BIO BIZ

Biotechnology Transforms

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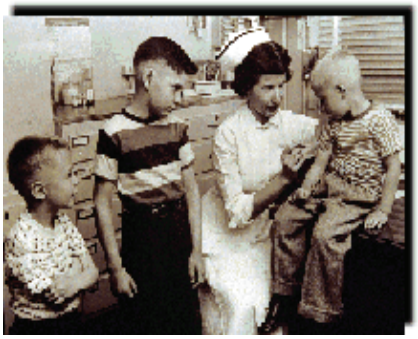


This month, Bio Biz is taking a look at vaccine biotechnology

By Mandy Latimer

It has been 212 years since Edward Jenner scratched the arm of an 8 yr old James Phipps with cowpox pus taken from a milkmaid carrying the cowpox virus in 1796. But, it wasn't until 1952 that Dr Jonas Salk developed a successful vaccine against polio by using a mixture of three types of viruses, grown in monkey kidney cultures which were then inactivated with formalin. Unfortunately, some of the virus remained active and the vaccine caused 260 cases of poliomyelitis with 10 deaths. In 1957, Albert Sabin began testing a live, oral form of the vaccine in which the infectious part of the virus was inactivated (attenuated). This vaccine became available for use in 1963. Since 1980, research has lead to a better understanding of the pathogenicity of disease causing microbes and the improvement of tissue-culture techniques. Scientists now have the ability to produce monoclonal antibodies and to transfer genetic information between unrelated species. The following articles in this months Bio-Biz cover some of the recent major advances that have been made in the last 4 years. Happy reading!

Employment opportunities

Athens Research & Technology Inc. are looking for research scientists.
artbio@athensresearch.com

USDA is looking for student workers. Contact Jodie Plumblee for more info:
Jodie.Plumblee@ARS.USDA.GOV

History Blurb

Ironically, before the 1900s, immunity was acquired primarily during infancy because sanitation conditions were poor and efforts at sewage and water treatment were primitive. Babies were frequently exposed to polioviruses. These infants did not contract the disease because their mothers[1] antibodies were passed on to them through breast feeding. The babies then developed their own antibodies to the virus.

Paradoxically, when sanitation improved, infants were no longer exposed at an age when they were protected, so they did not develop antibodies to the viruses. Consequently, when they were exposed to the virus in later childhood and adulthood, they were at risk of contracting polio.

Tests begin of Flu Vaccine grown In Insect Cell Lines

Science Daily (Oct. 28, 2004) - Scientists are launching a research study to check the effectiveness of a new type of flu vaccine that is made differently than the conventional vaccine, which is grown in eggs. The experimental vaccine instead relies on a cell line drawn from insects known as silk moths, which are best known for their role as pests attacking crops such as corn, cotton, barley & alfalfa.

Pandemic Fears? Try Growing Flu Vaccine Fast In Insect Cells (Not Eggs)

For the full article got to: Science Daily (Apr. 11, 2007) —- An experimental flu vaccine made in insect cells — not in eggs, where flu vaccines currently available in the United States are grown —- is safe and as effective as conventional vaccines in protecting people against the flu, according to results published in the April 11 issue of the Journal of the American Medical Association.

Removing eggs from the flu vaccine manufacturing process is one option for health officials seeking to protect the population from seasonal flu as well as a potential bird-flu pandemic. Using eggs to grow vaccine takes time; a flu vaccine that relies on a different technology is capable of being produced in large amounts much more quickly, a key advantage if a bird flu pandemic were to occur. "Eggs can be very cumbersome to work with," said John Treanor, M.D., the flu expert at the University of Rochester Medical Center who led the study of 460 people reported in JAMA. "When you need hundreds of millions of fertilized eggs, you're dealing with a whole host of agricultural issues, as well as scientific concerns regarding the flu virus itself. Flu viruses can be temperamental, and it's not always an easy matter to get the virus to grow as you want in eggs."

The use of cell culture systems to grow vaccines -- using viruses as tiny factories to churn out mass amounts of vaccines -- is a growing business. A similar technology using human cell lines is used to produce the hepatitis B vaccine, while one form of a vaccine against human papilloma virus is made using the same insect cell line used in the JAMA study.

