types of blood cell types like lymphocytes, monocytes, neutrophils, etc., but cannot differentiate into brain cells, bone cells or other non-blood cell types.

New research related to multipotent cells suggests that multipotent cells may be capable of conversion into unrelated cell types. In one case, fibroblasts were converted into functional neurons. In another case, human umbilical cord blood stem cells were converted into human neurons. Research is also focusing on converting multipotent cells into pluripotent cells.

Multipotent cells are found in many, but not all human cell types. Multipotent cells have been found in adipose tissue,[24] cardiac cells, bone marrow, and mesenchymal stromal cells (MSCs) which are found in the third molar.

MSCs may prove to be a good, reliable source for stem cells because of the ease in collection of molars at 8–10 years of age and before adult dental calcification. MSCs can differentiate into osteoblasts, chondrocytes, and adipocytes.

In biology, oligopotency is the ability of progenitor cells to differentiate into a few cell types. It is a degree of potency. Examples of oligopotent stem cells are the lymphoid or myeloid stem cells. A lymphoid cell specifically, can give rise to various blood cells such as B and T cells, however, not to a different blood cell type like a red blood cell. Examples of progenitor cells are vascular stem cells that have the capacity to become both endothelial or smooth muscle cells.

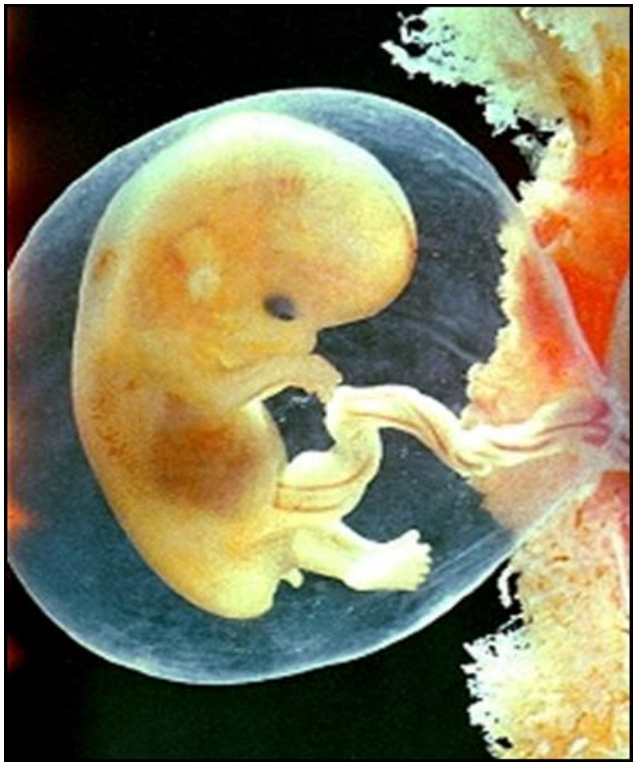
In cell biology, a unipotent cell is the concept that one stem cell has the capacity to differentiate into only one cell type. It is currently unclear if true unipotent stem cells exist. Hepatoblasts, which differentiate into hepatocytes (which constitute most of the liver) or cholangiocytes (epithelial cells of the bile duct), are bipotent. A close synonym for unipotent cell is precursor cell.

In practice, stem cells are identified by whether they can regenerate tissue. For example, the defining test for bone marrow or hematopoietic stem cells (HSCs) is the ability to transplant the cells and save an individual without HSCs. This demonstrates that the cells can produce new blood cells over a long term. It should also be possible to isolate stem cells from the transplanted individual, which can themselves be transplanted into another individual without HSCs, demonstrating that the stem cell was able to self-renew.

Properties of stem cells can be illustrated *in vitro*, using methods such as clonogenic assays, in which single cells are assessed for their ability to differentiate and self-renew. Stem cells can also be isolated by their possession of a

distinctive set of cell surface markers. However, *in vitro* culture conditions can alter the behavior of cells, making it unclear whether the cells will behave in a similar manner *in vivo*. There is considerable debate as to whether some proposed adult cell populations are truly stem cells.

Embryonic stem cells



Embryonic stem cells are derived from a four- or five-day-old human embryo that is in the blastocyst phase of development. The embryos are usually extras that have been created in IVF (in vitro fertilization) clinics where several eggs are fertilized in a test tube, but only one is implanted into a woman. Sexual reproduction begins when a male's sperm fertilizes a female's ovum (egg) to form a single cell called a zygote. The single zygote cell then begins a series of divisions, forming 2, 4, 8, 16 cells, etc. After four to six days - before implantation in the uterus - this mass of cells is called a blastocyst. The blastocyst consists of an inner cell mass (embryoblast) and an outer cell mass (trophoblast). The outer cell mass becomes part of the placenta, and the inner cell mass is the group of cells that will differentiate to become all the structures of an adult organism. This latter mass is the source of embryonic stem cells - totipotent cells (cells with total potential to develop into any cell in the body). In a normal pregnancy, the blastocyst stage continues until implantation of the embryo in the uterus, at which point the embryo is referred to as a fetus. This usually occurs by the end of the 10th week of gestation after all major organs of the body have been created.

However, when extracting embryonic stem cells, the blastocyst stage signals when to isolate stem cells by placing the "inner cell mass" of the blastocyst into a culture dish containing a nutrient-rich broth. Lacking the necessary stimulation to differentiate, they begin to divide and replicate while maintaining their ability to become any cell type in the human body. Eventually, these undifferentiated cells can be stimulated to create specialized cells.

Stem cells are either extracted from adult tissue or from a dividing zygote in a culture dish. Once extracted, scientists place the cells in a controlled culture that prohibits them from further specializing or differentiating but usually allows them to divide and replicate. The process of growing large numbers of embryonic stem cells has been easier than growing large numbers of adult stem cells, but progress is being made for both cell types In 1964, researchers isolated a single type of cell from a teratocarcinoma, a tumor now known to be derived from a germ cell. These cells isolated from the teratocarcinoma replicated and grew in cell culture as a stem cell and are now known as embryonal carcinoma (EC) cells. Although similarities in morphology and differentiating potential (pluripotency) led to the use of EC cells as the *in vitro* model for early mouse development, EC cells harbor genetic mutations and often abnormal karyotypes that accumulated during the development of the teratocarcinoma. These genetic aberrations further emphasized the need to be able to culture pluripotent cells directly from the inner cell mass.

In 1981, embryonic stem cells (ES cells) were independently first derived from mouse embryos by two groups. Martin Evans and Matthew Kaufman from the Department of Genetics, University of Cambridge published first in July, revealing a new technique for culturing the mouse embryos in the uterus to allow for an increase in cell number, allowing for the derivation of ES cells from these embryos. Gail R. Martin, from the Department of Anatomy, University of California, San Francisco, published her paper in December and coined the term “Embryonic Stem Cell”. She showed that embryos could be cultured *in vitro* and that ES cells could be derived from these embryos. In 1998, a breakthrough

occurred when researchers, led by James Thomson at the University of Wisconsin-Madison, first developed a technique to isolate and grow human embryonic stem cells in cell culture.

Neural stem cells (NSCs) are self-renewing, multipotent cells that generate the main phenotype of the nervous system. Stem cellsare characterized by their capability to differentiate into multiple cell types via exogenous stimuli from their environment. They undergo asymmetric cell division into two daughter cells, one non-specialized and one specialized. NSCs primarily differentiate intoneurons, astrocytes, and oligodendrocytes.

