[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.

FOR FURTHER INFORMATION: 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.

Therapeutic Hepatitis C Virus Antibodies

Description of Technology: Therapeutic antibodies against Hepatitis C Virus (HCV) have not been very effective in the past and there is evidence that this may result in part from interfering antibodies generated during infection that block the action of neutralizing antibodies. These neutralizing antibodies prevent HCV infection of a host cell.

The subject technologies are monoclonal antibodies against HCV that can neutralize different genotypes of HCV. Both antibodies bind to the envelope (E2) protein of HCV found on the surface of the virus. One of the monoclonal antibodies neutralizes HCV genotype 1a, the most prevalent HCV strain in the U.S., infection and in vitro data show that it is not blocked by interfering antibodies. The second antibody binds a conserved region of E2 and can cross neutralize a number of genotypes including genotypes 1a and 2a. The monoclonal antibodies have the potential to be developed either alone or in combination into therapeutic antibodies that prevent or treat HCV infection. These antibodies may be particularly suited for preventing HCV re-infection in HCV patients who undergo liver transplants; a population of patients that is especially vulnerable to the side effects of current treatments for HCV infection.

Potential Commercial Applications: Therapeutic antibodies for the prevention and/or treatment of HCV infection.

Competitive Advantages:

• Therapeutic antibodies have generally fewer side effects than current treatments for HCV infection.

• Potential to be developed into an alternative treatment for HCV infected liver transplant patients, who often cannot tolerate the side effects of current drug treatments.

Development Stage:

• Early-stage

• Pre-clinical

• In vitro data available

Inventors: Stephen M. Feinstone, Hongying Duan, Pei Zhang, Marian E. Major, Alla V. Kachko (all of FDA)

Publications:

1. Kachko A, et al. New neutralizing antibody epitopes in hepatitis C virus envelope glycoproteins are revealed by dissecting peptide recognition profiles. Vaccine. 2011 Dec 9;30(1):69-77. [PMID 22041300]

2. Duan H, et al. Amino acid residue-specific neutralization and nonneutralization of hepatitis C virus by monoclonal antibodies to the E2 protein. J Virol. 2012 Dec;86(23):12686-94. [PMID 22973024]

Intellectual Property:

• HHS Reference No. E-002-2012/0 — U.S. Provisional Patent Application No. 61/648,386 filed 17 May 2012

• HHS Reference No. E-167-2012/0 — International PCT Application No. PCT/US12/62197 filed 26 Oct 2012

Licensing Contact: Kevin W. Chang, Ph.D.; 301-435-5018; changke@mail.nih.gov

Live Attenuated Rubella Vector to Express Vaccine Antigens

Description of Technology: Live attenuated viruses make potent and effective vaccines. Despite the urgent need for an HIV vaccine, this approach has not been feasible because it has not been possible to attenuate the virus reliably and guarantee vaccine safety. Instead, live viral vectors have been proposed that could present HIV vaccine antigens in the most immunogenic way, in the context of an active infection.

The inventors have adapted a rubella vaccine strain as a vector to express HIV and SIV antigen and tested the effect of insert size and composition on vector stability and viral titer. The inventors have identified an acceptor site in the rubella nonstructural gene region, where foreign genes can be expressed as a fusion protein with the nonstructural protein P150 without affecting essential viral functions. The inserts were expressed as early genes of rubella, under control of the rubella genomic promoter. At this site, HIV and SIV antigens were expressed stably for at least seven passages, as the rubella vectors reached high titers. Rubella readily infects rhesus macaques, and these animals will provide an ideal model for testing the new vectors for replication in vivo, immunogenicity and protection against SIV or SHIV challenge.

