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Targeting multiple cancers: exploring the potential role of stem cells in treating 10 distinct types

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Abstract

Stem cell research has gained significant prominence due to its therapeutic potential in addressing diseases that are difficult to treat with conventional therapies, particularly cancer. Cancer remains a global health crisis responsible for one in six deaths worldwide and is characterized by uncontrolled cell growth, metastasis, and a generalized loss of growth control. Traditional cancer treatments, including surgery, radiation, and chemotherapy, have limitations, such as damaging healthy cells and tissues, and are often associated with cancer recurrence and metastasis. In response to these challenges, stem cell technology has emerged as a promising frontier, offering novel approaches to target and eliminate cancer cells while potentially reducing the side effects associated with conventional therapies. This review explores the biochemical properties of stem cells and their potential applications in treating ten distinct types of cancer. We analyze each cancer type to understand the potential use of stem cells in treatment. The article aims to contribute the growing body of knowledge and provide insights into the future directions of stem cell research in oncology.

Keywords: Stem Cell Therapy, Cancer Treatment, Oncology, Multi-cancer Therapy, Regenerative Medicine

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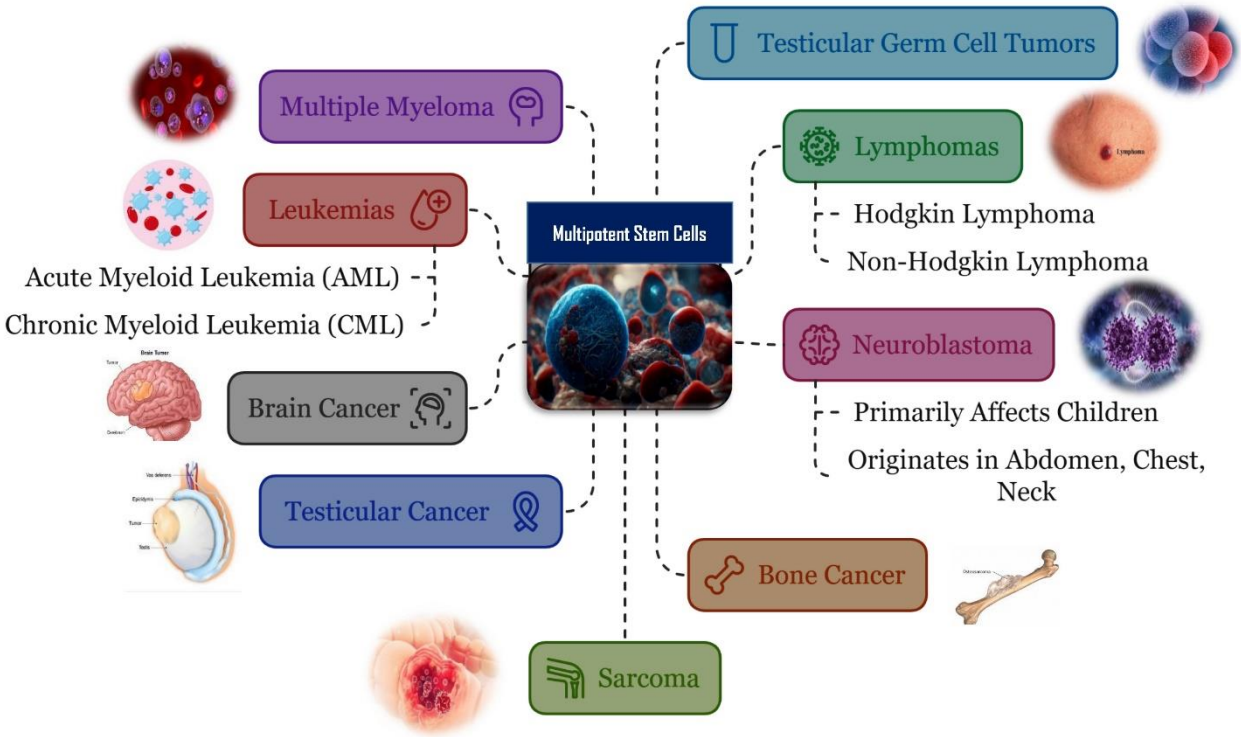
Graphical abstract



Introduction

In recent years, stem cell research has gained significant attention due to its potential therapeutic applications in addressing challenging diseases, many of which remain largely untreatable by conventional therapies, particularly cancer. Cancer represents a significant global health issue, accounting for one in every six deaths across the globe (1). This intricate and destructive disease, marked by the unregulated growth and multiplication of cells, continues to pose a substantial challenge to health systems worldwide. This condition arises from abnormal cell proliferation resulting from genetic mutations (2). Cancer cells possess the capability to proliferate without limit and circulate to various regions of the body through the process of metastasis. This represents a highly intricate series of medical conditions that advance progressively, resulting in a widespread loss of regulatory control over growth. For many decades, patients had limited options for cancer treatment, primarily consisting of surgery, radiation therapy, and chemotherapy, either as standalone therapies or in various combinations (3). Radiation therapy has the potential to harm healthy cells, organs, and tissues (4). Conversely, while chemotherapy has significantly decreased morbidity and mortality rates, it is important to note that nearly all chemotherapeutic agents adversely affect healthy cells, particularly those that are rapidly dividing and growing (5). While conventional treatment approaches can significantly decrease tumor size, the recurrence and spread of cancer remain persistent challenges.

