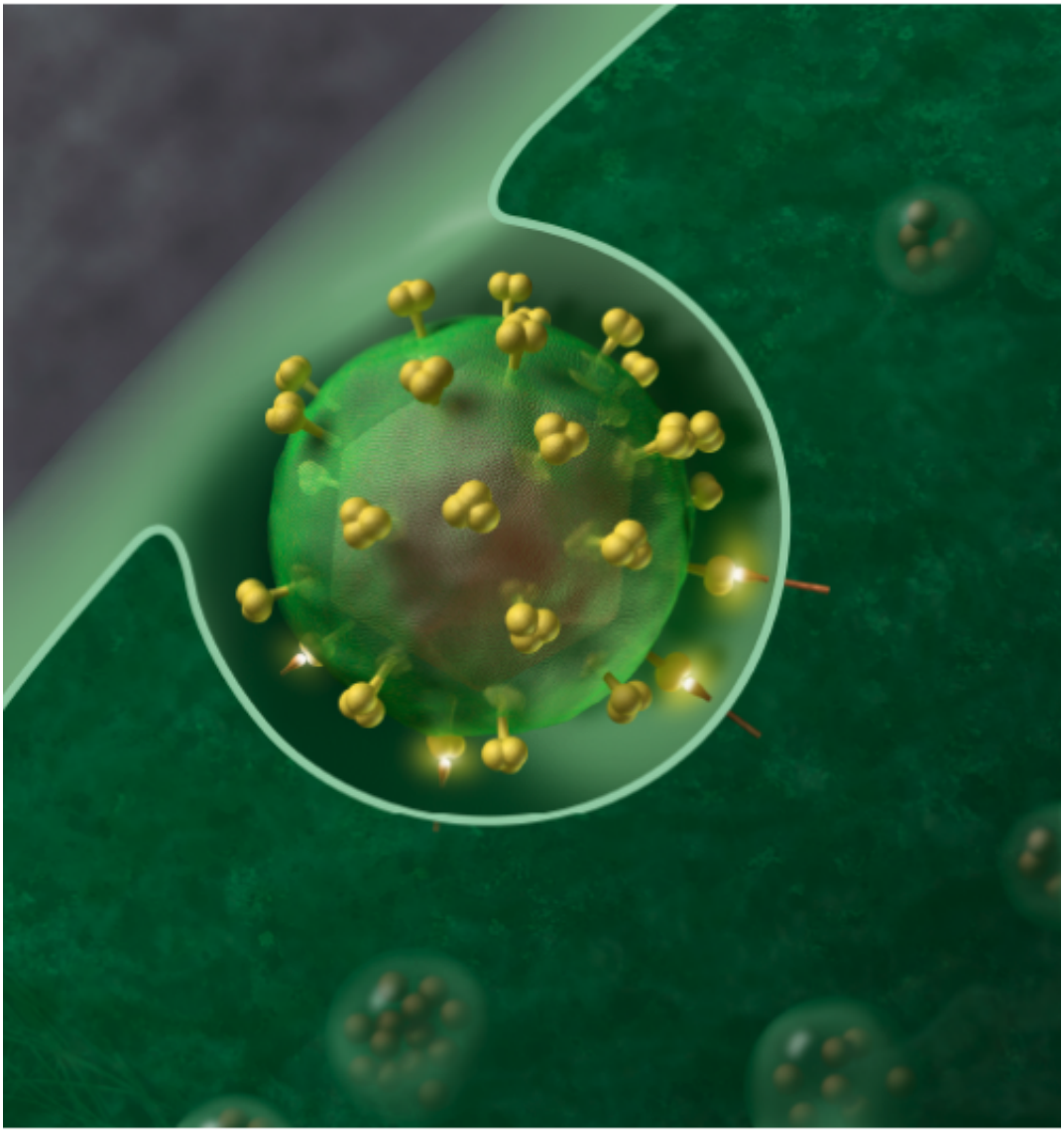
Infection with multiple HIV-1 variants leads to poorer clinical outcomes

August 31 2015



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

HIV-1 infection with multiple founder variants points to poorer clinical outcomes than infection with a single variant, according to a paper published today in the journal *Nature Medicine*.

In the study researchers analyzed large sample sets from two important HIV vaccine efficacy trials—the Step HIV vaccine clinical trial (HVTN 502) and RV144, the landmark vaccine clinical trial conducted in Thailand—to evaluate whether genetic characteristics of the founder viral populations could influence markers of clinical outcomes. Specifically, they examined viral loads and CD4 T-cell counts against measures of HIV-1 diversity. The study group included researchers from the U.S. Military HIV Research Program (MHRP), Fred Hutchinson Cancer Research Center, University of Washington, Armed Forces Research Institute of Medical Sciences (AFRIMS), Thai Ministry of Public Health and Mahidol University.

In both studies, data collected up to one year post HIV-1 diagnosis showed that subjects who had multiple founder viruses had significantly higher mean viral loads.

"Our results brings into sharp focus how the earliest interactions between virus and host have a profound impact on the course of the entire disease," said Morgane Rolland, PhD, of the Military HIV Research Program (MHRP), Walter Reed Army Institute of Research and senior author on the paper.

The researchers used two large data sets of viral sequences to test the association between HIV-1 diversity and markers of disease progression. The analysis included 63 Step study participants (infected with HIV-1 subtype B) and 100 RV144 participants (infected with CRF01_AE) who had viral load and CD4 T-cell measurements in the absence of antiretroviral therapy.

The setpoint for HIV-1 is the viral load of an infected person. It is established after the early HIV-1 infection phase and is generally stable over time. Given previously observed broad differences in viral load setpoint across subjects versus relatively stable viral loads over time, isolating characteristics that affect setpoint could be critical to understanding clinical outcomes.

"When studying the host response early after infection, we are looking at two types of infection. An homogeneous viral population will evolve in a stepwise manner, whereas the presence of two or more viral variants can immediately foster complex viral evolutionary processes," according to Rolland.

These findings point to new opportunities to analyze the effect of preventive interventions, including developing new analysis methods that will take into account viral diversity measures.

"This study emphasizes the value of vaccine efficacy trials for gathering rich datasets—even if a trial fails to show efficacy, the data may be used to investigate important questions regarding HIV pathogenesis which informs next steps for HIV vaccine development," according to Col. Nelson Michael, MHRP Director.

More information: HIV-1 infections with multiple founders are associated with higher viral loads than infections with single founders, *Nature Medicine*, DOI: 10.1038/nm.3932

S. Rerks-Ngarm et al., Vaccination with ALVAC and AIDSVAX to Prevent HIV-1 Infection in Thailand. NEJM DOI: 10.1056/NEJMoa0908492 (2009).

Provided by University of Washington