[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.

SUPPLEMENTARY INFORMATION: Technology descriptions follow.

Real Time Medical Image Processing Using Cloud Computing

Description of Technology:

The invention pertains to a system for reconstructing images acquired from MR and CT scanners in a robust Gadgetron based cloud computing system. A hardware interface connects clinical imaging instruments (e.g., MR or CT scanners) with a cloud computing environment that includes image data reconstruction and processing software not limited by the computational constraints typical of static hardware with finite processor power. Raw imaging data acquired from an MR or CT instrument is evaluated and categorized based on a pre-prioritized dimensionality parameter (e.g., spatial dimension parameter; three- or two-dimensionality, a time parameter, a flow/velocity parameter, an experiment timing dimension parameter, a diffusion encoding parameter, a functional/physiological testing dimension parameter, or a physiologic gating index parameter) and transmitted to a corresponding cloud computing environment for processing and reconstruction. The final processed image is retransmitted to a user interface that can be read by a radiologist or technician.

Potential Commercial Applications:

- MRI imaging
- CT imaging
- Image processing
- Diagnostic radiology

Competitive Advantages:

- Eliminates the need for purchasing expensive data processing equipment that becomes obsolete
- Less equipment leads to lowers costs and space efficiency
- Exponentially more robust computer power, data acquisition and image reconstruction

Development Stage:

- Early-stage
- In vitro data available
- In vivo data available (animal)
- In vivo data available (human)
- In situ data available (on-site)
- Prototype

Inventors:

Michael Hansen, Peter Kellman, Hui Xue (all of NHLBI)

Intellectual Property:

- HHS Reference No. E-074-2014/0 – US Provisional Application No. 61/934,987 filed 03 Feb 2014
- HHS Reference No. E-074-2014/1 – US Provisional Application No. 61/953,017 filed 14 Mar 2014

Licensing Contact:

Michael Shmilovich, Esq; 301-435-5019; shmilovm@mail.nih.gov

Collaborative Research Opportunity:

The National Heart Lung & Blood Institute is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize Gadgetron mediated clinical image processing. For collaboration opportunities, please contact Denise Crooks, Ph.D. at 301-435-0103 or crooksd@nhlbi.nih.gov.

Personal Respirator Safety: Flushed Seal for an Improved, More Protective, Negative-Pressure Respirator

Description of Technology:

This CDC-developed technology relates to improved, full-face flushed-seal personal respirators for lowering costs, improving user mobility, and ensuring occupational health and safety. Currently, the most common type of respirator in use, the negative pressure respirator, seals to a user's face so that inhaled air is pulled through a purifying filter by inhalation-generated negative pressure; the weakest link in this type of respirator is typically the seal at the face-to-mask interface. When there is face-seal leakage, toxic air will be drawn into the facepiece of the respirator and inhaled by the wearer, though designers and engineers of respirators attempt to minimize this face-seal leakage. Over the last several decades, facepiece design has been optimized by this design approach so that the ambient leakage of half-facepiece respirators and full-facepiece respirators are 10% and 2%, respectively.

This technology incorporates an additional element to reduce face-seal leakage and therefore increases user protection. In the respirator described by this technology, a primary sealing element is situated adjacent to the user's breathing space and a secondary

sealing element. Exhaled air (i.e., clean air obtained by filter passage) is passed from the breathing space into a flushing channel formed between the primary and secondary seals. If there is leakage in the primary seal, air from this flushing channel leaks into the breathing space rather than toxic, ambient air. Air within the flushing channel will predominately be air that has already passed through the filtering elements. The present invention provides, therefore, an inexpensive respirator which provides significantly more protection than conventional negative-pressure respirators. Further, at present the only alternative respirator types that offer such great levels of user protection are expensive, require heavy batteries and blowers or an airline, and have a limited service life.

