

# Promising Stem Cell therapy in the Management of HIV and AIDS: A Narrative Review

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**Abstract:** Stem cell therapies are becoming a major topic in biomedical research all over the planet. It may be a viable treatment choice for people suffering from a wide range of illnesses and injuries. It has recently emerged as an extremely intriguing and well-established science and research topic. Expectations have risen due to advancements in therapeutic approaches. Multiple laboratory testing of regulated stem cell culture and derivation is carried out before the formation of stem cells for the use of therapeutic process. Whereas HIV infection is contagious and can last a lifetime. Researchers are still working to develop a comprehensive and effective treatment for HIV and its associated condition, as well as AIDS. HIV propagation is primarily restricted to the immune system, notably T lymphocytes, as well as macrophages. Large numbers of research studies have contributed to a plethora of data about the enigmatic AIDS life cycle. This vast amount of data provides potential targets for AIDS therapies. Currently, stem cell transplantation, along with other procedures, provided novel insights into HIV pathogenesis and offered a glimpse of hope for the development of a viable HIV cure technique. One of its existing focus areas in HIV and AIDS research is to develop a novel therapeutic strategic plan capable of providing life-long complete recovery of HIV and AIDS without regular drug treatment and, inevitably, curative therapy for HIV and AIDS. The current paper tries to address the possibilities for improved stem cell treatments with “bone marrow, Hematopoietic, human umbilical cord mesenchymal, Genetical modifications with CRISPR/Cas9 in combination of stem cells, induced pluripotent stem cells applications” are discussed which are specifically applied in the HIV and AIDS therapeutic management advancement procedures.

**Keywords:** stem cell therapy, HIV/AIDS Management, HIV and AIDS advancements, stem cell in clinical practices, stem cell genetic applications/modifications

## Introduction

Stem cells are highly specialized cell types with an impressive ability to self-renew, able to transform into one or even more specific cell types that play a significant role in the regulation and tissue healing process.<sup>1-7</sup> To self-renew, a stem divides into two identical daughter stem cells and a progenitor cell and the embryonic and adult cells contain stem cells.<sup>1,2,8</sup>

Curing patients with serious medical conditions has been the focus of all disciplines of medical research for many years. Stem cell treatment has evolved into a highly exciting and progressed field of scientific research. Major advances have recently been introduced in fundamental and translational stem-cell-based treatment studies. As stem cell research progressed, many therapeutic options were investigated. The development of therapeutic procedures has sparked a great deal of interest.<sup>1,9</sup> Humanity has known for many years that it is possible to regenerate lost tissue. Recently, the regenerative medicine research has taken hold, defying the tremendous scientific advances in the molecular biology sciences only. Technological advances provide limitless opportunities for transformational and potentially restorative therapies for many of humanity’s most illnesses. A variety of human organs have successfully yielded stem cells. Besides this, the cell therapy is rapidly bringing good advancements in the healthcare system, intending to restore and possibly replace injured tissue, as well as organs, and ultimately restore the functional capacity of the body.<sup>2,10,11</sup>

## Sources of Stem Cells

The stem cells can be obtained from various sources of Adult (Adult body tissues), Embryonic (Embryos), Mesenchyma (Connective tissue or stroma), and Induced pluripotent stem [ips] cells (Skin cells or tissue-specific cells).<sup>3,6-8,12-15</sup>

## Characteristics

Due to various stem cells' cellular characteristics, the therapeutic clinical possibilities of stem-cell-based treatment are considered promising. These cells can regrow and restore various types of body tissues, for this reason, they are recognized as precursor cells to all kinds of cells.<sup>15</sup> The following are the distinguishing features: 1. *Self-renewal*- Divide without distinction to generate an infinite supply, 2. *Multi-potency*- One mature cell may distinguish more than one, 3. *Pluripotency*- Create all sorts of cells except for embryonic membrane cells, 4. *Toti-potency*- Produce various sorts of cells, including embryonic stem cells.<sup>1,2,6,7,16</sup>

## Hierarchy of Stem Cells

Stem cells are essential human cells that really can self-renew and make a distinction into particular mature cell types.<sup>3,6</sup> The different types of stem cells are “embryonic, induced pluripotent, and adult” kind of cell types. They all share the important feature of self-renewal, and the ability to discern themselves. It should be mentioned that, the stem cells are not homogeneous, but instead appear in a progressive order. Totipotent stem cells are the most basic and immature stem cells. The above cells can form a complete embryo and also extra-embryonic tissue. This one-of-a-kind efficiency is only present for a short period, starting with ovum development and completing whenever the embryo achieves the 4 to 8 cell phases. Having followed that, cells that divide until they approach the blastocyst, about which point they end up losing their totipotency and acquire a pluripotent character trait, at which cells can only distinguish through each embryonic germ stack. After a few divisions, the pluripotency character trait starts to fade and the distinguishing ability has become more lineage constrained, where its cells are becoming multipotent, indicating they could only transform into the cells connected to a cell or tissue of origin.<sup>10</sup> Many researchers believe that adult stem cells should be used in stem cell therapies.<sup>6,17</sup>

## Stem Cell Therapy

The stem cells can be transformed into a wide range of specialized functional cell types.<sup>3,18</sup> In response to injury or maturation, those same stem cells can propagate in massive quantities.<sup>19</sup> Adult, embryonic, and induced pluripotent stem cells are examples of stem cell-based therapies.<sup>14,15,19-21</sup> The stem cells, due to their capability to distinguish the specific cell types requisite for a diseased tissue regeneration, can provide an effective solution, while tissue and organ transplantation are considered necessary.<sup>10</sup> The sophistication of stem cell-based treatment interventions, on the other hand, probably leads researchers to seek stable, credible, and readily available stem cell sources capable of converting into numerous lineages. As an outcome, it is critical to exercise caution when selecting the type of stem cells to be used in therapeutic trials.<sup>12,14,22</sup>

## Translational Research on Stem Cells

Only with the explosive growth of basic stem cell research in recent years, the comparatively recent study sector of “Translational Research” had also grown exponentially, starting to build on major research knowledge and insight to advance new therapies. Once the necessary regulatory clearances have been obtained, the clinical translation process can start. Translational research is important because it acts as a filtration system, ensuring that only safe and effective therapeutic approaches start making it to the clinic.<sup>23</sup> Recent research illustrating, the successful application of stem cell transplantation to patient populations suggests that, such restorative approaches have been used to address a wide variety of complicated ailments of future concerns.<sup>19,24</sup>

Currently, clinical trials are available for a variety of stem cell-based treatments based on adult stem cells. To date, the WHO International Clinical Experiments Registration process has recorded more than 3000 experiments involved based on adult stem cells. Furthermore, preliminary trials involving novel and intriguing pluripotent stem cell therapies have

been registered. These studies' findings will assist the ability to comprehend and the timeframes required to obtain effective treatments and it will contribute to a better knowledge of the different disorders or abnormalities.<sup>10</sup>

