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SOMPONE THEERASURAKARN: INDUCTION OF APOPTOSIS IN SUCKLING MOUSE NEURAL CELLS DURING FIXED STRAIN OF RABIES VIRUS INFECTION. THESIS ADVISORS: SUKAATHIDA UBOL, Ph.D., MOLVIBHA VONGSAKUL, Ph.D., WITAYA THAMAVIT, Ph.D. 115 p. ISBN 974-662-933-6

Viruses such as HIV, influenza, picornavirus, and others are known as stimulators of apoptosis. This individual cellular elimination is a preferential host defense in regenerative tissues. In contrast, if this death occurrs in nonregenerating cells, such as neurons of the central nervous system, the result may be disease.

The pathogenesis of rabies is still unknown. Many reports indicate that there are no necrosis and neuronophagia in rabies virus infected brain. This result suggests that the viral replication does not destroy neurons directly but damage may be caused by the host immune mechanisms. The target cells for rabies virus are the neural tissues. Here, we studied the outcome of the interaction between rabies virus (CVS-11) and mouse brain cells. Replication of rabies virus in suckling mouse brain cells resulted in brain cell apoptosis, detected by DNA fragmentation and *in situ* apoptosis within 25 hours after infection and before evidence of intracerebral immune activation. There were several clinical signs of illness in infected newborn mice within 25 hours after the appearance of DNA fragmentation and before infiltration of lymphocytes, which suggested that onset of illness started independently of the immune function. This conclusion was supported by the occurrence of massive apoptosis followed by paralysis in rabies virus-infected immunosuppressed mice.

Direct, viral-induced, neuronal apoptosis was the earliest death mechanism detected in these mice. We propose that the pathogenesis of this fixed strain of rabies virus in mice begins with the induction of apoptosis by rabies virus replication. Cerebral damage may then be amplified by immunological mechanisms plus an additional unidentified factor.

The caspase family of protease, such as ICE and Nedd-2, plays a role in activation of apoptotic death of neuronal cells infected with rabies virus. Both ICE and Nedd-2 gene were activated after the cells were infected with rabies virus. However Bcl-2 gene which plays a significant role in apoptosis in other cell systems was not changed during the course of infection.