# Largest study of 'post-treatment controllers' reveals clues about HIV remission

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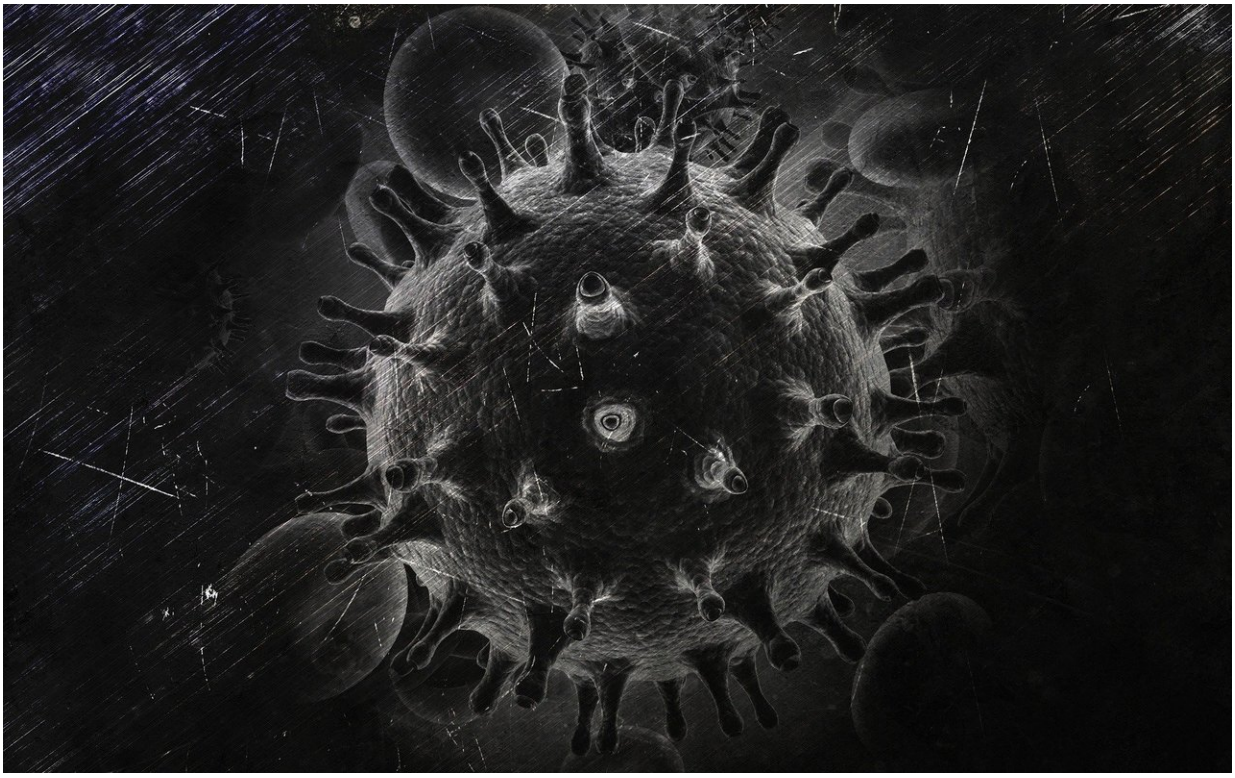

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Most HIV patients need to take daily anti-retroviral therapy—if they suspend treatment, HIV will rebound within 3-4 weeks. But clinical trials have revealed that a small fraction of patients can stop taking medications yet keep the virus suppressed for 24 weeks or longer,

maintaining viral control without the assistance of medication.

Much remains unknown about this unique group of individuals, known as HIV post-treatment controllers, including how rare this ability is. Two new studies—including the largest study of post-treatment controllers to date—explore the characteristics of this group as well as the biological mechanisms that may help explain this unique ability.

"Post-treatment controllers represent a natural model of sustained remission," said Jonathan Li, MD, of Brigham and Women's Hospital's Infectious Disease Clinic and lead author on both studies. "Understanding these individuals can lead to new insights for HIV therapies."

The researchers defined post-treatment controllers as having viral loads of 400 or fewer copies per milliliter of blood plasma for at least 24 weeks' post-treatment interruption. The study characterized 67 post-treatment controllers, the largest cohort to date. They found these post-treatment controllers by sifting through data collected from over 700 participants in 14 clinical studies involving treatment interruption.

The CHAMP (Control of HIV after Antiretroviral Medication Pause) study, published in *The Journal of Infectious Disease*, examined what post-treatment control can tell us about HIV's progression. The researchers observed that individuals treated early were significantly more likely to become post-treatment controllers. Previously published studies have found other benefits for early treatment, notably decreased risk of transmission to partners compared to treatment starting during chronic infection.

A second study published in *The Journal of Clinical Investigation* illuminated the biological mechanisms underlying post-treatment control. Li's team sequenced viral DNA, which the HIV virus had woven into the

patient's DNA.

The team observed that post-treatment controllers had lower levels of intact viral DNA prior to treatment interruption. In other words, post-treatment controllers carried smaller viral reservoirs. Li believes that reservoir size could represent a useful biomarker to help predict which patients will become post-treatment controllers.

In addition to intact viral DNA, Li and his team found that reservoirs of defective viral DNA may offer novel insights for treating HIV. They observed that defective HIV DNA seemed to give rise to proteins that could interact with the immune system. They plan to study this further.

"Each year, there are millions of new HIV infections," said Li. "The results of these studies may help inform the design of strategies and trials aimed at achieving HIV remission, which we hope will bend the curve of this epidemic."

**More information:** Radwa Sharaf et al, HIV-1 proviral landscapes distinguish posttreatment controllers from noncontrollers, *Journal of Clinical Investigation* (2018). DOI: 10.1172/JCI120549

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