## Progress of Stem Cell in Clinics

The role of stem cells in modern medicine is vital, both for their widespread application in basic research and for the opportunities they provide for developing new therapeutic strategies in clinical practice.<sup>6,16</sup> In recent times, the number of studies involving stem cells has expanded tremendously. Globally, thousands of studies claiming to use "stem cells" in experimental therapies have now been in the investigation field. This may give the impression that such treatments have already been shown to be extremely effective in the context of healthcare. Despite some promising results, the vast majority of stem cell-based therapeutic applications are still in the experimental stage itself.<sup>6,25</sup>

The stem cells are a valuable resource for understanding organogenesis as well as the body's continual regenerative capacity. These cells have brought up enormous anticipations among doctors, investigators, patients, and the public at large because of their ability to distinguish into a variety of cell types.<sup>25</sup> These cells are necessary for living beings for a variety of reasons and can play a distinguishable role. Several stem cells can play all cell types' roles, and when stimulated effectively, they can also repair damaged tissue. This capability has the potential to save lives as well as treat human injuries and tissue destruction. Moreover, different kinds of stem cells could be used for several purposes, including tissue formation, cell deficiency therapeutic interventions, and stem cell donation or retrieval.<sup>3,6,26</sup>

New research demonstrating that the successful application of stem cell treatments to patients has expressed hope that such regenerative strategies might very well one day be used to address a wide variety of problematic ailments. Furthermore, clinical trials incorporating stem cell-based therapeutics have advanced at an alarming rate in recent years. Some of these studies had a significant impact on a wide range of medical conditions.<sup>10</sup> As a regenerative medicine strategy, cell-based treatment is widely regarded as the most fascinating field of study in advanced science and medicine. Such technological innovation paves the way for an infinite number of transformational and potentially curable solutions to some of humanity's most pressing survival issues. Moreover, it is gradually becoming the next major concern in medical services.<sup>11</sup>

Modern data, which shows that the successful stem cell transplantation in beneficiaries has raised hopes on the certain rejuvenating approaches, will one day be used to treat many different types of challenging chronic conditions.<sup>24</sup> Preliminary data from highly innovative investigations have documented that the prospective advancement of stem cells provides a wide range of life-threatening ailments that have so far eluded current medical therapy.<sup>2,10,11</sup> Furthermore, clinical trials involving stem cell-based therapies have advanced at an unprecedented rate. Many of these studies had a significant impact on various disorders.<sup>19</sup> Despite the increasing significance of articles concerning viable stem cell-based treatments, the vast majority of clinical experiments have still yet to receive full authorization for stem cell treatments confirmation.<sup>11,12,27</sup>

## Brief Out on HIV and AIDs

Even though the first case of AIDS were noted nearly 27 years ago, and the etiologic agent was noticed 25 years ago, still for the effective control of the AIDS pandemic continues to remain elusive.<sup>28</sup> The HIV epidemic started in 1981 when a new virus syndrome defined by a weakened immune system was revealed in human populations across the globe. AIDS showed up to have a substantial reduction in CD4+ cell counts and also elevated B-cell multiplication.<sup>15,28-31</sup>

The agent that causes AIDS, later named HIV, is a retroviral disease with a genomic structural system made up of 2 identical single-stranded RNA particles.<sup>32-34</sup> According to the Centres for Disease Control and Prevention, with over 1.1 million Americans are presently infected with the virus.<sup>31</sup> Compromised immune processes in HIV and AIDS, as well as partial immune restoration, barriers are confirmed for HIV disease eradication. Innovative developmental strategies are essential to maximizing virus protection and enabling the host immune response to eliminate the virus.<sup>35</sup>

The progression of HIV infection in humans is divided into the following stages of acute infection, chronic infection, and AIDS.<sup>15,36</sup> During the acute infection phase, the circulation has a high viral replication, is extremely infectious, that may or may not demonstrate flu-like clinical signs. In the chronic stage, the viral load is lesser than in the acute stage, and

individuals are still infectious but may be symptomless. The patient has come to the end stage of AIDS whenever the CD4+ cell count begins to fall below 200 cells/mm or even when opportunistic infections are advanced.<sup>15,36</sup>

There are currently two types of HIV isolated HIV-1 and HIV-2.<sup>15,37,38</sup> However, HIV-1 is the most common cause of AIDS throughout the world, while HIV-2 is only found in a few areas of an African country. Although both virions can cause AIDS, HIV-2 infection is much more likely to occur in central nervous system disorder.<sup>15</sup> Besides this, HIV-2 seems to be less infectious than HIV-1, and HIV-2 infection induces AIDS to develop more slowly. Even though both HIV-1 and HIV-2 have a comparable genetic structure comprised of group-specific antigen, polymerase, and envelope genes, their genome organizational structures are differed.<sup>15,37–39</sup>

HIV infiltrates immune cell types, CD4+ T cell types, and monocytes, resulting in a drop in T-cell counts below a critical level and the failure of cell-mediated immune function.<sup>15,40</sup> The glycoprotein (gp120) observed in the virion envelope comes into contact with the CD4 particle with high affinity, allowing HIV to infect T cells. By interacting with their co-receptors, CXCR4 and CCR5, the virus infiltrates T cells and monocytes. The retrovirus uses reverse transcriptase to convert its RNA into DNA after attaching it to and entering the host cell. These newly replicated DNA copies then exit the host cell and infect other cells.<sup>15,40,41</sup>

HIV-1 is a retrovirus and belongs to a subset of retroviruses known as lentiviruses.<sup>38,42</sup> Infection is the most common global health concern around the world.<sup>15</sup> It has destroyed the millions of people's health and continues to wreak havoc on the individual health of millions more. The pandemic of HIV-1 is the most devastating plague in the history of humans, as well as a significant challenge in the areas of medicine, public health, and biological science of research activities.<sup>34,43</sup> Antiretroviral therapy is the only treatment that is commonly used. This is not a curative treatment; it must be used for the rest of one's life.<sup>15</sup> Although antiretroviral therapy has reduced significantly HIV intensity and transmission, the virus has not been eradicated, and its continued presence can lead to additional health issues.<sup>44</sup>

Infection with the human immunodeficiency virus necessitates entry into target cells, such as through adhesion of the viral envelope to CD4 receptor sites.<sup>43</sup> Cellular antiviral responses fail to eliminate the virus, resulting in a gradual depletion of CD4+ T cells and, finally, a severely compromised immune functioning system. Unfortunately, there is no cure for the virus that destroys immunity.<sup>44–47</sup> In advanced HIV infection, memory T-cell depletion primarily affects cellular and adaptive immune responses, with a minor impact on innate immune responses.<sup>48</sup> Globally, 37.7 million people were living with HIV in 2020, and with 1.5 million individuals are infected with the virus.<sup>49</sup> The advancement of stem cell therapy and the conduct of implemented clinical trials have revealed that stem cell treatment has high hopes for a range of medical conditions and implementations.<sup>15</sup>

