Dated: March 7, 2009.

Jeffrey Shuren,

Associate Commissioner for Policy and Planning.

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BILLING CODE 4160–01–S

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Government-Owned Inventions; Availability for Licensing

AGENCY: National Institutes of Health, 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.

Insect Salivary Proteins as Potent Adjuvants for Enhancing Immune Responses

Description of Technology: This invention relates to the discovery that specific sand fly salivary proteins have marked effects on the outcome of Leishmania infection. These proteins have the ability to stimulate strong Th1 and Th2 responses. The Th1 responses with one protein, PpSP15, result in immune protection while the Th2 responses to another protein, PpSP44, exacerbate infection. The protective protein enhanced a specific immune response to the infection, suggesting that it acts as an adjuvant to alter the environment and presentation of the parasite antigens.

These immunogenic salivary proteins, capable of driving Th1 or Th2 responses, can be used as adjuvants in vaccine development for a broad spectrum of diseases that require different immune responses. They may therefore be used to enhance immune responses to pathogens other than Leishmania parasites. They are also very potent in their effect, and small doses are sufficient to elicit a strong immune response. This potency can reduce the need to use chemical adjuvants, which often require large mounts of material and can have deleterious side effects.

Applications:

• Vaccine for Leishmania parasite and other pathogenic infections.

• Potent adjuvant for a broad spectrum of diseases.

Advantages: Efficient, potent, and less toxic than many chemical adjuvants.

Development Status: Early Stage.

Market:

• 88 countries with an estimated 2 million people affected each year.

• Estimated 350 million at risk worldwide.

Inventors: Jesus G. Valenzuela *et al.* (NIAID).

Publication: F Oliveira, PG Lawyer, S Kamhawi, JG Valenzuela. Immunity to distinct sand fly salivary proteins primes the anti-Leishmania immune response towards protection or exacerbation of disease. PLoS Negl Trop Dis. 2008 Apr 16;2(4):e226.

Patent Status: U.S. Provisional Application No. 61/089,884 filed 08 Aug 2008 (HHS Reference No. E–303–2008/0–US–01).

Licensing Status: Available for licensing.

Licensing Contact: Jeffrey A. James PhD; 301–435–5474; jeffreyja@mail.nih.gov.

Collaborative Research Opportunity: The NIAID, Office of Technology Development is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize the Insect Salivary Proteins as potent immune response adjuvants. Please contact Charles Rainwater at *crainwater@niaid.nih.gov* or 301/496–2644 for more information.

Anti-Cancer Oligodeoxynucleotides

Description of Technology: A majority of human cancers originate from epithelial tissue. A common cancer of epithelial cell origin is non-melanoma skin cancer (NMSC), including basal cell carcinoma (BCC) and squamous cell carcinoma (SCC), with more than seven hundred thousand (700,000) new cases diagnosed each year in the United States alone. BCC is rarely life-threatening because it is slow growing and is mostly localized. Unlike BCC, SCC metastasizes at a rate of two (2) to six (6) percent over several years after the initial diagnosis. A highly malignant form invades and destroys tissue, and then metastasizes, initially to a regional lymph node before more distant organs such as the lungs or brain are affected. SCC is commonly encountered in a number of epithelial tissues, including the oral cavity, esophagus, larynx, bronchi, intestines, colon, genital tract, and skin.

This application relates to suppressive CpG oligodeoxynucleotides (ODNs). This application claims suppressive ODN compositions and their use to prevent or delay the formation of a tumor, reducing the risk of developing a tumor, treating a tumor, preventing conversion of a benign to a malignant lesion, or preventing metastasis. Topical application of the ODNs of this invention in preclinical studies resulted in significantly fewer animals developing papillomas and fewer papillomas/animal. The invention also relates to use of suppressive ODNs to prevent/delay cancer when administered systemically as well as locally.

Application: Development of anti-cancer vaccines, therapeutics and diagnostics.

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

Inventors: Dennis M. Klinman and Hidekazu Ikeuchi (NCI)

Patent Status: U.S. Provisional Application No. 61/119,998 filed 04 Dec 2008 (HHS Reference No. E–296–2008/0–US–01).

