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The Role of Stem Cells in Cancer Treatments

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ABSTRACT: Stem cells have been the basis of, or used in, many cancer treatments. Bone marrow transplants, CAR-T cell immunotherapy, stem cell-based drug delivery systems, and differentiation therapy are four prime examples of the value of stem cells in the fight against cancer. This review will go through the mechanism of stem cells in these treatments, and analyze each treatment's effectiveness, advantages, and disadvantages of each approach. This is done using research papers backed by various clinical trials and studies. Whilst it was found that each treatment was indeed proven to help eradicate or alleviate its effects in cancer patients, each treatment also has its limitations and challenges. These obstacles range from safety implications to ethical concerns. Based on these findings, future research should focus on solving these issues by fully studying and understanding these unique challenges faced by stem cell cancer treatment to pinpoint solutions and allow patients to undergo these stem cell treatments safely and efficiently.

KEYWORDS: Biomedical and Health Sciences, Genetics and Molecular Biology of Disease, Cancer, Stem Cells.

Introduction

There are three different types of stem cells used in stem cell-mediated therapy: embryonic stem cells (ESCs), adult stem cells (ASCs), and induced pluripotent stem cells (iPSCs). ESCs are derived from the inner cell mass of the developing embryo at around 3 days post-fertilization, known as the blastocyst stage, and are pluripotent stem cells that can divide into more stem cells or can become any type of cell in the body.[1] On the other hand, ASCs are naturally found residing in small numbers in most adult tissues, such as bone marrow and the skin. Unlike ESCs, ASCs are multipotent stem cells, meaning that they can only differentiate into distinct cell types of their tissue of origin. Thus, their capacity to regenerate is limited. However, differentiated adult somatic cells can also be genetically reprogrammed back into an embryonic-like state via reintroducing the expression of four specific transcription factors discovered by Shinya Yamanaka in 2006, referred to as the Yamanaka factors, including Octamer-binding transcription factor 4 (Oct4), SRY-box transcription factor 2 (Sox2), Krüppel-like factor 4 (Klf4), and cellular MYC (c-Myc) by viral-based gene transfer methods into the cells.[2] As a result, these new, reprogrammed cells, known as iPSCs, can provide a pool of stem cells that are fully pluripotent for therapeutic use.

Stem cell therapy has already benefited patients affected by many diseases, including haematologic cancers like leukemia and various solid tumors. In fact, the most common method of stem cell therapy is in the treatment of blood cancers, where hematopoietic stem cell (HSC) transplantation is used to replace diseased leukemic cancer cells in the bone marrow with healthy stem cells that can proliferate and respond to environmental cues to restore normal blood and immune cell production.[3] Likewise, ASCs can also be utilized in other ways, especially in cancer. For example, mesenchymal stem cells (MSCs) and neural stem cells (NSCs) can be used in the delivery of cancer drugs to specific organ systems. Furthermore, ESCs and iPSCs can be utilized in CAR T-cell immunotherapies and differentiation therapies aimed at reducing donor variability and enabling more precise and scalable cancer treatments. This paper will highlight the different methods in which stem cells have been applied in cancer treatments, their use in various cancer therapies, and will also discuss their advantages, limitations, and potential future applications.

Bone Marrow Transplants:

Hematopoietic stem cells (HSCs) are commonly used to treat blood cancer via bone marrow transplantations. Blood cancers are defined by the uncontrolled growth of abnormal blood cells and can prevent one's blood from being able to perform most of its functions, such as transporting oxygen and fighting infections. Blood cancers also result in further dysfunctional blood cell production, leading to an overall weakened immune system and clotting ability. The diminishment of these functions is very detrimental to the already weakened patient. Furthermore, high-dose radiotherapy or chemotherapy are non-selective therapeutic approaches and can destroy functional blood cells as a side effect of fighting cancer cells.[4] To combat this, healthy bone marrow containing HSCs is transplanted into the body of immunocompromised patients who have near complete irradiation of their immune system. The first successful bone marrow transplant was performed by Dr. E. Donnall Thomas on a child with leukemia in 1956.[5] Since then, bone marrow transplants have been used in the treatment of many other types of blood cancers, such as multiple myeloma[6] and lymphomas.[7]

Upon successful engraftment, the addition of colony-stimulating factors (CSFs) to HSCs was found to activate intracellular signaling pathways, which allow the HSCs to differentiate to form any type of mature blood cell.[8] For example, the growth factor Granulocyte colony-stimulating factor (G-CSF) enables the proliferation and mobilization of HSCs,[9] hence, when HSCs are induced into a patient's body via a bone

