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Viral reservoirs and activation in animal models: SHIV-Infected macaques

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Abstract

NHP models of retroviral latency and reactivation will be of great utility for defining protocols to eradicate HIV and understanding *in vivo* mechanisms of virus activation. We are performing a systematic and comprehensive assessment in macaques with undetectable plasma virus load to define the reservoirs and activation of latently infected cells. We found 10-1000 provirus/10^6 PBMC, which remained stable in each animal, but varied among animals. Levels in most lymphoid organs were similar, but in many animals there were single compartments with 10-100X higher levels, and this site varied from animal to animal. Provirus levels in the gut were consistent with other lymphoid organs, regardless of route of infection. Provirus was also found in brain, epididymis, and other non-lymphoid organs, but generally at lower levels. The tissue distribution of provirus was remarkably similar to that reported for latency induced by ART in macaques. Latent virus was activated by CD8 depletion, resulting in a high-titered plasma viremia. We also detected 11-1790 transcripts per provirus during the activation phase. ART treatment prevented the development of plasma viremia. We have also observed lesser degrees of provirus activation with vorinostat and IL-7, and in some animals IL-2. A persistent viral replication was observed in the colon, even before activation of latent reservoir. These studies demonstrate that aviremic SHIV-infected macaques have a functional reservoir of latently infected cells. The mechanism whereby SHIV is driven into latency is not understood, but is surely different than ART-induced latency in humans. Nevertheless, the anatomic localization of provirus and kinetics of activation are very similar to that observed in other macaque models.

Biography

Dr. Hye Kyung Chung received her Ph.D from Kun-kuk University and she studied the pathogenesis and molecular mechanism of retroviruses as a postdoctoral fellow at the National Institutes of Health. She has spent the majority of her research career studying molecular virology, recently pathogenesis of human and animal lentiviruses. She studies NHP models of retroviral latency and reactivation collaborating with Dr. Pincus. Dr. Chung continues to develop cutting-edge new assays to study viral reservoirs.