Research Article

Mathematical Modeling to Study Multistage Stem Cell Transplantation in HIV-1 Patients

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1. Introduction

A virus called HIV (human immunodeficiency virus) causes AIDS (acquired immunodeficiency syndrome). HIV is a retrovirus that attacks the vital organs and the cells of the human immune system, making people more vulnerable to diseases and infections. Without treatment, HIV can develop into AIDS in many cases. In the absence of therapy the virus progresses. The developing rate of the virus differs between individuals and changes according to many factors. These factors include ability of the body to fight against HIV, the age of the individual, access to healthcare, the individual's genetic inheritance, the presence of other infections, and the resistance to certain strains of HIV.

According to the World Health Organization's guidelines issued in June 2018, there is no viable cure or vaccine for HIV, but treatments can improve patients' quality of life.

When given the right treatment, some patients can live with HIV and reduce their viral load to such a degree that it is not discoverable. Studies by the CDC (Centers for Disease Control and Prevention) proved that in individuals who have no discoverable viral load "through sex there is effectively no risk of transmitting HIV to an HIV-negative partner." Generally, people who live with HIV take a composition of medications called HAART (highly active antiretroviral therapy) or CART (combination antiretroviral therapy) [1]. This antiretroviral therapy (ART) prevents or slows the virus from developing.

We can find two types of HIV: HIV-1 and HIV-2. HIV-1 is more infective and more dangerous than HIV-2 as mentioned in [2]. Also HIV-1 concretes both lymphadenopathy associated virus (LAV) and human T-lymphotropic virus-3 (HTLV-III). HIV-2 is largely found in West Africa [3], according to its relatively poor capacity for transmission.

Understanding the dynamics of HIV-1 by mathematical modeling plays a basic role in medicine. All mathematical models of HIV-1 are based on the model in [4] where they considered the interaction between four components: uninfected CD4 + T-cells, latent infected CD4 + T-cells, infected CD4 + T-cells, and the free virus. Then, many researchers modified this model such as in [5] where they presented the same model without the latent infected CD4 + T-cells. The models that are studied in [6–10] focused on models interested in the dynamics of HIV and a hope for a cure for the infection.

Stem Cell Therapy. Nowadays, stem cell studies are a field of much interest, and within this area there is a need for mathematical model representation of the dynamics growth for stem cells. Inside any organism the new cells need a
source, which requires a continuous role to replace the older cells, to keep the balance of homeostasis for tissue, and to react to the external ecological stresses. In each organ adult stem cells [11, 12] are planning this important role to replace the older cells. Through its niche in the organism and its special nature, the stem cell is able to renew itself. The daughter cells are generated from the stem cells through cell divisions and will differentiate into one of any number of organ specific cell types; in this process of differentiation, they lose their initial capacity for self-renewal. Lie and Xie [13] discussed an accurate equilibrium between stem cell self-renewal and differentiation; also they studied the way stem cells regulate the body and treat human disease. A lot of interest has also been focused on embryonic stem cells [14, 15], a kind of stem cell from earlier in human development, and it is a smart cell that can be differentiated into any type of cells within the body.

Adult stem and embryonic cells have the same properties of proliferation, differentiation, and self-renewal. Hence, thinking about their transplantation in the patient can be a good idea to replace injured cells and help in restoring the function of damaged cells. Recent studies have shown the efficacy of this technique to regenerate some body organs [16]. All of the abovementioned properties are a critical field within the research of stem cells. According to the recent researches that studied proliferation of stem cells, this paper introduces a mathematical model. As discussed in Henrigou et al. [17] and Bonab et al. [18], many therapies of stem cells depend on the availability of the number of the stem cells to transfer. Therefore, the representation of the rate of growth for a population of stem cells as a function of the rate of growth for a population of stem cells to transfer. Therefore, the representation of stem cells depend on the availability of the number of stem cells to transfer. Therefore, the representation of the rate of growth for a population of stem cells as a mathematical model will be very useful. Several models applied to stem cell proliferation as in Loeffler and Wichman [19] and as in Cowan and Morris [20] have been reviewed and accordingly this paper’s mathematical model was constructed.

Depending on the ability of stem cells to differentiate into some of the specialized phenotypes in response to appropriate signals [21], this paper proposes to treat HIV-1 patients by engraftment of the type of cells able to transform to T-cells (CD4+T). Other varieties of cells were tested for restoring the heart [22–26], the cornea [27], and pancreatic functions [28, 29].

