This draft guidance, when finalized, will supersede ''Guidance for Industry: Revised Recommendations for the Assessment of Donor Suitability and Blood and Blood Product Safety in Cases of Known or Suspected West Nile Virus Infection,'' dated May 2003.

The draft guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The draft guidance, when finalized, will represent the agency's current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirement of the applicable statutes and regulations.

II. Paperwork Reduction Act of 1995

This draft guidance contains information collection provisions that are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501–3520). The information collection provisions in this guidance for 21 CFR 601.12 were approved under OMB control number 0910–0338; 21 CFR 606.170(b) was approved under OMB control number 0910–0116; and 21 CFR 606.171 was approved under OMB control number 0910–0458.

III. Comments

The draft guidance is being distributed for comment purposes only and is not intended for implementation at this time. Interested persons may submit to the Division of Dockets Management (see **ADDRESSES**) written or electronic comments regarding the draft guidance. Submit written or electronic comments to ensure adequate consideration in preparation of the final guidance. Submit a single copy of electronic comments or two paper copies of any mailed comments, except that individuals may submit one paper copy. Comments are to be identified with the docket number found in the brackets in the heading of this document. A copy of the draft guidance and received comments are available for public examination in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

IV. Electronic Access

Persons with access to the Internet may obtain the draft guidance at either *http://www.fda.gov/cber/guidelines.htm* or *http://www.fda.gov/ohrms/dockets/default.htm*.

Dated: April 13, 2005.

Jeffrey Shuren,

Assistant Commissioner for Policy.

[FR Doc. 05–7821 Filed 4–19–05; 8:45 am]

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, Public Health Service, DHHS.

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.

Methods for Tumor Treatment Using Dendrimer Conjugates

Hisataka Kobayashi and Peter Choyke (NCI)

U.S. Provisional Application filed 11 Mar 2005 (DHHS Reference No. E–107–2005/0–US–01)

Licensing Contact: Michael Shmilovich; 301/435–5019; *shmilovm@mail.nih.gov.*

Available for licensing and commercial development are dendrimer based methods for treating cancer. The dendrimer conjugate comprises an effective amount of an anti-tumor agent. A generation 5 DAB, generation 2 polylysine, or generation 6–8 PAMAM dendrimer (*e.g.,* PAMAM–G6) conjugate is administered to a cancer patient. The anti-tumor agent is selectively concentrated in the lymphatic system to treat metastatic disease. The anti-tumor agent can be one that is activated after selective aggregation in the lymphatic system. When an activatable anti-tumor agent is used, it may be activated by applying physical energy to the subject's body, for example by external application of that energy to the body. In particular examples, the external energy is heat, ultrasound, or electromagnetic energy. In particular, the physical energy can be a particle beam, such as a neutron beam.

The dendrimer conjugates may include an imaging agent, which permits the lymphatic system to be imaged when selective intra-lymphatic concentration of the dendrimer occurs. Further, when the dendrimer conjugate includes an activatable anti-tumor agent, the method may include selectively applying physical energy to the subject's body to selectively activate the anti-tumor agent in the lymphatic system. The dendrimer conjugate can include gadolinium, wherein the gadolinium acts as a contrast agent to image the lymphatic system.

In a particular example, the dendrimer conjugate includes a gadolinium-imaging agent that is activatable by a neutron beam. Once the gadolinium containing dendrimer conjugate is concentrated in the lymphatic system, detecting selective concentration of the dendrimer conjugate in the lymphatic system images the lymphatic system. The presence of tumor in lymph nodes can also be detected using this imaging technique. A neutron beam is then selectively applied to the imaged lymphatic system to selectively activate the anti-tumor agent at target areas in the lymphatic system for the treatment of metastatic tumor. In this example, the target area may be a lymph node, such as a sentinel lymph node, or a lymphatic vessel. The target area, when imaged, may show evidence of primary or metastatic tumor.

In addition to licensing, the technology is available for further development through collaborative research opportunities with the inventors.