During this time, cancer treatments have been the subject of more than half of all ongoing medical treatment research worldwide. Cancer remains a leading cause of mortality worldwide, despite advancements in traditional treatments such as surgery, chemotherapy, and radiation therapy. However, stem cell technology, emerging as a promising frontier, complements traditional cancer treatments by offering novel approaches to target and eliminate cancer cells while potentially reducing the side effects associated with chemotherapy and radiation (6). Researchers are harnessing the distinctive characteristics of stem cells, including their ability to self-renew and differentiate, to create innovative treatment approaches that are more precise, effective, and less harmful. Stem cell therapies have the potential to specifically target cancer cells by modifying stem cells to transport therapeutic agents

directly to tumor locations, thereby reducing harm to surrounding healthy tissues. This review article explores the biochemical underpinnings of stem cells and delves into the exciting possibilities of stem cell technology in combating various types of cancer. We will navigate the potential applications of stem cells in treating ten distinct types of cancers, including: myeloid leukemia (acute & chronic), brain tumor, lymphoma, multiple myeloma, germ cell tumor, testicular cancer, osteosarcoma (bone cancer), Neuroblastoma (develops from immature nerve cells), and sarcoma (develops in soft tissues).

Acute myeloid leukemia (AML) and chronic myeloid leukemia (CML) are both bone marrow cancers characterized by abnormal white blood cell production (7)**.** Brain cancer is a deadly disease with limited treatment options (8). Testicular cancer is a rare male cancer with two main types: seminomas and non-seminomas (9). Osteosarcoma is a prevalent bone cancer, primarily affecting adolescents (10). Lymphoma is a cancer of lymphatic tissue classified into Hodgkin and non-Hodgkin types, originating from B, T, or natural killer cells. Multiple myeloma is a cancer of plasma cells causing various health issues (11). Testicular germ cell tumors (TGCTs) originate from abnormal testicular stem cell development (12). One kind of cancer that arises in immature nerve cells is called Neuroblastoma. It primarily affects children and can originate in various parts of the body, including the abdomen, chest, and neck (13). Sarcoma is a cancer that arises in soft tissues, such as muscle, fat, blood vessels, or connective tissue. It can occur in people of all ages and often affects the arms, legs, or trunk (14).

This journey will also acknowledge the current challenges and ongoing research efforts aimed at translating this potential into effective and widely accessible clinical applications. As we embark on this exploration, one thing remains certain: stem cell technology has the potential to reshape the future of cancer treatment, presenting a future filled with renewed hope for patients worldwide. It's important to note that stem cell therapy for cancer is still under development. Several stem cell therapies are available; however, the majority remain in experimental phases, are expensive, or raise ethical concerns (15). While these characteristics hold promise, researchers are working on overcoming challenges such as assuring the safety and effectiveness of stem cell therapy. Despite the challenges, stem cell research offers a ray of hope for the future of cancer treatment. By utilizing the specialized characteristics of stem cells, scientists are developing novel approaches to combat this complex disease.

1. Therapeutic Potential of Stem Cells in Cancer Treatment

A stem cell is defined as a type of cell that possesses the capacity for continuous division and the ability to differentiate into diverse other cell types or tissues. Stem cells serve as a vital reservoir within the body's cellular system. In instances where there is a deficiency of specific cell types, stem cells can transform into those required cells, such as liver and kidney cells. Additionally, since blood cells and muscle cells lack the capability to divide and produce new cells, stem cells also play a crucial role in producing blood and muscle cells within the body. On the basis of origin or formation type, stem cells are commonly divided into Embryonic Stem Cells, Adult Stem Cells, and Induced Pluripotent Stem Cells. Based on the level of differentiation (potency), stem cells can be categorized as totipotent, pluripotent, multipotent, oligopotent and unipotent stem cells (16).

Stem cells possess the ability to self-renew through a process of continuous division over time. This characteristic allows them to serve as a potentially limitless source of cells for therapeutic purposes. In cancer treatment, this could be beneficial for replacing diseased or damaged blood-forming stem cells in bone marrow with healthy ones, often from a donor. Stem cells have the capability to generate similar stem cells. These cells possess the unique ability to differentiate into specific cell types within the body, such as blood cells, lung cells, and kidney cells, thereby contributing to the maintenance of cellular equilibrium (17). Furthermore, stem cells perform a crucial function in stimulating organs by providing necessary cellular support. They can replace aged, dying, or damaged cells, ensuring that organs consistently receive fresh cells to operate effectively.

Stem cells can be modified to transport therapeutic agents directly to tumor locations, thereby reducing harm to surrounding healthy tissues (18). This can be

accomplished through several approaches, including the genetic alteration of stem cells to generate and release therapeutic proteins (such as anti-cancer medications and cytokines), encapsulating drugs within the stem cells, or employing stem cells as carriers to deliver nanoparticles or alternative drug delivery systems to the tumor microenvironment. Stem cells possess the capability to be modified in order to strengthen the immune system's response to cancer cells through a variety of mechanisms (19). These cells can be designed to produce cytokines or other immune-activating substances that stimulate immune cells, including T cells and natural killer cells, thus enhancing the overall immune response. Furthermore, stem cells can be genetically altered to express tumor-specific antigens, which can initiate an immune reaction against cancer cells. This approach may also encompass the use of stem cells to develop adoptive cell therapies, such as chimeric antigen receptor T cells (CART cells), which are specifically tailored to identify and eliminate cancer cells (20).

