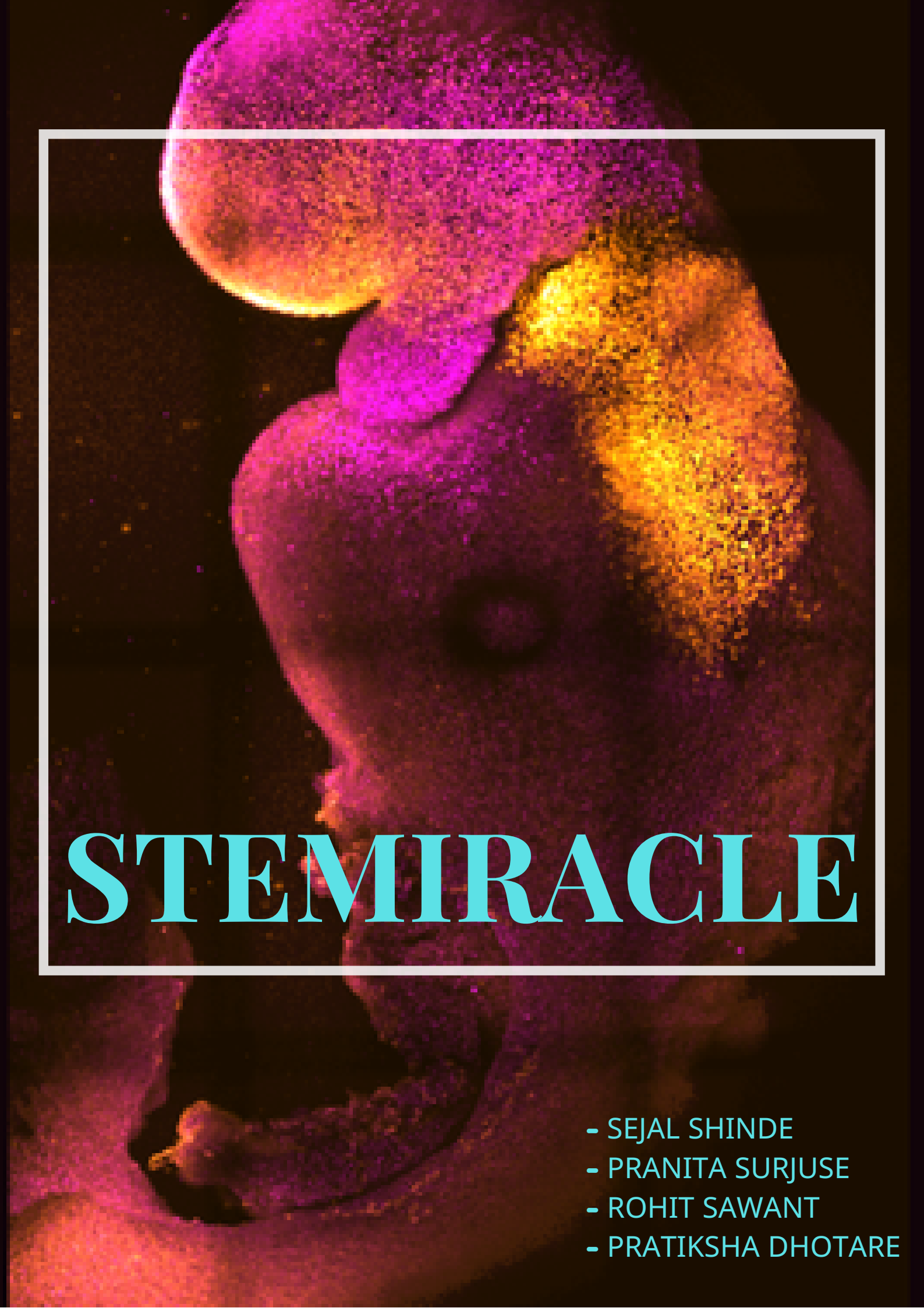




STEMIRACLE

- SEJAL SHINDE
- PRANITA SURJUSE
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- PRATIKSHA DHOTARE

Stem cells curing Cancer

By-Sejal Shinde

Cancer is the most dangerous disease by causing millions of deaths worldwide. Despite of rapid advancement in research of diagnostics and therapeutics, the death rate by cancer only declined ~1.5% annually in the period of 2006–2015 in United States. Comprehensive knowledge about cancer biology would allow scientists to design better therapeutic systems.

