novel anti-HIV human monoclonal antibody named X5. This antibody demonstrates promise over conventional anti-HIV antibodies because the X5 antibody exhibits a unique binding activity compared to its counterparts. It has been established that the initial stage of HIV–1 entry into cells is mediated by a complex between the viral envelope glycoprotein (Env) such as gp120-gp41, a receptor CD4 and a co-receptor CCR5. The X5 antibody binds to an epitope on gp120 that is induced by interaction between gp120 and the receptor CD4 and enhanced by the co-receptor CCR5. The X5 antibody also shows strong activity at very low levels (in the range from 0.0001—0.1 Mg/ml concentration based on the particular isolate). Because it is a human antibody, it can be administered directly into patients so that it is an ideal candidate for clinical trials. It also can be easily produced because it was obtained by screening of phage display libraries and its sequence is known. Finally, since it has neutralized all virus envelope glycoproteins, including those from primary isolates of different clades, the epitope is highly conserved and resistance is unlikely to develop. Therefore, this antibody and/or its derivatives including fusion proteins with CD4 are good candidates for clinical development.

The second invention (E–251–2004/0) provides for pharmaceutical compositions of, and methods of using potent cross-reactive human monoclonal antibodies to HIV. Specifically, the invention describes a competitive antigen panning (CAP) method of isolating antibodies that bind to the gp41 subunit of the HIV–1 envelope glycoprotein. Additionally, the invention includes compositions of the aforementioned antibodies and the epitopes recognized by the antibodies. Methods of using the invention in the development of vaccine immunogens for the treatment and prevention of HIV, as well as the detection of HIV in a mammal are also described. The invention has significant implications in the development of HIV inhibitors, vaccines, and research tools for understanding mechanisms of HIV entry. Further development of the disclosed invention may yield novel therapies and methods in the prevention of mother-to-child transmission of HIV, treatment of accidental exposure to HIV, and chronic infection in patients with resistance to current therapies.

The prospective exclusive license will be royalty bearing and will comply with the terms and conditions of 35 U.S.C. 209 and 37 CFR 404.7. The prospective exclusive license may be granted unless, within 60 days from the date of this published Notice, NIH receives written evidence and argument that establishes that the grant of the license would not be consistent with the requirements of 35 U.S.C. 209 and 37 CFR 404.7.

The field of use may be limited to the development of human monoclonal antibodies for use as a therapeutic or preventative in HIV infection either alone or in combination with other compounds.

Properly filed competing applications for a license filed in response to this notice will be treated as objections to the contemplated license. Comments and objections submitted in response to this notice will not be made available for public inspection, and, to the extent permitted by law, will not be released under the Freedom of Information Act, 5 U.S.C. 552.

Dated: January 16, 2008.

Steven M. Ferguson,

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

[FR Doc. E8–1258 Filed 1–24–08; 8:45 am]

BILLING CODE 4140–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Government-Owned Inventions; Availability for Licensing: Flavivirus Technologies

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.

Development of Antigenic Chimeric St. Louis Encephalitis Virus/Dengue Virus Type Four Recombinant Viruses (SLEV/DEN4) as Vaccine Candidates for the Prevention of Disease Caused by SLEV

Description of Invention: St. Louis Encephalitis Virus (SLEV) is a mosquito-borne flavivirus that is endemic in the Americas and causes sporadic outbreaks of disease in humans. SLEV is a member of the Japanese encephalitis virus serocomplex and is closely related to West Nile Virus (WNV). St. Louis encephalitis is found throughout North, Central, and South America, and the Caribbean, but is a major public health problem mainly in the United States. Prior to the outbreak of West Nile virus in 1999, St. Louis encephalitis was the most common human disease caused by mosquitoes in the United States. Since 1964, there have been about 4,440 confirmed cases of St. Louis encephalitis, with an average of 130 cases per year. Up to 3,000 cases have been reported during epidemics in some years. Many more infections occur without symptoms and go undiagnosed. At present, a vaccine or FDA approved antiviral therapy is not available.

