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## Modulation of interferon pathway by Chloroquine, Tunicamycin, and environmental pollutants: Correlation with the worsening of virus infection

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**P**reviously we have shown that treatment with chemotherapeutic agents such as chloroquine (CHL) or tunicamycin (TM) or exposure to environmental pollutants e.g., cadmium (Cd), manganese (Mn) or lead (Pb) and co-infection with malaria can cause increased pathogenesis and mortality associated with several viruses including Semliki Forest Virus (SFV), Venezuelan equine encephalitis virus (VEEV) and encephalomyocarditis virus (EMCV) in mice.In the present study, we have investigated the mechanism of enhanced pathogenesis by these agents. A global gene expression analysis of brains from mice infected with VEEV and treated with TM, revealed increased and early modulation of genes involved in VEEV pathogenesis such as interferon (IFN) signaling and antigen presentation pathway. Quantitative RT-PCR identified down-regulation of IFNA receptor-1 (IFNAR1) transcript levels. MicroRNAs predicted to down-regulate the IFNAR1 expression were also found to be significantly up-regulated in these mice. Similarly, down-regulation of IFNAR1 expression was also observed in SFV infected mice treated with Cd or VEEV infected mice treated with CHL.

Though the precise mechanism(s) underlying the potentiating effects of these agents on viral infections is not fully understood, results from our study revealed an impairment of the IFN pathway. These results are particularly important since the use of CHL as an antiviral agent has recently been advocated in humans based on in-vitro studies. Our findings are thus, of particular importance from a public health perspective, suggesting that indiscriminate exposure/use of agents like antimalarials can predispose the population to increased morbidity from viral infections. Therefore, in depth studies are warranted before recommending the use of CHL against important virus infections in humans especially in HIV and malaria endemic areas.

The opinions expressed herewith are those of the authors and do not reflect those of USUHS, BITS or FDA.

## Biography

Radha K Maheshwari received his PhD from Kanpur University, Kanpur, India in the field of Virology. He performed his post-doctoral research at National Institute of Arthritis, Metabolism and Digestive Diseases, NIH from 1977-1980. Currently, he is a Professor in the Pathology department at Uniformed Services University of The Health Sciences, Bethesda. He has been appointed as an adjunct faculty member at Birla Institute of Technology and Sciences, India to coordinate the research activity of exchange graduate students with the preceptor USUHS faculty. He has also served as an adjunct faculty member at Georgetown University, Washington, D.C. from 1977 to 1982. Over the past 30 years, he has established highly successful and productive national and international collaborations and published more than 125 scientific papers in highly reputed journals. Areas of research in his laboratory include: studying the molecular mechanisms of viral pathogenesis and neuro-degeneration by alphaviruses, development of vaccine candidates against alphavirus infections, prevention of ischemia/reperfusion and hemorrhage induced injuries, enhancement of wound healing and cancer chemoprevention by phytochemicals, identification of biomarkers against TBI and PTSD.

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