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

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.

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

gene expression of genes from cancer biopsies it is possible to identify patients that are unlikely to be cured by R–CHOP and could benefit from alternative treatments like anti-angiogenic drugs.

Applications: Diagnostic test for managing treatment of DLBCL patients; Design and analysis of clinical trials in DLBCL.

Market: About 16,000 new cases per year of DLBCL in U.S.; Affects mostly the middle-aged but it can afflict children.

Development Status: Clinical data is available.

Inventors: Louis M. Staudt (NCI).

Publication: A Rosenwald *et al.* The use of molecular profiling to predict survival after chemotherapy for diffuse large-B-cell lymphoma. N Engl J Med. 2002 Jun 20;346(25):1937–1947.

Patent Status: U.S. Provisional Application No. 61/059,678 filed 06 Jun 2008 (HHS Reference No. E–256–2008/0–US–01).

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

Licensing Contact: Sabarni Chatterjee, PhD; 301–435–5587; *stansbej@mail.nih.gov*.

A Simple Genetic Test for Kidney Disease

Description of Technology: This technology relates to methods of diagnosing a predisposition to diseases that cause chronic kidney disease (CKD) and end-stage kidney disease (ESKD). Variations in a gene, non-muscle myosin IIA (MYH9), are associated with 79% of the risk of focal segmental glomerulosclerosis (FSGS), the disease that causes ESKD, in African Americans with HIV, and 56% of African Americans as a whole. The variants are also associated with a 2–3 fold increased risk for end-stage kidney disease (ESKD) associated with hypertension. The variations are also present among European Americans, however they are less common.

A simple genetic screening test has been developed that identifies single nucleotide polymorphisms (SNP) and haplotypes in the non-muscle myosin gene MYH9. These variants confer genetic risk for the following kidney diseases: FSGS, collapsing glomerulopathy, HIV-associated nephropathy, hypertensive kidney disease, sickle cell nephropathy, lupus nephropathy, and possibly other kidney diseases.

Applications:

- Facilitate rigorous population (i.e. all individuals) screening for early kidney disease.
- Screen individuals with hypertension, to identify individuals who might benefit from more intensive therapy.
- Screen kidney donors for *MYH9* risk alleles to improve renal allograft survival.
- Screen patients with sickle cell disease to identify those at increased risk for CKD.
- Screen patients with lupus nephritis to identify those at increased risk for CKD.
- Screen patients with HIV–1 infection to identify those at increased risk for kidney disease.
- Screen patient with other kidney diseases, including idiopathic and secondary kidney disease, where MYH9 mutations may alter the propensity to develop kidney disease or the rate of progressive renal function decline.
- Pharmaceutical agents might be developed that reverse the susceptibility phenotype, reducing propensity to CKD. These agents might alter non-muscle myosin IIA function or its interactions with critical molecular partners.

Market: An estimated 26 millions have CKD, with impaired glomerular filtration rate and approximately 100,000 individuals in the United States develop ESKD every year. The lifetime risk for ESKD is 7.5% of individuals of African American descent and 2.1% for individuals of European descent. Early identification of individuals with MYH9 variants who are at increased risk for CKD might substantially reduce morbidity and mortality in this population, as impaired kidney function is associated with death from cardiovascular disease even in patients who do not progress to ESKD.

Development Status: Early-stage development for clinical applications, including diagnostic testing and therapeutic intervention.

Inventors: Cheryl A. Winkler (SAIC/NCI), George W. Nelson (SAIC/NCI), Jeffrey B. Kopp (NIDDK), Michael W. Smith (SAIC/NCI), Randall C. Johnson (SAIC/NCI).

Publication: JB Kopp *et al.* MYH9 is a major-effect risk gene for focal segmental glomerulosclerosis. Nat Genet. 2008 Oct;40(10):1175–1184.

Patent Status: U.S. Provisional Application No. 61/024,863 filed 30 Jan 2008 (HHS Reference No. E–090–2008/0–US–01); U.S. Provisional Application No. 61/095,590 filed 09 Sep 2008 (HHS Reference No. E–090–2008/1–US–01).

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

Licensing Contact: Steve Standley, PhD; 301–435–4074; *sstand@mail.nih.gov*.

Collaborative Research Opportunity: The National Cancer Institute, Laboratory of Genomic Diversity, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize genetic testing for MYH9. Please contact John D. Hewes, PhD at 301–435–3121 or *hewesj@mail.nih.gov* for more information.

Nanoparticles for Imaging and Treatment of Brain Tumors

Description of Technology: Malignant brain tumors, whether arising within the brain or invading the brain from other tissues, are difficult to treat. Conventional chemotherapy drugs do not reach therapeutic levels in brain tumor tissue, and do not remain in brain tumor tissue for long enough to enter brain tumor cells and kill them. As a consequence, these chemotherapy drugs are not effective at treating malignant brain tumors growing in patients, even though these drugs are effective at killing brain tumor cells growing in culture.

This invention claims that intravenously administered functionalized polyamidoamine (PAMAM) dendrimers of certain sizes can selectively cross the blood-brain barrier (BBB) of malignant brain tumors, and can accumulate over time within individual brain tumor cells. Gadolinium and fluorescent probe conjugated dendrimers with these properties can be used for simultaneous magnetic resonance and fluorescence imaging of brain tumor cells. Since these nanoparticles possess numerous additional surface functional groups, in addition to being useful for multi-modality imaging, functionalized dendrimers can also be useful for the simultaneous delivery of cytotoxic drugs and inhibitors of tumor cell metabolic or migratory pathways.

