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Flavivirus vaccine: Molecular basis for attenuation of live attenuated Japanese encephalitis virus vaccine SA14-14-2

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Diseases caused by flaviviruses including Zika, dengue, Japanese encephalitis, West Nile encephalitis and yellow fever have become increasingly frequent over the last couple of decades, aided by global warming and expanding geographies of the mosquito vector. The extremely safe and efficacious WHO-certified live attenuated vaccine for Japanese encephalitis virus (JEV) SA-$_{14}$-14-2 is used worldwide. We observed impressive enhancement in human CD8$^+$ T cell responses in vaccines relative to volunteers naturally exposed to circulating strains of JEV. Using cell lines that support JEV infection, we queried the molecular basis underlying the generation of enhanced CD8$^+$ T cells by the live vaccine SA-$_{14}$-14-2. Our studies revealed that the vaccine virus induced severe ER stress, viral protein was rapidly degraded in vaccine virus-infected cells and was differentially recognized by a panel of monoclonal antibodies. Sustained activation of the ER stress sensor PERK in vaccine virus-infected cells led to prolonged phosphorylation of eIF2α, activation of autophagy markers and upregulation of ER chaperones in SA-$_{14}$-14-2-infected cells. Interestingly, we also observed active dephosphorylation of eIF2α and inhibition of end stage autophagy in WT JEV infected cells. The mutated viral proteins responsible for these effects are being investigated. Our results can guide the rational design of efficacious vaccines against both flaviviruses such as Zika virus, dengue virus and West Nile virus and other pathogenic viruses belonging to other families.

Biography

Vijaya Satchidanandam has completed her PhD at Indian Institute of Science and Postdoctoral studies at National Institutes of Health, USA. She is a Professor in India's leading research institution located in Bangalore. Her laboratory investigates the "Molecular biology and immunology of flaviviral infections and *mycobacterium* tuberculosis". She has published 46 papers in reputed journals.

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