Safety and Immunogenicity of Candidate HSV-2 Vaccine

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Over 45 million people in the US are currently infected with herpes simplex virus type 2 (HSV-2). HSV-2 is the main cause of genital herpes and the virus can remain latent, with reactivations leading to new lesions and viral shedding. Antiviral treatments do not cure the infection, so a vaccine is sought to both prevent infection (prophylactic vaccine) and limit viral reactivation in those already infected (therapeutic vaccine). Previous findings that strong CD8+ T-cell responses are important for viral control, and the knowledge that there are many viral components, or antigens, targeted by the immune system make a vaccine that is capable of recognizing multiple targets and eliciting a strong T-cell response desirable. This led Dr. Anna Wald of the Vaccine and Infectious Disease Division (VIDD), along with VIDD's Dr. David Koelle and outside collaborators, to study the safety and immunogenicity of a polyvalent therapeutic vaccine, named HerpV, in HSV-2 seropositive patients.

The vaccine is comprised of multiple components designed to work together to elicit both CD4+ and CD8+ T-cell responses. These include recombinant human heat shock protein Hsc70, multiple peptides containing HSV-specific complexes, and a saponin adjuvant isolated from the South American soap bark tree (QS-21), which has been shown to increase both antibody and B-cell responses in previous experimental uses. The study enrolled 35 seropositive participants, and over the course of the study no serious adverse events occurred. All participants who received HerpV and QS-21 showed vaccine-induced CD8+ T-cell responses, and most showed CD4+ responses as well. Additionally, these responses are achieved using lower concentrations of peptides than in previous clinical trails, indicating that the use of the heat shock protein and/or QS-21 creates a more robust immune response.

The HerpV vaccine is the first candidate HSV-2 vaccine to show both CD4+ and CD8+ T-cell responses for a broad range of antigens. Additionally, this is the first human study where a heat shock protein-based vaccine has demonstrated an immune response against viral antigens. Given these results, the researchers are planning a follow-up study to test the clinical efficacy of this vaccine regimen.

Wald A, Koelle DM, Fife K, Warren T, LeClair K, Chicz RM, Monks S, Levey DL, Musselli C, Srivastava PK. 2011. Safety and immunogenicity of long HSV-2 peptides complexed with rhHsc70 in HSV-2 seropositive persons. *Vaccine* 29: 8520-8529.

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