STEM CELL IN CANCER DISEASE CURE VS CAUSE

By

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In partial fulfillment of the Bachelor of Pharmacy degree requirements, a thesis was submitted to the Department of Pharmacy.

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Declaration

It is made the following declaration:

1. The thesis I submitted was composed when I was studying at Brac University for my bachelor's degree.

2. No previously published or developed by a third party material may be utilized in the thesis unless it has been properly referenced with complete and correct referencing.

3. No material that has been approved or submitted for a degree or certificate from another university or institution may be included in the thesis.

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Approval

The thesis/project titled "**Stem cell in cancer disease cure vs cause**" submitted by Marisha Mansur Chowdhury (18146041), Summer 2021 has been acknowledged as acceptable in partial fulfilment of the Bachelor of Pharmacy degree requirement.

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Ethics Statement

There were no unethical works involved in doing the thesis. This study does not involve any kind of human or animal trial.

Abstract

Our bodies are made up of a variety of cell types. One of them is stem cells. Stem cells divide to make daughter cells in the body and in the lab. Daughter cells can self-renew or specialize into cells that fulfill a specific function (differentiation). Other cells in the body do not have the ability to regenerate. Disease, injury, or genetic illnesses may harm or destroy cells, tissues, and organs. Before being reintroduced into the body, stem cells are used to repair damaged or missing cells. New strategies for training embryonic stem cells to become specific cell types have been identified. Developing medicines that inhibit the self-renewal signals to cancer stem cells may be developed. The distinctions between normal and malignant stem cells might lead to novel cancer therapeutic targets.

Keywords

Stem cell, Embryonic, Pluripotent, Oncogenes, Leukemia, Immunotherapy, Apoptosis, Geminin, Cancer cell.

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List of Acronyms

ASC	Adult Stem Cell
MSC	Mesenchymal stem cells
NSC	Neural Stem cells
ESC	Embryonic Stem cell
iPSC	Induced Pluripotent Stem Cells
AMD	Age-Related Macular Degeneration
RPE	Retinal Pigment Epithelium
PDT	Photodynamic Therapy
CSC	Cancer Stem Cell
ECC	Embryonal Carcinoma Cells
TGF	Tumor Growth Factor
IFN	Interferon
TNF	Tumor Necrosis Factor
IL	Interleukin
HSC	Hematopoietic Stem Cell
PBSC	Peripheral Blood Stem Cells
EpiSC	Epiblast Stem Cell
AML	Acute Myeloid Leukemia

Chapter 1

Introduction

1.1 Background

Since 1990, the global cancer prevalence has increased from 0.54 percent to 0.64 percent (Sung et al., 2021). In 2020, 19.3 million new cancer patient are predicted to be diagnosed globally, with 10.0 million cancer deaths (Max Roser and Hannah Ritchie, 2019). Several studies shows that scientist developed stem cell therapy for cancer disease by targeting cancer stem cell pathways. Rituximab, a CD20 mAb, is effective in treating follicular and mantle-cell lymphoma (Yang et al., 2020). Anti-cancer vaccine development appears to be quite intriguing due to its high immunogenicity (Chu et al., 2020). Again some researchers examined ways to improve the functional potential, persistence, & homing of induced pluripotent stem cell (iPSC)-derived Natural killer (iPSC-NK) cells (Saetersmoen et al., 2019). For haematopoietic stem cell transplantation researcher endeavor to enhance patient outcomes and expand access to such a potentially life-saving therapy to people. It was first used to treat people with inherited anemias or immunological deficiencies via replacing the defective haematopoietic system with that of a healthy person. Second, it enabled the administration of myeloablative radiation and/or chemotherapy for cancer patients (Jenq & Van Den Brink, 2010). Again some researcher characterized and identified Cancer Stem Cell (CSC), and significant determinants and processes that influence CSC formation are depicted, as well as prospective targeted therapy for CSCs (Yang et al., 2020).

1.2 Research gap

If we form anti-cancer vaccine through stem cell then transplanted stem cells exposed to external circumstances during culture before transplantation may affect both genomic expression and phenotype. The longer stem cells are cultured, the more likely they are to become cancer cells. After one month in cultivation, 45.8% all Mesenchymal Stem Cell (MSCs) spontaneously changed into malignant cells, according to the research. Again there are some side effects and potential risk of stem cell therapy. They are tumorigen, Hematopoietice events in allogeneic Hematopoetic Stem Cell (HSC) transplantation, drug toxicity and drug resistance, increased immune responses and autoimmunity, viral infection (Chu et al., 2020). In past studies these type of limitations of stem cell therapy and cancer stem cell growth vs stem cell therapy still unanswered. This review paper is focused on how stem cell turns into malignant cell and how malignant cell can be treated by stem cell therapy as well as their side effects.

1.3 Objective

The review focuses on stem cell therapy in cancer diseases along with their causes and treatment. Furthermore, the significance of stem cell therapy as well as the mechanism of cancer cell growth are being over-viewed. On the other hand, the role of stem cells in cancer cell growth and cancer treatment are also described. Finally, the role of stem cells in causing and treating cancer is compared. The aim of this work is to show stem cell therapy as one of the most potential therapies for cancer disease.

1.4 Significance

By comparing between cause and cure of stem cells in cancer disease, this paper might be helpful in future that how far we should go for developing stem cell therapy in cancer disease. So that rate of differences between cause and cure of stem cell therapy in cancer disease, side effects or adverse effects of stem cell therapy can be reduced and getting a new way of succeed result of stem cell therapy in cancer. In that case we can find stem cell therapy as best of all therapy in cancer disease.

Chapter 2

Overview of stem cell

2.1 What exactly is a stem cell?

A number of cell kinds make up our body. Red blood cells, for example, are supposed to transfer oxygen throughout our bodies through the circulatory system, yet they can't divide (Genome, 2021).

Stem cells are the building blocks of the organism; they are the cells that give rise to each and every cells with specific activity. When stem cells cleave under the right circumstances in the body or in the lab, they produce daughter cells, which are new cells. These daughter cells may self-renew or develop into particularized cells such heart muscle cells blood cells, brain cells, or bone cells (differentiation). There is not at all cell in the body that can self-replicate new cell types (Clinic, 2019).

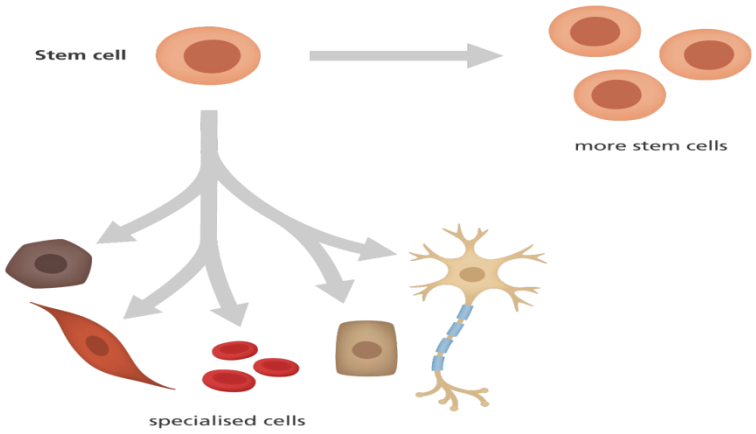

Figure 1 A stem cell may create more stem cells or specialized cells (Genome, 2021).

2.2 Different types of stem cells include

Stem cells are classified in a variety of ways. The three sort of stem cells are embryonic, adult, and induced pluripotent stem cells (iPSCs) (Genome, 2021).

2.2.1 Adult Stem Cells: Adult stem cells (ASC) are uniformed cells that have potentiality to regenerate or form new cells in our bodies' differentiated tissues to replace dead or damaged tissue. Adult stem cells, sometimes mentioned to as "somatic stem cells," are a kind of adult stem cell. The word "somatic" mentions to non-breeding cells in the body (eggs or sperm). Because ASCs are rare in native tissues, assessing and extracting them for research is difficult. ASCs are found in tiny quantities throughout most human tissues and make new cells to replace those lost as a result of spontaneous healing, disease, or damage. ASCs may be found in tissues for example the placenta, umbilical cord, muscle, bone marrow, brain, adipose tissue, skin, and gut throughout one's life. In 1948 the first ASCs were up-rooted and utilized to create blood. This plan of action was extended once mature bone marrow cells were transplanted initially worn in clinical treatment in consequence of the fact that blood disorders in 1968. Some research have shown particularly ASCs can solely create cell types found in their native tissue, while others have observed that ASCs can develop cell kinds not found in their original tissue. Further inquiry is necessary to confirm the disparity (NIH, 2019).

Adult stem cells come in many different shapes and sizes. They are:

- ✓ Hematopoietic Stem Cells (Blood Stem Cells)
- ✓ Mesenchymal Stem Cells
- ✓ Neural Stem Cells

- ✓ Epithelial Stem Cells
- ✓ Skin Stem Cells

White blood cells, platelets, red blood cells are wholly blood cells that may come from an immature cell. Hematopoietic stem cells may be detected in the marrow and blood plasma. A blood stem cell is another name for it (NIH, hematopoietic stem cell, 2019).