A Universal Antigen Delivery Platform for Enhanced Immune Response

John T. Patton and Zenobia F. Taraporewala (NIAID)

U.S. Provisional Application No. 60/633,036 filed 03 Dec 2004 (DHHS Reference No. E–322–2004/0–US–01)

Licensing Contact: Chekesha Clingman; 301/435–5018; *clingmac@mail.nih.gov.*

The present invention relates to a universal antigen delivery platform based on rotavirus NSP2 fusion proteins and methods for the use of such fusion proteins to enhance an immune response to an antigen. This technology

can potentially be used for rapid production of subunit vaccines against a wide range of infectious agents. Additional uses of the technology include development of diagnostic systems and production of specific antisera for research purposes. The antigen delivery platform comprises a monomeric fusion protein including (a) a self-aggregating polypeptide component (*e.g.* a viral NSP2 polypeptide); (b) a linear linking peptide; and (c) an antigenic polypeptide. Upon expression in prokaryotic or eukaryotic systems, multiple monomeric fusion protein subunits form a self-aggregating stable multimeric ring structure, which allows multivalent display of the antigen and enhances the immune response. Additionally, this delivery platform can be efficiently produced and recovered and is physically robust. The patent application also includes pharmaceutical compositions of vaccines for prophylactic and therapeutic administration.

Relevant publications: P. Schuck *et al.,* ''Rotavirus nonstructural protein NSP2 self-assembles into octamers that undergo ligand-induced conformational changes,'' J. Biol. Chem. (2001 March 30) 276(13):9679–9687, doi:10.1074/jbc.M009398200; H. Jayaram *et al.*, ''Rotavirus protein involved in genome replication and packaging exhibits a HIT-like fold,'' Nature (2002 May 16) 417(6886):311–315, doi:10.1038/417311a.

In addition to licensing, the technology is available for further development through collaborative research opportunities with the inventors.

Peptide Inhibitors of Yersinia Phosphatase (YopH) as Potential Treatments Against Plague

Terrence R. Burke, Jr., Kyeong Lee, Yang Gao, Jason Phan, David S. Waugh (NCI) U.S. Patent Application No. 10/341,607 filed 14 Jan 2003; International Application Number PCT/US04/00669 filed 12 Jan 2004, which published as WO 2004/065411 A3 on 05 Aug 2004 (DHHS Reference No. E–263–2002/0)

Licensing Contact: Cristina Thalhammer-Reyero; 301/435–4507; *thalhamc@mail.nih.gov.*

Available for licensing and commercial development are compounds that are useful as inhibitors of protein-tyrosine phosphatases (PTPs), and in particular, as inhibitors of the *Yersinia pestis* PTP (YopH). The compounds are tripeptides of the formula P–A–B–C, or prodrugs thereof, wherein A is an amino acid having a carboxy alkyl group (*e.g.*, carboxy C1-C6 alkyl group), B is a substituted tyrosine or phenylalanine, C is a hydrophobic amino acid, and P is an amine protecting group protecting the amine end of A. The inventors have discovered that a certain group on a specific residue is absolutely required to be present on those peptides in order to be active against YopH, and that another specific group results in higher affinity. These requirements are distinct from the requirements by other PTPs. Also disclosed are pharmaceutical compositions comprising such a compound and a pharmaceutically acceptable carrier. The invention also provides a method of inhibiting the YopH enzyme as well as a method of treating plague in an animal, *e.g.,* a human, exposed to or infected by *Yersinia pestis.* The compounds may be useful as anti-bioterrorism agents, and are potentially important for therapeutic development because they may facilitate bioavailablility, given the low ionic charge of the inhibitors.

The bacterium *Yersinia pestis* causes bubonic, pneumonic and septicemic plague, and it is considered as a potential bioterrorism agent. Within *Yersinia* is a 70 kb virulence plasmid, which encodes for a system of secreted proteins, called ''Yops'', which act either as intracellular effectors or as translocators. *Yersinia's* Yop system represents the archetype for one of the major virulence mechanisms in various pathogenic bacteria, referred to as type III, where extracellular bacteria that are in close contact with a eukaryotic cell deliver bacterial proteins into the cytosol of the cell. Other animal pathogens with related systems include the genera *Salmonella, Shigella, Pseudomonas, Chlamidia,* and *Bortedella,* as well as *E. coli.* One such effector protein, YopH, is a protein-tyrosine phosphatase (PTP) with a C-terminal catalytic domain that is essential to *Yersinia's* virulence, playing an antiphagocytic role by dephosporylating focal adhesion proteins. The phosphatase activity of YopH is required for bacterial pathogenesis.

