human cancers that overexpress human VEGFR2 by introducing anti-VEGFR2 CAR expressing T cells into patients with metastatic cancer.

• A possible prophylactic therapy to prevent the spread of cancer in patients whose cancer is predicted to metastasize.

• A drug component of a combination immunotherapy regimen aimed at targeting the specific tumor-associated antigens expressed by cancer cells within individual patients.

Advantages:

• *This discovery is widely applicable to many different cancers:* VEGFR2 is overexpressed in many metastatic cancers that utilize angiogenesis to spread from their initial site of development. An immunotherapy protocol using anti-VEGFR2 CAR could treat a variety of cancer types.

• *Antiangiogenic tumor therapy is anticipated to generate fewer side-effects compared to other treatment approaches:* These CARs can be delivered directly to the bloodstream to gain easy access to the targeted tumor vascular endothelial cells with minimal effects to normal tissues. Furthermore, destroying tumor blood vessels could accelerate tumor cell death so that the therapy can be administered for a shorter period of time. A reduced therapeutic timeframe and minimal access to normal tissues should contribute to reduced side-effects and lowered toxicity for this treatment.

• *The technology is anticipated to be highly effective and killing metastatic cells:* Most angiogenic tumor epithelial cells are believed to overexpress VEGFR2 to a similar degree. Administering a therapeutically effective amount of anti-VEGFR2 CARs to patients may leave no or little tumor cells remaining with an opportunity to metastasize. Many current angiogenesis therapies do not kill tumors, but rather stabilize the tumor, so they require long periods of administration.

Development Status: This technology could soon be ready for clinical development since the inventors plan to initiate clinical trials using CAR engineered lymphocytes for adoptive immunotherapy of cancer.

Market: The Food and Drug Administration (FDA) has approved eight therapies with antiangiogenic properties, including Avastin®, Erbitux®, Vectibix®, Herceptin®, Tarceva®, Nexavar®, Sutent®, Torisel™, Velcade®, and Thalomid®. The majority of these drugs produced worldwide sales exceeding an estimated $500 million in 2007. The fight against cancer and its spread will continue to benefit from the development of new therapeutics aimed at treating individual patients.

Cancer continues to be a medical and financial burden on U.S. public health. Statistically, in the U.S. cancer is the second leading cause of death with over 565,000 deaths reported in 2008 and almost 1.5 million new cases were reported (excluding some skin cancers) in 2008, many with the potential to metastasize. In 2007, the NIH estimated that the overall cost of cancer was $219.2 billion dollars and $89 billion went to direct medical costs.

Inventors: Steven A. Rosenberg et al. (NCI).

Patent Status: HHS Reference No. E–205–2009/0—U.S. Provisional Application No. 61/247,625 filed 01 Oct 2009.

Related Technologies:

• E–045–2009/0—U.S. Provisional Application No. 61/154,080 filed 20 Feb 2009

• E–312–2007/1—PCT Application No. PCT/US2008/077333 filed 23 Sep 2008

• E–059–2007/2—PCT Application No. PCT/US2008/050841 filed 11 Jan 2008, which published as WO 2008/089053 on 24 Jul 2008

• E–304–2006/0—U.S. Provisional Patent Application No. 60/847,447 filed 26 Sep 2006; PCT Application No. PCT/US2007/079487 filed 26 Sep 2007, which published as WO 2008/039818 on 03 Apr 2008

• E–093–1995/0—PCT Application No. PCT/US1996/04143 filed 27 Mar 1996, which published as WO 1996/30516 on 03 Oct 1996

• E–093–1995/2—U.S. Non-Provisional Application No. 08/084,994 filed 02 Jul 1993

Licensing Status: Available for licensing.

Licensing Contact: Samuel E. Bish, Ph.D.; 301–435–5282; *bishse@mail.nih.gov.*

Collaborative Research Opportunity: The Center for Cancer Research, Surgery Branch, 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, Ph.D. at 301–435–3121 or *hewesj@mail.nih.gov* for more information.

Dated: November 3, 2009.

Richard U. Rodriguez,

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

[FR Doc. E9–27199 Filed 11–10–09; 8:45 am]

BILLING CODE 4140–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Government-Owned Inventions; Availability for Licensing

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.