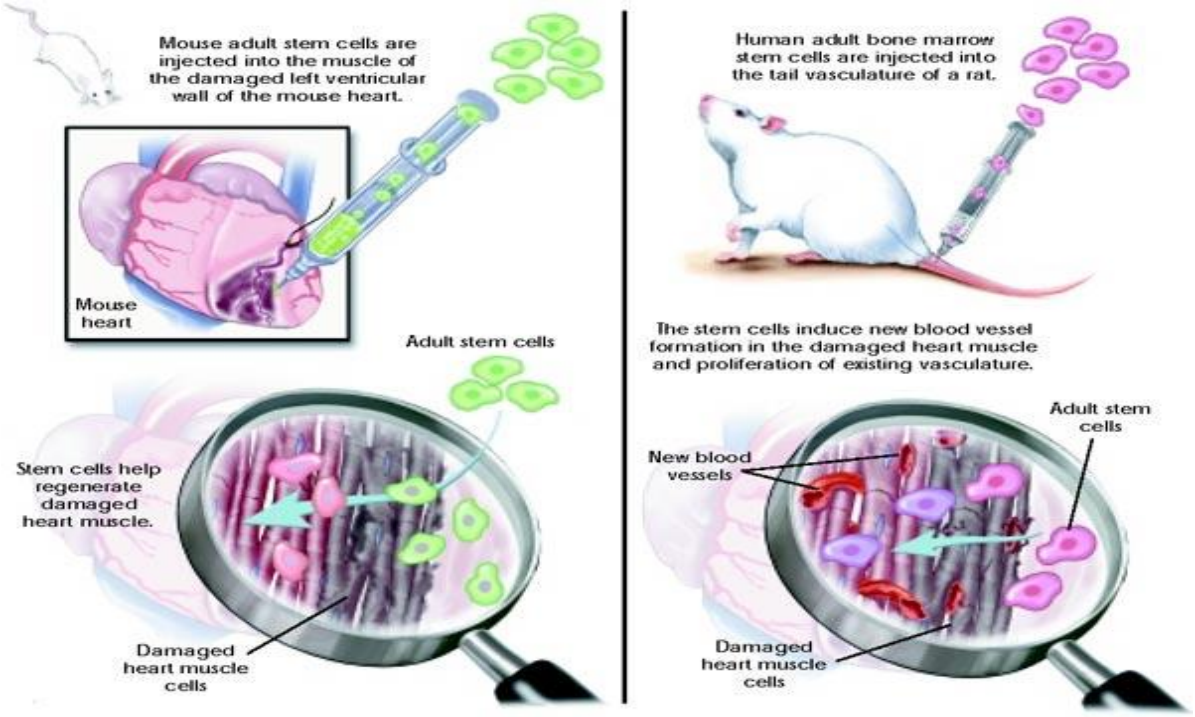
There are many ways in which human stem cells can be used in research and the clinic. Studies of human embryonic stem cells will yield information about the complex events that occur during human development. A primary goal of this work

is to identify how undifferentiated stem cells become the differentiated cells that form the tissues and organs. Scientists know that turning genes on and off is central to this process. Some of the most serious medical conditions, such as cancer and birth defects, are due to abnormal cell division and differentiation. A more complete understanding of the genetic and molecular controls of these processes may yield information about how such diseases arise and suggest new strategies for therapy. Predictably controlling cell proliferation and differentiation requires additional basic research on the molecular and genetic signals that regulate cell division and specialization. While recent developments with iPS cells suggest some of the specific factors that may be involved, techniques must be devised to introduce these factors safely into the cells and control the processes that are induced by these factors.

Human stem cells are currently being used to test new drugs. New medications are tested for safety on differentiated cells generated from human pluripotent cell lines. Other kinds of cell lines have a long history of being used in this way. Cancer cell lines, for example, are used to screen potential anti-tumor drugs. The availability of pluripotent stem cells would allow drug testing in a wider range of cell types. However, to screen drugs effectively, the conditions must be identical when comparing different drugs. Therefore, scientists must be able to precisely control the differentiation of stem cells into the specific cell type on which drugs will be tested. For some cell types and tissues, current knowledge of the signals controlling differentiation falls short of being able to mimic these conditions precisely to generate pure populations of differentiated cells for each drug being tested.

Perhaps the most important potential application of human stem cells is the generation of cells and tissues that could be used for cell-based therapies. Today, donated organs and tissues are often used to replace ailing or destroyed tissue, but the need for transplantable tissues and organs far outweighs the available supply. Stem cells, directed to differentiate into specific cell types, offer the possibility of a renewable source of replacement cells and tissues to treat diseases including

macular degeneration, spinal cord injury, stroke, burns, heart disease, diabetes, osteoarthritis, and rheumatoid arthritis.



For example, it may become possible to generate healthy heart muscle cells in the laboratory and then transplant those cells into patients with chronic heart disease. Preliminary research in mice and other animals indicates that bone marrow stromal cells, transplanted into a damaged heart, can have beneficial effects. Whether these cells can generate heart muscle cells or stimulate the growth of new blood vessels that repopulate the heart tissue, or help via some other mechanism is actively under investigation. For example, injected cells may accomplish repair by secreting growth factors, rather than actually incorporating into the heart. Promising results from animal studies have served as the basis for a small number of exploratory studies in humans (for discussion, see call-out box, "Can Stem Cells Mend a Broken Heart?"). Other recent studies in cell culture systems indicate that it may be possible to direct thedifferentiation of embryonic stem cells or adult bone marrow cells into heart muscle cells.

Cardiovascular disease (CVD), which includes hypertension, coronary heart disease, stroke, and congestive heart failure, has ranked as the number one cause of death in the United States every year since 1900 except 1918, when the nation

struggled with an influenza epidemic. Nearly 2,600 Americans die of CVD each day, roughly one person every 34 seconds. Given the aging of the population and the relatively dramatic recent increases in the prevalence of cardiovascular risk factors such as obesity and type 2 diabetes, CVD will be a significant health concern well into the 21st century. Cardiovascular disease can deprive heart tissue of oxygen, thereby killing cardiac muscle cells (cardiomyocytes). This loss triggers a cascade of detrimental events, including formation of scar tissue, an overload of blood flow and pressure capacity, the overstretching of viable cardiac cells attempting to sustain cardiac output, leading to heart failure, and eventual death. Restoring damaged heart muscle tissue, through repair or regeneration, is therefore a potentially new strategy to treat heart failure.

The use of embryonic and adult-derived stem cells for cardiac repair is an active area of research. A number of stem cell types, including embryonic stem (ES) cells, cardiac stem cells that naturally reside within the heart, myoblasts (muscle stem cells), adult bone marrow-derived cells including mesenchymal cells (bone marrow-derived cells that give rise to tissues such as muscle, bone, tendons, ligaments, and adipose tissue), endothelial progenitor cells (cells that give rise to the endothelium, the interior lining of blood vessels), and umbilical cord blood cells, have been investigated as possible sources for regenerating damaged heart tissue. All have been explored in mouse or rat models, and some have been tested in larger animal models, such as pigs.

A few small studies have also been carried out in humans, usually in patients who are undergoing open-heart surgery. Several of these have demonstrated that stem cells that are injected into the circulation or directly into the injured heart tissue appear to improve cardiac function and/or induce the formation of new capillaries. The mechanism for this repair remains controversial, and the stem cells likely regenerate heart tissue through several pathways. However, the stem cell populations that have been tested in these experiments vary widely, as do the conditions of their purification and application. Although much more research is

needed to assess the safety and improve the efficacy of this approach, these preliminary clinical experiments show how stem cells may one day be used to repair damaged heart tissue, thereby reducing the burden of cardiovascular disease.

In people who suffer from type 1 diabetes, the cells of the pancreas that normally produce insulin are destroyed by the patient's own immune system. New studies indicate that it may be possible to direct the differentiation of human embryonic stem cells in cell culture to form insulin-producing cells that eventually could be used in transplantation therapy for persons with diabetes.

To realize the promise of novel cell-based therapies for such pervasive and debilitating diseases, scientists must be able to manipulate stem cells so that they possess the necessary characteristics for successful differentiation, transplantation, and engraftment. The following is a list of steps in successful cell-based treatments that scientists will have to learn to control to bring such treatments to the clinic. To be useful for transplant purposes, stem cells must be reproducibly made to:

- Proliferate extensively and generate sufficient quantities of cells for making tissue.
- Differentiate into the desired cell type(s).
- Survive in the recipient after transplant.
- Integrate into the surrounding tissue after transplant.
- Function appropriately for the duration of the recipient's life.
- Avoid harming the recipient in any way.

Also, to avoid the problem of immune rejection, scientists are experimenting with different research strategies to generate tissues that will not be rejected.

To summarize, stem cells offer exciting promise for future therapies, but significant technical hurdles remain that will only be overcome through years of intensive research.