Selections of Genes and Methods of Using the Same for Diagnosis and for Targeting the Therapy of Select Cancers

Javed Khan, Jun S. Wei and Braden T. Greer (NCI)

U.S. Provisional Application No. 60/598,728 filed 03 Aug 2004 (DHHS Reference No. E–324–2001/2-US–01)

Licensing Contact: Cristina Thalhammer-Reyero; 301/435–4507; *thalhamc@mail.nih.gov.*

Available for licensing and commercial development are selections of expressed genes that function to characterize neuroblastoma in patients, and methods of using the same for targeting the therapy of neuroblastoma and for predicting the outcome of the therapy. The invention also relates to the use of supervised pattern recognition methods, such as artificial neural networks using high dimensional data, such as gene expression profiling data, for the prognosis of patients with neuroblastoma to predict their outcome.

Currently, patients with neuroblastoma are classified into risk groups (*e.g.*, according to the Children's Oncology Group risk-stratification) to guide physicians in the choice of the most appropriate therapy. Despite this careful stratification, the survival rate for patients with high-risk neuroblastoma remains <30%, and it is not possible to predict which of these high-risk patients will survive or succumb to the disease. The inventors performed gene expression profiling using cDNA microarrays containing 42,578 clones and used artificial neural networks to develop an accurate predictor of survival for each individual patient with neuroblastoma. Using principal component analysis we found that neuroblastoma tumors exhibited inherent prognostic specific gene expression profiles, achieving 88% accuracy. They identified 19 genes, including 2 prognostic markers reported previously, MYCN and *CD44,* which correctly predicted outcome for 98% of these patients.

The technology is further described in: Jun S. Wei, Braden T. Greer, Frank Westermann, Seth M. Steinberg, Chang-Gue Son, Qing-Rong Chen, Craig C. Whiteford, Sven Bilke, Alexei L. Krasnoselsky, Nicola Cenacchi, Daniel Catchpoole, Frank Berthold, Manfred Schwab, and Javed Khan, ''Prediction of Clinical Outcome Using Gene Expression Profiling and Artificial Neural Networks for Patients with Neuroblastoma'', Cancer Research 64, 6883–6891, October 1, 2004.

Amine Modified Random Primers for Microarray Detection

Charles Xiang and Michael J. Brownstein (NIMH)

U.S. Provisional Application No. 60/283,423 filed 11 Apr 2001; International Application PCT/US02/11656 filed 11 Apr 2002, which published as WO02083922 on 24 Oct 2002; corresponding U.S. Patent Application No. 10/474,611 filed 09 Oct 2003, and EP, CA and AU applications (DHHS Reference No. E–098–2001/0)

Licensing Contact: Cristina Thalhammer-Reyero; 301/435–4507; *thalhamc@mail.nih.gov.*

Available for licensing and commercial development is a new method for labeling nucleic acid molecules for use in hybridization reactions, and kits employing these methods. The fluorescence-labeled cDNA probes for DNA microarray studies only use about 1/20th as much input RNA as the conventional methods. The method allows making high quality probes from as little as 1 ug of total RNA without RNA or signal amplification. It is based on priming cDNA synthesis with random hexamers to the 5' ends of which amino allyl modified bases have been added. Coupling of the fluorescent dye to the amine residues is performed after the cDNA is reverse transcribed. The method can be used in tandem with RNA amplification (and/or signal amplification) to label probes from 10 or fewer cells.

Furthermore, the invention also relates to a novel method to amplify RNA derived from single cells using T3-random 9mers and a new lysing method, which allow probe-labeling capabilities that are approaching the single cell level.

