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Development of Vaxfectin®-formulated HSV-2 plasmid DNA vaccines for prophylactic and therapeutic applications

Genital infections caused by herpes simplex type 2 virus (HSV-2) present serious public health problems throughout the world. Initially HSV-2 infects the genital epithelium. Once the primary infection resolves, the virus establishes a permanent latent neuronal infection that undergoes periodic reactivation producing HSV-2 viral shedding, often without symptoms or lesions, which can transmit the virus. Ideally, an HSV-2 vaccine would not only prevent infection but could also serve to reduce lesion frequency and viral shedding in infected individuals. Unfortunately, no effective HSV-2 vaccine exists to date. Plasmid DNA-based vaccines may offer several advantages compared to other vaccine approaches, such as eliciting a broad immune response, including cytotoxic T-cell response, and employing a simple manufacturing process. Expression plasmids for HSV-2 glycoprotein D (gD), and tegument proteins VP11/12 (UL46) and VP13/14 (UL47) were evaluated as vaccine candidates. The plasmid DNAs were formulated with Vaxfectin®, a patented cationic liposome adjuvant. Prophylactically, the Vaxfectin®-formulated plasmid DNAs protected against primary and recurrent disease in both mice and guinea pigs. Viral loads from primary infection were significantly reduced and the vaccine protected against latent infections. Therapeutically, Vaxfectin® -formulated plasmid DNAs expressing the HSV-2 antigens produced a significant reduction in recurrence of viral lesions and also in viral shedding in HSV-2 infected guinea pigs. Preclinical studies required for an IND filing are in progress with the initiation of a Phase 1/2 safety clinical trial targeted for the second half of 2013.

Biography

Sean Sullivan is Executive Director of Pharmaceutical Sciences at Vical, Incorporated. He is in charge of formulation development and scale up manufacture of Vical's genetic vaccine product candidates. Prior to joining Vical, he was a tenured Associate Professor in the Department of Pharmaceutics, College of Pharmacy, and University of Florida with a joint appointment at Shands Cancer Institute. Prior to joining the University, he was in the biotechnology industry for 14 years developing liposome and polymer based nucleic acid delivery systems for the treatment of infectious disease (HIV, HSV and Hepatitis), arthritis and cancer.

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