Mesenchymal stem cells (MSCs) are stromal cells that can self-renew and differentiate into a range of cell types. The umbilical cord, uterine tumors, menstrual blood, marrow, and adipose are among the tissues from which MSCs may be extracted (Ding et al., 2011).

Neural stem cells (NSCs) divide throughout embryonic development to create radial glial progenitor cells, which eventually become the neurons and glia of the nervous system in all animals. The major results of NSC differentiation are neurons, astrocytes, and oligodendrocytes (Wikipedia, 2021).

Tissue homeostasis, wound healing, and carcinogenesis all need epithelial stem cells. Corneal epithelial stem cells are found in the limbal epithelium, whereas conjunctival epidermal layer cells are found in the conjunctiva's fornical zone. The corneal and conjunctival epithelia, and even the hair follicle and interfollicular dermis, may all self-renew, are mostly quiescent (slow-cycling), and can be encouraged to proliferate. The cornea's keratinocytes and hair follicles exhibit symptoms of suppleness (Lavker & Sun, 2003).

Skin Stem Cells: Adult stem cells that can renew itself and grow into a variety of skin cell lineages are known as skin stem cells. Adult skin may include them. Skin stem cells

have a function in both normal skin regeneration and post-injury skin repair. In patients who have sustained severe burns, skin stem cells may be employed to regenerate new skin (Hayakawa et al., 2022).

2.2.2 Embryonic Stem Cell: The embryo (referred to as a blastocyst) contains an inner cell mass capable of generating all of the specialized tissues that make up the human body from days 3-5 following conception and before implantation. ESCs are extracted from the inner cell mass of an in vitro fertilized embryo after receiving informed consent. ESCs aren't made from fertilized eggs from women. Pluripotent stem cells, which may change into nearly any cell type, are only found in the earliest phases of development. Scientists are attempting to comprehend how these cells develop and evolve. Along with scientists learn more about stem cells produced in vitro, we may be able to use similar developmental mechanisms to repair cells such as neurons, skin, intestines, livers, and other organs for transplantation (NIH, Stem Cells, 2019).

2.2.3 Induced Pluripotent Stem Cells: Induced pluripotent stem cells are a nice compromise between adult stem cells and laboratory-grown embryonic stem cells since they don't mingle. To turn a somatic cell (such as a skin cell) into a "stem cell-like" state, embryonic genes are injected. These cells, like ESCs, are pluripotent. Despite the fact that this approach of genetic reprogramming to make embryonic-like cells was found in 2007, additional study is required before it can be employed in clinical practice. On the other hand researchers found stem cells in both amniotic fluid and umbilical cord blood. These stem cells can differentiate into a wide range of cell types. The sac that surrounds and protects a developing fetus in the uterus is filled with amniotic fluid. During an amniocentesis technique to check for anomalies, researchers discovered stem cells in amniotic fluid samples taken from pregnant mothers. To fully comprehend the potential of amniotic fluid stem cells, further research is required (Mayo Clinic, 2021).

2.3 Uses of stem cells

Early-stage embryos, which are a collection of cells formed when a woman's egg is fertilized with a man's sperm in an in vitro fertilization facility, are used to make embryonic stem cells. Because human embryonic stem cells are sourced from human embryos, human embryonic stem cell research has raised a slew of ethical concerns. Human stem cell research guidelines were released by the National Institutes of Health in 2009. Embryonic stem cells and their potential for study as well as embryonic stem cell donation methods, are all outlined in the rules. Furthermore, according to the standards, embryonic stem cells from IVF embryos may only be utilized once the embryo is no longer required. Fertilized eggs obtained by in vitro fertilization (IVF) are employed in embryonic stem cell research, although they are never placed in a woman's uterus. When people donate stem cells, they are well aware that they are doing so. In test tubes or petri dishes, stem cells may survive and thrive under certain circumstances in the laboratory. Adult stem cells, despite their scientific potential, may not be as versatile and durable as embryonic stem cells. Adult stem cells may not be capable of producing all kinds of cells which would restrict their use in disease therapy. Adult stem cells are also more vulnerable to abnormalities generated by extrinsic stimuli like toxins or replication mistakes. Adult stem cells, on the other hand, have shown to be much more adaptable than previously thought (Mayo Clinic, 2021).

2.4 Stem cell line

A stem cell line is a group of cells produced from a single laboratory-grown stem cell. The cells of a stem cell line continue to develop but do not differentiate into other cell types. They should, in principle, be free of genetic defects and able to produce stem cells.

The clusters of cells that make up a stem cell line may be stored for subsequent use or shared with other researchers (Mayo Clinic, 2021).

2.5 Stem cell therapy

Cells, tissues, and organs may be irrevocably damaged or killed as a result of illness, injury, or genetic abnormalities. Stem cells have the potential to generate new cells, which could then be reintroduced into the body to replace those that have died or been damaged (Genome, 2021).

Stem cell treatment, also known as regenerative medicine, is the use of stem cells or their derivatives to aid in the repair of damaged, malfunctioning, or diseased tissue. It's the next step in organ transplantation, and it uses cells instead of donor organs, which are in short supply. In the lab, scientists create stem cells. These stem cells were genetically modified to produce a variety of cell types, including heart muscle cells, blood cells, and brain cells. The changed cells might then be implanted into a human. The cells might be put into the heart muscle if a person develops a cardiac problem, for example. The implanted healthy cardiac muscle cells may aid in the repair of damaged heart muscle. Adult bone marrow cells that have been converted into heart-like cells have previously been shown to repair cardiac tissue in patients, and further research is now being carried out. Stem cell transplants, also known as bone marrow transplantation, have been conducted by doctors. In stem cell transplants, stem cells are used to help the donor's immune system fight cancer and blood diseases such leukemia, lymphoma, myeloma, and multiple myeloma. Human embryos or umbilical cord are being used in these transplants. Induced pluripotent stem cells are being used to produce new RPE cells in the lab, which might subsequently be transplanted into the a retina of the eye to replace damaged cells. Researchers must be certain that embryonic stem cells will mature into

the necessary cell types before they may be used in patients. New ways for directing stem cells to be become specific cell kinds, including such heart cells from embryonic stem cells, have been created by researchers. This is an area where further research is needed. If embryonic stem cells are left to their own devices, they may grow improperly or specialize into other cell types. Scientists are looking for methods to stop embryonic cells from multiplying and growing. Embryonic stem cells may cause an immunological reaction in which the recipient's body assaults them as foreign invasions, or they may simply stop operating, leaving uncertain implications. Researchers are always looking for new ways to avoid these harmful repercussions (Mayo Clinic, 2021).

2.6 Therapeutic cloning

Therapeutic cloning, also known as somatic cell nuclear transfer, is a method of producing flexible stem cells that does not need the use of fertilized eggs. The nucleus, which carries the genetic material, is removed from an unfertilized egg during this operation. The nucleus of a donor cell is also removed. In a process known as nuclear transfer, the donor nucleus is injected into the egg to replace the nucleus that was removed. The blastocyst is formed when the egg is allowed to split. This procedure produces a genetically identical clone, or stem cell line, from the donor's cells. Therapeutic cloned stem cells may offer an advantage over fertilized egg stem cells, according to some experts, Because cloned cells are less likely to be rejected when transplanted back into the donor, researchers can more precisely follow disease development. Despite success in other species, researchers have yet to achieve therapeutic cloning results in humans. In recent investigations, researchers have altered the therapeutic cloning strategy to create human pluripotent stem cells. Scientists are constantly researching human therapeutic cloning (Mayo Clinic, 2021).

2.7 Stem cell research

The scientists want to learn further about stem cell qualities so they may understand better way human bodies grow and develop stem cell replacement therapies for cells and tissues that have been injured or are missing. Using stem cells, scientists may understand of how cells acquire specialized for certain functions in the human body, as well as what occurs when this process goes wrong in sickness. Researchers may be likely to duplicate this process to make cells, tissue, and organs if we get a deeper understanding of stem cell creation. Stem cells might be utilized to create tissue or organ structures, which could then be researched to learn more about how they work and how medications affect them (Mayo Clinic, 2021).

Chapter 3

Cancer Disease

3.1 What is cancer?

The scientists want to learn further about stem cell qualities so they may understand better way our bodies grow and develop stem cell replacement therapies for cells and tissues that have been injured or are missing. Using stem cells, scientists may understand more about how cells are specialized for certain functions in the human body, as well as what occurs when this process goes wrong in sickness. We could be able to recreate this process to make new skin cells, tissue, and organs if we get a deeper understanding of stem cell creation. Stem cells might be utilized to create tissue or organ structures, which could then be researched to learn more how they work and how medications affect them (NIH, What Is Cancer?, 2021).

