

VAXINNATE'S NOVEL TECHNOLOGY

Influenza Vaccines Today

Currently marketed influenza vaccines are based on a development, production and vaccination strategy that has changed little in 50 years. The seasonal nature of influenza, and the virus' ability to mutate and still cause disease, makes it necessary to formulate an entirely new influenza vaccine annually. Seasonal flu vaccine is based upon a prediction by the Centers for Disease Control (CDC, part of the U.S. government) and the World Health Organization (WHO) of the strains that are likeliest to circulate and cause disease during the next winter's flu season.

Current vaccines are formulated with hemagglutinin (HA) as the viral antigen, which is the protein component of the virus that serves as a target for an immune response. There is general concern, however, that traditional vaccines may not consistently meet the demands of seasonal influenza or potential pandemic virus outbreaks due to slow development and production cycles. These fears have been realized twice in just the past 4 years when annual influenza vaccine was in extremely short supply early in the season, the ideal time for vaccinating to prevent illness.

Conventional Production Technology

Currently, influenza vaccine is manufactured in live fertilized chicken eggs using a laborious process that involves harvesting, purifying and processing the virus to recover viral antigens. The entire process takes 6 to 9 months from start to finish and the result is far from optimal. Yields and immunogenicity can vary widely from year to year, making it difficult to predict supply, meet expected demand or respond quickly to surges in demand due to an extremely severe flu season, for example.

Vaccine production sites typically have devoted, non-convertible facilities, with no quick, easy or economical way to alter capacity. The size of these facilities and their production capacity are determined 5 to 7 years prior to the licensure of a vaccine. As a result, it's at best difficult and often impossible to adjust for unanticipated circumstances – including manufacturing problems at the few global sites approved for vaccine production, new public health usage recommendations, or public health emergencies, such as the emergence of pandemic influenza. The expense of keeping idle capacity operational precludes commercial firms from doing so in the event of unexpected demand.

The VaxInnate Approach

VaxInnate's approach overcomes the limitations of egg-based production. Our fusion vaccine can be efficiently and economically manufactured in bacteria. The technology for producing large quantities of proteins in bacteria has been in use for more than 20 years, and many currently available protein-based drugs are manufactured in this way.

The method involves the insertion of a circular DNA "vector" coding for the flagellin-antigen fusion product into bacteria. The DNA directs the synthesis of the fusion product, which either accumulates in the bacteria or is secreted into the surrounding media. The subsequent purification steps to isolate the recombinant protein are straightforward and scalable to industrial operations.

Applied to vaccines, bacteria-based production reduces the cost to manufacture the final product, and establishes a more rapidly scalable, readily transferrable manufacturing process.

Many existing fermentation facilities could convert their plant in and out of influenza vaccine production as commercial opportunity and medical needs change. Importantly, bacteria-based manufacturing eliminates the risk that an avian influenza pandemic could destroy egg-laying flocks and thereby thwart vaccine production.

VaxInnate's approach also eliminates erratic immunogenicity that results from egg-based production. We do this by leveraging both natural sources of immunity, using recent breakthroughs in understanding the inner workings of the immune system. We stimulate the two primary mechanisms of immune defense, referred to as "innate" and "adaptive" responses, using VaxInnate's proprietary Toll-Like Receptor (TLR) technology. This leads to a more effective vaccine against both variable antigens and antigens that remain conserved from one strain of virus to the next. Because the vaccines can be produced in bacteria, they can be developed and efficiently manufactured at a large scale within a short period of time.

VaxInnate's M2e vaccine candidate has completed its first Phase I trial, with the results accepted for presentation at a major scientific conference in 3Q 2008.

Meanwhile, VaxInnate's lead vaccine candidate against influenza HA demonstrated full protection against a lethal influenza challenge in mice, further supported by preclinical results in rabbits, ferrets and in vitro testing. These studies are highly predictive of successful human clinical trial outcomes. Production yields indicate that vaccine sufficient for national needs could be produced in standard industrial-scale fermenters within several months. We are testing the initial influenza HA vaccine candidate in humans in 3Q 2008, with results expected to be available in 4Q 2008.

Toll-Like Receptor (TLR) Technology

VaxInnate's TLR technology is based on the ability of TLRs to recognize certain molecular patterns, thereby triggering an innate immune response. When these molecular patterns are linked to an antigen, the target of adaptive immune response, robust antibody and cell-mediated immune responses are generated. The company's vaccines combine proteins of vaccine antigen (such as the influenza HA) and bacterial flagellin, a component of the long, hair-like tails that help bacteria swim and one of the molecular patterns recognized by TLRs. Physically linking flagellin to antigens leads to a more potent vaccine than merely administering a mixture of the two unattached components. This method has been demonstrated to produce robust protective immune responses in animal models for other diseases besides influenza, including West Nile Virus, Japanese Encephalitis Virus and Listeria.

The definitive proof-of-concept was completed in 2Q 2008 and in human studies the immune response against M2e was rapid, vigorous and of high affinity and avidity for the target antigen. Since flagellin is a stable bacterial protein, these fusion products are simple to make using recombinant DNA techniques. The ability to rapidly develop and manufacture large quantities of the fusion product vaccines makes them ideal for addressing seasonal variants of flu or emerging pandemic viruses.

