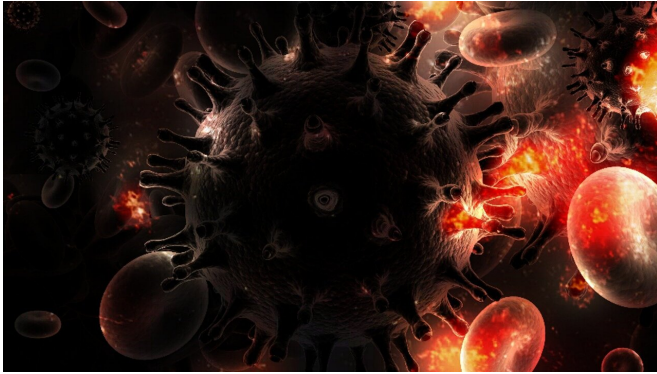


Formula predicts ideal dose of stem cells to cure HIV

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Scientists have determined the optimal conditions following a stem cell transplant that could control HIV without the need of an everyday pill, according to a study published today in *eLife*.

Finding the right balance of stem cell dose, cell type and timing of antiretroviral therapy (ART) could potentially lead to a spontaneous [cure](#) of HIV.

There are only two cases of HIV cure to date: the Berlin Patient and the London Patient, who both received stem cell transplants with stem [cells](#) from donors that lack a molecule called CCR5, which HIV is attracted to.

"The major obstacle to HIV eradication is a latent reservoir of long-lived infected cells, and cure strategies aim to eliminate all [infected cells](#) or permanently prevent viral reactivation from latency," explains first author E. Fabian Cardozo-Ojeda, Senior Staff Scientist at the Vaccine and Infectious Disease Division, Fred Hutchinson Cancer Research Center, Seattle, US. "We wanted to recreate the cures seen in the Berlin and London patients but with reduced toxicity."

The team investigated the use of autologous stem cell transplants, where bone marrow stem cells are removed from the patient, engineered using gene editing so that they lack CCR5, and then returned to patients. This technique is being tested in an early clinical trial in people with HIV, but the minimum number of CCR5-edited stem cells required for the long-term remission or cure seen in the Berlin and London patients was unknown.

To determine this, the researchers developed a multi-stage [mathematical model](#) to study the dynamics of residual and transplanted stem cells, HIV [viral load](#) (the amount of virus in the blood) and how these are affected by the timing of ART withdrawal. They based their model on data from 22 monkeys with simian HIV which were treated with a [stem cell transplant](#), with or without CCR5 gene editing. A subset of the animals then had their ART stopped after a year.

The immune cell dynamics and viral load differed between the animals, but a consistent theme was that the viral load after ART withdrawal was higher in transplanted animals than untreated. This suggests that stem cell transplantation might reduce existing immune cell immunity to HIV. The team speculated that this immunity might be recovered if CCR5 is sufficiently disrupted in the transplanted stem cells.

To explore this, they used their model to calculate the conditions required to achieve viral control after ART withdrawal. They found two important conditions: the first was ensuring a dose of at least five times as many transplanted stem cells as there are residual stem cells after the [transplant](#), and the second was allowing the CCR5-edited stem cells to be at least 76-94% of the total transplanted stem cell population.

"Our model predicts that viral control might be possible following autologous, gene-edited stem cell transplants if a sufficient proportion of edited

[stem cells](#) are allowed to repopulate the blood before ART is stopped," concludes senior author Joshua T. Schiffer, Associate Professor at the Vaccine and Infectious Disease Division, Fred Hutchinson Cancer Center. "The results illustrate the capabilities of mathematical models in optimizing strategies for HIV cure."

More information: E Fabian Cardozo-Ojeda et al, Thresholds for post-rebound SHIV control after CCR5 gene-edited autologous hematopoietic cell transplantation, *eLife* (2021). [DOI: 10.7554/eLife.57646](#)

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