A Method of Identifying Cdk5/p35 Modulators, and Possible Diagnostic or Therapeutic Uses for Neurodegenerative Diseases

Description of Invention: Cyclin-dependent kinase 5 (Cdk5) is a serine/threonine cyclin-dependent kinase that is highly expressed in the central nervous system and controls many biological processes that impact learning and memory, as well as pain and drug addiction. Studies have indicated that abnormal Cdk5 activity may be associated with the onset of neurodegenerative diseases, such as Alzheimer's disease, Parkinson's disease, and amyotrophic lateral sclerosis (ALS). The kinase activity of Cdk5 is turned on when it binds to one of the two proteins considered to be neuronal activators, p35 and p39.

Scientists at the NIH designed a cell-based assay to screen for p35 transcriptional regulators that work as upstream regulators of Cdk5. This technology may be useful for assessing the presence and risk of conditions associated with atypical Cdk5 kinase activity or for finding drug modulators that could be promising drug targets.

Applications:

• Diagnostic tool for assessing risk of conditions associated with abnormal Cdk5 kinase activity.

• Tool for screening Cdk5 modulators.

Development Status: Early stage.

Inventors: Ashok B. Kulkarni and Elias S. Utreras Puratich (NIDCR).

Patent Status: U.S. Provisional Application No. 61/198,246 filed 03 Nov 2008 (HHS Reference No. E–012–2009/0–US–01).

Licensing Status: Available for licensing.

Licensing Contact: Charlene Sydnor, Ph.D.; 301–435–4689; *sydnorc@mail.nih.gov.*

Collaborative Research Opportunity: The National Institute of Dental and Craniofacial Research, Laboratory of Cell and Developmental Biology, Functional Genomics Section, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize this technology. Please contact David W. Bradley, Ph.D. at 301–402–0540 or *bradleyda@nidcr.nih.gov* for more information.

A Phantom for Diffusion MRI: A Method of Enhancing Performance and Reliability

Description of Invention: The technology offered for licensing is in the field of Diffusion Magnetic Resonance Imaging (Diffusion MRI). Specifically, a novel imaging phantom is described and claimed. Such a phantom is specifically optimized for Diffusion MRI and is expected to enhance the performance and reliability of this now widespread imaging technology.

The phantom provided in this invention comprises a stable aqueous solution with a concentration of at least 30%, by weight, of a mixture of a high molecular-weight polymer or copolymer and a low molecular-weight polymer or copolymer, the aqueous solution having a resulting water diffusivity from about 2×10^{-4} mm²/s to about 3×10^{-3} mm²/s. Polyvinyl Pyrrolidone (PVP) is the polymer of choice used in this invention. The phantoms of this invention are uniquely stable, non-toxic, and transportable, and have shown to maintain constant water diffusivity after two years.

Applications: Combining a Diffusion MRI phantom with a resolution phantom would allow the same device to be used to calibrate an MR scanner's image quality and the accuracy and precision of its diffusion measurements. This would be useful particularly for Radiological QA and for use in assuring data quality in longitudinal and multi-subject studies.

Advantages:

• The imaging phantoms provided in the invention are optimized specifically for Diffusion MRI. They possess the following features and characteristics:

—Made of non-toxic, non-hazardous, non-flammable and easily transportable materials.

—Possess diffusivities similar to those of water in biological tissues, particular brain parenchyma.

—Possess stable diffusion properties over time. No appreciable change in water diffusivity was detectable after two years.

—Offers option to tailor diffusiveness of the phantoms to different applications by varying the ratios of the chemical components.

• In addition, the inventors established a procedure to make concentrated solutions (up to 80 wt% polymer content) from mixtures of different molecular weight polyvinyl pyrrolidone (PVP) polymer and/or vinylpyrrolidone-based copolymers in water in the presence of physiologically relevant ions and gadolinium-based MRI contrast agents. In general, preparation of homogeneous polymer solutions from hydrophilic glassy polymers with high solute content is problematic due to the inter- and intra-molecular interactions (*e.g.,* hydrogen bonds) leading to formation of entanglements and gelation. This discovery indicates that at certain PVP-water compositions the new preparation procedure gives rise to disengagement of polymer chains and considerably improves polymer solubility. Moreover, the addition of lower molecular weight PVP and/or vinylpyrrolidone-based copolymers decreases the intra molecular association among the polymer molecules without significantly affecting the diffusive and relaxation properties of the solvent (water) in the MRI phantom.

Development Status: The invention is fully developed.

Market:

• The market for medical imaging equipment industry is approximately $9.0 billion dollars now and has been growing by approximately 7.6% annually. MRI instrumentation constitutes a significant portion of this market.

