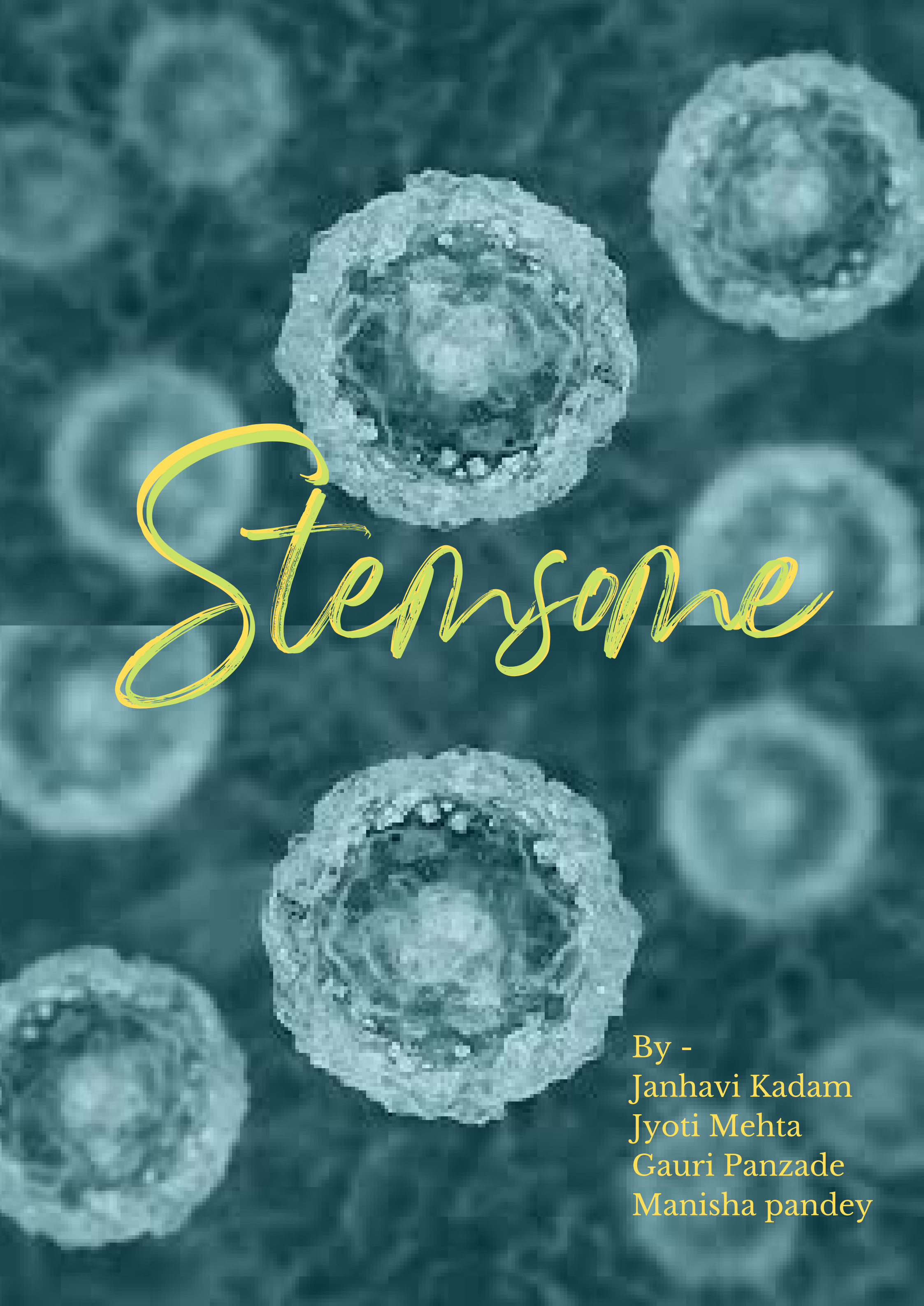




Stemsonne

By -
Janhavi Kadam
Jyoti Mehta
Gauri Panzade
Manisha pandey

EMBRYONIC STEM CELLS

By- Jyoti Mehta

Embryonic stem cells (ES cells) are pluripotent stem cells which are derived from the inner cell mass of a blastocyst, an early-stage embryo. Inner mass cells = embryonic stem cells = embryoblasts

The ES cells have high potential to differentiate into a wide variety of cell types. In other words, pluripotency, Undifferentiated embryonic stem cells can be functionally defined by their ability to differentiate into cells derived from the three germ layers.

Embryonic stem cells originate from early blastocysts and it retains the extraordinary plasticity to become any cell type of approximately 200 cell types that constitute the human body.

Given the right combination of signals, embryonic stem cells will develop into mature cells that can function as neurons, muscles, bone, blood or other needed cell types.

Another important feature of embryonic stem cells is their ability to remain in an undifferentiated state and to divide indefinitely.

These so-called self-renewing cells generate unlimited well-defined, identical, genetically and genomically characterized stem cells.

Various advantages of ES cells are as: 1. Flexible - have the potential to make any cell. 2. Immortal - can provide an endless supply of cells. 3. Availability - embryos from in vitro fertilization clinics.

Despite our growing knowledge about their enormous potential, we are limited to exploit ES cell-based therapeutic avenues. One of the challenging tasks is that markers that identify ESC also mark tumor stem cells i.e Tumorigenic- capable of forming tumors. Researchers face a formidable challenge in distinguishing ESCs, especially from TSCs. Another potential issue is that despite their embryogenic origin, human and mice differ in pluripotency mechanisms.

Immunogenic- cells from a random embryo donor may be rejected after transplantation.

Moreover ethical, legal, and jurisprudence concerns related to ES cells are: Destruction of embryo, increasing the rate of illegal abortion, lack of enough clear legal rules, commercial exploitation. Strategies involved in ethical, legal, and jurisprudence include obtaining stem cell from donated frozen embryos that would be discarded through IVF treatment process or obtaining informed consent from the both of donor and recipient. Trade prohibition of gamete and embryo. Compliance of national ethical. Guidelines in stem cell research and supervision on bio banks.

A black and white portrait of Martin Evans, an older man with white hair, wearing a dark suit, white shirt, and patterned tie. He is looking directly at the camera with a slight smile.

Martin Evans of Cardiff University, UK, then at the University of Cambridge, was the first researcher to isolate embryonic stem cells from mice in 1981

Identification of Stem Cells

SURFACE MARKERS:

SSEAs markers	Characteristics	Classification
SEA-1 (CD15/Lewis x)	Murine embryos, mouse ES cells, mouse and human germ cells, embryonal carcinoma (EC) cells	Carbohydrate-associated molecule
SSEA-3	Primate ES cells, human embryonic germ cells, human ES cells, embryonal carcinoma (EC) cells	Carbohydrate-associated molecule
CD markers		
CD324 (E-Cadherin)	Human ES cells, mouse ES cells, embryonal carcinoma (EC) cells	Surface marker (Binding to integrin alphaE/beta7, homotypic interactions mediate cell adhesion)
CD90 (Thy-1)	Human ES cells, mouse ES cells, hematopoietic stem cells, embryonal carcinoma (EC) cells	Surface marker (hematopoietic stem cell and neuron differentiation, T activation)
transcription factors		
Oct-3/4 (Pou5f1)	Mouse ES cells, human ES cells, embryonal carcinoma (EC) cells	POU family Transcription factors
Sox2	Mouse ES cells, human ES cells, embryonal carcinoma (EC) cells, neural stem (NS) cells	POU family binder Transcription factors

Application:

