An aggressive form of HIV uncovered in Cuba

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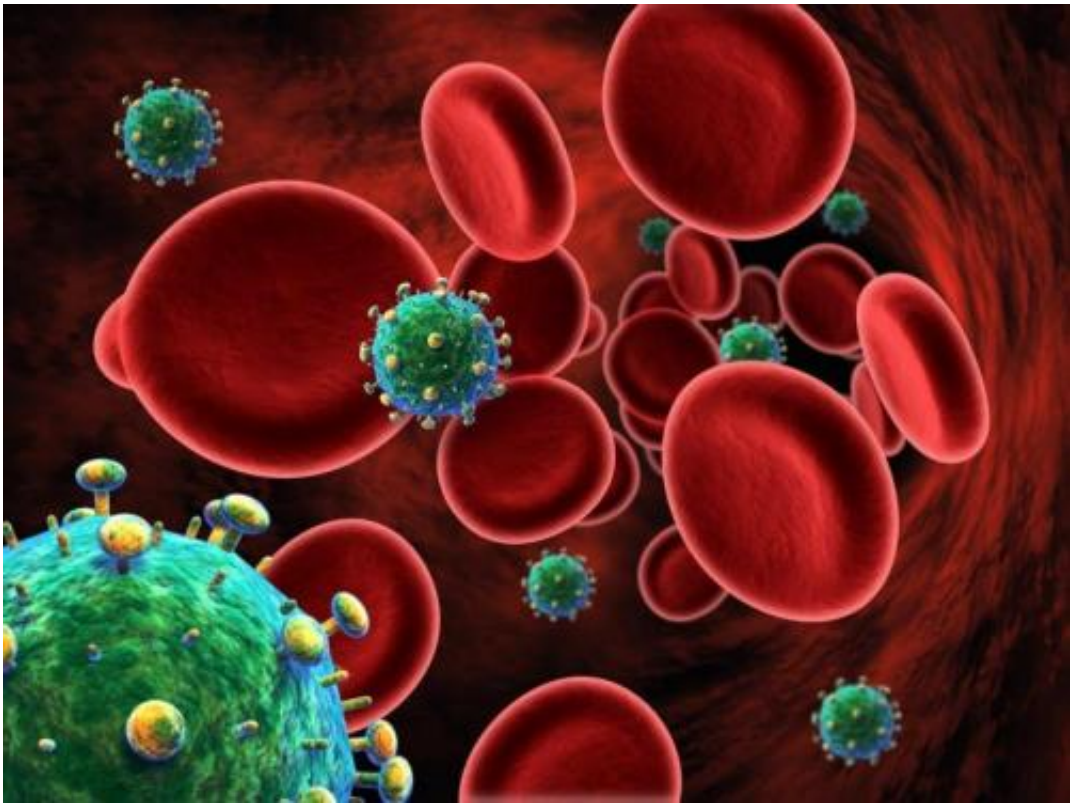

The unexpectedly rapid progression of this HIV variant increases the risk that patients become very ill before ever realising that they are infected.

Engaging in unprotected sex with multiple partners increases the risk of contracting multiple strains of HIV, the virus that causes AIDS. Once inside a host, these strains can recombine into a new variant of the virus. One such recombinant variant observed in patients in Cuba appears to be

much more aggressive than other known forms of HIV. Patients progress to AIDS within three years of infection - so rapidly that they may not even realise they were infected.

Before it can enter human cells, HIV must first anchor itself to them. The virus does this via anchor points, or co-receptors, which are proteins on the cell membrane. In a normal infection, the virus first uses the anchor point CCR5. In many patients, after a number of healthy years, the virus then switches to the anchor point CXCR4. This co-receptor switch coincides with a faster progression to AIDS.

Writing in the journal *EBioMedicine*, researchers at KU Leuven's Laboratory for Clinical and Epidemiological Virology now report a recombinant form of HIV observed in patients in Cuba that makes this transition much faster. The virus targets the anchor point CXCR4 early after infection, shortening drastically the healthy phase and triggering rapid progression to AIDS.

Professor Anne-Mieke Vandamme and an international team of researchers studied the blood of 73 recently-infected patients - 52 at AIDS diagnosis and 21 without AIDS - and compared results with blood from 22 patients who had progressed to AIDS after a normal healthy period with HIV.

In the patients infected with the HIV recombinant, the researchers observed abnormally high doses of the virus and of the defensive molecule RANTES. This molecule is part of our natural immune response and acts through binding to CCR5, to which most forms of HIV have to bind before entering the cell.

The high concentration of RANTES suggests that most of the CCR5 proteins were no longer available as anchor points for HIV. This may have caused the HIV recombinant to bypass that anchor point and go

straight to anchor point CXCR4. The observation that all study patients who were infected with the recombinant HIV variant went on to develop AIDS within three years of infection supports this theory.

The transition from anchor point CCR5 to CXCR4 is normally very difficult. The researchers suspect that the rapid transition observed in this HIV recombinant occurs as a result of combining fragments from different HIV subtypes. One of these fragments contains a protease (from subtype D), which acts very efficiently. Protease is an enzyme that cleaves the proteins that are used in new virus particles. This protease is very 'fit' - it enables the virus to replicate in greater numbers hence facilitating the transition to CXCR4 anchoring.

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More information: *EBioMedicine*, www.sciencedirect.com/science/ … ii/S2352396415000389

Provided by KU Leuven

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