



# Stem cell research finds possible HIV cure with cord blood transplant

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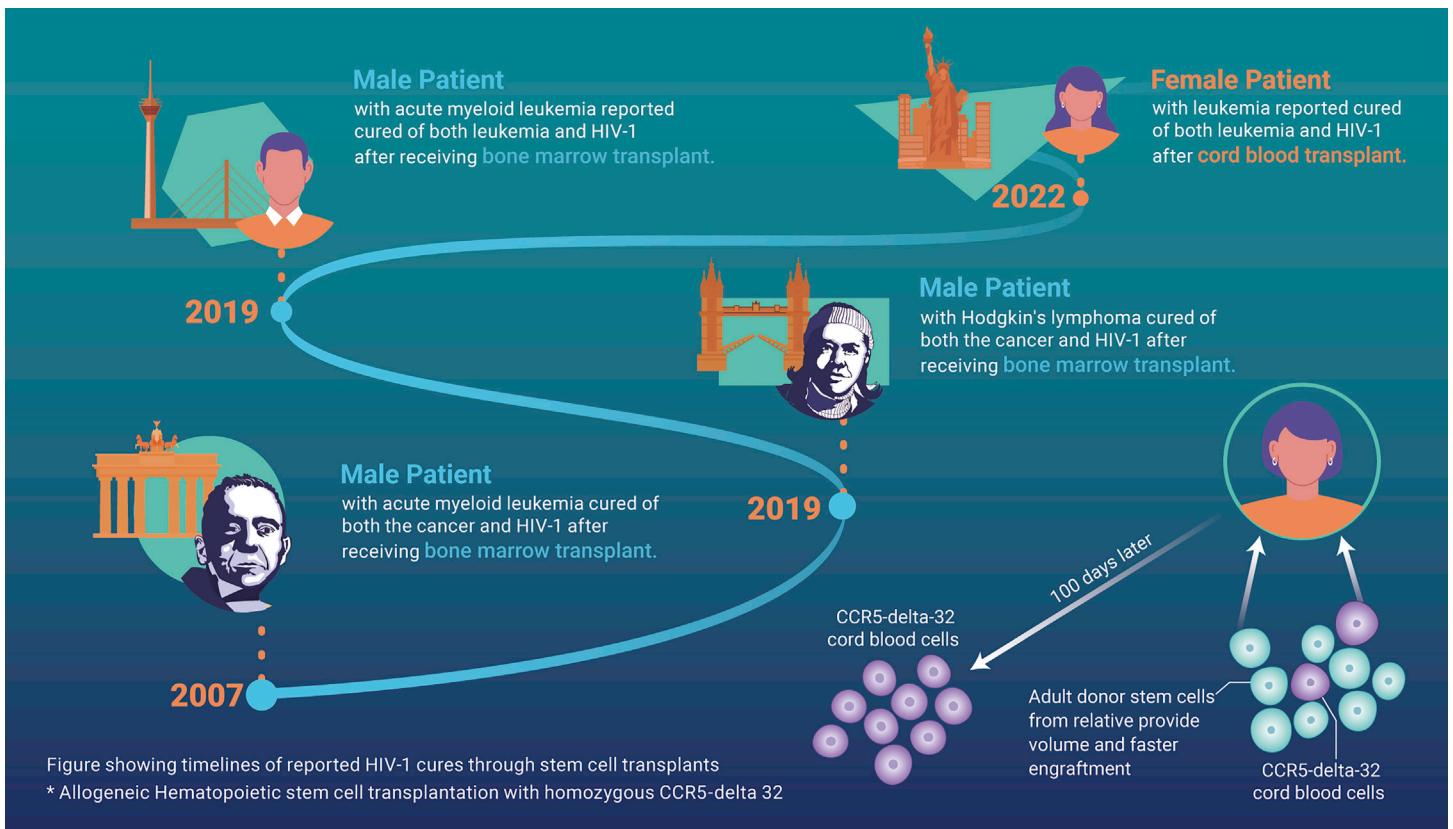
Recent reports of an American woman of mixed race cured of HIV through stem cell transplant suggest ground-breaking progress on the human immunodeficiency virus “HIV” war front as it marks significant progress in efforts to find a cure for the disease.

