A SIV molecular clone that induces neuroAIDS in infected rhesus macaques.


The development and application of Highly Active Anti-Retroviral Therapy (HAART) for use by human immunodeficiency virus 1 (HIV-1) infected individuals has led to a dramatic decrease in incidence of HIV-1 associated dementia or HIV encephalitis (HAD). Despite effective suppression of systemic viral replication by HAART, there have been an increased number of patients with HIV-1-associated neurocognitive disorder (HAND). To elucidate the mechanisms of HAD/HAND, our group has been developing a non-human primate model of neuroAIDS. We have recently reported on the isolation of SIVsm804E, that induces neuroAIDS in infected rhesus macaques with high frequency (Matsuda et al., 2014). In this present study, we have isolated and characterized a molecular clone from SIVsm804E, SIVsm804E-CL757. CL757 replicated in peripheral blood mononuclear cells (PBMCs), and in monocyte derived macrophages (MDMs) at comparable levels with the original swarm virus. To assess in vivo replication capacity, two animals were co-inoculated with SIVsmE543-3 and CL757, and another eight rhesus macaques were inoculated with CL757 alone. Preliminary data suggests CL757 robustly replicated in the central nervous system (CNS) of infected animals, suggested by high cerebrospinal fluid (CSF) viral RNA loads. The two co-inoculated animals developed encephalitis at 90 and 95 weeks post infection. In addition, Rh880, inoculated with CL757 alone, developed severe encephalitis at week 58, indicating that inoculation of CL757 alone was sufficient to induce neurological pathologies. The disease progression in CL757 infected animals was conventional, which recapitulates HAD better than the original SIVsm804E swarm infected animals since there were no rapid progressors. Thus, SIVsm804E-CL757 has the potential to be a novel nonhuman primate model for neuroAIDS to assess disease progression in the CNS during the chronic phase of infection.