Vaccine for Dengue Virus

Description of Technology: The claimed invention relates to viable chimeric dengue viruses or their derived recombinant mutants for use as vaccines against dengue and other flavivirus diseases, including tick-borne encephalitis and West Nile encephalitis. Dengue is a mosquito-transmitted viral disease which occurs in tropical and subtropical regions throughout the world. Inactivated whole dengue virus vaccines have been shown to be insufficiently immunogenic and live dengue virus vaccines prepared by serial passage in cell culture have not been shown to be consistently attenuated. A dengue vaccine is still not available. The present invention represents a technical breakthrough, which provides new approaches to dengue vaccines by construction of chimeric dengue viruses of all four serotypes and strategic modification to produce attenuated virus strains. Several fields of use remain available for licensing.

Applications: Prevention of dengue outbreaks, severe and fatal dengue caused by dengue viruses, a major public health problem in tropical and subtropical regions.

Inventors: Ching-juh Lai, et al. (NIAID).

Patent Status: U.S. Patent 6,184,024 issued 06 Feb 2001 (HHS Reference No. E–171–1988/1–US–02); U.S. Patent 6,676,926 issued 13 Jan 2004 (HHS Reference No. E–171–1988/1–US–03).

Licensing Status: Available for non-exclusive licensing.

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

Murine Monoclonal Antibodies Effective To Treat Respiratory Syncytial Virus

Description of Technology: Available for licensing through a Biological Materials License Agreement are the murine MAbs described in Beeler et al, ''Neutralization epitopes of the F glycoprotein of respiratory syncytial virus: effect of mutation upon fusion function,'' J Virol. 1989 Jul;63(7):2941–2950. The MAbs that are available for licensing are the following: 1129, 1153, 1142, 1200, 1214, 1237, 1112, 1269, and 1243. One of these MAbs, 1129, is the basis for a humanized murine MAb (see U.S. Patent 5,824,307 to humanized 1129 owned by MedImmune, Inc.), recently approved for marketing in the United States. MAbs in the panel reported by Beeler et al. have been shown to be effective therapeutically when administered into the lungs of cotton rats by small-particle aerosol. Among these MAbs several exhibited a high affinity (approximately 109M–1) for the RSV F glycoprotein and are directed at epitopes encompassing amino acid 262, 272, 275, 276 or 389. These epitopes are separate, nonoverlapping and distinct from the epitope recognized by the human Fab of U.S. Patent 5,762,905 owned by The Scripps Research Institute.

Applications: Research and drug development for treatment of respiratory syncytial virus.

Inventors: Robert M. Chanock, Brian R. Murphy, Judith A. Beeler, and Kathleen L. van Wyke Coelingh (NIAID).

Patent Status: HHS Reference No. B–056–1994/1—Research Tool.

Licensing Status: Available for non-exclusive licensing under a Biological Materials License Agreement.

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

Dated: December 1, 2006.

Steven M. Ferguson,

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

[FR Doc. E6–21028 Filed 12–11–06; 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.

Noncovalent HIV Env-CD4 Complexes as HIV Vaccines

Description of Technology: HIV vaccine technology based on HIV envelope protein (Env) have been less successful than anticipated to date. One possible reason for this is the potential conformational masking of neutralizing epitopes. The current technology combines HIV Env and cell surface polypeptides CD4 in non-covalent complexes to expose epitopes not present on the uncomplexed Env molecules. These complexes can thus be used to elicit neutralizing antibodies when used as vaccines, immunogenic compositions or immunotherapies. The CD4 inducing epitopes found in regions of the virus that are most conserved across clades are unmasked and immune sera generated with this technology neutralized primary HIV–1 viruses from several clades. Additionally, cell surface polypeptide CD4 is in its native conformation and masked by Env, therefore it is unlikely to induce autoantibodies.