In 1968, doctors performed the first successful bone marrow transplant. Bone marrow contains somatic stem cells that can produce all of the different cell types that make up our blood. It is transplanted routinely to treat a variety of blood and bone marrow diseases, blood cancers, and immune disorders. More recently, stem cells from the blood stream (called peripheral blood stem cells) and umbilical cord stem cells have been used to treat some of the same blood-based diseases.

Leukemia is a cancer of white blood cells, or leukocytes. Like other blood cells, leukocytes develop from somatic stem cells. Mature leukocytes are released into the bloodstream, where they work to fight off infections in our bodies.

Leukemia results when leukocytes begin to grow and function abnormally, becoming cancerous. These abnormal cells cannot fight off infection, and they interfere with the functions of other organs.

Successful treatment for leukemia depends on getting rid of all the abnormal leukocytes in the patient, allowing healthy ones to grow in their place. One way to do this is through chemotherapy, which uses potent drugs to target and kill the abnormal cells. When chemotherapy alone can't eliminate them all, physicians sometimes turn to bone marrow transplants.

In a bone marrow transplant, the patient's bone marrow stem cells are replaced with those from a healthy, matching donor. To do this, all of the patient's existing bone marrow and abnormal leukocytes are first killed using a combination of chemotherapy and radiation. Next, a sample of donor bone marrow containing healthy stem cells is introduced into the patient's bloodstream.

If the transplant is successful, the stem cells will migrate into the patient's bone marrow and begin producing new, healthy leukocytes to replace the abnormal cells.

New evidence suggests that bone marrow stem cells may be able to differentiate into cell types that make up tissues outside of the blood, such as liver and muscle.

Scientists are exploring new uses for these stem cells that go beyond diseases of the blood.

While most blood stem cells reside in the bone marrow, a small number are present in the bloodstream. These peripheral blood stem cells, or PBSCs, can be used just like bone marrow stem cells to treat leukemia, other cancers and various blood disorders.

Since they can be obtained from drawn blood, PBSCs are easier to collect than bone marrow stem cells, which must be extracted from within bones. This makes PBSCs a less invasive treatment option than bone marrow stem cells. PBSCs are sparse in the bloodstream, however, so collecting enough to perform a transplant can pose a challenge.

Newborn infants no longer need their umbilical cords, so they have traditionally been discarded as a by-product of the birth process. In recent years, however, the stem-cell–rich blood found in the umbilical cord has proven useful in treating the same types of health problems as those treated using bone marrow stem cells and PBSCs.

Umbilical cord blood stem cell transplants are less prone to rejection than either bone marrow or peripheral blood stem cells. This is probably because the cells have not yet developed the features that can be recognized and attacked by the recipient's immune system. Also, because umbilical cord blood lacks well-developed immune cells, there is less chance that the transplanted cells will attack the recipient's body, a problem called graft versus host disease.

Both the versatility and availability of umbilical cord blood stem cells makes them a potent resource for transplant therapies.

For over 30 years, bone-marrow have been used to treat cancer patients with conditions such as leukaemia and lymphoma; this is the only form of stem cell therapy that is widely practiced. During chemotherapy, most growing cells are

killed by the cytotoxic agents. These agents, however, cannot discriminate between the leukaemia or neoplastic cells, and the hematopoietic stem cells within the bone marrow. It is this side effect of conventional chemotherapy strategies that the stem cell transplant attempts to reverse; a donor's healthy bone marrow reintroduces functional stem cells to replace the cells lost in the host's body during treatment. The transplanted cells also generate an immune response that helps to kill off the cancer cells; this process can go too far, however, leading to graft vs host disease, the most serious side effect of this treatment.

Another stem cell therapy called Prochymal, was conditionally approved in Canada in 2012 for the management of acute graft-vs-host disease in children who are unresponsive to steroids. It is an allogenic stem therapy based on mesenchymal stem cells (MSCs) derived from the bone marrow of adult donors. MSCs are purified from the marrow, cultured and packaged, with up to 10,000 doses derived from a single donor. The doses are stored frozen until needed.

The FDA has approved five hematopoietic stem cell products derived from umbilical cord blood, for the treatment of blood and immunological diseases.

In 2014, the European Medicines Agency recommended approval of Holoclar, a treatment involving stem cells, for use in the European Union. Holoclar is used for people with severe limbal stem cell deficiency due to burns in the eye.

Research has been conducted to learn whether stem cells may be used to treat brain degeneration, such as in Parkinson's, Amyotrophic lateral sclerosis, and Alzheimer's disease.

Healthy adult brains contain neural stem cells which divide to maintain general stem cell numbers, or become progenitor cells. In healthy adult animals, progenitor cells migrate within the brain and function primarily to maintain neuron populations for olfaction (the sense of smell). Pharmacological activation of endogenous neural stem cells has been reported to induce neuroprotection and behavioral recovery in adult rat models of neurological disorder.[12][13][14]

Brain and spinal cord injury

Stroke and traumatic brain injury lead to cell death, characterized by a loss of neurons and oligodendrocytes within the brain. A small clinical trial was underway in Scotland in 2013, in which stem cells were injected into the brains of stroke patients.

Clinical and animal studies have been conducted into the use of stem cells in cases of spinal cord injury.

Heart

The pioneering workby Bodo-Eckehard Strauer has now been discredited by the identification of hundreds of factual contradictions.[20] Among several clinical trials that have reported that adult stem cell therapy is safe and effective, powerful effects have been reported from only a few laboratories, but this has covered old and recent infarcts as well as heart failure not arising from myocardial infarction. While initial animal studies demonstrated remarkable therapeutic effects, later clinical trials achieved only modest, though statistically significant, improvements. Possible reasons for this discrepancy are patient age, timing of treatment and the recent occurrence of a myocardial infarction. It appears that these obstacles may be overcome by additional treatments which increase the effectiveness of the treatment or by optimizing the methodology although these too can be controversial. Current studies vary greatly in cell procuring techniques, cell types, cell administration timing and procedures, and studied parameters, making it very difficult to make comparisons. Comparative studies are therefore currently needed.

Stem cell therapy for treatment of myocardial infarction usually makes use of autologous bone marrow stem cells (a specific type or all), however other types of adult stem cells may be used, such as adipose-derived stem cells.[32] Adult stem cell therapy for treating heart disease was commercially available in at least five continents as of 2007.

Possible mechanisms of recovery include:

Generation of heart muscle cells

- Stimulation of growth of new blood vessels to repopulate damaged heart tissue
- Secretion of growth factors
- Assistance via some other mechanism

It may be possible to have adult bone marrow cells differentiate into heart muscle cells

The first successful integration of human embryonic stem cell derived cardiomyocytes in guinea pigs (mouse hearts beat too fast) was reported in August 2012. The contraction strength was measured four weeks after the guinea pigs underwent simulated heart attacks and cell treatment. The cells contracted synchronously with the existing cells, but it is unknown if the positive results were produced mainly from paracrine as opposed to direct electromechanical effects from the human cells. Future work will focus on how to get the cells to engraft more strongly around the scar tissue. Whether treatments from embryonic or adult bone marrow stem cells will prove more effective remains to be seen.

In 2013 the pioneering reports of powerful beneficial effects of autologous bone marrow stem cells on ventricular function were found to contain "hundreds" of discrepancies. Critics report that of 48 reports there seemed to be just 5 underlying trials, and that in many cases whether they were randomized or merely observational accepter-versus-rejecter, was contradictory between reports of the same trial. One pair of reports of identical baseline characteristics and final results, was presented in two publications as, respectively, a 578 patient randomized trial and as a 391 patient observational study. Other reports required (impossible) negative standard deviations in subsets of patients, or contained fractional patients, negative NYHA classes. Overall there were many more patients published as having receiving stem cells in trials, than the number of stem cells processed in the

hospital's laboratory during that time. A university investigation, closed in 2012 without reporting, was reopened in July 2013.

Heart

One of the most promising benefits of stem cell therapy is the potential for cardiac tissue regeneration to reverse the tissue loss underlying the development of heart failure after cardiac injury.

