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Innovation Advancement & Commercialization

Low-Dose Vaccine Platform for T-Cell Based Immunity

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Reference: Low-Dose Vaccine

Patent Status

- Two issued U.S. Patents (8,647,636 and 9,107,875)
- EPO, Canadian patent applications have also been filed
- Additional applications pending in US, EPO, Canada & China for delivery formulation

Licensing Opportunities

- This technology is available for exclusive and non-exclusive licensing in most fields of use; obligations exist for diseases in livestock and poultry
- Joint development opportunities include funded research or joint venture

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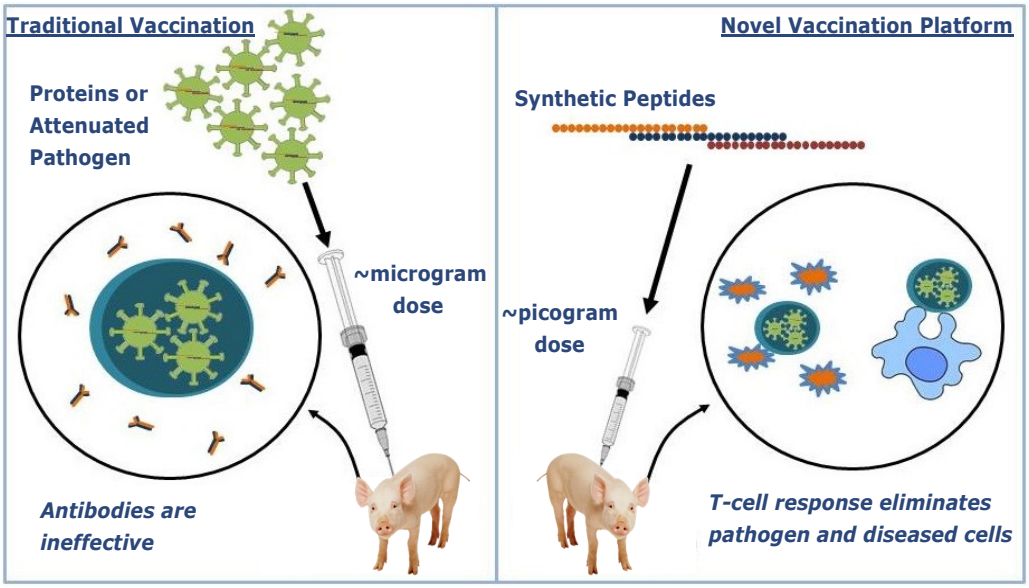
Overview

Auburn University is seeking a licensee or development partner for a novel low-dose vaccine platform. Vaccination against pathogens is a cornerstone of modern medicine. However, there is a persistent need for better protection and therapy against diseases caused by intracellular pathogens in both human and animal healthcare. Traditional vaccines use a relatively high dose of antigen — proteins or inactivated/modified pathogens — to elicit an antibody response. However, antibody responses are ineffective against many intracellular infections. Further, these formulations are often costly to produce and can pose an increased risk to the patient.

This novel method uses an extremely low dose of peptides from the target disease. This creates a T-cell response to provide improved protection against intracellular diseases. Further, the use of synthetic peptides in such small amounts allows for a lower cost and safer formulation than many existing vaccines. Up to hundreds of peptides can be combined in a fully synthetic vaccine to provide broad coverage. Generally speaking, diseases that currently do not have a vaccine or have vaccines utilizing attenuated live pathogens are the best suited targets for this platform. Infectious diseases, cancer, and autoimmune diseases can all potentially be treated. Preventative or therapeutic care can be given by this platform depending on the disease target.

Advantages

- T-cell response creates protective effect on targets that currently have little/no treatment
- Multiple strains of a pathogen or multiple pathogens can be treated with one formulation
- Use of synthetic peptides allows for low cost scale-up and provides a safer product with fewer quality control problems than formulations derived from biological manufacturing



In traditional vaccines (left), large amounts of protein or inactivated/attenuated pathogen from the disease of interest are administered. This generates a B-cell-based response that results in antibody production. While these antibodies are highly specific and can bind to pathogens which can provide protection, they are often ineffective against intracellular infections. With the administration of ultra-low doses of synthetic peptides from the disease target (right), a T-cell-based response is generated. This response eliminates pathogens and infected cells by cytokines or induced cell death, thereby creating superior protection against intracellular diseases.