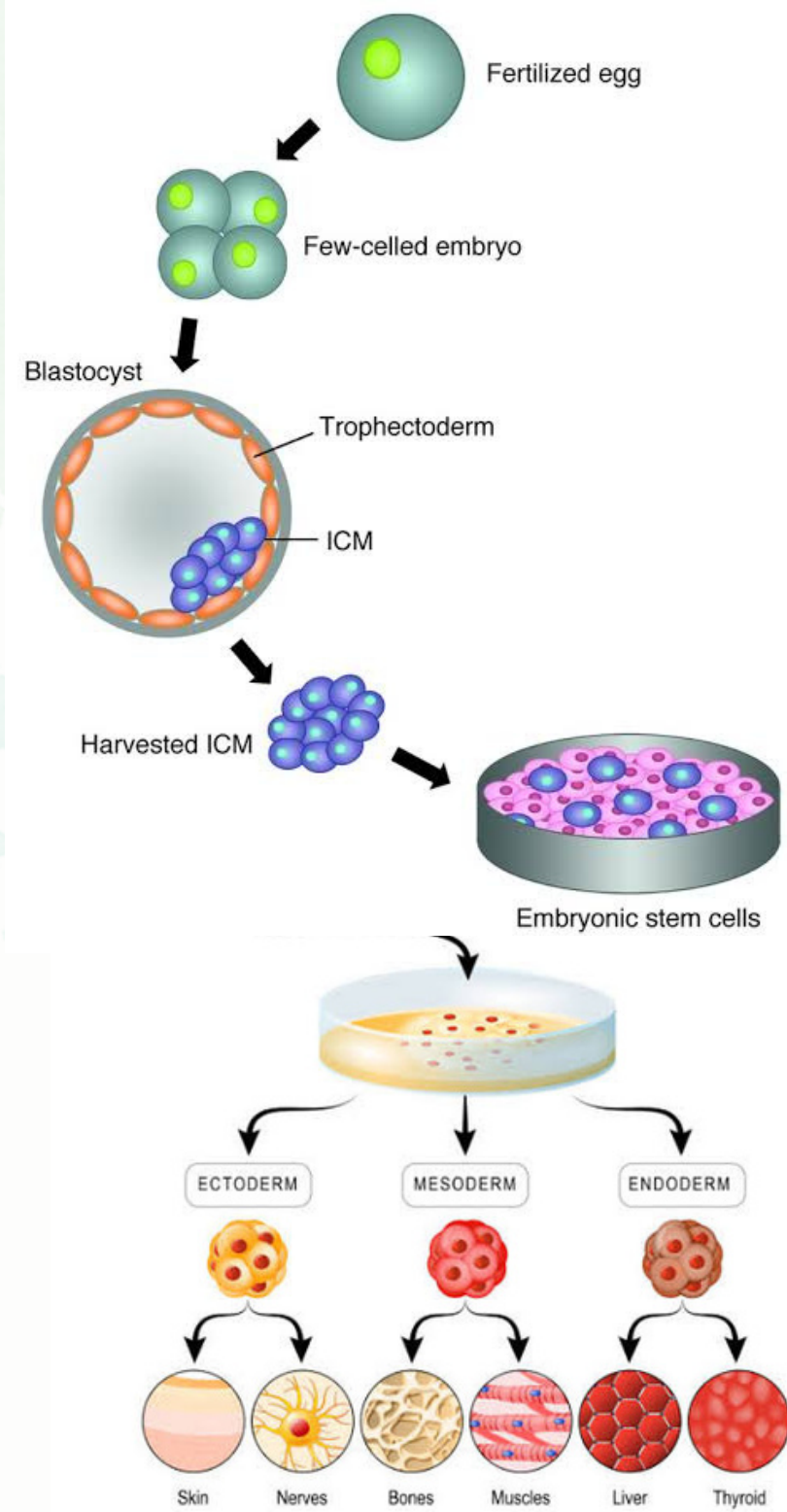
- The ES cells are an important material in developmental biology, genomics, and transgenic methods, as well as in potential clinical applications, gene therapy and tissue engineering.
- Human stem cells are most commonly employed in regenerative medicine, therefore the idea of using them in cell replacement therapy is highly alluring.
- The therapeutic use of ES cells.
- Cancer cell lines, for example, are used to screen potential anti-tumour drugs.
- Treatment of neural diseases such as Parkinson's disease, Huntington's disease and Alzheimer's disease.
- Stem cells could be used to repair or replace damaged neurons. Repair of damaged organs such as the liver and pancreas. Treatments for AIDS.



<https://www.nature.com/articles/s41586-022-05246-3>

By Magdalena Zernicka-Goetz

Recent research conducted by the University of Cambridge and Caltech have created model mouse embryos from stem cells—the body's master cells, which can develop into almost any cell type in the body—that have beating hearts, as well as the foundations for a brain and all of the other organs in the mouse body.



Stem cells Facts and myths

- A stem cell transplant only treats leukaemia. 
- A blood stem cell transplant can be a potentially life-saving treatment for more than 70 different diseases.
- There are plenty of donors on the system. 
- Every year, over 80,000 people in need of a blood stem cell donation search globally for an unrelated matching donor (i.e. not a relative).
- Stem cell matches depend on your blood type. 
- Blood stem cell donor matches depend on tissue types, not blood types. These are inherited genetic characteristics, and are often unique to a particular race group.
- It's complicated and time consuming to register as a stem cell donor. 
- It takes less than 10 minutes to register as a donor. When you register as a donor, you remain on the global database until you are a match for a patient, turn 60 or report any health reasons why you need to be removed.
- If I'm a match for someone, they will drill into my bones! 
- The life-saving bone marrow stem cells are found in your blood stream. A cell separator machine is used to collect stem cells from your blood.

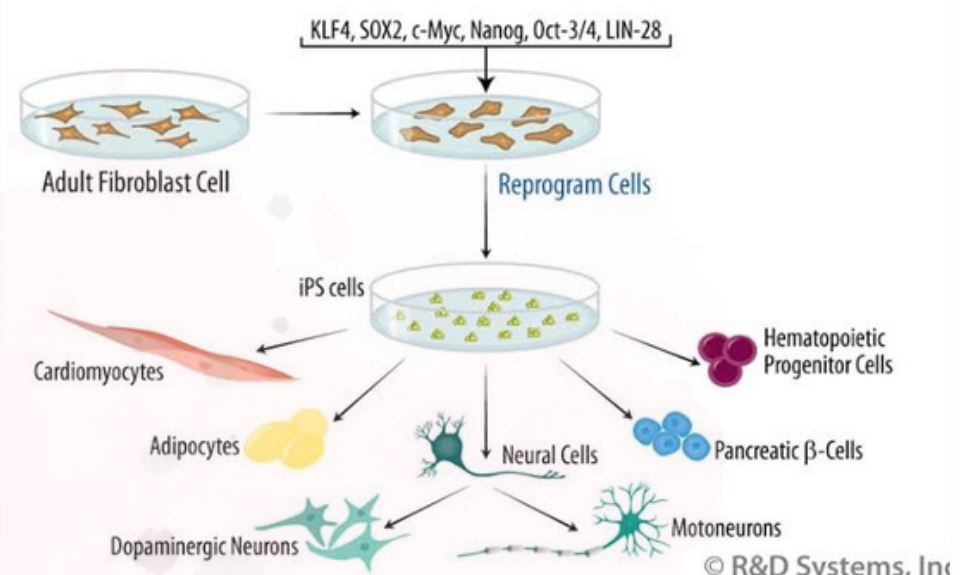
INDUCED PLURIPOTENT STEM CELLS

By - Janhavi kadam

- **IPS CELLS OR INDUCED PLURIPOTENT STEM CELLS (IPSCS)?**

Induced pluripotent stem cells (iPS cells or iPSCs) are a type of pluripotent stem cell that can be generated from adult somatic cells such as skin fibroblasts or peripheral blood mononuclear cells (PBMCs) by genetic reprogramming or the 'forced' introduction of reprogramming genes (Oct4, Sox2, Klf4 and c-Myc).

Human iPSCs were obtained with a somewhat altered gene set: Oct4, Sox2, Nanog, and Lin28. Induced PSCs closely resemble ESCs in a broad spectrum of features. They possess similar morphologies and growth manners and are equally sensitive to growth factors and signaling molecules. Like ESCs, iPSCs can differentiate in vitro into derivatives of all three primary germ layers (ectoderm, mesoderm, and endoderm) and form teratomas following their subcutaneous injection into immunodeficient mice.



- **WHERE CAN YOU OBTAIN HUMAN IPS CELLS?**

The European Bank of Induced Pluripotent Stem Cells (EBiSC) is a collection of high quality human iPS cells available for researchers for use in disease modelling and other forms of stem cell research. The stem cell bank includes iPSC cell lines derived from neurodegenerative diseases (Alzheimer's Disease, Parkinson's Disease, Dementia, Motor Neuron Disease (ALS) - and Huntington's Disease), eye and heart diseases, and lines from healthy control donors for age and sex matching.

- **WHAT ARE THE ADVANTAGES OF IPS CELLS OVER EMBRYONIC STEM CELLS?**

The advantage of iPS cells is that they are derived from somatic cells, which has less ethical concern in this field. By removing the bioethical issues, the scientists are more likely to obtain more federal funding and support. Another significant benefit of iPS cell technology would permit for creation of isogenic control cell lines using CRISPR/Cas9 gene editing that are genetically tailored to model a disease phenotype.

- **ISSUES FACED WHILE USING IPSC'S**

With iPSC research being a hotspot for several years now, many of the problems the technology first faced have been studied and resolved. The main issue is the use of retroviruses to generate iPSCs as they are associated with cancer. More specifically, retroviruses can insert their DNA anywhere in the genome and subsequently trigger cancer-causing gene expression. Also, as mentioned before, the c-Myc (one of the genes used in reprogramming) is a known oncogene, and its overexpression can cause cancer.

Also, in certain non-dividing cell types (such as PBMCs or elderly skin fibroblasts) the reprogramming rate of somatic cells to iPSCs is very low (less than 0.02 %). There is also a need to assess the quality and variability of the reprogramming process.

For example, iPSCs often have a tendency not to fully differentiate. Hence, there is a need to pursue a quantitative assessment of the final quality of cells and screen for any genetic or epigenetic alterations during the reprogramming process.