Potential Commercial Applications:

- Increased protection for first responders
- Biodefense, military and/or chemical/environmental clean-up applications
- Industrial-use personal respirator applications where extensive worker mobility is a requisite
- Inexpensive alternatives for air-line systems or powered air-purifying respirators (PAPRs) that are currently in use

Competitive Advantages:

- Inexpensive to implement
- Provides significantly more protection than conventional negative-pressure respirators
- Unlike PAPR devices, no heavy, mobility-limiting battery packs are required for this technology; no battery recharge time or noisy blowers with this respirator technology

- Compared to "air-line" respirators, this technology is significantly less expensive to purchase and maintain and does not limit the range of a user's mobility

Development Stage:

- In situ data available (on-site)
- Prototype

Inventors:

Donald L. Campbell, Christopher C. Coffey, William A. Hoffman, Judith B. Hudnall (all of CDC)

Intellectual Property:

HHS Reference No. E-241-2013/0 –

- PCT Application No. PCT/US2001/040957 filed 12 Jun 2001
- US Patent No. 6,957,653 issued 25 Oct 2005

Related Technologies:

- HHS Reference No. E-174-2013/0
- HHS Reference No. E-291-2013/0

Licensing Contact:

Whitney Blair, J.D., M.P.H.; 301-435-4937; whitney.blair@nih.gov

Multi-specific Chimeric Antigen Receptors Against HIV

Description of Technology:

The present disclosure is directed to novel CD4-based multi-specific chimeric antigen receptor (CAR) proteins composed of an extracellular targeting moiety containing at least two HIV Env-binding motifs, linked to a transmembrane domain and a

cytoplasmic signaling domain. The invention further discloses nucleic acids encoding the novel chimeric antigen receptors to enable their expression in host T cells for treatment of HIV infection and disease. Importantly, CAR-transduced CD8 T cells recognize HIV-infected target cells in MHC independent fashion by binding the highly conserved regions of the HIV Env glycoprotein, thus minimizing the selection of viral escape mutants. Furthermore, the present invention also relates to methods of generating a recombinant CD8 T cells expressing a CAR with a CD4-based targeting moiety that does not confer susceptibility to HIV infection.

Potential Commercial Applications:

- Therapy for HIV infection
- Research on antiretroviral infection
- Generate HIV-unsusceptible T cells

Competitive Advantages:

- Target highly conserved regions of Env of HIV
- Target non-MHC-expressing HIV-infected cells
- Eliminate emergence escape HIV variants

Development Stage:

- In vitro data available
- In vivo data available (animal)

Inventors:

Li Liu (NIAID), Bhavik Patel (NIAID), Edward Berger (NIAID), Steven Rosenberg (NCI), Richard Morgan (NCI)

Publications:

1. Dey B, et al. Neutralization of human immunodeficiency virus type 1 by sCD4-17b, a single-chain chimeric protein, based on sequential interaction of gp120 with CD4 and coreceptor. J Virol. 2003 Mar;77(5):2859-65. [PMID 12584309]
2. Lagenaur LA, et al. sCD4-17b bifunctional protein: extremely broad and potent neutralization of HIV-1 Env pseudotyped viruses from genetically diverse primary isolates. Retrovirology. 2010 Feb 16;7:11. [PMID 20158904]
3. Berger EA. Targeted cytotoxic therapy: adapting a rapidly progressing anticancer paradigm for depletion of persistent HIV-infected cell reservoirs. Curr Opin HIV AIDS. 2011 Jan;6(1):80-5. [PMID 21242898]

Intellectual Property:

HHS Reference No. E-170-2013/0 – US Patent Application No. 61/908,691 filed 25 Nov 2013

Licensing Contact:

John Stansberry, Ph.D.; 301-435-5236; stansbej@mail.nih.gov

Methods for Near Real-time Chemical Analysis of Aerosols using Microwave-induced Plasma Spectroscopy

Description of Technology:

This CDC developed technology entails a novel method of near real-time elemental analysis of aerosols by corona assisted microwave induced plasma spectroscopy (CAMPS).

Analysis of elemental composition of aerosol particles holds significant implications for environmental and workplace pollution monitoring. Various plasma

based analytical techniques, including laser-induced breakdown spectroscopy (LIBS) and spark-induced breakdown spectroscopy (SIBS), have been successfully used for multi-elemental analyses in solids, liquids, and gases, including aerosols. However, the characterization of fine and ultrafine aerosols using these techniques is particularly challenging due to small plasma volume, miniscule sample mass, and inferior sampling statistics, often leading to poor detection limits and precision.