Some day, stem cells will be enlisted to help repair or replace damaged tissues and organs. They will rescue us from diseases for which drugs can only treat the symptoms.

Stem cells are key to our normal development and health from conception through adulthood. Embryonic stem cells produce the progenitors and determine how our organs, muscles, sinews, and skeletons are formed and how they are arranged in the body..

Stem cells survive much longer than ordinary cells, increasing the chance that they might accumulate genetic mutations. It might take only a few mutations for one cell to lose control over its self-renewal and growth and become the source of cancer.



Ernest McCulloch and James Till

The idea that the remnants of our embryonic past could lead to our demise through cancer is actually a longstanding hypothesis, tracing back to 1829.

Throughout the mid-19th century, theories and observations accumulated that tumors were linked to embryonal tissue growth, culminating in a comprehensive **“Embryonal rest”** theory put forward by Julius Cohnheim in 1875.



Dr. John Dick

The theory stated that tumors may arise from embryonic cells left over from development, and that lie dormant until activated to become **cancerous**.

Today's theories about the involvement of stem cells in cancer are really an update of the embryonal rest theory, only now we know more precisely which types of cells are involved. This advance in knowledge, more than 150 years after the theory was first proposed, came about because we now know how to identify stem cells within tumors by the protein markers on their surface.

Searching for these markers, John Dick and colleagues at the University of Toronto confirmed in 1997 that certain types of leukemia originated from a subpopulation of stem cells. In 2003, Michael Clarke of the University of Michigan and now at Stanford, found **cancer** stem cells in breast tumors and demonstrated that most other cells in the tumor were incapable of seeding growth on their own. Others followed with similar discoveries in brain cancer, colon cancer, bone cancer and melanoma.

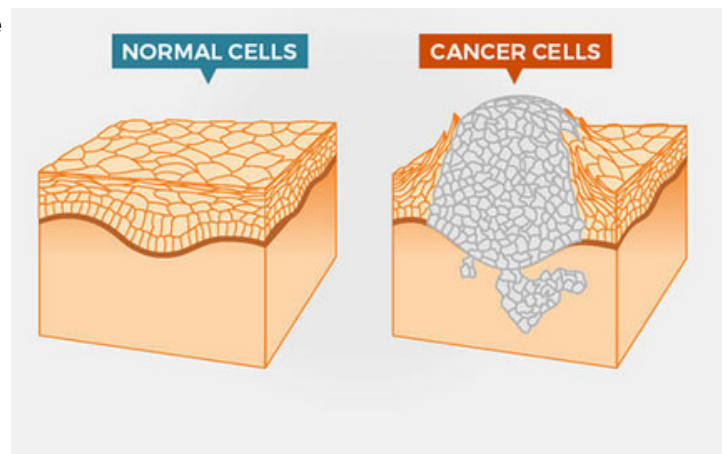
A TALE OF TWO CELLS

-PRATIKSHA DHOTARE

Stem cells are the undifferentiated stage cell in animal development, that have a potential to differentiate into one or more cell types depending on their level of differentiation along with indefinite self-renew capacity.

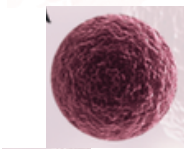
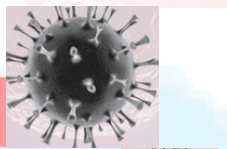
Cancer is the abnormal growth of cells that proliferate uncontrollably and, in some cases, metastasize (spread).

Cancer stem cells are cells within the cancer microenvironment and niche that have the ability to self-renew and cause the tumor's heterogeneous lineages of cancer cells.