This paper begins by recalling a known mathematical model for multilineage stem cells, which was used to formulate a new mathematical model of the viral dynamic of HIV-1 treatment by stem cell therapy. The study of the model enables us to choose the best stage in the lineage to engraft these cells and help medicine make the good decision.

2. Mathematical Modeling of n-Multistage Stem Cell Maturation

Let \( s_i \) be the density of stem cells at the \( i \)th stage for \( i = 1, 2, \ldots, n - 1 \), of differentiation and the density of mature cells for \( i = n \). Let \( h(t) \) be the concentration of signaling molecules which depends only on the density of mature cells \( s_n \); thus the dynamics of a cytokine (a protein, polypeptide, or glycoprotein that are used in signaling and intracellular signaling and also aid in cell-to-cell communication in immune responses and stimulate the movement of cells towards sites of inflammation and infection) can be represented as a first-order differential equation:

\[
\frac{dh}{dt} = \mu(1 - h - y s_n(t)),
\]

where \( \mu \) is the death rate of a mature cell population and \( y \) is a +ve constant; solving this equation using the approximation of the quasi-steady state we get \( h = h_i(t) = 1/(1 + y s_n(t)) \). The stem cell lineage can be expressed as an ODEs system [30]:

\[
\begin{align*}
\frac{ds_1}{dt} &= f_1(h(t), s_1(t)), \\
\frac{ds_2}{dt} &= f_2(h(t), s_2(t)) + g_1(h(t), s_1(t)), \\
&\vdots \\
\frac{ds_n}{dt} &= f_n(h(t), s_n(t)) + g_{n-1}(h(t), s_{n-1}(t)).
\end{align*}
\]

Here \( f_i(h(t), s_i(t)) \) is the change of \( s_i(t) \) that is caused by processes at the \( i \)th stage of maturation. If gains cells caused by the loss of differentiation or death are more weakened than the self-renewal and proliferation, then \( f_i(h(t), s_i(t)) \geq 0 \); otherwise \( f_i(h(t), s_i(t)) < 0 \). But if we suppose that mature cells are postmitotic (they cannot proliferate), then since \( f_n \) is accounted only for cell death, we have \( f_n(h(t), s_n(t)) < 0 \). We denote \( g_i(h(t), s_i(t)) \geq 0 \) to be the flux of cells from the maturation stage \( i \) to maturation stage \( i + 1 \) due to differentiation.

Let \( p_i(t) \) denote the proliferation rate of the subpopulation of type \( i \) at time \( t \), \( a_i(t) \) denote the fraction of self-renewal, and \( \mu_i(t) \) denote the death rate. Then, the flux to mitosis at time \( t \) will be \( p_i(t) s_i(t) \). The fraction \( a_i(t) \) of daughter cells dose not differentiate. Thus, the influx to cell population \( i \) after cell division is \( 2a_i(t)p_i(t)s_i(t) \) and the flux to the next cell compartment is \( 2(1 - a_i(t))p_i(t)s_i(t) \). The flux to death at time \( t \) is given by \( \mu_i(t)s_i(t) \). Hence we obtain

\[
\begin{align*}
 f_i(t) &= (2a_i(t) - 1) p_i(t) s_i(t) - \mu_i(t) s_i(t), & \text{for } i < n, \\
 g_i(t) &= 2(1 - a_{i-1}(t)) p_{i-1}(t) s_{i-1}(t), & \text{for } 1 < i < n, \\
 f_n(t) &= -\mu_n(t) s_n(t).
\end{align*}
\]

Assume that the proliferation rates and the death rates are constant with time, and self-renewal fractions are controlled by the signal feedback \( a_i(t) = a_i(h(s_i(t))) = a_{i,max} h(s_i(t)) \), where \( a_{i,max} = a_i \) is the maximal fraction of self-renewal. Therefore, system (1) can be written as
\[
\frac{ds_1}{dt} = (2a_1h - 1) p_1 s_1 - \mu_1 s_1, \\
\frac{ds_2}{dt} = (2a_1h - 1) p_2 s_2 + 2(1 - a_1h) p_1 s_1 - \mu_2 s_2,
\]
\[
\vdots
\]
\[
\frac{ds_n}{dt} = (2a_1h - 1) p_n s_n + 2(1 - a_{n-1}h) p_{n-1} s_{n-1} - \mu_n s_n.
\]

