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Blocking virus mediated evasion of host immunity as a strategy for prevention and treatment of genital herpes

In a recent phase III trial, HSV-2 glycoprotein D (gD2) subunit antigen vaccine failed to meet the primary endpoint of preventing genital herpes in HSV-1/HSV-2seronegative women; however, the vaccine was efficacious in preventing HSV-1genital disease, which made up 60% of the cases. Our approach is to improveupon a gD2-containing vaccine by adding glycoproteins C (gC2) and E (gE2), which are immune evasion molecules that inactivate complement (gC2) and antibody effector functions (gE2). We postulated that gC2 and gE2 subunit antigens would induce antibodies that block the evasion of complement and effector functions of vaccine induced antibodies mediated by HSV-2 gC and gE respectively. Guinea pigs were immunized three times with a gC2/gD2/gE2 (trivalent) subunit vaccine given with CpG and alum as adjuvants and challenged intravaginally with HSV-2. Acutegenital lesions were observed on 1/135(0.7%)days in the trivalent vaccine group compared with 34/67 (51%) days in the mock group (P<0.001). Recurrent genital disease developed on 8/690 days (1.2%) in the vaccine group and 56/184 (30%) days in the mock group (P<0.001). Vaginal HSV-2 DNA shedding was detected on 18/315 (5.7%) days in the vaccine group and 8/84 (9.5%) days in the mock group (reduced by 40%). We evaluated the trivalent vaccine astherapy for genital herpes by infecting guinea pigs intravaginally with HSV-2 and once recovered, immunizing three times with the trivalent vaccine with CPG and alum. A 49% reduction in lesion days was noted in the vaccine group (29/738, 3.9%) compared with the mock group (48/624, 7.7%) (P<0.01). Vaginal shedding of HSV-2 DNA was detected on 5/144 (3.5%) days in the vaccine group compared with 21/162 (13.0%) days in the mock group (P<0.01). Therefore, the trivalent subunit antigen vaccine is highly efficacious as a prophylactic and therapeutic vaccine for genital herpes.

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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