• Diffusion MRI is now a mature technology that has received FDA approval; Diffusion MRI methods are ''made, used and sold'' by all major MRI manufacturers. The installed base of clinical scanners using Diffusion MRI methods, including DTI, must now be in the thousands, worldwide.

• Imaging phantoms are necessary components of any imaging system as they provide the means for the systems' standardization and quality control, and are thus a required components for their reliable performance. Commercial success of these phantoms described in the invention is therefore expected, in particular in view of the unique characteristics possessed by these phantoms as outlined above. Due to these properties they can be stored in a medical facility without special permits or requirements.

• The phantoms described in this invention could be sold with new MRI scanners supporting DTI and other diffusion MRI methods or for existing MRI scanners that support diffusion MRI applications. These phantoms could be used by MRI companies internally for product sequence testing and development as well as to ensure that MRI scanners shipped to users operate properly and to within ''specs'' following installation. The phantoms should be of interest to medical physicists, technicians and bioengineers charged with the responsibility of assuring quality and reproducibility in their routine and research scans.

Inventors: Ferenc Horkay, Carlo Pierpaoli, Peter Basser (NICHD).

Patent Status: U.S. Provisional Application No. 61/147,314 filed 26 Jan 2009 (HHS Reference No. E–249–2008/0–US–01).

Licensing Status: Available for licensing.

Licensing Contacts: Uri Reichman, Ph.D., MBA; 301–435–4616; *UR7a@nih.gov*; John Stansberry, Ph.D.; 301–435–5236; *stansbej@mail.nih.gov*.

Collaborative Research Opportunity: The Eunice Kennedy Shriver National Institute of Child Health and Human Development's Section on Tissue Biophysics & Biomimetics (STBB) is seeking statements of capability or interest from outside parties who are interested in entering into a Collaborative Research and Development Agreement (CRADA) to develop and commercialize the Diffusion MRI Phantom described above. Please contact Alan Hubbs, Ph.D. at 301–594–4263 or *hubbsa@mail.nih.gov* for more information.

Viral Inactivation Using Crosslinkers and Detergents

Description of Invention: The subject technology is a method of inactivating enveloped viruses by hydrophobic photoactivatable chemical crossing-linking compounds and detergent treatment. The inactivated viruses may be used as vaccines against the diseases caused by those viruses or as reagents in experimental procedures that require

inactivated viral particles. The compounds diffuse into the lipid bilayer of biological membranes and upon UV irradiation will bind to proteins and lipids in this domain, thereby inactivating fusion of enveloped viruses with their corresponding target cells. Furthermore, the selective binding of these chemical crosslinking agents to protein domains in the lipid bilayer may preserve the structural integrity and therefore immunogenicity of proteins on the exterior of the inactivated virus. The additional detergent step effectively eliminates the infectivity of any residual viral particles that are not adequately crosslinked.

Applications:

• Vaccines for enveloped viruses.

• Vaccine for Human Immunodeficiency Virus.

Advantages:

• Novel method of inactivating enveloped viruses.

• May maintain native conformational structures and viral epitopes for generating an effective immune response.

Development Status: In vitro data can be provided upon request.

Market: Vaccines.

Patent Status: International Patent Application PCT/US2009/000623 filed 30 Jan 2009 (HHS Reference No. E–331–2007/2–PCT–01).

Licensing Status: Available for licensing.

Licensing Contact: Kevin W. Chang, Ph.D.; 301–435–5018; *changke@mail.nih.gov*.

Collaborative Research Opportunity: The National Cancer Institute, Center for Cancer Research, Nanobiology Program is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize the use of hydrophobic crosslinkers for their use in vaccine development. Interested collaborators are also invited to provide statements for proposed *in vitro* or *in vivo* studies using various enveloped viruses. Please contact John D. Hewes, Ph.D. at 301–435–3121 or *hewesj@mail.nih.gov* for more information.

New Derivative of Dextromethorphan for Use in Neuronal Therapy

Description of Invention: This invention describes a derivative of dextromethorphan, which is a non-competitive inhibitor of the nicotinic acetylcholine receptor. Dextromethorphan is an antitussive drug used as one of the active ingredients to prevent coughs in many over-the-counter cold and cough medicines. It has also found other uses in medicine, ranging from pain relief to psychological applications. The disclosed compound may display attractive properties compared to the closely related dextromethorphan or other drugs currently in use as non-competitive inhibitors of the nicotinic acetylcholine receptors, including extended receptor inhibition and reduced side effects.

