



Retroviruses and Amyotrophic Lateral Sclerosis

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A small set of HIV-infected patients have been reported with an Amyotrophic Lateral Sclerosis (ALS)-like syndrome that show reversal with antiretroviral drugs. However, ALS is a devastating neurodegenerative disease for which there is not treatment available. Genetic mutations have been identified in nearly 20% patients but the remaining are sporadic cases. Several studies have shown that retroviral activity can be detected in the brain and blood of these patients however an extensive search for exogenous retroviruses has been unrevealing. We reasoned that this may suggest activation of endogenous retroviral elements. RNA sequence analysis for human endogenous retroviruses (HERV) of brain tissue from patients with ALS suggested that exclusively HERV-K

was expressed. This was confirmed by quantitative polymerase chain reaction for the pol, gag and env genes. Immunostaining with an antibody to the env protein showed that HERV-K was expressed in cortical neurons and anterior horn cells of the spinal cord in patients with ALS but not in controls. In vitro and in vivo studies showed that expression of HERV-K was toxic to neurons. A panel of antiretroviral drugs were screened for their effects on HERV-K replication. Dose response curves were established and compared against their effects on HIV replication.