

Foreign patent applications are filed on selected inventions to extend market coverage for U.S. companies and may also be available for licensing.

**ADDRESSES:** Licensing information and copies of the U.S. patent applications listed below may be obtained by writing to Robert Benson at the Office of Technology Transfer, National Institutes of Health, 6011 Executive Boulevard, Suite 325, Rockville, Maryland 20852-3804 (telephone 301/496-7735 ext 267; fax 301/402-0220). A signed Confidential Disclosure Agreement will be required to receive copies of the patent applications.

#### **Polysaccharide-Protein Conjugates**

Shouson Szu, Rachel Schneerson, and John B. Robbins (NICHD), Serial No. 07/155,799, Patent Issued 20 Apr 93, U.S. Patent Number 5,204,098.

The invention concerns conjugates of pathogenic microorganism capsular polysaccharides and proteins useful as vaccines. The broadest claim reads: "A composition for enhancing the antibody response of a host comprising a capsular polysaccharide having carboxyl groups conjugated through a thio derivative of said carboxyl groups to a protein in a physiologically acceptable carrier." Applications are pending in Japan and Canada.

The conjugates having capsular polysaccharide from *Staphylococcus* have been exclusively licensed and are not available.

#### **Pertussis Toxin Used as a Carrier Protein With Non-Charged Saccharides in Conjugate Vaccines**

Rachel Schneerson, Lily Levi, and John B. Robbins (NICHD), Serial No. 07/932,960, Filed 21 Aug 92.

This invention concerns conjugates of non-charged capsular polysaccharides from pathogenic bacteria with pertussis toxin for use as vaccines. Bacteria having non-charged capsular polysaccharides include *Streptococcus pneumoniae* types 7 and 14. The invention is described in *Infection and Immunity* 60(9), 3528-3532, 1992. Mice injected with Pn14-pertussis toxin conjugates raised serum antibodies against both type 14 capsular polysaccharide and pertussis toxin. Also claimed are methods of synthesis, immunization methods and vaccines. The application has been foreign filed, PCT/US93/07732.

#### **Immunogenic Polysaccharide-Protein Conjugates Containing Poly Alpha (2-8), Alpha (2-9) Neunac Capsular Polysaccharides**

Rachel Schneerson, John B. Robbins, and Sarvamangala Devi (NICHD), Filed

12 Mar 91 (priority date), Serial No. 08/153,263 (CON of 07/667,170).

The invention concerns conjugates of *E. coli* K92 capsular polysaccharide and carrier proteins, such as tetanus toxoid. The conjugates have been shown to raise antibodies that react with Group B and Group C *Neisseria meningitis* and *E. coli* K1 capsular polysaccharides. The conjugate is a potential vaccine against Group B meningitis. Infant rats have been protected from lethal injections of *E. coli* K1 using antisera raised against the conjugates. The invention is described in P.N.A.S. 88, 7175-7179 (1991). Applications are pending in Canada, Australia, Japan and Europe.

#### **Detoxified LPS-Cholera Toxin Conjugate Vaccine for Prevention of Cholera**

Shouson Szu, John B. Robbins, and Rajesh K. Gupta (NICHD), Filed 16 Jan 92 (priority date), Serial No. 08/171,188 (CON of 07/821,453).

The invention concerns a conjugate of detoxified lipopolysaccharide (LPS) from *V. cholera* and proteins, potentially useful as a cholera vaccine. The LPS is detoxified by treatment with anhydrous hydrazine, resulting in a detoxified LPS that is less toxic and more immunogenic than cholera LPS's detoxified by other means. The invention has been foreign filed, PCT/US93/00253. In a phase I clinical trial, 38 volunteers were injected with a conjugate of the detoxified LPS and tetanus toxoid. The conjugate vaccines of the invention elicit higher levels of anti-LPS IgG antibodies than whole cell vaccine. IgG can penetrate the intestinal membrane to reach the gut, and, thus, is the primary reason for protection. The serum from the volunteers is vibriocidal for at least nine months; tests are continuing. In the field trials of the whole cell vaccine, protection is correlated with the level of serum vibriocidal antibodies.

#### **Synthesis of Typhoid Fever Vaccine From a Plant or Fruit Polysaccharide**

Shouson Szu and Slavomir Bystrisky (NICHD), Filed 17 Oct 94, Serial No. 08/323,918.

The invention is a synthetic *Salmonella typhi* capsular polysaccharide, Vi, made by chemically modifying fruit pectin. The synthetic Vi is useful as a component of a subunit vaccine for typhoid fever. The synthetic Vi is made by acetylating the C<sub>2</sub> and C<sub>3</sub> hydroxyls of the galacturonate subunits of pectin. A vaccine is made by conjugating the synthetic Vi to a carrier protein, such as tetanus toxoid. The synthetic Vi-tetanus toxoid conjugates were shown to react with *S. typhi*

antisera, and when injected into mice raised antibodies reactive with natural *S. typhi* Vi antigen. The conjugates were able to elicit a booster effect. Antibodies or antisera raised against the conjugates and useful for diagnostic purposes and for passive immunization are also part of the invention. The invention is described in *Infection & Immunity* 62, 5545-5549 (1994).

#### **Glucuronoxylomannan-Protein Conjugates of Cryptococcus Neoformans**

Sarvamangala Devi, Rachel Schneerson, John E. Bennett, and John B. Robbins (NICHD), Filed 16 Sep 91 (priority date), Serial No. 08/231,444 (CON of 07/760,143).

*Cryptococcus neoformans* is an encapsulated fungus that causes systemic infections in humans, particularly in those who are immunocompromised. The incidence of infection is high in AIDS patients. The invention concerns conjugates of the glucuronoxylomannan (GXM) capsular polysaccharide of *C. neoformans* and carrier proteins such as tetanus toxoid or cholera toxin. These conjugates are potential vaccines to be given to people at high risk of HIV infection. Another facet of the invention is passive immunization, a therapeutic treatment, using antisera or antibodies raised against the conjugates. Passive protection has been demonstrated in mice. Human clinical trials are ongoing. The basic invention is described in *Infection & Immunity* 59, 3700-3707 (1991).

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**Barbara M. McGarey,**

*Deputy Director, Office of Technology Transfer.*

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#### **National Cancer Institute; Notice of Meetings**

Pursuant to Pub. L. 92-463, notice is hereby given of the meetings of the National Cancer Institute for February, March and April 1995.

These meetings will be open to the public to discuss administrative details or other issues relating to committee activities as indicated in the notice and for the review of concepts being considered for funding. Attendance by the public will be limited to space available.

These meetings will be closed to the public as indicated below in accordance with the provisions set forth in secs. 552b(c)(4) and 552b(c)(6), Title 5, U.S.C. and sec. 10(d) of Pub. L. 92-463, for the