Vaccination Platform for Persistent Viruses

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BACKGROUND

While successful vaccines have been developed against acute infections, persistent infections have remained refractory to both natural immunity and vaccination protocols. The standard strategy of selecting immunogens on their ability to generate a strong T-cell response has proven ineffective. In reality, one observes immunogens that generate a surfeit of T-cells but are completely ineffective as vaccines. On the other hand, one can immunize with DNA and get protection using a gene against which no immunity is generated during natural infection. Therefore, to vaccinate against persistent infections, a vaccine may have to be better than natural immunity. An effective approach may be evolved by learning from and targeting the "Achilles heel" of natural immunity.

TECHNOLOGY DESCRIPTION

Using numerous animal models of persistent infections and immunity, UC San Diego inventors have demonstrated the efficacy of a vaccination protocol, which includes plasmid DNAs and killed/attenuated virus. The approach is differentiated by the choice of plasmid DNAs, which encode conserved, essential genes that are normally expressed in an active infection but do not prime a T cell response in the context of an infection. However, these plasmids do elicit specific CD8+ T cell responses against the conserved, essential proteins of the virus. Also included is a plasmid DNA that encodes a viral glycoprotein targeted by neutralizing antibody. By combining plasmid DNA immunization with immunization using whole, killed cytomegalovirus (CMV) or herpes simplex virus (HSV), broad T-cell and B-cell immune responses are generated to prevent viral infection.

APPLICATIONS

- Utility as a prophylactic or therapeutic vaccine.
- Platform, which is validated for CMV and HSV, may readily translate to other persistent viral infections, including Herpes, AIDS, hepatitis, and papillomaviruses.

ADVANTAGES

This two-pronged approach simultaneously neutralizes virus spread from organ to organ and allows the recognition and destruction of persistently infected cells within the host.

STATE OF DEVELOPMENT

In addition to the published *in vivo* validation of efficacy in a murine model of CMV (see references), protective efficacy has been demonstrated in murine and guinea pig models of genital infection with HSV-2. Specifically, immunization of both mice and guinea pigs using proprietary genes and methods resulted in a significant reduction of HSV-2 viral shedding and acute and recurrent genital disease. Notably, the protection was greater than that afforded by the most successful vaccination strategy in HSV-2 clinical trials to date, subunit vaccination with gD2 protein in MPL/alum. Current work is focused on optimizing adjuvant for greatest efficacy and a single formulation vaccination protocol.

INTELLECTUAL PROPERTY INFO

Pending international and U.S. applications, see publication number WO/2007/106404); also see information for U.S., Canada, Europe, and Japan.

RELATED MATERIALS

- Morello, C. S., et. al. 2007. DNA Immunization Using the Highly Conserved Murine Cytomegalovirus Genes Encoding the Homologs of Human Cytomegalovirus UL54 (DNA Polymerase) and UL105 (Helicase) Elicits Strong CD8 T Responses and Is Protective Against

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OTHER INFORMATION

KEYWORDS

cytomegalovirus virus, Herpes, AIDS, hepatitis, HSV, CMV, papillomavirus, prevention, prophylaxis, prophylactic, therapy, therapeutic, vaccine, vaccination, platform, single formulation, infection, infectious, pre-clinical

CATEGORIZED AS

- **Medical**
- Disease: Infectious Diseases
- Vaccines

RELATED CASES

2006-121-0

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▶ Morello, C.S., et. al. (2005). Systemic Prime-Boost Immunization with a Trivalent Plasmid DNA and Inactivated Murine Cytomegalovirus (MCMV) Vaccine Provides Long-Term Protection Against Viral Replication Following Systemic or Mucosal MCMV Challenge. J. Virol. 79:159-175.

▶ Ye, M., et. al. (2004). Multiple Epitopes in the Murine Cytomegalovirus Early Gene Product M84 Are Efficiently Presented in Infected Primary Macrophages and Contribute to Strong CD8+ T-Lymphocyte Responses and Protection Following DNA Immunization. J. Virol. 78:11233-11245.

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▶ Gonzalez Armas, J. C., et. al. (1996). DNA Immunization Confers Protection Against Murine Cytomegalovirus Infection. J. Virol. 70:7921-7928.

▶ http://cmm.ucsd.edu/Lab_Pages/Spector

PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Issued Patent	8,501,194	08/06/2013	2006-121

ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

▶ Novel Inactivated Virus Vaccine Against Herpesviruses

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