Stem cell treatment has shown impressive outcomes in HIV management and has the potential to have significant implications for HIV treatment and prevention in the future. In HIV patients, stem cell therapy helps to suppress the viral load even while enabling antiretroviral regimens to be tapered. Interestingly, this practice led to a significant improvement in procedure outcomes soon after starting antiretroviral treatment.<sup>15</sup> Stem cell transplantation can alleviate a wide variety of diseases that are currently incurable. They could also be used to create a novel anti-infection therapy strategic plan and to enhance the treatment of immunologic conditions such as HIV infection. HIV wreaks havoc on immune system cells.<sup>30,50</sup>

The virus infects and replicates within T-helper cells (T-cells), which are white immune system cells. T-cells are also referred to as CD4 cells. HIV weakens a person's immune system over time by pulverizing more CD4 cells and multiplying itself. More pertinently, if the individual has been unable to obtain anti-retroviral medicine, he will progressively fail to control the infectious disease and illnesses.<sup>3,15,42</sup>

Despite 36 years of scientific research, investigators are still trying to cure human HIV and its potential problem, AIDS.<sup>3,51–53</sup> HIV continues to face unconquerable dangers to human survival. This virus has developed the potential to avoid anti-retroviral therapy and tends to result in victim death.<sup>52</sup> Investigators are still looking for effective and all-encompassing treatment for HIV and its complexity, AIDS.<sup>54</sup> This massive amount of data revealed potential AIDS treatment targets.<sup>55</sup> Thousands of research projects have yielded a great deal of information on the elusive AIDS life cycle to date.<sup>54–56</sup> These massive amounts of data supplied possible targets for AIDS treatment.<sup>33,55,56</sup> In HIV-infected patients, using stem cell therapy can augment the process of keeping the viral load stagnant by permitting antiretroviral regimens to be tapered.<sup>15</sup>

## History of Stem Cell Transplantation Among HIV-Positive Individuals

Overall, stem cell-based strategies for HIV and AIDS treatment have recently emerged and have become a key area of research. Ideally, effective stem cell-based therapeutic approaches might have several benefits.<sup>30</sup> Clinical studies encompassing stem cell therapy have shown substantial therapeutic effects in the treatment of various autoimmune, degenerative, and genetic problems.<sup>15,25</sup> Substantial progress has been developed in the treatment of HIV infection using stem cell-based techniques.<sup>30</sup>

Successfully treated, clinical studies have shown that total tissue recovery is feasible.<sup>15,57</sup> In the early 1980s, the first stem cell transplants were accomplished on HIV-positive patients who were unsure of their viral disease. Following the above preliminary aspects, many HIV-positive patients with concurrent malignant tumours or other hematologic disorders underwent allogeneic stem cell transplantation around the world.<sup>42</sup> After ART became a common treatment option for patients,<sup>58,59</sup> the procedure's prognosis improved dramatically. In addition, a retrospective study of 111 HIV+ transplant patients demonstrated a mildly lower overall survivorship performance in comparison to an HIV-uninfected comparison group.<sup>60</sup>

Earlier, the primary problem for people living with HIV and AIDS was immunodeficiency caused by a loss of productive T-cells. Some clinicians intended to replenish lost lymphocytes through adoptive cell transplants in the initial days before efficacious antiretroviral therapy options were available. Immunologically, it is relatively simple in an isogenic condition, as illustrated on HIV-positive individuals with just a correlating identical twin who received T-lymphocytes and stem cell transfusions to rebuild the weak immune status of the patient.<sup>60</sup> Cell therapy transfusion may be used to remove resting virion genomes from CD4+ immune cells and macrophages mostly through genome-editing or cytotoxic anti-viral cells.<sup>15,60</sup> Cell technology and stem cell biological reprogramming developments have made a significant contribution to novel strategies that may give confidence to HIV healing process.<sup>3</sup> However, human embryonic stem cells can be distinguished into significant HIV target cells, according to several research findings.<sup>30,61,62</sup>

## Stem Cell Applications in HIV/AIDS Management

Initially, stem cell transplantation was believed to influence the clinical significance of HIV infection, but viral regulation was not accomplished in the discipline. Moreover, improvements in stem cell transplants utilizing synthetic or natural resistant cell resources, in combination with novel genetic manipulative tactics or the advancement of cytotoxic anti-HIV effector cells, have significantly accelerated this sector of HIV cell management.<sup>60</sup> Multiple techniques are being introduced to overcome HIV, either through protecting cells from infectious disease or by continuing to increase immune responses to the viral infection.<sup>30</sup> The various methods are as follows: Bone marrow stem cells Therapies, Autologous stem cell transplantations, Hematopoietic stem cell transplantation, Genetical modifications of Hematopoietic stem cells (HSCT), HSCT and HAART therapeutic approach, Human umbilical cord mesenchymal stem cell transplantation, Mesenchymal stem/stromal cells (MSCs) applications, CCR5 Delta32/Delta32 Stem-Cell Transplantation, CRISPR and stem cell applications, Induced Pluripotent Stem Cells applications.

## Bone Marrow Stem Cells Therapies

According to the findings, circulating replicative HIV remains the most significant threat to effective AIDS therapy. As a result, a method for conferring resistance to circulating HIV particles is required. The effective viral burden in the human body would be significantly reduced if it were possible to defeat reproducing HIV particles.<sup>43,44</sup> For the treatment of AIDS, a restorative approach that relies on bone marrow stem cells has been suggested.<sup>52</sup> The proposed treatment method captures and eventually destroys circulating HIVs using receptor-integrated red blood cells. Red blood cell membranes can be equipped with the CD4 receptor and the C-C chemokine receptor type 5 and C-X-C chemokine receptor type 4 co-receptors, which will selectively bind circulating HIV particles.<sup>15,30,32,33,43,44,46,63-65</sup>