COMMON FEATURES FOUND IN NORMAL AND CANCER STEM CELLS:

- Capacity for asymmetric divisions (self-renewal) that produces a quiescent stem cell and a dedicated progenitor and plays important role toward emerging a dangerous cell mass.
- Regulation of self-renewability by similar signaling pathways (Wnt, Sonic Hedgehog, MAPK and Notch) and at the epigenetic level by BMI-1.
- Extended telomeres and telomerase activity that increases the cellular life span.
- Stimulation of angiogenesis through secretion of angiopoietic factors.
- Expression of similar surface receptors (e.g., CXCR4, CD133, $\alpha 6$ integrin, c-kit, c-met, LIF-R) those are either identified as stem cell markers or are associated with homing and metastases.

	Normal stem cell	Cancer Stem Cell	
	Extensive but limited self-renewal capacity	Extensive and indefinite self-renewal capacity	
	Organogenic capacity	Tumorigenic capacity	
	Highly regulated self-renewal and differentiation	Highly dysregulated self-renewal and differentiation	
	Rare in normal adult tissues	Infrequent or rare within tumors	
	Can be identified based on surface markers	Similar types of surface markers as ordinary stem cells in the same tissue	
	Normal karyotype	Abnormal karyotype	

Article: STEM CELL AND CANCER STEM CELL;A Tale of Two Cells

MdShaifur Rahman , Hossen Mohammad Jamil , Naznin Akhtar K.M.T. Rahman , Rashedul Islam , S.M. Asaduzzaman

Types Of Stem Cells for Cancer Treatment

By-Pranita Surjuse

Stem cells from different sources exhibit different capacities of proliferation, migration, and differentiation, which determine their application in anti-tumor therapy.

- **Embryonic Stem Cells (ESCs):**

ESCs, isolated from the undifferentiated inner mass cells of embryo, possess the ability to give rise to all types of cells except those in the placenta. However, the applications of ESCs for clinical trials are restricted due to ethical considerations.

- **Pluripotent Stem Cells (iPSCs)**

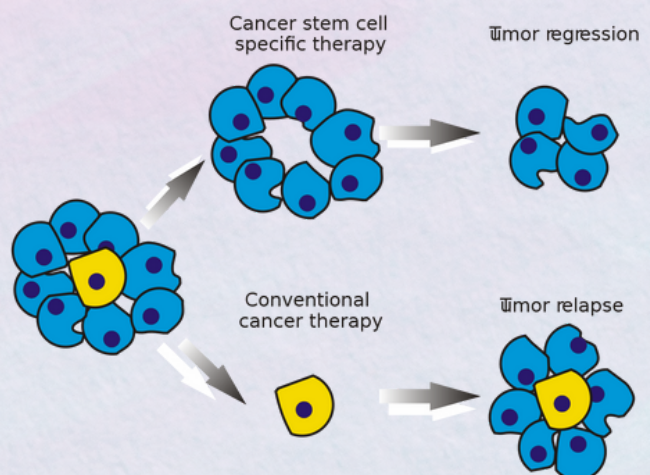
In 2006, the invention of Yamanaka factors to Induce pluripotent stem cells (iPSCs) from somatic cells in culture marked breakthrough in cell biology. iPSCs have same characteristics as ESCs, removing ethical concerns from embryo destruction, and both hESCs and iPSCs are important sources for the induction of effector T- and NK cells, and for the production of anti-cancer vaccines.

- **Adult Stem Cells (ASCs):**

- ASCs give rise to hematopoietic stem cells (HSCs), mesenchymal stem cells (MSCs) and NSCs that are often utilized in cancer treatment.
- HSCs, located in bone marrow, can **form all mature blood cells** in the body. Contributing to cancer treatment, the infusion of HSCs derived from cord blood is the only procedure of stem cells that were approved by the FDA to treat multiple myeloma, leukemia, and some kinds of blood system disorders.
- MSCs, found in many tissues and organs, playing important roles in tissue repair and regeneration, possess unique biological properties and have been extensively used to support other therapies or to deliver therapeutic agents in treating a variety of cancers.
- NSCs, originally present in the central nervous system, can self-renew and generate **new neurons** and glial cells. They treat both primary and metastatic breast, lung, and prostate cancers in murine models.