Applications and Advantages: (1) HIV vaccine based on conformationally masked epitopes; (2) Presents epitopes to immune system that are the same or similar as with actual HIV infection; (3) Multiple copies of Env may enhance immune response and limit dosage.

Inventors: Jinhai Wang and Michael Norcross (CDER/FDA).

Patent Status: U.S. Provisional Application No. 60/711,985 filed 25 Aug 2005 (HHS Reference No. E–173–2005/0–US–01); PCT Application filed 25 Aug 2006 (HHS Reference No. E–173–2005/1–PCT–01).

Licensing Contact: Susan Ano, PhD; 301–435–5515; *anos@mail.nih.gov.*

Collaborative Research Opportunity: The FDA Center for Drug Evaluation and Research is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize this HIV Env-CD4 technology. Please contact Beatrice A. Droke at 301/827–7008 or *bea.droke@fda.hhs.gov* for more information.

Modified Bacterial Strain for Otitis Media Vaccine

Description of the Technology: This invention relates to a strain of Moraxella catarrhalis containing a gene mutation that prevents endotoxic lipooligosaccharide (LOS) synthesis and potential use of the mutant for developing novel vaccines against the pathogen, for which there is currently

no licensed vaccine. M. catarrhalis is one of the causative agents of otitis media (middle ear infection), sinusitis, and lung infections. The mutant is defective in the lpxA gene, whose enzyme product is relevant in lipid A biosynthesis (lipid A is part of the LOS). The nontoxic mutant was found to elicit high levels of antibodies with bactericidal activity and provided protection against wild type bacterial challenge. Use of this mutant bacterium is envisioned as a new approach for vaccines against M. catarrhalis.

Applications: Otitis media vaccine, sinusitis, and lung infections.

Inventors: Xin-Xing Gu and Daxin Peng (NIDCD).

Patent Status: U.S. Provisional Application No. 60/577,244 filed 04 Jun 2004 (HHS Reference No. E–174–2004/0–US–01); U.S. Provisional Application No. 60/613,139 filed 23 Sep 23 (HHS Reference No. E–174–2004/1–US–01); PCT Application No. PCT/US2005/019479 filed 03 Jun 2005 (HHS Reference No. E–174–2004/2–PCT–01).

Licensing Status: Available for non-exclusive licensing—biological materials.

Licensing Contact: Susan Ano, PhD; 301/435–5515; *anos@mail.nih.gov.*

Collaborative Research Opportunity: The Vaccine Research Section in the National Institute on Deafness and Other Communication Disorders (NIDCD) is seeking statements of capability or interest from parties interested in collaborative research. NIDCD is interested in developing outer membrane proteins (OMP), outer membrane vesicle (OMV), and whole cell vaccines generated from the mutant. The mutant strain can also be used as an effective vehicle to express and deliver protective antigens from other important human pathogens. Please contact Dr. Xin-Xing Gu by phone (301–402–2456) or e-mail (*guxx@nidcd.nih.gov*) for more information.

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.*

HIV Entry Inhibitor

Description of Technology: The technology relates to a chimeric molecule, N_{CCG}-gp41, in which the internal trimeric helical coiled-coil of the ectodomain of gp41 is fully exposed and stabilized by both fusion to a minimal ectodomain core of gp41 and by engineered intersubunit disulfide bonds. N_{CCG}-gp41 inhibits HIV envelope mediated cell fusion at nanomolar concentrations with an IC_{50} of 16 nM. It is proposed that N_{CCG}-gp41 targets the exposed C-terminal region of the gp41 ectodomain in its pre-hairpin intermediate state, thereby preventing the formation of the fusogenic form of the gp41 ectodomain that comprises a highly stable trimer of hairpins arranged in a six-helix bundle. Antibodies have been raised against N_{CCG}-gp41 that inhibit HIV envelope mediated cell fusion.

Applications: (1) Entry inhibitor HIV therapeutic; (2) HIV/AIDS vaccine; (3) As a component of a high throughput screening assay for small molecule inhibitors of HIV envelope mediated cell fusion.

