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SIV/HIV latency in the CNS: role of innate immune responses

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In order to model the molecular events that lead to HIV infection and pathogenesis in the brain, we developed an accelerated, consistent simian model of HIV infection in which pigtailed macaques are inoculated with a neurovirulent SIV clone and an immunosuppressive SIV strain. Infected animals invariably develop AIDS and over 90% develop central nervous system disease with lesions typical of HIV encephalitis as well as peripheral nervous system disease with neurodegeneration by 3 months postinoculation. This model has allowed us to identify early events in the brain that lead to the downregulation of SIV replication and the establishment of latency in macrophages. We have demonstrated that SIV infection is established in the brain during acute infection and this is accompanied by increased levels of inflammatory cytokines/chemokines and increased expression of macrophages inflammatory markers. Further, our studies have delineated the effects of IFNβ in suppressing early virus replication, suppressing virus transcription and inducing viral latency as well as downregulation of early inflammation. We have identified a novel pathway of IFNβ signaling that affects viral gene expression as well as expression of cellular genes involved in inflammation. The molecular mechanisms involved in these processes will be discussed.

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