M.Sc.2

Biotechnology

THE STEM STORY

STEM CELLS IN RESEARCH

Chief Editor: Dr. Dhanashri Godbole

Shreya Aasore	21163
Shweta Pawar	21164
Siddhi Mahudkar	21165
Srijani Deb	21166

SD

Content

STEM CELLS: PAST, PRESENT, AND FUTURE

BACKGROUND:

Stem cell, an undifferentiated cell that can divide to produce some offspring cells that continue as stem cells and some cells that are destined to differentiate (become specialized). Stem cells are an ongoing source of the differentiated cells that make up the tissues and organs of animals and plants. There is great interest in stem cells because they have potential in the development of therapies for replacing defective or damaged cells resulting from a variety of disorders and injuries, such as Parkinson disease, heart disease, and diabetes.

REFERENCES:

https://stemcellres.biomedcentral.com/articles/10.1186/s13287-019-1165-5

https://www.britannica.com/science/stem-cell/Neural-stem-cells

Date:November 2022

STEM CELL CLASSIFICATION

As the cells undergo differentiation, their developmental potency decresases. According to their level of tifferentiations, they cells can be classified.

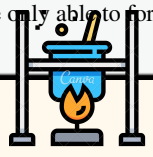
Totipotent stem cells are able to divide and differentiate into cells of the whole organism. Totipotency has the highest differentiation potential and allows cells to form both embryo and extra-embryonic structures. One example of a totipotent cell is a zygote, which is formed after a sperm fertilizes an egg. These cells can later develop either into any of the three germ layers or form a placenta. After approximately 4 days, the blastocyst's inner cell mass becomes pluripotent. This structure is the source of pluripotent cells.

Pluripotent stem cells (PSCs) form cells of all germ layers but not extraembryonic structures, such as the placenta. Embryonic stem cells (ESCs) are an example. ESCs are derived from the inner cell mass of preimplantation embryos. Another example is induced pluripotent stem cells (iPSCs) derived from the epiblast layer of implanted embryos. Their pluripotency is a continuum, starting from completely pluripotent cells such as ESCs and iPSCs and ending on representatives with less potency—multi-, oligo- or unipotent cells. One of the methods to assess their activity and spectrum is the teratoma formation assay. iPSCs are artificially generated from somatic cells, and they function similarly to PSCs. Their culturing and utilization are very promising for present and future regenerative medicine.

Multipotent stem cells have a narrower spectrum of differentiation than PSCs, but they can specialize in discrete cells of specific cell lineages. One example is a haematopoietic stem cell, which can develop into several types of blood cells. After differentiation, a haematopoietic stem cell becomes an oligopotent cell. Its differentiation abilities are then restricted to cells of its lineage. However, some multipotent cells are capable of conversion into unrelated cell types, which suggests naming them pluripotent cells.

Oligopotent stem cells can differentiate into several cell types. A myeloid stem cell is an example that can divide into white blood cells but not red blood cells.

Unipotent stem cells are characterized by the narrowest differentiation capabilities and a special property of dividing repeatedly. Their latter feature makes them a promising candidate for therapeutic use in regenerative medicine. These cells are only able to form one cell type, e.g. dermatocytes



STEM CELL BIOLOGY :

A blastocyst is formed after the fusion of sperm and ovum fertilization. Its inner wall is lined with short-lived stem cells, namely, embryonic stem cells. Blastocysts are composed of two distinct cell types: the inner cell mass (ICM), which develops into epiblasts and induces the development of a foetus, and the trophectoderm (TE). Blastocysts are responsible for the regulation of the ICM microenvironment. The TE continues to develop and forms the extraembryonic support structures needed for the successful origin of the embryo, such as the placenta. As the TE begins to form a specialized support structure, the ICM cells remain undifferentiated, fully pluripotent and proliferative. The pluripotency of stem cells allows them to form any cell of the organism. Human embryonic stem cells (hESCs) are derived from the ICM. During the process of embryogenesis, cells form aggregations called germ layers: endoderm, mesoderm and ectoderm , each eventually giving rise to differentiated cells and tissues of the foetus and, later on, the adult organism. After hESCs differentiate into one of the germ layers, they become multipotent stem cells, whose potency is limited to only the cells of the germ layer. This process is short in human development. After that, pluripotent stem cells occur all over the organism as undifferentiated cells, and their key abilities are proliferation by the formation of the next generation of stem cells and differentiation into specialized cells under certain physiological conditions.

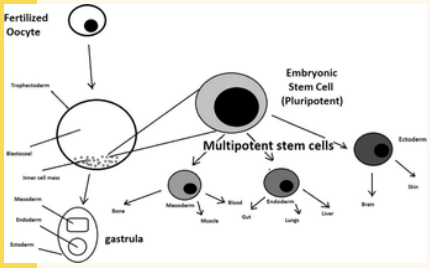


Fig : oocyte development and formation of stem cells: the blastocoel, which is formed from oocytes, consists of embryonic stem cells that later differentiate into mesodermal, ectodermal, or endodermal cells. Blastocoel develops into the gastrula

SRIJANI DEB – 21166

TYPES OF STEM CELLS IN RESEARCH :

Embryonic stem cells

Embryonic stem cells (often referred to as ES cells) are stem cells that are derived from the inner cell mass of a mammalian embryo at a very early stage of development, when it is composed of a hollow sphere of dividing cells (a blastocyst). Embryonic stem cells from human embryos and from embryos of certain other mammalian species can be grown in tissue culture.