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

Inventors: G. Marius Clore et al. (NIDDK).

Publications:

1. JM Louis et al. Design and properties of N_{CCG}-gp41, a chimeric gp41 molecule with nanomolar HIV fusion inhibitory activity. J Biol Chem. 2001 Aug 3;276(31):29485–29489.

2. CA Bewley et al. Design of a novel peptide inhibitor of HIV fusion that disrupts the internal trimeric coiled-coil of gp41. J Biol Chem. 2002 Apr 19;277(16):14238–14245.

3. JM Louis et al. Covalent trimers of the internal N-terminal trimeric coiled-coil of gp41 and antibodies directed against them are potent inhibitors of HIV envelope-mediated cell fusion. J Biol Chem. 2003 May 30;278(22):20278–20285.

4. JM Louis et al. Characterization and HIV–1 fusion inhibitory properties of monoclonal Fabs obtained from a human non-immune phage library selected against diverse epitopes of the ectodomain of HIV–1 gp41. J Mol Biol. 2005 Nov 11;353(5):945–951.

Patent Status: U.S. Patent Application No. 10/499,094 filed 14 Jun 2004 (HHS Reference No. E–252–2001/0–US–03); EP application 02795951.9 and IN application 1535/CHENP/2004.

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

Licensing Contact: Susan Ano, Ph.D.; 301/435–5515; *anos@mail.nih.gov.*

Subgenomic Replicons of the Flavivirus Dengue

Description of Technology: Dengue virus, with its four serotypes Den-1 to Den-4, is the most important member of the Flavivirus genus with respect to infection of human producing diseases that range from flu-like symptoms of dengue fever (DF) to severe or fatal illness of dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS). Dengue outbreaks continue to be a major public health problem in densely populated areas of the tropical and subtropical regions, where mosquito vectors are abundant. This invention relates to the construction of all four types of dengue subgenomic replicons (chromosome and plasmid which contain genetic information necessary for their own replication) containing large deletions in the structural region (C-preM–E) of the genome. Immunization using these replicons should be effective in eliciting not only a humoral-mediated immune response but also a cell-mediated

immune response. These replicons should be safer than a live attenuated vaccine because they cannot cause disease in the host and they should be better than subunit vaccines because they can replicate in the host.

Applications: Prevention of severe and/or fatal human disease caused by dengue virus, a major health concern in tropical and subtropical regions.

Inventor: Xiaowu Pang (CBER/FDA).

Patent Status: U.S. Patent Application 10/656,721 filed 05 Sep 2003, claiming priority to 09 Mar 2001 (HHS Reference No. E–228–2000/0–US–03).

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

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

Dated: December 1, 2006.

Steven M. Ferguson,

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

[FR Doc. E6–21029 Filed 12–11–06; 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.

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ARH3, a Therapeutic Target for Cancer, Ischemia, and Inflammation

Description of Technology: ADP-ribosylation is important in many cellular processes, including DNA replication and repair, maintenance of genomic stability, telomere dynamics, cell differentiation and proliferation, and necrosis and apoptosis. Poly-ADP-ribose is important in a number of critical physiological processes such as DNA repair, cellular differentiation, and carcinogenesis. Until recently, only one human enzyme, PARG, had been identified that degrades the ADP-ribose polymer. Another ADP-ribose, O-acetyl-ADP ribose, is formed via the deacetylation of proteins, such as acetyl-histone, by proteins in the Sir2 family. Sir2 proteins have been implicated in regulation of chromatin structure and longevity.

