[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, 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. 209 and 37 CFR Part 404 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: 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.

Rabbit Antibody to Mouse Sphingosine-1-phosphate (S1P) lyase

Description of Technology: The cleavage of sphingoid base phosphates by sphingosine-1-phosphate (S1P) lyase to produce phosphoethanolamine and a fatty aldehyde is the final degradative step in the sphingolipid metabolic pathway. Researchers at NIH injected rabbits with the C-terminal peptide of the mouse S1P lyase — 551-TTDPVTQGNQMNGSPKPR-568 — to develop an antibody that can be used in western blotting to study this pathway.

Potential Commercial Applications: The antibody can be used to detect and measure S1P lyase.

Competitive Advantages: The antibody works very well for western blotting.

Development Stage: In vitro data available

Inventor: Richard L. Proia (NIDDK)

Publication: Bektas M, et al. Sphingosine 1-phosphate lyase deficiency disrupts lipid homeostasis in liver. J Biol Chem. 2010 Apr 2;285(14):10880-9. [PMID 20097939]

Intellectual Property: HHS Reference No. E-465-2013/0 – Research Tool. Patent protection is not being pursued for this technology.

Licensing Contact: Jaime M. Greene, M.S.; 301-435-5559; greenejaime@mail.nih.gov

Rabbit Antibody to Mouse Sphingosine kinase 2 (SphK2)

Description of Technology: Two isoforms of sphingosine kinase, sphingosine kinase 1 (SphK1) and sphingosine kinase 2 (SphK2), convert sphingosine to sphingosine

1-phosphate (S1P) in mammalian cells. While the importance of SphK1 has been known for some time, information about SphK2 is still being revealed. Therefore, researchers at NIH have developed an antibody against mouse SphK2, which can be used to further understand the role of this enzyme.

Potential Commercial Applications: The antibody can be used to detect and measure SphK2.

Competitive Advantages: The antibody works very well for western blotting.

Development Stage: In vitro data available

Inventor: Richard L. Proia (NIDDK)

Publication: Olivera A, et al. IgE-dependent activation of sphingosine kinases 1 and 2 and secretion of sphingosine 1-phosphate requires Fyn kinase and contributes to mast cell responses. J Biol Chem. 2006 Feb 3;281(5):2515-25. [PMID 16316995]

Intellectual Property: HHS Reference No. E-466-2013/0 – Research Tool. Patent protection is not being pursued for this technology.

Licensing Contact: Jaime M. Greene, M.S.; 301-435-5559; greenejaime@mail.nih.gov

Video Monitoring System for Vivarium Cage Racks

Description of Technology: This invention pertains to a system for continuous observation of rodents in home-cage environments with the specific aim to facilitate the quantification of activity levels and behavioral patterns for mice housed in a commercial ventilated cage rack. The home-cage in-rack provides daytime and nighttime monitoring with the stability and consistency of a home-cage environment. The system is made up of

a dual-video camera hardware design mounted on a video rack and an executable software means for automatic detection and processing for tracking multiple animals.

Potential Commercial Applications:

• vivarium monitoring

• laboratory test animal management

Competitive Advantages:

• real-time monitoring

• day or night monitoring

Development Stage: Prototype

Inventors: James Mitchell (NCI), Ghadi Salem (CIT), Thomas Pohida (CIT)

Intellectual Property: HHS Reference No. E-090-2013/0 – US Provisional Patent Application 61/841,064 filed June 28, 2013

Licensing Contact: Michael Shmilovich, Esq., CLP; 301-435-5019; shmilovm@mail.nih.gov

Collaborative Research Opportunity: The National Cancer Institute is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize Video Monitoring System for Vivarium Cage Racks. For collaboration opportunities, please contact John D. Hewes, Ph.D. at hewesj@mail.nih.gov.

MRI Scanner Bore Covering

Description of Technology: This invention pertains to a bore covering for creating controlled environments and specifically for maintaining temperature within the

bore of an MRI scanner. The bore covering includes a covering sheet with fastening means (e.g., weak-tack adhesive, pressure-sensitive adhesive or low-tack adhesive) around its inner surfaces that permits reversible attachment to the scanner. The adhesive ends can be peeled away to expose an edge of the bore opening or the entire sheet may be constructed with peel away gaps so that warm air can be pumped into the bore. On the inner surface the bore covering may include a gap that is connected to a climate control device or an exhaust vent to expel air out of the MRI scanner bore.