Initially, the observed improvements were attributed to a transdifferentiation of BM-MSCs into cardiomyocyte-like cells.[24] Given the apparent inadequacy of unmodified stem cells for heart tissue regeneration, a more promising modern technique involves treating these cells to create cardiac progenitor cells before implantation to the injured area.

Blood-cell formation

The specificity of the human immune-cell repertoire is what allows the human body to defend itself from rapidly adapting antigens. However, the immune system is vulnerable to degradation upon the pathogenesis of disease, and because of the critical role that it plays in overall defense, its degradation is often fatal to the organism as a whole. Diseases of hematopoietic cells are diagnosed and classified via a subspecialty of pathology known as hematopathology. The specificity of the immune cells is what allows recognition of foreign antigens, causing further challenges in the treatment of immune disease. Identical matches between donor and recipient must be made for successful transplantation treatments, but matches are uncommon, even between first-degree relatives. Research using both hematopoietic adult stem cells and embryonic stem cells has provided insight into the possible mechanisms and methods of treatment for many of these ailments.

Fully mature human red blood cells may be generated *ex vivo* by hematopoietic stem cells (HSCs), which are precursors of red blood cells. In this process, HSCs are grown together with stromal cells, creating an environment that mimics the conditions of bone marrow, the natural site of red-blood-cell

growth. Erythropoietin, a growth factor, is added, coaxing the stem cells to complete terminal differentiation into red blood cells.[38] Further research into this technique should have potential benefits to gene therapy, blood transfusion, and topical medicine.

Baldness

Hair follicles also contain stem cells, and some researchers predict research on these follicle stem cells may lead to successes in treating baldness through an activation of the stem cells progenitor cells. This treatment is expected to work by activating already existing stem cells on the scalp. Later treatments may be able to simply signal follicle stem cells to give off chemical signals to nearby follicle cells which have shrunk during the aging process, which in turn respond to these signals by regenerating and once again making healthy hair. Most recently, Aeron Potter of the University of California has claimed that stem cell therapy led to a significant and visible improvement in follicular hair growth . Results from his experiments are under review by the journal Science (journal).

Missing teeth

In 2004, scientists at King's College London discovered a way to cultivate a complete tooth in mice and were able to grow bioengineered teeth stand-alone in the laboratory. Researchers are confident that the tooth regeneration technology can be used to grow live teeth in human patients.

In theory, stem cells taken from the patient could be coaxed in the lab into turning into a tooth bud which, when implanted in the gums, will give rise to a new tooth, and would be expected to be grown in a time over three weeks. It will fuse with the jawbone and release chemicals that encourage nerves and blood vessels to connect with it. The process is similar to what happens when humans grow their original adult teeth. Many challenges remain, however, before stem cells could be a choice for the replacement of missing teeth in the future.

Research is ongoing in different fields, alligators which are polyphyodonts grow up to 50 times a successional tooth (a small replacement tooth) under each mature functional tooth for replacement once a year.

Deafness

Heller has reported success in re-growing cochlea hair cells with the use of embryonic stem cells.

Blindness and vision impairment

Since 2003, researchers have successfully transplanted corneal stem cells into damaged eyes to restore vision. "Sheets of retinal cells used by the team are harvested from aborted fetuses, which some people find objectionable." When these sheets are transplanted over the damaged cornea, the stem cells stimulate renewed repair, eventually restore vision.[45] The latest such development was in June 2005, when researchers at the Queen Victoria Hospital of Sussex, England were able to restore the sight of forty patients using the same technique. The group, led by Sheraz Daya, was able to successfully use adult stem cells obtained from the patient, a relative, or even a cadaver. Further rounds of trials are ongoing.

In April 2005, doctors in the UK transplanted corneal stem cells from an organ donor to the cornea of Deborah Catlyn, a woman who was blinded in one eye when acid was thrown in her eye at a nightclub. The cornea, which is the transparent window of the eye, is a particularly suitable site for transplants. In fact, the first successful human transplant was acornea transplant. The absence of blood vessels within the cornea makes this area a relatively easy target for transplantation. The majority of corneal transplants carried out today are due to a degenerative disease called keratoconus.

The University Hospital of New Jersey reports that the success rate for growth of new cells from transplanted stem cells varies from 25 percent to 70 percent.

In 2014, researchers demonstrated that stem cells collected as biopsies from donor human corneas can prevent scar formation without provoking a rejection response in mice with corneal damage.

In January 2012, The Lancet published a paper by Steven Schwartz, at UCLA's Jules Stein Eye Institute, reporting two women who had gone legally blind from macular degeneration had dramatic improvements in their vision after retinal injections of human embryonic stem cells.

Diabetes

Diabetes patients lose the function of insulin-producing beta cells within the pancreas. In recent experiments, scientists have been able to coax embryonic stem cell to turn into beta cells in the lab. In theory if the beta cell is transplanted successfully, they will be able to replace malfunctioning ones in a diabetic patient.

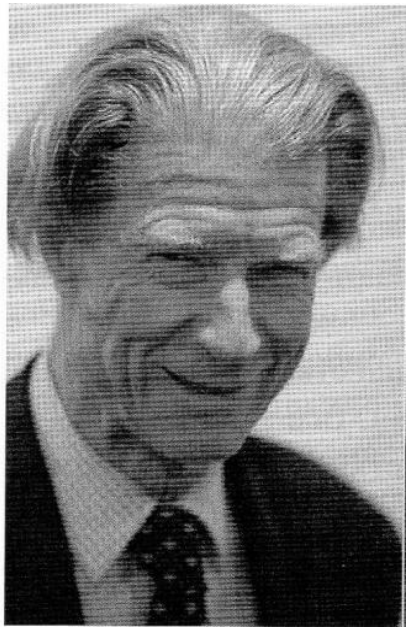
Transplantation

Human embryonic stem cells may be grown in cell culture and stimulated to form insulin-producing cells that can be transplanted into the patient.

However, clinical success is highly dependent on the development of the following procedures:

- Transplanted cells should proliferate
- Transplanted cells should differentiate in a site-specific manner
- Transplanted cells should survive in the recipient (prevention of transplant rejection)
- Transplanted cells should integrate within the targeted tissue
- Transplanted cells should integrate into the host circuitry and restore function

Induced pluripotent stem cells (also known as **iPS** cells or **iPSCs**) are a type of pluripotent stem cell that can be generated directly from adult cells. The iPSC technology was pioneered by Shinya Yamanaka's lab in Kyoto, Japan, who showed in 2006 that the introduction of four specific genes encoding transcription factors could convert adult cells into pluripotent stem cells. He was awarded the 2012 Nobel Prize along with Sir John Gurdon "for the discovery that mature cells can be reprogrammed to become pluripotent."



Pluripotent stem cells hold great promise in the field of regenerative medicine. Because they can propagate indefinitely, as well as give rise to every other cell type in the body (such as neurons, heart, pancreatic, and liver cells), they represent a single source of cells that could be used to replace those lost to damage or disease.

The most well-known type of pluripotent stem cell is the embryonic stem cell. However, since the generation of embryonic stem cells involves destruction (or at least manipulation) of the pre-implantation stage embryo, there has been much controversy surrounding their use. Further, because embryonic stem cells can only be derived from embryos, it has so far not been feasible to create patient-matched embryonic stem cell lines.