The name of metastatic cancer is the same as the name of the original cancer, and the cancer cells are the same as the original cancer cells (also known as primary cancer). Breast cancer that has progressed to the lungs and established a metastatic tumor, for example, is called metastatic breast cancer rather than lung cancer. Metastatic cancer cells seem almost similar to the cells that caused the original sickness under a microscope. Furthermore, metastatic cancer cells and cells from the original tumor share certain genetic traits that identify them from one another, such as the existence of specific chromosomal abnormalities. Some persons with metastatic cancer may benefit from therapy that extends their lives. If cancer has spread to another organ, the main objective of therapy is to limit the disease's course or to relieve the symptoms it causes. Metastatic

tumors may seriously impair a person's capacity to function, and metastatic illness is the leading cause of mortality among cancer patients (NIH, What Is Cancer?, 2021).

3.2 Cancer Cells vs. Normal Cells: What's the Difference?

In certain aspects, cancer cells differ from normal ones. For example,

- ✓ Cancer cells grow in the absence of external signals. Only in response to such signals can normal cells form.
- ✓ Signals telling cells to stop dividing or die are disregarded (Apoptosis, or programmed cell death, is a kind of cell death that occurs when a cell is intended to die..).
- ✓ Invade surrounding regions to spread to other sections of the body. Normal cells stop growing when they come into touch with other cells, and most normal cells do not migrate throughout the body.
- ✓ Instruct blood arteries to grow in the direction of tumors. These blood vessels provide oxygen and nutrients to tumors while also eliminating waste.
- ✓ Isolate yourself as much as possible from the immune system. Damaged or aberrant cells are normally eliminated by the immune system.
- ✓ Get the immune system to help cancer cells survive and flourish by tricking it. For example, some cancer cells urge immune cells to defend the tumor rather than fight it.
- ✓ Chromosomes accumulate multiple modifications, such as duplications and deletions of chromosomal regions. Cancer cells may contain double the number of chromosomes as healthy ones.

- ✓ In a different manner than regular cells, they rely on nutrition. Furthermore, unlike most normal cells, certain cancer cells use nutrients in an unusual method to create energy. This enables cancer cells to grow more quickly.

Cancer cells frequently depend so heavily on abnormal activity that they can't live without them. As a result, drugs that target cancer cells' abnormal features have been developed. For example, certain cancer therapies prevent blood vessels from growing toward tumors, depleting the tumor of nutrients (NIH, What Is Cancer?, 2021).

3.3 How Does Cancer Develop?

Cancer is a hereditary illness in which changes in genes that govern how our cells function, especially how they divide and proliferate, cause the disease. The following causes may result in cancer-causing genetic alterations:

- ✓ As a consequence of errors that arise during cell division
- ✓ DNA damage is caused by harmful substances in the environment, such as chemicals in cigarette smoke and UV rays from the sun. (See our Cancer Causes and Prevention section for more information.)
- ✓ They were passed down to us from our parents.

The body usually eliminates cells with damaged DNA before they become cancerous. Our bodies' capacity to do so, however, diminishes as we age. One of the reasons individuals are more prone to acquire cancer later in life is because of this.

A unique collection of genetic mutations causes each person's cancer. More changes will occur as the malignancy adva nces. Within the same tumor, distinct cells may contain different genetic mutations (NIH, What Is Cancer?, 2021).

3.4 Types of Genes that Cause Cancer

Proto-oncogenes, tumor suppressor genes, and DNA repair genes are all affected by the genetic alterations that produce cancer. In cancer, these anomalies are referred to as "drivers." Proto-oncogenes help normal cell division and proliferation. Certain genes may become cancer-causing genes (or oncogenes) if they are changed in certain ways or become more active than usual, allowing cell growth and survive even when they shouldn't Tumor suppressor genes are also associated with cell division and development regulation. Tumor suppressor gene mutations may cause cells to proliferate uncontrolled. Repairing damaged DNA is the job of DNA repair genes. Changes in these genes are more likely to cause mutations in other genes as well as chromosomal abnormalities including duplications and deletions. If all of these changes occur at the same time, the cells may become cancerous. m As scientists understand more about the molecular alterations that lead to cancer, they've learned that some mutations are common in a variety of cancers. Many cancer treatments that target cancer-causing gene mutations are already accessible. A number of these therapies are available to anybody with cancer who has the targeted mutation, regardless of where the tumor began to form (NIH, What Is Cancer, 2021).

3.5 Tissue Changes that Are Not Cancer:

Changes in the body's tissues may not always indicate the presence of cancer. When left untreated, some tissue alterations may progress to the point where they cause cancer. Here are some instances of tissue alterations that are not cancerous but are being monitored in some cases because they have the potential to become cancerous:

Hyperplasia is a condition in which cells within a tissue multiply at a quicker rate than usual, resulting in the accumulation of additional cells. The cells as well as the structure of the tissue, on the other hand, seem to be perfectly normal under a microscope. Multiple reasons or situations, including prolonged inflammation, can contribute to the development of hyperplasia.

When compared to hyperplastic disease, dysplasia is more advanced disease. There is also an accumulation of additional cells in the case of dysplasia. The cells, on the other hand, have an uneven appearance, and the tissue's organization has changed. The more aberrant the cell and tissue seem, the more likely they are to be cancerous. the more likely cancer will develop. Some varieties of dysplasia need the patient to be monitored or treated, while others do not. A dysplastic nevus (also known as a dysplastic mole) is an abnormal mole that grows on the skin that is an example of dysplasia. A dysplastic nevus has the potential to develop into melanoma, albeit the majority do not.

Carcinoma in situ is a condition that is significantly more advanced than the previous one. Even though it is usually referred to as stage 0 cancer, it is not a kind of cancer since the abnormal cells do not enter nearby tissue in the same way as cancer cells do. However, certain carcinomas in situ are regularly treated since they have the potential to develop to malignancy (NIH, What Is Cancer, 2021).

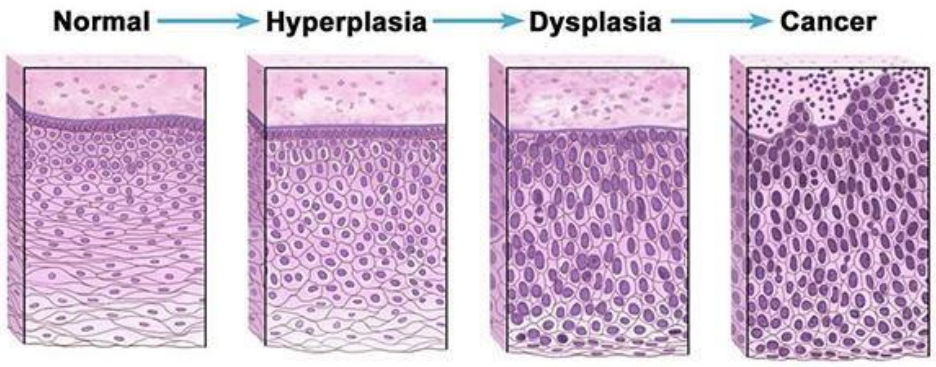

Figure 2 Normal cells to cancer cells

(NIH, What Is Cancer, 2021).

3.6 Cancer types include

The four primary forms of cancer are as follows:

Carcinoma: A carcinoma may start inside the epidermis or even in the layer that surrounds the exterior of inner organs and glands, based on where tumor is located.Solid tumor formation is a frequent hallmark of carcinomas. Ovarian cancer is the most common kind of cancer. Carcinoid tumors may be seen in prostate cancer, breast cancer, lung cancer, and colon cancers (Cancer.Net, What is cancer, 2019).

Sarcomas: Sarcomas are cancerous tumors that start in the body's supporting and connecting tissues and spread throughout the body. Sarcomas may occur in fat, muscle, neurons, tendon, joints, blood vessels, lymphatic vessels, bone, along with many other tissues (Cancer.Net, What is cancer, 2019).

Leukemias: Leukaemia is a type of cancer that may affect adults and children. Leukemia is a disease that causes healthy blood cells to change and grow uncontrolled. Acute

lymphocytic, chronic lymphocytic, acute myeloid lymphoma, and chronic myeloid leukemia are the four forms of leukemia to consider (Cancer.Net, What is cancer, 2019).

Lymphomas: Lymphoma is a cancer that starts in the lymph system and then spreads throughout the body. The lymphatic system consists of channels and glands that aid the immune system in the fight against infection and illness. Hodgkin and non-Hodgkin lymphoma are the two forms of lymphoma (Cancer.Net, What is cancer, 2019).

3.7 Types of treatment

Surgery, chemotherapy, and radiation therapy are the most commonly used cancer treatment methods today. Targeted therapy, immunotherapy, laser therapy, hormone therapy, and other treatments are also available.

The following are the methods of cancer treatment:

Many types of cancer are treated with surgery, which is a common procedure. During the procedure, the surgeon removes the mass of cancerous cells (tumor) as well as some of the surrounding tissue from the body. When a tumor causes adverse effects, it is sometimes necessary to perform surgery to alleviate the symptoms (Gersten, 2019).