The inventors have previously developed a WNV/Dengue4Delta30 antigenic chimeric virus as a live attenuated virus vaccine candidate that contains the WNV premembrane and envelope (prM and E) proteins on a dengue virus type 4 (DEN4) genetic background with a thirty nucleotide deletion (Delta30) in the DEN4 3'-UTR. Using a similar strategy, the inventors have generated an antigenic chimeric virus, SLE/DEN4Delta30. Preclinical testing results indicate that chimerization of SLE with DEN4Delta30 decreased neuroinvasiveness in mice, did not affect neurovirulence in mice, and appeared to overattenuate the virus for non-human primates. Modifications of the SLE/DEN4Delta30 vaccine candidate are underway to improve its immunogenicity.

This application claims live attenuated chimeric SLE/DEN4Delta30 vaccine compositions and bivalent WNV/SLE/DEN4Delta30 vaccine compositions. Also claimed are methods of treating or preventing SLEV infection in a mammalian host, methods of producing a subunit vaccine composition, isolated polynucleotides comprising a nucleotide sequence encoding a SLEV immunogen, methods for detecting SLEV infection in a biological sample and infectious chimeric SLEV.

Application: Immunization against SLEV or SLEV and WNV.

Development Status: Live attenuated vaccine candidates are currently being developed and preclinical studies in mice and monkeys are in progress. Suitable vaccine candidates will then be evaluated in clinical studies.

Inventors: Stephen S. Whitehead, Joseph Blaney, Alexander Pletnev, Brian R. Murphy (NIAID).

Patent Status: U.S. Provisional Application No. 60/934,730 filed 14 Jun 2007 (HHS Reference No. E–240–2007/0–US–01).

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

Collaborative Research Opportunity: The NIAID Laboratory of Infectious Diseases is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize live attenuated virus vaccine candidates for St. Louis encephalitis virus. Please contact Dr. Whitehead at 301–496–7692 for more information.

Live Attenuated Virus Vaccines for La Crosse Virus and Other Bunyaviridae

Description of Invention: La Crosse virus (LACV), family Bunyaviridae, is a mosquito-borne pathogen endemic in the United States. LACV infection results in 70–130 clinical cases a year and is the major cause of pediatric arboviral encephalitis in North America. LACV was first identified as human pathogen in 1960 after its isolation from a 4 year-old girl from Minnesota who suffered meningoencephalitis and later died in La Crosse, Wisconsin. The majority of LACV infections are mild and never reported, however serologic studies estimate annual infection rates of 10–30/100,000 in endemic areas. LACV is a member of the California serogroup of viruses in the genus *Orthobunyavirus.* The serogroup contains members found on five continents that include human pathogens such as La Crosse, Snowshoe hare, and Jamestown Canyon viruses in North America; Guaroa virus in North and South America; Inkoo and Tahyna viruses in Europe; and Lumbo virus in Africa. Children who recover from severe La Crosse encephalitis may have significantly lower IQ scores than expected and a high prevalence (60% of those tested) of attention-deficit-hyperactivity disorder. Seizure disorders are also common in survivors. LACV can also cause encephalitis in immunosuppressed adults. Projected lifelong economic costs associated with neurologic sequelae range from $48,775–3,090,398 per case. At present, a vaccine or FDA approved antiviral therapy is not available.

This application principally claims live attenuated LACV vaccine compositions, but also includes subunit vaccine compositions including California encephalitis virus (CEV) serogroup immunogens, attenuated and inactivated CEV serogroup and chimeric *Bunyaviridae.* Also claimed are methods of treating or preventing CEV serogroup infection in a mammalian host, methods of producing a subunit vaccine composition, isolated polynucleotides comprising a nucleotide sequence encoding a CEV serogroup immunogen, methods for detecting LACV infection in a biological sample and infectious chimeric *Bunyaviridae.*

Application: Immunization against *Bunyaviridae.*

Developmental Status: Live attenuated vaccine candidates are currently being developed and preclinical studies in mice and monkeys are in progress. Suitable vaccine candidates will then be evaluated in clinical studies.