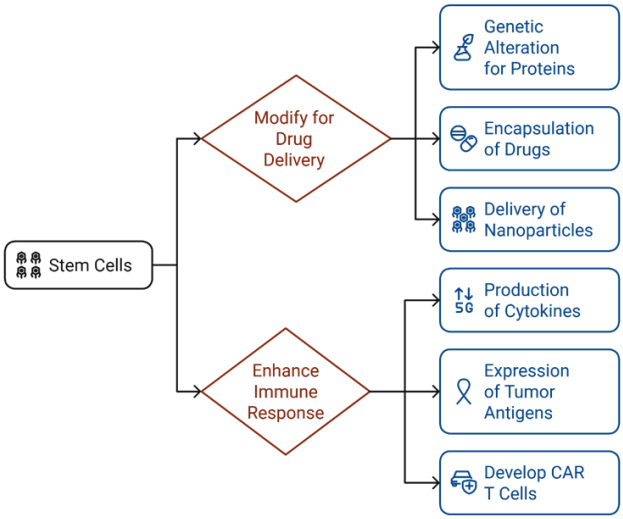


Figure 1. The role of stem cells in targeted drug delivery and immune modulation for cancer treatment.

Stem cell therapy is commonly referred to as regenerative medicine (21). Depending on the type of stem cell, they can differentiate into various specialized cell types. In some cancers, healthy tissue is damaged during treatment. Stem cells could potentially be used to regenerate healthy tissue, such as liver or bone, after cancer treatment. Certain stem cells exhibit immunomodulatory characteristics, indicating their ability to affect the immune system's reaction. This could be beneficial for suppressing tumor growth by stimulating the immune system to attack cancer cells, reducing inflammation caused by cancer or its treatment (22). Due to these characteristics, stem cells hold immense potential in many diseases, especially cancer treatment. Their distinctive capability for self-renewal and differentiation into multiple cell types offers novel therapeutic avenues. By targeting cancer stem cells, researchers aim to eradicate the root cause of tumor growth. Additionally, stem cells can be engineered to deliver therapeutic agents directly to cancer sites or to boost the immune system's anti-tumor response (18). While significant challenges remain, such as the ethical considerations associated with the utilization of embryonic stem cells in cancer treatment, the potential of stem cell-based therapies to improve patient outcomes is driving extensive research and clinical development. But our question is, can stem cell-based therapies offer a more personalized approach to cancer treatment in the future?

2. The Role of Stem Cells in Cancer Treatment: Addressing Diverse Cancer Types and Challenges

Because of their exceptional capacity to self-renew, differentiate into a various cell types, and potentially target malignant cells, stem cells have become a viable tool in the treatment of several forms of cancer. This review delves into the therapeutic potential of stem cells in addressing a spectrum of cancers. Each type of cancer presents unique challenges and complexities, which we have thoroughly examined and discussed. By exploring the diverse applications of stem cells in these cancer types, this study underscores the potential of stem cell-based therapies to revolutionize cancer treatment. However, challenges such as tumor heterogeneity (23), immune suppression (24), and ethical considerations must be carefully addressed to realize the full potential of this approach. Tumor heterogeneity refers to the genetic and phenotypic variations present among cancer cells within a single tumor. These differences can significantly reduce the overall effectiveness of treatments. To enhance the efficacy of targeted therapies and ensure consistent treatment results, it is essential to recognize and address the issue of heterogeneity (25). Tumors generate an immunosuppressive environment that reduces the effectiveness of immunotherapies, including those that involve stem cells. Mechanisms like cytokine modulation and the function of regulatory

T-cells allow tumors to escape detection by the immune system. Addressing immune suppression to improve therapeutic results continues to be a key area of research (26).

3.1. Acute myeloid leukemia

A study by Hahn et al. (2015) revealed that approximately 14,000 new cases of Acute Myeloid Leukemia (AML) were identified, and 10,000 deaths were recorded in the United States during the year 2013 (27). Acute Myeloid Leukemia (AML) is a bone marrow-derived malignancy leading to the rapid proliferation of abnormal white blood cells. It is caused by genetic alteration that affects hematopoietic stem cells and causes an excess production of malignant clonal myeloid stem cells. Abnormal leukemic cells cause disruptions in the normal synthesis of blood cells, which results in bleeding, infections, and exhaustion. While extra-medullary manifestations may arise, the primary cause of the disease lies in abnormalities related to hematopoietic cell production. A small percentage of cases can be linked to prior chemotherapy or chemical exposures; however, the vast majority are attributed to chromosomal anomalies or mutations in single genes, without an apparent cause (28). Hematopoietic stem cells, a specific type of stem cell, have been used to treat acute myeloid leukemia. Hematopoietic stem cells are employed in the treatment of Acute Myeloid Leukemia (AML) by replacing the affected bone marrow with healthy stem cells that can yield normal blood cells and may also eradicate cancerous cells. This approach aims to reset the immune system and achieve long-term remission by eradicating leukemia cells and restoring healthy hematopoiesis.

3.2. Chronic Myeloid Leukemia

A bone marrow-derived malignancy known as chronic myeloid leukemia (CML) is distinguished by a high concentration of white blood cells and the Philadelphia chromosome. Edition et al. (2017) reported the incidence of CML to be 1-2 cases per 100,000 adults (29). However, it's important to note that the incidence of CML can vary depending on factors such as age, geographic location, and population demographics This disease progresses through three stages: chronic, accelerated, and blast crisis. Each stage has a higher severity and more difficult treatment options. A study by Champlin et al. (2011) revealed that treatment for CML involves the use of stem cell therapy, including allogeneic hematopoietic stem cell transplantation (HSCT), in which the patient receives transplants of healthy stem cells from a donor (30). This technique is thought to be the only viable approach for CML. Because of the possibility of reintroducing leukemic cells, autologous stem cell transplantation—which employs the patient's own stem cells—is less prevalent in CML patients. However, patients who do not have a compatible donor may still undergo this procedure. Moreover, stem cell transplants are frequently used in conjunction with targeted therapy like tyrosine kinase inhibitors (TKIs), which include medications like imatinib, dasatinib, and nilotinib to lessen the impact of the disease and sustain recovery (31) (32). Identifying an appropriate donor, controlling graft-versus-host disease (GVHD), and coping with a high risk of infection and other problems after transplantation are some of the difficulties associated with HSCT. Clinical results for CML patients receiving stem cell therapy have greatly improved, and many of them have achieved long-term recovery, especially when HSCT is carried out when the illness is still in its chronic stage (33).