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Low-Dose Vaccine Platform for T-Cell Based Immunity *(Cont'd)*

Lead Inventors

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Candidate Disease Targets

Viral
- Norovirus
- Pan-influenza
- Rhinovirus
- RSV
- HIV
- Dengue & Yellow Fevers
- SARS/MERS (Coronavirus)
- Herpesvirus (Human, Animal)
- Hepatitis B & C
- PRRSV (Swine)
- African Swine Fever
- Swine Influenza
- Parvovirus (Canine, Swine)
- Scours (Bovine)
- BVD/BRD (Bovine)
- ILT (Poultry)
- IBV (Poultry)
- Foot-and-Mouth (Multiple)
- Rift Valley Fever (Multiple)

Bacterial
- Tuberculosis
- Leprosy
- Typhoid
- Lyme Disease
- Mycoplasma (Swine, others)
- Johne's Disease (Bovine)
- Anaplasmosis (Bovine)
- Chlamydia (Human, Animal)

Protozoan (e.g., Malaria)

Cancer

Autoimmune Disorders

* Diseases in production animals not available

Detailed Description

This vaccine platform uses extremely low doses of small, overlapping peptide fragments to generate a protective T-cell response against intracellular diseases. These fragments are derived from the amino acid sequences of key proteins related to the disease. Preferably, the peptides are about 20 amino acids in length. By overlapping the peptide sequences, all possible 8-10 amino acid segments from the target protein can be presented to the T-cells. When combined with a synthetic adjuvant, fully synthetic, safe and low-cost vaccines can be produced. Thus, difficult manufacturing using chicken embryo or cell culture methods can be avoided.

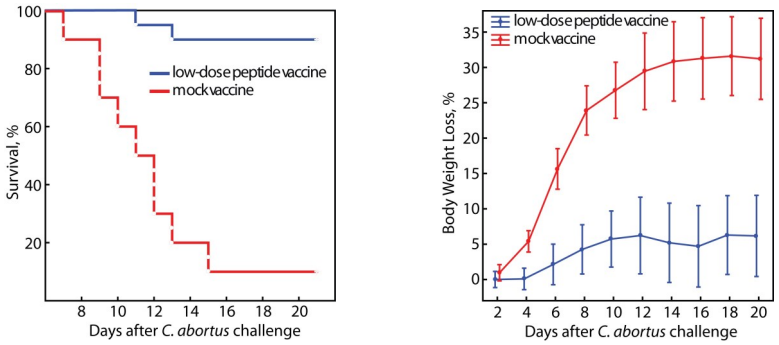
Numerous different peptides can be incorporated into a single formulation because of the extremely low antigen dosage (at least three orders of magnitude less than traditional vaccines) and the low cost of production. This allows for targeting of multiple proteins, including proteins from multiple pathogens. Further, multiple antigenic variant sequences of a pathogen can be included. This enables both extremely rapid adaptation of a vaccine to antigenic drift and shift and potentially universal vaccines against rapidly changing pathogens.

Vaccine formulations for pathogens with small genomes, including many viruses, could be made up of overlapping peptides comprising the complete viral proteome. Such vaccines could be produced for testing almost immediately. For more complex pathogens and diseases, such as bacterial infections or cancer, a vaccine could be based on key protective proteins. Typically, further research would be needed to determine the ideal protein targets. However, if such protective proteins have already been identified, formulations could again be finalized quickly.

Other features include the ability to: 1.) tune formulations to preferentially induce a Th1 response versus other types of immune responses (e.g., Th17 or Th2); 2.) generate an immune response during the window of maternal immunity, which is potentially beneficial for diseases such as canine parvovirus; 3.) differentiate infected from vaccinated animals (DIVA).

Development Status

- Proof of concept shown in *Chlamydia abortus* mouse model (see figure below). Vaccinated mice showed significantly enhanced survival (left) and lower body weight loss (right). *Currently no commercial vaccine with proven high efficacy against Chlamydia is available.*
- Demonstrated with several different commercial and proprietary carriers and adjuvants
- Statistically significant protection against IBDV demonstrated in chickens (host species) over unprotected control and commercial vaccine.



Twenty C3H/HeJ mice (Toll-4 receptor-deficient LPS non-responders) were vaccinated with short peptides derived from the five most protective *C. abortus* proteins to generate anti-chlamydial Th1 immunity. Protection is shown in enhanced survival (left) and lower body weight loss (right) after intranasal challenge with 10^8 *C. abortus* bacteria (P<0.01).