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14-3-3 Protein in the CNS of SIV-Infected Macaques

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Abstract:

The presence of 14-3-3 protein in cerebrospinal fluid (CSF) has been reported to be a marker of neuronal damage in several central nervous system (CNS) diseases including Creutzfeldt Jakob disease (CJD) and multiple sclerosis (MS). Our studies using the simian immunodeficiency virus (SIV)/macaque model of human immunodeficiency virus (HIV) CNS disease have demonstrated that 14-3-3 protein is present in the CSF of a subset of SIV-infected macaques during asymptomatic infection where it persists until terminal disease in animals that develop high CSF and CNS viral burdens, thus serving as an early predictive marker of the level of CNS viral replication. Furthermore, the zeta isoform of 14-3-3 appears to be predominate in CSF as a marker of neuronal damage induced by SIV. In addition to serving as a CSF marker of neuronal damage, 14-3-3 proteins likely play key regulatory roles in neurodegenerative diseases by modulating neuronal and/or glial apoptosis. For example, by binding to phosphorylated Bcl-2-associated death protein (BAD), 14-3-3 protein can sequester BAD thus preventing BAD-triggered pro-apoptotic pathways. To test the hypothesis that 14-3-3 protein serves this neuroprotective role in the SIV model, 14-3-3-BAD interactions were evaluated by co-immunoprecipitating 14-3-3 and BAD from brain homogenates. The results suggest that 14-3-3 and BAD are dissociated in animals with SIV encephalitis, thereby promoting apoptosis.