Deletions in variable region 1 of the HIV envelope accelerate V3-glycan bNAb induction in SHIV-infected rhesus macaques.

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Eliciting broadly neutralizing antibodies (bNAbs) is a major goal of HIV-1 vaccine research. V3-glycan bNAbs were previously identified in human participant CH848, and two of six rhesus macaques (RMs) infected with a simian-human immunodeficiency virus (SHIV) expressing the CH848 transmitted/founder envelope (Env) glycoprotein. In all cases, neutralization breadth developed after years of infection and only after the variable region 1 (V1) of Env had shortened in response to neutralizing antibodies. These observations suggested that V3-glycan bNAb elicitation might be accelerated if RMs were infected with SHIVs bearing CH848 Envs with truncated V1 loops. To test this hypothesis, we analyzed antibody responses in 10 RMs infected with SHIV.CH848 variants containing V1 deletions that mimicked those observed in natural infection. In three RMs, potent V3-glycan bNAbs developed within one year of infection, nearly three times faster than in wildtype CH848 infection. Longitudinal sequencing of B cell immunoglobulin genes revealed a single bNAb lineage in each RM that was primed as early as 8–12 weeks post-infection and that largely recapitulated plasma breadth. We conclude that truncations in the V1 loops of CH848 Envs accelerate precursor priming, findings that may guide HIV-1 vaccine design and support with the HVTN307 clinical trial in humans.