Inventors: Stephen S. Whitehead, Richard S. Bennett, Brian R. Murphy (NIAID).

Publication: RS Bennett *et al.* Genome sequence analysis of La Crosse virus and in vitro and in vivo phenotypes. Virol J. 2007 May 8;4:41.

Patent Status: U.S. Provisional Application No. 60/920,691 filed 29 Mar 2007 (HHS Reference No. E–158–2007/0–US–01); U.S. Provisional Application No. 60/928,406 filed 08 May 2007 (HHS Reference No. E–158–2007/1–US–01); U.S. Provisional Application filed 29 Jun 2007 (HHS Reference No. E–158–2007/2–US–01).

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 NIAID Laboratory of Infectious Diseases is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize live attenuated virus vaccine candidates for La Crosse virus and other *Bunyaviridae.* Please contact Dr. Whitehead at 301–496–7692 for more information.

Development of Dengue Virus Type 3 Vaccine Candidates Containing Either (1) Nucleotide Deletions in the 3′-UTR of the Genome Consisting of More Than 30 Contiguous Nucleotides in One or Multiple Regions, or (2) a 3′-UTR Derived From DEN4 and Containing the A30 Nucleotide Deletion

Description of Technology: The disease burden associated with dengue virus infection has increased over the past several decades in the tropical and semi-tropical regions of the world, where over 2 billion people live at risk of dengue infection. Annually, there are an estimated fifty (50) to one hundred (100) million cases of dengue fever, making development of an effective vaccine a priority. In addition, there is a need for a ''travelers vaccine'' to protect those visiting dengue virus endemic areas, similar in scope to other currently available ''travelers vaccines'', such as hepatitis A vaccine.

The previously identified Δ30 attenuating mutation, created in each dengue virus serotype by the removal of 30 homologous nucleotides from the 3′-UTR, is capable of attenuating wild-type strains of dengue virus type 1 (DEN1), type 4 (DEN4) and to a limited extent type 2 (DEN2). These DEN1Δ30 and DEN4Δ30 viruses have been shown to be both safe and immunogenic in humans. However, the Δ30 mutation failed to have an attenuating effect on dengue virus type 3 (DEN3). To generate DEN3 vaccine candidates with a clearly attenuated phenotype, viruses were produced containing 3′-UTR deletions consisting of extensions of the original Δ30 mutation or additional mutations which remove stem-loop structures similar to those removed by Δ30. In addition, the entire 3′-UTR of DEN3 was replaced with the 3′-UTR derived from DEN4 and containing the Δ30 mutation. Studies in monkeys demonstrated that these newly developed viruses are highly attenuated, yet sufficiently immunogenic to warrant their further development for use as live attenuated vaccine candidates. Such viruses are anticipated to become the DEN3 component of a tetravalent vaccine formulation designed to immunize against all four dengue virus serotypes.

Application: Immunization against all four serotypes of dengue virus.

Developmental Status: Vaccine candidates have been synthesized and preclinical studies have been performed. The vaccine candidates of this invention are slated to enter Phase I clinical trials in the next year.

Inventors: Stephen S. Whitehead, Joseph E. Blaney, Brian R. Murphy (NIAID).

Patent Status: PCT Application No. PCT/US2007/076004 filed 15 Aug 2007, claiming priority to 15 Aug 2006 (HHS Reference No. E–139–2006/0–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.*

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 these vaccines. Please contact Dr. Brian Murphy at 301–594–1616 or *bm25f@nih.gov* for more information.

