

Curcumin inhibits rift valley fever virus replication in human cells

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Rift Valley fever virus (RVFV) is an arbovirus that is classified as a select agent, an emerging infectious virus and an agricultural pathogen. Understanding RVFV-host interactions is imperative to the design of novel therapeutics. Here, we report that an infection by the MP-12 strain of RVFV induces phosphorylation of the p65 component of the NF κ B cascade. We demonstrate that phosphorylation of p65 (serine 536) involves phosphorylation of I κ B α and occurs through the classical NF κ B cascade. A unique low molecular weight complex of the IKK- β subunit can be observed in MP-12 infected cells that we have labeled as IKK- β 2. The IKK- β 2 complex retains kinase activity and phosphorylates an I κ B α substrate. Inhibition of the IKK complex using inhibitors impairs viral replication thus alluding to the requirement of an active IKK complex to the viral life cycle. Curcumin, a well-documented NF κ B inhibitor, strongly down regulates levels of extracellular infectious virus. Our data demonstrate that curcumin binds to and inhibits the kinase activity of the IKK- β 2 complex in infected cells. Curcumin partially exerts its inhibitory influence on RVFV replication by interfering with IKK- β 2 mediated phosphorylation of the viral protein NSs and by altering cell cycle of treated cells. Curcumin also demonstrates efficacy against ZH501, the fully virulent version of RVFV.

Curcumin treatment down regulates viral replication in the liver of infected animals. Our data point to the possibility that RVFV infection may result in the generation of novel versions of host components (such as IKK- β 2) that by virtue of altered protein interaction and function, qualify as unique therapeutic targets.

Biography

Dr. Aarthi Narayanan received her Ph.D. in Genetics and Biochemistry from The University of Georgia at Athens. She did her post-doctoral research at the NIH where the focus of her research was on host-virus interactions. In 2007 she took up the position of Research Assistant Professor in the National Center for Biodefense and Infectious Diseases. Dr. Narayanan's research focus is to understand the interactions between the human host and viruses belonging to diverse families including Bunyaviruses, Alphaviruses, and HIV.

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