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Research illuminating long-term non-progression suggests novel vaccination strategy for HIV

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A major problem researchers have faced in attempting to develop a vaccine for HIV is that the virus mutates incredibly quickly, which means that its antigens—the target molecules of a vaccine—are moving targets. A comparison of individuals who are able to control HIV without antiretroviral medication with those who are unable to do so suggests that a novel approach to vaccination might work around this problem. The research is published in the July Journal of Virology.

Human DNA contains so-called human endogenous retroviruses (HERVs), which are remnants of ancient retroviruses—genetic fossils—that under normal circumstances sit silently, and always genetically stably, within human DNA. In earlier work, a team of researchers led by Douglas Nixon of the University of California, San Francisco, showed that infection with HIV activates HERVs that lie inside HIV-infected cells in some individuals (but not those in non-infected cells), by interfering with regulatory compounds that normally prevent expression of these HERVs. The activated HERVs produce proteins that attract immune system T cells to the HIV-infected cells, targeting them for destruction. The researchers also showed that the greater T cell response, the lower an individual's viral load.

In the new research, Devi SenGupta of the University of California, San Francisco et al. extended these findings to include individuals who have long-term chronic HIV-1 infection. They compared the responses of a

tiny subset of individuals who are unique in their ability to suppress the virus indefinitely without the aid of combination therapy to those of patients on highly active antiretroviral therapy (HAART), virologic noncontrollers, immunologic progressors, and uninfected controls. A strong anti-HERV response corresponded to a lower viral load, and a higher CD4+ T cell count. “Interestingly, controllers who lack HLA alleles [critical immune system components] that are associated with protection from HIV-1 disease progression… constituted a large proportion of the subjects with the strongest HERV responses, suggesting that there may be an alternative mechanism of HIV control (such as HERV-specific cytotoxic T cells) in these controllers,” the researchers write.

The findings suggest that a vaccination targeting proteins produced by the HERV genes could help the immune system keep HIV in check, says SenGupta. “Our research helps lay the groundwork for developing a new therapeutic or preventive vaccine against HIV. If this leads to a new anti-HIV therapy, millions of lives could be improved all over the world.”

More information: D. SenGupta, R. Tandon, R.G.S. Vieira et al. Strong human endogenous retrovirus-specific T cell responses are associated with control of HIV-1 in chronic infection. *J. Virol.* 85:6977-5985

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