Since iPSCs can be derived directly from adult tissues, they not only bypass the need for embryos, but can be made in a patient-matched manner, which means that each individual could have their own pluripotent stem cell line. These unlimited supplies of autologous cells could be used to generate transplants without the risk of immune rejection. While the iPSC technology has not yet advanced to a stage where therapeutic transplants

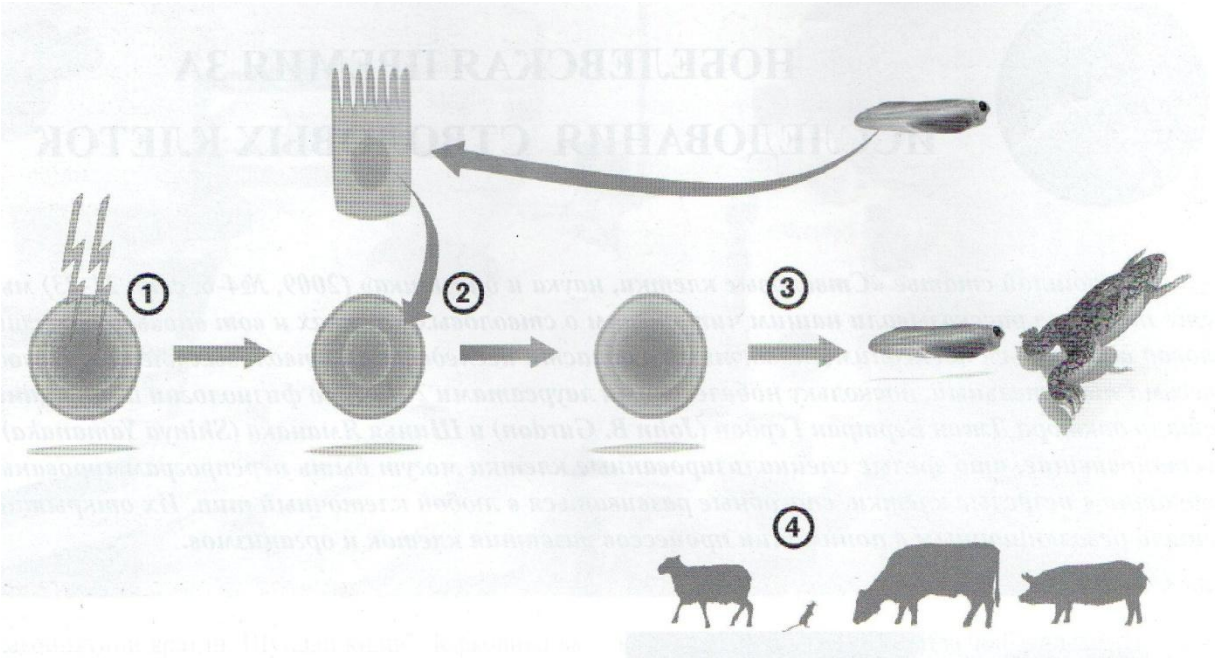
have been deemed safe, iPSCs are readily being used in personalized drug discovery efforts and understanding the patient-specific basis of disease.

Depending on the methods used, reprogramming of adult cells to obtain iPSCs may pose significant risks that could limit their use in humans. For example, if viruses are used to genomically alter the cells, the expression of cancer-causing genes "oncogenes" may potentially be triggered. In February 2008, scientists announced the discovery of a technique that could remove oncogenes after the induction of pluripotency, thereby increasing the potential use of iPS cells in human diseases. In April 2009, it was demonstrated that generation of iPS cells is possible without any genetic alteration of the adult cell: a repeated treatment of the cells with certain proteins channeled into the cells via poly-arginine anchors was sufficient to induce pluripotency. The acronym given for those iPSCs is piPSCs (protein-induced pluripotent stem cells). [24]

The 2012 Nobel Prize in Physiology or Medicine was awarded jointly to Sir John B. Gurdon and Shinya Yamanaka "for the discovery that mature cells can be reprogrammed to become pluripotent."

Historical Background leading up to Yamanaka's research

The prevalent view during the early 20th century was that mature cells were permanently locked into the differentiated state and cannot return to a fully immature, pluripotent stem cell state. They thought that cellular differentiation can only be a unidirectional process. Therefore, non-differentiated egg/early embryo cells can only develop into specialized cells. However, stem cells with limited potency (adult stem cells) remain in bone marrow, intestine, skin etc. to act as a source of cell replacement.



The fact that differentiated cell types had specific patterns of proteins suggested irreversible epigenetic modifications or genetic alterations to be the cause of unidirectional cell differentiation. So, cells progressively become more restricted in the differentiation potential and eventually lose pluripotency.

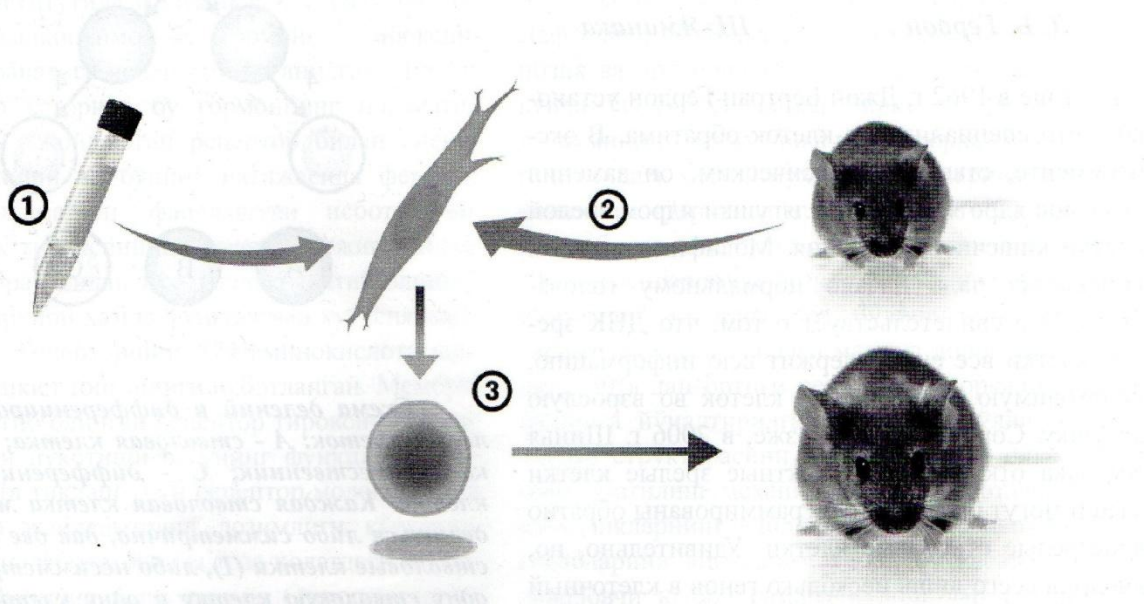
In 1962, John B. Gurdon demonstrated that the nucleus from a differentiated frog intestinal epithelial cell can generate a fully functional tadpole via transplantation to an enucleated egg. Gurdon used somatic cell nuclear transfer (SCNT) as a method to understand reprogramming and how cells change in specialization. He concluded that differentiated somatic cell nuclei had the potential to revert to pluripotency.[11] This was a paradigm shift during the time. It showed that a differentiated cell nucleus has retained the capacity to successfully revert to an undifferentiated state, with the potential to restart development (pluripotent capacity).

However, the question still remained whether an intact differentiated cell could be fully reprogrammed to become pluripotent.

Yamanaka's research

Shinya Yamanaka proved that introduction of a small set of transcription factors into a differentiated cell was sufficient to revert the cell to a pluripotent state.

Yamanaka focused on factors that are important for maintaining pluripotency in embryonic stem (ES) cells. Knowing that transcription factors were involved in the maintenance of the pluripotent state, he selected a set of 24 ES cell transcriptional factors as candidates to reinstate pluripotency in somatic cells.



First, he collected the 24 candidate factors. When all 24 genes encoding these transcription factors were introduced into skin fibroblasts, few actually generated colonies that were remarkably similar to ES cells. Secondly, further experiments were conducted with smaller numbers of transcription factors added to identify the key factors, through a very simple and yet sensitive assay system. Lastly, he identified the four key factors. They found that 4 transcriptional factors (Myc, Oct3/4, Sox2 and Klf4) were sufficient to convert mouse embryonic or adult fibroblasts to pluripotent stem cells (capable of producing teratomas in vivo and contributing to chimeric mice).

These pluripotent cells are called iPS (induced pluripotent stem) cells; they appeared with very low frequency. iPS cells can be selected by inserting the b-geo gene into the Fbx15 locus. The Fbx15 promoter is active in pluripotent stem cells which induce b-geo expression, which in turn gives rise to G418 resistance; this resistance helps us identify the iPS cells in a culture.

Moreover, in 2007, Yamanaka and his colleagues found iPS cells with germ line transmission (via selecting for Oct4 or Nanog gene). Also in 2007, they were the first to produce human iPS cells.

However, there are some difficulties to overcome. The first is the issue of the very low production rate of iPS cells, and the other is the fact that the 4 transcriptional factors are shown to be oncogenic.