Mouse embryonic stem cells

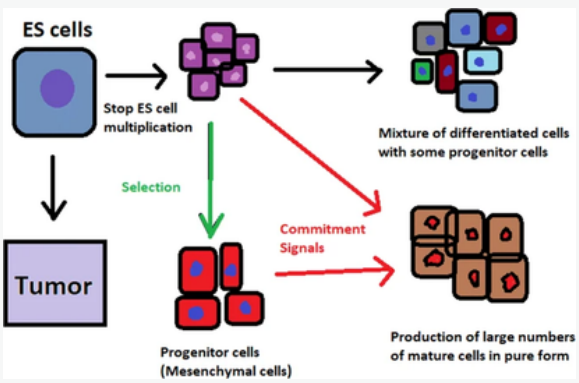
The most-studied embryonic stem cells are mouse embryonic stem cells, which were first reported in 1981. This type of stem cell can be cultured indefinitely in the presence of leukemia inhibitory factor (LIF), a glycoprotein cytokine. If cultured mouse embryonic stem cells are injected into an early mouse embryo at the blastocyst stage, they will become integrated into the embryo and produce cells that differentiate into most or all of the tissue types that subsequently develop.

Human embryonic stem cells

Extensive experience with mouse embryonic stem cells made it possible for scientists to grow human embryonic stem cells from early human embryos, and the first human stem cell line was created in 1998.The human embryonic stem cells form a wide variety of differentiated tissues in vitro, and they form teratomas when grafted into immunosuppressed mice. they are indeed pluripotent cells, and they therefore are regarded as a possible source of differentiated cells for cell therapy.

Embryonic germ cells

Embryonic germ (EG) cells, derived from primordial germ cells found in the gonadal ridge of a late embryo, have many of the properties of embryonic stem cells. The primordial germ cells in an embryo develop into stem cells that in an adult generate the reproductive gametes (sperm or eggs).



Adult stem cells

Some tissues in the adult body, such as the epidermis of the skin, the lining of the small intestine, and bone marrow, undergo continuous cellular turnover. They contain stem cells, which persist indefinitely, and a much larger number of "transit amplifying cells," which arise from the stem cells and divide a finite number of times until they become differentiated. The stem cells exist in niches formed by other cells, which secrete substances that keep the stem cells alive and active. In such tissues there is probably no special stem-cell population, and any cell can participate in tissue regeneration when required.

Epithelial stem cells

The epidermis of the skin contains layers of cells called keratinocytes. Only the basal layer, next to the dermis, contains cells that divide. A number of these cells are stem cells, but the majority are transit amplifying cells. The keratinocytes slowly move outward through the epidermis as they mature, and they eventually die and are sloughed off at the surface of the skin. The epithelium of the small intestine forms projections called villi, which are interspersed with small pits called crypts. The dividing cells are located in the crypts, with the stem cells lying near the base of each crypt. Cells are continuously produced in the crypts, migrate onto the villi, and are eventually shed into the lumen of the intestine. As they migrate, they differentiate into the cell types characteristic of the intestinal epithelium.

Bone marrow and hematopoietic stem cells

Bone marrow contains cells called hematopoietic stem cells, which generate all the cell types of the blood and the immune system.

Bone marrow is a source for mesenchymal stem cells (sometimes called marrow stromal cells, or MSCs), which are precursors to non-hematopoietic stem cells that have the potential to differentiate into several different types of cells, including cells that form bone, muscle, and connective tissue.

Induced pluripotent stem cells

IPSCs can be stimulated to differentiate into select types of cells that could in principle be used for disease-specific treatments. Patient-specific induced pluripotent stem cells and dedifferentiated cells are highly valuable in terms of their therapeutic applications because they are unlikely to be rejected by the immune system.

WHAT ARE STEM CELLS USED FOR? WHY ARE THEY IMPORTANT IN SCIENCE AND MEDICINE?

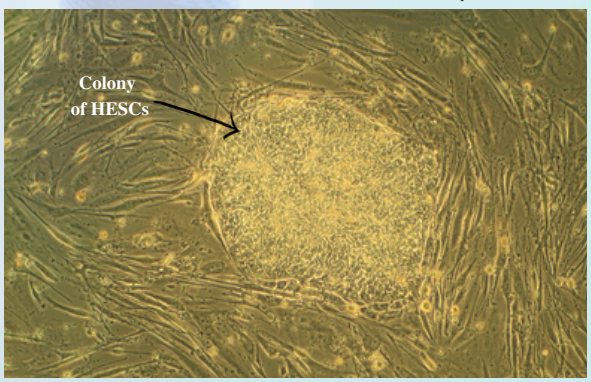
Stem cells are hot topics in scientific research today. The importance of stem cells lies in their amazing potential to become virtually any type of cell in our body. So, if someone has certain cells that don't function properly or that have been damaged, then stem cells could be used to replace those damaged cells. This is not a new concept. In fact, stem cells have already been used for years in medicine.

Have you ever heard of a bone marrow transplant? Did you know that this therapy for treatment of leukemia is completely dependent on the ability of multipotent adult stem cells to renew themselves and differentiate into white blood cells? When a person has leukemia (a blood related cancer), their white blood cells, called leukocytes, grow abnormally and cannot carry out their usual functions. The patient can't fight off infection, and the abnormal cells also interfere with the proper functioning of other organs. The idea behind bone marrow transplants is to replace the stem cells that are giving rise to cancerous leukocytes, with ones that will generate healthy leukocytes. In order to do this, chemotherapy is first used to kill off the cancerous leukocytes and then the donor's bone marrow containing stem cells are introduced to the patient's blood stream. If all goes well, the stem cells from the donor will migrate to the patient's bone marrow and begin producing healthy leukocytes. Since this method of treatment has been very successful, scientists have good reason to try to uncover all the untapped information and potential treatments that stem cells could offer.