Licensing Status: Available for licensing.

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

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

Neutralization of Hepatitis C Virus (HCV)

Description of Technology: Available for licensing and commercial development are compositions and methods for preventing and/or treating infection caused by hepatitis C virus (HCV). The invention is based on mapping studies conducted by the inventors of two epitopes within HCV E2: epitope I and epitope II. It has been discovered that epitope I is involved in virus neutralization but that epitope II mediates antibody interference,

probably an adaptation of the virus to obfuscate the immune system. In an effort to attenuate or disable the interference effect of HCV–E2 epitope II, the present invention is directed to a HCV E2 polypeptide substitution/deletion of native amino acids LFY in epitope II, a HCV E2 polypeptide insertion of amino acids between the native LFY in epitope II, or the use of epitope II as a molecular decoyant or to affinity-purify an immune globulin to deplete interfering antibodies from, and enrich neutralizing antibodies in, the preparation.

Applications: HCV vaccines; HCV therapeutics.

Advantages: Improved HCV vaccines and therapeutics.

Development Status: The technology is currently in the preclinical stage of development.

Inventors: Pei Zhang, Marian Major, Stephen Feinstone (FDA).

Publications:

1. P Zhang *et al.* Hepatitis C virus epitope-specific neutralizing antibodies in Igs prepared from human plasma. Proc Natl Acad Sci USA. 2007 May 15;104(20):8449–8454.

2. MY Yu *et al.* Neutralizing antibodies to hepatitis C virus (HCV) in immune globulins derived from anti-HCV-positive plasma. Proc Natl Acad Sci USA. 2004 May 18;101(20):7705–7710.

Patent Status:

U.S. Provisional Application No. 61/002,031 filed 06 Nov 2007 (HHS Reference No. E–276–2007/0–US–01).

PCT Application No. PCT/US2008/082368 filed 04 Nov 2008 (HHS Reference No. E–276–2007/1–PCT–01).

Licensing Status: Available for licensing.

Licensing Contact: RC Tang, JD, LLM; 301–435–5031; *tangrc@mail.nih.gov*.

Collaborative Research Opportunity: The FDA Center for Biologics Evaluation and Research, Laboratory of Plasma Derivatives, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize this technology. Please contact Alice Welch, PhD at 301–827–0359 or *Alice.Welch@fda.hhs.gov* for more information.

Live-Attenuated West Nile Virus Vaccines with Improved Immune Responses

Description of Technology: West Nile virus (WNV), the etiologic agent of West Nile virus fever and encephalitis, is an emerging human and veterinary pathogen in North America. WNV also periodically poses a serious threat to public health in Africa, Australia, Europe, the Middle East, and Asia. There is no vaccine available. WNV strains are phylogenetically grouped into two distinct lineages based primarily on differences within the envelope (Env) protein gene segment. The highly virulent strains recently emergent on the North American continent are of lineage I. Lineage I viruses are primarily also isolated in the Middle East, Europe, and parts of Africa. Lineage II viruses are mostly isolated in Africa. Both lineages include highly neurovirulent as well as relatively attenuated strains of WNV.

WN vaccine viruses developed by others are chimeric live attenuated WN vaccine viruses. The genomes of these viruses encode the C and NS proteins of dengue or yellow fever virus, respectively, along with the WNV prM and Env proteins, which are the major targets of the humoral immune response to flaviviruses. These chimeric live attenuated WN vaccines have been successful in animal testing and some are currently in clinical trials. However, these vaccines have two potential disadvantages due to their heterogeneous genetic composition: (i) Animal host range may be different from that of wild-type WNV, rendering the vaccines less than optimal for immunization of some at-risk species and (ii) the elicited immune response may be suboptimal in duration or quality, due to the absence from these vaccines of homologous WN NS proteins.