Nonetheless, this is a truly fundamental discovery. This was the first time an intact differentiated somatic cell could be reprogrammed to become pluripotent. This opened up a completely new research field.

In July 2014, a scandal regarding the research of Haruko Obokata was connected to Yamanaka. He could not find the lab notes from the period in question [25] and was made to apologise.

Further research and future prospects

Since the original discovery by Yamanaka, much further research has been done in this field, and many improvements have been made to the technology. Here we discuss the improvements made to Yamanaka's research as well as the future prospects of his findings.

1. The delivery mechanism of pluripotency factors has been improved. At first retroviral vectors, that integrate randomly in the genome and cause deregulation of genes that contribute to tumor formation, were used. However, now, non-integrating viruses, stabilised RNAs or proteins, or episomal plasmids (integration-free delivery mechanism) are used.

2. Transcription factors required for inducing pluripotency in different cell types have been identified (e.g. neural stem cells).

3. Small substitutive molecules were identified, that can substitute for the function of the transcription factors.

4. Transdifferentiation experiments were carried out. They tried to change the cell fate without proceeding through a pluripotent state. They were able to

systematically identify genes that carry out transdifferentiation using combinations of transcription factors that induce cell fate switches. They found trandifferentiation within germ layer and between germ layers. E.g.) exocrine cells to endocrine cells, fibroblast cells to myoblast cells, fibroblast cells to cardiomyocyte cells, fibroblast cells to neurons

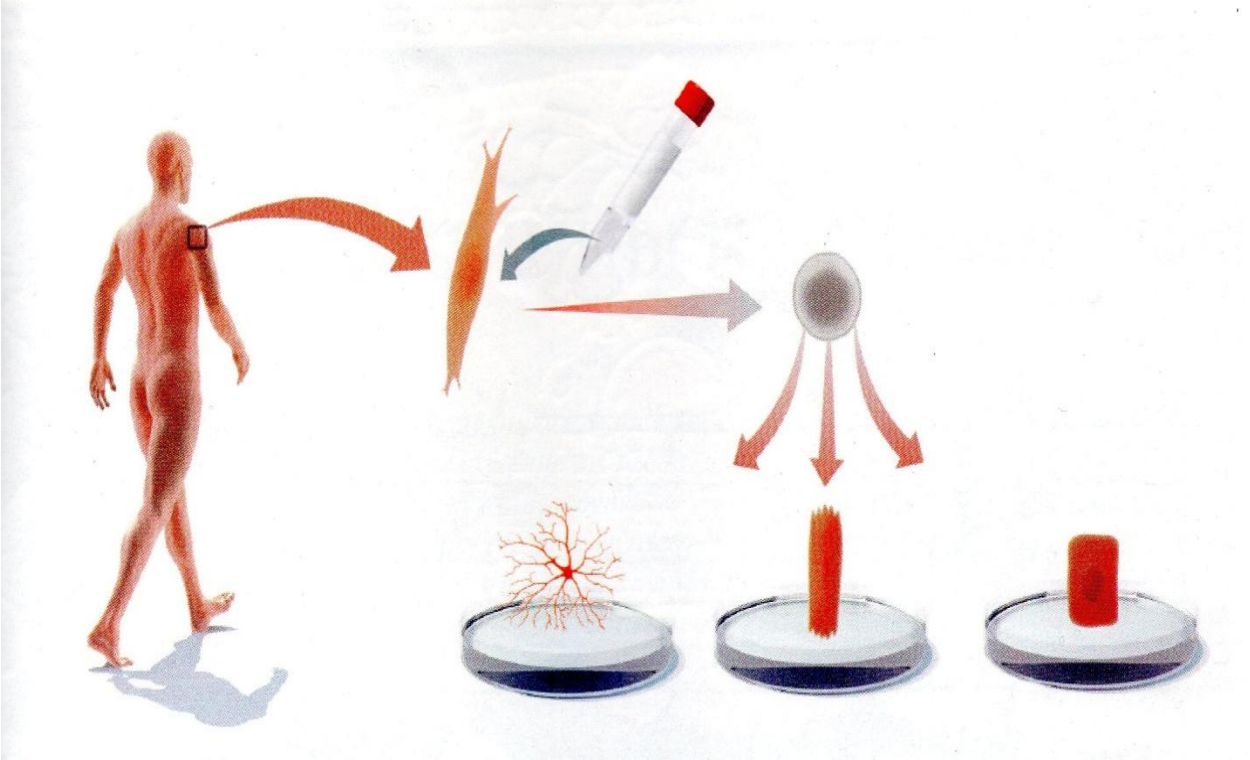
5. Cell replacement therapy with iPS cells is a possibility. Stem cells can replace diseased or lost cells in degenerative disorders and they are less prone to immune rejection. However, there is a danger that it may introduce mutations or other genomic abnormalities that render it unsuitable for cell therapy. So, there are still many challenges, but it is a very exciting and promising research area. Further work is required to guarantee safety for patients.

6. Can medically use iPS cells from patients with genetic and other disorders to gain insights into the disease process. - Amyotrophic lateral sclerosis (ALS), Rett syndrome, spinal muscular atrophy (SMA), α1-antitrypsin deficiency, familial hypercholesterolemia and glycogen storage disease type 1A. - For cardiovascular disease, Timothy syndrome, LEOPARD syndrome, type 1 and 2 long QT syndrome - Alzheimer's, Spinocerebellar ataxia, Huntington's etc.

7. iPS cells provide screening platforms for development and validation of therapeutic compounds. For example, kinetin was a novel compound found in iPS cells from familial dysautonomia and beta blockers & ion channel blockers for long QT syndrome were identified with iPS cells.

Yamanaka's research has "opened a new door and the world's scientists have set forth on a long journey of exploration, hoping to find our cells' true potential.

In January 2014, two articles were published claiming that a type of pluripotent stem cell can be generated by subjecting the cells to certain types of stress (bacterial toxin, a low pH of 5.7, or physical squeezing); the resulting cells were called STAP cells, for stimulus-triggered acquisition of pluripotency.



In light of difficulties that other labs had replicating the results of the surprising study, in March 2014, one of the co-authors has called for the articles to be retracted. On 4 June 2014, the lead author, Obokata agreed to retract both the papers after she was found to have committed ‘research misconduct’ as concluded in an investigation by RIKEN on 1 April 2014.

To follow stem cells to organism regeneration (experiment)

Plan to experiment:

1. To take red blood marrow from the object experiment (rabbit).
2. To make a wound two legs of rabbit for experiment.
3. To put bone marrow one of the leg.
4. To compare quality of wounds which is setting stem cells and which is not setting stem cells.
5. To write results.

Information about experiment`s object.

Phylum: Chordata

Last phylum: Vertebrata

Main class: Tetrapoda

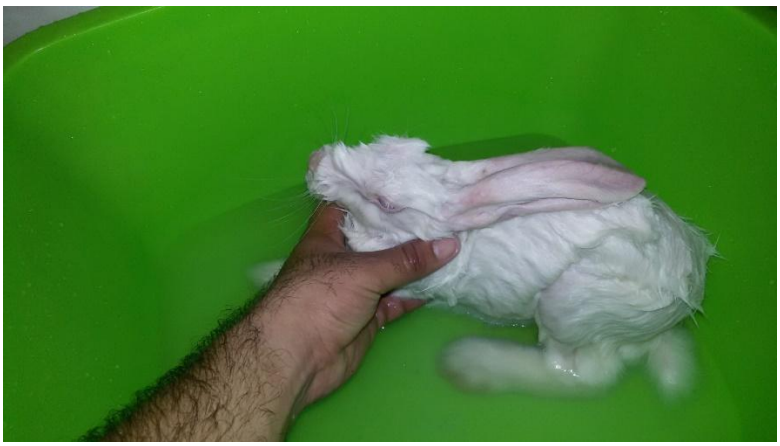
Class: Mammalia

Order: Logomorpha

Species: White rabbit

The statement of experiment.

A rabbit is washed and get improved the hygiene.



The first of all a rabbit was slept by chloroform and cut thorax with scalpel and opened it.