- **Cancer Stem Cells (CSCs):**

CSCs, so-called stem-like cells or immature progenitors of tumor cells or tumor-initiating cells, are generated by epigenetic mutations in normal stem cells or in precursor/progenitor cells. CSCs are found within tumor tissues, playing important roles in cancer growth, metastasis, and recurrence. Therefore, targeting CSCs could provide a promise to treat various types of solid tumors.



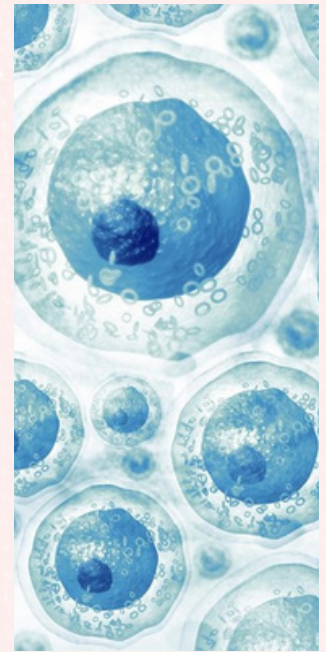
Cancer stem cell markers

- Each type of cancer cell exhibit a unique set of molecular and biochemical markers.
- Cancer cell biomarkers can be used to target residual cancer Stem cells and used for target therapy.
- Some cancer types and their common marker proteins are:

1. Glioma/Medulloblastoma, head and Neck cancers, Lung, Prostate, Melanoma, Osteosarcoma - Marker ABCG2

(ATP-binding cassette transporter)

2. Breast, Pancreas, Liver, Oesophagus, Gastric - Marker CD24
Osteosarcomas, Leukemia, ovarian cancers, Melanomas,
Laryngeal cancers - Marker CD105/Endoglin



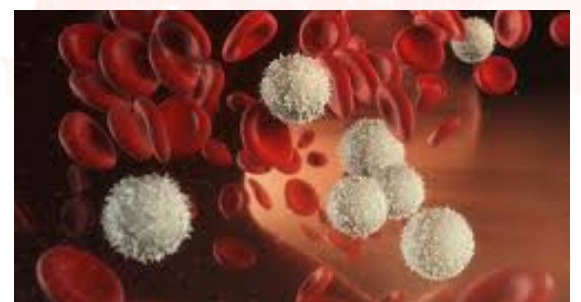
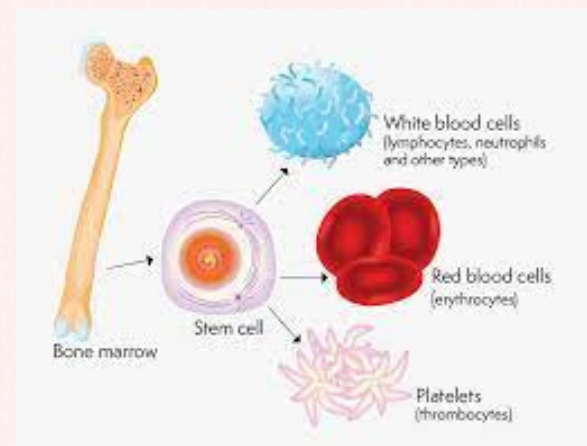
Is Embryonic stem cells (ESCs) or adult stem cells (ASCs) be the source of stem cells for Cancer therapy?

Ideally, ESCs would be the source of stem cells for therapeutic purposes due to higher totipotency and indefinite Life span compared to ASCs with lower totipotency and restricted life span. Because of ethical constraints ,their use for research and therapeutic purposes are restricted and prohibited in many countries throughout the world. ESCs with higher totipotency have been shown to be more tumorigenic in mice. Thus, for ease of availability and lesser constrained on ethical issue, ASCs are the stem cells most commonly used for research and therapeutic purposes.