DNA Microarray technology has become one of the most important tools for high throughput studies in medical research with applications in the areas of gene discovery, gene expression and mapping. The suitability of DNA Microarray for profiling diseases and for identifying disease-related genes has also been also well documented. Most studies using DNA arrays involve preparation of fluorescent-labeled cDNA from the mRNA of the studied organism. The cDNA probes are then allowed to hybridize to the DNA fragments printed on the array, and the array is scanned and the data analyzed. Good results depend on a number of factors including high quality arrays and well-labeled probes. In order to achieve adequate sensitivity and reproducibility, probes have had to be prepared from rather large amounts of RNA using other methods.

The technology is further described in Xiang CC, Kozhich OA, Chen M, Inman JM, Phan QN, Chen Y, Brownstein MJ. ''Amine-modified random primers to label probes for DNA microarrays.'' Nat Biotechnol. 2002 Jul; 20(7): 738–42.

Methods for Manipulating Nucleic Acids

Charles Xiang and Michael J. Brownstein (NIMH)

U.S. Patent Application No. 10/269,515 filed 11 Oct 2002, published as US2003170675 on 11 Sept 2003 (DHHS Reference No. E–098–2001/1) and International Application PCT/US03/33319 filed 10 Oct 2003, published as WO 200/033669 on 22 April 2004 (DHHS Reference No. E–098–2001/2)

Licensing Contact: Cristina Thalhammer-Reyero; 301/435–4507; *thalhamc@mail.nih.gov.*

Available for licensing and commercial development are methods of labeling nucleic acid probes for the detection of nucleic acids molecules, for instance producing labeled probes for detecting hybridization signals, such as those from a microarray. This disclosure provides new methods for amplifying nucleic acid templates from very small samples, even as small as one cell. Nucleic acid templates amplified by the disclosed methods can be used in combination with any method that requires amplified nucleic acid. In addition, the amplified nucleic acid can be labeled with any labeling method, such as the labeling method disclosed herein. Also provided are methods for preparing modified nucleotide probes, from either amplified or unamplified nucleic acid templates. In one embodiment, the method includes the incorporation of modified nucleic acids into random primers that are used to initiate polymerization of a probe molecule. In another embodiment, the random primers include nucleotides that are modified by amine groups (such as aminoallyl moieties). In yet other embodiments, the modified nucleotides comprise a detectable molecule, such as a fluorophore or hapten. The disclosure also provides an improved method of extracting RNA from fixed cells or tissue sections for subsequent use as RNA templates or for generating labeled probe. In one specific embodiment, the cells are fixed with Dithio-bis (Succinimidyl Propionate) (DSP). Also disclosed are kits for producing a labeled hybridization probe, using a modified random primer, or for probing an array, and kits for amplifying nucleic acid templates from very small samples.

The technology is further described in: Xiang CC, Chen M, Kozhich OA, Phan QN, Inman JM, Chen Y, Brownstein MJ. ''Probe generation directly from small numbers of cells for DNA microarray studies.'' Biotechniques. 2003 Feb;34(2):386–8, 390, 392–3; Xiang CC, Chen M, Ma L, Phan QN, Inman JM, Kozhich OA, Brownstein MJ. ''A new strategy to amplify degraded RNA from small tissue samples for microarray studies.'' Nucleic Acids Res. 2003 May 1; 31(9):e53; Xiang CC, Brownstein MJ. ''Preparing fluorescent probes for microarray studies.'' Methods Mol Biol. 2003; 224:55–60; and Xiang CC, Mezey E, Chen M, Key S, Ma L, Brownstein MJ. ''Using DSP, a reversible cross-linker, to fix tissue sections for immunostaining, microdissection and expression profiling'' Nucleic Acids Res. 2004 Dec 16; 32(22): e185.

Dated: April 11, 2005.

Steven M. Ferguson,

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

[FR Doc. 05–7848 Filed 4–19–05; 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, DHHS.

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Triptolide To Induce Immunotolerance

Xin Chen *et al.* (NCI).

U.S. Provisional Application 60/638,640 filed 22 Dec 2004 (DHHS Reference No. E–358–2004/0–US–01).

Licensing Contact: Fatima Sayyid; (301) 435–4521; *sayyidf@mail.nih.gov.*

Dendritic cells represent a heterogeneous population of antigen-presenting cells that initiate primary immune responses by activating naive T cells and subsequently the effector cells of the adaptive immune system. Accordingly, dendritic cells play an