A skin was opened by scalpel for a minute. And the chest of a rabbit was seen. They poured Sol. Ditsinon 0,1% solution for stopping blood letting from the wound.

They took 1 ml clean sterile water with 10 ml syringe. I gave chest an injection.

At the first 1 ml clean sterile water was sent for bone. Then syringe was sent for sucking. For result of sucking I could get red blood marrow which was mixed with water. Then I put stem cells to the sterile dish for saving. Then I made artificial wound on the palms of two legs for general regeneration of stem cells.

Blood was stopped by Sol. Ditsinon 0.1%. The artificial wound was made on the two legs. I put stem cells to the left leg and right leg was clean. Before putting stem cells to left leg I poured ferment ligaza 0.5 ml. The aim of that experiment stem cells were combined with new condition.

After that thorax was stitched for getting bone marrow. I fastened to wound with bunch.

Rabbit was stirred up and gave muscle an injection anaesthetic Sol. Ketanol 1 ml. The condition of rabbit got improved and fed it.

In 2015 on April 18 artificial wound was appeared I looked over two wounds and measured them which was setting stem cells and another for results. Both of the wounds dimension were 10 mm.

	Date of the review	Dimension of the wound which is setting stem cell	Dimension of the wound which is not setting stem cell
Day of the appearance wound	18.04.2015 10:30	10mm	10mm
	20.04.2015 17:50	8mm	8.5mm
	22.04.2015 17:50	6mm	7mm
	23.04.2015 17:50	5mm	6mm
	24.04.2015 17:50	3mm	4.5mm
	25.04.2015 17:50	1.5mm	3.5mm
	26.04.2015 17:50	0mm	2mm
	27.04.2015 17:50	-	0.5mm
	28.04.2015 8:00	-	0mm

Date: 20th April. The condition of rabbit was good. Nourishment and movement were good.

The dimension of wounds: The wound was setting stem cells was about 8 mm. The wound which wasn't setting stem cells was about 8.5 mm.

Date: 22nd April. The condition of rabbit was good. Nourishment and movement were good.

The dimension of wounds: The wound was setting stem cells was about 6 mm. The wound which wasn't setting stem cells was about 7 mm.

Date: 23rd April. The condition of rabbit was good. Nourishment and movement were good.

The dimension of wounds: The wound was setting stem cells was about 5 mm. The wound which wasn't setting stem cells was about 6 mm.

Date: 24th April. The condition of rabbit was good. Nourishment and movement were good.

The dimension of wounds: The wound was setting stem cells was about 3 mm. The wound which wasn't setting stem cells was about 4.5 mm.

Date: 25th April. The condition of rabbit was good. Nourishment and movement were good.

The dimension of wounds: The wound was setting stem cells was about 1.5 mm. The wound which wasn't setting stem cells was about 3.5 mm.

Date: 26th April. The condition of rabbit was good. Nourishment and movement were good.

The dimension of wounds: The wound was setting stem cells was about 0 mm. The wound which wasn't setting stem cells was about 2 mm.

Date: 27th April. The condition of rabbit was good. Nourishment and movement were good.

The dimension of wounds: The wound was setting stem cells was recovered. The wound which wasn't setting stem cells was about 0.5 mm.

Date: 28th April. It was 8 o'clock: The condition of rabbit was good. Nourishment and movement were good.

The dimension of wounds: The wound was setting stem cells was recovered.

The wound which wasn't setting stem cells was about 0 mm.

Shayxontohur district School № 59 class 9A

The lesson plan of the technology cooperation teaching (method is working with small groups).

Subject: Biology

Lesson theme: The stem cells.

Class: 9A

Teacher: Mullayev Dilshod.

Type of lesson: To teach with new technologies and separate to a small groups. Discussion and debate.

To use tests: oral, writing.

The kind of lesson: conversation.

The method of teaching: to use active methods

Time: 80 minute

Study room № 45

The aim of the lesson: to introduce with biological news to pupils.

The educational aim of the lesson:

- to remember the past lesson to develop pupil's knowledge of the new theme.
- to introduce biotechnological news with using active method.

The developing aim:

- to appear knowledge of the pupils about biotechnology and to introduce news about it.
- to revise the outlook of pupils,

The aim of the lesson biology:

- to create new methods for all steps of the lesson.
- to use new technology, active sketch, diagrams table, slides.
- to use differencial methods according to pupil's knowledge.

The methods of the lesson:

- Intellectual attack
- Discussion and debate
- To separate small groups and hold a competition
- Working with tests
- Tasks, working with diagrams

The equipments:

Computer, videoprojector and so on.

Chronological map of the lesson:

1. Organizational part, to make psychological atmosphere 5 minute.
2. To repeat the past lesson 5 minute.
3. To study stem cells 20 minute.
4. To discuss about stem cells 30 minute.
5. To conclude and marking 15 minute.
6. To end the lesson and give homework 5 minute.

The recommendation of the theory lesson:

Organizational part.

Teacher will enter classroom and greet with pupils and control the cleaning of the room, preparing of the pupils.

To base activity study:

Teacher will introduce with new theme and aim and pupils will write it.

To define knowledge about stem cells.

To check support knowledge "Rotatsiya" method. Pupils will separated into 4 groups. All of the groups will make question to the question part the second team will change it. They will write answer and also change the answer again. The group which was given answer should know very well. Because this group will check it and put review. Teacher will control answers. Teacher will mark teams and make a mark on notebook.

To well-developed of the knowledge:

Carrying out debate about the new theme with pupils.

In this case pupils should take a questions and answer with using technic aids, tables and blackboard. Another pupil should complete answer. The question which is answer will put into sun card. In this way debate will continue. Then pupil will give information and developed.

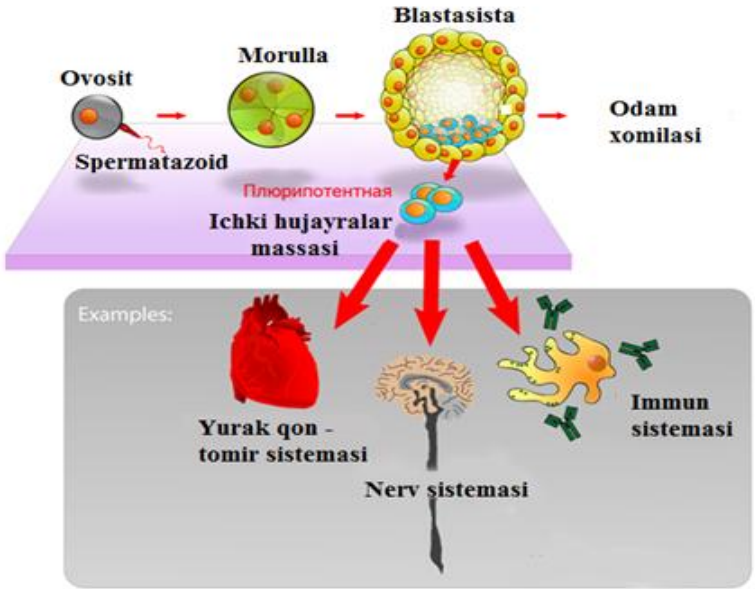
To end of the lesson teacher will well-developed knowledge of pupils.

To generalize lesson, marking and commentary. During the lesson teacher will mark pupils, knowledge and comment it. Teacher will put mark on the pupils sheet.

Homework.

Teacher will give same tasks which are belonged to theme.

Stem cells are mother cells that have the potential to become any type of cell in the body. One of the main characteristics of stem cells is their ability to self-renew or multiply while maintaining the potential to develop into other types of cells. Stem cells can become cells of the blood, heart, bones, skin, muscles, brain etc. There are different sources of stem cells but all types of stem cells have the same capacity to develop into multiple types of cells.



Stem cells (center ones) can develop into any cell type. They are valuable as research tools and might, in the future, be used to treat a wide range of diseases.