Potential Commercial Applications:

• HIV vaccines

• Bivalent rubella

• Research tools

Competitive Advantages:

• Ease of manufacture

• Low cost vaccines

Development Stage:

• Pre-clinical

• In vitro data available

• In vivo data available (animal)

Inventors: Ira Berkower and Konstantin Virnik (FDA/CBER)

Publication: Virnik K, et al. Live attenuated rubella viral vectors stably express HIV and SIV vaccine antigens while reaching high titers. Vaccine. 2012 Aug 10;30(37):5453-8. [PMID 22776214]

Intellectual Property:

• HHS Reference No. E-004-2012/0 — US Application No. 61/621,394, filed 6 Apr 2012

• HHS Reference No. E-004-2012/1 — US Application No. 61//642,333 filed 3 May 2012

Related Technologies:

• HHS Reference No. E-156-2008/0 — US Application No. 13/501,893 filed 13 Apr 2012, claiming priority to 16 Oct 2009

• HHS Reference No. E-291-2008/0 — US Application No. 13/057,414 filed 03 Feb 2011, claiming priority to 04 Aug 2008

• HHS Reference No. E-299-2008/0 — US Application No. 12/714,085 filed 26 Feb 2010, claiming priority to 26 Feb 2009

Licensing Contact: Peter A. Soukas; 301-435-4646; soukasp@mail.nih.gov

DNA Promoters and Anthrax Vaccines

Description of Technology: Currently, the only licensed vaccine against anthrax in the United States is AVA BioThrax®, which, although efficacious, suffers from several limitations. This vaccine requires six injectable doses over 18 months to stimulate protective immunity, requires a cold chain for storage, and in many cases has been associated with adverse effects.

This application claims a modified *B. anthracis* protective antigen (PA) gene for optimal expression and stability, linked it to an inducible promoter for maximal expression in the host, and fused to the secretion signal of the *Escherichia coli* alpha-hemolysin protein (HlyA) on a low-copy-number plasmid. This plasmid was introduced into the licensed typhoid vaccine strain, *Salmonella enterica* serovar Typhi strain Ty21a, and was found to be genetically stable. Immunization of mice with three vaccine doses elicited a strong PA-specific serum immunoglobulin G response with a geometric mean titer of 30,000 (range, 5,800 to 157,000) and lethal-toxin-neutralizing titers greater than 16,000. Vaccinated mice demonstrated 100% protection against a lethal intranasal challenge with aerosolized spores of *B. anthracis* 7702.

Potential Commercial Applications: Anthrax vaccines, therapeutics and diagnostics.

Competitive Advantages:

• Vector is well-characterized.

• Simple manufacturing process.

• Potential low-cost vaccine.

• Oral vaccine – avoids needles and can be administered rapidly during emergencies.

• Temperature-stable manufacturing allows for vaccine distribution without refrigeration.

Development Stage:

• Pre-clinical

• In vitro data available

• In vivo data available (animal)

Publication: Osorio M, et al. Anthrax protective antigen delivered by Salmonella enterica serovar Typhi Ty21a protects mice from a lethal anthrax spore challenge. Infect Immun. 2009 Apr;77(4):1475-82. [PMID: 19179420]

Intellectual Property: HHS Reference No. E-344-2003/1 —

• EP Application No. 04809769.5 filed 20 Sep 2004

• US Patent No. 7,758,855 issued 20 Jul 2010

• US Patent No. 8,247,225 issued 21 Aug 2012

• US Application No. 13/551,168 filed 17 Jul 2012

Licensing Contact: Peter A. Soukas; 301-435-4646; soukasp@mail.nih.gov

Collaborative Research Opportunity: The FDA Center for Biologics Evaluation and Research is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize oral anthrax vaccine. For collaboration opportunities, please contact Dr. Dennis J. Kopecko at dennis.kopecko@fda.hhs.gov or 301-661-8839.

Live Oral *Shigella dysenteriae* Vaccine

Description of Technology: This application claims a *Salmonella* typhi Ty21a construct comprising a *Shigella dysenteriae* O-specific polysaccharide (O-Ps) inserted into the Salmonella typhi Ty21a chromosome, where heterologous *Shigella dysenteriae* serotype 1 O-antigen is stably expressed together with homologous *Salmonella* typhi O-antigen. The constructs of this invention elicit immune protection against virulent *Shigella dysenteriae* challenge, as well as *Salmonella* typhi challenge. Also claimed in this application are methods of making the constructs of this invention and methods for inducing an immune response.