Table 1. Comparison of Acute Myeloid Leukemia (AML) and Chronic Myeloid Leukemia (CML).

Sr No	Feature	Acute Myeloid Leukemia (AML)	Chronic Myeloid Leukemia (CML)
1	**Definition**	Malignant disorder of bone marrow leading to rapid proliferation of abnormal white blood cells	Chronic bone marrow disorder characterized by increased white blood cells and the Philadelphia chromosome
2	**Incidence**	Approximately 14,000 new cases and 10,000 deaths in the US in 2013	1-2 cases per 100,000 adults
3	**Disease Stages**	Single acute phase	Chronic, accelerated, and blast crisis phases
4	**Genetic Abnormalities**	Various chromosomal abnormalities and single gene mutations	Presence of the Philadelphia chromosome

5	**Treatment Approach**	Primarily hematopoietic stem cell transplantation (HSCT)	HSCT and targeted therapy (TKIs)
6	**Challenges**	Finding suitable donor, graft-versus-host disease	Finding suitable donor, graft-versus-host disease, resistance to TKIs

3.3. Brain tumor

One of the hardest tumors to cure is brain cancer (34). The latest worldwide cancer statistics issued by the World Health Organization (WHO) in 2020 indicate that brain tumors make up around 1.6% of all reported cases and account for 2.5% of all tumor-related deaths. Brain tumors may be classified into two categories: primary and secondary brain cancer. Primary brain cancer arises from brain cells and develops inside the central nervous system (CNS), often without spreading to other parts of the body outside the CNS. Secondary brain cancer arises and spread from outside the central nervous system (CNS), namely from organs such as lung, skin, breast, colon, and kidney (35). Brain cancer that is very malignant, aggressive, and usually fatal is called glioblastoma multiforme (GBM). The frequent and fast recurrence of GBM leads to a low 5-year survival rate of just 4%, despite the use of gold-standard therapies such as temozolomide-based chemotherapy and radiotherapy. The Blood Brain Barrier (BBB) makes it difficult to treat brain tumors effectively because it prevents medications from getting to the afflicted region. Lengel et al. (2020) investigated that a unique therapeutic method to treat brain damage has been the use of exosomes derived from stem cells (36). Stem cells are important for the treatment of brain tumors because they show promise for both specific cancer treatment and regenerative therapies. Cancer stem cells (CSCs) are hypothesized to be present in brain tumors and to be the cause of the tumor's proliferation and resistance to conventional therapies. Targeting these CSCs can result in more successful treatments, while regular stem cells can be used in regenerative therapies to repair damage caused by malignancies or their treatment (37).

3.4. Testicular Cancer

Testicular carcinoma is an uncommon form of tumor that makes up only 1% of all cancers in males; it is also known as testicular germ cell carcinoma (TGCC). 50% of all TGCC are seminomas, while the remaining 50% are non-seminomas. A study by Popovic et al. (2015) revealed that most testicular germ cell cancers (TGCC) originate from the gonads, whereas approximately 5% originate from extragonadal areas along the body's mid-line, such as the retroperitoneum, mediastinum, or brain (38). Various surgical and hormonal interventions are available for TGCC treatment; however, in recent years, there has been a significant concentration on stem cell therapy (39). The notion of cancer stem cells (CSCs) states that CSCs are accountable for the growth, invasion, and spread of tumors (40). Spermatogonial stem cells (SSCs) are a type of stem cell found in the testis that perform a crucial role in the process of spermatogenesis, which is necessary for male fertility (41). Stem cells can be obtained from numerous resources, such as bone marrow, peripheral blood, dental pulp, hair follicles, and adipose tissue, with adipose tissue being considered one of the more accessible sources for isolating stem cells to treat these types of cancers.

3.5. Osteosarcoma (Bone cancer)

Osteosarcoma is the predominant tumor of the bone, primarily affecting individuals in the infant and adolescent age groups. Eaton et al. (2021) estimated that reports of osteosarcoma cases in youngsters are 4.4 per million annually (42). Lin et al. (2021) investigated that osteosarcoma primarily develops from the metaphysis of long bones, primarily affecting the proximal and distal ends of the humerus and femur (43). The substantial side effects and high dose levels necessary for the effectiveness are the constraints of this commonly used anticancer drug (44). Mesenchymal stem cells (MSCs) are found locally next to tumor tissues and may interact directly with malignancies, according to recent investigations. Through genetic engineering or spontaneous transformation, human bone marrow mesenchymal stromal cells (BMSCs) can support OS development (45). According to accumulating data, Hinoi et al. (2024) suggest that targeting OSCs may be a successful tactic for enhancing OS treatment (46).

