[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.

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.

Zirconium-89 PET Imaging Agent for Cancer

Description of Technology: This technology is a new generation of rationally designed chelating agents which improve the complexation of Zirconium-89 for PET imaging of cancers. The technology uses cyclic or acyclic chelators made of 4 hydroxamate donors groups for improved stability compared to the currently used natural product siderophore desferrioxamine B (DFB), a chelator that consists of only 3 hydroxamate donors that fails to saturate the coordination sphere of Zr(IV). DFB, which has been the object of many pre-clinical and clinical studies exhibits insufficient stability resulting in progressive radioisotope accumulation in bone once injected that can contribute to toxicity and increased background. The new chelators described in this invention have shown improved kinetic inertness compared to DFB with stability up to 90% after 7 days compared to 28% for DFB. In association with an adequate targeting agent such as an antibody, toxicity to the bone can be reduced and images with better contrast can be obtained with these new chelators.

Potential Commercial Applications:

• Cancer imaging

• PET imaging

• ImmunoPET

Competitive Advantages:

• High stability

• Low toxicity

• Better imaging contrast

Development Status:

• Prototype

• In vitro data available

Inventors: Francois Guerard (NCI), Yong Sok Lee (CIT), Martin Brechbiel (NCI)

Publications:

1. Zhou Y, et al. Mapping biological behaviors by application of longer-lived positron emitting radionuclides. Adv Drug Deliv Rev. In Press; doi: 10.1016/j.addr.2012.10.012. [PMID 23123291]

2. Deri MA, et al. PET imaging with 89Zr: from radiochemistry to the clinic. Nucl Med Biol. 2013 Jan;40(1):3-14. [PMID 22998840]

3. Vosjan MJ, et al. Conjugation and radiolabeling of monoclonal antibodies with zirconium-89 for PET imaging using the bifunctional chelate p-isothiocyanatobenzyl-desferrioxamine. Nat Protoc. 2010 Apr;5(4):739-43. [PMID 20360768]

4. 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]

5. Evans MJ, et al. Imaging tumor burden in the brain with 89Zr-transferrin. J Nucl Med. 2013 Jan;54(1):90-5. [PMID 23236019]

6. Guerard F, et al. Investigation of Zr(IV) and 89Zr(IV) complexation with hydroxamates: progress towards designing a better chelator than desferrioxamine B for immuno-PET imaging. Chem Commun (Camb). 2013 Feb 1;49(10):1002-4. [PMID 23250287]

Intellectual Property: HHS Reference No. E-111-2013/0 – U.S. Provisional Application No. 61/779,016 filed 13 Mar 2013

Related Technologies:

• HHS Reference No. E-194-2007/0 – U.S. Patent Application No. 12/667,790 filed 05 Jan 2010

• HHS Reference No. E-226-2006/0 – U.S. Patent No. 8,288,530 issued 16 Oct 2012

• HHS Reference No. E-067-1990/0

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

Collaborative Research Opportunity: The Radioimmune & Inorganic Chemistry Section, ROB, CCR, NCI, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize Zirconium-89 chelation technology for ImmunoPET imaging and other applications. For collaboration opportunities, please contact John D. Hewes, Ph.D. at hewesj@mail.nih.gov.

Novel Methods for Generating Retinal Pigment Epithelium Cells from Induced Pluripotent Stem Cells

Description of Technology: High efficiency methods for producing retinal pigment epithelial cells (RPE) from induced pluripotent stem cells (iPSCs) are disclosed. The RPE is a polarized monolayer in the vertebrate eye that separates the neural retina from the choroid, and performs a crucial role in retinal physiology by forming a blood-

retinal barrier and closely interacting with photoreceptors to maintain visual function. Many ophthalmic diseases, such as age-related macular degeneration, are associated with a degeneration or deterioration of the RPE. The iPSCs are produced from somatic cells, including retinal pigment epithelial cells, such as fetal RPE. These methods involve producing embryoid bodies from human iPSCs, culturing the embryoid bodies using specific media to induce differentiation into RPE and growing the differentiated RPE cells in a defined media to generate human RPE cells. The investigators also developed methods for detecting RPE cells and authenticating RPE cells; determining agents that can affect the production of RPE cells from an iPSC; and identifying an agent that can increase RPE survival in response to a proteo toxic insult or stress. The novel methods and RPE cells disclosed here can be useful for both pre-clinical and clinical studies involving RPE. **Potential Commercial Applications:** The methods described here can be used to:

