Retrovirology

Poster presentation

Higher Virus Replication and Rapid Disease Progression Correlate Inversely With SIV tat exon 1 Evolution in Morphine-addicted SIV/SHIV-infected Macaques

Richard J Noel Jr*‡ and Anil Kumar

Address: IDS Research Program, Ponce School of Medicine, Ponce, PR

Email: Richard J Noel* - rnoel@psm.edu

* Corresponding author ‡Presenting author

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We analyzed the association between evolution of the 5' exon of *tat* and disease progression in a SIV/SHIV macaque model of opiate-dependence and AIDS. We cloned *tat* sequences using RT-PCR of plasma virus from eight animals at three time points following infection. Six of these monkeys were part of a morphine-dependent cohort, while two served as non-drug using controls. We found a significant inverse correlation between disease progression and *tat* diversity in plasma by 20 weeks. The morphine cohort segregated into two classifications based on progression: a rapidly progressing group (Group A) and a second set (Group B) that progressed at a rate similar to the two non-morphine controls (Group C). The three animals in Group A exhibited -40% ($p = 0.01$) and -50% ($p = 0.028$) less diversity than Group B and C animals, respectively. Group A animals showed prominent re-emergence of the wild-type inoculum *tat* sequence as illness progressed. This suggests that the virus from the original infection represented the most pathogenic form in these cohorts throughout the first 20 weeks of infection. Our results indicate that *in vivo* morphine dependence can contribute to the pathogenesis of SIV/SHIV infection and that it may do so in conjunction with the evolution of viral proteins, such as Tat. It is unclear if this is a direct effect of morphine on the virus replication/evolution or if it is mediated indirectly through modulation of the immune response, or through the enhanced vulnerability of a protected compartment such as the CNS.