FDA's technology that is available for licensing comprises live attenuated West Nile viruses that are not chimeric, but instead have one or more mutations in the 3′ terminal stem loop secondary structure, resulting in decreased neurovirulence. The related patent application also claims methods of making the viruses claimed in the application and methods for using these viruses to prevent or treat WN infection. More specifically, the inventors modified infectious WN DNA such that all or segments of the wild-type WN 3′ stem loop nucleotide sequence was replaced with analogous dengue virus serotype 2 3′ stem loop sequences. The inventors also created a number of point mutations in the nucleotide sequence of the WN 3′ stem loop sequence.

Application: Development of live attenuated West Nile Virus vaccines, therapeutics and diagnostics.

Development Status: Vaccine candidates have been prepared and preclinical (mouse) studies have been performed.

Inventors: Lewis Markoff and Li Yu (FDA/CBER).

Publication: L Yu *et al.* Attenuated West Nile viruses bearing 3′SL and envelope gene substitution mutations. Vaccine. 2008 Nov 5;26(47):5981–5988.

Patent Status:

HHS Reference No. E–022–2004/0—

- U.S. Provisional Patent Application No. 60/579,396 filed 14 Jun 2004.
- PCT Patent Application No. PCT/US2005/0207327 filed 14 Jun 2005.
- U.S. Patent Application No. 11/629,560 filed 14 Dec 2006.

Licensing Status: Available for licensing.

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

Collaborative Research Opportunity: The FDA Office of Vaccines Research & Review is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize West Nile Virus vaccines. Please contact Alice Y. Welch, PhD, at 301–827–0359 or *Alice.Welch@fda.hhs.gov* for more information.

Neuronal Decoding Algorithm for Prosthetic Limbs

Description of Technology: The invention is a new algorithm for decoding neuronal responses based on the discovery that neuronal spike trains can be described using order statistics. The device has applications in the direct control of prosthetic limbs by neuronal signals originating from electrodes placed in the brain. The method allows for decoding neuronal responses by monitoring sequences of potentials from neurons while specific motor tasks are carried out. The sequences are then characterized using the innovative technique of applying order statistics to the spike train, such that subsequent action potentials representing unidentified motor tasks can be decoded to determine the unknown task. The invention is of substantial importance because it appears to have achieved a closed form interpretation of neuronal responses upon which a motor prosthetic device might be based.

Applications: Direct control of prosthetic limbs by neurons; Closed form interpretation of neuronal response for prosthetic devices.

Development Status: Early Stage.

Inventors: Barry J. Richmond and Matthew C. Wiener (NIMH).

Patent Status: U.S. Patent No. 7,442,212 issued 28 Oct 2008 (HHS Reference No. E–038–2001/0–US–03).

Licensing Status: Available for licensing.

Licensing Contact: Jeffrey A. James, PhD; 301–435–5474; *jeffreyja@mail.nih.gov*.

Collaborative Research Opportunity: The National Institute of Mental Health, Laboratory of Neuropsychology, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize decoding algorithm for neuronal responses. Please contact Suzanne Winfield at *winfiels@mail.nih.gov* or 301–402–4324 for more information.

Dated: April 7, 2009.

Richard U. Rodriguez,

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

[FR Doc. E9–8473 Filed 4–13–09; 8:45 am]

BILLING CODE 4140–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Government-Owned Inventions; Availability for Licensing: Methods for Improvements and Enhancements of Diffusion Tensor MRI

AGENCY: National Institutes of Health, 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 CONTACT: Licensing information and copies of the U.S. patent applications listed below may be obtained by contacting either Uri Reichman, PhD, MBA (Phone: 301–435–4616; Fax: 301–402–0220; E-mail: *UR7a@nih.gov*) or John Stansberry, PhD (Phone: 301–435–5236; Fax: 301–402–0220; E-mail: *stansbej@mail.nih.gov*) at the Office of Technology Transfer, National Institutes of Health, 6011 Executive Boulevard, Suite 325, Rockville, Maryland 20852–3804. A signed Confidential Disclosure Agreement will be required to receive copies of the patent applications.

SUPPLEMENTARY INFORMATION: The technology offered for licensing is in the field of Diffusion Magnetic Resonance Imaging (MRI). Specifically, three new methods have been described and claimed that enhance the scope and applicability of Diffusion Tensor MRI (DTI or DT–MRI).