• produce RPE cells for use in screening for novel ocular therapeutics and for identifying toxic side

effects of drugs

• produce RPE cells for use in novel cell-based therapies

• produce cells to study pathophysiology of RPE

Competitive Advantages: The methods described here:

• dramatically increase the efficiency of iPSC differentiation into RPE

• produce superior quality RPE

• produce RPE cells that are fully authenticated

• provide ways to perform high throughput screens with RPE cells

Development Stage:

• Prototype

• Early-stage

• In vitro data available

Intellectual Property: HHS Reference No. E-251-2012/3 – U.S. Provisional Application No. 61/759,988 filed 01 Feb 2013

Licensing Contact: Suryanarayana (Sury) Vepa; 301-435-5020; vepas@mail.nih.gov

Collaborative Research Opportunity: The National Eye Institute is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize iPSC to RPE differentiation protocol, its clinical, screening, and translational applications. For collaboration opportunities, please contact Alan Hubbs, Ph.D. at hubbsa@mail.nih.gov.

Novel Tocopherol and Tocopheryl Quinone Derivatives as Therapeutics for Lysosomal Storage Disorders

Description of Technology: Novel tocopherol derivatives and tocopheryl quinone derivatives useful in the decrease of lysosomal substrate accumulation, the restoration of normal lysosomal size, and the treatment of lysosomal storage disorders (LSDs) are provided. The inventors have discovered that tocopherol and tocopheryl quinone derivatives with side chain modifications (such as terminal tri-halogenated methyl groups) exhibit improved pharmacokinetics, modulation of mitochondrial potential and restoration of some LSDs phenotypes. These molecules by themselves or

in combination with Cyclodextrins (CDs) increase intracellular Ca2+ and enhance exocytosis. Also, the treatment with these compounds reduced the pathological changes in the ultrastructure of LSD cells as observed using electron microscopy analysis. The inventors also found that there is a synergy between CDs and the new tocopherol analogues when tested on the NPC cells and cells from six other lysosomal storage diseases including Wolman, Niemann Pick Type A, Farber, TaySachs, MSIIIB and CLN2 (Batten) diseases. These new tocopherol analogues are as good or better than natural occurring tocopherols and tocotrienols in reducing cholesterol accumulation in several LSDs.

Potential Commercial Applications: To develop new therapeutics to treat LSDs.

Competitive Advantages:

• The main advantage of the compounds disclosed here is their improved pharmacokinetics.

• The combination of CD and the novel tocopherol analogues may reduce the dosage of each drug and thereby reduce the potential side effects.

Development Stage:

• Prototype

• Early-stage

• Pre-clinical

• In vitro data available

Inventors: Juan Jose Marugan, Wei Zheng, Jingbo Xiao, and John McKew (NCATS)

Intellectual Property: HHS Reference No. E-148-2012/0 — U.S. Provisional Application No. 61/727,296 filed 16 Nov 2012

Related Technologies:

• HHS Reference No. E-294-2009/0 — PCT Application No. PCT/US2011/044590 filed 19 Jul 2011, which published as WO 2012/012473 on 26 Jan 2012

• HHS Reference No. E-050-2012/0 — US Provisional Application No. 61/679,668 filed 12 Aug 2012

Licensing Contact: Suryanarayana (Sury) Vepa; 301-435-5020; vepas@mail.nih.gov

Collaborative Research Opportunities: 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 Novel Tocopherol and Tocopheryl Quinone Derivatives as Therapeutics for Lysosomal Storage Disorders. For collaboration opportunities, please contact the NCATS Technology Development Coordinator at NCATSPartnerships@mail.nih.gov.

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Date

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