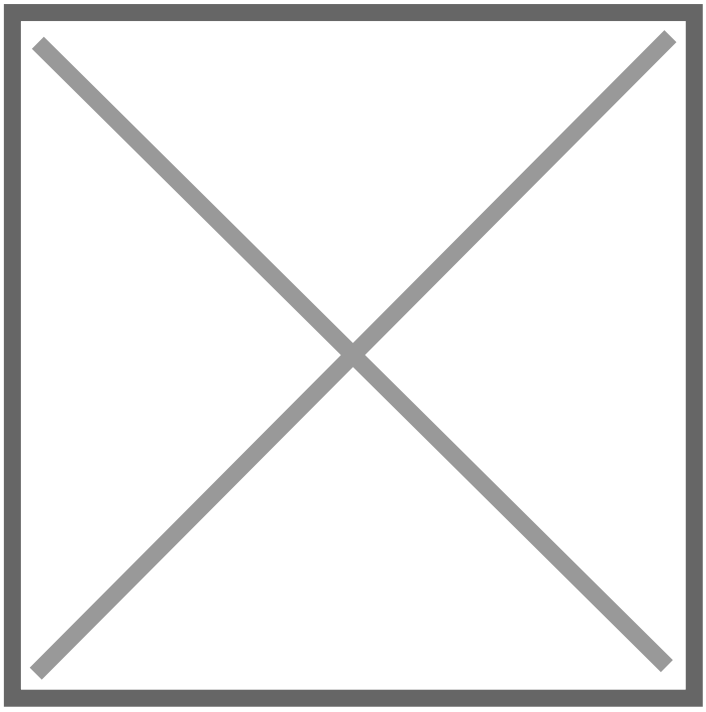
BioSpect
the business of Bi
24 years of leveraging the business of Bio
www.biospectrumindia.co

GSK

06 January 2006 | News



GSK's Cervarix induces higher immune response in adolescents

Cervarix, GlaxoSmithKline's candidate cervical cancer vaccine, formulated with the proprietary adjuvant AS04, induced antibody levels against the two most common cancer-causing HPV types (HPV 16/18) at least two-fold higher in 10-14 year-old adolescent girls, than in women 15-25 years old, a new study shows. The candidate vaccine for cervical cancer was also shown to induce antibodies in 100 per cent of volunteers in both age groups one month after completion of the course of vaccination. The vaccine in the present study was well tolerated and adverse event rates were similar in each age group. No vaccine-related serious adverse events were reported.

Recent positive findings have demonstrated that the AS04 adjuvant in the candidate vaccine induces a stronger, sustained immune response when compared to a formulation with aluminum salt alone in young adult women. In the study presented recently, the higher antibody levels observed in the pre-teen/adolescent group Ã¢â?¬â?? compared to that observed in women 15-25 years old Ã¢â?¬â?? are important as the elevated levels demonstrated in this younger age range may result in longer duration of protection. It would be beneficial to vaccinate adolescents against infection with cancer-causing HPV types 16/18 well before the start of sexual activity with a vaccine with sustained efficacy.

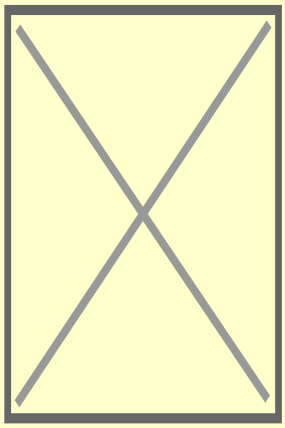
While GSK's goal is to provide a cervical cancer vaccine for women over a broad age range, the study was designed specifically to compare the immunogenicity and safety of the candidate vaccine in the younger 10-14 year-old group with the 15-25 year-old group. The results were presented at the Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC), in Washington DC, USA.