Dengue Tetravalent Vaccine Containing a Common 30-Nucleotide Deletion in the 3′-UTR of Dengue Types 1, 2, 3, and 4

Description of Technology: The invention relates to a dengue virus tetravalent vaccine containing a common 30-nucleotide deletion (Δ30) in the 3′-untranslated region (UTR) of the genome of dengue virus serotypes 1, 2, 3, and 4. The previously identified Δ30 attenuating mutation, created in dengue virus type 4 (DEN4) by the removal of 30 nucleotides from the 3′-UTR, is also capable of attenuating a wild-type strain of dengue virus type 1 (DEN1). Removal of 30 nucleotides from the DEN1 3′-UTR in a highly conserved region homologous to the DEN4 region encompassing the Δ30 mutation yielded a recombinant virus attenuated in rhesus monkeys to a level similar to recombinant virus DEN4Δ30. This established the transportability of the Δ30 mutation and its attenuation phenotype to a dengue virus type other than DEN4. The effective transferability of the Δ30 mutation establishes the usefulness of the Δ30 mutation to attenuate and improve the safety of commercializable dengue virus vaccines of any serotype.

A tetravalent dengue virus vaccine containing dengue virus types 1, 2, 3, and 4 each attenuated by the Δ30 mutation is being developed. The presence of the Δ30 attenuating mutation in each virus component precludes the reversion to a wild-type virus by intertypic recombination. In addition, because of the inherent genetic stability of deletion mutations, the Δ30 mutation represents an excellent alternative for use as a common mutation shared among each component of a tetravalent vaccine.

Inventors: Stephen S. Whitehead (NIAID), Brian R. Murphy (NIAID), Lewis Markoff (FDA), Barry Falgout (FDA), Kathryn A. Hanley (NIAID), Joseph E. Blaney (NIAID).

Patent Status: U.S. Patent Application No. 10/970,640 filed 21 Oct 2004, claiming priority to 03 May 2002 (HHS Reference No. E–089–2002/1–US–02).

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 these vaccines. Please contact Dr. Brian Murphy at 301–594–1616 or *bm25f@nih.gov* for more information.

Development of Mutations Useful for Attenuating Dengue Viruses and Chimeric Dengue Viruses

Description of Technology: Although flaviviruses cause a great deal of human suffering and economic loss, there is a shortage of effective vaccines. This invention relates to dengue virus mutations that may contribute to the development of improved dengue vaccines. Site directed and random mutagenesis techniques were used to introduce mutations into the dengue virus genome and to assemble a collection of useful mutations for incorporation in recombinant live attenuated dengue virus vaccines. The resulting mutant viruses were screened for several valuable phenotypes, including temperature sensitivity in Vero cells or human liver cells, host cell restriction in mosquito cells or human liver cells, host cell adaptation for improved replication in Vero cells, and attenuation in mice or in mosquitoes. The genetic basis for each observed phenotype was determined by direct sequence analysis of the genome of the mutant virus. Mutations identified through these sequencing efforts have been further evaluated by re-introduction of the identified mutations, singly, or in combination, into recombinant dengue virus and characterization of the resulting recombinant virus for phenotypes. In this manner, a menu of attenuating and growth promoting mutations was developed that is useful in fine-tuning the attenuation and growth characteristics of dengue virus vaccine candidates. The mutations promoting growth in Vero cells have usefulness for the production of live or inactivated dengue virus vaccines.

Inventors: Stephen S. Whitehead, Brian R. Murphy, Kathryn A. Hanley, Joseph E. Blaney (NIAID).

Patent Status: U.S. Patent No. 7,226,602 issued 05 Jun 2007 (HHS Reference No. E–120–2001/0–US–04); U.S. Patent Application No. 11/446,050 filed 02 Jun 2006 (HHS Reference No. E–120–2001/0–US–10).

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 these vaccines. Please contact Dr. Brian Murphy at 301–594–1616 or *bm25f@nih.gov* for more information.

Date: January 10, 2008.

Steven M. Ferguson,

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

[FR Doc. E8–1234 Filed 1–24–08; 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.

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Monoclonal Antibodies Against Dengue and Other Viruses With Deletion in Fc Region

Description of Invention: The four dengue virus (DENV) serotypes (DENV–1 to DENV–4) are the most important arthropod-borne flaviviruses in terms of morbidity and geographic distribution. Up to 100 million DENV infections occur every year, mostly in tropical and subtropical areas where vector mosquitoes are abundant. Infection with