The invention of DTI represented a breakthrough in MRI. It provides a method and system for measuring the effective diffusion tensor of spin-labeled molecules, and for generating images of key tensor-derived parameters that indicate features of tissue microstructure, organization and even physiological state. DTI data has improved the diagnosis of a large number of diseases, disorders, and conditions, and is also being used therapeutically, for instance, to aid neurosurgical planning.

One of the pioneers in Diffusion MRI, Dr. Peter Basser, a Principal Investigator in NIH's Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), is the primary inventor of DTI. Dr. Basser's first contribution in this field is described in US Patent #5,539,310 (issued July 23, 1996), entitled ''Method and System for Measuring the Diffusion Tensor and for Diffusion Tensor Imaging.'' His new inventions (described below) extend the specificity and clinical value of diffusion MRI data, particularly in elucidating fine microstructural details and features that are not detectable using DTI.

Diffusion Tensor and q-Space MRI Specimen Characterization

Description of Technology

Diffusion Tensor MRI (DTI or DT–MRI) provides information primarily about how water diffuses in the extracellular compartment of tissues, where water mobility is hindered (*i.e.*, where water diffuses freely but encounters barriers from which it is reflected). However, DTI does not provide a complete characterization of diffusion in the intracellular compartment of some cells, particularly myelinated axons, where water mobility is restricted by impermeable membranes (*i.e.*, where water is trapped but otherwise free to diffuse within the cell).

The subject invention provides a new modeling framework that self-consistently describes 3–D anisotropic diffusion within a hindered extracellular compartment and within a restricted intra-axonal compartment. It results in an improved characterization and measurement tissue and cell microstructure in neuronal tissue, which promises to advance diagnosis of neurological conditions (*e.g.*, Stroke, MS, Alzheimer's disease), possibly cognitive and behavioral disorders (*e.g.*, schizophrenia), as well as our ability to follow normal development and aging processes.

More specifically, this new in vivo diffusion MRI method, especially suited for the characterization of brain white matter, marries q-space and DTI concepts: Diffusion within axons is modeled as hindered diffusion parallel to the axis of the axon, and restricted diffusion perpendicular to the axis. Diffusion exterior to axons is modeled as hindered diffusion with differing diffusivities parallel and perpendicular to the nerves' axis. To practice this method, diffusion weighted (DW) MRI data are acquired from specimens at different q-values (with different diffusion gradient magnitudes and directions). Parameters associated with tissue microstructure, such as the intra and extra-axonal principal diffusivities and their corresponding principal directions, and the volume fractions of intra and extra-axonal space are then estimated from these data. Improved angular resolution of fiber tract orientation can be obtained for tractography studies and more microstructural information can be gleaned for both diagnostic and therapeutic purposes than from conventional DTI. This technology has been named CHARMED (Composite Hindered and Restricted Model of Diffusion).

Inventors

Peter J. Basser (NICHD) *et al.*

Publications

1. Y Assaf, RZ Freidlin, GK Rohde, PJ Basser. New modeling and experimental framework to characterize hindered and restricted water diffusion in brain white matter. Magn Reson Med. 2004 Nov;52(5):965–978.

2. Y Assaf and PJ Basser. Composite hindered and restricted model of diffusion (CHARMED) MR imaging of the human brain. Neuroimage 2005 Aug 1;27(1):48–58.

3. L Avram, E Özarslan, Y Assaf, A Bar-Shir, Y Cohen, PJ Basser. Three-dimensional water diffusion in impermeable cylindrical tubes: theory versus experiments. NMR Biomed. 2008 Oct;21(8):888–898.

4. A Bar-Shir, L Avram, Y Assaf, PJ Basser, Y Cohen. Experimental Parameters and Diffraction Patterns at High q Diffusion MR: Experiments and Theoretical Simulations. Proc Intl Soc Mag Reson Med. 2007;15:1530.

Patent Status

U.S. Patent Application No. 10/888,917 filed 08 Jul 2004, claiming