

Abstract



Control of Alphavirus Replication in Neurons +

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Abstract: Sindbis virus causes age-dependent encephalomyelitis in mice. Young mice and immature neurons replicate the virus to high titers and die from infection while older mice and mature neurons restrict replication and survive infection. Studies to identify factors that affect maturation-dependent virus replication in neurons have used AP-7 rat olfactory neuronal cells that can be differentiated in vitro, and have identified roles for host transcription factors interferon regulatory protein (IRF) 7 and NF-κB and viral proteins E2 and nsP3. IRF7 is required for neuronal survival and deficiency leads to paralysis and death of 4–6 weeks old C57BL/6 mice. Activation of NF-κB works in conjunction with PKR to facilitate replication in mature neurons by promoting shut-off of host protein synthesis and increasing translation of the viral structural proteins from ADP-ribosylated proteins and is important for initiation of neuronal infection and for synthesis of viral structural proteins. Thus, neurons regulate translation of the structural proteins from subgenomic RNA required for the production of the infectious virus.

Keywords: Sindbis virus; NF-kB; IRF7; encephalomyelitis; mice; nonstructural protein 3



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