Using that \(h = 1/(1 + \gamma s_n)\), then system (3) becomes
\[
\frac{ds_1}{dt} = \left( \frac{2a_1}{1 + \gamma s_n} - 1 \right) p_1 s_1 - \mu_1 s_1, \\
\frac{ds_2}{dt} = \left( \frac{2a_2}{1 + \gamma s_n} - 1 \right) p_2 s_2 + 2\left( 1 - \frac{a_1}{1 + \gamma s_n} \right) p_1 s_1 - \mu_2 s_2,
\]
\[
\vdots
\]
\[
\frac{ds_n}{dt} = 2\left( 1 - \frac{a_{n-1}}{1 + \gamma s_n} \right) p_{n-1} s_{n-1} - \mu_n s_n.
\]

For the initial data and the model parameters, we add the following biologically relevant assumptions as in [30]:

\[ te [0, \infty), \]

\[ s_i(0) \geq 0, \quad \text{for } i = 1, \ldots, n, \]

\[ \mu_i \geq 0, \quad \text{for } i = 1, \ldots, n - 1, \]

\[ \mu_n > 0, \]

\[ p_i > 0, \quad \text{for } i = 1, \ldots, n - 1, \]

\[ a_{i, \text{max}} \in [0, 1), \quad \text{for } i = 1, \ldots, n - 1, \]

\[ \gamma > 0. \]

3. Mathematical Modeling of the n-Multistage Stem Cell Therapy for HIV-1 Patients

In our previous work [31], we proposed for the first time in literature a model that explains the effect of stem cell transplantation on HIV-1 viral dynamics. The basic model structure that describes the therapy uses four state variables: stem cells (S), healthy T-cells (T), infected T-cells (T_i), and the virus (V):

\[
\frac{dS}{dt} = \left[ b(s_{S} - \alpha_{D}) - \delta_{S} \right] S \\
\frac{dT}{dt} = \lambda_{T} - d_{T} T - k_{T} TV + (2\alpha_{D} + \alpha_{A}) bAS \\
\frac{dT_i}{dt} = k_{T} TV - \rho_{T} T_i \\
\frac{dV}{dt} = \pi_{T} T_i - cV,
\]

where the parameters \(b, \alpha_{S}, \alpha_{D}\) are nonnegative and \(b(\alpha_{S} - \alpha_{D}) - \delta_{S}\) are nonpositive. We know there are three possibilities for a stem cell to divide [32]:

(i) Symmetric self-renewal, where a stem cell can divide to become two stem cells, with probability \(\alpha_{S}\).

(ii) Asymmetric self-renewal, where one daughter cell remains a stem cell while the other does not inherit this characteristic, with probability \(\alpha_{D}\).

(iii) Symmetric commitment differentiation, where a stem cell can divide to become two committed cells, with probability \(\alpha_{A}\).

Therefore \(\alpha_{A} + \alpha_{S} + \alpha_{D} = 1\). We suppose that the stem cells \(S\) divide at rate \(b\) and die at rate \(\delta_{S}\). We need to introduce an amplification factor \(A\) to finally get the simplified ODE: 
\[
\frac{dS}{dt} = \left[ b(s_{S} - \alpha_{D}) - \delta_{S} \right] S
\]

Since stem cells \(S = S_1\) need many stages to transform to mature cells \(S_\infty = T\), in this paper we shall perform our previous work [31] by including the stages of the lineage of stem cells given by system (4). Our system (6) can then transform to a new system that describes the n-multistage stem cells transformation in the therapy of HIV-1 patients. This new model describes the dynamics of stem cell transplantation on the virus using \((n+2)\) state variables \((n+2)\) ODEs:

\[
\frac{dS_1}{dt} = \left( \frac{2a_1}{1 + \gamma T} - 1 \right) p_1 S_1 - \mu_1 S_1, \\
\frac{dS_2}{dt} = \left( \frac{2a_2}{1 + \gamma T} - 1 \right) p_2 S_2 + 2\left( 1 - \frac{a_1}{1 + \gamma T} \right) p_1 S_1 - \mu_2 S_2,
\]
\[
\vdots
\]
\[
\frac{dS_n}{dt} = \left( \frac{2a_n}{1 + \gamma T} - 1 \right) p_n S_n + 2\left( 1 - \frac{a_{n-1}}{1 + \gamma T} \right) p_{n-1} S_{n-1}
\]
4. Study of the Mathematical Model of the 2-Multistage Stem Cell Therapy for HIV-1 Patients

In this section, we are going to discuss the stability of the model of viral dynamics corresponding to the stem cell therapy given by system (8). We shall try to find out equilibrium points of system (8) in the form \((S_1, S_2, T, T_i, V)\). As in [36] we take \(\gamma\) to be very small; therefore we replace \(a_i/(1 + \gamma T)\) by \(a_i\) for \(i = 1, 2, \ldots, n - 1\), which is equivalent to choosing \(h = 1/(1 + \gamma T)\) as in [37].