3.7.1 Chemotherapy: Chemotherapy is a term that refers to the process of using medications to kill cancer cells. The drugs may be administered orally or injected into a blood vessel directly (IV). Various drugs may be given at the same time or in a different order (Gersten, 2019).

3.7.2 Radiation: Radiation therapy is a kind of cancer treatment in which cancer cells are destroyed using x-rays, particles, or radioactive seeds. Cancer cells multiply more

quickly than normal cells in the body. Because radiation is more destructive to rapidly reproducing cells, it causes cancer cells to be injured more severely than normal cells during treatment. The cancer cells' capacity to grow and divide is hampered as a consequence, and they finally die.The two most common types of radiation therapy are as follows:

- ✓ External beam: This is the most often observed variant. This kind of therapy uses X-rays or particles from outside the body to target the tumor.
- ✓ Internal beam: This type of radiation is delivered to the inside of your body. It may be administered through the use of radioactive seeds that are implanted in or near the tumor, a liquid or pill that you consume, or through the vein (intravenous, or IV).

3.7.3 Targeted therapies: Using medications to block cancer from growing and spreading, targeted treatment is used to treat cancer. It accomplishes this while causing less harm to normal cells than other therapies. Chemotherapy, in its current form, destroys both cancerous and non-cancerous cells. To eliminate cancer cells, targeted treatment concentrates on particular targets (molecules) located in the cells. These anti-cancer targets are important in cancer cell proliferation and survival. Because of the drug's utilization of these receptors, cancer cells are rendered inoperable (Gersten, 2019).

Targeted treatment medications have a variety of mechanisms of action. They may do any of the following:

- ✓ Turning off the mechanism that allows cancer cells to grow and spread inhibits their development and spread.
- ✓ Cancer cells can be induced to die on their own.
- ✓ Cancer cells are killed in the direct path of the virus.

Targeted therapies are administered intravenously or as pills.

3.7.4 Immunotherapy: Immunotherapy is a cancer treatment that makes use of the body's inherent defense mechanisms to combat infection (immune system). It makes use of chemicals produced by the body or in a lab to help the immune system fight cancer more effectively and accurately. This aids in the removal of cancer cells from your body (Gersten, 2019).

Immunotherapy operates in the following ways:

- ✓ Cancer cell proliferation can be stopped or slowed by a variety of methods.
- ✓ It is critical to prevent cancer from spreading to other places of the body.
- ✓ Increasing the immune system's capacity to rid the body of cancer cells.

These drugs are specifically designed to target and destroy certain components of a cancer cell. Some of them are tainted with poisons or radioactive substances. Immunotherapy is administered intravenously.

3.7.5 Hormonal therapy: Hormonal Therapy is a sort of therapy in which hormones are used. Treatment for malignancies that are fuelled by hormones, such as breast, ovarian, and prostate cancers, is accomplished by the use of hormone therapy. It employs surgical procedures or pharmaceuticals to suppress or prevent the production of the body's natural hormones. This has been demonstrated to help cancer cells grow slower. The ovaries and testicles are removed during the procedure, as are other hormone-producing organs. The medications are administered either intravenously or orally as pills (Gersten, 2019).

3.7.6 Hyperthermia: Hyperthermia is a technique that employs heat to burn and kill cancer cells while causing no harm to normal cells. It can be used for a variety of things, including:

- ✓ A tumor, for example, is a collection of cells in a small area.
- ✓ Individual body components, such as an organ or limb
- ✓ The entire body is involved.

The heat is provided from outside the body, either through a needle or probe inserted into the tumor or through a machine outside the body.

3.7.7 Laser therapy: Laser Therapy is a treatment that uses lasers to treat patients. Laser treatment is a method of destroying cancer cells by delivering an extremely narrow, focused beam of light. Laser therapy can be used to treat the following conditions:

- ✓ Tumors and precancerous growths should be eliminated.
- ✓ Tumors that are blocking the stomach, colon, or esophagus can be reduced in size.
- ✓ Aid in the treatment of cancer symptoms such as bleeding.
- ✓ Nerve terminals should be sealed following surgery to reduce pain.
- ✓ Sealing lymph veins after surgery helps to minimize edema and prevent tumor cells from spreading further.

Laser therapy is frequently administered by the use of a narrow, illuminated tube that is implanted within the body. The light is directed toward the cancer cells by Thin fibers at the end of the tube. In addition, lasers are employed on the skin. The use of laser cancer

treatment in conjunction with other cancer treatment methods including radiation and chemotherapy is common (Gersten, 2019).

3.7.8 Photodynamic therapy: PDT is an abbreviation for Photodynamic Therapy. In photodynamic therapy, a patient is given a shot of a medication that is only activated when exposed to a specific type of light. The medicine remains in cancer cells for a longer period than it does in healthy ones. Once this is done, the cancer cells are targeted using laser or other light sources by the doctor. The light causes the medicine to transform into a chemical that destroys the cancer cells in the body (Gersten, 2019).

3.7.9 Cryotherapy: This therapy, also known as cryosurgery, involves the use of extremely cold gas to freeze and kill cancer cells. In some cases, it is used to treat cells that have the potential to become cancer (known as precancerous cells) on the skin or cervix, for instance. The use of special equipment to deliver cryotherapy to tumors inside the body, such as those in the liver or prostate, is also an option available to doctors (Gersten, 2019).

3.8 Success and failure rate of different stages of Geminin by cancer treatment

The term "staging" refers to the process of describing cancer. The stage of cancer refers to where it is situated and how big it is, as well as how far it has progressed into neighboring tissues and if it has migrated to nearby lymph nodes or other sections of the body. Cancer's stage is determined by the location and size of cancer, as well as how far it has spread into nearby tissues. A multitude of procedures may be used to identify the stage of cancer, including physical examinations, imaging scans, and another testing

before any cancer therapy can begin. It is possible that staging will not be completed until all of the tests have been performed (Cancer.Net, Stages of Cancer, 2021).

Stage 1 and treatment: The phrase "stage 1 cancer" refers to cancer that is tiny and limited to a single location on the body, and has not yet progressed to the lymph nodes or other parts of the body. Cancer will still be referred to by the stage at when it was discovered, regardless of whether it has spread or improved. Cancers that are in the same stage of development are frequently treated in the same way. For example, surgery is typically used in the treatment of stage 1 cancer (America, 2021).

Stage 2 and treatment: In general, stage 2 tumors are treated locally with surgery and/or radiation to maximize their chances of survival. Cancer treatment for stage 2 might sometimes include chemotherapy or other pharmacological therapies in addition to surgical intervention (America, 2021).

Stage 3 and treatment: Generalized chemotherapy and radiation, as well as a combination of the two, are used to treat stage 3 malignancies. Surgery is usually followed by treatment to decrease the tumor before surgery, such as chemotherapy or radiation (America, 2021).

Stage 4 and treatment: Stage 4 cancer is the most severe stage of the disease, and it carries the highest risk of death. On the other hand, a person's life expectancy is impacted by a number of things. The treatment approach for stage 4 cancer is determined by the kind of disease and the degree to which it has spread. Some treatments are designed to improve a person's overall quality of life while also controlling their symptoms. Others aim to halt the progression of cancer. Treatment options at this stage may include the following:

- ✓ Chemotherapy is a reliable treatment option, though the risks may be too great when cancer has spread extensively.
- ✓ Treatment with radiation therapy, which can help shrink tumors and alleviate symptoms
- ✓ Tumor removal surgery is used in conjunction with immunotherapy to assist the body's immune system in fighting cancer.
- ✓ The goal of targeted therapy is to slow the growth of tumors (Kandola, 2021).

Chapter 4

Stem cell are one of the causes of cancer

4.1 Stem cell in cancer disease

Stem cells may be used in the future to assist repair or replace damaged tissues and organs. They will save us from diseases that can only be treated symptomatically with medications. They may, however, play a different function in our lives, one that is not as beneficial as we would want. They might be the cause of a variety of malignancies, including the majority. According to some experts, every tumor has a few stem cells that have lost their genetic marbles and are feeding a malignant mass with cancerous cells on a regular basis. Beginning at conception and continuing through maturity, stem cells are essential for our regular development and wellbeing. Embryonic stem cells help produce our organs, muscles, sinews, and skeletons, as well as their location within our bodies after birth, by forming progenitors and patterns. They leave a guardian population of stem cells in charge of mending each tissue as needed after they've accomplished their mission. One progenitor is produced when a stem cell splits into two, and the renewal process continues. The new stem cell prepares for the next stage of tissue regeneration, when it will be called upon to replace the tissue that has been lost, while the progenitor cell continues to grow into mature, specialized cells.