Shigella cause millions of cases of dysentery every year, which result in about seven hundred thousand deaths worldwide. *Shigella dysenteriae* serotype 1, one of about forty serotypes of *Shigella*, causes a more severe disease with a much higher mortality rate than other serotypes. There are no licensed vaccines available for protection against *Shigella*. The fact that many isolates exhibit multiple antibiotic resistance complicates the management of dysentery infections.

Potential Commercial Applications:

• One component of a multivalent anti-shigellosis vaccine under development.

• Shigella vaccines, therapeutics and diagnostics.

Competitive Advantages:

• Vector is well-characterized.

• Simple manufacturing process.

• Potential low-cost vaccine.

• Oral vaccine – avoids need for needles.

• Temperature-stable formulation allows for vaccine distribution without refrigeration.

Development Stage:

• Pre-clinical

• In vitro data available

• In vivo data available (animal)

Inventors: Dennis J. Kopecko and De Qi Xu (FDA/CBER)

Publication: Xu DQ, et al. Core-linked LPS expression of Shigella dysenteriae serotype 1 O-antigen in live Salmonella typhi vaccine vector Ty21a: preclinical evidence of immunogenicity and protection. Vaccine. 2007 Aug 14;25(33):6167-75. [PMID 17629369]

Intellectual Property: HHS Reference No. E-214-2004/0 —

• EP Application No. 05754091.6 filed 24 May 2005

• EP Application No. 12186545.5 filed 24 May 2005

• US Patent No. 8,071,113 issued 06 Dec 2011

• US Patent No. 8,337,831 issued 25 Dec 2012

• US Application No. 13/687,797 filed 28 Nov 2012

Licensing Contact: Peter A. Soukas; 301-435-4646; soukasp@mail.nih.gov

Collaborative Research Opportunity: The FDA Center for Biologics Evaluation and Research is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize combination typhoid-shigellosis oral vaccine. For collaboration opportunities, please contact Dr. Dennis J. Kopecko at dennis.kopecko@fda.hhs.gov or 301-661-8839.

Oral Shigellosis Vaccine

Description of Technology: This application claims a *Salmonella* typhi Ty21a construct comprising a *Shigella sonnei* O-antigen biosynthetic gene region inserted into the *Salmonella* typhi Ty21a chromosome, where heterologous *Shigella sonnei* form 1 O-antigen is stably expressed together with homologous *Salmonella* typhi O-antigen. The constructs of this invention elicit immune protection against virulent *Shigella sonnei* challenge, as well as *Salmonella* Typhi challenge. Also claimed in this application are methods of recombineering a large antigenic gene region into a bacterial chromosome.

Bacillary dysentery and enteric fevers continue to be important causes of morbidity in both developed and developing nations. *Shigella* cause greater than one hundred and fifty million cases of dysentery and enteric fever occurs in greater than twenty-seven million people annually. Currently, there is no licensed vaccine to prevent the occurrence of shigellosis. Increasing multiple resistance in *Shigella* commonly thwarts local therapies.

Potential Commercial Applications:

• One component of a multivalent Shigellosis vaccine under development

• Research tool

Competitive Advantages:

• Low cost production

• Lower cost vaccine

• Oral vaccine – no needles required

• Temperature-stable manufacturing process - avoids need for refrigeration during vaccine distribution

Development Stage:

• Pre-clinical

• In vitro data available

• In vivo data available (animal)

Inventors: Dennis J. Kopecko and Madushini N. Dharmasena (FDA/CBER)

Publication: Dharmasena MN, et al. Stable Expression of Shigella sonnei Form I O-Polysaccharide Genes Recombineered into the Chromosome of Live Salmonella Oral Vaccine Vector Ty21a. Int J Med Microbiol. 2013 (accepted).

Intellectual Property: HHS Reference No. E-168-2012/0 — US Application No. 61/701,939 filed 17 Sep 2012

Licensing Contact: Peter A. Soukas; 301-435-4646; soukasp@mail.nih.gov

Collaborative Research Opportunity: The FDA Center for Biologics Evaluation and Research is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize oral Shigellosis vaccine. For collaboration opportunities, please contact Dr. Dennis J. Kopecko at dennis.kopecko@fda.hhs.gov or 301-661-8839.

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Date

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