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Analysis of phospho-signaling events in human cells following infection by Rift valley fever virus

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Rift Valley Fever (RVF) is a zoonotic disease caused by Rift Valley fever virus (RVFV). RVF is a disease that primarily affects livestock and can spread to humans by mosquito bites. RVFV is an emerging infectious pathogen and a Category A select agent. Although Ribavarin is used to treat RVF, there are associated side effects, emphasizing the need for novel therapeutics. One of the recurrent themes in recent studies of many infectious diseases is the therapeutic targeting of host signaling responses by specific inhibitors. While traditionally antiviral drugs are directed against the proteins and functional pathways of the virus itself, the major caveat to virus-based antivirals is that drug resistance almost invariably ensues. However, as cellular pathways are important components for viruses to successfully multiply, it is of great benefit to develop antivirals based on host responses.

In our preliminary studies using high throughput Reverse Phase protein MicroArrays (RPMA), we have identified specific phosphorylation events that are associated with infection by ZH501 and MP12 strains of RVFV. Some examples of strongly phosphorylated molecules include p38, JNK, NFkB and p53. Based on critical signaling cues obtained from these studies, we have screened multiple host-signaling based inhibitors. Of the inhibitors studied, MEK inhibitors appear to be successful in lowering viral replication in cultured cells. Collectively, our data demonstrates that RPMA is a powerful, high throughput approach to study host-based signaling events following viral infection and provides an excellent starting platform for identification of novel inhibitors.

Biography

Dr. Narayanan received her Ph.D. from the University of Georgia at Athens in Genetics and Biochemistry. She continued her post-doctoral research in virology at the NIH (NIAID) for five years where her research was focused on transcriptional regulation of herpesviruses. She is currently a research assistant professor at George Mason University's National Center for Biodefense and Infectious Diseases. Her current research is geared towards understanding the interactions of alphaviruses, bunyaviruses and retroviruses with their host cells. Her research also includes development of novel host-based therapeutics for emerging infectious viruses.