This technology utilizes a microwave plasma-based detection system for aerosol analysis that features increased microplasma lifetime, repeatability, and stability over currently-available pulsed microplasma-based methods. This system produces microplasma lifetimes in the range of 5 to 50 milliseconds, a duration that is orders of magnitude larger than lifetimes for laser-induced or spark plasmas, as well as larger plasma volumes, which together are expected to provide improved detection limits over currently-available techniques.

Potential Commercial Applications:

- Elemental quantification of aerosols in near real-time
- Air pollution studies, Particulate Matter monitoring
- Hazardous materials exposure determinations and identification
- Biodefense, chemical-defense, homeland-security applications
- Environmental and occupational epidemiology
- Evaluation of engineering controls

Competitive Advantages:

- Makes it possible to conduct accurate, near-real-time measurement of the elemental composition of aerosols in industrial and ambient atmospheres

- Corona field stabilizes the microwave plasma and results in repeatable plasma formation
- Larger size of CAMPS plasma provides sufficient plasma volume which can lead to complete ablation of deposited aerosol in the tip of the electrode
- Longer duration of CAMPS plasma (~10-50 ms) allows longer integration time which results in signal enhancement

Development Stage:

- In situ data available (on-site)
- Prototype

Inventors:

Pramod Kulkarni (CDC), et al.

Intellectual Property:

HHS Reference No. E-163-2013/0 –

- US Patent Application 61/652,593 filed 02 May 2012
- US Patent Application 13/804,512 filed 14 Mar 2013

Related Technology:

HHS Reference No. E-205-2013/0

Licensing Contact:

Whitney Blair, J.D., M.P.H.; 301-435-4937; whitney.blair@nih.gov

Local Positioning System for Increasing Occupational Safety

Description of Technology:

This CDC-developed technology describes an automated system for monitoring worker hazard exposures by recording data about where and when hazards occur in a workplace or other environment. This allows the hazards to be avoided and harmful exposures and risks reduced. This field-tested technology consists of an integrated, hand-held electronics instrument and software system that will precisely correlate multiple exposure levels with position coordinates of the user and features real-time data acquisition.

Workers in many outdoor occupations move about frequently during a typical day of work. Certain workers, such as agricultural and construction workers, are particularly mobile. This exposure monitoring system combines geographical location with real-time sensors and outputs the information to a user-friendly interface. By linking worker location throughout the workday to exposure levels from real-time monitors, Local Positioning System (LPS) units (with integrated software processing of data) identify and document where to direct hazard exposure analysis and control efforts. Post-processing of LPS data enables researchers, regulatory inspectors, and industry safety and health personnel to map exposure intensity and location, reveal hot spots to identify sources, and provide exposure intensity distributions to increase workplace safety.

Potential Commercial Applications:

- Collection of real-time condition data and real-time position data generated over time at one or more locations
- Outdoor occupational exposure assessment with various real-time sensors/monitors (e.g., HAZMAT crews, safety inspection, etc.)
- Solid state "bread crumbs" allowing a person or machine to retrace their path

- Tracking of objects, animals or people at a short distance, including sensing of their internal condition or environmental conditions

Competitive Advantages:

- Correlates real-time position and real-time condition data for multiple commercial/industrial applications
- An add-on capability for any sensor(s) when measurement of a location is also useful
- System is highly customizable and can be easily adapted for additional monitoring of noise, dust, gases, and vapor, heat stress, etc. exposures
- Automated system provides greater efficiency and greater feedback than video monitoring systems
- An integrated alarm will alert users to potential hazards

Development Stage:

- In situ data available (on-site)
- Prototype

Inventors:

Larry A. Lee, Sidney C. Soderholm, Michael Flemmer, Jennifer L. Hornsby-Myers, Ramesh Gali (all of CDC)

Publication:

Lee LA, et al. Field test results of an automated exposure assessment tool, the local positioning system (LPS). J Environ Monit. 2005 Jul;7(7):736-42. [PMID 15986055]

Intellectual Property:

HHS Reference No. E-274-2013/0 – US Patent No. 7,191,097 issued 13 Mar 2007

Licensing Contact:

Whitney Blair, J.D., M.P.H.; 301-435-4937; whitney.blair@nih.gov

Novel Dopamine D2 Receptor Antagonists and Methods of Their Use

Description of Technology:

