LETTER

Evidence for HIV weakening over time

Payne et al. (1) present evidence that HIV may be evolving into a less virulent form over time. Central to this evidence is a documented difference in the results from an in vitro assay measuring HIV replication capacity in the two populations studied (in Botswana and South Africa). Because there are significant cross-sectional correlations between the results of this assay and viral load and CD4 counts, Payne et al. (1) suggest that the significantly lower HIV replication capacity documented in study participants in Botswana can be equated to slower disease progression from HIV infection to AIDS and death.

However, prior research by many of the same authors specifically assessed whether results from the HIV replication capacity assay can predict the pace of disease progression in cohorts of HIV-positive individuals followed longitudinally. In the first study that addressed the question, no correlation was observed between results of the HIV replication capacity assay and CD4 T-cell decline over time in a cohort of 339 individuals with chronic HIV infection (Spearman's rank correlation; $r = -0.01$ and $P = 0.79$) (2). In a subsequent, smaller study involving individuals with recent HIV infection, there was no correlation between HIV replication capacity and viral load setpoint (Pearson's correlation, $r = 0.12$ and $P = 0.37$) and only a trend for an association with CD4 T-cell decline in 45 individuals with baseline CD4 T-cell counts over 300 (Spearman's correlation, $r = -0.25$ and $P = 0.09$) (3).

These prior results appear difficult to reconcile with the suggestion in the PNAS paper that the lower HIV replication capacity documented in the population in Botswana can be straightforwardly equated to slower disease progression. To better assess whether HIV is evolving into a weaker form, it would be helpful to have additional longitudinal data on disease progression rates to corroborate the inferences drawn from the HIV replication capacity assay results.

Richard J. Jefferys[1]
Basic Science, Vaccines & Cure Project, Treatment Action Group, New York, NY 10016

1 Payne R, et al. (2014) Impact of HLA-driven HIV adaptation on virulence in populations of high HIV seroprevalence. *Proc Natl Acad Sci USA* 111(50):E5393–E5400.
2 Wright JK, et al. (2010) Gag-protease-mediated replication capacity in HIV-1 subtype C chronic infection: Associations with HLA type and clinical parameters. *J Virol* 84(20): 10820–10831.
3 Wright JK, et al. (2011) Influence of Gag-protease-mediated replication capacity on disease progression in individuals recently infected with HIV-1 subtype C. *J Virol* 85(8):3996–4006.

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[1]Email: richard.jefferys@treatmentactiongroup.org.

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