ESCs are derived from a 5-day old pre-implantation human embryos, however it posses potential risk of destroying the embryo. ASCs can be obtained from many tissues including bone, synovium, deciduous teeth, adipose tissue, brain, blood vessels, blood and umbilical cord blood. Most commonly, ASCs are acquired from the bone marrow and peripheral blood.

Choice of type of stem cell : bone marrow or peripheral blood

The source of stem cells is most commonly either from the bone marrow or the peripheral blood. The procedure of the bone marrow aspiration is invasive and is associated with the potential possible complications including fracture, wound infection and sepsis while the procedure for PBSCs isolation is much less invasive and less morbid. PBSCs have also been shown to induce higher number of CD4 T and NK cells compared to stem cells obtained from the bone marrow . Thus, the stem cells from peripheral blood are considered the preferred source of stem cells "however various clinical trials have publicized controversial conclusions comparing PBSCs and BM stem cells".



Implications for Cancer Treatment

By-Pranita Surjuse

Treatments for cancer vary according to cancer type and severity, in which surgery, radiation therapy, chemotherapy or hormonal therapy represents the traditional approaches. Tumor metastasis is a complex process. It is the key to improve the prognosis of patients by removing CSCs selectively with no significant toxicity. Several pieces of instances have been put forward surrounding this conclusion:

1. Appropriate microenvironment exhibits vital importance for CSCs, thus **inhibiting the cell survival microenvironment** and mechanism can aid in treatment.
2. The **exploration of self-renewal pathways** of the defective cancer cells may provide a new treatment for cancer.
3. Potential approaches to killing CSCs also include inducing **tumor cell differentiation**.

Wnt pathway plays a critical role in the self-renewal and maintenance of stem cells. A recent report documents that rapamycin-mediated inhibition of mTOR signaling may prevent CSC self-renewal and circumvent CSC-mediated resistance to cancer therapeutics.

Metformin not only selectively killed existing CSCs, but also indirectly lowered the CSC burden by inhibiting the conversion of non-stem cancer cells to CSCs.

Recent study indicates that salinomycin, a specific inhibitor of P-glycoprotein, can restore a normal drug sensitivity of Multiple Drug Resistance (MDR) cell lines and induce CSC death.

Cell differentiation is regulated, at least in part, by a recent discovered class of molecules-microRNAs (miRNAs), and as a consequence, a potential therapeutic use of miRNAs is to correct these aberrant transcript levels involved in the signaling pathways of cancer cells, especially CSCs.

Review Article: *The Implications of Cancer Stem Cells for Cancer Therapy*

STEM CELL THERAPY: MYTHS AND FACTS

Ref :onlymyhealth



-PRATI KSHA DHOTARE

Myth:

Stem cells are sourced from the embryo

Fact: One of the major controversies though is the source of stem cells. It is believed that embryonic stem cells are used for treatment, which is not only unethical but can also result in tumor formation. The preferable source are adult stem cells.

Myth: Stem cells results are temporary

Facts: While it is true that cells in our bodies are constantly renewing, this is a normal part of the ageing process, once injected, stem cells tend to enhance the functions of other cells while also setting off with their inherent functions. As a result, even if the stem cells eventually differentiate and 'grow old,' a series of healing events have already occurred, aiding in the continuation of the regenerative processes.

Myth:

There are only a few diseases that stem cell therapy can treat

Fact: Stem cell therapy is thought to be the only treatment for conditions such as sports injuries, arthritis, wounds, and so on. However, because stem cells have immunomodulatory properties, autoimmune conditions (such as type 1 diabetes) respond to therapy as well. Cancer immunotherapy, which uses immune system cells to treat cancer, has opened up new avenues of target-specific treatments that have overcome the drawbacks of traditional chemo- and radiotherapy.

conclusion:

Overall, the possibilities of stem cell therapy are endless. Be aware of fraudulent claims obtaining correct information from qualified professionals regarding stem cell therapy is the need of the hour.