## Autologous Stem Cell Transplantations

The term autologous pertains to blood-forming stem cells obtained from the patient for use as a source of fresh blood cells followed by high-dose chemotherapeutic agents.<sup>66</sup> Lymphoma is still the biggest cause of mortality in HIV patients. Autologous stem cell recovery or transplantation with high-dose treatments has long been supported as a treatment for

certain types of cancer in HIV-negative patients, including leukaemia and lymphoma. Individuals over the age of 65, as well as those with health problems such as HIV, were excluded from initial transfusion experiments. Moreover, the treatment regimen mortality of transplantation has also been reduced significantly due to its use of peripheral blood stem cells rather than bone marrow and the use of newer marginal conditioning therapeutic strategies. HIV-infected clients may be able to utilize enough stem cells for an autologous transplant advancement in HIV management. High-dose Autologous stem cell transplant (ASCT) treatments are better than conventional treatment in people with relapsed non-Hodgkin lymphoma, according to randomized trial evidence. Similarly, studies on HIV-negative people with Hodgkin Lymphoma have shown that ASCT would provide patients with repetitive illness with long-term progression-free survival.<sup>66,67</sup> Even so, the clinical trial on Allogeneic Hematopoietic Cell Transplant for HIV Patients with Hematologic Malignancies report was explained as, the cell-associated HIV DNA and inducible infectious virus were not detectable in the blood of patients who attained complete chimerism.<sup>68</sup>

The study on long-term multilineage engraftment of autologous genome-edited hematopoietic stem cells in nonhuman primates report findings was Genome editing in hematopoietic stem and progenitor cells (HSPCs) is a potential innovative approach for the treatment of numerous human disorders. This report shows that genome-edited HSPCs engraft and contribute to multilineage repopulation following autologous transplantation in a clinically relevant large animal model, which is an important step toward developing stem cell-based genome-editing therapeutics for HIV and possibly other illnesses.<sup>69</sup>

Research on comprehensive virologic and immune interpretation in an HIV-infected participant again just after allogeneic transfusion and analytical interruption of antiretroviral treatment findings are the instance of HIV-1 cure having followed allogeneic stem cell transplantation (allo-SCT), resulting allo-SCTs in HIV-1 positive participants have failed to cure the disease. It describes adjustments in the HIV reservoir in a single chronically HIV-infected client who had undergone allo-SCT for acute lymphoblastic leukaemia treatment and was obtaining suppressive antiretroviral treatment.

To estimate the size of the HIV-1 reservoir and describe viral phylogenetic and phenotypic modifications in immune cells, the investigators just used leukapheresis to obtain peripheral blood mononuclear cells (PBMCs) from a 55-year-old man with chronic HIV infection prior and after allo-SCT. Once HIV-1 was found to be unrecognizable by numerous tests, including the PCR measurement techniques both of overall and fully integrated HIV-1 DNA, recompilation virus precise measurement by significant cell input quantifiable viral outgrowth assay, and in situ hybridization of intestine tissue, the client accepted to an analytic treatment interruption (ATI) with recurrent clinical observing on day 784 post-transplantation. He continued to remain aviremic off ART until ATI day 288, once a reduced virus rebound of 60 HIV-1 copies/mL resulted, which expanded to 1640 HIV-1 copies/mL five days later, urging ART reinitiation. Rebounding serum HIV-1 action sequences were phylogenetically distinguishable from pro-viral HIV-1 DNA discovered in circulating PBMCs before transplantation. It was indicated that allo-SCT tends to result in significant reductions in the magnitude of the HIV-1 reservoir and a >9-month ART-free cessation from HIV-1 multiplication.<sup>34</sup>

The Impact of HIV Infection on Transplant Outcomes after Autologous Peripheral Blood Stem Cell Transplantation: A Retrospective Study of Japanese Registry Data reported as ASCT is a successful treatment option for HIV-positive patients with non-Hodgkin lymphoma and multiple myeloma (MM). HIV infection was associated with an increased risk of overall mortality and relapse after ASCT for NHL in a study population.<sup>70</sup>

## Hematopoietic Stem Cell Transplantation

The procedure of delivering hematopoietic stem cells mostly through intravenous infusion to restore normal haematopoiesis or treat cancer is known as hematopoietic stem cell transplantation.<sup>71</sup> There has recently been a rise in the desire to develop strategies for treating HIV/AIDS diseases employing human hematopoietic stem cells,<sup>30</sup> along with this Hutter and Zaia were evaluated the background of Haematopoietic stem cell transplantation (HSCT) in HIV-infected individuals.<sup>42</sup>

Attempts to use HSCT as a technique for immunologic restoration in AIDS patients or as a therapeutic intervention for malignant tumours were initially insufficient. Regretfully, in the absence of sufficient ART, HSCT seemed to have no impact on the evolution of HIV infection, and the majority of the patients ended up dead of rapidly deteriorating

immunosuppression or reoccurring lymphoma or leukaemia. A specific instance report described how an un-associated, matched donor supplied allogeneic HSCT to a patient with refractory lymphoma. The virus was unrecognizable by isolating or PCR of peripheral blood mononuclear cells commencing on day 32 after transplantation. Although HIV-1 was unrecognizable by cultural environment or PCR of several tissues examined at mortem, the patient died of recurring lymphoma on day 47. Another client who obtained both allogeneic HSCT and zidovudine had similar results, with HIV-1 becoming unnoticeable in the blood by PCR analysis. In some other particular instances, a 25-year-old woman with AIDS who obtained an allogeneic HSCT from a corresponding, unfamiliar donor after controlling with busulfan and cyclophosphamide and ART with zidovudine and IFN-2 regimen continued to live for 10 months before falling victim to adult respiratory distress. However, PCR testing of autopsy tissues revealed that they were HIV-1 negative.<sup>72</sup>

Recent research discovered significant progress towards the clinical application of stem cell-based HIV therapeutic interventions, principally illustrating the opportunity to effectively undertake a large-scale phase two HSC-based gene therapy experiment. In this investigation, the research team used autologous adult HSCs that had been transduced to a retroviral vector that usually contains a tat-vpr-specific anti-HIV ribozyme to develop cells that were less vulnerable to productive infection,<sup>73</sup> whereas vector-containing cells have been discovered for extended periods (more than 100 weeks in most people) and CD4+ T cell gets counted were significantly high within anti-HIV ribozyme treating people group compared with the placebo group, the impacts on viral loads were minimal. The study's success, even so, is based on the realization that a stem cell-based strategy like this is being used as a more conventional and efficacious therapeutic approach.<sup>30</sup> Some other latest clinical studies used a multi-pronged RNA-based strategic plan which included a CCR5-targeted ribozyme, an shRNA targeting tat/rev transcripts, and a TAR segment decoy.<sup>74</sup>

These crucial research findings are explained on lentiviral-based gene therapy vectors that can genetically manipulate both dividing and non-dividing HSCs and are less likely to cause cellular changes than murine retro-viral-based vectors. Long-term engraftment and multipotential haematopoiesis have been demonstrated in vector-containing and expressing cells, according to the researchers. Whereas the antiviral effectiveness was not reviewed, the results demonstrate the strategy's protection, which helps to expand well for the possibility of a lentiviral-based approach in the upcoming years.<sup>30</sup>