Investigators at the NIH have identified a series of novel, small molecule antagonists of the dopamine D2 receptor. Among the dopamine receptor (DAR) subtypes, D2 DAR is arguably one of the most validated drug targets in neurology and psychiatry. For instance, all receptor-based anti-Parkinsonian drugs work via stimulating the D2 DAR, whereas all FDA approved antipsychotic agents are antagonists of this receptor. Unfortunately, most agents that act as antagonists of D2 DAR are problematic, either they are less efficacious than desired or cause multiple adverse effects. Thus, it is desirable to develop a class of novel therapeutic agents with high selectivity for the D2 DAR. This invention describes dihydrobenzo[b,f][1,4]thiazepine-8-carboxamide compounds, methods of making these compounds, methods of characterizing their in vitro activity, demonstration of in vivo activity in animals, as well as methods of using these compounds to treat central nervous system (CNS) related disorders.

Potential Commercial Applications:

- Antipsychotic agent
- Treatment for schizophrenia, Tourette's syndrome, depression
- Alternative therapy for disorders currently treated with non-selective D2 antagonists

Competitive Advantages:

Highly selective

Development Stage:

- In vitro data available
- In vivo data available (animal)

Inventors:

David Sibley (NINDS), R. Benjamin Free (NINDS), Juan J. Marugan (NCATS), Jingbo Xiao (NCATS), Marc Ferrer-Alegre (NCATS), Noel T. Southall (NCATS)

Publication:

Xiao J, et al. Discovery, optimization, and characterization of novel D2 dopamine receptor selective antagonists. J Med Chem. 2014 Apr 24;57(8):3450-63. [PMID 24666157]

Intellectual Property:

HHS Reference No. E-030-2013/0 – U.S. Provisional Application No. 61/859532 filed 29 Jul 2013

Licensing Contact:

Charlene S. Maddox, Ph.D.; 301-435-4689; maddoxcs@mail.nih.gov

Collaborative Research Opportunity:

The National Institute of Neurological Disorders and Stroke is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize Novel Dopamine D2 Receptor Antagonists and Methods of Their Use. For collaboration opportunities, please contact Laurie Arrants at ArrantsL@ninds.nih.gov.

Therapeutic Compounds Targeting Thioesterase Deficiency Disorders

Description of Technology:

Compositions comprising N-t-butyl hydroxylamine (NtBuHA), a small molecule that partially or fully mimics thioesterase activity are provided to treat or prevent thioesterase deficiency disorders. Lysosomal storage disorders (LSDs) represent a group of >50 genetically distinct, inherited diseases. Included amongst these are a group of neurodegenerative LSDs called neuronal ceroid lipofuscinoses (NCLs), also commonly known as Batten disease. The infantile type of NCL (or INCL) is one of the most devastating diseases. It is caused by mutations in the *CLN1* gene encoding palmitoyl-protein thioesterase-1 (PPT1). Hydroxylamine (HA) is a potent nucleophilic small molecule and it functionally mimics thioesterase activity including that of PPT1. Unfortunately, the inherent toxicity of HA precludes its clinical use for any disorder. The inventors evaluated several non-toxic derivatives of HA for anti-oxidant properties, the ability to cleave thioester linkage in S-acylated proteins, the ability to mediate ceroid depletion, to suppress apoptosis in cultured cells from INCL patients and in *Ppt1*-knockout (*Ppt1-/-*) mice. Specifically, the inventors have discovered that NtBuHA is non-toxic, manifests potent antioxidant property, cleaves thioester linkages in S-acylated proteins, depletes intracellular ceroid in *Ppt1-/-* mice and extends lifespan. These results demonstrated that NtBuHA may be broadly useful as therapeutic agents for thioesterase deficiency disorders including INCL.

Potential Commercial Applications:

Compositions and methods to treat or prevent thioesterase deficiency disorders

Competitive Advantages:

• Currently there are no effective treatments for INCL and N-t-BuHA will be the first specific treatment targeting INCL.

• N-t-BuHA can be developed as a broad spectrum therapeutic against thioesterase deficiency disorders.