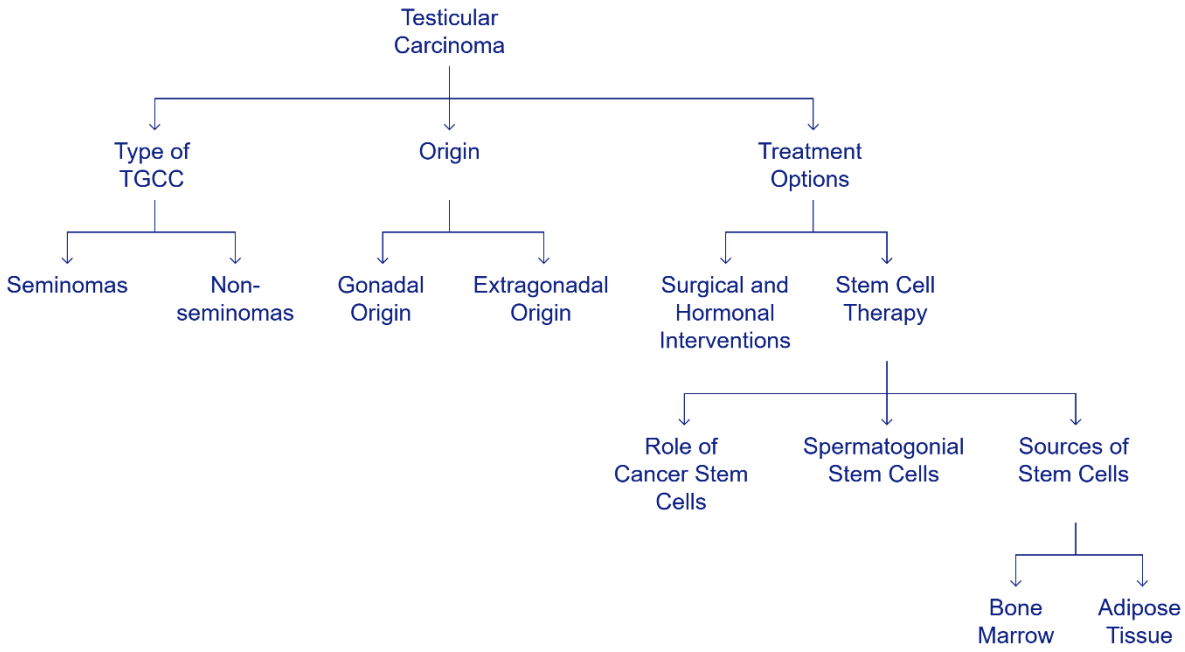


Figure 2. Testicular germ cell tumors: origin, treatment, and the role of stem cells.

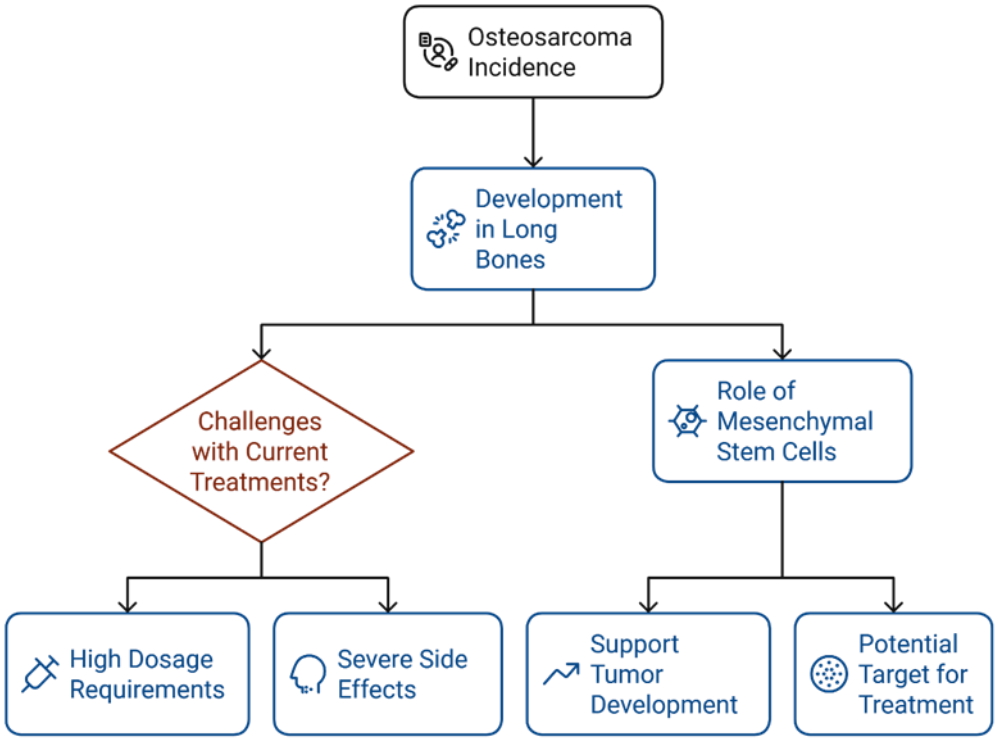


Figure 3. Osteosarcoma: a pediatric bone cancer with significant therapeutic challenges.

3.6. Lymphoma

Lymphoma constitutes a diverse group of malignant neoplasms of lymphocytes that includes lymphatic tissue, bone marrow, or extra-nodal sites. Lymphoma develops due to its expansion through extra-nodal sites by direct invasion or by circulatory flow to the spleen, liver, lungs, or bone marrow. He et al. (2023) reported that the primary classification of lymphoma is obtained from B-cell, T-cell, or natural killer cell origin (47). On the other hand, Hazani and Isaac (2019) noted that lymphoma commonly presents as painless adenopathy, with symptoms such as fever, severe weight loss, or

night sweats often occurring in the critical stage of the disorder (48). It is conventionally categorized usually as non-Hodgkin and Hodgkin lymphoma.