Potential Commercial Applications: MR imaging of infants and neonates

Competitive Advantages:

• Temperature control

• Comfort

Development Stage: Prototype

Inventors: Robert Balaban, Robert Lederman, Michael Hansen, Anthony Faranesh, Kanishka Ratnayaka (all of NHLBI)

Intellectual Property: HHS Reference No. E-026-2013/0 – US Provisional Patent Application 61/836,817 filed June 19, 2013

Licensing Contact: Michael Shmilovich, Esq., CLP; 301-435-5019; shmilovm@mail.nih.gov

Collaborative Research Opportunity: The National Heart, Lung, and Blood Institute (NHLBI) is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize MRI Scanner Bore Covering. For collaboration opportunities, please contact Dr. Denise Crooks at crooksd@mail.nih.gov.

Cotranslational Protein Expression System for High-throughput Screening

Description of Technology: Reporter gene-based assays are used extensively in high-throughput screening (HTS) to identify chemical modulators of cellular pathways for drug discovery and development. However, such screening frequently results in a large number of false "hits" due to interactions of screened compounds with reporter proteins, producing confounding results. Thus, validation of results using these assays often involves significant time and expense.

The inventors have developed an assay system that significantly improves detection of target-relevant active compounds by discriminating between signals arising from the target activity and those caused by reporter bias. This system utilizes simultaneous detection (also known as "coincidence detection") of non-homologous reporter proteins with dissimilar properties, such as differing catalysis, light emission, or fluorescence characteristics; simultaneous observation of signals from these reporters indicates a high probability that it is a true target response. The reporters are cotranslationally expressed from a single RNA transcript, which ensures stable stoichiometry of the expressed proteins.

Potential Commercial Applications: High-throughput screening of chemical libraries in a single assay platform for commercial or research use.

Competitive Advantages: This method will significantly enhance the ability to identify and prioritize active compounds from reporter gene-based assays.

Development Stage: Early-stage

Inventors: James Inglese, Ken C-C Cheng, Samuel A. Hasson (all of NCATS)

Publication: Chan K, Inglese J. A coincidence reporter-gene system for high-throughput screening. Nat Methods. 2012 Oct;9(10):937. [PMID 23018994]

Intellectual Property: HHS Reference No. E-300-2012/0 – PCT Application No. PCT/US2013/032184 filed March 15, 2013

Licensing Contact: Tara L. Kirby, Ph.D.; 301-435-4426; tarak@mail.nih.gov

Collaborative Research Opportunity: The National Center for Advancing Translational Sciences (NCATS) is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize Cotranslational Protein Expression System for High-throughput Screening. For collaboration opportunities, please contact NCATS Technology Development Coordinator at NCATSPartnerships@mail.nih.gov.

Human Melanoma Metastasis Cell Lines Harboring Bcl-2-Like Protein 12 (BCL2L12) Mutations

Description of Technology: Using whole-genome and whole-exome sequencing to identify somatic (e.g., tumor-specific) alternations in human melanoma samples, the researchers at the NIH have found a recurrent synonymous (or silent) somatic mutation in the Bcl-2-Like Protein 12 (BCL2L12). The mutant BCL2L12 bound to p53 and inhibited UV-induced apoptosis more efficiently than wild-type BCL2L12 and therefore could be a novel melanoma oncoprotein. This appears to be the first report of a mutation that does not alter the encoded protein, yet affects the protein function in the cancer genome. Consequently, these cell lines could be used to further investigate the effects of BCL2L12 in melanoma and to develop therapeutics targeting this gene and protein.

Potential Commercial Applications:

• Diagnostic array for the detection of BCL2L12 mutations.

• In vitro and in vivo cell model for the BCL2L12 mutation in melanoma. This is a useful tool for investigating BCL2L12 phenotype biology, including growth, motility, invasion, and metabolite production.

Competitive Advantages:

• Cell lines are derived from melanoma patients.

• The BCL2L12 mutation is frequent in melanomas.