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marrow transplant, they help restore the patient's ability to produce new blood cells from both myeloid and lymphoid lineages.[10]

Till now, bone marrow transplants and the infusion of HSCs are the only FDA-approved stem cell treatments[11] with an increased survival rate for patients post-transplant. The survival rates after transplant for patients with acute leukemia in remission are 55% to 68% with related donors and 26% to 50% if the donor is unrelated.[12] Other than leukemia, patients with Ewing sarcoma and lymphoma have benefited from improved survival rates after going through an autologous bone marrow transplant when combined with traditional cancer treatments.[7,13]

However, side effects and risks such as graft-versus-host-disease (GVHD) and low platelet count regarding bone marrow transplants still pose challenges. Fortunately, modern medicine can help solve these issues. For example, the occurrence of GVHD when using matched (allogeneic) sources of HSCs, which occurs when immune cells from the transplanted bone marrow attack healthy cells in the patient, can be treated with immunosuppressive drugs or therapies, such as using genetically modified mesenchymal stem cells (MSCs) to suppress overactive T-cells.[14] The conditioning treatment for bone marrow transplants can lead to low platelet count as well, which can lead to an increased bleeding risk. However, this risk can be lowered by following special precautions to avoid injury, and extremely low platelet counts can be treated via blood transfusions.[15]

Furthermore, according to research by Smita Bhatia on the long-term health impacts of HSC transplantation (HSCT), whilst 70-80% of those who survive the first 2 years following HSCT are expected to become long-term survivors, chronic mortality is still a big issue.[16] In a cohort of 854 individuals who had survived for >2 years after autologous bone marrow transplantation, it was found that the cohort was still at a 13-fold increased risk for premature death compared with the general population, and bone marrow transplant recipients are at a 2.3- to 4.0-fold increased risk of death due to cardiac issues when compared with the general population.[16] Similarly, results from another study, which closely followed 548 long-term bone marrow transplant recipients, also support the increased mortality risk reported by Bhatia *et al*.[17] Here, the transplant recipients had a 9.8-fold increase in the risk of arterial embolism/thrombosis, which are cardiac events in which blood clots block blood flow in the arteries.

Overall, HSC transplantation has transformed the treatment of blood cancers by restoring the patient's ability to produce healthy blood cells and significantly improving survival rates, particularly in leukemia, lymphoma, and other hematologic malignancies. However, long-term risks such as graft-versus-host disease and cardiovascular complications remain substantial, highlighting the need for ongoing clinical vigilance and supportive care. Looking forward, advances in genetic engineering and immunomodulation may further reduce these risks and enhance the efficacy of HSC transplants, potentially expanding their use and improving long-term outcomes for patients with cancers other than blood cancer.

CAR T-cell cancer immunotherapy:

The second way stem cells have been used in cancer treatment is through the production of immune cells for Chimeric Antigen Receptor T-cell (CAR T-cell) therapy. In this approach, immune cells, such as T-cells and natural killer (NK) cells, are taken from the patient and genetically modified in order to specifically recognize and attack cancer cells, making them a highly targeted method of cancer treatment.[18] This method of therapy is a form of treatment that essentially utilizes certain parts of a person's immune system to recognize and fight disease by stimulating the natural defenses of one's immune system to improve its efficiency in finding and killing cancer cells.[19]

However, generating CAR T- and NK cells from one's body has its limitations, as the quality and quantity of the cells are hard to control *in vivo*, leading to a low standard of cell health and less efficient immunotherapy. This is where stem cells come in: outsourcing to iPSCs and ESCs can offer unlimited sources of immune cells and enable a larger number of eligible patients to undergo immunotherapy.[20] To allow the iPSCs and ESCs to differentiate into immune cells for immunotherapy, they are incubated in the growth medium containing NK cell or T-cell initiating cytokines, such as stem cell factor (SCF), IL-3, IL-7, and IL-15. The T-cells are then genetically modified via viral-based gene transfer methods or CRISPR-Cas9 gene editing to express a CAR specific for a tumor antigen, enabling their receptor to directly bind to and kill cancer cells.[21] This is followed by *ex vivo* cell expansion and re-infusion to the patient.[22]