"Vaccination of pre-teen/adolescent girls against cancer-causing HPV before onset of sexual activity will be an important part of the overall strategy for cervical cancer prevention," said Anna-Barbara Moscicki, Professor of Pediatrics, University of California, San Francisco. "Prevention of high-risk HPV 16 and HPV 18 infection is key to reducing cervical cancer, and a prophylactic vaccine against these types of HPV is necessary to prevent infection in the first place. The higher levels of antibody titers seen in the vaccinated preteens/teens than the vaccinated adults offers encouraging evidence that in this age group, a stronger immune response could translate into longer protection. Ongoing studies should further demonstrate these findings."

HPV is the leading cause of cervical cancer. Although there are many oncogenic types of HPV, globally, approximately 70 per cent of all cervical cancer cases are associated with just these two cancer-causing types, HPV 16 and HPV 18. GlaxoSmithKline's cervical cancer vaccine candidate targeting HPV 16/18 is currently undergoing Phase III clinical trials involving more than 30,000 women worldwide. This was a Phase III, randomized, double-blinded trial conducted in multiple centers in Denmark, Estonia, Finland, Greece, the Netherlands and the Russian Federation.

Cervical cancer is a major global health problem, with nearly 500,000 new cases occurring each year worldwide. It is the second most common cancer Ã¢â?¬â?? and the third leading cause of cancer deaths Ã¢â?¬â?? in women worldwide. Each year an estimated 270,000 women die from the disease, and it is the leading cancer killer of women in the developing world.

Sneaking drugs into the brain may be possible



Clive Svendsen, professor of anatomy and director, Stem Cell Research Program.

One of the great challenges for treating Parkinson's Disease and other neurodegenerative disorders is getting medicine to the right place in the brain.

The brain is a complex organ with many different types of cells and structures, and it is fortified with a protective barrier erected by blood vessels and glial cells - the brain's structural building blocks - that effectively block the delivery of most drugs from the bloodstream.

Scientists have now found a novel way to sneak drugs past the blood-brain barrier by engineering and implanting progenitor brain cells derived from stem cells to produce and deliver a critical growth factor that has already shown clinical promise for treating Parkinson's Disease.

Clive Svendsen, a neuroscientist at the University of Wisconsin-Madison and his colleagues have demonstrated that engineered human brain progenitor cells, transplanted into the brains of rats and monkeys, can effectively integrate into the brain and deliver medicine where it is needed.

The Wisconsin team obtained and grew large numbers of progenitor cells from human fetal brain tissue. They then engineered the cells to produce a growth factor known as glial cell line-derived neurotrophic factor (GDNF). In some small but promising clinical trials, GDNF showed a marked ability to provide relief from the debilitating symptoms of Parkinson's. But the drug, which is expensive and hard to obtain, had to be pumped directly into the brains of Parkinson's patients for it to work, as it is unable to cross the blood-brain barrier.

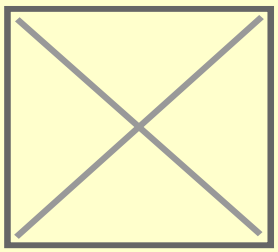
In an effort to develop a less invasive strategy to effectively deliver the drug to the brain, Svendsen's team implanted the GDNF secreting cells into the brains of rats and elderly primates. The cells migrated within critical areas of the brain and produced the growth factor in quantities sufficient for improving the survival and function of the defective cells at the root of Parkinson's.

In the new Wisconsin study, the GDNF-producing cells transplanted in the striatum, a large cluster of cells in the brain that controls movement, balance and walking, of animals with a condition like Parkinson's showed that not only a critical drug could be delivered to the right place but also the drug was delivered in a way that promoted its therapeutic potential. The researchers reported new nerve fiber growth in the striatum and the transport of the critical nerve growth factor GDNF from the striatum to the substantia niagra, the part of the brain that harbors the cells that produce dopamine. The transplanted cells survived and continued to produce GDNF in laboratory animals for up to three months.

One hurdle that needs to be overcome before such a technique could be attempted in human patients, said Svendsen, is developing a method to switch transplanted cells on or off and thus control their drug delivery capabilities. Working with engineered cells in culture, the Wisconsin group found they could switch the cells on and off using a second drug.

