MEDICAL TECHNOLOGY TRANSFER

U.S. Army Medical Research and Development Command
Fort Detrick Maryland

Platform Technology for Vaccine Development

Optimization of Virus-Like Particle Vaccines using a Tobacco Mosaic Virus (TMV) Platform.

The Army seeks a partner interested in commercializing this technology.

Status

Patent Applications
US Provisional 62/561,956 filed 22 September 2018

PCT/US2018/052193 filed 21 September 2019

Title
Tobamovirus-Based Virus-Like Particles and Vaccines

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Publications
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The Tobacco Mosaic Virus (TMV) particle platform allows rapid expression of antigenic epitopes. The resulting TMV particles are less expensive and less reactogenic than vaccine approaches using protein carriers derived from human pathogens.

The Market Need

A need exists for improved and less expensive vaccine development approaches. Vaccines based on short epitope sequences are inherently non-immunogenic. The protein carriers often used to make epitopes more immunogenic are based in non-lethal or attenuated forms of human pathogens including adenovirus, influenza, hepatitis B, yellow fever, shigella, and salmonella etc. However, there can be pre-existing immunity to many of these human pathogens that affects the immune responses to target epitopes displayed on these carriers. Researchers at WRAIR solved this problem by engineering a Tobacco Mosaic Virus capsid to which no pre-existing immunity exists in humans to express antigenic epitopes for new vaccines.

The Technology

WRAIR inventors developed a TMV particle platform to test new malaria vaccines and compare them to the existing malaria vaccine (RTS,S/AS01) which is a Circumsporozoite protein (CSP)-based malaria vaccine conferring partial protection. After testing various epitope structures, a TMV vaccine containing CSP repeats displayed as a loop induced 10X better antibody titer than a nearly full-length CSP in mice. A similar 5X improvement in antibody titer was seen in rhesus monkeys. The rhesus antibodies to the TMV vaccine inhibited parasite invasion for up to 11 months after vaccination. The TMV vaccine containing CSP repeats is not just an improvement over existing malaria vaccines, but demonstrates that utilization of the TMV particle platform may be an effective strategy for other types of vaccines as well.

Applications

The TMV particle based platform was initially designed to test new malaria vaccines. The approach is suitable for other vaccines as there is an acute need for vaccines with improved immunogenic profiles that will protect the recipient without the risk of reactogenicity.

Highlighted Benefits

- Tobamovirus capsid protein assembles in an array of monomers that forms an interior region (pore) and an external region (exposed loop)
- Immunogenic epitope is displayed on the external region of the TMV disk
- TMV particle platform expressed in E. coli is less expensive to produce
- Resulting TMV particles are thermo-stable
- TMV particles are not reactogenic
- Purified TMV particles contain very low endotoxin levels (< 5 endotoxin units/microgram) and very low amounts of bacterial host proteins (<1 nanogram/milliliter)

Stage of Development

Antigen configuration and copy-number of CSP proteins were displayed on a TMV particle platform. The resulting vaccine produced a 10X better antibody titer than a nearly full-length CSP in mice. Antibodies raised using this TMV platform in rhesus, inhibited parasite invasion for up to 11 months after vaccination.

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