Stem cells have a significantly longer lifespan than conventional cells, which increases the likelihood that they may collect genetic mutations over time. A cell may lose control of its self-renewal and development with only a few mutations, causing it to become a malignant source. Tumors might grow from embryonic cells that were left behind after development and stayed latent until they were stimulated and developed malignant, according to prior theories. Despite

the fact that today's views on stem cells' function in cancer are based on the embryonal rest hypothesis, the types of cells involved are now well known. Despite the fact that the concept was first postulated more than 150 years ago, we have gone a long way in our understanding, since we now know how to find stem cells inside malignancies using protein markers on their surfaces (Institute H. S., 2021).

4.2 DNA mutation of stem cells

Malignancies may be divided into two categories: those that increase in frequency with age and those caused by developmental abnormalities in animals. In the first category, the multiplication of genetically gained stem cells, who give birth to and sustain tissues and organs, causes genetic modifications linked to DNA replication. Aneuploidy is caused by genome destabilizing mutations, which abnormal genomic multiplication and chromatid missegregation are caused by these mutations. Genome destabilizing mutations produce aneuploidy by generating excessive genome duplication and chromatid missegregation, while cancer driver mutations promote carcinogenesis. Carcinogenesis is caused by cancer driver mutations, whereas genome destabilizing mutations produce aneuploidy by triggering chromatid missegregation. Because of the increased genomic instability, clonal evolution moves more quickly, leading in the formation of more aggressive clones that are more resistant to pharmacological therapy. The mismatch between pluripotent stem cells even during early stages of development creates progenitor cell hyperplasia, the second type of cancer. Pluripotent stem cells that emerge in human embryo rise to all the derived cells in the embryo and adult during normal development; nevertheless, malignancies occur whenever they mislocalize to ectopic locations. Interestingly, the Geminin enzyme is necessary to prevent DNA damage-dependent mortality through excessive DNA

replication in pluripotent and many cancer cells. Given the relationship among Dna synthesis regulation throughout initial stages and germ cell neoplasia, geminin might be a potential chemotherapy target in the treatment of cancer progenitor cells (Institute H. S., 2021).

4.3 Origin of cancer through stem cells

Two opposing ideas exist about the genesis of human cancer. Cancer is assumed to be caused mostly by genetic alterations inherited or acquired via DNA replication errors and environmental stresses. This idea explains the relationship between aging and the risk of cancer. Another notion is that cancer stem cells (CSCs) are to blame. CSCs are cells that may replicate endlessly without losing their potential to commence uncontrolled development, which ultimately leads to tumor formation and progression. All cancer cells can live in conditions where normal cells can't, but only CSCs can start from scratch and develop tumors. CSCs were initially discovered in the setting of leukemia, but their uses have subsequently extended to encompass breast, brain, prostate, colon, and other organ solid cancers. CSCs may form as a consequence of genetic mutations accumulating during mammalian development, therefore these two concepts are not mutually incompatible. CSCs might also be latent stem cells that awaken in a new environment and respond to proliferation and migratory signals that they weren't programmed to respond to during development.

The emergence of stem cells in the embryonic development of mice has been widely studied, with the majority of research focusing on the mouse. Stem cells are cells that may divide indefinitely while still retaining the ability to specialize into certain cell types (a process known as self-renewal). It's usual to speak to them in terms of how many distinct cell lineages they've spawned. In this way, unipotent cell giving birth to a single lineage cells, whereas multipotent

cell give birth to multiple cell lines. Pluripotent cells can produce every cell lineage in the embryo and adult, but totipotent cells can only produce the embryo and placenta. Geminin mutations in unipotent and multipotent tissue-specific stem cells When 'pluripotent,' which commence mammalian development, appear in the wrong place at the wrong time, they have the potential to cause cancer (Institute H. S., 2021).

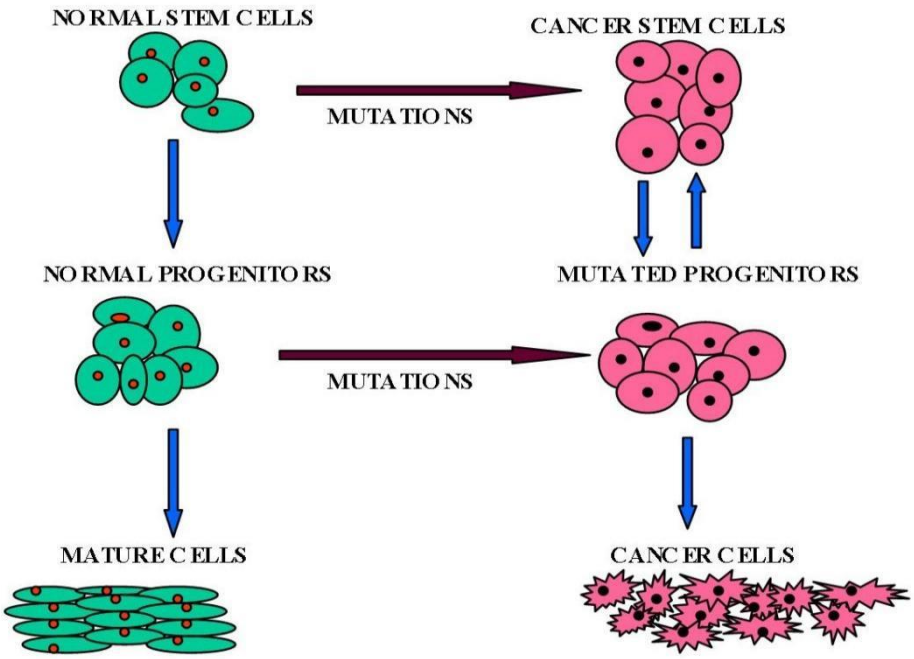

Figure 3 Origin of cancer

(Institute H. S., 2021).

4.4 Pluripotent stem cells are potential cancer stem cells

Cancer stem cells (CSC) or embryonic (ESC) have certain similarities (ESC). CSCs and ESCs can develop into a variety of cells and retain these characteristics during self-renewal. CSCs and ESCs have genetic signatures that are similar, reproduce fast, have little interaction inhibition, and have genetic signatures that are comparable. Because they both operate under low oxygen tension and depend on glyco rather than oxidative phosphorylation, embryonic cells and also most cancerous cells have a lot in common. In vitro, both have chromosomal fragility and reduced oxygen tension (particularly human ESCs). The most eye-catching finding is whether pluripotent stem cells either mice or humans transplanted into ectopic areas of isolates or immuno-compromised fetus and adult animals all develop symptoms. Germ cell tumors and teratocarcinomas, which appear in humans and mice during infancy and develop spontaneously, are very comparable to pluripotent stem cell cancers. Germ cell tumors are benign tumors made up of a homogeneous mass of cells made up of tissues of at least 2 embryonic germ layers, but not all three. Teratomas are a kind of cancer that exclusively affects children and adolescents. CSCs, also known as "embryonal carcinoma cells (ECCs)," have been discovered and studied in teratocarcinomas, which are cancerous teratomas. ECCs resemble embryonic stem cells (ESCs) in appearance, but they have undergone unknown genetic modifications that distinguish them from ESCs. Individual ECC lines have diverse properties, despite the fact that ECCs may contribute to the development of all tissues in the host embryo. Cancers usually arise in chimera animals because their contributions to embryonic development are generally restricted, and they display a broad variety of differentiation traits. Despite this, broad expression of Oct4 in the body does not mimic pluripotent cells' ability to form extragonadal cancers. As a consequence, teratoma production has been used as a tool for evaluating pluripotency for stem cell therapy and

a template for embryonic development, illness, and cancer both in animal and human studies reproduce fast, have little interaction inhibition, and have genetic signatures that are comparable. Because they both operate under low oxygen tension and depend on glyco rather than oxidative phosphorylation, embryonic cells and also most cancerous cells have a lot in common. In vitro, both have chromosomal fragility and reduced oxygen tension (particularly human ESCs). The most eye-catching finding is whether pluripotent stem cells either mice or humans transplanted into ectopic areas of isolates or immuno-compromised fetus and adult animals all develop symptoms. Germ cell tumors and teratocarcinomas, which appear in humans and mice during infancy and develop spontaneously, are very comparable to pluripotent stem cell cancers. Germ cell tumors are benign tumors made up of a homogeneous mass of cells made up of tissues of at least 2 embryonic germ layers, but not all three. Teratomas are a kind of cancer that exclusively affects children and adolescents. CSCs, also known as "embryonal carcinoma cells (ECCs)," have been discovered and studied in teratocarcinomas, which are cancerous teratomas. ECCs resemble embryonic stem cells (ESCs) in appearance, but they have undergone unknown genetic modifications that distinguish them from ESCs. Individual ECC lines have diverse properties, despite the fact that ECCs may contribute to the development of all tissues in the host embryo. Cancers usually arise in chimera animals because their contributions to embryonic development are generally restricted, and they display a broad variety of differentiation traits. Despite this, broad expression of Oct4 in the body does not mimic pluripotent cells' ability to form extragonadal cancers. As a consequence, teratoma production has been used as a tool for evaluating pluripotency for stem cell therapy and a template for embryonic development, illness, and cancer both in animal and human studies. As a result, pluripotent cells such as ESCs, EpiSCs, and PGCs can eventually develop into CSCs (Vassilev & DePamphilis, 2017).