Advantages:

- Intravenously administered nanoparticles selectively cross the BBB of brain tumors and accumulate within brain tumor cells but not normal brain cells.
- Nanoparticles accumulate in and are retained in brain tumor tissue for long enough to result in the effective uptake of nanoparticles by individual brain tumor cells.
- Nanoparticle size can be adjusted to achieve the desired particle blood half-life.
- A wide variety of agents can be attached to the functional groups on the nanoparticle exterior.

Applications:

• Anatomic and metabolic imaging of brain and spinal cord tumors for diagnostic and therapeutic purposes.
• Intravenous treatment of brain and spinal cord tumors.
• Imaging of intravenous drug delivery to brain and spinal cord tumors.
• Potential to be used for imaging and treatment of other neurological disorders in which the BBB becomes porous.

Market: In 2008, it is estimated that malignant tumors of the brain and spinal cord will account for about 1.5% of all cancers and 2.3% of all expected cancer-related deaths.

Development Status: Early stage development; Pre-clinical data available.

Inventor: Hemant Sarin (CC).

Patent Status: U.S. Provisional Application No. 61/055,328 filed 22 May 2008 (HHS Reference No. E–063–2008/0–US–01).

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

Licensing Contact: Surekha Vathyam, PhD; 301–435–4076; *vathyams@mail.nih.gov*.

Induced Internalization of Surface Receptors

Description of Technology: Cell-surface receptors are responsible for the biological activities of many molecules. Specific ligands bind to them, causing the cell-surface receptors to internalize or bring the receptor and ligand inside the cell. A number of diseases, including cancer, metabolic disorders, and viral infections are known to require the expression of cell-surface receptors for critical pathogenetic steps. This has prompted significant research efforts towards the development of pharmaceutical agents that block the signals from cell-surface receptors. While this current research shows great promise, there is a strong need for new therapeutic strategies that utilize the mechanistic properties of cell-surface receptors.

This technology describes a strategy for artificially inducing the internalization of surface receptors, and thereby blocking the effects of the ligands associated with that receptor. This method employs bifunctional ligands that bind to both a scavenger receptor and a target receptor. As proof of concept, the inventors Drs. Narazaki and Tosato have shown that a ligand capable of binding to the scavenger receptor SREC–1 and the neuropilin-1 receptor NRP1 induces the internalization of NRP1 and inhibits NRP1 signaling. The inventors propose that this strategy can be used to inhibit signaling from any target receptor if an appropriate bifunctional ligand is used. For example, the concept could be expanded to other receptors, such as HDL and LDL receptors. Likewise the bifunctional ligand could include specific antibodies or modified ligands that recognize cell surface receptors of biological importance. Accordingly, this approach could be used to limit tumor angiogenesis, limit tumor growth, block metastasis formation, block inflammation, block viral infection, and treat just about any disease where we identify a cell surface receptor as the molecular basis for disease.

Applications:
• Method of inducing the internalization of target receptors.
• Inhibiting diseases or conditions associated with target receptors, such as HIV infection, cancer, or angiogenesis.
• Treating diseases or conditions associated with target receptors, such as cancer, viral infections, or HIV infections.

Market:
• Cancer is one of the leading causes of death in the United States and it is estimated that there will be more than half a million deaths caused by cancer in 2008.
• It is estimated that over one million people in the U.S. are living with HIV/AIDS and approximately 50,000 new infections occur each year.

Development Status: The technology is currently in the pre-clinical stage of development.

Inventors: Masashi Narazaki and Giovanna Tosato (NCI).

Patent Status: U.S. Provisional Application No. 61/023,397 filed 24 Jan 2008 (HHS Reference No. E–250–2007/0–US–01).

Licensing Status: Available for licensing.

Licensing Contact: Whitney A. Hastings; 301–451–7337; *hastingw@mail.nih.gov*.

Collaborative Research Opportunity: The National Cancer Institute, Laboratory of Cellular Oncology, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize the technology aimed at promoting selective receptor internalization as a means to neutralize ligand function and receptor signaling. Please contact John D. Hewes, PhD at 301–435–3121 or *hewesj@mail.nih.gov* for more information.

Methods of Determining the Prognosis of an Adenocarcinoma

Description of Technology: Available for licensing and commercial development is a novel method for determining the prognosis of a subject with adenocarcinoma in an organ, such as the lung, and to aid in the selection of a specific therapeutic regimen. Lung adenocarcinoma (AC) is the predominant histological subtype of lung cancer, which is the leading cause of cancer deaths worldwide. The risk of metastasis remains substantial in AC patients, even when a curative resection of early-stage AC is performed. The prognosis includes the determination of the likelihood of survival, the likelihood of metastasis, or both. The method includes quantization of the expression of a plurality of Th1 and Th2 cytokines of interest in the adenocarcinoma and in non-cancerous tissue in the organ. Altered expression of one or more of the Th1 and Th2 cytokines in the adenocarcinoma as compared to the non-cancerous tissue determines the prognosis for the subject. The method is capable of distinguishing patients with lymph node metastasis versus those with short term survival. Furthermore, methods are provided for evaluating the effectiveness of anti-cancer agents.

Applications: Prognosis of adenocarcinoma, aid in the selection of specific therapeutic regimens and evaluation of the effectiveness of anti-cancer agents.

Development Status: The technology is in early stage of development.

Inventors: Curtis C. Harris, Masahiro Seike, Xin Wei Wang (NCI).

Patent Status: PCT Application No. PCT/US2007/073637 filed 16 Jul 2007, which published as WO 2008/009028 on 17 Jan 2008; claiming priority to 14 Jul 2006 (HHS Reference No. E–263–2006/1–PCT–01).

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

Licensing Contact: Susan Ano, PhD; 301–435–5515; *anos@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. E8–25221 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.