Monoclonal Antibodies Against Orthopoxviruses

Description of Technology: Concerns that variola (smallpox) virus might be used as a biological weapon have led to the recommendation of widespread vaccination with vaccinia virus. While vaccination is generally safe and effective for prevention of smallpox, it is well documented that various adverse reactions in individuals have been caused by vaccination with existing licensed vaccines. Vaccinia immune globulin (VIG) prepared from vaccinated humans has historically been used to treat adverse reactions arising from vaccinia immunization. However, VIG lots may have different potencies and carry the potential to transmit other viral agents.

Chimpanzee Fabs against the B5 and A33 outer extracellular membrane proteins of vaccinia virus were isolated and converted into complete mAbs with human gamma1 heavy chain constant regions. The two mAbs displayed high binding affinities to B5 and A33. The mAbs inhibited the spread of vaccinia virus as well as variola virus (the causative agent of smallpox) *in vitro,* protected mice from subsequent intranasal challenge with virulent vaccinia virus, protected mice when administered 2 days after challenge, and provided significantly greater protection than that afforded by VIG.

Application: Prophylactics or therapeutics against orthopoxviruses.

Development Status: Preclinical studies have been performed.

Inventors: Zhaochun Chen, Robert Purcell, Suzanne Emerson, Patricia Earl, Bernard Moss (NIAID).

Publications:

1. Z Chen *et al.* Chimpanzee/human mAbs to vaccinia virus B5 protein neutralize vaccinia and smallpox viruses and protect mice against vaccinia virus. Proc Natl Acad Sci USA. 2006 Feb 7; 103(6): 1882–1887.

2. Z Chen *et al.* Characterization of chimpanzee/human monoclonal antibodies to vaccinia virus A33 glycoprotein and its variola virus homolog in vitro and in a vaccinia virus mouse protection model. J Virol. 2007 Sep; 81(17): 8989–8995.

Patent Status: U.S. Patent Application No. 12/142,594 filed 19 Jun 2008, claiming priority to 22 Dec 2005 (HHS Reference No. E–145–2004/3–US–02).

Licensing Status: Available for exclusive or non-exclusive licensing.

Licensing Contact: Peter A. Soukas, J.D.; 301–435–4646; *soukasp@mail.nih.gov.*

Collaborative Research Opportunity: The National Institute of Allergy and Infectious Diseases, Laboratory of Infectious Diseases, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize Chimpanzee/human neutralizing monoclonal antibodies against orthopoxviruses. Please contact Dr. Robert Purcell at 301–496–5090 for more information.

Methods for Conjugation of Oligosaccharides or Polysaccharides to Protein Carriers Through Oxime Linkages via 3-Deoxy-D-Manno-Octulsonic Acid

Description of Technology: This technology comprises new methods for the conjugation of O-specific polysaccharides/oligosaccharides (O–SP/OS) derived from bacterial lipooligosaccharides/ lipopolysaccharides (LOS/LPS), after their cleavage from Lipid A, to carrier proteins, to serve as potential vaccines. Conjugation is performed between the carbonyl group on the terminal reducing end of the saccharide and the aminooxy group of a bifunctional linker bound further to the protein.

The inventors have carried out the reaction under mild conditions and in a short time resulting in binding 3-deoxy-D-manno-octulosonic acid (KDO) on the saccharide to the protein. These conjugates preserve the external non-reducing end of the saccharide, are recognized by antisera, and induce immune responses in mice to both conjugate components (i.e., the OS and the associated carrier protein).

Application: Cost effective and efficient manufacturing of conjugate vaccines.

Inventors: Joanna Kubler-Kielb (NICHD), Vince Pozsgay (NICHD), Gil Ben-Menachem (NICHD), Rachel Schneerson (NICHD), *et al.*

Patent Status: PCT Application No. PCT/US2007/016373 filed 18 Jul 2007, which published as WO 2008/013735 on 31 Jan 2008; claiming priority to 21 Jul 2006 (HHS Reference No. E–183–2005/0–PCT–02).