A further approach, with a different emphasis, has been started up in the hopes of trying to direct immune function to target specific HIV to overcome barriers to attempting to clear the virus from the patient's body. These strategies use gene treatment innovations on peripheral blood cells to biologically modify cells so that they assert a receptor or chimeric particle that enables them to especially target a specific viral antigen,<sup>75</sup> deception of HIV-infected people's peripheral blood T cells raises issues to be addressed, such as the effects of ongoing HIV infection and ex vivo modification on the capabilities and lifetime of peripheral blood cells. Further to that, the above genetically manipulated cells would demonstrate their endogenous T cell receptors, and the representation of the newly introduced receptor could outcome in cross-receptor pairing, resulting in self-reactive T cells. Most of these deficiencies could be countered by enabling specific developmental strategies to take place that can start generating huge numbers of HIV-specific cells in a renewable, consistent way that can restore defective natural immune activity against HIV.<sup>30</sup>

One strategy being recognized is the application of B cells obtained from HSCs to demonstrate anti-HIV neutralizing specific antibodies. While animal studies have shown that neutralizing antibodies could protect against infection, and extensively neutralizing antibodies have been noticed in some HIV-infected persons, safety from a single engineered antibody might be exceptional.<sup>76,77</sup> Realizing antibody binding and virus neutralization may assist in the development of chimeric receptors or single-chain therapeutic antibodies with recognition domains for other techniques that identify cellular immunity against HIV-infected cells.<sup>78,79</sup> Thereby, genetically modifying HSCs to generate B cells that produce neutralizing anti-HIV specific antibodies, or engineering HSCs to enable multipotential haematopoiesis of cells that express a chimeric cellular receptor usually contains an antibody recognition domain, indicate one arm of an HSC-based "engineered immunity" process.<sup>30</sup>

A further technique of using HSCs that were genetically altered with molecularly cloned T-cell receptors or chimeric molecules particular to HIV to yield antigen-specific T cells. The basic difference in this strategy is that the cells produced from HSCs after "standard" advancement in the bone marrow and thymus are made subject to normal central tolerance modalities and are antigen-specific "naive" cells, and therefore do not have the ex-vivo manipulation and

impaired functioning or exhaustion problems that other external cell modification methods would have. In this context, the latest actual evidence research using a molecularly cloned T cell receptor particular to an HIV-1 Gag epitope in the aspect of HLA-A\*0201 revealed that HSC altered in this ability can progress into fully functioning, mature HIV specialized CD8+ T cells in human thymic tissue that conveys the acceptable constrained HLA-A\*0201 particles.<sup>80</sup> This explores the possibility of genetically engineering HSCs with a molecularly cloned receptor and signifies a step toward a better understanding and application of initiated T cell responses, which would probably result in the eradication of HIV infection from the body, similar to the natural immune function of other virus infections and pathogenic organisms.<sup>30</sup>

In an “allogeneic” transplantation, donor stem cells replace the patient’s cells.<sup>66</sup> Allogeneic hematopoietic stem cell transplantation (HSCT) has appeared as one of the most potent treatment possibilities for many people who suffer from hemopoietic system carcinomas and non-malignant ailments.<sup>81</sup> Both HIV-cured people have received HSCT utilizing CCR5 132 donor cells.<sup>82,83</sup> This implies that HIV eradication necessitates a decrease in the viral reservoir through the myeloablative procedures,<sup>84–86</sup> Having followed that, immune rebuilding with HIV-resistant cells was carried out to prevent re-infection.<sup>45</sup> The possibility of adoptive transfer of ex vivo-grown, virus-specific T-cells to prevent and control infectious diseases (eg, Cytomegalovirus and EBV) in immunocompromised patients helps to make adoptive T-cell treatment a feasible strategy to inhibit HIV rebound having followed HSCT.<sup>81,87,88</sup>

The Engineered Zinc Finger Protein Targeting 2LTR Inhibits HIV Integration in Hematopoietic Stem and Progenitor Cell-Derived Macrophages: In Vitro Study, the researchers investigated the efficacy and safety of 2LTRZFP in human CD34+ HSPCs. Researchers used a lentiviral vector to transduce 2LTRZFP with the mCherry tag (2LTRZFPmCherry) into human CD34+ HSPCs. The study findings suggest that the anti-HIV-1 integrase scaffold is an enticing antiviral molecule that could be utilised in human CD34+ HSPC-based gene therapy for AIDS patients.<sup>89</sup>

## Genetical Modifications of Hematopoietic Stem Cells (HSCT)

The fundamental element of HIV management is stem cell genetic modification, which involves genetically enhanced patient-derived stem cells to overcome HIV infection. In this sector, numerous experimental studies, in vitro as well as in vivo examinations, and positive outcomes for AIDS patients have been conducted.<sup>65,74</sup> Genetic engineering for HIV-infected individuals can provide a once-only intervention that minimizes viral load, restores the immune system, and minimizes the accumulated toxicities concerned with highly active antiretroviral therapy (HAART).<sup>73</sup> HSCs can be genetically altered, permitting for the addition of exogenous components to the progeny that protects them from direct infectious disease and/or enables them to target a specific antigen. Besides that, HSC-based strategies can enhance multilineage hemopoietic advancement by re-establishing several arms of the immune function. Eventually, as HSCs can be produced autologously, immunologic tolerance is typically high, enabling effective engraftment and subsequent distinction into the fully functioning mature hematopoietic cells.<sup>30</sup>

The utilization of human HSCs to rebuild the immune function in HIV disease is one application that tries to preserve newly formed cells from HIV infection, while another attempts to develop immune cells that attack HIV infected cells. While each initiative has many different aspects at the moment, they represent huge attention to HIV/AIDS therapies that, most likely when integrated with the other therapeutic approaches, would result in the body trying to overcome the obstacles needed for the virus to be effectively cleaned up.<sup>30</sup>

While HSC transplantation technique and processes are not accurately novel, as they are commonly and effectively used to address a wide variety of haematological diseases and malignant neoplasms,<sup>90</sup> trying to combine them with a gene therapeutic strategy represents a unique and possibly potent therapeutic approach for HIV and AIDS-related ailments. As the results of HIV-infected patients who obtained autologous HSCT continued to improve, there was growing interest in genetically altered stem cells that were tolerant to HIV disease. Multiple logistical challenges have impeded the advancement of genetically modified hematopoietic stem cells as a conceivable therapeutic option for HIV/AIDS.<sup>72,73</sup>