The NIH announces the discovery of a novel PARG-like enzyme, ARH3. ARH3 possesses PARG activity, yet is structurally distinct from PARG. ARH3 also hydrolyzes O-acetyl-ADP-ribose, and is the only protein recognized to date with such activity. ARH3 thus appears to function in two important signaling pathways, serving to regulate both poly-ADP-ribose and O-acetyl-ADP-ribose levels. It may affect chromatin structure through effects on both pathways. Since ARH3 structures differs from PARG or other enzymes that participate in these pathways, it may be possible to design specific inhibitors to target both the poly-ADP-ribose and Sir2 pathways. These drugs may be used as anticancer agents, radiosensitizers or antiviral agents, or for treating disorders involving oxidative damage, such as acute tissue injury, ischemia, and inflammation.

Applications: (1) Development of therapeutics for cancer or disorders associated with excessive DNA damage; (2) Development of therapeutics for diseases involving oxidative damage, such as acute tissue injury, ischemia and inflammation.

Market: (1) Patients with chemotherapy-resistant tumors, or with cancers that are genetically deficient in DNA repair; (2) Patients with inflammatory or ischemia/reperfusion diseases, particularly those associated with acute cardiovascular disease.

Development Status: Early stage.

Inventors: Joel Moss et al. (NHLBI).

Related Publications:

1. S Oka, J Kato, J Moss. Identification and characterization of a mammalian 39-kDa poly(ADP-ribose) glycohydrolase. J Biol Chem. 2006 Jan 13;281(2):705–713.

2. T Ono, A Kasamatsu, S Oka, J Moss. The 39-kDa poly(ADP-ribose) glycohydrolase ARH3 hydrolyzes *O*-acetyl-ADP-ribose, a product of the Sir2 family of acetyl-histone deacetylases. Proc Natl Acad Sci USA 2006 Nov 7;103(45):16687–16691. Epub 2006 Oct 30, doi 10.1073/pnas.0607911103.

Patent Status: U.S. Provisional Application No. 60/716,807 filed 12 Sep 2005 (HHS Reference No. E–347–2004/0-US–01); PCT Application No. PCT/US2006/035771 filed 12 Sep 2006 (HHS Reference No. E–347–2004/0–PCT–02).

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

Licensing Contact: Tara L. Kirby, PhD; 301/435–4426; *tarak@mail.nih.gov.*

Collaborative Research Opportunity: The Pulmonary Critical Care Medicine Branch in the National Heart, Lung, and Blood Institute is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize the invention. Please contact Marianne Lynch in the NHLBI Office of Technology Transfer and Development by phone (301–594–4094) or e-mail (*lynchm@nhlbi.nih.gov*) for more information.

Antisera To Detect Phosphorylated Phosphoinositide-Dependent Kinase 1 (PDK–1)

Description of Technology: PDK–1 phosphorylates and activates a number of cellular kinases, and plays a major role in insulin and growth factor signaling. PDK–1 also represents a promising drug target for a number of cancers. Autophosphorylation at Ser244 (mouse) or Ser241 (human) is critical for PDK–1 activity.

Available for licensing are polyclonal rabbit antisera that specifically detect mouse PDK–1 protein phosphorylated at Ser244. These antisera are also expected to be specific for the human PDK–1 protein phosphorylated at Ser241.

Applications: (1) Tool for screening PDK–1 autophosphorylation inhibitors for cancer and other indications; (2) Tool for studying insulin and growth factor signaling.

Inventor: Michael J. Quon (NCCAM).

Publication: MJ Wick, FJ Ramos, H Chen, MJ Quon, LQ Dong, F Liu. Mouse 3-phosphoinositide-dependent protein kinase-1 undergoes dimerization and trans-phosphorylation in the activation loop. J Biol Chem. 2003 Oct 31;278(44):42913–42919.

Patent Status: HHS Reference No. E–330–2003/0—Research Tool.

Licensing Status: This technology is available as a research tool under a Biological Materials License.

Licensing Contact: Tara Kirby, PhD; 301/435–4426; *tarak@mail.nih.gov*

Collaborative Research Opportunity: The NIH, NCCAM, Diabetes Unit is seeking statements of capability or interest from parties interested in collaborative research to further