The nicotine acetylcholine receptor is a ligand gated ion channel. These receptors specifically control rapid permeation of cations through the postsynaptic cell membrane, and are key targets in drug discovery for a number of diseases such as Alzheimer's and Parkinson's disease. This superfamily of receptor proteins is separated into the nicotinic receptor superfamily (muscular and neuronal nicotinic), the excitatory amino acid superfamily, and the ATP purinergic ligand gated ion channels, and they differ only in the number of transmembrane domains found in each subunit. This newly discovered derivative of dextromethorphan may have potential therapeutic use for several conditions involving these nicotinic acetylcholine receptors.

Advantages:

• Derivative of dextromethorphan may have superior properties on target receptors including increased selectivity, potency and receptor occupancy.

• Potential other therapeutic uses for the new compound.

Development Status: Early stage.

Inventors: Irving W. Wainer *et al.* (NIA).

Publication: K Jozwiak *et al.* Displacement and non-linear chromatographic techniques in the investigation of the interaction of noncompetitive inhibitors with an immobilized alpha3beta4 nicotinic acetylcholine receptor liquid chromatographic stationary phase. Anal Chem. 2002 Sep 15;74(18):4618–4624.

Patent Status: U.S. Patent Application No. 10/820,809 filed 09 Apr 2004, claiming priority to 11 Apr 2003 (HHS Reference No. E–158–2003/1–US–02).

Licensing Status: Available for licensing.

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

Collaborative Research Opportunity: The National Institute on Aging, Laboratory of Clinical Investigation, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize a series of noncompetitive inhibitors of neuronal nicotinic acetylcholine receptors based upon the dextromethorphan and levomethorphan scaffolds including molecular modeling and synthesis of new derivatives, receptor binding and occupancy studies and non-competitive inhibition of nicotinic acetylcholine receptors subtypes and related ligand gated ion channels. Please contact Nicole Darack, Ph.D. at 301–435–3101 or *darackn@mail.nih.gov* for more information.

Methods and Compositions for the Diagnosis of Neuroendocrine Lung Cancer

Description of Invention: The technology relates to the use of cDNA microarrays to facilitate the identification of pulmonary neuroendocrine tumors. In order to identify molecular markers that could be used to classify pulmonary tumors, the inventors examined the gene expression profiles of clinical samples from patients with small cell lung cancer (SCLC), large cell neuroendocrine carcinoma (LCNEC), and typical carcinoma (TC) tumors by cDNA microarray analysis to detect hybridization between cDNA from tumor cells and DNA from a panel of 8,897 human genes. Gene expression was found to be nonrandom and to exhibit highly significant clustering that divided the tumors into their assigned World Health Organization (WHO) classification with 100% accuracy. The inventors concluded that pulmonary neuroendocrine tumors could be classified based on the genome-wide expression profile of the clinical samples without further manipulations.

Applications:

• Method to differentiate three types of pulmonary neuroendocrine tumors.

• Method to diagnose pulmonary neuroendocrine cancer.

• Neuroendocrine Microarray.

Advantages: Accurate, rapid, easy to use diagnostic to stratify patients according pulmonary tumors.

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

Market:

• Cancer is the second leading cause of death in United States and it will be responsible for an estimated 562,340 deaths.

• It is estimated that the cancer therapeutic market would double to $50 billion a year in 2010 from $25 billion in 2006.

Inventors: Curtis C. Harris et al. (NCI)

Publication: P He *et al.* Identification of carboxypeptidase E and gamma-glutamyl hydrolase as biomarkers for pulmonary neuroendocrine tumors by

cDNA microarray. Human Pathol. 2004 Oct;35(10):1196–1209.

Patent Status: U.S. Patent Application No. 10/533,459 filed 02 May 2005 (HHS Reference No. E–248–2002/0–US–04).

Licensing Status: Available for licensing.

Licensing Contact: Jennifer Wong; 301–435–4633; *wongje@mail.nih.gov*.

Immunotoxin Useful for Treatment of AIDS

Description of Invention: Human Immunodeficiency Virus (HIV) attacks and destroys T cells, leading to the development of Acquired Immunodeficiency Syndrome (AIDS) in patients. Although significant progress has been made treating patients with AIDS, an effective cure has yet to be identified. For example, highly active antiretroviral therapy (HAART) has shown dramatic reduction of viral replication while allowing recovery of the immune system in HIV patients. However, HAART does not directly kill HIV-infected T cells, allowing the virus to persist in the body and resume replication and infection of T cells after HAART is stopped. This ultimately results in a return to pre-treatment levels of viral replication and the persistence of the disease in patients.