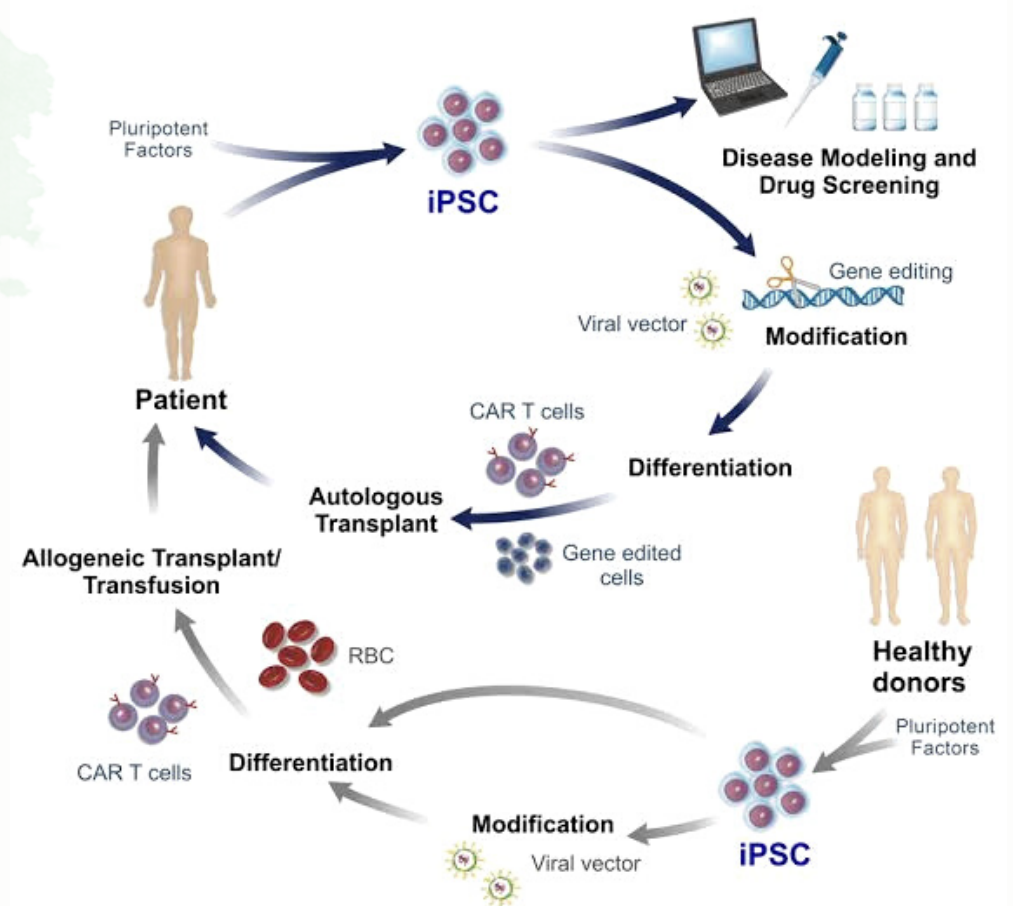
• APPLICATIONS

Induced pluripotent stem cells (iPSCs) are widely used in regenerative medicine, pharmacological research, and genetic disease analysis. However, knockout iPSC generation with CRISPR-Cas9 has been difficult to achieve using approaches such as frameshift mutations to reproduce genetic diseases with full-length or nearly full-length gene deletions.

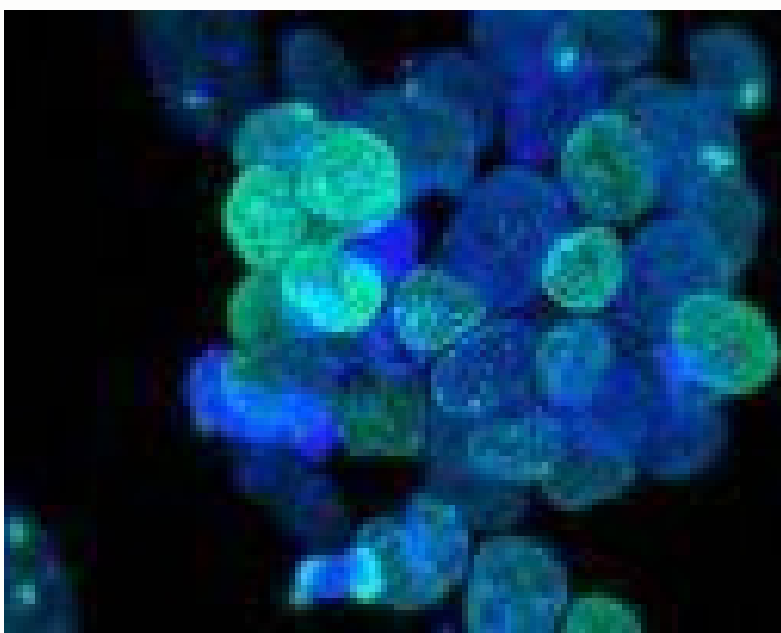
Full-length gene deletion methods in iPSCs might solve these problems, although no such approach has been reported yet.

In a new study, researchers presented a practical two-step gene-editing strategy leading to the precise, biallelic, and complete deletion of the full-length NPHP1 gene in iPSCs, which is the first report of biallelic full-gene deletion in iPSCs using CRISPR-Cas9 and single-stranded oligodeoxynucleotides mainly via single-strand template repair (SSTR).

This strategy requires no selection or substances to enhance SSTR and can be used for the analysis of genetic disorders that are difficult to reproduce by conventional knockout methods.



- The human iPSCs injected into the host animals might give rise to human gametes in the chimeric animals, posing a serious ethical conundrum
- iPSCs could also be used for the generation of humanized organs inside large animals through interspecies blastocyst complementation.



Researchers Generate Blood-Forming Stem Cells in the Lab Using Pluripotent Stem Cells

For the first time, researchers have generated blood-forming stem cells in the lab using pluripotent stem cells, which can make virtually every cell type in the body. Although the cells made from the pluripotent stem cells are a mix of true blood stem cells and other cells known as blood progenitor cells, they are capable of generating multiple types of human blood cells when put into mice.

This step opens up an opportunity to take cells from patients with genetic blood disorders, use gene editing to correct their genetic defect, and make functional blood cells,” said Ryohichi Sugimura, the study’s first author and a postdoctoral fellow in the Daley Lab. “This also gives us the potential to have a limitless supply of blood stem cells and blood by taking cells from universal donors. This could potentially augment the blood supply for patients who need transfusions.”

ADULT STEM CELLS

Adult stem cells are undifferentiated cells that live in a tissue or organ alongside developed cells. They have the capacity to renew and differentiate into multiple cell types. Adult stem cells can only differentiate into unique cell types of their tissue of origin, making them multipotent or unipotent stem cells. Adult stem cells' principal functions are to maintain and repair the tissue in which they dwell. Adult stem cells are uncommon and often tiny in quantity, but they can be discovered in a variety of adult organs.

Types of Adult/Somatic Stem Cells

1. Hematopoietic Stem Cells
2. Mesenchymal Stem Cells
3. Intestinal Stem Cells
4. Neuronal Stem Cells
5. Stem Cells of Epidermis and Hair Follicle

1. Hematopoietic Stem Cells:

Hematopoietic stem cells (HSCs) are uncommon cells of mesodermal origin seen in the adult mammalian bone marrow that sit atop a hierarchy of progenitors that become increasingly confined to multiple or single lineages. True HSCs remain primarily quiescent in adult tissue and give rise to short-term HSCs with limited self-renewal ability (6-8 weeks). When a short-term HSC changes from an undifferentiated self-renewing state, it can become a common myeloid progenitor (CMP) or a common lymphoid progenitor (CLP). Erythrocytes, monocytes and macrophages, neutrophils, basophils, eosinophils, megakaryocytes/platelets, and dendritic cells are all derived from the myeloid lineage.

