



International Conference and Exhibition on VIRIOLOGY

5-7 September 2011 Baltimore, USA

Blocking HSV-2 mediated evasion of host immunity: A novel strategy to improve gD-2 subunit vaccine for HSV-2 genital disease

Sita Awasthi

University of Pennsylvania, USA

There are about a billion people worldwide infected with Herpes simplex virus type 2 (HSV-2). HSV-2 infection increases the risk of HIV acquisition by 3 fold. Currently there is no FDA approved vaccine for genital herpes. HSV-2 glycoprotein D (gD-2) is a potent immunogen and a candidate antigen for a subunit vaccine. Clinical trials using recombinant gD-2 as subunit immunogen revealed protection against genital ulcer disease in seronegative women but not in men regardless of their sero status. In a more recent trial it failed to protect seronegative women from genital infection. Our approach is to use HSV-2 glycoprotein C (gC-2) in addition to gD-2. gC-2 is an immune evasion protein binds complement component C3b and inhibits complement-mediated immunity. Immunizations with gC-2 in mice shows that anti-gC-2 antibody blocks gC-2 binding to C3b and prevents virusmediated evasion of host immunity. We further investigated whether combined immunization with gD-2 and gC-2 provides better protection against challenge than gD-2 alone based on antibodies to gC-2 preventing HSV-2-mediated immune evasion. IgG purified from mice immunized with gC-2 blocked C3b binding to gC-2 and greatly increased neutralization by gD-2 IgG in the presence of complement. Unlike anti- gC-1, anti-gC-2 IgG neutralized HSV-2 in absence of complement, and was greatly enhanced in presence of complement. Passive transfer of gC-2 IgG protected complement intact mice against HSV-2 challenge significantly better than C3 knockout mice, indicating that gC-2 antibody activity in vivo is complement-dependent. Immunizing mice with gD-2 and gC-2 provided better protection than gD-2 alone in preventing vaginal disease, and most importantly, infection of dorsal root ganglia in the vaginal models. Combined immunizations with gD-2 and gC-2 also provided better protection against acute and recurrent vaginal infection in guinea pigs. gD-2 and gC-2 vaccine protects mice against multiple HSV-2 strains from North America and Africa. Therefore, we conclude that gC-2 immunization prevents HSV-2 evasion from complement and enhances the protection provided by gD-2 immunization.

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 at University of Pennsylvania, Pearlman School of Medicine, Infectious Disease Division. 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.