Bacteriophage Virus-Like Particle Vaccines against Flavivirus Non-Structural Protein 1

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Technology description

Background

Dengue serotypes (DENV1-4) are mosquito-borne viruses that infect over 390 million people worldwide annually, primarily in developing nations. There are no current antiviral treatments for DENV, and prevention methods rely on local control of a specific mosquito vector,Aedes aegypti. There is one licensed vaccine, Dengvaxia (Sanofi-Pasteur), available; however, it has recently been removed from vaccination campaigns due to safety concerns regarding the increased risk of Severe Dengue. The development of Severe Dengue originates from the unique pathogenesis features of the DENV serotypes. In response to the primary infection, antibodies bind to the serotype present. If an additional infection occurs, these non-neutralizing antibodies facilitate entry of the new DENV into the immune cells, resulting in plasma leakage, hemorrhage, shock, and cytokine storm. Thus, current vaccine efforts have been targeting all four DENV serotypes through tetravalent vaccine preparation to eliminate the chance of vaccine-elicited Severe Dengue.
A promising treatment target emerging is DENV Non-Structural Protein 1 (NS1). NS1 is produced from the viral genome in infected cells, and is secreted in large quantities throughout the early stages of infection. When present in the bloodstream, NS1 can directly and indirectly cause plasma leakage; through interaction with endothelial cells and activation of cytokine production, respectively. It has been shown that antibodies against NS1 protect mice from lethal DENV infections, and NS1-mediated vascular leakage. Therefore, NS1 is proven to be a promising target for a DENV vaccine against all four serotypes. However, complications arise due to the cross-reactivity of a subset of antibodies against NS1; in addition to, eliciting a long-lasting, high titer antibody response with subunit vaccines. Thus, there exists a present need for a vaccine targeting DENV NS1 that is capable of eliciting antibodies to block NS1 activity, while eliminating the potential for harmful cross-reactions.

Technology Description

Researchers at the University of New Mexico utilize a bacteriophage virus-like platform (VLP) to elicit high titer, long-lasting antibodies to NS1 epitopes of interest.

By eliciting antibodies to NS1 peptides, they are able to focus the antibody response to the specific regions responsible for pathogenic activity, reducing the likelihood of cross-reactions. The utilization of VLPs provides several benefits outside of antibody production, including improved feasibility and safety. Increased feasibility is also present through the possibility of single immunization. Finally, both safety and immunogenicity of bacteriophage VLPs have been established in number of clinical trials. These benefits provide a significant advantage in the production of a successful DENV NS1 vaccine.

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Application area

High titer, long-lasting antibody response to NS1 without dangerous cross-reactivity
Highly immunogenic vaccine platform
Thermostable properties for transportation to remote regions
Epitope-specific vaccines
Potential protection against Zika Virus (additional flaviviruses)

Institution

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