Currently, scientists are working on developing therapies that may one day be able to treat diseases such as Parkinson's, cerebral palsy and diabetes. The idea here is to grow compatible tissues in vitro for transplant to replace damaged neurological cells, or pancreatic cells. Another method may be to use drugs to stimulate the body's stem cells to produce more healthy cells and avoid transplantation altogether. There has been some success already just by injecting patients with stem cells which eventually find their way to the damaged cells.

Revolution in the petri dish: Induced pluripotent stem cells (iPSC)

Stem cells are the all-rounders of the body. All types of tissue are formed from them, making them particularly valuable. A few years ago, reprogramming of adult cells by Japanese researcher and Nobel laureate Shinya Yamanaka sparked a revolution in the world of research. Up until that point, the purpose of a cell within the body had been considered unchangeable, because even though the entire genome is contained in every cell, skin or never cells, for example, can no longer access all parts of it.



A colony of embryonic stem cells, from the H9 cell line

Today, a biological trick makes it possible to reprogram adult stem cells into the state of pluripotent stem cells. These so-called induced pluripotent stem cells (iPSCs) can theoretically be differentiated into any type of cell and, therefore, any tissue type.

Small cell, big effect: How iPSCs help in research

Working with iPSCs and the cells differentiated from them offers a broad range of possibilities to researchers: They can artificially reconstruct entire organs from their various components (cell types), even making it possible to simulate diseases in the organs. iPSCs are used to create organ cells – nerve cells, myocardial or liver cells – that show classical symptoms of disease. Thus, illnesses – from Parkinson's to cardiovascular diseases and even cancer – can be simulated in the petri dish.

Specific genetic damage can also be created with iPSCs. It is possible to generate models of patients suffering from certain genetic defects and the resulting illnesses. Testing of substances in the diseased cells enables researchers to examine new therapeutic approaches and the effects of potential active substances.

Another possible use: With cardiomyocytes created from induced stem cells, it is possible to gain information at an early stage about possible side effects of active substances that might become dangerous for a patient's cardiac function.

- References: - American Association for the Advancement of Science. 2009. Science and Policy: Stem Cells. - https://www.bayer.com/en/pharma/stem-cells-new-age-medical-research

SIDDHI MAHUDKAR – 21165

HOW ARE STEM CELLS USED IN BIOMEDICAL RESEARCH AND THERAPIES?

Given their unique regenerative abilities, there are many ways in which human stem cells are being used in biomedical research and therapeutics development.

Understanding the biology of disease and testing drugs

Scientists can use stem cells to learn about human biology and for the development of therapeutics. A better understanding of the genetic and molecular signals that regulate cell division, specialization, and differentiation in stem cells can yield information about how diseases arise and suggest new strategies for therapy. Scientists can use iPSCs made from a patient and differentiate those iPSCs to create "organoids" (small models of organs) or tissue chips for studying diseased cells and testing drugs, with personalized results.

Cell-based therapies

An important potential application is the generation of cells and tissues for cell-based therapies, also called tissue engineering. The current need for transplantable tissues and organs far outweighs the available supply. Stem cells offer the possibility of a renewable source. There is typically a very small number of adult stem cells in each tissue, and once removed from the body, their capacity to divide is limited, making generation of large quantities of adult stem cells for therapies difficult. In contrast, pluripotent stem cells are less limited by starting material and renewal potential.

To realize the promise of stem cell therapies in diseases, scientists must be able to manipulate stem cells so that they possess the necessary characteristics for successful differentiation, transplantation, and engraftment. Scientists must also develop procedures for the administration of stem cell populations, along with the induction of vascularization (supplying blood vessels), for the regeneration and repair of three-dimensional solid tissues.

What laboratory tests are used to identify stem cells?

At various points during the process of generating stem cell lines, scientists test the cells to see whether they exhibit the fundamental properties that make them stem cells. These tests may include:

- Verifying expression of multiple genes that have been shown to be important for the function of stem cells.
- Checking the rate of proliferation.
- Checking the integrity of the genome by examining the chromosomes of selected cells.
- Demonstrating the differentiation potential of the cells by removing signals that maintain the cells in their undifferentiated state, which will cause pluripotent stem cells to spontaneously differentiate, or by adding signals that induce adult stem cells to differentiate into appropriate cell phenotypes.

To be useful for transplant purposes, stem cells must be reproducibly made to:

- Proliferate extensively and generate sufficient quantities of cells for replacing lost or damaged tissues.
- Differentiate into the desired cell type(s).
- Survive in the recipient after transplant.
- Integrate into the surrounding tissue after transplant.
- Avoid rejection by the recipient's immune system.
- Function appropriately for the duration of the recipient's life.