Freedom from the egg brings implications important to a world facing the threat of pandemic bird flu. For decades the nation's efforts to prevent flu have centered on growing flu virus in hundreds of millions of fertilized eggs, with each egg containing less than a teaspoonful of material that will ultimately become part of a vaccine. It's typically a six-month process to produce enough flu vaccine to protect the public. Taking eggs out of the process would likely slice one or two months off the production process, Treanor said. In case of a bird-flu pandemic, that would allow manufacturers to ramp up vaccine production more quickly than if they had to wait for the production of millions of eggs.

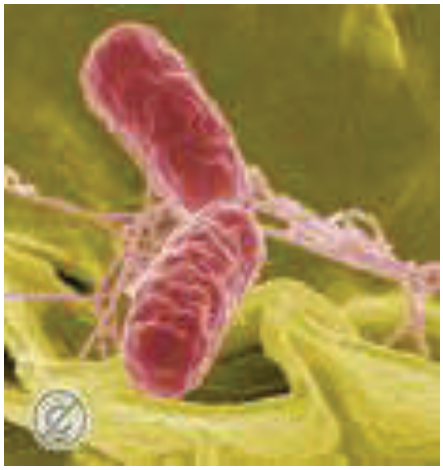
The experimental vaccine differs from approved vaccines in another way as well. The experimental vaccine focuses on a portion of the flu virus known as the hemagglutinin, which the virus uses to attach to blood cells. Unlike conventional vaccines, FluBlOk does not also include neuraminidase, an enzyme that allows a flu virus to replicate and spread.

From Foe To Friend: Researchers Use Salmonella As A Way To Administer Vaccines In The Body

For full article see: Science Daily (July 8, 2008) - researchers at the Biodesign Institute at Arizona State University have made a major step forward in their work to develop a biologically engineered organism that can effectively deliver an antigen in the body. The researchers report that they have been able to use live salmonella bacterium as the containment/delivery method for an antigen.

The work is a major step forward in development of a new means of biological containment that would be a key component to a new way to deliver vaccines in animals and humans. If fully developed, the new method could be used to administer vaccines to many of those who do not benefit from traditional vaccines because of their cost, because of drug resistance or because of limited effects on children.

A key to the project, according to Curtis, is "turning a foe into a friend." That foe is the salmonella bacterium--the leading cause of human food-borne illness and which is currently in the news due to contaminated tomatoes and other food crops. Curti's team, through genetic know-how, has developed a variety of ways to tame salmonella in the lab and use it as a delivery vector for vaccines.



"We try to genetically modify the salmonella bacterium to eliminate its harmful effects -- the diarrhea, gut inflammation and fluid secretion -- while keeping the wherewithal to induce immunity against the bacteria causing pneumonia or other infectious diseases," Curtis said. Several in his research team attack the problem from different angles, with some focusing on weakening salmonella, others boosting the immune response and others optimizing the self-destruct mechanism.

In experiments, the genetically modified *Salmonella enterica* bacterium colonizes the lymph tissues of the host and manufactures a protein from the *S. pneumoniae* bacterium, which then triggers a strong antibody response. Unlike most vaccines that are entirely manufactured by a vaccine company, the attenuated recombinant salmonella vaccine after entry into the immunized individual serves as its own factory to produce (manufacture) the protective antigens (proteins) from the *S. pneumoniae* pathogen. This ability to cause manufacture in the immunized individual dramatically decreases the cost of such vaccines to make them affordable for use in the developing world, Curtis said.

An important factor for the research team was to genetically program the *S. enterica* bacterium to destroy itself so that it is not released into the environment, Curtis said.

The research was funded by the U.S. Department of Agriculture and the National Institutes of Health.

Arizona State University. "From Foe To Friend: Researchers Use Salmonella As A Way To Administer Vaccines In The Body." Science Daily 8 July 2008. 9 July 2008 <http://www.sciencedaily.com- / releases/2008/07/080708141546.htm>.