Development Stage: Pre-clinical

Inventors: Yardena Samuels (NHGRI) and Steven Rosenberg (NCI)

Publication: Gartner JJ, et al. Whole-genome sequencing identifies a recurrent functional synonymous mutation in melanoma. Proc Natl Acad Sci U S A. 2013 Jul 30; Epub ahead of print. [PMID 23901115]

Intellectual Property: HHS Reference No. E-145-2012/0 – Research Tool. Patent protection is not being pursued for the BCL2L12 melanoma metastatic cell lines.

Related Technologies: HHS Reference Nos. E-029-2012/0 (research tool), E-013-2011/0 (patent app: US), E-024-2012/0 (research tool), E-272-2008/0 (patent app: US, EP), E-229-2010/0 (research tool), E-232-2010/0 (research tool)

Licensing Contact: Whitney Hastings; 301-451-7337; hastingw@mail.nih.gov

Collaborative Research Opportunity: The NHGRI is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize this technology. For collaboration opportunities, please

contact Claire Driscoll, Director, NHGRI Technology Transfer Office, at cdriscol@mail.nih.gov or 301-594-2235.

Gag-Based DNA Vaccines Against HIV

Description of Technology: Novel DNA vaccine constructs against HIV that express highly conserved elements (CE) within the HIV Gag protein and elicit strong, cross-clade cellular and humoral responses. The DNA vaccine vectors were engineered to express CEs for protection against different clades of HIV and prevention of immunodominance, two issues associated with current HIV vaccine candidates.

In vivo studies of Rhesus macaques vaccinated with variants of these constructs expressing seven highly CEs covering >99 of all known Gag sequences elicited strong, cellular T-cell and humoral antibody immune responses. The Gag-specific antibody responses were high titer and cross-clade. Cross-clade protection is important given the sequence diversity of HIV as is the absence of immunodominant epitopes that generate antibodies which are not protective against HIV.

Potential Commercial Applications: HIV vaccines

Competitive Advantages: Addresses two key hurdles faced by current HIV vaccines: sequence diversity of HIV and immunodominance.

Development Stage:

• Early-stage

• Pre-clinical

• In vitro data available

• In vivo data available (animal)

Inventors: George N. Pavlakis (NCI), Barbara K. Felber (NCI), James Mullins (University of Washington)

Intellectual Property: HHS Reference No. E-132-2012/0 – PCT Application No. PCT/US2013/028932 filed March 4, 2013

Related Technology: HHS Reference No. E-308-2000/0 — Patent family filed in the U.S., Canada, Australia, Europe, and Japan

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

Diffusion Through Skull as Route of Delivery for Treatment of Brain Injury and Disease

Description of Technology: Traumatic Brain injury (TBI) often results from head impact and is a major cause of death and disability. Brain injuries vary in severity and can be associated with hemorrhaging, swelling, inflammation, and death of brain tissue. Inventors at NINDS developed a novel approach to treating brain injuries that involves transcranial application of small molecules. They discovered, using two photon laser scanning microscopy, that compounds as large as 40,000 molecular weight (MW) can pass directly through the intact skull into the underlying cerebral spinal fluid (CSF) that circulates through the brain and spinal cord. Small molecular weight compounds (e.g. 600 MW) pass through the skull more quickly than large ones and appear to do so by simple diffusion. Researchers have shown that application of a variety of agents, including glutathione, TNP-ATP hydrase (P2X4 inhibitor), oxidated ATP (P2X7 inhibitor), MRS2578 (P2Y6 inhibitor), MeSAMP (P2Y12 inhibitor) and Carbenoxelone

(Connexin Hemichannel Inhibitor) directly to the head results in delivery of the agents to the brain. Transcranial drug application can be used to pharmacologically target several tiers of brain injury responses, from the toxic mediators that cause cell death to the molecular signals that drive inflammation. Application can be by direct application to the skull through the scalp (e.g. rubbing it in), transdermal patch, or subcutaneous injection under the scalp.

Potential Commercial Applications:

• Treating Traumatic Brain Injury

• Treating stroke

• Treating other acute CNS conditions, including encephalitis and meningitis

• Treating chronic CNS disorders such as brain tumors, Alzheimer's, Parkinson's, and multiple sclerosis

Competitive Advantages:

• Quickly achieves a high local drug concentration at the site of brain injury.

• Bypasses the blood brain barrier and allows rapid administration of therapeutic agents directly into injured or inflamed brain.

• Current therapies to treat Traumatic Brain Injury with neuroprotective agents are often limited by ability to achieve therapeutic concentrations of therapeutic agent in the brain.