The following theorem gives us the equilibrium points for the following system:

\[
\begin{align*}
\frac{dS_i}{dt} &= (2a_1 - 1) p_i S_1 - \mu_1 S_i, \\
\frac{dS_2}{dt} &= \left( \frac{2a_2}{1 + \gamma T} - 1 \right) p_i S_2 + 2 \left( 1 - \frac{a_1}{1 + \gamma T} \right) p_i S_1 - \mu_2 S_2, \\
\frac{dT}{dt} &= \lambda_T - (d_T + \mu_3) T - k_T TV + 2 \left( 1 - \frac{a_2}{1 + \gamma T} \right) p_2 S_2, \\
\frac{dT_i}{dt} &= k_T TV - \rho_T T_i, \\
\frac{dV}{dt} &= \pi_T T_i - cV.
\end{align*}
\]

If the basic reproduction ratio of the virus is given by \(R_0 = k_T \lambda_T \pi_T / (c \rho_T)\), then we get the following theorem.

**Theorem 1.** System (9) has two equilibrium points given by \(P_1 = (0, 0, \lambda_T/\beta, 0, 0)\) corresponding to the free disease case and \(P_2 = \beta c/k_T \pi_T (R_0 - 1, (\beta/\lambda_T)(R_0 - 1))\) corresponding to the endemic case.

**Proof.** To find the equilibrium points, we solve the following system for \((S_1, S_2, T, T_i, V)\):

\[
\begin{align*}
(2a_1 - 1) p_1 S_1 - \mu_1 S_i &= 0, \\
(2a_2 - 1) p_2 S_2 + 2 (1 - a_1) p_1 S_1 - \mu_2 S_2 &= 0, \\
\lambda_T - \beta T - k_T TV + 2 (1 - a_2) p_2 S_2 &= 0, \\
k_T TV - \rho_T T_i &= 0, \\
\pi_T T_i - cV &= 0.
\end{align*}
\]

By introducing \(R_0 = k_T \lambda_T \pi_T / (c \rho_T \beta)\), we get the result. \(\square\)

In the next theorems we study the stability at the equilibrium points \(P_1\) and \(P_2\).

**Theorem 2.** The free disease case \(P_1\) is asymptotically stable if \(R_0 < 1\) and unstable if \(R_0 > 1\).

**Proof.** The Jacobian matrix corresponding to system (9) is given by
At the health point \( P_1 \) the Jacobian matrix becomes
\[
J_1 = \begin{bmatrix}
(2a_1 - 1)p_1 - \mu_1 & 0 & 0 & 0 \\
2(1 - a_1)p_1 & (2a_2 - 1)p_2 - \mu_2 & 0 \\
0 & 2(1 - a_2)p_2 & -\beta - k_T V & 0 \\
0 & 0 & k_T V & -\rho_T - k_T T \\
0 & 0 & 0 & \pi_T - c
\end{bmatrix}.
\] (12)

So the characteristic equation \( \det(J_1 - rI) = 0 \) has the eigenvalues
\[
\begin{align*}
    r_1 &= (2a_1 - 1)p_1 - \mu_1, \\
r_2 &= (2a_2 - 1)p_2 - \mu_2, \\
r_3 &= -\beta, \\
r_{4,5} &= -\beta(c + \rho_T) \pm \sqrt{\left(\beta(c + \rho_T)\right)^2 - 4\beta \left(k_T \rho_T - k_T \lambda_T \pi_T \rho_T\right)}.
\end{align*}
\] (13)