The use of stem cells to produce CAR T-cells and NK cells for the process of immunotherapy has been very rewarding thus far,[23-25] especially in the treatment of hematological cancers, which are cancer that begins in blood-forming tissue, such as the bone marrow, or in the cells of the immune system. According to clinical trials, end-stage Acute Lymphocytic Leukemia patients who have undergone this treatment have up to 92% chance of a full recovery.[22] However, it should be noted that most patients in these trials were children or young adults, and elderly patients may have a lower chance of a full recovery due to their different tumour microenvironments. It can be seen that patients with multiple myeloma have benefited from CAR T-cell immunotherapy, too, as a study found evidence of tumor reduction in 87% of patients with multiple myeloma who underwent this therapy.[26] Several CAR-T therapies treating certain patients with hematological cancers have already been FDA approved,[27-29] and with many clinical trials aiming to improve the safety and efficacy of CAR-T cell therapies,[30-32] hopefully stem cell-induced CAR-T cell immunotherapy will also gain approval in the future.

However, CAR T-cell therapy remains a very inaccessible treatment for many people worldwide.[33] It is estimated that CAR T-cell therapy can cost between $500,000 and $1,000,000, and the added costs of stem cell differentiation to produce CAR T-cells do not help with the hefty sum. Furthermore, only three pharmaceutical companies, Bristol Myers Squibb, Gilead Sciences, and Novartis, hold FDA approval to produce CAR T-cells commercially. Thus, the limited production of

CAR T-cells makes the treatment both expensive and exclusive.[34] Patients who live in rural areas far from major transplant centers also do not have easy access to this therapy. For example, a patient by the name Suzanne Behanna claims she had to travel nearly 800 miles from rural New Mexico to Houston's University of Texas MD Anderson Cancer Center just to receive this treatment,[35] and unfortunately, many are not as lucky as she to be ultimately able to travel long distances for access to CAR T-cell immunotherapy.

CAR T-cell therapy has also been controversial for another reason. Many suspected that the cells that were genetically engineered for the immunotherapy were cancer-causing following reports of many patients diagnosed with various T-cell cancers post-therapy. In November 2023, the FDA warned that CAR T-cell therapy may be associated with secondary cancers.[36] Researchers at the Stanford Cancer Institute used genetic profiling on 724 patients treated with CAR T-cell therapy to conduct a study to find out if the warnings and controversy surrounding CAR T-cell therapy were warranted.[37] Their results showed that the incidence of secondary blood cancers approached 6.5% over a median of three years of follow-up, which is around the same for patients who underwent stem cell transplantation to treat their cancers. The analysis also found that the T-cells responsible for the patient's second cancer were genetically distinct from those engineered for CAR T-cell therapy. The research results at Stanford also correlate with another study at UPenn, which found that roughly 3.6% of patients treated with CAR-T cell therapies were diagnosed with a second cancer. Furthermore, molecular analysis of a CAR T-cell-treated patient who developed a secondary lung tumor did not find the CAR transgene in his T-cell lymphoma.[38] Thus, both studies indicate a lack of evidence linking CAR T-cell therapy to secondary tumors.

In summary, stem cells can be used to generate CAR T-cells, which offer a highly targeted immunotherapy approach for cancer. Clinical trials have demonstrated impressive remission rates, and several CAR T-cell therapies are already FDA-approved, although high costs and limited accessibility remain significant barriers. Ongoing advances in stem cell biology and gene-editing technologies may make this therapy safer, more effective, and accessible to a wider range of patients in the future.

MSCs and NSCs as drug delivery carriers:

Stem cells such as mesenchymal (MSCs) and neural stem cells (NSCs) can also be utilized as cancer drug delivery carriers. Cell-based targeted drug delivery systems generally offer low immunogenicity and cytotoxicity, specific tropism to injured tissue, prolonged circulation time, and extended half-lives.[39] This makes them more efficient than other drug delivery systems, such as oral and parenteral drug delivery that bypass the gastrointestinal tract. On top of these benefits, stem cells also offer other advantages when acting as drug carriers. The specific pros and cons of MSCs and NSCs will be discussed in the following paragraphs, as well as their unique properties that make them suitable for this treatment, which other stem cells may lack.

