[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.

ADDRESS: 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.

Novel NSAIDs for the Treatment of Human Diseases

Description of Technology: The invention relates to novel compounds which are hybrids between two moieties, i.e. non-steroidal anti-inflammatory drugs (NSAID) and Nitroxyl (HNO) releasing agents as well as Nitroxide (an antioxidant and superoxide scavenger). Such modified NSAIDs have shown to be advantageous to conventionally used NSAID, as their toxicity is significantly reduced and they can thus be used in medical treatment for extended periods of time without severe side effects. The adverse side effects (i.e. heart attack, thrombosis and severe gut toxicity) presented by conventional NSAIDs are well documented and some of them (i.e. Vioxx) were therefore withdrawn from the market. The present compounds may alleviate these problems, and may render more anti-inflammatory agents suitable for human use. The HNO releasing moiety of these novel compounds will expand the medical utility of these compounds, as HNO releasing agents possess anticancer activity as well as good antioxidant activities, a property that is beneficial for a variety of human diseases, including acute and chronic inflammation. In summary, the hybrid compounds provided in the invention can be useful in treatment of variety of human diseases (i.e. inflammatory diseases, heart diseases and cancer) with relatively low level of side effects.

Potential Commercial Applications: The drugs of this invention will be useful in treatment of anti-inflammatory diseases, and as therapeutic or preventative drugs for cardiovascular diseases, diabetes and cancer.

Competitive Advantages: The hybrid structure of the present drugs will render them useful in therapy and prevention of a wide variety of disorders, with reduced toxicity.

Development Stage: In vitro data available

Inventors: David A. Wink et al. (NCI)

Publication: Flores-Santana W et al. Redox-Modified Non-Steroidal Anti-Inflammatory Drugs as Potential Anti-Cancer Agents with the SOD Mimetic Nitroxide. Br J Pharmacol. 2011 Jun 9; doi: 10.1111/j.1476-5381.2011.01527.x (Epub ahead of print). [PMID 21658022]

Intellectual Property: HHS Reference No. E-131-2011/0 — U.S. Provisional Application No. 61/472,770 filed 07 Apr 2011

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

Fibroblast Growth Factor Receptor 1 (Fgfr1) Conditional Knock Out Mouse

Description of Technology: Scientists at NIDDK have developed a fibroblast growth factor receptor 1 (Fgfr1) conditional knock out mouse. Fgfr1 is a member of the Fgfr family of transmembrane protein receptors with intrinsic tyrosine kinase activity. Fgfr1 is important in multiple biological processes, including mesoderm induction and patterning, cell growth and migration, organ formation and bone growth. Fgfr1 is highly expressed in central nervous system tissues and plays a critical role in proliferation, migration, and survival of neurons and glial cells. Additionally, overexpression of Fgfr1 has been associated with mammary gland transformation and may be crucial for the development of some cancers. The Fgfr1 conditional knockout mouse can be used to study development and biological processes in a variety of tissues and can provide information on signaling pathways that interact with Fgfr1 to induce genes important for

critical cellular events, such as proliferation, differentiation, adhesion, movement, survival, and transformation.

Potential Commercial Applications:

• Basic research tool to investigate intracellular pathways dependent on Fgfr1.

• Tool to study skeletal and neural development.

• Model of stress-related environments such as bone fractures or tumorigenic induction.

Competitive Advantages:

• Unlike Fgfr1 null mice that are embryonic lethal, Fgfr1 conditional knockout mice are viable and can be used to study the role of Fgfr1 in tissue and organ development.

• Mice carrying the Fgfr1 conditional knockout mutation can be cross-bred using, for example, Cre-expressing mice to generate tissue specific knockouts of Fgfr1 and used for more detailed tissue studies of Fgfr1 signaling.

Development Stage: In vivo data available (animal)

Inventor: Chu-Xia Deng (NIDDK)

Publication: Xu X, Qiao W, Li C, Deng CX. Generation of Fgfr1 conditional knockout mice. Genesis. 2002 Feb;32(2):85-86. [PMID 11857785]

Intellectual Property: HHS Reference No. E-071-2011/0 — Research Tool. Patent protection is not being pursued for this technology.

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

Biomarkers for Cancer-Related Fatigue and Their Use in the Management of Such Fatigue (CRF)

Description of Technology: The invention relates to the diagnosis and management of cancer-related fatigue (CRF). More specifically the invention relates to identification and measurement of a single Biomarker or a group of biomarkers (e.g. genes) that are associated with cancer related fatigue. The identification and measurement of such biomarkers can be utilized in the diagnosis and management of fatigue and may facilitate the development of therapy for such fatigue. In particular, the invention provides for a method of diagnosing a subject with CRF by detecting expression of at least one gene associated with CRF in a sample obtained from the subject; and comparing expression of the gene to a control. The invention also describes a method of treating a patient with CRF by administering to the subject an agent that alters expression or activity of a gene associated with CRF. Further provided in the invention is array that includes a plurality of genes associated with CRF, such as TNFRSF25, SLC6A8, OGT, SNCA, APBA2, CASK, OR2W3, MYL4, IL7R, ARHGEF10 and ITGA6. Some of these genes are over expressed in a CRF patient (e.g., SNCA and SLC6A8) while others (e.g., IL7R, ARHGEF10) are under expressed. The array can provide detailed and comprehensive information that can result in improved diagnostics and in increased options for therapeutic treatment.

Potential Commercial Applications: Diagnostics and therapeutic of cancer-related fatigue.