Hodgkin lymphoma (HL) is an abnormal B-cell lymphoma that is specifically distinguished by some malignant cells, such as cancerous Reed-Sternberg cells in an inflammatory environment (49). Non-Hodgkin lymphoma (n-HL) is a diverse group of malignant diseases emerging from the cells of the immune system, such as lymphoid tissue (50). Almost all non-Hodgkin lymphomas emerge from mature B lymphocytes, while few of them are produced from T lymphocytes or natural killer (NK) cells. According to Chu et al. (2023), several risk factors for both lymphomas include genetics, viral infections, immune-deficiency disorders (such as HIV), physical relationships, and environmental hazards (51).

Repeated or refractory disorder can be efficiently handled or treated by high-dose chemotherapy following autologous stem cell transplantation (ASCT), yet there is a notable portion of some patients that relapse after the treatment. Allogeneic stem cell transplantation (All-SCT) can be utilized for those patients who have repeated disorders or those who have failed ASCT (52). Therefore, the development of some novel agents, such as antibody-based therapies and checkpoint inhibitors, has remarkably increased the outgrowth of patients with HL or n-HL that repeats after ASCT. Probably, the development of some latest drugs in the first-line setting will efficiently enhance prolonged outcomes of ASCT (53).

Table 2. List of some novel agents/antibody-based therapies or checkpoint inhibitors for the treatment of Hodgkin's lymphoma and non-Hodgkin's lymphoma after ASCT.

Lymphomas	Antibody-based therapies	Checkpoint inhibitors	Reference
Hodgkin's lymphoma	Brentuximab Vedotin (BV) AFM13 ADCT-301 Camidanlumab Tesirine (Cami)	Nivolumab Pembrolizumab Histone deacetylase inhibitors Chimeric antigen receptor (CAR) T-cells	(54)
Non-Hodgkin's lymphoma	Rituximab Brentuximab vedotin (BV) Alemtuzumab Ofatumumab	Pembrolizumab (Anti-PD1) Nivolumab (Anti-PD1) Atezolizumab (Anti-PD-L1) Ipilimumab (Anti-CTLA-4)	(55)

3.7. Multiple myeloma

Multiple myeloma is a hemostatic malignancy of plasma cells that develops monoclonal immunoglobulin in an abnormal way, arising from the bone marrow. Rajkumar (2018) reported that this disorder usually presents with hypercalcemia, renal failure, anemia, and a large number of infections (56). Nearly all patients with multiple myeloma arise from an asymptomatic pre-malignant stage called monoclonal gammopathy of undetermined significance (MGUS) that is described by the appearance of a monoclonal protein. Various risk factors are involved, such as high levels of monoclonal protein, the presence of plasma cells in the bone marrow, or a high percentage of IgA monoclonal protein (57).

The establishment of high-dose therapy after autologous stem cell transplantation (ASCT) is an ordinary treatment for young patients with early stages of multiple myeloma (58). Advanced therapies for these patients as a medicinal application conveyed before ASCT or after ASCT, such as induction, consolidation, and maintenance treatment in order to eliminate tumor overburden and minimize attainable infections on normal hematopoietic cells. An enlargement of immunomodulatory drugs such as thalidomide, lenalidomide, pomalidomide, and monoclonal antibodies like daratumumab, along with second-generation proteasome inhibitors for example, carfilzomib, bortezomib etc., gave rise to the remarkable advancement in the survey of patients having multiple myeloma (MM), appropriate for autologous stem cell transplantation (ASCT) (59).

3.8. Testicular germ cell tumor

Human germ cell tumors (GCTs) are believed to emerge from stem cells of premature embryos and the germ line that are present in the gonads (ovaries or testes) as well as in extragonadal sites, where primordial germ cells (PGCs) are found during embryogenesis (60). Dieckmann et al. (2018) found that testicular germ cell tumor (TGCT) is the most frequent malignant GCT in adults or young men, accounting for almost 95%, with variations observed across different geographical regions (61). The phenomena of TGCT are a complex procedure where many molecular deformities give rise to its evolution, characterized by some environmental or hormonal factors. Spermatogenesis is a basic principle to a male's progress and prolongation of fertility. TGCTs occur due to the failure of normal maturation of testicular stem cells (TSCs) controlled by clinical procedure, where TSCs do not encounter exact spermatogenic differentiation yet convert into intratubular germ cell neoplasia (IGCN) or carcinoma in situ (CIS) that presents as the precursor cells for first stage TGCTs (62).

Differentiation therapy has the ability, just like chemotherapy, to utilize non-cytotoxic advanced procedures to minimize tumor development, such as pluripotent embryonal stem cells, particularly influence the separation of Cancer Stem Cells (CSCs), whereby decreasing the possibility for metastasis that leads to repetition of the disorder (40). Specific applications utilized in order to produce CSC-targeted therapies that include some drugs such as salinomycin, an antibiotic that diminishes mammary development of tumors, as well as Thioridazine, an antipsychotic, which particularly influences the depletion of CSCs without changing normal hematopoietic stem cells.