Docs transplant stem cells in Cancer patient

Mangaluru: The medical oncology specialist team of Dr Guruprasad Bhat and Dr Najeeb Behzad Mohammed successfully performed an autologous stem cell transplant in a 20-year-old cancer patient at Unity Hospital recently.

The patient was suffering from Hodgkin's Lymphoma, a type of blood cancer.

He initially received chemotherapy.

When the cancer relapsed, he was referred for bone marrow transplant.

The procedure involved stem cell apheresis and cryopreservation followed by high-dose chemotherapy for four days. This was followed by a reinfusion of stem cells. Then the patient was under intensive care till the engraftment of stem cells on the tenth day.

The patient was discharged the next day after engraftment.

Cancer patient gets stem cell transplant

Bhubaneswar: The Institute of Medical Sciences and Sum Hospital, of Siksha O Anusandhan deemed to be university, has successfully conducted bone marrow transplant (BMT) or autologous stem cell transplantation on a lymphoma patient. The challenging procedure was conducted on a 33-year-old patient suffering from lymphoma, a type of blood cancer, by following the cryopreservation process. Head of the department of clinical haematology and haemato oncology, Priyanka Samal, said it is the first hospital in the state to have undertaken stem cell transplantation on a lymphoma patient.

Son lost to leukaemia, man donates stem cells to save teenage girl's life

AHMEDABAD: Kishor Patel, 45, is haunted by the day in 2004 when his son Mohit, only one year and nine months old, died in his lap. "He slipped into a deep sleep and never woke up.

He was my first child, and the sheer helplessness of not being able to save his life cut into me day and night," says Kutch and Bengaluru-based timber businessman. Mohit lost his battle to terminal blood Cancer. The Patel family, which desperately reached out to even doctors in the US for consultation, were crestfallen as the cancer was detected in advanced third stage and did not respond to drugs. Patel finally got closure 17 years after his son's death when he became the means to save another family's daughter. "I donated stem cells for a teenage girl battling leukemia in 2021 to save her life. I see this as a divine intervention. It also motivated me to be a crusader for the cause of stem cell donation to save other children's lives."

Patel had donated his stem cells for the cause in December 2020 when the spectre of Covid pandemic loomed large. Officials of DKMS-BMST, the foundation established to create awareness about blood Cancer, thalassemia and other blood disorders and promoting stem cell donation, said that the transplant was a success. In 2017, in an event by DKMS-BMST, he got to know about the stem cell donation and got himself enrolled with his blood sample. He got a call in December 2020 from the foundation to donate and he agreed immediately.

Patrick Paul, CEO of DKMS BMST Foundation, said that Patel donated his stem cells through peripheral blood stem cell (PBSC) method, which is similar to blood platelet donation.





Intra-Tumor Heterogeneity of Cancer Stem Cell-Related Genes and Their Potential Regulatory

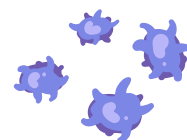


Snail Maintains the Stem/Progenitor State of Skin Epithelial Cells and Carcinomas through the Autocrine Effect of Matricellular Protein Mindin

Non-Coding RNAs and Glioma: Focus on Cancer Stem Cells

Functions and Underlying Mechanisms of lncRNA HOTAIR in Cancer Chemotherapy Resistance

Differential Expression of Hepatic Cancer Stemness and Hypoxia Markers in Residual Cancer After Locoregional Therapies for Hepatocellular Carcinoma



An Experimental Model for Ovarian Cancer: Propagation of Ovarian Cancer Initiating Cells and Generation of Ovarian Cancer Organoids