These possess the capacity to divide for long periods and retain their ability to make all cell types within the organism. The best known type of pluripotent stem cell is the one present in embryos that helps babies grow within the womb. These are termedembryonic stem cells. These cells form at the blastocyst stage of development. A blastocyst is a hollow ball of cells that is smaller than a pinhead. The embryonic stem cells lie within this ball of cells. Recent research has enabled scientists to derive pluripotent cells from adult human skin cells. These are termed induced pluripotent stem cells or iPS cells. Normally muscles cells, nerve cells, blood cells and other specialized cells do not normally replicate themselves but stem cells have the capability to do so. This replication is calledproliferation. Proliferation over months can give rise to millions of cells. If the resulting cells are unspecialized, self renewal continues for long periods of time.

The well-developed and marking of the new theme:

Results of the first test:

The first group excellent mark “5”

The second group was “4”

The third group was marked with “5”

The third terms of second task:

The first group was 14 b.

The second group was 15 b.

The third group was marked with 14 b.

The results of the third test

The first group was “5”

The second group was “5”

The third group was marked with “5”

The fourth task is answer the questions

The first group was “3”b

The second group was “2” b.

The third group was marked with “3”.

General results:

The first group was 27 b.

The second group was 26 b.

The third group was collected 27 b.

Conclusion.

A cell is a very basic structural and functional unit of life. While bacteria are unicellular because they consist of only one cell, humans are considered multicellular in that they have literally trillions of cells. Your cells are responsible for everything that you do, whether that is taking in nutrients, providing energy for you to go about your day, or reproducing. Cells in your body have many different functions and they 'stem' from simpler cells that are not yet specialised. These simpler cells are known as stem cells. What this means is that a stem cell is basically a cell that does not yet have a specific job in the body. The word 'simple' is even a bit deceiving because it implies that these cells are not important, which is far from the case.

Stem cells have an enormous potential to benefit different areas of disease research and management. By learning more about stem cells, scientists and the public can understand how these multi-purpose cells can develop into the specific and specialised cells that make humans what they are today. By studying stem cells, we can learn about the actual process that occurs from a single stem cell to a huge array of specialised cells that let us live and function each day.

Glossary.

Antiokislitelniy – kasallikga qarshi kurashish

Blostasista - homila 1qavatlik davri

Deferensatsiya – ixtisoslashish

Epimorfichakiy– yo'qotilgan o'rganni tiklash

Fenom – tashqi tuzilishi

Fetal – abort qoldig'i.

Gemopoetik hujayralar –qon hosil qiluvchi o'zak hujayralar

Glioblastli - tog'ay hosil qiluvchi

Mezenximal - mezinximadan olinuvchi

Neyroblastli - nerv to'qimasini hosil qiluvchi

O'zak hujayralar –harqanday hujyraga aylana oladigan hujayralar

Plyurapatent – embreonal o'zak hujayralar.

Potipatentli - yetuk organizmdagi saqlanib qolgan o'zak hujayralar.

Pupovin - qondagi o'zak hujayralar

Qizil qon iligi - g'ovak suyagini qon shaklli elementlarini hosil qiluvchi iligi

Regeniratsiya –o'zini tiklash

Retsikulyar – nisbatan doimiy ssaqlanuvchi

Reysipent – qoyiladigan , qabul qiluvuvchi

Steril – mikraorganizimlardan xoli

Stroma - ichki g'ovak qism

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Annatatsiya

Ushbu diplom ishida o’zak hujayralarni hosil bo’lishi, kelib chiqishi va turlari haqida ma’lumotlar keltirilgan. Hozirgi zamon biologiyasi o’zak hujayralar ustida olib borilgan izlanishlar, yutuqlari va ko’zlangan maqsadlar bayon etilgan. O’zak hujayralar turlari, kelib chiqish xillari shular jumlasidan. Tajriba bobida o’zakzhujayralar organizm regeneratsiyasiga yo’naltrishga oid eksperement qilingan, natijalari bayon etilgan. Xo’rdalilar tipi, To’rt oyoqlilar kata sinfi, Sutemizuvchilar sinfi, Tovushqonlar turkumiga mansub oq quyonni qizil qon iligi olinib old oyoq qismini sunniy jarohat hosil qilinganligi. Jarohatga yo’naltrildi. Jarohat bitish tezligi va sifati kuzatishlar va natijalari bayon etilgan.

Аннотация

В данной дипломной работе приведены сведения об образовании, происхождении и видах стволовых клеток. Изложены поисковые работы достижения и намеченные цели проводимые по стволовым клеткам. Виды стволовых клеток и виды происхождения также относится к этому. В главе опыта изложены результаты эксперимента направленный на регенерацию организма стволовыми клетками. Была извлечена красный костный мозг из передней лапы у белого кролика, относящегося к отряду Зайцеобразных, классу Млекопитающих, надклассу Четвероногих, Типу Хордовых, направленная на нанесение искусственной травмы. В качестве результатов изложена скорость заживления раны и качественные наблюдения.

Abstract

This research paper presents data on education, origin and types of stem cells. It sets out search operations and to achieve the intended goals of the stem cell. Types of stem cell origin and types also belong to this. This chapter presents the results of the experiment of experience aimed at the regeneration of the body's stem cells. Was removed from the red bone marrow in the front paws white rabbit belonging to the order of lagomorphs, the class of mammals, superclass quadrupeds Tipu chordates aimed at applying artificial injury. As the results stated rate of wound healing and qualitative observations.

Dictionary

1. Elektromagnit maydon – electromagnet board
2. Tirik organizmlar – a live organs
3. Nurlanish – radiation
4. Nerv sistemasi – nerv system
5. Bosh miya – main brain
6. Odam – person
7. Organlar – organs
8. Elektr asboblar – electrical tools
9. Salbiy – negative
10. Ijobiy – positive
11. Past chastotali – low
12. Tajriba - experiment
13. Pedagogik texnologiya – pedagogic technology
14. Tibbiyot – medical
15. Sog`lomlashtirish – invigorate
16. Ruhiy – intellectual
17. Hayot – life
18. Kasallik – disease
19. Barkamol avlod – perfect generation
20. Asrash – preserving
21. Falokat – disaster
22. Himoya – defence
23. Maydon – areal
24. Biologiya – biology
25. Tarbiya – ypbringing
26. Ta`lim – education
27. Sog`lom – health
28. Qon – blood
29. Oqsil – protein

30. Muhit – environment
31. Shahar – town
32. Ta`sir ko'rsatish – influence
33. Yurak – heart
34. Harorat – temperature
35. Hayvon – animals
36. Turmush – lifestyle
37. Ko'z – sight
38. Teri – leather
39. Vazifa – duty
40. Malaka – skill
41. Kasal – sick
42. Ko'rinish – appearance
43. O'lim – death
44. Zaif – weak
45. Asab – nerve
46. Asabiylik – nervousness
47. Tashqi – externol
48. Zamon – time
49. Dars – lesson
50. Mavzu – scubjest
51. Metodika – methodology
52. Adabiyotlar tahlili – the list of the litera
53. Axvol – situation
54. Asr – century
55. Atom – atom
56. Atrof-muhit – the ennironment
57. Bosh miya – brain
58. Bob – the chopter
59. Chidamli – tough

60. Faol – active
61. Jala – downpour
62. Turar joy – home
63. Noyob nemat – rare blessing
64. Ma`naviy boylik – spiritual material
65. Transport – transport
66. Ilmiy tadqiqot – research invertigution
67. Kirish – inroduction
68. Maqsad – infent
69. Og`iz – mouth
70. Tajriba – experiment
71. Tuxum – breed
72. Vatan – homeland
73. Yil – year
74. Metallar – metals
75. Ion – ion
76. Zarracha – tiny particle
77. Rivojlanish – progress
78. Labaratoriya – labaratory
79. O'quvchilar – puppils
80. Ma`ruza – lecture
81. Suxbat – conversation
82. Ma`lumot – information
83. Savol-javob – answer-question
84. Uy vazifasi – homework
85. Tabiat – nature
86. Omil – agent
87. Global muammo – global problem
88. Er kurrasi – earths sphere
89. Avlod-ajdod – generation

90. Biotop – biotophe
91. Etishmaslik – deficienty
92. Barqaror rivojlanish – the stable aleve lopment
93. Reja – plan
94. Malaka – skill
95. Zamon – time
96. Dars – lesson
97. Mavzu – scubjest
98. Metodika – metodology
99. Taqriz – review
100. Belgilar – sign