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

For all purposes: iPSCs are useful in pharmaceutical research and regenerative medicine

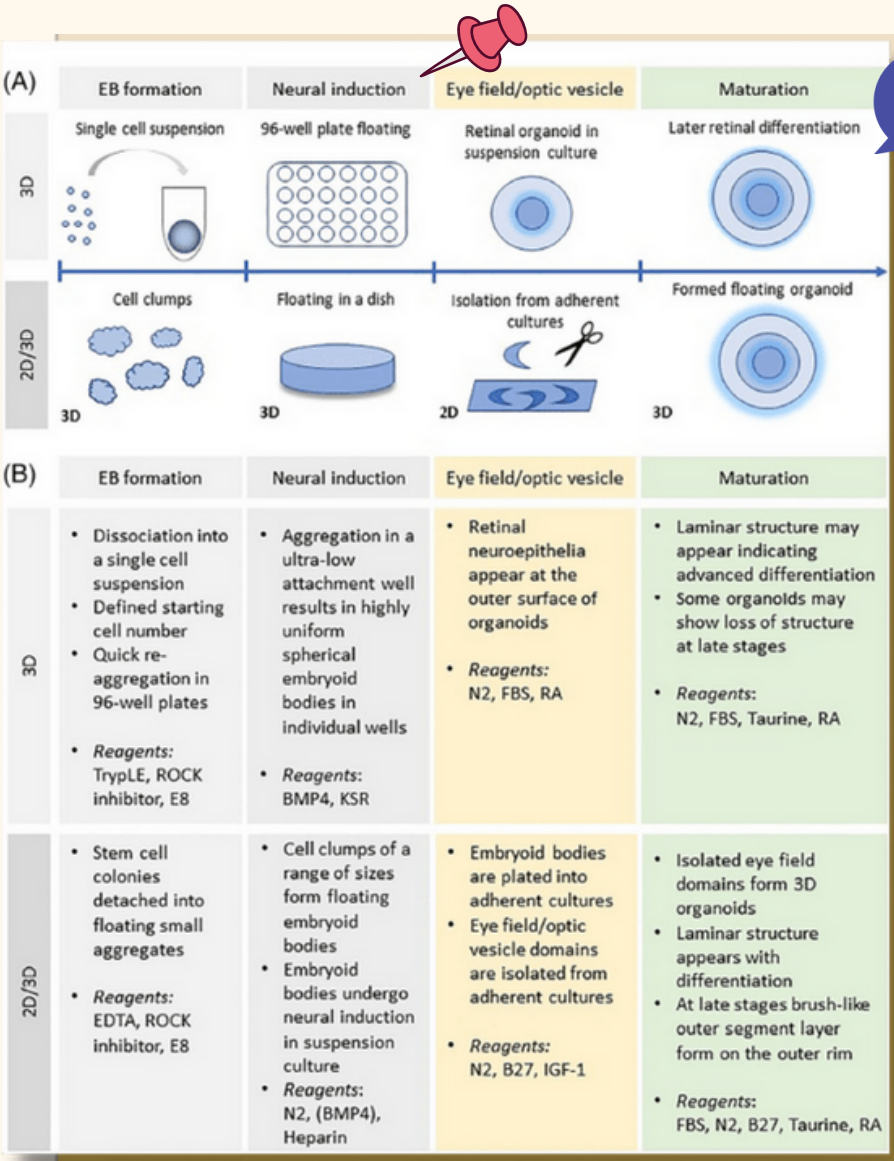
Besides drug research, stem cell-based approaches are also very promising in the field of regenerative medicine. For instance, iPSCs could be differentiated into cells which are defective in a patient (e.g., dopaminergic neurons in the case of Parkinson's disease). These cells can be transplanted into the patient and help halt the progression of the disease or even bring about a cure. In addition, specific genetic modifications can be used to minimize or completely prevent rejection reactions in the patient.

- References:
http://stemcells.nih.gov/info/basics/
-https://www.bayer.com/en/pharma/stem-cells-new-age-medical-research

SIDDHI MAHUDKAR – 21165

PLURIPOTENT STEM CELL-DERIVED RETINAL ORGANOIDS

Loss of sight is one of the most feared disabilities. The retina is often called the window to the brain, and dysfunction of retinal neurons in complex multifactorial diseases such as age-related macular degeneration (AMD), glaucoma, or diabetic retinopathy is a major cause of incurable blindness worldwide. Mutations in over 200 genes can lead to inherited retinal and macular diseases (IRDs). As retinal diseases constitute a genetically and phenotypically diverse group of clinical conditions leading to vision impairment or blindness with limited treatment options; Advances in reprogramming of somatic cells to induced pluripotent stem cells and generation of three-dimensional organoids resembling the native retina offer promising tools to interrogate disease mechanisms and evaluate potential therapies for currently incurable retinal neurodegeneration.



DIFFERENTIATION METHODS AND STAGING OF RETINAL ORGANOIDS

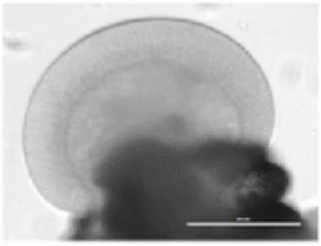
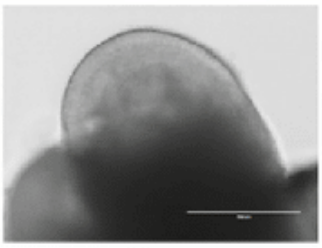
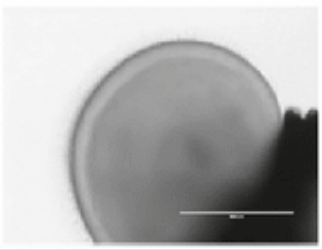
Groundbreaking discoveries in reprogramming of somatic cells into iPSCs and their differentiation into retinal lineages have greatly facilitated the study and treatment design of retinopathies. Labrotories have pioneered the methods for 3D optic cup morphogenesis in vitro from mouse embryonic stem cells, followed by adaptation of the protocol to produce human retinal organoids.

