HHV-6 causes Inflammatory demyelination in non-human primates

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Objectives: To create laboratory systems for investigation of causal links between HHV-6 and multiple sclerosis (MS).

Methods: Common marmosets are susceptible to central nervous system (CNS) diseases and viral infections. We showed that PBMC of this species are susceptible to HHV-6 infection. Naïve animals (n=10) were infected with either HHV-6A or HHV-6B and monitored for up to a year. We investigated viral persistence by nested PCR and a direct PCR method capable of differentiating variants A and B, in blood, cerebrospinal fluid, and brain and spinal cord at autopsy. For in vitro studies, human glial and neuronal cell lines were exposed to HHV-6 and signs of toxicity were monitored.

Results: Only animals exposed to HHV-6A developed significant neurological deficits with inflammation located sub-pial space, and demyelination in brain parenchyma. Two HHV-6A infected animals were observed chronically and developed a relapsing remitting course of symptoms resembling MS attacks. Serial immunological studies showed delayed appearance of immunity against myelin proteins. HHV-6A could be detected in blood at distance from infection, and in CNS at autopsy in 2 animals. Apoptosis induced by exposure to the virus was observed in CNS tissue (Tunel), and in glial and neuronal cell lines (staining with Hoechst and annexin V).

Conclusion: 1. Exposure to HHV-6A in marmosets is capable of inducing a typical MS-like disease, without primary sensitization against any CNS components. 2. Entry and persistence of HHV-6A and direct toxicity to CNS resident cells is suggested as a causal mechanism.