Researchers Apply DNA Biology to Vaccination Technique

Feb 1, 2006 Science Daily

London– A new flu vaccine could save lives and protect us from a deadly outbreak. But can the United States handle a widespread flu epidemic? Most experts would agree — not with the way we currently mass-produce the vaccine. It currently takes at least six months to a year to make flu vaccines, but that is soon to change. Spraying viral genes directly through the skin is a new technique that turns infinitesimal amounts of DNA into an effective vaccine. If approved for use in humans, the new procedure could save lives in case of a flu pandemic, by skipping the current time-consuming production of vaccines in chicken eggs.

Infectious disease researchers extract just a few genes from the DNA of the flu virus to make a vaccine. Then, microscopic particles are coated with the vaccine and shot into the body at super-fast speeds using this new, needle free device. "It's because the DNA gets into the cells of the skin that it produces such a strong immune response, "Dr Beadle says.

BACKGROUND: Researchers have been working on a DNA-based vaccine for the flu for several years. While not yet ready for widespread use, if there were a global outbreak of the potentially deadly virus, such a vaccine could be fast-tracked into use. The Center for Disease Control estimates that more than 200,000 people in the U.S. are hospitalized each year as a result of the flu, and more than 30,000 die from it. Globally, the flu kills close to half a million people every year.

HOW VACCINES WORK: There are three basic strains of the flu virus: A, B and C. A is the most common strain, and the most severe. The flu vaccine works by triggering the body's immune system response. The body recognizes the vaccine as a foreign invader and produces antibodies to it. However, flu strains differ from year to year; that's why there is a different vaccine each year.

Currently, flu vaccines are made by incubating the three strains of the flu virus expected to strike in a given year are injected into millions of chicken eggs to multiply before being extracted and packaged. It is a labor-intensive and time-consuming technique that is much the same as when it was first invented in the 18th century.

WHAT ARE DNA VACCINES?: DNA vaccines are a form of gene therapy in which just a few genes are extracted from the virus and injected into people. Unlike the standard process, which takes up to six months, DNA-based vaccines could be ready in less than three months. The downside is they have never been tested in full-blown clinical trials.

WHAT IS THE FLU: The flu is caused by the influenza virus, which targets the respiratory tract by binding to the surface of cells. Then the virus releases its genetic information (RNA) into the cell's nucleus to replicate itself. When the cell dies, those copies are released into the body, infecting other cells. Flu symptoms are unpleasant, but not life-threatening by themselves. However, the flu weakens the immune system, making the body vulnerable to more serious infections, such as pneumonia.

History Blurb

Many vaccines begin as a fluke. For example, Louis Pasteur discovered the notion of attenuated vaccines when old cholera cultures-forgotten on a lab bench-lost their virulence. Inoculated with the aged cultures, chickens unexpectedly developed immunity to a fowl form of cholera.

Similarly, DNA vaccines emerged as a surprise. In a 1990 experiment, researchers at publicly owned Vical Inc., then a biotech startup in San Diego, and the University of Wisconsin injected a control group of mice with "naked" viral DNA. Unexpectedly, the control mice began churning out significant amounts of viral proteins.

Vical presented its results to Merck, which decided to fund further DNA vaccine research. In 1993, a collaborating Merck/ Vical team reported that a DNA vaccine could indeed prevent influenza infection in mice (J.B. Ulmer et al., *Science*, **259**:1745-9, 1993).

Notice

What should a school do with outdated Chemicals?

Contact the EPA Schools Chemical Cleanout Campaign

www.epa.gov/sc3/

Calling all kids! Cornell University wants you to find and photograph ladybugs. John Losey, a professor of entomology at Cornell University, hopes children will help document ladybug populations around the country. Some native species are dwindling, while exotics are on the rise.

To participate in the project, go to the Lost Ladybug Project Web site or send an e-mail to ladybug@cornell.edu.

Ladybug Classification:

Kingdom: Animalia
Phylum: Arthropoda
Class: Insecta
Order: Coleoptera
Family: Coccinellidae
Genus: Hippodamia

Bio Biz Editor: Michael Mouat

GBTI: Is a collaboration of the Gwinnett and Athens Technical Colleges Biotechnology Programs

For information about High School Outreach & Equipment Loan programs contact:

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