In the first approach, PSCs are suspended as single cells, followed by quick aggregation into embryoid bodies in a multiwell format, and then retinal neuroepithelium differentiation is stimulated by addition of basal lamina components present in Matrigel.
The second set of protocols combine 2-D and 3-D approaches with initial formation of embryoid bodies from detached human PSC (hPSC) colonies and neural induction in suspension, then plating and eye field formation in adherent conditions, followed by isolation of retinal domains and suspension culture as retinal organoids. The initial step of embryoid body formation can be omitted with growth of hPSCs to confluence and neural induction in adherent cultures.

Another alternative is mixing hPSC clumps with Matrigel to form epithelialized cysts, which can be then plated, later followed by gentle lifting with dispase to form welllaminated organoids.Replacement of widely used all-trans retinoic acid with 9-cis retinal accelerates differentiation of rod photoreceptors in retinal organoids,whereas signaling by thyroid hormone facilitates the specification of L/M cone subtypes,consistent with S-cones being the default fate of photoreceptors. Interestingly, scraping of the adherent culture and selection of subsequently formed optic vesicles improves the yield and efficiency of generating retinal organoids.Typically, the combination of 2-D and 3-D approaches achieves higher organization and maturity levels in late-stage organoids.

SRIJANI DEB – 21166

Staging retinal organoids

	Stage	Morphological features	Molecular markers	Fetal retina epoch
Stage 1		○ Phase-bright neuroepithelium ○ Often columnar organization visible ○ Cup-like shape ○ Rapid growth ○ Several weeks post isolation	○ Retinal progenitors: RAX, VSX2, PAX6 ○ Neurogenesis: ASCL1, NEUROD1, NEUROG1, ATOH1 ○ Ganglion and Starburst amacrine cells: BRN3A/B, SNCG, HuC/D, CHAT, NEFL	○ **First epoch** ○ Mitosis and retinal progenitor genes (*FGF19, LIN28B, PRTG, SFRP2*) ○ Retinal ganglion cell genes (*ATOH7, DLX2, POU4F2*)
Stage 2		○ Phase dark core develops ○ Grown together tend to merge forming multi-lobular aggregates ○ May remain at this stage	○ Interneurons: ONECUT1/2, TFAP2A/C, CALB2 ○ Photoreceptor precursors: OTX2, CRX, NRL, NR2E3, THRB2, RXRG ○ Synaptogenesis: VAMP2, SNAP25, STX3, SYP, SYT1, CPLX3, PCLO	○ **Second epoch** ○ Horizontal and amacrine cell genes (*PROX1, ASCL1*) ○ Synapse genes (*NRXN1/3, SCN2A, CACNA1C*)
Stage 3		○ Outer lamina clearly defined ○ Brush-like apical protrusions at the rim ○ Center dense and opaque ○ Arise around 15-20 weeks post-isolation	○ Opsins: OPN1SW, OPN1MW, RHO ○ Phototransduction: GNAT1/2, GNGT1/2, SAG, ARR3, CNGB1/3 ○ Outer segment: ROM1, ABCA4, PRPH2, RPGR ○ Müller glia: RLBP1, VIM	○ **Third epoch** ○ Photoreceptor and bipolar cells genes (*OTX2, NRL, RCVRN, TULP1, GNAT1/2, GRM5/6/7/8*)

RETINAL ORGANOIDS AS DISEASE MODELS

Studies using iPSC lines from retinitis pigmentosa patients differentiated in adherent conditions identified endoplasmic reticulum stress as a common disease signature. Subsequently progress in 3-D cultures allowed examining disease mechanisms in organoids with more native spatial cell arrangement. Defects in early retinogenesis were modeled in cells carrying R200Q mutation in the transcription factor visual system homeobox (VSX2). During retinal development, a distinct profile of alternative splicing is established, and retinal organoids have been used for disease modeling of patients with mutations in splicing factor PRPF31 (RP11).Many disease causing mutations in IRDs are specifically located in genes related to sensory cilia and can be modeled in organoids. One of the published studies examined effects of mutations in a centrosome-cilia protein CEP290.Cilia formation was shown to be impaired in fibroblasts. derived from CEP290 patients with a more severe syndromic disease Joubert syndrome, but not in those diagnosed with LCA, a blinding retinal disease. However, retinal organoids from CEP290-LCA patients exhibited abnormal ciliogenesis demonstrating tissue-specific impact of pathogenic mutations and correlating broader defects with increased disease severity. Retinal organoids from patients with an intronic CEP290 mutation common in LCA patients revealed a more frequent cryptic exon inclusion compared to fibroblasts, iPSCs or RPE cells from the same patient.Reduced CEP290 protein levels in CEP290-LCA organoids led to impaired cilia development.

GENE-BASED & CELL THERAPIES

AAV vector platform has become a gene delivery method of choice for retinal diseases. Transduction of mouse and human retinal organoids as well as RPE tissues has been examined by a panel of commonly used AAV capsid serotypes.Interestingly, ShH10 capsid serotype, which was developed through directed evolution approach of screening AAV mutant libraries,was highly efficient in transducing all stem cell-derived tissues examined.In mouse retinal organoids, AAV2 vector rescued the CEP290-associated disease phenotype. For human photoreceptor transduction AAV2 capsid serotype also appears to be highly potent, whereas AAV5 is most effective for RPE cells of both mouse and human origin.

