Evaluation of Rift Valley Fever Virus Neurotropism

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Rift Valley fever virus (RVFV) is one of the most important viral zoonotic agents affecting humans and economically valuable livestock species on the African continent. Recent outbreaks in South Africa have infected hundreds of humans. The possible spread of RVFV to areas outside Africa and the Arabian Peninsula is of great concern. The life threatening clinical manifestations of RVFV in humans consist of hepatitis, hemorrhagic fever, and encephalitis. While pathogenesis studies have revealed that RVFV exhibits a broad cellular tropism in vivo and in vitro the exact cellular and molecular mechanisms mediating RVFV entry into the brain are not understood. We have established that human primary glial cells inoculated with RVFV were highly susceptible to infection. In addition the cytokine profile of RVFV infected astrocytes revealed a restricted ability of inoculated cells to secrete proinflammatory cytokines, as observed by the more intense production of cytokines when glial cells were inoculated with NSs mutant RVFV. Human neuronal cells were also permissive to infection with RVFV. Both neuronal and glial cells displayed prominent cytopathic effects as a result of pathogenic strain and live attenuated MP-12 strain infection. The presented findings suggest primary human glial cells provide a useful scientific model for the study of cellular and molecular mechanisms of RVFV neuroinvasion and neuropathogenesis.