4.5 Stem cell the fact rate for cancer

A stem cell scientist feels that stem cell malfunction is a primary cause of most ailments in the industrialized world, based on his or her egocentric perspective. As we become older, our stem cells collect more mutations, resulting in a loss of self-renewal and adaptability. At some point, the renewal of the entire tissue or organ is delayed and hampered. Mutations in our stem cell pool may change stem cells and their clonal progeny over time, leading to the development of aggressive cancer. Stem cells may be traced back to the creation of multicellular creatures with specialized cells and tissues, as well as their role in tissue regeneration and cancer. While multicellular tissues encounter less obstacles than single-celled organisms, they do face certain obstacles, such as the necessity for self-renewal for tissue regeneration, as well as cell differentiation and 'cell-to-cell contact.' Organized tissues lose their capacity to develop on their own as they get more organized as a consequence of the cooperation that is necessary among single cells. It is possible to recuperate this loss by an accident, with one significant side effect being the development of cancer (Lagasse, 2008).

Chapter 5

Stem cell therapy is one of the best cancer treatment

5.1 Stem cell in immune-reconstitution

It has been many years since stem cells have been utilized in immune reconstitution following the development of cancer or the therapy of cancer. Chemotherapy at large doses can have negative effects on the bone marrow, leading to myelosuppression. Because of complicated interactions between hematopoietic progenitor cells and their surroundings, blood cell recovery is normally performed by using hematopoietic progenitor cells present in the bone marrow. which are influenced by a variety of stimulatory and inhibitory stimuli. On the other hand, the time it takes for hematopoietic recovery is dictated by the chemotherapy dosage and cycles utilized. Chemotherapy has been proven to generate tumor growth factors (TGF), interferon (IFN), tumor necrosis factor (TNF), and interleukin (IL)-4, as well as myelosuppressive cytokines. HSCs are the commonest and advised cell lines for hematopoietic transplantation after high-dose chemotherapy. These are the stem cells chosen preference for recovering bone marrow and immune response functioning to pre-chemotherapy levels after high-dose chemotherapy. In randomised clinical research, HSCs have been employed in hematopoietic transplantation with varied degrees of effectiveness. The studies' outcomes, however, have proven contentious. A sufficient volume of stem cell treatment has also been found as one of the most essential criteria in a speedy recovery. Several chemotherapeutic medications, notably alkylating agents, have been demonstrated to have a deleterious influence on stem cell production and hematopoietic recovery, according to certain research. Throughout the post-transplant period, re-infusion of ex

vivo created myeloid precursors and ex vivo enlarged peripherals blood stem cells (PBSC) may help to reduce thrombocytopenia and neutropenia (Sagar et al., 2007).

5.2 How treatment can be targeted

The first step in using stem cell therapy to treat particular cancer types is to understand how the diseases developed. If this is the case, the focused treatment will be determined. In adult mammals, totipotent and pluripotent cells are distinguished from the majority of other cells by the presence of a key gene called Geminin (Geminin, also known as Gmnn, is a DNA replication inhibitor). Geminin is not required for the survival of most of the other cells in adult mammals. In mice or human embryos fibroblast and human primary mammary epithelia, geminin reduction promotes DNA re-replication instead of senescence, although Gmnn ablation leads trophoblast stem cells to develop into nonproliferating large cells. As a consequence of these findings, geminin becomes a therapeutic target for cancers arising from pluripotent stem cells (Vassilev & DePamphilis, 2017).

Preimplantation embryos and embryonic stem cells (ESCs) need Geminin to maintain the expression of pluripotency-related genes, according to many studies.Others believe Geminin is needed to protect the cells investigated from DNA damage and death, rather than to retain or exit pluripotency. This is puzzling since these two jobs in the same cell are mutually incompatible. The riddle of Geminin's function in ESCs seems to have been solved. Gmnn ablation caused DNA re-replication in ESCs attempting self-renewal in vitro, which has been preceded with cell injury, a DNA damage response, but eventually death. These studies found no relationship between Geminin expression and the expression of pluripotency or differentiation genes, and ESCs no longer needed Geminin to survive after differentiation in vitro. To investigate whether

the results were attributable to experimental artifacts, naturally resistant mice was transplanted in ESCs carrying Gmnn genes that could have been otherwise this by intravenous injections of tamoxifen. The mice were then given some time to recover. Gmnn ablation will result in the production of teratomas, and the tumors will be devoid of Gmnn alleles if Geminin is required for pluripotency maintenance. However, if Geminin is required for ESC survival, Gmnn ablation would delay the formation of trophozoites because the most of ESCs would die, leaving only those that survived Gmnn ablation to create teratomas, as previously indicated. Geminin was shown to be required for ESC survival but not pluripotency, as previously thought. Another finding was that differentiated cells, including pluripotent stem cells, may maintain their proliferative potential after the development of a teratoma, even when missing Gmnn alleles and the Geminin protein. As a consequence, Geminin is no longer needed for differentiated cells to survive in a solid tissue environment (Vassilev & DePamphilis, 2017).

The importance of Geminin for ESC survival in both vitro and in vivo experiments explains the ramifications of Gmnn deletion in preimplantation embryos. When embryos reached the morula stage after fertilization, Gmnn ablation stopped development, most likely owing to a shortage of Geminin, which was inherited from the mother throughout development. The aberrant embryos looked to be experiencing DNA damage-dependent apoptosis in some instances, whereas early differentiation into trophoblast large cells appeared to be occurring in others. In embryos that got enough With Geminin to attain the early morula stage, the outermost blastomeres would have transformed into trophoblast cells throughout development. In this case, reduction of gene encoding Geminin could kill totipotent blastomeres, whereas trophoblast cells proliferated in large numbers (Vassilev & DePamphilis, 2017).

Furthermore, Geminin's function in pluripotent cells could explain why Gmnn ablation causes neural tube defects in the post-implantation epiblast by altering progenitor specification and neuronal differentiation, but not in later-appearing neural stem cells by altering progenitor specification and neuronal differentiation. The epiblast contains pluripotent progenitor cells, which are the source of pluripotent ESCs and EpiSCs. As a consequence, eliminating Gmnn from the epiblast would result in the loss of pluripotent progenitor cells, which are required for development to continue. Gmworkation, on the other hand, has no impact or hampers brain development because it has no effect on the survival or developmental capacity of later-appearing multipotent neural stem cells.According to the results, geminin is necessary for the mitotic growth of immature germ cells (spermatogonia) produced from PGCs. During in the initial surge of mitotic multiplication, that happens in the first week of life, Gmnn ablation induced death in mouse spermatogonia. Despite having more double-stranded DNA strand breaks that control cells, spermatogonia retained undifferentiated expression of genes and did not prematurely release genes involved with differentiated spermatogonia (ESCs). In contrast, knocking down Gmnn in meiotic spermatocytes had no impact upon meiosis or spermatid maturation into mature sperm. During the mitotic phase, geminin is required for spermatogonia proliferation, but never for spermatogonia development, as it is for ESCs. Geminin might be used to effectively treat germ cell neoplasias since it is required for longevity rather than regulation of gene expression in mice embryonic cells (ESCs) or male sperm cell (Vassilev & DePamphilis, 2017).

5.3 Types of Stem cell therapy/transplants

The stem cell transplant that involves injecting normal plasma stem cells into the a vein using a syringe. After entering your circulation, the stem cells go to your marrow, wherein they repair cells that have been damaged either chemotherapy or radiation. Bone marrow, circulation, and the umbilical cord may all be used to acquire blood-forming stem cells (NIH, Stem Cell Transplants in Cancer Treatment, 2015).

The stem cell transplant that involves injecting normal blood-forming stem cells into a veins using a syringe. After entering your circulation, the stem cells travel to your bone marrow, wherein they repair cells that have been damaged by chemotherapy or radiotherapy. Bone marrow, circulation, and the umbilical cord may all be used to acquire blood-forming stem cells (Center, 2021).

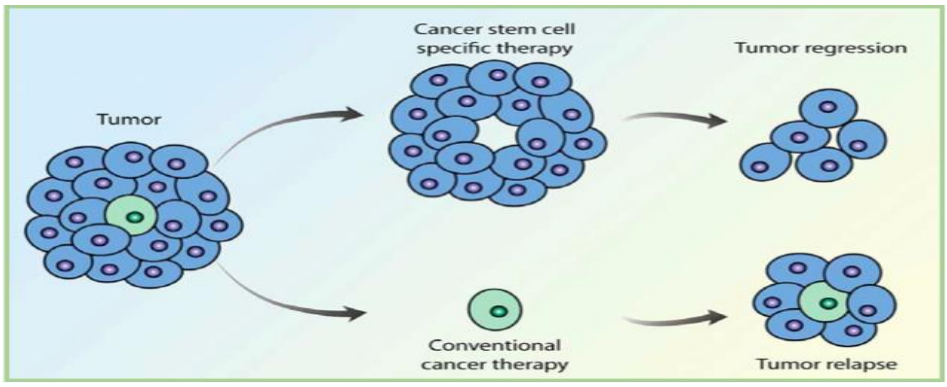

Figure 4 Novel therapeutic method of cancer stem cell

(Institute, 2021).

