Production of the first generation of mucosally transmissible SHIV challenge stocks from HIV-1 clade AE env sequences


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Abstract:

The generation and evaluation of simian immunodeficiency virus/human immunodeficiency virus (SHIV) challenge stocks are important for preclinical testing of vaccines, antibodies, and other interventions aimed to prevent HIV-1. We sought to develop and produce the first generation of mucosally transmissible SHIV challenge stocks from HIV-1 clade AE env sequences. The sequences were identified from acutely infected HIV-1 individuals from Thailand. SHIV-AE6, SHIV-AE6RM, and SHIV-AE16 sequences were 99.2 to 100% identical to the original HIV-1 isolate and did not require in vivo passaging. These viruses exhibited CCR5 tropism and displayed resistance to tier 2 neutralizing antibodies. These challenge stocks efficiently infected rhesus monkeys by the intrarectal route (i.r.), replicated to high levels during acute infection, and established chronic setpoint viremia in 21/24 (88%) animals. SHIV-AE16 was also titrated for use in single, high dose and repetitive, low dose i.r. challenge studies which resulted in viremia
21/24 (88%) animals. The SHIV challenge stocks should facilitate the evaluation of vaccines and other interventions targeted at controlling the spread of clade AE HIV-1.