Analysis of activation of the NF-κB pathway by SHFV infection

Aisabor, A., Vatter, H., Di, H. and Brinton, M.A.

Simian Hemorrhagic Fever Virus (SHFV) is a positive strand RNA virus that is classified as a member of the family Arteriviridae. SHFV causes asymptomatic infections in African non-human primates such as baboons, which are natural hosts for this virus, but causes hemorrhagic fever and high mortality rates in non-natural hosts, such as Asian macaques. Macrophages and dendritic cells from macaques, but not baboons produce proinflammatory cytokines after infection with SHFV. In this study, we analyzed whether SHFV infection of disease resistant baboon and disease susceptible macaque macrophages and dendritic cells activates the NF-κB signaling pathway. The NF-κB complex is located within the cytosol and remains inactive through its association with the protein IκBα. When the NF-κB pathway is induced, IκBα becomes phosphorylated and ubiquitinated, and dissociates from the NF-κB complex. IκBα is degraded by the proteasome and the p65/p50 complex translocates into the nucleus and acts as a transcription factor on the promoters of proinflammatory cytokine genes. Western blotting was used to analyze the activation of the NF-κB pathway by detecting the levels of the individual proteins that are a part of the complex. TNF-α was used as a control activator of the NF-κB pathway. Macrophages and dendritic cells from different baboons and macaques were cultured and infected with SHFV. The cell lysates were harvested at various times after infection and then analyzed. MA-104 cells treated with TNF-α or infected with SHFV were analyzed for the activation of the NF-κB pathway.