The high proliferative capacity of MSCs, alongside their multi-potency and anti-inflammatory properties, are qualities that increase MSC effectiveness in drug delivery.[39] Furthermore, MSCs can carry microcapsules containing drugs without harm to their structural integrity due to unexpressed cytokine secretion that suppresses cell damage responses. This makes MSCs particularly suitable for use as encapsulated drug transporters.[39] Their retained motility and ability to target and migrate towards cancer cells, even through minuscule eight μm pores, are also key to drug delivery efficacy.[40] This is achieved as the microenvironment of tumors acts as a chemoattractant to guide the migration of MSCs to the cancer.[41] Cancer cells release the chemokines CCL2, CCL15, CCL20, CCL25, CXCL1, and CXCL8, which are detected by chemokine receptors on the surface of MSCs, guiding their migration to the tumor.[42] MSCs then release nano-sized exosomes, containing various biological materials, to regulate cell-cell interaction with the cancer cells and anti-cancer drugs into the cancer cells to damage the tumor.[43]

So far, MSC-based drug delivery systems have been quite successful in research involving mice as animal models. In one study, MSCs containing the chemotherapy drug paclitaxel were injected into lung tumor-bearing mice, and it was found that after three MSC injections, metastasis of the tumor was no longer observed, indicating that the damage to cancer cells was successful.[44] In an attempt to further research the drug delivery efficacy of MSCs, a team of Japanese researchers compared the efficacy of liposomal doxorubicin, a type of chemotherapy drug, and doxorubicin-modified MSCs in mice suffering from colon cancer.[45] Results analysis using the avidin-biotin complex method showed that the drug-loaded MSCs suppressed the proliferation of the mice's colon cancer cells significantly more than the liposomal doxorubicin alone. In the co-cultures of the doxorubicin-loaded MSCs, localized distribution of the drug was detected at the cancer cell contact surface, which was not observed when only liposomal doxorubicin was added to the cancer cells alone.[46] This correlates with the aforementioned study to support that the MSC drug delivery system is effective in targeting the cancerous cells.

However, this treatment is not without its limitations. One major challenge of the MSC drug delivery system is the pulmonary first-pass effect, in which the drug contained by the MSCs is metabolized before reaching the tumor.46 In fact, research *in vivo* using MSC-based drug delivery in rats has shown that most MSCs were trapped inside the lungs post intravenous infusion.[47] Furthermore, multiple studies have shown that the spontaneous malignant transformations that MSCs undergo can promote tumor growth,[48] notably the metastasis of breast cancer in mouse models.[49, 50] Research on *ex vivo* handling of MSCs has also found that *ex vivo* factors, such as the microenvironment of culture conditions, can cause MSCs to lose their homing ability,[51] effectively rendering only 1% of MSCs able to effectively target the cancer cells.[52, 53] However, it should be noted that more extensive clinical trials and research are required to utilize the MSC drug delivery system in humans, as the success in the MSC studies in mice may

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not necessarily translate to success in human biological contexts, owing to their vast genetic and physiological differences.

Aside from MSC-based drug delivery, NSCs are another type of stem cell with great potential to be utilized in cancer drug delivery systems, with clinical research in mouse models proving to be successful so far.

NSCs are promising carriers that protect and deliver oncolytic viruses (OVs) to tumors to kill cancer cells selectively. These cells can differentiate into any central nervous system cell, such as neurons and glial cells. Their self-renewing ability and multipotent characteristics make them a good OV delivery carrier.[54] Furthermore, the tumor-trophic nature of NSCs allows them to deliver the OVs to the cancer cells with minimal off-target effects,[55] while also protecting the OVs from immune neutralization from antibodies, allowing for repeat administrations,[56] and more effective OV delivery. After reaching the tumor, OVs undergo selective replication within the cancer cells to induce lysis, thus causing the cancer cells to disintegrate.[57] Additionally, in reaction to the viral particles being replicated, the patient's body produces an immune response; therefore, OVs effectively induce long-term host antitumor immunity.[58]

OVs transported by NSCs have led to successful results in treating gliomas, a type of brain tumor. Research has shown that NSCs loaded with the CRAD-S-pk7, a glioma-restricted oncolytic adenovirus, have led to inhibited tumor growth in mice models of human glioma and a 50% increased median survival rate compared to treatment using CRAd-S-pk7 without NSCs.[59] Another study also found that NSCs loaded with the anti-cancer medication Irinotecan transiently expressed and delivered high levels of active carboxylesterase enzymes to human glioma xenograft tumors in mice. This enzyme helps in drug metabolism and increases Irinotecan's cytotoxicity in glioma cells.[60] Separately, NSCs have been proven to directly inhibit glioma tumor cells as well.[61,62] The ability of glioma cells to proliferate and metastasize was found to be significantly inhibited when co-cultured with embryonic NSCs.[61] Additionally, culturing malignant glioma cells in NSC condition medium was also found to suppress their growth and prevent invasion into surrounding healthy tissue, indicating that NSCs themselves may secrete certain factors that slow cancer development.[62]