3.9. Neuroblastoma

Morgenstern et al. (2013) reported that neuroblastoma (NB) is a solid tumor that constitutes 6% of all pediatric cancers and is the most prevalent cancer diagnosed in infants (63). Neural crest cells are the progenitors of the sympathetic nervous system and the source of neuroblastoma. Neuroblastoma begins in the adrenal glands but also finds its way in nerve tissues along the spine, chest, abdomen, or pelvis. Systemic spread and recurrent relapses are clinical features of NB disease development, with a short survival timeline (1st relapse in 18 months, 2nd relapse in 8.7 months, and 3rd relapse in 3.8 months). Obtaining a cure after a relapse of progressive non-communicable bone disease is extremely difficult due to the disease's heterogeneous behavior (64). There are many different treatment options for neuroblastoma, and these generally combine several methods. Surgical procedures, chemotherapy, radiation therapy, and immunotherapy are examples of conventional treatments. Surgery by alone may be curative in low-risk patients. Intense chemotherapy is usually required for intermediate- and high-risk neuroblastoma, and the tumor may occasionally be surgically removed after treatment. When a tumor is incurable or there is leftover disease, radiation therapy is frequently used to treat it. Additionally, Kushner et al. (2005) highlighted that immunotherapy—especially using anti-GD2 antibodies—has emerged as a key component of neuroblastoma treatment, aiding in the more precise targeting and elimination of cancer cells (65).

Two consecutive autologous stem cell transplants (tandem ASCT) increased event-free survival rates in children with high-risk neuroblastoma when compared to a single transplant, according to a noteworthy research conducted by the Children's Oncology Group (COG) (66). Although long-term results are still being investigated, preliminary trials employing CAR-T cells and stem cell-derived treatments show promise. These treatments aim to lower recurrence rates and enhance patients' quality of life. Using stem cells in conjunction with precision medicine techniques like gene editing and immunomodulation to customize therapies to each patient's requirements is becoming more and more supported by research (67). The use of genetically modified natural killer T cells to combat neuroblastoma was investigated in a recent clinical experiment. Early-phase studies of this immunotherapeutic strategy have demonstrated preliminary safety and effectiveness, giving optimism for further advancements. To produce NK cells for targeted treatment, researchers are looking into using human induced pluripotent stem cells (iPSCs). Scalability and immunological compatibility are two benefits of iPSCs that are essential for treating pediatric malignancies (68). Neuroblastoma treatment has been revolutionized by stem cell technology,

particularly for high-risk cases. Mora (2022) indicated that following intense chemotherapy, autologous stem cell transplantation (ASCT), which involves harvesting and reinfusing hematopoietic stem cells from the patient's bone marrow or blood, is now considered standard therapy (69). By mending the damage that chemotherapy has caused to the bone marrow, this mechanism improves survival rates and permits greater chemotherapy dosages. Furthermore, continuing studies on mesenchymal stem cells (MSCs) have shown promise in directly delivering targeted therapeutics to tumors, potentially leading to less toxic and more effective therapy options.

3.10. Sarcoma

Sarcoma is a diverse group of cancers that arise in the bones and soft tissues, involving fat, muscle, blood vessels, deep skin tissues, and nerves (14). It accounts for about 1% of adult cancers and 15% of pediatric cancers, making it relatively rare but challenging due to its diverse presentation and aggressive nature. Sarcomas are broadly classified into two main categories: bone sarcomas, such as osteosarcoma and Ewing sarcoma, and soft tissue sarcomas, including liposarcoma, leiomyosarcoma, and angiosarcoma (70). These tumors have the capability to arise in any region of the body; in spite of this, they are mainly located in the arms, legs, and trunk. Bindal et al. (1994) highlighted that the clinical manifestations of sarcoma vary based on the tumor's size and location, often leading to a delayed diagnosis. Additionally, sarcomas are known for their ability to metastasize, particularly to the lungs, which complicates treatment and significantly worsens prognosis (71). Standard treatment options for sarcoma typically involve a combination of surgery, radiation therapy, and chemotherapy. Surgical resection with clear margins is the primary approach for localized sarcoma, while radiation therapy is often used to shrink the tumor before surgery or to eliminate residual disease postoperatively. Chemotherapy is more commonly employed for high-grade or metastatic sarcomas, although its effectiveness can be limited (72).

Stem cell technology has recently emerged as a promising avenue for improving sarcoma treatment outcomes. For high-risk cases, autologous stem cell transplantation (ASCT) following high-dose chemotherapy has been explored as a means to restore the patient's bone marrow function and allow for more aggressive chemotherapy regimens (73). Moreover, ongoing research into mesenchymal stem cells (MSCs) offers hope for the development of novel therapies that could directly target sarcoma cells, reduce tumor growth, and enhance the precision of treatment while minimizing damage to surrounding healthy tissues. The ability of mesenchymal stem cells (MSCs) to directly transport anti-cancer drugs to tumors is being investigated. In order to stop tumor growth, researchers are investigating whether modified MSCs can target sarcoma sites and release therapeutic chemicals like cytokines or gene-editing tools (74). Clinical research is looking into how stem cell-derived therapies may be used in conjunction with more conventional treatments like radiation and chemotherapy. By decreasing tumor recurrence and promoting tissue healing after therapy, this strategy seeks to improve the effectiveness of current techniques (3). Regenerative therapy is another area of attention for stem cell research in sarcoma. Stem cells are being investigated for fostering tissue regeneration and reducing harm from invasive therapies after surgically excising malignancies. The genetic manipulation of stem cells for precise sarcoma targeting is still being refined in lab research. Among these initiatives is altering the cells to withstand immune suppression techniques frequently used by sarcoma tumor (75). Although still in the experimental stages, these approaches represent a potential paradigm shift in the management of this complex and often deadly group of cancers.

Table 3. Overview of Stem Cell-Based Therapies for Different Cancer Types.