To get the asymptotically stable case for the free disease equilibrium point we shall have for the first and the second roots \((2a_1 - 1)p_1 < \mu_1\) and \((2a_2 - 1)p_2 < \mu_2\) which are true and agree with [30, 31, 36]; since the population of mature cells \(S_i\) reaches some value, then the term \((2a_i(t) - 1)p_i(t)S_i(t) < 0\), for \(i < n\), and the number of cells at stage \(i\) decreases, while the lowness of the density for the mature cells causes \((2a_i(t) - 1)p_i(t)S_i(t) < 0\), for \(i < n\), and if the death rates are not too high, then the number of cells at stage \(i\) increases. These show how the level of mature cells affects the dynamics of each cell subpopulation. Also it is clear that \(r_i < 0\), and if \(R_0 = k_T \lambda_T \pi_T / c \rho_T < 1\), then \(c \rho_T \beta > k_T \lambda_T \pi_T \beta\), so \( (\beta + \rho_T)^2 > \beta(\beta^2 - 2\beta c \rho_T + 4k_T \lambda_T \pi_T \rho_T + \beta^2 \pi_T)\); then \(r_{4,5} < 0\).

If \(R_0 = k_T \lambda_T \pi_T / c \rho_T \beta > 1\), then \(c \rho_T \beta^2 < k_T \lambda_T \pi_T \beta\), so \( (\beta + \rho_T)^2 < \beta(\beta^2 - 2\beta c \rho_T + 4k_T \lambda_T \pi_T \rho_T + \beta^2 \pi_T)\); then \(r_{4,5} > 0\). Thus, we get the result.

**Remark 3.** (1) If \(R_0 = 1\), then \(P_1 = P_2\)

(2) If \(R_0 < 1\), then \(P_2\) is impossible

To study the endemic point \(P_2\), we need the following lemma.

**Lemma 4** (see [37]). The polynomial \(f(r) = r^3 + a_1 r^2 + a_2 r + a_3\) has the following results:

(i) If \(a_3 < 0\), then \(f(r)\) has at least one positive root

(ii) If \(a_1 > 0\), \(a_2 \geq 0\), and \(a_3 \geq 0\), then \(f(r)\) has no positive root

(iii) If \(a_1 > 0\), \(a_3 \geq 0\), and \(a_2 < 0\), then \(f(r)\) has a positive root:
\[
r = \frac{1}{3} \left(-a_1 + \sqrt{a_1^2 - 3a_2}\right) \quad (14)
\]

**Theorem 5.** If \(R_0 \geq 1\), then the endemic point \(P_2\) is asymptotically stable.

**Proof.** At the point \((0, 0, (\lambda_T / \beta)(1/R_0), (\beta c / k_T \pi_T))(R_0 - 1), (\beta / k_T)(R_0 - 1))\) the Jacobian matrix becomes
\[
J_2 = \begin{bmatrix}
(2a_1 - 1)p_1 - \mu_1 & 0 & 0 & 0 & 0 \\
2(1 - a_1)p_1 & (2a_2 - 1)p_2 - \mu_2 & 0 & 0 & 0 \\
0 & 2(1 - a_2)p_2 & -\beta R_0 & 0 & -k_T \frac{\lambda_T}{\beta R_0} \\
0 & 0 & \beta (R_0 - 1) - \rho_T & k_T \frac{\lambda_T}{\beta R_0} & -c \\
0 & 0 & 0 & \pi_T - c
\end{bmatrix}.
\] (15)
So the characteristic equation $\det(J_2 - rI) = 0$ has the eigenvalues $r_1 = (2a_1 - 1)p_1 - \mu_1, r_2 = (2a_2 - 1)p_2 - \mu_2,$ and the other eigenvalues are roots of the polynomial $f(r) = r^3 + a_1 r^2 + a_2 r + a_3 = 0$, where $a_1 = c + \rho_T + \beta R_0, a_2 = \beta R_0 (c + \rho_T), \text{ and } a_3 = \gamma p_T \beta (R_0 - 1).$

Since $R_0 > 1$, then $\beta R_0 (c + \rho_T) > 0$, and $\gamma p_T \beta (R_0 - 1) > 0$. Then, according to Lemma 4, we deduce that $P_2$ is asymptotically stable.

5. Study of the Mathematical Model of the n-Multistage Stem Cell Therapy for HIV-1 Patients

In this section, we will consider previously given $(n + 2)$-dimensional system (7). As mentioned in the previous section, we can replace $a_i/(1 + yT)$ by $a_i$ for $i = 1, \ldots, n - 1$. Then (7) can be written as

$$\frac{dS_i}{dt} = (2a_i - 1)p_i S_i - \mu_i S_i,$$

$$\frac{dS_2}{dt} = (2a_2 - 1)p_2 S_2 + 2(1 - a_1)p_1 S_1 - \mu_2 S_2,$$

$$\vdots$$

$$\frac{dS_{n-1}}{dt} = (2a_{n-1} - 1)p_{n-1} S_{n-1} + 2(1 - a_{n-2})p_{n-2} S_{n-2} - \mu_{n-1} S_{n-1},$$