The new study, Svendsen argued, proves that progenitor cells - cells that can now be made in large quantities in the laboratory - can be crafted to help clinicians deliver drugs where they are needed most in the body. Delivering medicine to the brain, whose blood-brain barrier effectively excludes more than 70 percent of all drugs, would be an especially valuable use for the cells. Such a new method may be useful for treating a number of neurodegenerative diseases beyond Parkinson's, he added.

Tiny self-assembling cubes could carry medicine, cell therapy



(A) Optical image showing a collection of biocontainers. (B-D) Optical and Scanning electron microscopy images at different stages of the fabrication process: (B) the 2D precursor with electrodeposited surfaces, (C) the precursor with surfaces and hinges, and (D) the self-assembled biocontainer.

Johns Hopkins researchers have devised a self-assembling cubeshaped perforated container, no larger than a dust speck that could serve as a delivery system for medications and cell therapy.

The relatively inexpensive microcontainers can be mass-produced through a process that mixes electronic chip-making techniques with basic chemistry. Because of their metallic nature, the cubic container's location in the body could easily be tracked by magnetic resonance imaging.

The method of making these self-assembling containers and the results of successful lab tests involving the cubes were reported in a paper published in the December 2005 issue of the journal Biomedical Microdevices. In the tests, the hollow cubes housed and then dispensed microbeads and live cells commonly used in medical treatment.

David H Gracias, who led the team is an assistant professor in the Department of Biomolecular and Chemical Engineering in the Whiting School of Engineering at Johns Hopkins. He focuses on building micro and nanosystems with medical applications. He believes the microcontainers developed in his lab could someday incorporate electronic components that would allow the cubes to act as biosensors within the body or to release medication on demand in response to a remote-controlled radio frequency signal. Gracias is of the view that this is an entirely new encapsulation and delivery device that could lead to a new generation of 'smart pills.'

The long-term goal is to be able to implant a collection of these therapeutic containers directly at the site or an injury or an illness.

To make the self-assembling containers, Gracias and his colleagues begin with some of the same techniques used to make microelectronic circuits: thin film deposition, photolithography and electrodeposition. These methods produce a flat pattern of six squares, in a shape resembling a cross. Each square, made of copper or nickel, has small openings etched into it, so that

it eventually will allow medicine or therapeutic cells to pass through.

The researchers use metallic solder to form hinges along the edges between adjoining squares. When the flat shapes are heated briefly in a lab solution, the metallic hinges melt. High surface tension in the liquified solder pulls each pair of adjoining squares together like a swinging door. When the process is completed, they form a perforated cube. When the solution is cooled, the solder hardens again, and the containers remain in their box-like shape.

The tiny cubes are coated with a very thin layer of gold, so that they are unlikely to pose toxicity problems within the body. The microcontainers have not yet been implanted in humans or animals, but the researchers have conducted lab tests to demonstrate how they might work in medical applications.

Gracias and his colleagues used micropipettes to insert into the cubes a suspension containing microbeads that are commonly used in cell therapy. The lab team showed that these beads could be released from the cubes through agitation.

The researchers also inserted human cells, similar to the type used in medical therapy, into the cubes. A positive stain test showed that these cells remained alive in the microcontainers and could easily be released.

At the Johns Hopkins School of Medicine's In Vivo Cellular and Molecular Imaging Center, researcher Barjor Gimi and colleagues then used MRI technology to locate and track the metallic cubes as they moved through a sealed microscopic s-shaped fluid channel. This demonstrated that physicians will be able to use non-invasive technology to see where the therapeutic containers go within the body. Some of the cubes (those made mostly of nickel) are magnetic, and the researchers believe it should be possible to guide them directly to the site of an illness or injury.

The researchers are now refining the microdevices so that they have nanoporous surfaces. Gimi, whose research focuses on magnetic resonance microimaging of cell function, envisions the use of nanoporous devices for cell encapsulation in hormonal therapy. He also envisions biosensors mounted on these devices for non-invasive signal detection.