EXECUTIVE SUMMARY [NON-CONFIDENTIAL, NON-TECHNICAL ABSTRACT FOR PUBLIC INFORMATION OR PROGRAM PROMOTION]: State in layman's terms the application's broad, long-term objectives and specific aims, making reference to the potential public benefits of the project relevant to California. Do not include proprietary or confidential information. This may be distributed before the funding decision has been finalized.

Genital Herpes virus infection in adults is one of the most important and common sexually transmitted diseases, with as many as 1 out of 6 American adults having Herpes genitalis. The disease is highly infectious, affecting both normal and immunosuppressed adults, and leads to increased susceptibility to other infectious diseases, including HIV which continues to be a serious health problem in California and throughout the rest of the world. Genital Herpes virus also causes serious clinical disease in neonates following its transmission from infected mothers. Infected women who have Herpes genitalis are 5X more likely to develop cervical cancer than non-infected women. Despite the availability of effective antiviral drugs for treating HSV-2 infection, the incidence of genital herpes in the United States continues to increase and a major factor contributing to this spread of genital herpes is the ability of the virus to be shed from the genital tract in the absence of signs of infection. For these reasons, there is a critical need for developing new approaches to the prevention of herpes infections, including most prominently an effective HSV-2 vaccine to reduce the frequency of the disease and recurrent infections. The nature of the infection suggests that an effective vaccine will be required to stimulate a potent T cell mediated response in order to control both primary and recurrent disease. The preclinical results in our laboratory have demonstrated that a novel HSV2 gD epitope/liposome vaccine displays advantages over the current technology, including higher levels of protection against lethal challenge of female and male mice and the stimulation of effective immune responses in female and male mice without the potential complications associated with using live or killed virus preparations. In the present study, we propose to expand our preliminary investigation of the use of this unique liposome delivery vehicle to examine the nature of the protective responses generated to the specific HSV-2 peptides incorporated into the liposomes. The liposomal vaccine delivery vehicle that we have designed is innovative in that it involves a fusion protein, consisting of a recombinant viral peptide fused to a hydrophobic protein, which can then be easily incorporated into liposome membranes to form very small liposomes (<100nm) which mimic the appearance of a non-infectious virus. The protected mice given this unique liposomal vaccine have displayed some evidence of T cell dependent immune responses, suggesting that this vaccine induces T cell responses that are primarily responsible for the vaccine's protection. Our promising preclinical data has led us to propose testing the hypothesis that a prolonged, protective CD4 and CD8 T cell response to HSV-2 stimulated by the non-microbial, liposomal HSV2-gD epitope vaccine will provide the primary protection to lethal HSV-2 viral challenge and that this type of T cell response will reduce or eliminate primary and recurrent HSV-2 infection.