Certain mutations give HIV infection an advantage that sticks

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(Medical Xpress)—Varieties of HIV that replicate more quickly can cause infected individuals' immune systems to decline faster, new research demonstrates. The results were published by the journal *PLOS Pathogens*.

"These results are exciting because they demonstrate a novel early impact of HIV replicative capacity that can define the trajectory of immune decline and disease," says senior author Eric Hunter, PhD, co-director of the Emory Center for AIDS Research and a member of the Emory Vaccine Center. Hunter is a Georgia Research Alliance Eminent Scholar and a professor of pathology and laboratory medicine in Emory School of Medicine.

Generally, when HIV is transmitted from one person to another, only one virus out of a swarm of frequently mutating viruses establishes the new infection. Soon after that, the virus continues to mutate to avoid the new host's immune system.

Hunter and his colleagues wanted to find out: does the replicative capacity of the new virus stick? Or does the struggle to elude the new host's immune system shake things up enough that any early advantage a virus has is lost?

They obtained samples of HIV from 149 newly infected individuals, and isolated the Gag gene, which encodes the main structural proteins, from each one. They examined the effect each Gag variant's mutations had on

the viral capacity to replicate in cell culture.

They found that high replicative capacities correlated with higher viral loads (the amount of virus in the body) as well as faster CD4 T cell count decline over the first three years of infection. Thus individuals infected with poorly replicating viruses progressed to low CD4 T cell counts more than two years after those infected with highly replicating viruses.

"This suggests that the trajectory of pathogenesis may be affected very early in infection, before adaptive immunity can respond," Hunter says. "It raises the possibility that a vaccine that can attenuate early virus replication would have a positive impact on disease progression."

The research team also found previously unknown mutations linked with replicative capacity, which could point to vulnerable targets in the HIV genome.

Access to patient samples came through collaboration with co-investigators and volunteers at Emory's HIV research program in Zambia .

More information: J.L Prince et al. Role of Transmitted Gag CTL Polymorphisms in Defining Replicative Capacity and Early HIV-1 Pathogenesis. *PLoS Pathog* 8(11): e1003041. doi:10.1371/journal.ppat.1003041 (2012). www.plospathogens.org/article/info%3Adoi%2F10.1371%2Fjournal.ppat.1003041

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