- Sources of stem cells:

1. Bone Marrow (BM)
2. Umbilical cord blood (UCB)
3. Peripheral blood hematopoietic stem cells (PBSC)

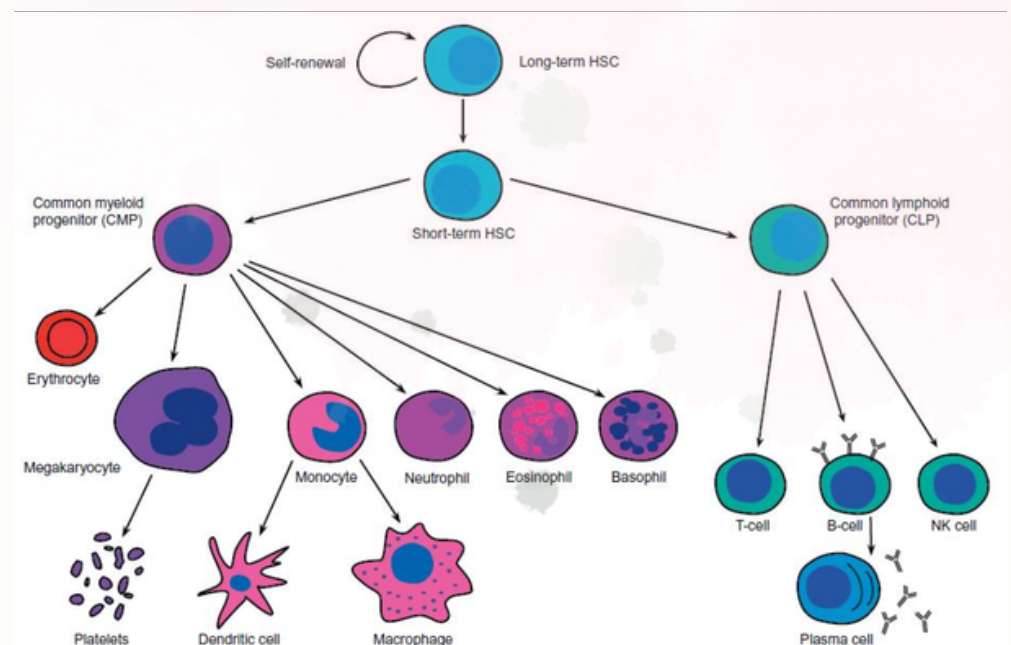
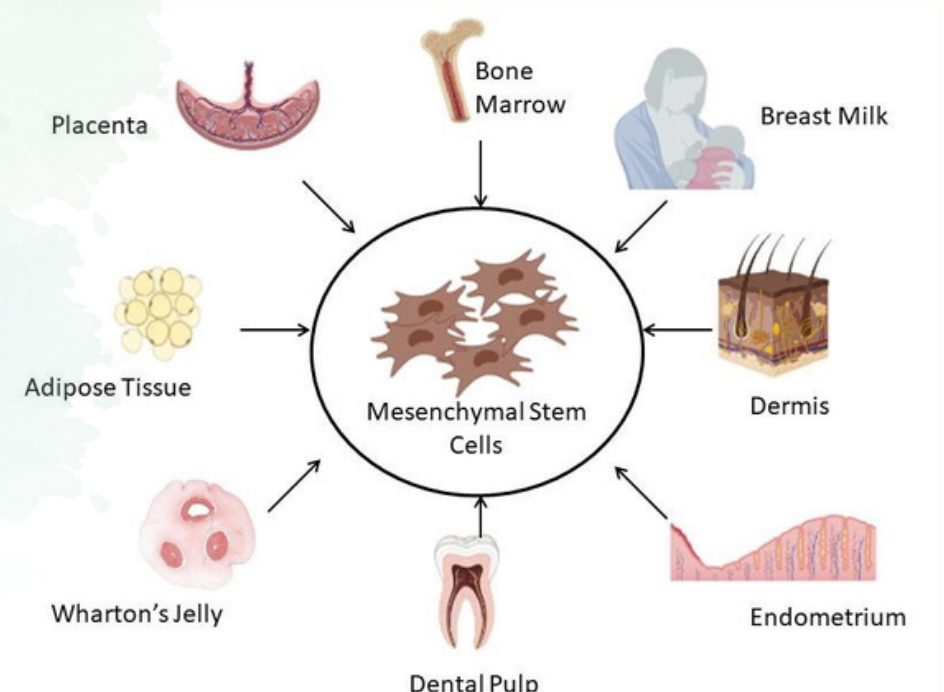


Figure 1. Simplified diagram of differentiation of hematopoietic stem cells

2. Mesenchymal Stem Cells

The majority of mesenchymal stem cells (MSCs) are found in the stroma of bone marrow. MSCs derived from bone marrow have the ability to develop naturally into mesodermal tissues such as muscle, tendon, adipocyte, osteocyte, and chondrocyte lineages. MSCs have been discovered in adipose tissue, intestinal stroma, the corneal limbal stroma of the eye, the trachea, and the dental pulp. MSCs are primarily found in niches around the pericyte



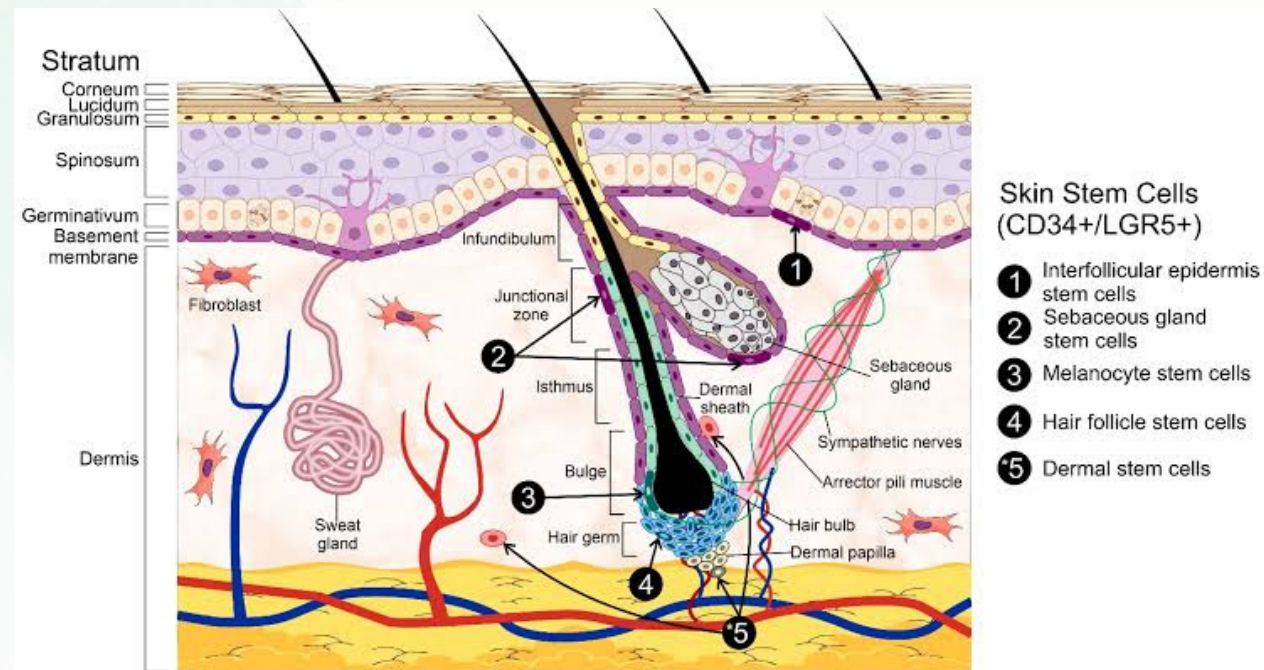
area of capillaries in various tissues. Neonatal tissues such as placenta, cord blood, and Wharton's jelly are also essential medical sources of MSCs. MSCs are used in the regenerative processes of adult tissues, such as the heart after an infarction. MSCs can direct cell differentiation from damaged tissues and act as paracrine regulators of healing processes.

• **SOURCES OF STEM CELLS:**

1. Bone Marrow
2. Adipose Tissue-Derived Stem Cells (ADSCs)
3. Dental Stem Cells (DSCs)

3. SKIN STEM CELLS:

- Skin stem cells are multipotent adult stem cells present in the adult skin, which can self-renew and differentiate into different cell lineages of the skin. Skin stem cells are active during skin renewal, which occurs throughout life, and in skin repair after injury.

