HIV Encephalitis (HIVE) Mouse Model

Early attempts to reflect HIV disease of the CNS were re-evaluated following the introduction of combination antiretroviral therapeutics (cART). Historically, encephalitis fueled by active viral replication in mononuclear phagocytes (MPs) reflected the histopathological correlate of disease in the pre-cART era. In the cART era persistence of HIV-1 in the CNS is seen nearly exclusively in macrophages. To study HIV persistence and disease pathology in the CNS, a mouse model was developed wherein HIV-1 infected human monocyte derived macrophages (MDMs) were injected into the basal ganglia of immunodeficient mice. This gave rise to the name HIV encephalitic (HIVE) mice. The histopathological changes observed in the murine brains parallel those in human HIVE. This includes HIV-1 infected human macrophages, the formation of multinucleated giant cells, astrocytosis, microglial activation and neuronal cell death. The model has been used to examine neuronal function in HIVE using a range of behavioral and electrophysiological tests. Mice injected with MDMs develop cognitive impairments and associated deficits in synaptic long-term potentiation. HIV-1 viral strain-specific differences in inducing neuropathogenesis have also been assessed. Importantly, this mouse model has been used extensively for evaluating new drugs and delivery systems for HIVE. Since macrophage-induced inflammation affects hippocampal plasticity and neuronal development in HIVE mice, these mice have been used to develop adjunctive therapies that can reduce microglial activation resulting in neuroprotection.

Reference:

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