UCLA’s Eli and Edythe Broad Center for Restorative Medicine and Stem Cell Studies is one bit closer to constructing an instrument to arm the body’s immune system to attack and defeat HIV. Dr. Kitchen et al are the first ones to disclose the use of a chimeric antigen receptor (CAR), a genetically manipulated molecule, in blood-forming stem cells. In the



experiment, the research team introduced a CAR gene into blood-forming stem cells, which were then moved into HIV-infected mice that had been genetically programmed. The scientists found that CAR-carrying blood stem cells efficiently transformed into fully functioning T cells that have the ability to kill HIV-infected cells in mice. The outcome was an 80-to-95 percentage reduction in HIV levels, suggesting that stem-cell-based genetic engineering with a CAR might be a viable and effective approach for treating HIV infection among humans. The CAR initiative, according to Dr. Kitchen, is much more able to adapt and ultimately more efficient, which can conceivably be used by others. If any further experiment showcases keep promising, the scientists expect that a practice based on their strategy will be accessible for clinical development within the next 5–10 years.<sup>91</sup>

## HSCT and HAART Therapeutic Approach

HSCT and HAART therapeutic approaches in treating HIV/AIDS as the emergence of highly active antiretroviral therapy (HAART) in the 1990s improved survival rates of HIV infection, leading to a major dramatic drop in the occurrence of AIDS and AIDS-related mortalities. As an outcome, there is much less involvement with using HSCT as a therapy for HIV infection.<sup>28,33,43,67,86</sup>

## Human Umbilical Cord Mesenchymal Stem Cell Transplantation

A randomized clinical trial of human umbilical cord mesenchymal stem cell transplant among HIV/AIDS immunological non – responders' investigation, the researchers examined the clinical efficacy of transfusion of human umbilical cord mesenchymal stem cells (hUC-MSC) for immunological non-responder clients with long-term HIV disease who have an unmet medical need in the aspect of effective antiretroviral therapy. From May 2013 to March 2016, 72 HIV-infected participants were admitted in this stage of the randomized, double-blind, multi-center, placebo-controlled dose-determination investigation. They were either given a high dose of hUC-MSC of 1.5106/kg body weight as well as small doses of hUC-MSC of 0.5106/kg body weight, or a placebo application. During the 96-week follow-up experiment, interventional and immunological character traits were analysed. They found that hUC-MSC therapy was both safe and efficacious among humans. There was a significant rise in CD4+ T counts after 48 weeks of treatment in both the high-dose (P 0.001) and low-dose (P 0.001) groups, but no changes in the comparison group.<sup>92</sup>

## Mesenchymal Stem/Stromal Cells (MSCs) Applications

One interesting invention made by a team of UC Davis investigators is the recognition of a particular form of stem cell that can minimize the quantity of the virus that tends to cause AIDS, thus dramatically increasing the body's antiviral immune activity. Mesenchymal stem/stromal cells (MSCs) furnish an incredible opportunity for a creative and innovative, multi-pronged HIV cure strategic plan by augmenting prevailing HIV potential treatments. Even while no antivirals have been used, MSCs have been able to increase the host's antiviral responses. MSC therapeutic approaches require specialized delivery systems and good cell quality regulation. The study's findings lay the proper scientific foundation for future research into MSC in the ongoing treatment of HIV and other contagious diseases in the clinical organization.<sup>35</sup>

## CCR5 Delta32/Delta32 Stem-Cell Transplantation

Infection with HIV-1 necessitates the existence of both specific receptors and a chemokine receptor, particularly chemokine receptor 5 (CCR5).<sup>46</sup> Resistance to HIV-1 infection is attained by homozygosity for a 32-bp removal in the CCR5 allele.<sup>93</sup> In this investigation, stem cells were transplanted in a patient with severe myeloid leukaemia and HIV-1 infection from a donor who was homozygous to Chemokine receptor –5 delta 32. The client seemed to have no viral relapses after 20 months of transplantation and attempting to stop antiretroviral medicine. This finding highlights the essential role that CCR5 tries to play in HIV-1 infection maintenance.<sup>86</sup>

In comparison, additional HIV-1-infected people who have received allogeneic stem cell transplants with cells from CCR5 truly wild donors did not have long-term relapses from HIV-1 rebound, with 2 of these patients trying to report viral reoccurrence 12 as well as 32 weeks after analytic treatment interruption, respectively. Among these 2 patients, allogeneic stem cell transplantation probably reduced but did not eliminate latently HIV-infected cells, enabling persistent viral reservoirs to activate viral rebound. This viewpoint may not rule out the potential that allogeneic

hematopoietic stem cell transplantation might result in a much more comprehensive or near-complete elimination of viral reservoirs, enabling long-term drug-free relapse of HIV-1 infection in some contexts.<sup>84</sup> As just one report demonstrated a decade earlier, a curative treatment for HIV-1 remained elusive. The “Berlin Patient” has undergone 2 allogeneic hematopoietic stem cell transplantations to cure his acute myeloid leukaemia utilizing a potential donor with a homozygous genetic mutation in HIV coreceptor CCR5 (CCR532/32).<sup>15,34,46,64,65,72,82,84,86,94–96</sup> Other similar studies with CCR5 receptor targets are as follows: Automated production of CCR5-negative CD4+T cells in a GMP compatible, clinical scale for treatment of HIV-positive patients,<sup>97</sup> Mechanistic Models Predict Efficacy of CCR5-Deficient Stem Cell Transplants in HIV Patient Populations,<sup>98</sup> Conditional suicidal gene with CCR5 knockout.<sup>99</sup>

## CRISPR and Stem Cell Applications

Clustered regularly interspaced short palindromic repeats CRISPR/Cas9 is a promising gene editing approach that can edit genes for gain-of-function or loss-of-function mutations in order to address genetic abnormalities. Despite the fact that other gene editing techniques exist, CRISPR/Cas9 is the most reliable and efficient proven method for gene rectification.<sup>100–103</sup>

Genome engineering employing CRISPR/Cas has proven to be a strong method for quickly and accurately changing specific genomic sequences. The rise of innovative haematopoiesis research tools to examine the complexity of hematopoietic stem cell (HSC) biology has been fuelled by considerable advancements in CRISPR technology over the last five years. High-throughput CRISPR screenings using many “new flavours” of Cas and sequential and/or functional outcomes, in specific, have become more effective and practical.<sup>104,105</sup>

The power of the CRISPR/Cas system is that it can specifically and efficiently target sequences in the genome with just a single synthetic guide RNA (sgRNA) and a single protein. Cas9 is directed to the specific DNA sequence by the sgRNA, which causes double stranded breaks and activates the cell’s DNA repair processes. Non-homologous end joining can cause insertion–deletion (indel) substitutions at the target location, whereas homology-directed repair can use a template DNA to insert new genetic material.<sup>104,106</sup>