While using NSCs to deliver OVs and eradicate tumor cells in mouse models has been effective, scientists have had trouble translating this success to human patients. Unlike the ease of inducing NSCs in mice xenograft tumors, intratumoral injections for tumor patients are often invasive, making repeat injections difficult and casting doubt on the efficacy of NSCs successfully migrating to the cancer cells.[63] Furthermore, certain human OVs may damage normal tissues by destroying cancer cells. For example, studies have shown that the neurotropic virus HSV-1, often used in gene delivery, can cause fatal encephalitis and neonatal herpes in certain cases when induced in humans.[64] Finally, most cancer therapies using a single agent generally cannot eradicate tumors, and NSC-based therapy is no exception. It should instead be used in combination with, rather than as a replacement for, other cancer drugs to increase treatment durability and ultimately gain clinical utility. This was proven in a study showing that the combination of NSCs carrying oncolytic adenoviruses and temozolomide, a type of anticancer medication or radiation, led to a 46% increase in the median survival of mice suffering from glioblastoma multiforme.65 Furthermore, cases in which the stem cells were injected before, not after, chemoradiotherapy application were found to provide the greatest efficacy.[65]

Overall, stem cells such as MSCs and NSCs offer promising platforms for targeted cancer drug delivery, efficiently transporting chemotherapeutics or OVs directly to tumors. In preclinical studies, they have been shown to suppress tumor growth, reduce their ability to metastasize, and appear to improve overall survival in mouse models. However, challenges such as delivery limitations, potential off-target effects, and species differences highlight the need for further research. With more experimentation and optimization, and by testing its efficacy when combined with conventional therapies, MSC- and NSC-based drug delivery has the potential to become a safe and effective treatment option for human brain and solid-tumour cancers.

Differentiation Therapy:

The last stem cell-based anticancer therapy this paper will cover is differentiation therapy. For some context, it is known that stem cells can survive longer than regular cells, and their high pluripotency can lead to an accumulation of genetic mutations that can result in a loss of control over their growth and long-term ability to regenerate.[66] This is very similar to the general nature of cancer cells.[67] Cancer stem cells (CSCs) are tumor cells that function like stem cells and have stem-cell-like characteristics such as pluripotency and self-renewal capabilities. Indeed, such CSCs are believed to play a role in cancer progression, recurrence, and treatment resistance.[68] Thus, targeting CSCs is important in preventing cancer progression and relapse, and differentiation therapy essentially uses our existing knowledge of stem cells to achieve this.[69]

It has been found that various hormones and cytokines can influence cell communication to stimulate the early maturity of stem cells.[70] This causes the stem cells to lose their ability to regenerate and instead pushes them to differentiate into specialized cell/tissue types.[71] Thus, differentiation therapy uses various pharmacological agents, most commonly retinoic acid, to force CSCs to differentiate into more mature cells and stop them from multiplying uncontrollably,[72,73] effectively halting one of the hallmarks of cancer. One example that demonstrates the mechanism of differentiation therapy is its use in treating acute promyelocytic leukemia.[74] To treat this aggressive blood cancer, retinoic acid and arsenic are used in combination to inhibit the expression of the proto-oncogene Bcl-2 in myeloid CSCs. The Bcl-2 protein functions to inhibit apoptosis in leukemia cells, leading to the prolonged survival of the cancer cells. Hence, the downregulation of Bcl-2 due to retinoic acid prevents the myeloid CSCs from undergoing uncontrolled cellular proliferation, leading to a loss of their cancerous traits and instead the activation of the cell's internal death pathways.[75]

One benefit of differentiation therapy is that it simply aims to selectively push CSCs to differentiate into mature non-cancerous cells, hence avoiding the surrounding healthy cells.[76] This is unlike conventional anticancer therapy, such as chemotherapy, as the harmful chemicals used in traditional therapy to kill cancer cells may also harm healthy cells as a side effect.[77] Thus, the less toxic nature of differentiation therapy and lack of negative side effects make it an effective cancer treatment. For example, a study demonstrated that out of 50 advanced thyroid cancer patients treated with retinoic acid, 26% showed a distinct increase in radioiodine uptake (26%), and 40% showed a lower risk of cardiovascular issues (40%). The total number of patients who benefited from the differentiation therapy by having their tumors reduced was 38%.[78] Furthermore, whilst the importance of targeting CSCs to eradicate cancer has already been emphasized, it is important to note that CSCs are highly resistant to classic anticancer drugs, even more so than other cancer cells,[79] thus differentiation therapy offers a promising strategy by forcing CSCs to mature into non-proliferative, non-cancerous cells, effectively overcoming their inherent drug resistance and suppressing tumor growth at its source.