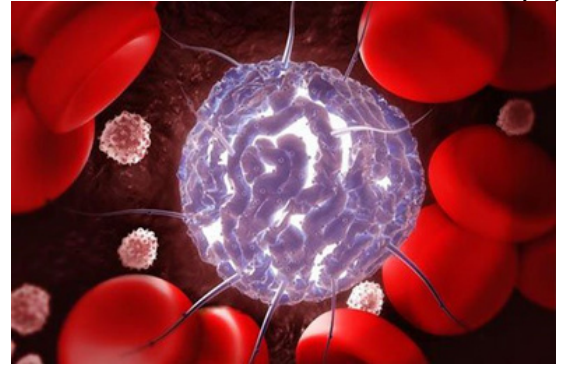
Fucoidan from Sargassum hemiphyllum Inhibits the Stemness of Cancer Stem Cells and Epithelial-Mesenchymal Transitions in Bladder Cancer Cells



An Anti-Alcoholism Drug, Disulfiram and Copper Complex Improves Radio-Resistance of Tumor-Initiating Cells in Esophageal Squamous Cell Carcinoma

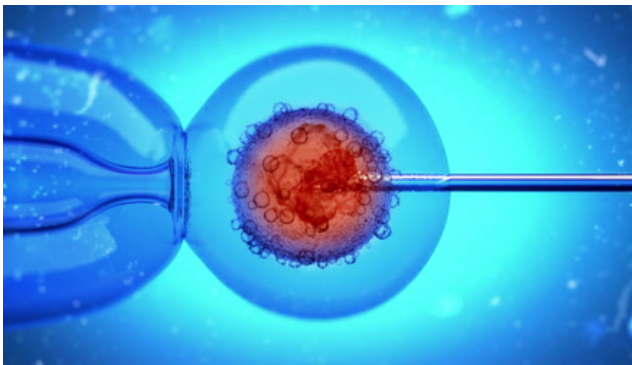
ETHICAL ISSUES

- Major issues in stem cell research are Obtaining, saving, maintenance, Using.
- Use of early embryonic stem cells has caused many ethical debates.
- Ethical, legal concerns are Destruction of embryo.
- Increasing rate of illegal abortion.
- Commercial exploitation. In case of both ESC'S and ASC'S.
- Embryos can not be created for research purpose.



Controversy

- Embryonic stem cells have not been adequately researched and dangers inherent in their medical use are largely unknown
- The harvesting of ESC'S requires death of the embryo.
- Donated embryos are in limited supply.



Alternatives

- Stem cells derived from bone marrow of adult can be reprogrammed to become pluripotent like ESC'S.
- Donation of adult stem cells between blood relatives
- Stem cells derived from amniotic fluid during amniocentesis

QUIZ TIME



1. What is a stem cell?

- a. A cell only found in the stem of plants.
- b. An unspecialized cell with the ability to create specialized cells
- c. A specialized cell who can only generate cells of the same type

2. What is the process of cell specialization called?

- a. Proliferation
- b. Differentiation
- c. Cryopreservation

3. What is the least invasive source of stem cells from the human body?

- a. Cord blood
- b. Adipose tissue

4. Cells or tissue donated by a related or unrelated individual are called

- a. Syngeneic
- b. Allogeneic

5. A stem cell transplant using a patient's own stem cells is described as...

- a. Syngeneic
- b. Autologous

6. Stem cell treatments are risk-free if they come from your own body.

- a. True b. False

7. In the treatment of burns, scientists can use stem cells to help them replace...

- a. All parts of the patient's skin
- b. Hair follicles and sweat glands
- c. The outermost layer of the skin

8. Which stem cells have the most potency?

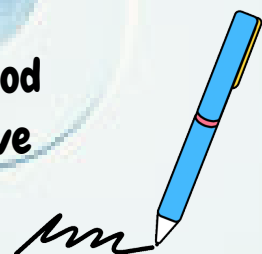
- a. multipotent
- b. pluripotent
- c. totipotent

9. ____ refers to the varying ability of stem cells to differentiate into specialized cell types.

- a) Cell potency
- b) Cell-regeneration
- c) Cell-therapy

10. Name two sources of "ethical" stem cell ?

- a. Cord blood
- b. Bone marrow
- c. Peripheral blood
- d. All of the above



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