The possibility for CRISPR/Cas9 to be used in the hematopoietic system was emphasised as pretty shortly after it was initiated as a new genome editing method.<sup>106,107</sup> The efficiency with which CRISPR-mediated alteration can be used to evaluate hematopoietic stem/progenitor and mature cell function via transplantation. As a result, hematopoietic research has significantly advanced with the implementation of these technologies. Whilst single-gene CRISPR/Cas9 programming is a significant tool for testing gene function in primary hematopoietic cells, high-throughput screenings potentially offer CRISPR/Cas9 an even greater advantage in hematopoietic research.<sup>104</sup>

While understanding human haematological disorders requires the ability to mimic diseases, the ultimate goal is to transfer this innovation into therapies. Despite significant advancements in CRISPR technology, there are still barriers to overcome before CRISPR/Cas9 can be used effectively and safely in humans. CRISPR has also been used to target CCR5 in CD34+ HSPCs in an effort to make immune cells resistant to HIV infection, as CCR5 is an important coreceptor for HIV infection.<sup>104</sup>

CRISPR is a modern genome editing technique that could be used to treat immunological illnesses including HIV. The utilization of CRISPR in stem cells for HIV-related investigation, on the other end, was ineffective, and much of the experiment was done in vivo. The new research idea is about increasing CRISPR-editing efficiencies in stem cell transplantation for HIV treatment, as well as its future perspective. The possible genes that enhance HIV resistance and stem cell engraftment should be explored more in the future studies. To strengthen HIV therapy or resistance, double knockout and knock-in approaches must be used to build a positive engraftment. In the future, CRISPR/SaCas9 and Ribonucleoprotein (RNP) administration should be explored in the further investigations.<sup>108</sup> As well as some different title studies were explained the effectiveness of the CRISPR gene editing technology on the management of HIV/AIDS including: CRISPR view of hematopoietic stem cells: Moving innovative bioengineering into the clinic,<sup>104</sup> CRISPR-Edited Stem Cells in a Patient with HIV and Acute Lymphocytic Leukaemia,<sup>109</sup> Sequential LASER ART and CRISPR Treatments Eliminate HIV-1 in a Subset of Infected Humanized Mice,<sup>110</sup> Extinction of all infectious HIV in cell culture by the CRISPR-Cas12a system with only a single crRNA,<sup>111</sup> HIV-specific humoral immune responses by CRISPR/Cas9-edited B cells,<sup>112</sup> CRISPR-Cas9 Mediated Exonic Disruption for HIV-1 Elimination,<sup>113</sup> RNA-directed gene editing

specifically eradicates latent and prevents new HIV-1 infection,<sup>114</sup> CRISPR/Cas9 Ablation of Integrated HIV-1 Accumulates Pro viral DNA Circles with Reformed Long Terminal Repeats,<sup>115</sup> CRISPR-Cas9-mediated gene disruption of HIV-1 co-receptors confers broad resistance to infection in human T cells and humanized mice,<sup>116</sup> Inhibition of HIV-1 infection of primary CD4+ T-cells by gene editing of CCR5 using adenovirus-delivered CRISPR/Cas9,<sup>117</sup> Transient CRISPR-Cas Treatment Can Prevent Reactivation of HIV-1 Replication in a Latently Infected T-Cell Line,<sup>118</sup> CCR5 Gene Disruption via Lentiviral Vectors Expressing Cas9 and Single Guided RNA Renders Cells Resistant to HIV-1 Infection,<sup>119</sup> CRISPR/Cas9-Mediated CCR5 Ablation in Human Hematopoietic Stem/Progenitor Cells Confers HIV-1 Resistance In Vivo.<sup>109</sup>

## Induced Pluripotent Stem Cells Applications

Induced pluripotent stem cells (iPSCs) have significantly advanced the field of regenerative medicine by allowing the generation of patient-specific pluripotent stem cells from adult individuals. The progress of iPSCs for HIV treatment has the potential to generate a continuous supply of therapeutic cells for transplantation into HIV-infected patients. The title of the study is reported on Generation of HIV-1 Resistant and Functional Macrophages from Hematopoietic Stem Cell-derived Induced Pluripotent Stem Cells. In this investigation, researchers used human hematopoietic stem cells (HSCs) to produce anti-HIV gene expressing iPSCs for HIV gene therapy. HSCs were dedifferentiated into constantly growing iPSC lines using 4 reprogramming factors and a combination anti-HIV lentiviral vector comprising a CCR5 shRNA and a human/rhesus chimeric TRIM5 $\alpha$  gene. After directing the anti-HIV iPSCs toward the hematopoietic lineage, a large number of colony-forming CD133+ HSCs were acquired. These cells were distinguished further into functional end-stage macrophages with a normal phenotypic profile. Upon viral challenge, the anti-HIV iPSC-derived macrophages displayed good protection against HIV-1 infection. Researchers have clearly shown how iPSCs can establish into HIV-1 resistant immune cells and explain their prospective use in HIV gene and cellular therapies.<sup>120</sup>

Some other similar titles of the studies reported on the effectiveness of iPSCs on HIV/AIDS managements are as follows: Generation of HIV-Resistant Macrophages from iPSCs by Using Transcriptional Gene Silencing and Promoter-Targeted RNA,<sup>121</sup> Generation of HIV-1-infected patients' gene-edited induced pluripotent stem cells using feeder-free culture conditions,<sup>122</sup> A High-Throughput Method as a Diagnostic Tool for HIV Detection in Patient-Specific Induced Pluripotent Stem Cells Generated by Different Reprogramming Methods,<sup>123</sup> Genetically edited CD34+ cells derived from human iPS cells in vivo but not in vitro engraft and differentiate into HIV-resistant cells,<sup>124</sup> Engineered induced-pluripotent stem cell-derived monocyte extracellular vesicles alter inflammation in HIV humanized mice,<sup>125</sup> Sustainable Antiviral Efficacy of Rejuvenated HIV-Specific Cytotoxic T Lymphocytes Generated from Induced Pluripotent Stem Cells.<sup>126</sup>

## The Reality of Berlin and London Patient from HIV

Recently, one HIV patient appeared to be virus-free after having undergone a stem-cell transfusion in which their WBCs were changed with HIV-resistant variations.<sup>84</sup> Timothy Ray Brown also noted as the "Berlin patient", who is still virus-free, was the first individual to undertake stem-cell transplantation a decade earlier. The most recent patient, like Brown, had a type of leukaemia that was vulnerable to chemo treatments. They required a bone marrow transplantation, which involved removing their blood cells and replacing them with stem cells from a donor cell.<sup>5,31,34,41,127-130</sup> Rather than simply choosing a suitable donor, Ravindra Gupta et al chose one who already had 2 copies of a mutant within the CCR5 gene,<sup>128,131</sup> which provides resistance to HIV infection.<sup>3</sup>