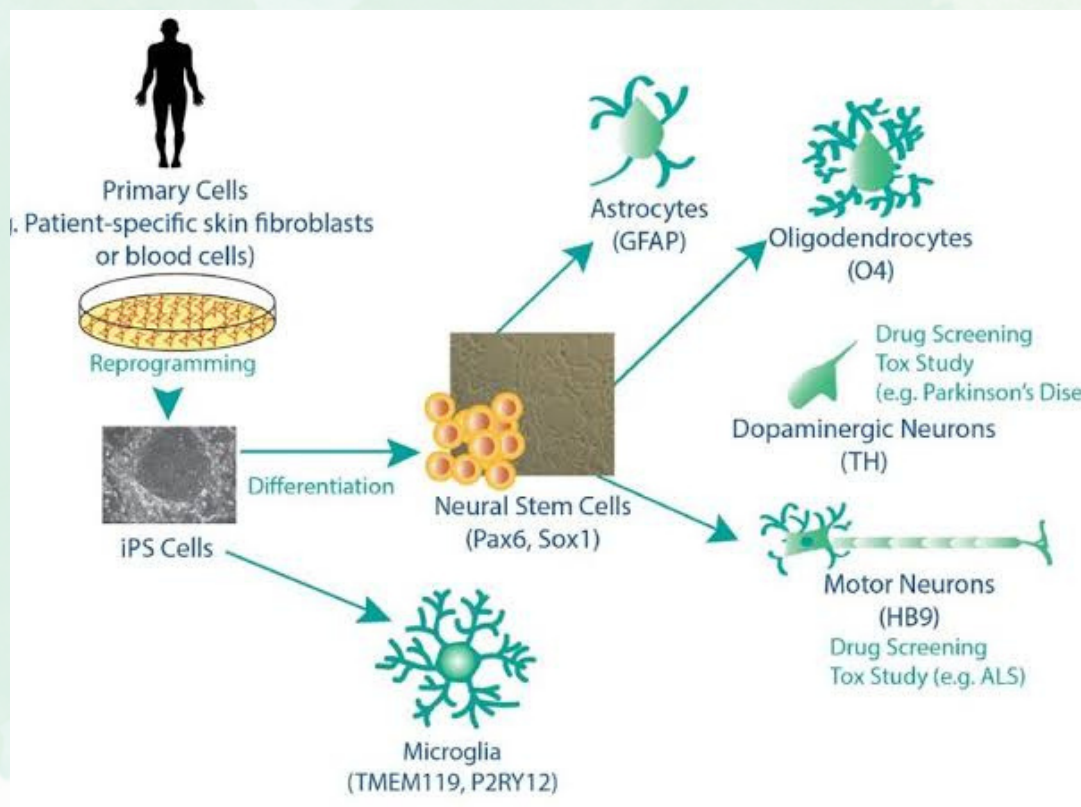


- Skin stem cells as well fall into the classification as somatic stem cells, however, due to the cellular heterogeneity of skin, various types of skin stem cells were found in past decades. Recently, significant advances have been made in identifying different types of skin stem cells with the aid of molecular tools. Subgroups of skin stem cells are listed as below.

SUBGROUPS OF SKIN STECELLS ARE LISTED AS BELOW:

- Epidermal stem cells- Most resided in the basal layer of epidermis, can derive into transient amplifying cells and terminal-differentiated epidermal cells. Specified cell markers are p63, β 1high/melanoma chondroitin sulfate proteoglycan + (MCSP+), α 6high/CD71dim.
- Follicular stem cells- Located at the follicle bulge region, can derive into hair follicle epithelium, including outer root sheath, inner root sheath, and hair shaft. Specified cell markers are K15, CD34, Lgr5, Sox9, Lhx2, NFATC1, NFIB, K15, PHLDA1, CD200, K19, etc.
- Melanocyte stem cells- Located at the follicle bulge region and hair germ. Specified cell markers are Dct, Sox, and Pax3
- Mesenchymal stem-cell-like cells- Located at dermis, might divide into Mesodermal derivatives and some neural cell types. Specified cell markers are CD70, CD90, and CD105 whereas negative for CD34
- Neural progenitor cells- Located at the follicle dermal papillae, might divide into neural and glial lineages, shared similar cell markers as counterparts in other organs or tissues.

4. Neuronal Stem Cells



- Neural stem cells are largely undifferentiated cell originating in the central nervous system.
- They have the potential to give rise to offspring cells that grow and differentiate into neurons and glial cells.
- Typically, NSCs are defined by three cardinal characteristics: self-renewal potential, neural tripotency (i.e., the capability to give rise to all of the major neural lineages: neurons, astrocytes and oligodendrocytes) and competence for in vivo regeneration
- They are located in two distinct re-gions of brain. One population is located in the subventricular zone of the forebrain (SVZ), which is the most active neurogenetic area and the richest source of NSCs

- Transplantation of neural stem cells or their derivatives into a host brain and the proliferation and differentiation of endogenous stem cells by pharmacological manipulations are potential treatments for many neurodegenerative diseases and brain injuries, such as Parkinson's disease, brain ischemia and spinal cord injury.
- Several studies have shown that NSCs can be extracted from neural tissue or generated from pluripotent cellular sources, genetically manipulated and differentiated in vitro.

5. Intestinal Stem Cells:

- These are multipotent stem cells that can generate all kinds of differentiated cell types of the small intestine and the colon including the predominant enterocytes (the absorptive cells); the mucus-secreting Goblet cells; the peptide hormone se-creting enteroendocrine cells and the Paneth cells.).
- They are responsible for the remarkable ability of the intestinal epithelium to efficiently renew and repair itself throughout life.
- The intestinal stem cells reside within specialized instructive niches at the crypt base. WNT is an essential niche factor supplied by both Paneth cells and non-epithelial cells.
- ISCs are scarce in number, not concentrated in distribution, and lack of highly specific markers.
- Active ISCs are usually localized to the base of crypts and characterized by expression of Leucine-rich repeat-containing G protein-coupled receptor 5
- ISCs are a type of adult stem cells located at the base of the intestinal mucosal crypts. Normally, they continue to proliferate, differentiate, and migrate to the top of the crypts.



RESEARCH : DONE TILL DATE



By - Janhavi Kadam



CHENNAI-BASED INSTITUTE TO BEGIN CLINICAL TRIAL ON STEM CELL THERAPY FOR LIVER DISEASE

Doctors at the Stem Cell Research Centre, Government Stanley Medical College Hospital (GSMCH), are in the process of recruiting patients for conducting phase I and II clinical trials of Stem Cell Therapy for end-stage liver disease to assess its safety and efficacy.

The clinical trial comes as a significant move as presently, liver transplant is the only treatment available for end-stage liver disease, but scarcity of donor organs necessitates alternative modalities.

Dr Secunda Rupert, Co-Investigator at Stem Cell Research Centre, GSMCH told TNIE that liver transplant is currently the only option for end-stage liver disease. "Many patients are on the waiting list for liver transplant. So these stem cells can be used as a bridge till they get donor liver for transplant and in some cases, it can be a wholesome therapy.

According to data from the Transplant Authority of Tamil Nadu (TRANSTAN), there are 418 patients waiting for liver transplant in the State alone.

"The CDSCO gave approval and also directed to conduct more animal studies. We will first conduct them and then will start the clinical trials.

Total of 30 patients will be recruited for clinical trials, and among them 15 will be put on Stem Cell Therapy and 15 on standard treatment, added Secunda.

IIT MADRAS RESEARCHERS OBTAIN CANCER CELLS WITH STEM CELL CHARACTERISTICS USING MICROGRAVITY

Researchers from Institute of Technology Madras (IIT-M) have found that subjecting cancer cells to microgravity results in the formation of giant cancer cells with stem-cell characteristics. These cells can conceivably be used for cancer research and drug development.

The research was led by Prof Rama S Verma, Stem Cell and Molecular Biology Laboratory, and School of Biosciences, Department of Biotechnology, IIT Madras.

Speaking about the practical application of this research, Prof Verma said, "We have shown that simulated microgravity can be used for development of stem cell structures for drug testing, instead of animal models. Cancer Stem Cells (CSC) are important in cancer research because they not only instigate formation of tumour, but are also involved in recurrence of tumours after cancer treatment."

The research team found that microgravity causes the formation of giant, haploid (containing more than one nucleus) cancer cells that have stem-cell characteristics. The team found that these giant cells are formed because microgravity affects the 'Hippo pathway', a signalling mechanism that controls organ size in animals through balance of cell growth and death. It also causes the localization of YAP, a regulator of cell growth, in the nucleus, which causes extensive cell growth and differentiation.