The current technology concerns an invention that can be used to address this limitation of HAART. An immunotoxin has been created that targets a toxin (PE38) to the HIV-specific Envelope glycoprotein (gp120) that is displayed on the surface of T cells that have been infected with the HIV virus. The immunotoxin kills the HIV-infected T cells and other infected cell types that serve as a viral reservoirs during HAART, thereby reducing the ability of the virus to replicate and infect other cells after HAART is stopped. Recent data shows that the immunotoxin blocks the spread of HIV–1 *in vitro* and does not induce hepatotoxicity in rhesus monkeys, suggesting the procedure could be effective in human patients. By combining the immunotoxin with a treatment regimen such as HAART, it may be possible to significantly improve treatment of HIV infection.

Applications:

- Reduction of HIV–1 infected cell populations in patients to reduce viral reservoirs.
- Treatment of HIV infection in combination with therapeutic regimens such as HAART.

Advantages:

- Overcomes a limitation of current HIV therapies by specifically depleting infected cell reservoirs.
- Specific targeting of HIV-infected cells allows depletion of infected cells without affecting uninfected cells.
- Combination therapy combines inhibition of HIV replication and selective killing of infected cells that still persist.

Development Status: Preclinical stage of development.

Patent Status:

- US Patent Application 09/673,707 (HHS Reference No. E–201–1998/0–US–06), pending.
- European Patent 1085908 (HHS Reference No. E–201–1998/0–EP–05).

For more information, see:

- PE Kennedy et al. Anti-HIV–1 immunotoxin 3B3(Fv)-PE38: enhanced potency against clinical isolates in human PBMCs and macrophages, and negligible hepatotoxicity in macaques. J Leukoc Biol. 2006 Nov;80(5):1175–1182.
- TK Bera et al. Specific killing of HIV-infected lymphocytes by a recombinant immunotoxin directed against the HIV–1 envelope glycoprotein. Mol Med. 1998 Jun;4(6):384–391.

Inventors: Ira Pastan *et al.* (NCI)

Licensing Status: Available for licensing.

Licensing Contact: David A. Lambertson, Ph.D.; 301–435–4632; *lambertsond@mail.nih.gov*.

Collaborative Research Opportunity: The Center for Cancer Research, Laboratory of Molecular Biology, 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, Ph.D. at 301–435–3121 or *hewesj@mail.nih.gov* for more information.

Dated: November 4, 2009.

Richard U. Rodriguez,

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

[FR Doc. E9–27196 Filed 11–10–09; 8:45 am]

BILLING CODE 4140–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2009–D–0508]

Guidance for Industry on Registration and Product Listing for Owners and Operators of Domestic Tobacco Product Establishments; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of the guidance entitled ''Registration and Product Listing for Owners and Operators of Domestic Tobacco Product Establishments.'' The guidance document is intended to assist persons making tobacco product establishment registration and product listing submissions to FDA under the Family Smoking Prevention and Tobacco Control Act (Tobacco Control Act).

DATES: Submit written or electronic comments on this guidance at any time. General comments on agency guidance documents are welcome at any time.

ADDRESSES: Submit written requests for single copies of the guidance document entitled ''Registration and Product Listing for Owners and Operators of Domestic Tobacco Product Establishments'' to the Center for Tobacco Products, Food and Drug Administration, 9200 Corporate Blvd., Rockville, MD 20850–3229. Send one self-addressed adhesive label to assist that office in processing your request or include a fax number to which the guidance document may be sent. See the **SUPPLEMENTARY INFORMATION** section for information on electronic access to the guidance document.

Submit written comments on the guidance to the Division of Dockets Management (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit electronic comments to *http://www.regulations.gov*. Identify comments with the docket number found in brackets in the heading of this document.

FOR FURTHER INFORMATION CONTACT: Michele Mital, Center for Tobacco Products, Food and Drug Administration, 9200 Corporate Blvd., Rockville, MD 20850–3229, 301–796–4800, *Michele.Mital@fda.hhs.gov*.

SUPPLEMENTARY INFORMATION:

I. Background

In the **Federal Register** of October 21, 2009 (74 FR 54052), FDA announced the availability of a draft guidance document entitled ''Registration and Product Listing for Owners and Operators of Domestic Tobacco Product Establishments.'' The agency considered received comments as it finalized this guidance. This guidance document is designed to assist domestic owners and operators with submitting tobacco product establishment registration and tobacco product listing information. Under section 905(b) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 387e(b)), added by the