Stem cells and organoids have been widely used as a source for

evaluating cell replacement therapy approaches.The degenerative process in retinopathies primarily affects two retinal cell types: the light-sensitive photoreceptors and RPE.As a simple monolayer easily distinguishable by pigmentation and cuboidal morphology, RPE has been one of the first cell types to be efficiently differentiated from PSC sources and the first hESC-derived cell type to be transplanted into humans. Implanting intact RPE sheets alone or grown on a bioscaffold is likely to result in improved outcomes.

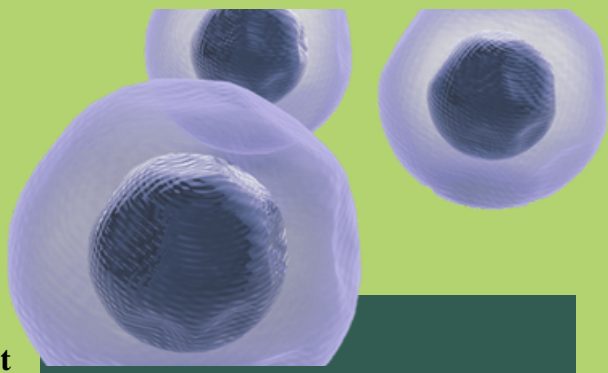
HTTPS://WWW.SCIENCEDIRECT.COM/SCIENCE/ARTICLE/PII/S0169409X1830108X
HTTPS://ACADEMIC.OUP.COM/STMCLS/ARTICLE/38/10/1206/6409281

SRIJANI DEB – 21166

Stem Cells in research

CHALLENGES

Grand challenges in stem cell treatments



Stem cells mainly include embryonic stem cells (ESC), pluripotent stem cells (iPS), Epiblast-derived stem cells (Epi-SC), and adult tissue stem cells. ESC are pluripotent, being able to differentiate into the ectoderm, mesoderm and endoderm.However, there are ethical issues when using human embryos, and ESC trans-plants into mouse models can result in malignant tumors. Further challenges facing research in the use of ESC are how to reduce contamination, and prevent cancer risk. Human ESC lines derived from single blastomeres have been reported. This method may create new stem cell lines and therapies without destroying embryos, and would thus address the ethical concerns and allow the generation of matched tissues for children and siblings born from transferred preimplantation genetic diagnosis embryos.Another current challenge is that the cells used in research are rejected by the recipient's immune system.One challenge facing researchers is how to control and regulate the process to successfully triggerdifferentiation into the desired cell type after the stem cells have been isolated. When some defined transcription factors are transferred into somatic cells, somaticcells can directly reprogram to differentiate into other cell types without passing through a pluripotent state.

Stem cell treatments include new technologies and therapies that aim to replace damaged tissues and cells in order to treat disease or injury. A number of stem cell therapies are still in the experimental stages, and are controversial. The first challenge researchers face when considering stem cell treatment is to understand the mechanisms by which stem cells function in the injured microenvironment using animal models, and then to translate the results of these studies to humans. Another challenge is how to identify and isolate stem cells from tissue, and then induce their differentiation into the desired cell types. The third challenge is how to prevent immunorejection after stem cell transplantation. Immunological rejection is a major barrier to successful stem cell transplantation. A person's immune system may also recognize the transplanted cells as foreign bodies and this can trigger an immune reaction that results in the rejection of the transplanted cells. Recipients of the transplant usually have to take strong immunosuppressive drugs to reduce the chances of rejection but these drugs induce infection by viruses or microbes in the environment.

Challenges in Developing Countries

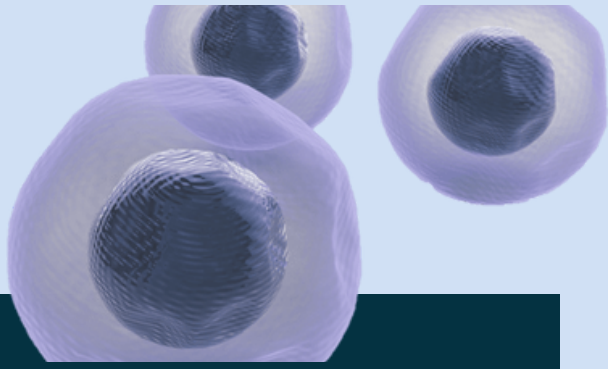
There are many challenges that are suppressing the growth of stem cell therapy in developing country. The first challenge is dominancy of peasant therapeutic methodology. People still have a belief on primitive therapy due to lack of upgrading knowledge of modern medicine. Second challenge is lack of skilled human resources, poor transfusion servicesservices. Third challenge is poor socioeconomic status, ethical issue and financial limitations when committed to treat the disease by stem cell, it requires the huge money which is in many cases impossible to spend. The fourth challenge is difficulty in keeping pace with technological advancement. The fifth challenge is poor government support and policy even though lots of fund become freeze without doing research every year. Therefore there should be the policy to take care of such artifact to strengthen the existing facilities and they should use such fund in the development of more centers for research and translational work. In addition, private sector should also be forced by government to start research and clinical therapies in reasonable price in area of stem cells. International collaborations with advanced centers should be beneficial for this purpose.

