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Humanized mouse model to study viral infections and evaluate antivirals

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HSV-2 infections cause genital ulcer disease and their by increasing the risk of HIV-1 acquisition approximately three-fold in human. Efforts to prevent recurrent genital ulcer disease with acyclovir failed to reduce HIV-1 acquisition or transmission. HIV-1 vaccine trials have also been unsuccessful to date. A recent population-based model explored the impact of a prophylactic HSV-2 vaccination on HIV-1 incidence in Africa and reported that a vaccination campaign that reduces HSV-2 acquisition and reactivation by 75% in 10 years will reduce HIV-1 incidences by 30-40% after 20 years. If accurate, an HSV-2 vaccine can have a tremendous impact on controlling HIV globally; we have developed a trivalent HSV-2 subunit vaccine that is highly effective in preventing HSV-2 disease and latent infection of dorsal root ganglia in the mouse model and, genital recurrences and vaginal viral shedding in guinea pig model of recurrent HSV-2 infection. Our ultimate goal is to determine whether an HSV-2 vaccine will prevent genital ulcer disease and reduces susceptibility to HIV-1 infection.

To accomplish our goal, we have first established an HSV-2 vaginal infection in humanized mice. These animals have B- and T-cells of human origin. We have shown that severity of vaginal disease is dose dependent. The LD50 value for HSV-2 vaginal infection for a clinical isolate of HSV-2 strain 2.12 is 37 PFU. We have also shown that virus successfully replicates in mouse vaginal tissue and develop vaginal disease. Histochemical and immuno-histochemical analysis of infected humanized mice showed that vaginal tissue was disrupted, and immune cells migrated to the site of infection within first 3 days of infection. While no staining for HSV-2 was observed in liver and spleen, the proliferation of immune cells was observed in spleen within first 3 days of vaginal infection. We plan to infect HSV-2 infected humanized mice with HIV-1 and evaluate the markers of HIV-1 infection and HSV-2 infection.

Biography

Sita Awasthi has received her Ph.D in Biochemistry from Devi Ahilya University at Indore, India and her postdoctoral training from University of Pennsylvania at Philadelphia. Currently she is a Research Assistant Professor in Infectious Disease Division, Department of Medicine, Perelman School of Medicine at University of Pennsylvania, Philadelphia. Her research interests are HSV-2 vaccine development against genital herpes disease and HSV-2 HIV-2 co-infections. She has published numerous research articles and serving as an editorial board member of Journals of antivirals and anti retrovirals, Journal of Immunoassay and Immunochemistry. She has been a Board Member for the Association of Women in Science, Philadelphia chapter.

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