Development Stage:

In vivo data available (animal)

Inventors:

Anil Baran Mukherjee, Chinmoy Sarkar, Zhongjian Zhang (all of NICHD)

Publication:

Sarkar C, et al. Neuroprotection and lifespan extension in Ppt1(-/-) mice by NtBuHA: therapeutic implications for INCL. Nat Neurosci. 2013 Nov;16(11):1608-17. [PMID 24056696]

Intellectual Property:

HHS Reference No. E-157-2011/0 –

• US Patent Application No. 14/110,393 filed 07 Oct 2013

• EP Patent Application No. 12716889.6 filed 07 Oct 2013

Licensing Contact:

Suryanarayana Vepa, Ph.D., J.D.; 301-435-5020; vepas@mail.nih.gov

Collaborative Research Opportunity:

The *Eunice Kennedy Shriver* National Institute of Child Health and Human Development is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize hydroxylamine-derivatives or other small molecules with similar properties for treating thioesterase deficiency diseases including infantile neuronal ceroid lipofuscinosis (INCL). For

collaboration opportunities, please contact Joseph M. Conrad, Ph.D., J.D. at jmconrad@mail.nih.gov or 240-276-5495.

Non-Invasive In Vivo MR Method to Image Salient Features of Nerves

Description of Technology:

The invention consists of a novel diffusion MRI experiment and modeling framework that describes white matter in the central nervous system (CNS) and nerves in the peripheral nervous system (PNS) as composite media having intra- and extra axonal spaces with different water diffusion characteristics. Specifically, fascicles in the nervous system are modeled as having a hindered extracellular region and a restricted intracellular or intra-axonal region. Diffusion of water in these two distinct compartments contributes to the total measured diffusion MRI signal. This method provides a voxel-by-voxel measurement of the intra- and extra- axonal volume fractions, and an estimate of the mean axon diameter. This technology is also incorporated in NIH's AxCaliber MRI technology, which extends it, treating fascicles as a bundle of impermeable cylinders having a distribution of internal diameters.

The significance of this invention is that it provides measurements of new and useful microanatomical features of white matter (and gray matter) that are closely related to the function of the nervous system--particularly the speed that information travels along axons--critically important in medicine and the neurosciences. Previously, the data provided by this non-invasive MR imaging method were only available using invasive and laborious histological means requiring tissue biopsy.

Potential Commercial Applications:

- clinical MRI
- small animal or pre-clinical MRI

Competitive Advantages:

- non-invasive, painless, in vivo measurement of microanatomical features of nerves and muscles.
- no contrast agents required
- modest data requirements allow for scans to be performed in a clinically feasible time-frame

Development Stage:

- Early-stage
- In vitro data available
- In vivo data available (animal)
- In vivo data available (human)
- In situ data available (on-site)
- Prototype

Inventors:

Peter J. Basser (NICHD), Yaniv Assaf (Tel Aviv University)

Publications:

1. Assaf Y, et al. New modeling and experimental framework to characterize hindered and restricted water diffusion in brain white matter. Magn Reson Med. 2004 Nov;52(5):965-78. [PMID 15508168]

2. Assaf Y, Basser PJ. Composite hindered and restricted model of diffusion (CHARMED) MR imaging of the human brain. Neuroimage 2005 Aug 1;27(1):48-58. [PMID 15979342]
3. Assaf Y, Basser PJ. Combining DT and q-space MRI: a new model of white matter in the brain. In Proc. Intl. Soc. Mag. Reson. Med. 2003;11:588. [http://cds.ismrm.org/ismrm-2003/ismrm03.pdf]
4. Assaf Y, et al. A New Modeling and Experimental Framework to Characterize Hindered and Restricted Water Diffusion in Brain White Matter. In Proc. Intl. Soc. Mag. Reson. Med. 2004;11:251. [http://cds.ismrm.org/ismrm-2004/Files/Program04.pdf]

Intellectual Property:

HHS Reference No. E-079-2003/1 – US Patent No. 8,380,280 filed 19 Feb 2013

Related Technologies:

- HHS Reference No. E-203-1993/0 – US Patent No. 5,539,310 issued 23 Jul 1996
- HHS Reference No. E-079-2003/0 – US Patent No. 7,643,863 issued 05 Jan 2010
- HHS Reference No. E-276-2008/0 – US Patent No. 8,704,515 issued 22 Apr 2014

Licensing Contact:

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 is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize novel MRI methods to probe tissue structure and organization, particularly for neuroimaging applications.

For collaboration opportunities, please contact Alan E. Hubbs at hubbsa@mail.nih.gov or 240-276-5530.

Dated: May 12, 2014

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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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