$$\frac{dS_n}{dt} = (2a_n - 1)p_n S_n - \mu_n S_n,$$

$$\frac{dT}{dt} = \lambda_T - (d_T + \mu_n) T - k_T TV + 2(1 - a_{n-1})p_{n-1} S_{n-1},$$

$$\frac{dT_i}{dt} = k_T TV - \rho_T T_i,$$

$$\frac{dV}{dt} = \pi_T T_i - c V.$$

Assume that $d_T + \mu_n = \beta'$. If the basic reproduction ratio of the virus (that depends on the patient) is given by $R_0 = k_T \lambda_T \pi_T / \gamma p_T \beta'$, then, using mathematical induction, we can deduce the following theorem.

Theorem 6. System (16) has two equilibrium points given by the following:

$$P_1(S_1, S_2, \ldots, S_{n-1}, T, T_i, V) = (0, 0, \ldots, 0, \lambda_T / \beta', 0, 0),$$

corresponding to the free disease case, and

$$P_2(S_1, S_2, \ldots, S_{n-1}, T, T_i, V) = \left(0, 0, \ldots, 0, \frac{\lambda_T}{\beta'} \frac{1}{R_0}, \frac{\beta' c}{k_T \pi_T} (R_0 - 1), \frac{\beta' c}{k_T} (R_0 - 1)\right),$$

corresponding to the endemic case.

Theorem 7. The free disease case $P_1$ is asymptotically stable if $R_0 < 1$ and unstable if $R_0 > 1$.

Remark 8. (1) If $R_0 = 1$, then $P_1 = P_2$

(2) If $R_0 < 1$, then $P_2$ is impossible.

Theorem 9. If $R_0 \geq 1$, then the endemic point $P_2$ is asymptotically stable.

6. Conclusion

We have formulated an n-multistage system of ODEs model to study the influence of the treatment of HIV-1 infection with stem cell transplantation. Evidently the effect of the therapy on the viral dynamics depends on the patient (depends on $R_0$).

(i) If $R_0 \leq 1$, we have only one equilibrium point corresponding to the free disease case $P_1(S_1, S_2, \ldots, S_{n-1}, T, T_i, V) = (0, 0, \ldots, 0, \lambda_T / d_T, 0, 0)$, which is asymptotically stable. We can then conclude that the infected T-cells and virus particles will be cleared and the stem cells exhausted. In this case, the patient is healed.

Here we can also add a comment on the best stage we can choose for the mutant cells to be transplanted on the patient. Since all the components $S_1, S_2, \ldots, S_{n-1}$ of the point $P_1$ are equal to zero, then it is better to transplant the stem cells when they are nearly transformed to mature T-cells. This result is known in the cases of corneal transplantation, skin transplantation, and cardiac disease.

(ii) If $R_0 > 1$, the free disease case $P_1$ is unstable, and the infected state $P_2(S_1, S_2, \ldots, S_{n-1}, T, T_i, V) = (0, 0, \ldots, 0, \lambda_T / d_T (1/R_0), (d_T c_T / k_T \pi_T) (R_0 - 1), (d_T / k_T) (R_0 - 1))$ is asymptotically stable, which means that any HIV-1 infection for that patient will progress to chronic infection after stem cell exhaustion.

Therefore, stem cell therapy will not offer a cure to that infected person ($R_0 > 1$) but simply will help delay progression to the chronic stage. If we repeat the transplantation of stem cells in a manner to prevent its exhaustion from the patient, we can prevent AIDS.

We advise medicine to try to replace the chemical drug therapy with the apparently safe stem cell therapy. But will clinical experiments meet the expectations?

7. Future Works

For more interest we will study a fractional order of mathematical modeling to study multistage stem cell transplantation on HIV-1 patients based on [38, 39]. The presence of a fractional differential order in differential equations can lead to more consistency and more accuracy to real life than the integer-order models because the fractional derivatives enable the description of the memory and hereditary properties inherent in various processes and materials. The most important property of these models is their nonlocal property which does not exist in the integer-order differential operators. We mean by this property that the next state of a model depends not only on its current state but also on all of its historical states.
Data Availability
No data were used to support this study.

Conflicts of Interest
The authors declare that they have no conflicts of interest regarding the publication of this paper.

References


