

Scientists discover that defective HIV DNA can encode HIV-related proteins

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HIV-1 Virus. Credit: J Roberto Trujillo/Wikipedia

Investigators from the National Institutes of Health have discovered that cells from HIV-infected people whose virus is suppressed with treatment harbor defective HIV DNA that can nevertheless be transcribed into a template for producing HIV-related proteins. This finding may affect scientists' understanding of the long-term effects of HIV infection and what a cure would require.

When HIV infects a cell, it inserts its genetic instructions into the cell's DNA. Effective [treatment](#) with anti-HIV drugs does not eliminate this HIV DNA (called proviral DNA or a provirus), so in theory it could give rise to new viruses during treatment. However, scientists previously have found that 95 percent or more of HIV proviruses are unable to encode intact viruses due to genetic mutations and deletions. As a result, researchers have come to think of these defective HIV proviruses as biological dead-ends.

This thinking may change thanks to the new finding by scientists in the Laboratory of Immunoregulation at the National Institute of Allergy and Infectious Diseases (NIAID), part of NIH.

Hiromi Imamichi, Ph.D., and colleagues used a technique for creating multiple copies of nearly full-length proviral DNA and cell-associated HIV RNA. The scientists showed that HIV RNAs complementary to defective proviruses could be found in cells from two of four people in whom treatment had suppressed the [virus](#) to undetectable levels for more than 8 years. This was evidence that the defective provirus had been transcribed from DNA into an RNA molecule. The researchers then demonstrated that these RNAs could encode novel HIV-related proteins. Thus, while unable to encode a virus, the defective proviral DNA could encode an intact protein.

This finding could help explain the persistent immune activation observed in people living with HIV who have undetectable levels of

virus, say the study authors. The discovery also suggests another potential barrier to an HIV cure. More research is needed, however, to determine the impact of HIV RNA transcripts from defective proviruses, the authors add.

More information: Defective HIV-1 proviruses produce novel protein-coding RNA species in HIV-infected patients on combination antiretroviral therapy, www.pnas.org/cgi/doi/10.1073/pnas.1609057113

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