Licensing Status: Available for exclusive or non-exclusive licensing.

Licensing Contact: Peter A. Soukas, J.D.; 301–435–4646; *soukasp@mail.nih.gov.*

Dated: October 14, 2008.

Richard U. Rodriguez,

Director, Division of Technology Development and Transfer, Office of Technology Transfer, National Institutes of Health.

[FR Doc. E8–25219 Filed 10–22–08; 8:45 am]

BILLING CODE 4140–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Government-Owned Inventions; Availability for Licensing

AGENCY: National Institutes of Health, Public Health Service, HHS.

ACTION: Notice.

SUMMARY: The inventions listed below are owned by an agency of the U.S. Government and are available for licensing in the U.S. in accordance with 35 U.S.C. 207 to achieve expeditious commercialization of results of federally funded research and development. Foreign patent applications are filed on selected inventions to extend market coverage for 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 the indicated licensing contact at the Office of Technology Transfer, National Institutes of Health, 6011 Executive Boulevard, Suite 325, Rockville, Maryland 20852–3804; telephone: 301–496–7057; fax: 301–402–0220. A signed Confidential Disclosure Agreement will be required to receive copies of the patent applications.

Vaccine for Protection Against *Shigella sonnei* Disease

Description of Technology: Shigellosis is a global human health problem. Transmission usually occurs by contaminated food and water or through person-to-person contact. The bacterium is highly infectious by the oral route, and ingestion of as few as 10 organisms can cause an infection in volunteers. An estimated 200 million people worldwide suffer from shigellosis, with more than 650,000 associated deaths annually. A recent CDC estimate indicates the occurrence of over 440,000 annual shigellosis cases in the United States alone, approximately eighty percent (80%) of which are caused by *Shigella sonnei. Shigella sonnei* is more active in developed countries. *Shigella* infections are typically treated with a course of antibiotics. However, due to the emergence of multidrug resistant *Shigella* strains, a safe and effective vaccine is highly desirable. No vaccines against *Shigella* infection currently exist. Immunity to *Shigellae* is mediated largely by immune responses directed against the serotype specific O-polysaccharide. Claimed in the invention are compositions and methods for inducing an immunoprotective response against *S.*

sonnei. Specifically, an attenuated bacteria capable of expressing an *S. sonnei* antigen comprised of the *S. sonnei* form I O-polysaccharide expressed from the *S. sonnei* rfb/rfc gene cluster is claimed. The inventors have shown that the claimed vaccine compositions showed one hundred percent (100%) protection against parenteral challenge with virulent *S. sonnei* in mice.

Inventors: Dennis J. Kopecko (FDA), De-Qi Xu (NIDCR), John O. Cisar (NIDCR).

Patent Status: U.S. Patent Application No. 10/346,706 filed 15 Jan 2003, claiming priority to 16 Jan 2002 (HHS Reference No. E–210–2001/0–US–02)

Licensing Contact: Peter A. Soukas, J.D.; 301–435–4646; *soukasp@mail.nih.gov*.

Methods for Preparing Complex Multivalent Immunogenic Conjugates

Description of Technology: Claimed in this application are novel methods for preparing complex multivalent immunogenic conjugates and conjugate vaccines. The multivalent conjugates and conjugate vaccines are synthesized by conjugating mixtures of more than one polysaccharide at a desired ratio of the component polysaccharides to at least one carrier protein using hydrazide chemistry. Because of the high efficiency of hydrazide chemistry in conjugation, the polysaccharides are effectively conjugated to the carrier protein(s) so that the resulting complex synthesized vaccine conjugate products, without requiring tedious and complicated purification procedures such as chromatography and/or ammonium sulfate precipitation, are efficacious in inducing antibodies in mice against each component polysaccharide. The methods claimed in this application simplify the preparation of multivalent conjugate vaccines by utilizing simultaneous conjugation reactions in a single reaction mixture or batch that includes at least two immunogenic-distinct polysaccharides. This single-batch simultaneous reaction eliminates the need for multiple parallel synthesis processes for each polysaccharide vaccine conjugate component as employed in conventional methods for making multivalent conjugate vaccines.