As presented at the recent Conference on Retroviruses and Opportunistic Infections, the cured patient was discovered in the ongoing USA-supported stem cell research study led by Dr. Deborah Persaud of Johns Hopkins University and Dr. Yvonne Bryson of the University of California Los Angeles (UCLA).<sup>1</sup> The study follows up on 25 people living with HIV that received umbilical cord blood transplants as part of treatment for cancer and other life-threatening conditions. The middle-aged leukemia patient also living with HIV was deemed cured of her HIV-1 infection after researchers found no traces of either HIV-1-specific antibody responses or replication-competent latent reservoir of the virus in her blood samples 55 weeks post treatment with cord blood transplant. The hypothesized cure was further grounded when no viral rebound occurred 14 months after her antiretroviral treatment ceased and an HIV-1 DNA PCR test was negative<sup>1</sup> (Figure 1).

Stem cell research into HIV cure has been ongoing for decades, with promising outcomes found in some studies. For example, a previous study highlighted how to implement gene therapy trials in conventional and reproducible ways, and another emphasized the need for multi-pronged approaches using lentiviral-based gene therapy vectors. The results from such studies served as the foundation for developing alternative methods that may have contributed to the three

cases of HIV cure reported in recent years.<sup>2</sup> However, progress toward finding suitable long-term stem cell-based treatment strategies that would result in complete immune clearance of the virus from the body for all population types has been slow. The first case of a successful stem cell-based HIV cure was widely reported in 2007 when a man living with HIV was found to have cleared his HIV infection after receiving a bone marrow transplant as part of cancer treatment therapy for acute myeloid leukemia.<sup>3</sup> More recent reports indicate that two men (the London and Dusseldorf patients) have also continued to live free of HIV years later after receiving similar bone marrow transplant (hematopoietic stem-cell transplant [HSCT]) with homozygous CCR5-delta 32 for Hodgkin’s lymphoma and leukemia treatment, respectively.<sup>4,5</sup>

However, scaling up further research into bone marrow transplant is limited by the method being a painful and expensive procedure mainly reserved as a last resort treatment option for a patient that is not manageable with medication. Also, the clinical requirements that donors of bone marrow need to have the rare HIV-resistant blood and be well matched with the recipient for a successful transplant to avoid rejection and potential death among recipients further complicates the situation. Thus, even if approved for global use in HIV treatment, large-scale implementation of HIV treatment based on bone marrow transplant would be an expensive procedure and impossible. However, unlike bone marrow transplants, umbilical cord blood is an equally good source of stem cells with a higher potential of compatibility for unrelated members of the population



**Figure 1. Timelines of reported HIV-1 cures through stem cell transplant** A middle-aged woman was diagnosed with HIV in 2013 and subsequently with acute myeloid leukemia in 2017. She required a stem cell transplant and joined a study designed to use previously screened umbilical cord blood with the double CCR5-delta-32 mutation. The procedure, called a haplo-cord transplant, combined CCR5-delta-32 cord blood cells with partially matched adult donor stem cells from one of the woman’s relatives without the CCR5 mutation. Full engraftment with 100% CCR5-delta-32 immune cells derived from the cord blood cells was achieved 100 days later.

(non-family relatives). It has the added advantages of being easier to obtain (like the umbilical cord of newborn babies), easily matches multiple recipients, low risk of rejection in recipients, and can be stored for decades when frozen correctly. Hence, using cord blood transplant for HIV treatment has the potential to successfully circumvent the clinical challenges and risks associated with treatment based on bone marrow transplant and could be cheaper. Therefore, the recent discovery that cord blood transplant could play an essential role in developing an HIV cure fuels researchers' hopes of discovering an HIV cure soon and brightens the light at the end of the tunnel for younger persons living with HIV.

Nonetheless, there are still more relevant issues to be further investigated before cord blood transplant could be hailed as the "holy grail" in HIV cure achievements. First, there is a need for more evidence on a longer-term non-viral rebound in the cured patient to ensure acquired immunity is not temporary. Second, more research is needed to verify or debunk any role that cancer, especially leukemia, and its related chemotherapy may have in the success of the HIV cure. This investigation is crucial as cancer, especially leukemia, and chemotherapy are but a few common factors underlying how the three individuals cured of HIV are similar.

Fourth, there is a substantial need for more clinical trials to research the potential use of cord blood transplants in treating persons living with HIV without pre-exposure to any cancer.

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## DECLARATION OF INTERESTS

The authors declare no competing interests.