

## VACCINE TECHNOLOGIES

### **Influenza Vaccines**

Currently marketed influenza vaccines are based on a development, production and vaccination strategy that has not changed significantly in the past five decades. Due to the seasonal nature of the disease and the genetic instability of the virus, it is necessary to formulate a new influenza vaccine each year based on an epidemiological prediction of the strains most likely to be circulating in the human population in the next winter's flu season. Current vaccines are formulated with hemagglutinin (HA) as the viral antigen (the component of the virus, usually a protein, which serves as a target for an immune response). Due to slow development and production cycles, there is general concern that traditional vaccines may not consistently meet the demands of seasonal influenza or potential pandemic virus outbreaks.

### **The VaxInnate Approach**

The novel approach championed by VaxInnate is designed to meet those demands by drawing upon breakthroughs in our knowledge of the way the immune system works and taking advantage of efficient manufacturing technology. By leveraging both of the two primary mechanisms of immune defense, referred to as "innate" and "adaptive" responses, VaxInnate's proprietary TLR technology 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.

Recently, a VaxInnate lead vaccine candidate against influenza HA demonstrated full protection against a lethal influenza challenge in mice, while production yields indicate national needs could be produced in standard industrial-scale fermenters within several months.

### **TLR Technology**

VaxInnate's TLR technology is based on the ability of "toll-like receptors" (TLRs) to recognize certain molecular patterns, 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 just administering a mixture of the two unattached components. This method has been

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Technology Backgrounder

demonstrated to produce robust protective immune responses in animal models to several pathogens including West Nile Virus, Japanese Encephalitis Virus and Listeria, in addition to influenza. Because 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 ideally suited for responding to seasonal variants of influenza, or emerging pandemic viruses.

In addition to rapid development and production, TLR vaccine technology offers a further advantage. The viral antigen-flagellin fusion product can generate a response even against targets that are not very immunogenic, including highly conserved regions of viral proteins. That means instead of developing a new vaccine for every seasonal variant or emerging strain of virus, one vaccine could be effective against a wider variety of strains and even pandemic viruses. Such a vaccine strategy could facilitate stockpiling for public health and biodefense purposes.

## **Production Technology**

Current vaccine manufacturing is based on growing virus in live fertilized chicken eggs. In a laborious process, the virus is then harvested, purified and processed to recover viral antigens. Egg-based systems take six to nine months to manufacture and release a year's batch of vaccine, making it difficult to predict demand or respond quickly to public health emergencies.

VaxInnate's fusion vaccine can be efficiently and economically manufactured in bacteria. The technology for producing large quantities of proteins in bacteria has been practiced for over two decades, 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 scaleable to industrial operations. Applied to vaccines, bacteria-based production avoids traditional egg-based manufacturing, lowers the cost of goods of the final product, and establishes a more rapidly scaleable manufacturing process. In addition, a bacteria-based manufacturing process avoids the risk that an avian flu pandemic will destroy egg-laying flocks.