5.4 How stem cells transplants work

To be clear, cancer transplants are seldom beneficial in the treatment of the disease. Instead, when you've been subjected to strong doses of radiation, chemotherapy, or a combination of the two, they aid your body's capacity to create stem cells. However, stem cell transplantation may have a direct influence on the malignancy in rare instances of multiple myeloma and leukemia. This is related to the possibility of graft-versus-tumor syndrome following allogeneic transplantation. When a donor's white blood cells are used (the graft) are used to target cancer cells in your body that have survived high-dose chemotherapy, it is known as graft versus tumor (the tumor). The treatment's effectiveness improves as a result of this effect (NIH, Stem Cell Transplants in Cancer Treatment, 2015).

5.5 Stem cell transplants in leukemia or lymphoma

A patient's stem cells are harvested of his or her marrow or blood and utilized to replenish those that have perished in an autologous transplant. During treatment (high-dose chemotherapy and/or radiation), they are frozen and kept safe. Purging is a scientific technique for attempting to remove any leukemia cells that may have been present in the samples. After treatment, the stem cells then make these kinds into the patient's bloodstream to continue the operation (Society, 2021).

If you still have Acute Myeloid Leukemia (AML) but don't have a matching donor for an allogeneic transplant, you may require an autologous transplant. Some physicians believe that traditional "consolidation" chemotherapy is superior for these patients, however this is not widely agreed upon. Autologous transplants are frequently more acceptable than allogeneic transplants since patients get their own cells back. As a consequence, patients are less likely to

have complications after the treatment. On the other hand, high-dose chemotherapy might have substantial adverse effects. This kind of transplant may be done on anybody who is usually healthy; however, people who are extremely elderly or have other health issues may not be good candidates (Society, 2021).

In bone marrow or blood samples, distinguishing between normal stem cells and leukemia cells is difficult, making autologous transplants tricky. Even after purging, some leukemia cells may reappear following the stem cell transplant (In the lab, stem cells are being processed in an attempt to destroy or eradicate any remaining leukemia cells (Society, 2021).

5.6 Stem cell transplants in bone cancer

A patient's stem cells are harvested from his or her marrow or blood and utilized to restore those that have perished in an autologous transplant. During treatment (high-dose chemotherapy and/or radiation), they are frozen and kept secure. Purging is a scientific method of removing any leftover leukemia cells from the samples. The stem cells are former (reinfused) into the person's circulation to continue the cycle after therapy.

If you already have Acute Myeloid Leukaemia (AML) but do not have a matching donors for an allogeneic transplant, you may require an autologous transplant. Some physicians believe that traditional "consolidation" chemotherapy is superior for these patients, however this is not widely agreed upon. Autologous transplants are preferred over allogeneic transplants because patients get their own cells back. As a result, patients are less likely to have problems after therapy. On the other hand, high-dose chemotherapy has the potential to cause major adverse effects. Anyone in excellent health may receive this kind of transplant; however, people who are exceedingly old or have other health conditions may not be ideal candidates. With bone marrow

or blood samples, distinguishing among self - renewal and leukemia cells is difficult, making autologous transplants tricky. Even after purging, some leukemia cells may reappear following the stem cell transplant (In the lab, stem cells are being processed in an attempt to destroy or eradicate any remaining leukemia cells).

Surgery, chemotherapy, and radiation treatments for bone cancer are all accompanied with a considerable risk of negative side effects, which is particularly true for the typical therapeutic modules. Drugs intended to treat comorbidities associated with bone cancer (such as osteolysis), for example, may not always have good anti-tumor activity. Cell-based targeted treatments, which utilize genetically altered cells to deliver a specific sort of drug, are not believed to be especially safe. On the other hand, using mRNA-based engineering of mesenchymal stem cells provides significant benefits. It's a simple and safe procedure, for instance, since it doesn't need the use of genetic engineering. This approach enables the rapid and transitory production of several proteins at the same time, which may aid cancer cell death while minimizing adverse effects (Dutta, 2020).

5.7 Stem cell therapy and the success rate for cancer

The cancer stem cell idea offers a wide range of therapeutic applications, some of which might be significant. It might not only offer a new pathophysiological mechanism for understanding tumor resistance to treatment, but it could also aid clinicians in better diagnosing, prognosticating, and treating cancer in the future (Dikomey et al., 2016).

Since cells (CSCs) generally assumed to be the source of uncontrolled tumor development, therapy failure in the clinic could be attributed in part to CSC resistance to therapy. Treatment should result in a larger proportion of cancer stem cells inside the tumor than ever before

treatment since cancer stem cells are more difficult to treat (such as chemotherapy or radiation). Contrary to popular belief, if all cells respond to therapy in the same manner, the ratios between tumorigenic or non-tumorigenic cells should stay steady as the tumor shrinks (Dikomey et al., 2016).

Cancer treatment has reached an amazing new phase, as seen by recent advancements in stem cell therapy, with traditional medicines including such chemotherapy, radiation, or surgery on the one side, and stem cells on another. Stem cells have lately received a lot of interest due to their well-known role in immune restoration. This is particularly the case that now new gene techniques have emerged, including such gene integration in living cells, allowing for more targeted anti-cancer drug delivery. Cancer is now thought to become a stem cell issue, rather than a disease marked by rapidly increasing cells. Regardless of the fact that cancer stem cells' origins are unclear, the concept that cancer stem cells might lead to revolutionary cancer treatment strategies in the future. In order to distinguish cancer stem cells between healthy cells and many other cancer cells inside a variety of malignancies, further study is required in this field. To develop breakthrough therapies with the ultimate objective of removing residual sickness and avoiding recurrence, further study is required to discriminate between both the genes or signaling pathways implicated in carcinogenesis or cancer stem cells (Sagar et al., 2007).

The category of stem cells, there own differentiation status, as well as proliferation capacity, the administration route, the intended location, throughout vitro culture and/or other manipulation stages, irreversibility of treatment, in need of concurrent tissue regeneration throughout case of irreversible tissue loss, as well as long-term survival of engrafted cells all influence the risk profile of stem cell-based medicinal products (Herberts et al., 2011).

Chapter 6

Cure vs Cause

Cancer stem cells, a type of cancer cell discovered inside certain tumors, are considered to be responsible again for origin and development of the malignancy in question, as per a body of research. Understanding the factors that control cancerous and healthy stem cell growth, self-renewal, survivability, differentiation, and differentiation might aid researchers in better understanding cancer mechanisms and developing more effective cancer treatments (Clarke & Fuller, 2006).

6.1 Comparison between fact and treatment

Individuals may be at danger in the losing proposition that leads to cancer since cells must proliferate throughout an organism's existence. Adult stem lineages may have developed to reduce the chances of cells escape procedures that limit their ability to divide by limiting the chances for cell escaping processes that affect their ability to grow. According to a recent research, the cancer cell hierarchy in some blood malignancies and tumors mimics that of healthy tissue from whence they formed, with cancer stem cells producing children with limited replication potential (Clarke & Fuller, 2006).

Only a tiny number all cancerous cells of breast and brain tumors have the capacity to self-renew, whereas the remainder have little or no growth potential. This raises the possibility that CSC are to responsible for the tumor's development and dissemination. Furthermore, the presence of a tissue stem population of cells has implications for cancer diagnosis and treatment, since cancer cases must be targeted to cure the disease. The tumor will recur after treatment if

these identity cells are not completely destroyed. If cancer stem cells can be detected before they reach the circulation, it will be able to explore necessary aspects or pathways that could be addressed to eradicate them (Clarke & Fuller, 2006).

Typical developmental stages in long-lived eukaryotes fail to satisfy the demands of replacement short-lived cell types found in the skin, gut, or blood could be a key stage in cancer progression. Cancer is a condition that causes the body's capacity to renew cells to be disrupted. The bulk of malignancies develop in organs including the epidermis, stomach, or blood, where continual proliferation is required to provide a steady supply of newly differentiated cells. A complex process is used to substitute mature cells in these tissues, where a small community of self-renewing adult stem cells generates replicating progenitor cells (also called transit-amplifying cells) that undertake a limited amount of mitotic divisions before terminal illness trying to distinguish as well as losing their proliferative ability. Only stem cells can survive for an extended amount of time in this hierarchical framework. Although progenitor cells may live for months or years, their lifetime is usually measured in days or weeks (Clarke & Fuller, 2006).