RESEARCHERS AT SRU IN CHENNAI ISOLATE STEM CELLS FROM HUMAN GUM TISSUE, TURN THEM INTO NERVE CELLS

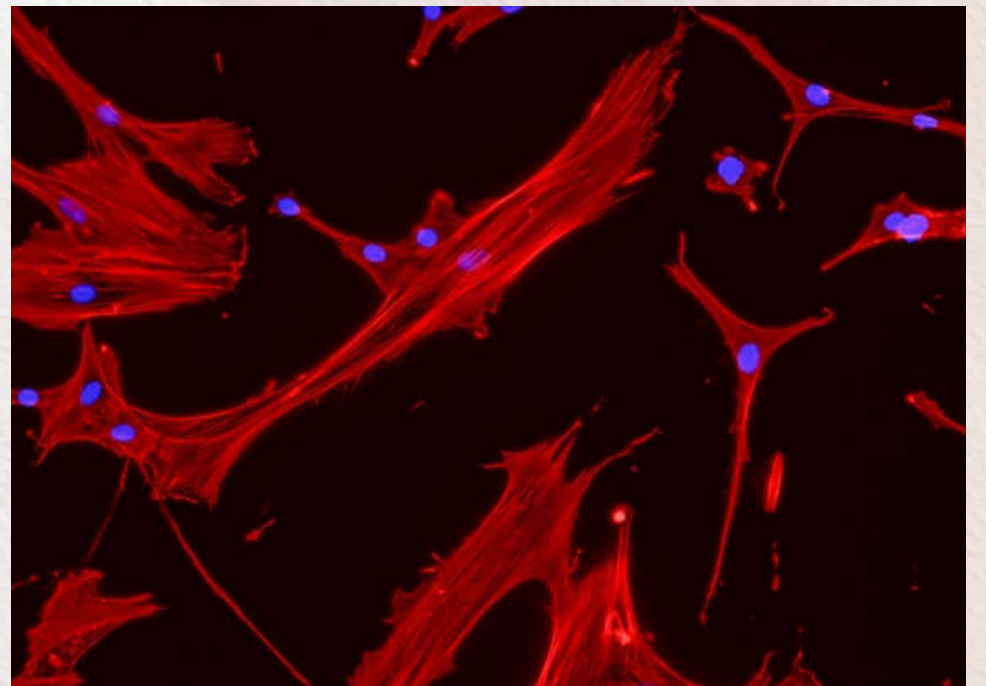
For the first time in the country the stem cell research group at the Sri Ramachandra University (SRU) in Chennai has isolated stem cells from human gum tissue and turned them into nerve cells. Currently, these stem cells are being tried in spinal cord injury in animals at the SRU, sources from the university informed. Stem cells aid in regenerating to original form. But there is a limitation on procuring ideal potent cells and gingiva (gum) fills the gap. Gum has tremendous healing capacity and they heal without scar. Hence we wanted to observe if the gum has stem cells and to analyse their nature, said Dr Suresh. The research wing at SRU, within last one year, grew stem cells after obtaining gum tissue from humans. After certain period of time they were able to separate stem cells from gum tissue. By using specific identification markers they confirmed the cells as stem cells

SCIENTISTS CREATE FIRST COMPREHENSIVE MAP OF HUMAN BLOOD STEM CELL DEVELOPMENT

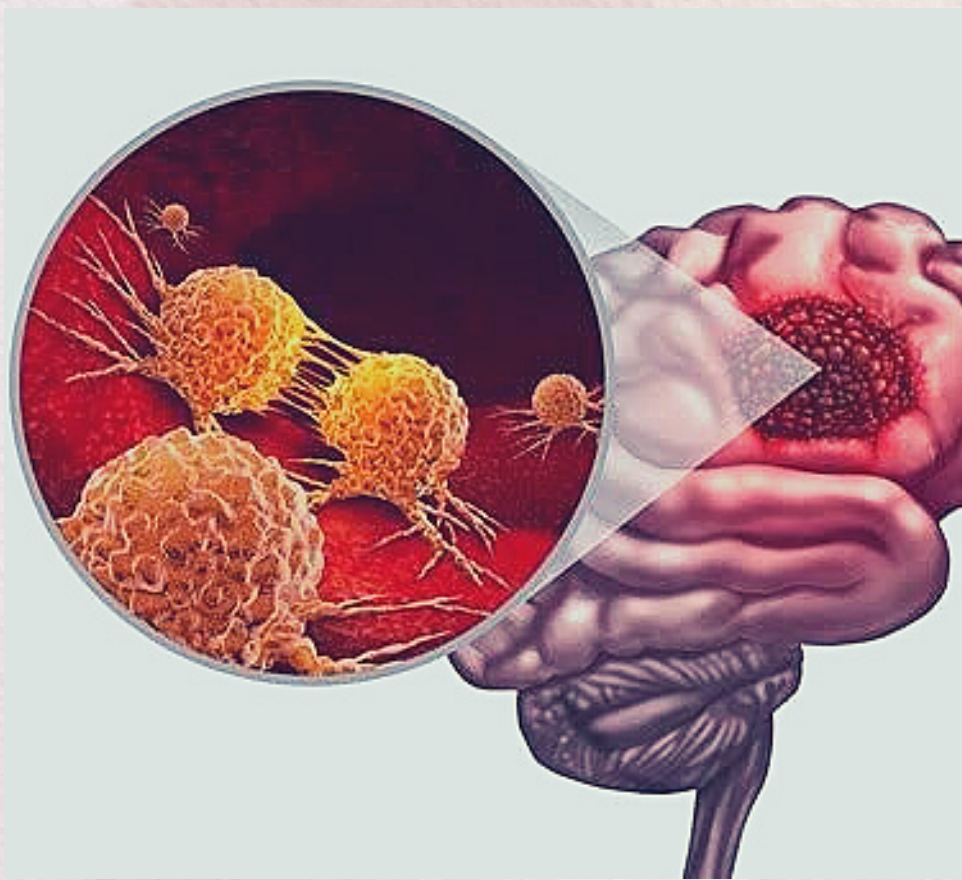
UCLA scientists and colleagues have created a first-of-its-kind roadmap that traces each step in the development of blood stem cells in the human embryo, providing scientists with a blueprint for producing fully functional blood stem cells in the lab.

The research team, which included scientists from Germany's University of Tübingen and Australia's Murdoch Children's Research Institute, created the resource using single-cell RNA sequencing and spatial transcriptomics, new technologies that enable scientists to identify the unique genetic networks and functions of thousands of individual cells and to reveal the location of these cells in the embryo.

The data make it possible to follow blood stem cells as they emerge from the hemogenic endothelium and migrate through various locations during their development, starting from the aorta and ultimately arriving in the bone marrow. Importantly, the map unveils specific milestones in their maturation process, including their arrival in the liver, where they acquire the special abilities of blood stem cells.



<https://scitechdaily.com/innovative-experiment-reveals-the-complex-dynamics-of-stem-cell-tethers-and-slings/amp/>



“OFF THE SHELF” ENGINEERED STEM CELLS CREATED TO TREAT AGGRESSIVE BRAIN CANCER

Glioblastomas (GBMs) are highly aggressive cancerous tumors of the brain and spinal cord. Brain cancers like GBM are challenging to treat because many cancer therapeutics cannot pass through the blood-brain barrier, and more than 90% of GBM tumors return after being surgically removed, despite surgery and subsequent chemo- and radiation therapy being the most successful way to treat the disease. In a new study led by investigators at Brigham and Women’s Hospital and Harvard Medical School, scientists devised a novel therapeutic strategy for treating GBMs post-surgery by using stem cells taken from healthy donors engineered to attack GBM-specific tumor cells. This strategy demonstrated profound efficacy in preclinical models of GBM, with 100 percent of mice living over 90 days after treatment. Results will be published today (May 19, 2022) in the journal Nature Communications.

<https://doi.org/10.1038/s41467-022-30558-3>



Muscling in: stem cells are injected into a patient’s heart during bypass surgery.

Cardiologists take heart from stem-cell treatment success

Erika Check, Washington

NATURE | VOL 428 | 29 APRIL 200

INNOVATIVE EXPERIMENT REVEALS THE COMPLEX DYNAMICS OF STEM CELL TETHERS AND SLINGS

An innovative experiment design shows, in real time and at the scale of a single molecule, how stem cells slow their rolling inside the circulatory system by growing long tethers that attach to the inner surfaces of blood vessels. The strategy could help researchers to improve stem cell transplantations and to find new treatments for metastasizing cancers.