Competitive Advantages: The technology provides for an array of multiple biomarkers, all associated with CRF. Thus it may offer a more detailed and accurate diagnosis of CRF as well as larger number of therapeutic options.

Development Stage:

• In vitro data available (animal)

• In vivo data available (human)

Inventor: Leorey Saligan (NINR)

Intellectual Property: HHS Reference E-280-2010/0 — U.S. Provisional Application No. 61/442,605 filed 14 Feb 2011

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

Characterizing Compartment Distributions from Diffusion Weighted Magnetic Resonance (MR) Data

Description of Technology: The National Institutes of Health seeks licensees with MR software expertise to commercialize a method of imaging the structural and dimensional characteristics (microstructure) of microscopic specimens. Microstructure is elucidated using MR scanning and the diffusion weighted MR signal is transformed into statistical moments of the underlying compartment size distribution associated with restricted diffusion. Essentially, the method includes the steps of: 1) acquiring diffusion weighted image or spectroscopic data, 2) applying the new modeling framework relating pore size distribution to the diffusion weighted (DW) data, and 3) using this framework to estimate moments of the pore diameter distribution from the DW data.

Potential Commercial Applications: Examination of tissue/cellular microstructures

Competitive Advantages: Refined imaging

Development Stage: In vitro data available

Inventors: Evren Ozarslan and Peter J. Basser (NICHD)

Publications:

1. Assaf Y, et al. AxCaliber: a method for measuring axon diameter distribution from diffusion MRI. Magn Reson Med. 2008 Jun;59(6):1347-1354. [PMID 18506799]

2. Shemesh N, et al. Accurate noninvasive measurement of cell size and compartment shape anisotropy in yeast cells using double-pulsed field gradient MR. NMR Biomed. 2011 July 22. E-pub ahead of print, doi: 10.1002/nbm.1737. [PMID 21786354]

3. Ozarslan E, et al. NMR characterization of general compartment size distributions. New J Phys. 2011 Jan;13:15010. [PMID 21709780]

4. Komlosh ME, et al. Pore diameter mapping using double pulsed-field gradient MRI and its validation using a novel glass capillary array phantom. J Magn Reson. 2011 Jan;208(1):128-135. [PMID 21084204]

5. Nevo U, et al. A system and mathematical framework to model shear flow effects in biomedical DW-imaging and spectroscopy. NMR Biomed. 2010 Aug;23(7):734-744. [PMID 20886564]

6. Shemesh N, et al. From single-pulsed field gradient to double-pulsed field gradient MR: gleaning new microstructural information and developing new forms of contrast in MRI. NMR Biomed. 2010 Aug;23(7):757-780. [PMID 20690130]

7. Shemesh N, et al. Noninvasive bipolar double-pulsed-field-gradient NMR reveals signatures for pore size and shape in polydisperse, randomly oriented, inhomogeneous porous media. J Chem Phys. 2010 Jul 28;133(4):044705. [PMID 20687674]

Intellectual Property: HHS Reference No. E-273-2010/0 — U.S. Provisional Patent Application No. 61/522,421 filed 11 Aug 2011

Related Technologies:

• HHS Reference No. E-079-2003/0 — U.S. Patent 7,643,863 issued 05 Jan 2010; International Patent Application PCT/US2004/22027 filed 08 Jul 2004, which published as WO 2005/012926 on 10 Feb 2005

• HHS Reference No. E-079-2003/1 — U.S. Patent Application 12/114,713 filed 02 May 2008

Licensing Contact: Michael Shmilovich, Esq.; 301-435-5019; mish@codon.nih.gov

One Step Fluorine-18 Peptide Labeling Strategy of Biological Substrates

Description of Technology: A one-step process is now available for licensing that allows direct 18F labeling of any biological substrate that is modified with 4-nitro-3-trifluoromethyl arene. Normally, 18F labeling requires several time-consuming radio synthesis steps using prosthetic groups, resulting in a low labeling yield. Other attempts at one step labeling methods have also shown relatively low yields.

This new process eliminates time-consuming radiosynthesis steps and associated low labeling yields with a single step process that displaces a nitro group in an arene.

Relatively low amounts of precursor and short time radiosynthesis times are required compared to direct peptide-labeling. Higher yields by this simplified process improve time and cost efficiencies and may make 18F labeling more amenable for automation.

Potential Commercial Applications:

• Radiological imaging

• Radiological diagnosis

• Radiological therapy

Competitive Advantages:

• Significantly shorter reaction and synthesis times

• Lower amounts of precursor required

• Relatively high yield of specific activity product

Development Stage:

• Early-stage

• Pre-clinical

• In vitro data available

• In vivo data available (animal)

Inventors: Xiaoyuan (Shawn) Chen and Orit J. Weiss (NIBIB)

Publication: Jacobson O, et al. Rapid and simple one-step F-18 labeling of peptides. Bioconjug Chem. 2011 Mar 16;22(3):422-428. [PMID 21338096]

Intellectual Property: HHS Reference No. E-238-2010/0 — U.S. Provisional Patent Application No. 61/429,671 filed 04 Jan 2011

Licensing Contact: Tedd Fenn; 301-435-5031; Tedd.Fenn@NIH.gov

Collaborative Research Opportunity: The NIBIB is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize the technology for One Step Fluorine-18 Peptide Labeling Strategy of Biological Substrates. For collaboration opportunities, please contact Shawn Chen, Ph.D. at shawn.chen@nih.gov.

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Date

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

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