References: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4206984/
https://medcraveonline.com/JSRT/challenges-of-stem-cell-therapy-in-developing-country.html

Shreya Aasore 21163

Stem Cells in research

DID YOU KNOW



- **Birth Defects**

According to Joseph Yanai, director of the Ross Laboratory for Studies in Neural Birth Defects at the Hebrew University-Hadassah Medical School, in Jerusalem, stem cell therapies are helpful to treat birth defects when the mechanism of damage is not fully understood. He says that if neural stem cells are used, they act as little doctors that can diagnose the defect and differentiate into the desired cell type to repair it. When stem cells are derived from an individual who is genetically different from the patient, the transplant can lead to immunological rejection. To overcome this challenge, researchers will have to find a way to isolate stem cells from the patient's own body, to program them to function as stem cells, and then transplant them into the patient's blood.

- **Nervous System Disorders**

Neurogenesis results from cells that are possibly the remnants of stems cells that existed during brain development in the fetus.Neurons are generated only in some regions of the brain. However, there are chances of these cells being of use in replacing those lost due to degenerative diseases or injuries. Researchers are identifying growth factors used by the brain as they could be used to reduce brain damage and to activate stem cells to repair the damage caused.

In the 1970s, cells from the substantia nigra of the fetal tissue of a mouse were transplanted into a rat. The cells were found to develop into mature dopamine neurons. Later, it was found that this transplant could reverse Parkinson's-like symptoms in rats and monkeys. In two clinical trials funded by NIH, tissue from aborted fetuses was transplanted into the striatum of Parkinson's disease patients. While some patients showed improvement, many showed side effects. In some patients, their immune system did not accept the transplant.

AMAZING! WORLD'S FIRST BABY BORN USING STEM CELL IVF TECHNIQUE

- **Zain Rajani, born April 13, 2015, is the world's first baby to be born using an in vitro fertilization technique called AUGMENT, which some believe could significantly boost IVF success rates**
- **AUGMENT is an innovative treatment targeted at improving a mother's egg health by injecting stem cells from the ovarian lining to mature egg cells. These stem cells enhance necessary energy production from existing mitochondria**
- **Though AUGMENT is not yet available in the US, its success in other countries, such as Canada, gives great hope to parents wishing to start a family, but face fertility problems due to poor egg quality or age**

Stem cells in Drug Discovery

As human stem cells can be made to differentiate in an artificial environment to form various specialized cells, they are of use in the discovery of drugs. Cells derived from tumors in animals or humans can be used to test their reaction to compounds.The effectivity and toxicity of newly developed drugs can be tested on animals. But considering the cost and ethical issues involved, in vitro testing that stem cells allow is more beneficial.

To test a drug for chronic toxicity, the cells that it is being tested on, should have a long life. For it to be tested on all cell types, the cells should be available. As embryonic stem cells can differentiate into different cell types and for long periods, these constraints in drug testing are almost eliminated.By deriving stem cells from different organisms, the efficacy of a drug can be tested across species.Using the induced pluripotent stem cell (iPSC) technology, new cellular models can be created with varying degrees of susceptibility and resistance to drug.

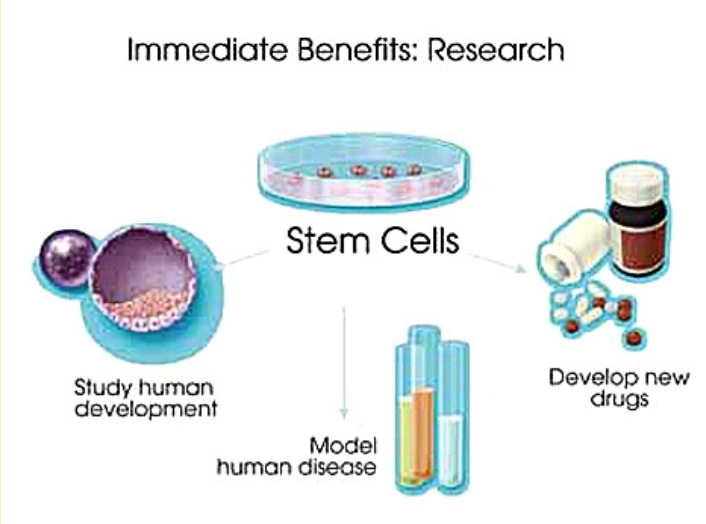
https://biologywise.com/stem-cell-research-facts

Shreya Aasore 21163

Shweta Pawar

Role of stem cell in basic research

Stem cells offer opportunities for scientific advances that go far beyond regenerative medicine. They offer a window for addressing many of biology's most fundamental questions. Watching embryonic stem cells give rise to specialized cells is like peeking into the earliest development of the many tissues and organs of the human body. Stem cell research may help clarify the role genes play in human development and how genetic mutations affect normal processes. They can be used to study how infectious agents invade and attack human cells, to investigate the genetic and environmental fctors that are involved in cancer and other diseases, and to decipher what happens during aging.



Stem cells may also revolutionize tradi-ional chemical medicine. Because embryonic stem cells can continue to divide for long periods of time and produce a variety of cell types, they could provide a valuable source of human cells for testing drugs or measuring the effects of toxins on normal tissues without risking the health of a single human volunteer. In the future, thousands of compounds could be quickly tested on a wide assortment of cell types derived from stem cells, making drug discovery more efficient and cost effective.

Using nuclear transfer to produce stem cells could be particularly useful for testing drugs for disorders that are of genetic origin. For example, it is difficult to study the progression of Alzheimer's and Parkinson's diseases in the brains of live patient but by using the cells of an Alzheimer's patient to create stem cell lines with nuclear transfer, scientists could trace the development of the disease in a culture dish and test drugs that regenerate loste nerve cells with no danger to the patient.

Stem cells may also help scientists calculate the effects of toxic substances in drugs, food, and the environment.

