lymphocytic lineages bearing Fc receptors. ADE of DENV–2 infection has also been demonstrated in monkeys infused with a human dengue immune serum.

We have identified chimpanzee-human chimeric IgG1 mAbs capable of neutralizing or binding to one or more DENV serotypes. Cross-reactive IgG 1A5 neutralizes DENV–1 and DENV–2 more efficiently than DENV–3 and DENV–4, and type-specific IgG 5H2 neutralizes DENV–4 at a high titer. Analysis of antigenic variants has localized the IgG 1A5 binding site to the conserved fusion peptide in E. Thus, IgG 1A5 shares many characteristics with the cross-reactive antibodies detected in flavivirus infections.

This application claims a variant of an antibody comprising a polypeptide in the Fc region, which binds an Fc gamma receptor (FcgammaR) with lower affinity than the parent antibody. The variant polypeptide comprises a deletion of nine amino acids at the N-terminus of the C_H2 domain in the Fc region. Introduction of the Fc variant abrogates the antibody-mediated dengue virus replication enhancing activity. This invention has important implications for the antibody-mediated prevention of dengue virus infection.

Application: Immunization against Dengue and/or flaviviruses.

Developmental Status: Antibody candidates have been synthesized and preclinical studies have been performed.

Inventors: Ana Goncalvez, Robert Purcell, C.J. Lai (NIAID).

Publication: AP Goncalvez *et. al.* Monoclonal antibody-mediated enhancement of dengue virus infection in vitro and in vivo and strategies for prevention. Proc Natl Acad Sci USA. 2007 May 29; 104(22): 9422–9427.

Patent Status: PCT Application No. PCT/US2008/059313 filed 03 Apr 2008, claiming priority to 04 Apr 2007 (HHS Reference No. E–159–2007/3–PCT–01).

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

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

Monoclonal Antibodies That Bind or Neutralize Dengue Virus

Description of Technology: Among the arthropod-borne flaviviruses, the four dengue virus serotypes, dengue type 1 virus (DENV–1), dengue type 2 virus (DENV–2), dengue type 3 virus (DENV–3), and dengue type 4 virus (DENV–4 are most important in terms of human morbidity and geographic distribution. Dengue viruses cause dengue outbreaks and major epidemics in most tropical and subtropical areas where *Aedes albopictus* and *Aedes aegypti* mosquitoes are abundant. Dengue infection produces fever, rash, and joint pain in humans. A more severe and life-threatening form of dengue, characterized by hemorrhagic fever and hemorrhagic shock, has occurred with increasing frequency in Southeast Asia and Central and South America, where all four dengue virus serotypes circulate. A safe and effective vaccine against dengue is currently not available. Passive immunization with monoclonal antibodies from non-human primates or humans represents a possible alternative to vaccines for prevention of illness caused by dengue virus.

The application claims monoclonal antibodies that bind or neutralize dengue type 1, 2, 3, and/or 4 viruses. The application also claims fragments of such antibodies retaining dengue virus-binding ability, fully human or humanized antibodies retaining dengue virus-binding ability, and pharmaceutical compositions including such antibodies. The application also claims isolated nucleic acids encoding the antibodies of the invention. Additionally, application claims prophylactic, therapeutic, and diagnostic methods employing the antibodies and nucleic acids of the invention.

Application: Prophylaxis against dengue serotypes 1, 2, 3 and 4.

Development Status: Antibodies have been synthesized and preclinical studies have been performed.

Inventors: Ching-Juh Lai and Robert Purcell (NIAID).

Publications: The antibodies are further described in:

1. R Men *et al.* Identification of chimpanzee Fab fragments by repertoire cloning and production of a full-length humanized immunoglobulin G1 antibody that is highly efficient for neutralization of dengue type 4 virus. J Virol. 2004 May; 78(9): 4665–4674.

2. AP Goncalvez *et al.* Chimpanzee Fab fragments and a derived humanized immunoglobulin G1 antibody that efficiently cross-neutralize dengue type 1 and type 2 viruses. J Virol. 2004 Dec; 78(23): 12910–12918.

3. AP Goncalvez *et al.* Epitope determinants of a chimpanzee Fab antibody that efficiently cross-neutralizes dengue type 1 and type 2 viruses map to inside and in close proximity to fusion loop of the dengue type 2 virus envelope glycoprotein. J Virol. 2004 Dec; 78(23): 12919–12928.

4. AP Goncalvez *et al.* Monoclonal antibody-mediated enhancement of dengue virus infection in vitro and in vivo and strategies for prevention. Proc Natl Acad Sci U.S.A. 2007 May 29; 104(22): 9422–9427.

Patent Status: U.S. Patent Application No. 10/582,006 filed 07 Jun 2006 (HHS Reference No. E–066–2003/5–US–02); Canadian Patent Application No. 2548808 filed 03 Dec 2004 (HHS Reference No. E–066–2003/5–CA–03).

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 this technology. Please contact Ching-Juh Lai at 301–594–2422 for more information.

Dated: October 14, 2008.

Richard U. Rodriguez,

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

[FR Doc. E8–25210 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.

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.

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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.

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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.*