Strict procedures for regulating cellular growth were necessary when single-celled animals evolved into multicellular creatures with particular cell types and sophisticated organ systems. The ensuing tumor has the capacity to ruin the whole organism if any cells in the tissues communities are able to break free from such cell growth constraints. Lengthy multicellular animals have developed a number of cancer-fighting techniques that have been shown to work. The following are a few examples: As a consequence, a large somatic mutation must collect in a single cell stem and collaborate to overcome these protective systems in order enable cancer to spread. The deactivation of fail-safe processes, which may cause abnormal cells to die and prohibit cells from expanding into adjacent tissues, or the absence of normal growth controllers,

which can lead to the creation of polyps, can all lead to cell development (Clarke & Fuller, 2006).

Lengthy animals, on the other hand, are more likely to resort to cancer at a young age, regardless of the fact that cancer is caused by a huge number of mutations in a single malignant cell (as is the case with humans). Whenever it come to cancer prevention, it all boils down to a simple math problem. During the typical course of a human existence, billions of cells develop, and at most another of those cells acquires enough mutations to enable the creature to become cancerous while it still is a young adult. As a result, organisms have devised a technique for restricting the number of long-lived, self-renewing cells that can live in their surroundings. Reducing the long-term regeneration of short-lived types of cells might lessen the likelihood of a single proliferating cell accumulating the mutations required for cancer development in the future (Clarke & Fuller, 2006).

Counting systems that normally control and cap the number of cycles of subsequent transit-amplifying cell divisions may safeguard cancer-prone cells with heightened transit-amplifying capabilities. Despite the fact that stem cells and transit-amplifying cells multiply and produce the identical final (a spectrum of differentiating progeny), their ability to stay undifferentiated for lengthy periods of time differs (as opposed to stem cells that divide and differentiate). Even single hematopoietic stem cell could aid in the rebuilding of a mouse's blood system (HSC). The transit-amplifying progenitor cell produced from such an HSC is unable to self-renew if implanted into the a lethally irradiated host, and thus can only add to the circulatory system for just a limited time. A hematopoietic transit-amplifying cell's offspring grow progressively differentiated with each division, culminating in a drastically diminished ability to proliferate. Progenitor cells may cease multiplying and terminally differentiate as a result of this regulated

reduction in replication capacity before accumulating the many mutations required for tumor formation (Clarke & Fuller, 2006).

The ability to self-renew is one of the most essential characteristics shared by cancer stem cells or normal stem cells. The amount of daughter cells that preserve stem cell identity should be carefully managed to maintain tissue homeostasis. When the stem cell pool was maintained but not increased, differentiated cells may well be created in response to injury. The stem cell pool's development is controlled, limiting the formation of cancerous stem cells (Clarke & Fuller, 2006).

Cellular niches are critical in stopping mammalian stem cells in reproducing, according to a recent research. It's possible that critical aspects of the niche's self-renewal or stem cell differentiation activities failed. Throughout evolution, mutations have remained constant. Paracrine signaling pathways, negativity loops that limit the response to mitogenic input, or systems that stop the differentiation program from initiating in stem cells are all example of these characteristics. Other stem cell suppression strategies are translational repression or chromatin regulators, which limit the transcription of genes encoding in differentiation. It is feasible to ensure that development is the default situation by instructing adult stem cells towards differentiate. As a result, adult stem cells become programmed that differentiate and thus are lost to the pool for long-term proliferating cells unless they are placed in a specific location inside the niche (Clarke & Fuller, 2006).

6.2 Cancer stem cell leads to more specific cancer therapy

For cancer to develop, a population of continually reproducing (self-renewing) cells is required. At least two theories exist to explain the occurrence or cscs in tumors. For example, oncogenic mutations may be able to escape typical stem cell multiplication constraints, allowing cancer stem cells to be created from healthy stem cells. According to the second hypothesis, oncogenic mutations may allow transit-amplifying cells to keep reproducing while transiting to the a postmitotic notable change, producing inside a pool or self-renewing cells where further mutations may collect. This collection of cells may one day give birth to differentiated cancer stem cells (Clarke & Fuller, 2006).

In the first scenario, normal stem cells can acquire oncogenic mutations, resulting in defects of stem cell niche dependence systems. For example, mutations within systems to make stem cells rely just on niche for self-renewal may limit their efficiency. Another theory has been that cscs secrete substances which recruit tumor-forming cells towards the tumor, thereby widening the niche. In a separate situation, cscs could be able to enable self-renewal systems in response to stimulation apart from cell division signals. Cancer stem cells may be able to promote niche cell self-renewal routes via activating intracellular signals typically activated by niche cells, or by generating ligands normally produced by niche-forming cells, or by constitutively activating receptors that react to these ligands.

In the second scenario, oncogenic mutations may develop, allowing improper activating of a stem cell self-renewal regulating machinery within transit-amplifying cells, ultimately leading to cancer genesis. This could give transport progenitor cells stem-cell-like characteristics, resulting in the development of the a population of cells that could become completely malignant if

additional genetic events occur. The loss of regulatory domains essential for the activation of hierarchical position genes, cell-cycle inhibitors, or cell death genes, all of which were demonstrated to have a deleterious influence on self-renewal, are all examples of oncogenic alterations. Oncogenic mutations may trigger postmitotic differentiation or interfere with mechanisms that limit transit-amplifying cell division. Aside from that, it's possible that transit-amplifying cells may split more cells while reaching the post - mitotic phase than normal cells. Because transit-amplifying cells outweigh stem cells by a substantial margin, mutations that allow these to proliferate rather than terminal differentiate might be a key stage in tumor progression (Clarke & Fuller, 2006).

A succession of mutations disrupting normal embryonic processes, ending in the creation of cancer stem cells that drive tumor development, might be the origin of the vast majority of malignancies. The particular interactions with the niche required for stem cell maintenance will most likely decide whether a cancer stem cell starts from a normal stem cell or even a transit-amplifying progenitor cell. The differences between normal and cancerous stem cells could lead to the discovery of new targets again for development of appropriate cancer treatments. Medicines that stop the niche's self-renewal impulses in entering cancer stem cells, similarly to just how normal stem cells have indeed been repressed, may be produced since the niche and various stem cell types have various molecular links. Many mechanisms may be involved in controlling the intended decrease in transportation progenitor cell replication capacity with normal stem cell self-renewal, according to the findings. With a better understanding of such pathways including how they are disturbed in cancer stem cells, more efficient Geminin cancer treatments might be developed (Clarke & Fuller, 2006).

Table 1: The comparison between the cause and cure

Cause	Cure
Some malignancies begin in cells have the capability to self-renew that is called cancer stem cell.	.A major focus in stem cell biology is on a type of cell growth known as self-renewal, which is unique to stem cells.
The CSC model is based on the premise that non-tumorigenic cells in cancer evolve from parent tumorigenic cells inside a hierarchical and stable fashion, similar to how differentiated cells emerge from stem cells in normal tissue development and homeostasis.	If stem cell and tumorigenic cell have different renewal mechanism then it will have selective targeting as well as high therapeutic index. On the other hand this scenario will be totally vice versa if stem cell and tumorigenic cell have shared renewal mechanism.
The growth of tumorigenic cell is fast and aggressive.	In the stem cell therapy in cancer the progress rate is very slow compare to differentiation rate of cancer cell.

Chapter 7

Finding a new path in stem cell therapy for cancer

7.1 Limitations

On the basis of four types of cancer, cancer is classified in many ways, like glioma, colon adenocarcinoma, metastatic lung cancer, hepatocellular carcinoma, and so on. These classes of cancer have a different rate of abnormal cell growth and also have various stem cell therapies like neural stem cell's retroviral transduction, baculoviral transduction, adenoviral transduction, and so on (Zhang, 2017). In this paper, all types of cancer growth rates as well as their various stem cell therapies were not possible to describe.

7.2 Future direction

Despite advances in -pre-clinical and clinical studies, stem cell treatment still faces numerous difficulties. Further research would be carried out to provide insight on the role of stem cell signalling in tumor progression in certain situations, allowing a suitable stem cell engineering technique to be selected. Furthermore, given the intricacy and immunosuppressive qualities of something like the solid tumor microenvironment, combining additional medicines, such as immune checkpoint inhibitors, may improve the efficacy of cancer treatment and recurrence prevention. In conclusion, current stem cell technology outcomes for tumor treatment are very promising, but more work is wanted to enhance the safety and effectiveness before clinical trials can begin.

Chapter 8

Conclusion

In this paper the differences between cause and cure of stem cell for cancer disease as well as the obstacles of stem cell therapy are emphasized. In future to develop this process for cancer treatment we should minimize the differences of cause and cure. We should work on stem cell therapy and should find alternative way so that the stem cell therapy progress rate will increase and growth rate of cancer cell will be decrease. Also the research's obstacles of stem cell should be considered. Finally targeting cancer stem cell growth along with finding proper stem cell therapy with low cost and less defection for specific cancer disease should be reviewed.

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