Role of Animals in Stem Cell Research

Refrence:

https://nap.nationalacademies.org

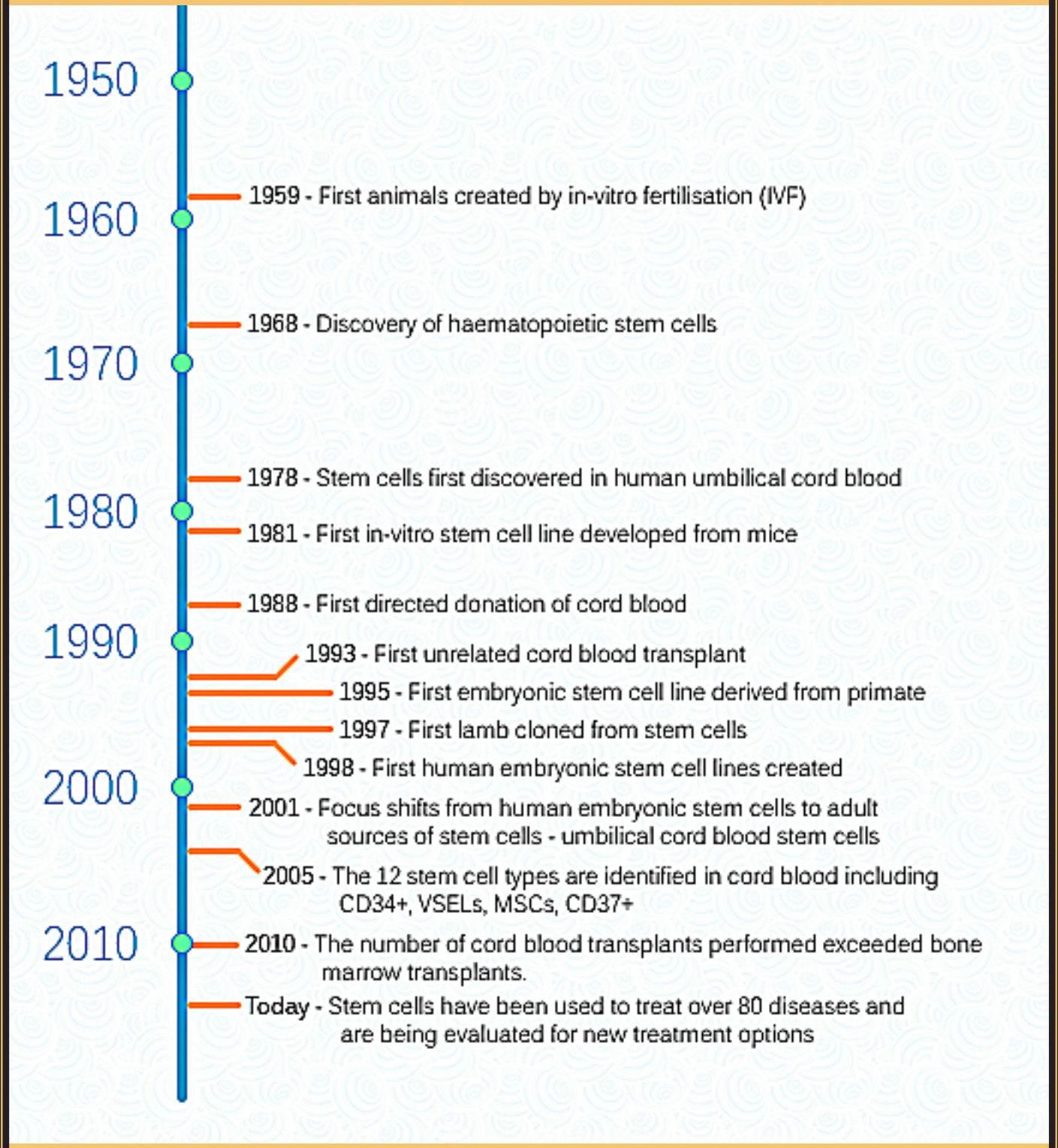
For medical research, as well as for research that explores the basic processes in the development of organisms and diseases, scientists often rely on animals. Implanting human cells into animals such as mice has long been common practice in order to test the safety and effectiveness of new drugs, procedures, and medical devices before clinical testing in human volunteers. For steml Cell research, scientists use animals to make sure the stem cells are able to incorporate into the tissue do not cause any harmful consequences, And function in concert with the rest of the body.For example, before using stem cells to replace the pancreatic cells that are destroyed by type 1 diabetes in humans, scientists will transplant human stem cells into a mouse to see whether the stem cells yield healthy, insulin-producing cells If their methods prove successful in mice,scientists may eventually apply the technology that developing treatments for diabetes in humans.

Animal studies can also reveal how human cells differentiate during normal development.For example, scientists may implant human stem cells into a developing mouse to observe processes involved in building and organizing the different tissue types that make up the human body. Scientists can also trace the development and progression of certain diseases within an animal. By implanting human stem cells that lead to a particular disease into a mouse blastocyst, scientists can observe when and how the afflicted cells begin to show signs of disease and can test drugs that might prevent that process .

Organisms that contain cells or tissues from another inividual of the same or a different species are called chimeras. A common example of a chimera is a mouse that has been injected with some humans Cell so that it can be used for studying a human disease or testing a new drug. A person who has had blood transfusion or a person who has received heart valve transplant from a pig is technically a chimera, as well.

Shweta Pawar

History- Stem cells in research



Siddhi Mahudkar 21165