However, a major disadvantage of differentiation therapy is that tumors can resist the differentiating agent used to mature the CSCs. Retinoic acid and other retinoids are the preferred pharmacological agent used in differentiation therapy owing to their high success rates in the treatment.[80, 81] Despite treatment success, patients treated with retinoids often develop resistance to this therapy,[82] leading to secondary drug resistance in the tumors that then cause the CSCs to no longer respond to retinoid differentiation therapy despite having been successfully treated by this therapy in past treatments.[83] Furthermore, intrinsic resistance to retinoids has been exhibited in the development of some solid tumors.[84] In fact, the effectiveness of differentiation therapy has also been questioned; those who were given retinoic acid to undergo differentiation therapy showed that many patients had no signs of tumor reduction, and the median survival time post-treatment was only nineteen months.[85]

In summary, the use of differentiation therapy to target CSCs by inducing them to mature into non-proliferative, non-cancerous cells has shown to effectively suppress tumor growth while sparing healthy surrounding tissue. Indeed, it has shown clinical success in cancers such as acute promyelocytic leukemia and advanced thyroid cancer alongside other cancers, offering a less toxic alternative to conventional chemotherapy. However, resistance to differentiating agents, such as commonly used retinoids, and limited efficacy in certain solid tumors, remain significant challenges. Future research should focus on overcoming these resistance mechanisms, identifying novel differentiation-inducing compounds aside from those mentioned above, and exploring combination therapies with conventional or targeted treatments. With continued advancements, differentiation therapy has the potential to become a more effective and widely applicable strategy against cancer by offering an alternative fate for the cancerous cells rather than destroying them.

Conclusion

To conclude, stem cell-based therapy offers promising and novel alternatives to traditional cancer treatments and holds high potential to target cancer more efficiently and effectively.

The use of stem cells in cancer treatments offers an increased capacity for treatment success, but progress is hindered by negative side effects and unclear translation into the human system, respectively. HSCs, used in bone marrow transplants, have improved survival in hematologic cancers, but their application is limited by serious side effects, including graft-versus-host disease, reduced blood cell counts (cytopenias), and long-term cardiovascular risks. Similarly, though MSC- and NSC-based drug delivery systems enhance the targeted delivery of chemotherapeutics or oncolytic viruses and minimize off-target toxicity, they still face challenges such as the pulmonary first-pass effect, loss of homing ability, and difficulty translating preclinical success to humans. In addition, the use of stem cells has given rise to more innovative strategies such as CAR T-cell therapy, offering highly targeted and effective immunotherapy options to cancer patients, although with limitations in accessibility, cost, and potential safety concerns. Via future scientific research, such challenges in treatment will hopefully decrease as we gain a deeper understanding of stem cell treatment mechanisms, so as to increase treatment viability and lower medical risks for patients.

In addition, to a certain extent, the nature of tumor cells is very related to stem cells,[86] as both types of cells have a high ability for proliferation, viability, and resistance to apoptosis. We have already used insight from stem cells to fight cancer in differentiation therapy, in which CSCs are matured into cells with non-cancerous traits despite limitations such as inaccessibility and treatment resistance. This unique nature of differentiation therapy, which aims to repurpose cancerous cells instead of killing them, therefore poses reduced risk for rejection and toxicity concerns to healthy cells in comparison to conventional treatments. Further developments in our knowledge of stem cell characteristics that relate to cancer cells can no doubt lead to even more novel treatments henceforth.

As of now, amongst the 4 treatments discussed, bone marrow transplants and CAR T-cell therapy are the more immediate and commonly used treatments, as much research and fine-tuning have been put into these treatments over the years. On the other hand, differentiation therapy and stem cell-based drug delivery systems are currently in the premature infancy and explorative stage of research, but hold great potential for the future.

In the future, more stem-cell-based cancer treatments and improvements to existing treatments can be discovered as we learn more about stem cells themselves. Indeed, the future of stem cell therapy will likely involve combinatorial approaches, integrating the strategies mentioned in this paper to maximize long-term efficacy. Thus, continued advancements will be imperative in reducing treatment risks and providing improved and novel cancer treatments that are more widely accessible to patients worldwide.

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