Development Stage:

• In vitro data available

• In vivo data available (animal)

Inventors: Dorian McGavern and Theodore Roth (NINDS)

Publication: Manuscript in preparation.

Intellectual Property: HHS Reference No. E-025-2012/0 – PCT Application No. PCT/US2013/24741 filed February 5, 2013

Licensing Contact: Betty B. Tong, Ph.D.; 301-594-6565; tongb@mail.nih.gov

Collaborative Research Opportunity: The National Institute of Neurological Disorders and Stroke (NINDS) is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize treatment of brain injury or disease through transcranial drug delivery. For collaboration opportunities, please contact Melissa Maderia, Ph.D., M.B.A. at maderiam@mail.nih.gov or 240-276-5533.

Tri-functional Imaging Agent for Monoclonal Antibody Tumor-Targeted Imaging

Description of Technology: This is a novel lysine-based trifunctional chelate which bears both a chelating moiety (CHX-A") for sequestering radiometals (86Y or 111In) and a near-infrared dye, e.g., Cy5.5, for dual modality PET (or SPECT) and fluorescence imaging. Successful conjugation of monoclonal antibody trastuzumab (Herceptin) or cetuximab (Erbitux), has also been achieved by efficient thiol-maleimide chemistry, thereby yielding an immunoconjugate (Signaling agent (Cy5.5-Lys(SMCC)-CHX-A") conjugated to trastuzumab) or (Signaling agent (Cy7-Lys(SMCC)-CHX-A") conjugated to cetuximab). Both specifically target antigen expressing cells and internalization of the agent has been imaged over time. Trastuzumab can be radiolabeled with isothiocyanate derivatives of the bifunctional chelating agents 1B4M (2-(4-aminobenzy1)-6-methyldiethylenetriaminepentaacetic acid); and CHX-A" (N-[(R)-2-

amino-3-(p-aminophenyl)propyl]-trans-(S,S)-cyclohexane-1,2-diamine-N,N,N',N'',N''-pentaacetic acid).

Potential Commercial Applications:

• Cancer imaging

• Cancer diagnostics

Competitive Advantages:

• Target specific

• Multifunctional (imageable through multiple platforms)

Development Stage:

• Early-stage

• In vivo data available (animal)

Inventors: Martin W. Brechbiel, Heng Wu, Kwamena E. Baidoo (all of NCI)

Publications:

1. Xu H, et al. Design, synthesis, and characterization of a dual modality positron emission tomography and fluorescence imaging agent for monoclonal antibody tumor-targeted imaging. J Med Chem. 2007 Sep 20;50(19):4759-65. [PMID 17725340]

2. Nayak TK, et al. PET and MRI of metastatic peritoneal and pulmonary colorectal cancer in mice with human epidermal growth factor receptor 1-targeted 89Zr-labeled panitumumab. J Nucl Med. 2012 Jan;53(1):113-20. [PMID 22213822]

3. Dadwal M, et al. Synthesis and evaluation of a bifunctional chelate for development of Bi(III)-labeled radioimmunoconjugates. Bioorg Med Chem Lett. 2011 Dec 15;21(24):7513-5. [PMID 22047687]

4. Song HA, et al. Efficient bifunctional decadentate ligand 3p-C-DEPA for targeted alpha-radioimmunotherapy applications. Bioconjug Chem. 2011 Jun 15;22(6):1128-35. [PMID 21604692]

5. Bumb A, et al. Preparation and characterization of a magnetic and optical dual-modality molecular probe. Nanotechnology. 2010 Apr 30;21(17):175704. [PMID 20368682]

Intellectual Property: HHS Reference No. E-194-2007/0 – US Patent Application No. 12/667,790 filed 05 Jan 2010 (allowed)

Related Technology: HHS Reference No. E-111-2013/0 – US Provisional Application No. 61/779,016 filed 13 Mar 2013

Licensing Contact: Michael A. Shmilovich, Esq., CLP; 301-435-5019; shmilovm@mail.nih.gov

Collaborative Research Opportunity: The National Cancer Institute Radiation Oncology Branch is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize Trifunctional Imaging Agent for Monoclonal Antibody Tumor-Targeted Imaging. For collaboration opportunities, please contact John D. Hewes, Ph.D. at hewesj@mail.nih.gov.

August 6, 2013
Date

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

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