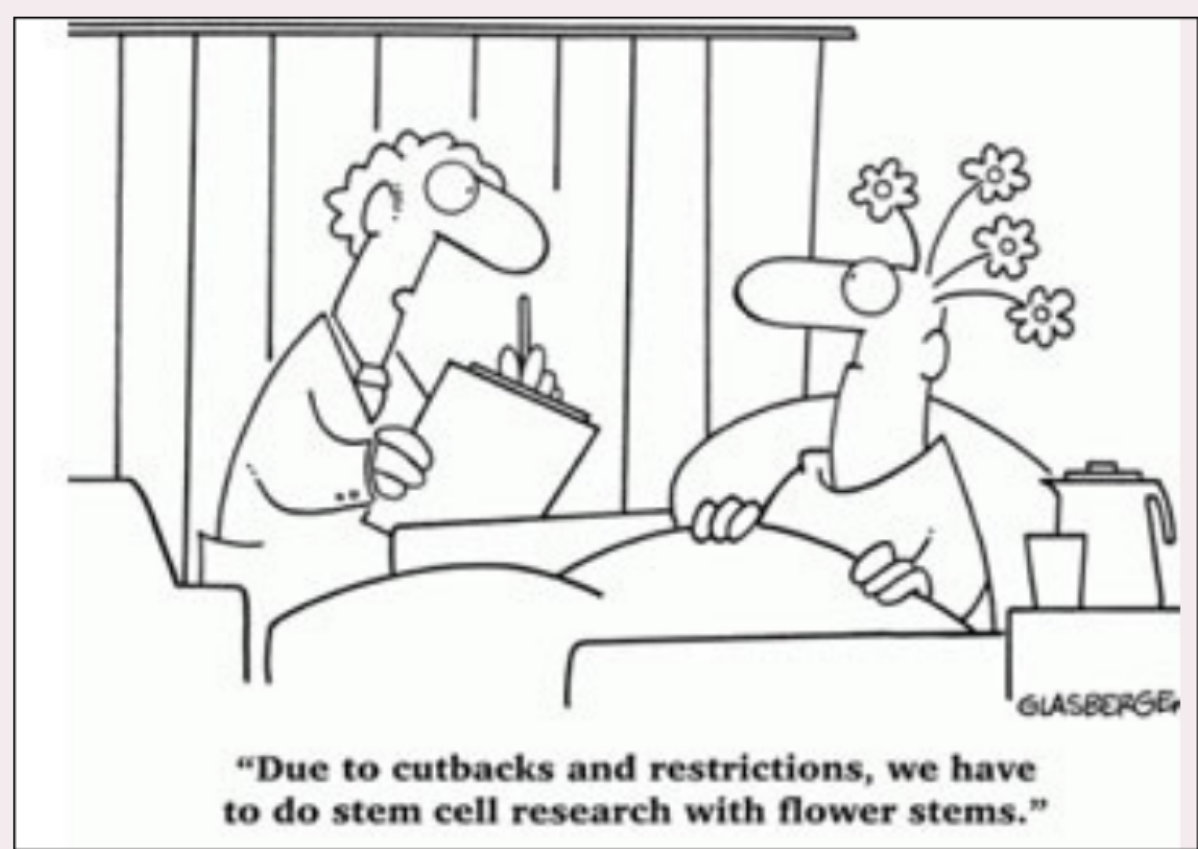
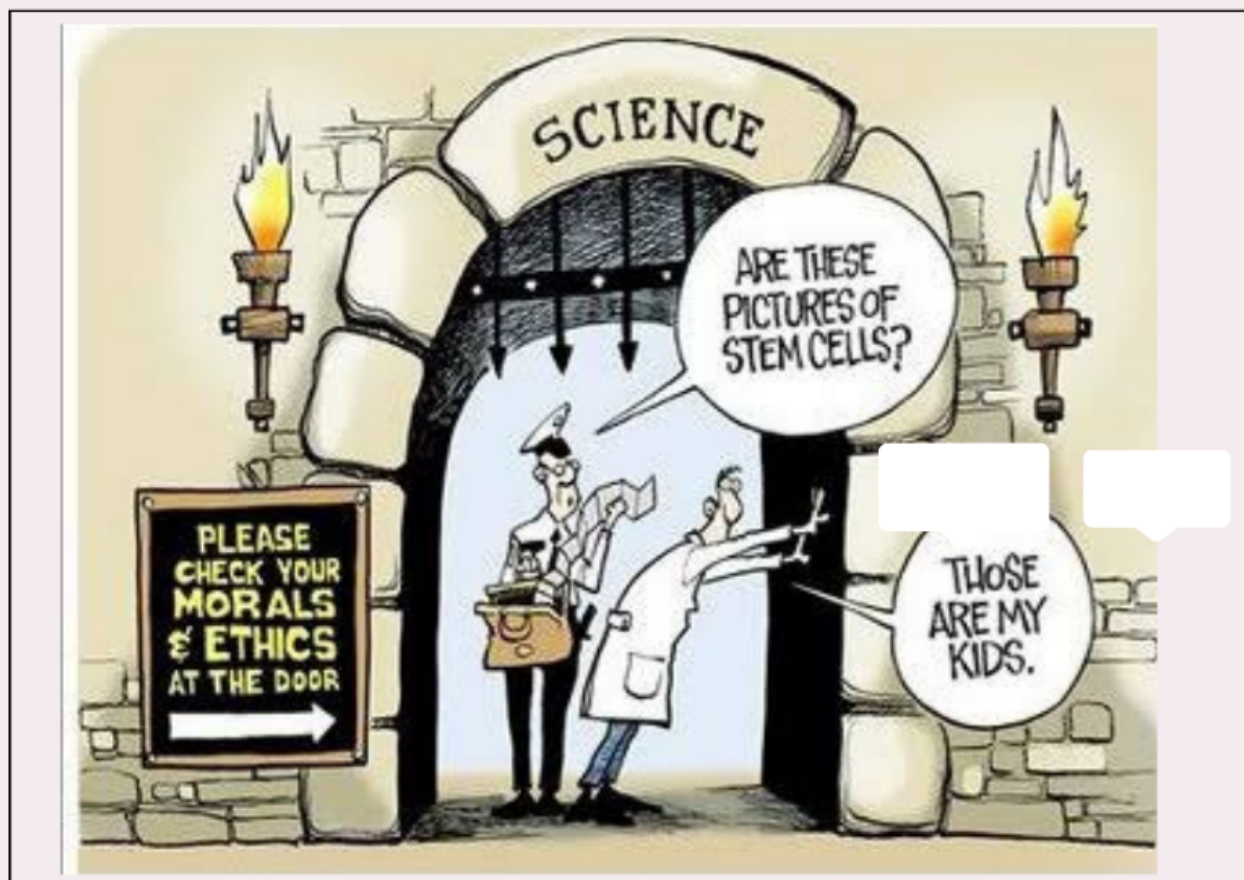
“Our research is focused on understanding how various cells move in the body using adhesion systems. For example, one goal is to improve stem cell movement in the body so they can get where they are needed following transplantation or in other disease settings. We are also focused on understanding how and why cancer cells outperform normal cells in their ability to migrate so that we can develop methods to inhibit their



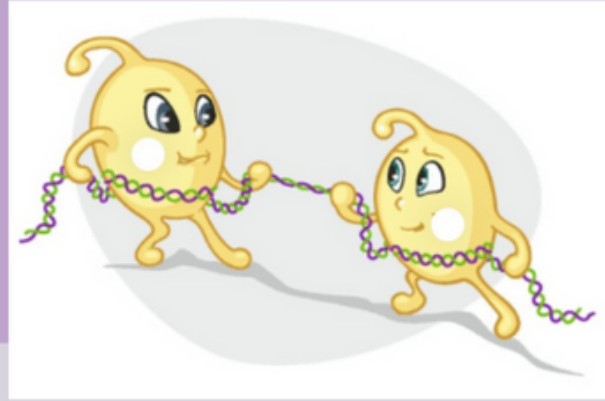
metastasis. Using the sophisticated assays developed by Satoshi and his team.