Application: Cost effective and efficient manufacturing of conjugate vaccines.

Inventors: Che-Hung Robert Lee (CBER/FDA).

Patent Status: PCT Application No. PCT/US2007/006627 filed 16 Mar 2007, which published as WO 2007/109129 on 27 Sep 2007 (HHS Reference No. E–085–2005/0–PCT–02); U.S. Patent Application filed 15 Sep 2008 (HHS Reference No. E–085–2005/0–US–03).

Licensing Status: Available for exclusive or non-exclusive licensing. The technology is not available for licensing in the field of use of multivalent meningitis vaccines.

Licensing Contact: Peter A. Soukas, J.D.; 301–435–4646; *soukasp@mail.nih.gov*.

A Method With Increased Yield for Production of Polysaccharide-Protein Conjugate Vaccines Using Hydrazide Chemistry

Description of Technology: Current methods for synthesis and manufacturing of polysaccharide-protein conjugate vaccines employ conjugation reactions with low efficiency (about twenty percent). This means that up to eighty percent of the added activated polysaccharide (PS) is lost. In addition, inclusion of a chromatographic process for purification of the conjugates from unconjugated PS is required.

The present invention utilizes the characteristic chemical property of hydrazide groups on one reactant to react with aldehyde groups or cyanate esters on the other reactant with an improved conjugate yield of at least sixty percent. With this conjugation efficiency the leftover unconjugated protein and polysaccharide would not need to be removed and thus the purification process of the conjugate product can be limited to diafiltration to remove the by-products of small molecules. The new conjugation reaction can be carried out within one or two days with reactant concentrations between 1 and 25 mg/mL at PS/protein ratios from 1:2 to 3:1, at temperatures between 4 and 40 degrees Centigrade, and in a pH range of 5.5 to 7.4, optimal conditions varying from PS to PS.

Application: Cost effective and efficient manufacturing of conjugate vaccines.

Inventors: Che-Hung Robert Lee and Carl E. Frasch (CBER/FDA).

Patent Status: U.S. Patent Application No. 10/566,899 filed 01 Feb 2006, claiming priority to 06 Aug 2003 (HHS Reference No. E–301–2003/0–US–10); U.S. Patent Application No. 10/566,898 filed 01 Feb 2006, claiming priority to 06 Aug 2003 (HHS Reference No. E–301–2003/1–US–02); International rights available.

Licensing Status: Available for non-exclusive licensing.

Licensing Contact: Peter A. Soukas, J.D.; 301–435–4646; *soukasp@mail.nih.gov*.

Dated: October 14, 2008.

Richard U. Rodriguez,

Director, Division of Technology Development and Transfer, Office of Technology Transfer, National Institutes of Health.

[FR Doc. E8–25220 Filed 10–22–08; 8:45 am]

BILLING CODE 4140–01–P

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Gene Expression Profiling for Prognosis of a Non-Hodgkin Lymphoma

Description of Technology: Diffuse large B cell lymphoma (DLBCL) is a quickly progressing cancer of the white blood cells, which is the most common type of non-Hodgkin lymphoma. Most commonly, DLBCL is treated aggressively with combination chemotherapy referred to as R–CHOP. Fortunately, with this treatment more than half of these patients can be cured or show remission. However, other patients do not respond to treatment and succumb to the disease. Therefore, it would be helpful to predict which patients are likely not to respond to R–CHOP and would benefit from alternate treatments.

This invention provides gene microarrays and method of use claims for a survival predictor calculated for DLBCL patients undergoing combination therapy. By measuring the