Additionally, this gene encodes for a specific receptor of white blood cells that are assisted in the body's immunological responses. The transplant, according to Gupta's team, completely replaced the client's White cells with HIV-resistant forms.<sup>41,83</sup> Cells in the patient's blood disrupted expressing the CCR5 receptor, making it unfeasible for the client's form of HIV to infect the above cells again. The scientists determined that the virus had been cleared from the patient's blood after the transplantation. Besides that, after 16 months, the client has withdrawn antiretroviral treatment. The infection was not detected in the most recent follow-up, which occurred 18 months after the treatment was discontinued. Adam, also known as the "London patient", was the second person to be cured of HIV as a result of a stem cell transfusion. This discovery is an important step forward in HIV research because it may aid in the detection of

potential future therapeutic interventions. It must be noted, but even so, that this is not an extensively used HIV treatment. For HIV-infected patients, antiretroviral drugs have been the foremost therapeutic option.<sup>3,31,41,94,129,130</sup> It also encourages many investigators and clinicians to look at the use of stem cells in the treatment of a wide range of serious medical conditions. The reprogramming abilities of stem cells, as well as their accessibility, have created a window of opportunity in medical research. The clinical utility of stem cells is forecast to expand rapidly in the coming years.

## The Recovery of 3rd Individual from HIV

On Feb 15, 2022, scientific researchers confirmed that a woman had become the 3rd person in history to be successfully treated for HIV, the virus that causes AIDS, after just receiving a stem-cell transfusion that has used cells from cord blood. Within those transplant recipients, adult hematopoietic stem cells have been used; these are stem cells that eventually develop into all blood cell types, which include white blood cells, these are a vital component of the immune framework. Even so, the woman who had fairly recently been completely cured of HIV infection had a more unique experience than that of the 2 men who were actually cured before her.<sup>132</sup>

The client's physician, Dr. JingMei Hsu of Weill Cornell Medicine in New York, informed them that, she had been discharged from the hospital just 17 days after her procedure was performed, even with no indications of graft vs host ailment. The woman was HIV-positive but also had acute myeloid leukaemia, a blood cancer of the bone marrow that affects blood-forming cells. She had likely received cord blood as a successful treatment for both her cancer and HIV once her doctors decided on a potential donor well with HIV-blocking gene mutation. Cord blood comprises a high accumulation of hematopoietic stem cells; the blood is obtained during a child's birth and donated by the parents.<sup>132</sup>

The patient's donor was "partly nearly matched", and she received stem cells from a close family member to enhance her immune function after the transfusion. The procedure was performed on the woman in August of 2017. She chose to discontinue taking antiretroviral drugs, the standardized HIV intervention, 37 months upon her transfusion. After more than 14 months, there is no evidence of the viral infection or antibodies against it in her blood. Umbilical cord blood, in reality, is much more commonly accessible and simpler to try to match to beneficiaries than bone marrow. Perhaps, some research suggests that the method could be more available to HIV patients than bone marrow transplantation. Nearly 38 million people worldwide are infected with HIV. The potential for using partly matched umbilical cord blood transplantation increases the chances of choosing appropriate suitable donors for these clients considerably.<sup>132</sup>

## Discussion

It is really exciting to see the earlier terminally ill diseases of being effectively treated. In recent times, there has been a surge of focus on stem cell research.<sup>3</sup> Stem cell therapy advancements in inpatient care are receiving a growing amount of attention.<sup>20</sup> HIV/AIDS has been and remains a significant health concern around the world. Effective control of the HIV pandemic will necessitate a thorough understanding of the virus's transmission.<sup>32</sup>

Despite concerns about full compliance and adverse reactions, HAART has demonstrated to be able to succeed and is a sign specifically targeted form of treatment against HIV advancement. As illustrated by the first case of HIV infection relapse attained by bone marrow transplant, anti-HIV HPSC-based stem cell treatment and genotype technology have established a possible future upcoming technique to try to combat HIV/AIDS.

Investigators have conducted experiments with engineering distinct anti-HIV genetic traits trying to target different phases of HIV infection utilizing advanced scientific modalities. In numerous in vivo and in vitro animal studies, HSPCs and successive mature cells were secured from HIV infection by trying to target genetic factors in the infection. Anti-HIV gene engineering of HSPCs is safe and efficacious.<sup>15</sup>

The number of stem-cell-based research trials has risen in recent years. Thousands of studies claiming to use "stem cells" in experimental therapies have been registered worldwide. Despite some promising results, the majority of clinical stem cell technologies are still in their early life. These achievements have drawn attention to the possibility of the potential and advancement of various promising stem cell treatments currently in development.<sup>11</sup>

HIV remains a major danger to humanity. This virus has developed the ability to evade antiretroviral medication, resulting in the death of individuals. Scientists are constantly looking for a treatment for HIV/AIDS that is both effective and efficient.<sup>52</sup> The 1st treatments in HIV+ clients were conducted in the early 1980s, even though they were cognizant of their viral disease. Following these early cases, allogeneic SCT was used to treat HIV+ patients with associated cancer or other haematological disorders all over the world. Stem cell transplantation developments have also stimulated the improvement of innovative HIV therapeutic approaches, especially for large goals like eradication and relapse.<sup>60</sup>

Numerous stem cell therapy progressions have been recognized with autologous and allogeneic hematopoietic stem cell transplantation, as well as umbilical cord blood mesenchymal stem cell transplant in AIDS immunologic non-responders. Whereas this sector continues to advance and distinguishing directives for these cells become much more effective, totipotent stem cells such as hESC and the recently reported induced pluripotent stem cells (iPSC) could be very useful for genetic engineering methods to counter hematopoietic abnormalities such as HIV disease.<sup>133–135</sup>

## Conclusion

Immunocompromised people are at a higher risk of catching life-threatening diseases. The perseverance of latently infected cells, which is formed by viral genome inclusion into host cell chromosomes, is a significant challenge in HIV-1 elimination. Stem cell therapy is producing impressive patient outcomes, illustrating not only the broad relevance of these strategies but also the huge potential of cell and gene treatment using adult stem cells and somatic derivative products of pluripotent stem cells (PSCs).

Stem cells have enormous regeneration capacity, and a plethora of interesting therapeutic uses are on the frontier. This is a highly interdisciplinary scientific field. Evolutionary biologists, biological technicians, mechanical engineers, and others that have evolved novel concepts and decided to bring them to medical applications are required to make important contributions. Further to that, recent advancements in several different research areas may contribute to stem cell application forms that are novel. Several hurdles must be conquered, however, in the advancement of stem cells. On the other hand, this discipline appears to be a promising and rapidly expanding research area.

Stem cell-based approaches to HIV treatment resemble an innovative approach to trying to rebuild the ravaged body's immune system with the utmost goal of eliminating the virus from the body. We will probably see effective experiments from the next new generation of stem cell-based strategies shortly, which will start serving as a base for the further development and use of these techniques in a range of treatment application areas for other chronic diseases.

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