MEMES CORNER

JANHAVI KADAM



*Listen daughter, you have got to want
to be more than a epithelial cell*



Demanding stem cell parents

JANHAVI KADAM

**You can be anything
you want to be when
you grow up**



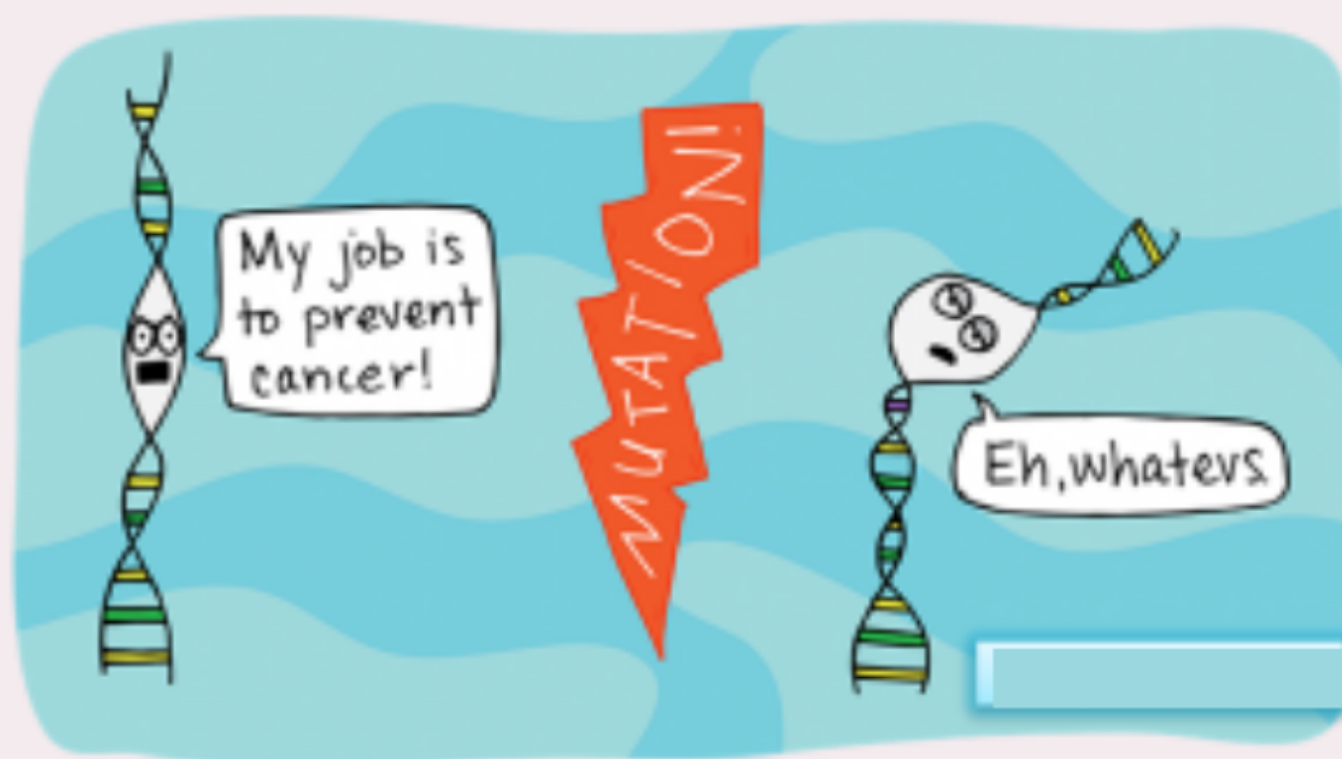
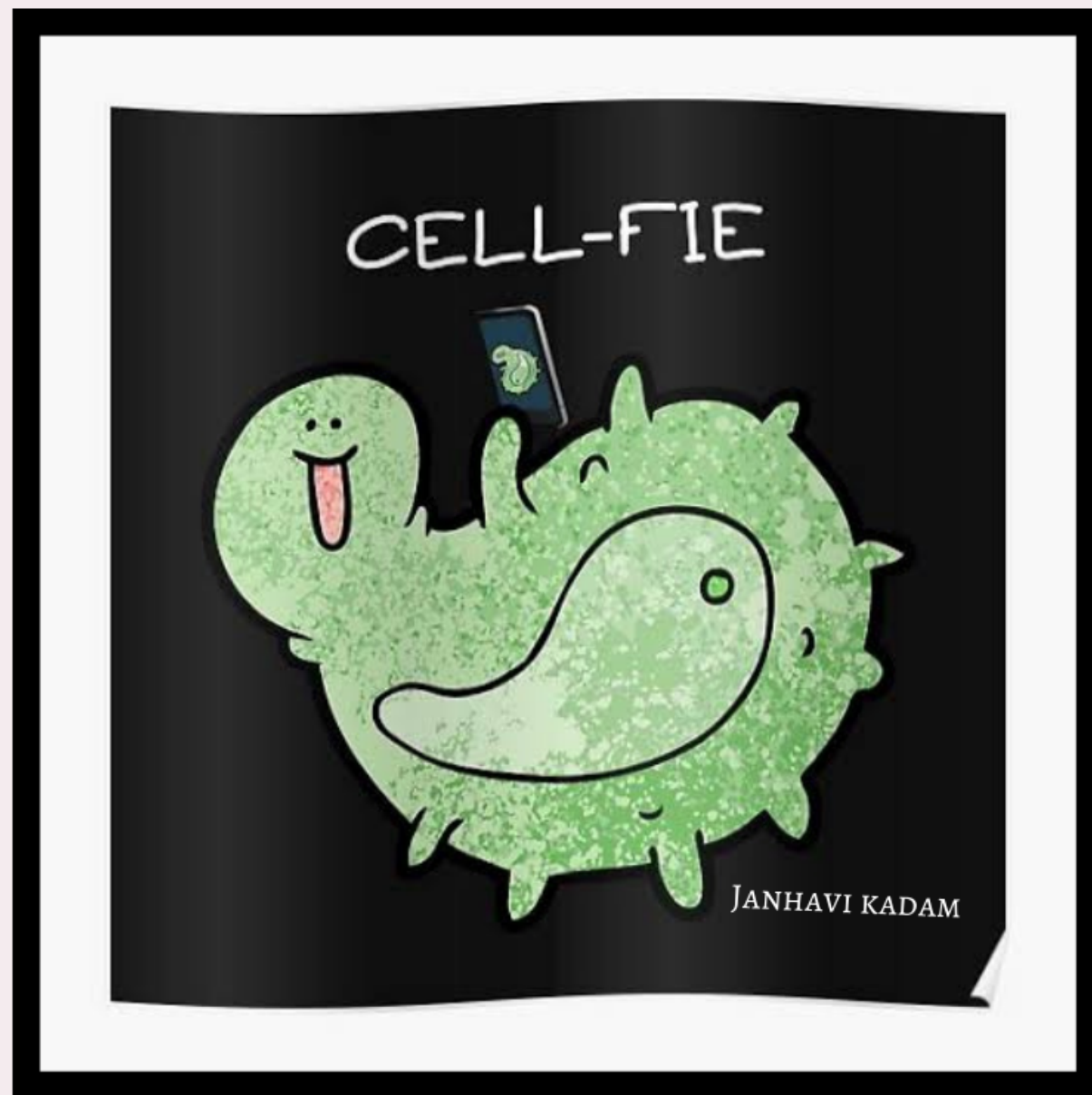
STEM CELL parental advice

JANHAVI KADAM

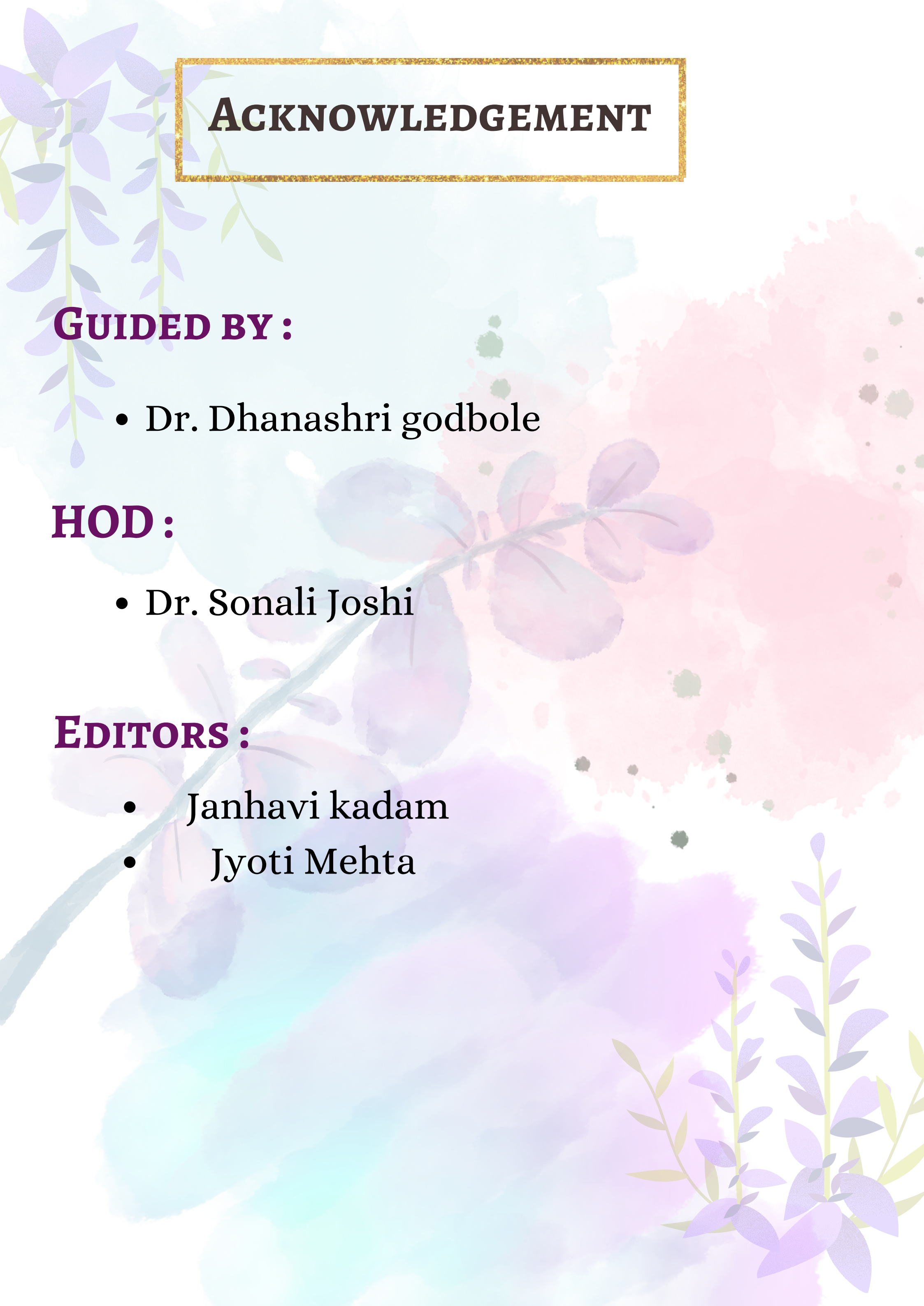
Stem Cell Therapy is the
miraculous new formula whose
testing suggests
it can help your skin's stem cells
generate smooth new skin cells.

Reminds me of:





The most common cause of cancer: mutation.



ACKNOWLEDGEMENT

GUIDED BY :

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HOD :

- Dr. Sonali Joshi

EDITORS :

- Janhavi kadam
- Jyoti Mehta