Sr No	Cancer Type	Stem Cell Type(s)	Potency	Clinical Applications	References
1	Acute Myeloid Leukemia	Hematopoietic	Multipotent	Bone marrow transplantation	(76)
2	Chronic Myeloid Leukemia	Hematopoietic	Multipotent	Bone marrow transplantation (allogenic)	(77)

3	Brain Tumor	Mesenchymal, Neural Stem Cells	Multipotent	Tumor targeting, immune modulation, tissue repair	(78)
4	Testicular Cancer	Spermatogonial stem cells	Multipotent	Tumor replacement, immune modulation, tissue repair	(79)
5	Osteosarcoma	Mesenchymal stem Cells	Multipotent	Bone regeneration, tumor suppression	(80)
6	Lymphoma	Hematopoietic, Mesenchymal	Multipotent	Immune modulation, tumor targeting, tissue repair	(81)
7	Multiple Myeloma	Autologous Hematopoietic stem cells	Multipotent	Bone marrow regeneration, immune modulation	(82)
8	Germ Cell Tumor	Embryonic Induced Pluripotent Stem Cells	Pluripotent	Tumor replacement, differentiation therapy	(83)
9	Neuroblastoma	Neural Stem Cells, Mesenchymal Stem Cells	Multipotent	Tumor targeting, immune modulation, tissue repair	(84)
10	Sarcoma	Mesenchymal Stem Cells	Multipotent	Tumor suppression, tissue regeneration	(85)

4. Challenges

There's a potential risk of uncontrolled cell growth and tumor formation if transplanted stem cells are not properly controlled. Stem cells, particularly induced pluripotent stem cells (iPSCs) and embryonic stem cells (ESCs), have the ability to differentiate uncontrollably, leading to the formation of tumors themselves (86). Ensuring the safety and minimizing side effects of stem cell-based treatments is crucial for clinical translation. Stem cell therapy is often expensive and may be inaccessible to patients due to high treatment costs. Ensuring that these treatments are cost-effective and widely available is an important challenge (87). Variability in stem cell sources, isolation methods, culture conditions, and differentiation protocols can lead to inconsistencies in cell quality and therapeutic outcomes. Immune rejection continues to pose a considerable obstacle in the field of stem cell transplantation therapies. The immune system may recognize stem cells as foreign and reject them, particularly if the stem cells are derived from donors or are genetically modified (88). This poses a challenge for the long-term effectiveness of stem cell-based cancer therapies. Strategies to mitigate immune rejection, such as immunosuppression. The long-term effects of stem cell therapy in cancer treatment are not yet fully known. Monitoring patients over time to assess the safety and efficacy of these treatments is a critical aspect of their development (89).

5. Future prospects

The exploration of stem cells in cancer treatment holds significant promise, yet much remains to be discovered and refined before these therapies can be fully realized in clinical practice. One of the key future directions is the enhancement of targeted delivery systems, ensuring that stem cells can accurately locate and treat cancer cells without affecting healthy tissues. Lotfi et al. (2023) suggested that advances in nanotechnology and gene editing, such as CRISPR, may play an essential role in enhancing the precision and efficacy of stem cell-based therapies (90). Another important area of future work involves overcoming the risks associated with stem cell therapy, particularly the potential for tumorigenicity and immune rejection (91). Developing safer stem cell lines, along with improved methods for controlling stem cell differentiation, will be critical for the success of these treatments. The convergence of immunotherapy and stem cell therapy presents significant potential for transforming the landscape of cancer treatment (92). By harnessing the power of the immune system and the regenerative potential of stem cells, this synergistic approach offers novel strategies

to combat cancer. The use of engineered stem cells is another method that is being actively pursued (93). New approaches have been developed in light of our growing knowledge of the molecular mechanisms underlying stem cell self-renewal and proliferation as well as the identification of additional genes governing stem cell differentiation and proliferation. Nanomedicine is another strategy that has lately been considered as a potential method in cancer treatments (94).

Conclusion

In conclusion, stem cell research represents a transformative approach in the fight against cancer, offering new hope for patients facing this devastating disease. As cancer remains one of the prominent causes of death globally, traditional therapies like surgery, radiation, and chemotherapy, though effective in many cases, often fall short due to their inability to fully eradicate cancer cells and prevent recurrence. Stem cell-based therapies present a promising alternative, with their unique capability to identify and eradicate cancer stem cells, potentially reducing the risk of relapse and metastasis. The potential of stem cells to distinguish into multiple cell types, along with their ability for self-renewal, opens new avenues for cancer treatment, particularly for types of cancer that have limited treatment options. However, significant challenges remain, including the risk of tumorigenicity, immune rejection, and the high cost of treatment. Despite these challenges, the future of stem cell-based cancer therapy is bright. Advances in technology, such as gene editing and targeted delivery systems, are likely to overcome many of the current obstacles, bringing us closer to acknowledging the full potential of these therapies. The integration of stem cell therapy with existing treatments, such as immunotherapy, could revolutionize cancer care, offering more effective and less harmful treatment options. As research continues to advance, stem cell-based therapies may soon become a cornerstone of cancer treatment, offering new hope for millions of patients worldwide.

Author contribution

MA, **LB**, and **SAI** design the study. **MA**, **SAI, HMC, LB,** and **AA**, wrote the first draft of the manuscript. **MUA** wrote a section of the manuscript. **LB** and **FEM** made tables. **HMS** revised the manuscript. All the authors contributed to the article and approved the submitted version.

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There is no Conflicts of interest/competing interests.

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