[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.

Delta Tocopherol for the Treatment of Lysosomal Storage Disorders

Description of Technology: Delta Tocopherol is identified as a novel therapeutic to treat lysosomal disorders characterized by defective cellular cholesterol and other lipid trafficking and storage. Currently, there is no treatment for many of Lysosomal Storage Disorders. In some cases, such as Gaucher disease, enzyme replacement therapy and substrate deduction treatment are available with very high cost (over $100,000 per patient per year). NIH investigators have identified an unexpected and previously unrecognized use for delta tocopherol, which is a form of vitamin E, in the treatment of diseases and conditions related to lysosomal storage disorders. Scientists at the National Center for Advancing Translational Sciences, NIH discovered a clear difference between the effects of delta-tocopherol and alpha tocopherol on the cell-based disease models of Niemann Pick C (NPC) disease. They found that while delta-tocopherol significantly reduced the cholesterol accumulation in NPC cells and reduced the size of enlarged lysosomes, alpha-tocopherol only showed weak effects in the same cells.

The present invention can be used to develop new therapies involving delta-tocopherol to treat lysosomal disorders, such as Niemann-Pick type C disease, Mucopolysaccharidoses disorder, and Neuronal Ceroid Lipofuscinoses. This invention provides potential novel methods for the modulation of cholesterol and other lipids'

recycling. It may be also possible to use delta-tocopherol for the reduction of the size of enlarged lysosomes caused by accumulation of lipids and macromolecules.

Potential Commercial Applications:

• Therapeutics for lysosomal disorders

• Therapeutics for Niemann-Pick type C disease

Competitive Advantages: delta-tocopherol is a novel lead compound for drug development to treat a variety of lysosomal storage diseases characterized by lipid/macromolecule accumulation and defective lipid trafficking.

Development Stage:

• Early-stage

• In vitro data available

Inventors: Wei Zheng et al. (NCATS)

Publications:

1. Xu M, et al. delta-Tocopherol reduces lipid accumulation in Niemann-Pick type C1 and Wolman cholesterol storage disorders. J Biol Chem. 2012 Nov 16;287(47):39349–60. [PMID 23035117]

2. Yu D, et al. Niemann-Pick Disease Type C: Induced Pluripotent Stem Cell-Derived Neuronal Cells for Modeling Neural Disease and Evaluating Drug Efficacy. J Biomol Screen. 2014 Jun 6. pii: 1087057114537378. [PMID 24907126]

Intellectual Property: HHS Reference No. E-294-2009/0 -

• US Patent Application No. 13/810,774 filed 17 Jan 2013

• EP Patent Application No. 11741023.3 filed 19 July 2011

Related Technology: HHS Reference No. E-148-2011/0 - PCT Patent Application No. PCT/US2013070156 filed 14 Nov 2013, entitled "Tocopherol and Tocopheryl Quinone Derivatives as Correctors of Lysosomal Storage Disorders"

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

Collaborative Research Opportunity: The National Center for Advancing Translational Sciences is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize particular therapeutic uses of delta tocopherol. Please contact Dr. Wei Zheng at wzheng@mail.nih.gov for more information.

^{18}F-labeled Calcofluor Derivatives for PET Imaging and Diagnosis of *Aspergillus* Infection

Description of Technology: *Aspergillus* is a common fungal lung infection with high mortality rates in immune compromised patients. The inability to diagnose this infection impedes treatment. Blood based diagnostic tests for this infection lack sensitivity and specificity due to cross reactivity. Other methods of diagnosis are invasive and labor intensive. The ability to accurately and non-invasively diagnose infection in *Aspergillus* immune compromised populations may greatly improve treatment and lower mortality rates. This technology uses ^{18}F-labeled calcofluor derivatives for positron emission tomography (PET) imaging of filamentous fungal infections. ^{18}F-labeled calcofluor derivatives have low toxicity, high binding specificity to *Aspergillus* species due to uptake by *Aspergillus*-specific siderphore system, and low

binding affinity to patient tissue. These compounds may be used for rapid and accurate PET diagnostic imaging of infection by species of *Aspergillus*.

Potential Commercial Applications: Diagnosis of *Aspergillus* infection

Competitive Advantages: Non-invasive, low toxicity, specific for *Aspergillus*

Development Stage: In vivo data available (animal)

Inventors: Peter Williamson (NIAID), John Panepinto (Univ. Buffalo), Dale Kiesewetter (NIBIB), Jin Qui (NIAID)

Publications:

1. Palmer GE, et al. The diverse roles of autophagy in medically important fungi. Autophagy. 2008 Nov;4(8):982-8. [PMID 18927489]

2. Panepinto JC, et al. Deletion of the Aspergillus fumigatus gene encoding the Ras-related protein RhbA reduces virulence in a model of invasive pulmonary aspergillosis. Infect Immun. 2003 May;71(5):2819-26. [PMID 12704156]

3. Desoubeaux D, et al., Diagnosis of invasive pulmonary aspergillosis: updates and recommendations, Med Mal Infect. 2014 Mar; 44(3):89-101. [PMID 24548415]

Intellectual Property: HHS Reference No. E-449-201/0 - US Provisional Application No. 61/894,754 filed 23 Oct 2013

Licensing Contact: Edward (Tedd) Fenn; 424-297-0336; Tedd.fenn@nih.gov

Collaborative Research Opportunity: The National Institute of Allergy and Infectious Diseases 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 Nadine Chien at 301-827-0258.

Multifunctional RNA Nanoparticles as Therapeutic Agents

Description of Technology: The promise of RNA interference based therapeutics is made evident by the recent surge of biotechnological drug companies that pursue such therapies and their progression into human clinical trials. The present invention discloses novel RNA and RNA/DNA nanoparticles including multiple siRNAs, RNA aptamers, fluorescent dyes, and proteins. These RNA nanoparticles are useful for various nanotechnological applications. This technology has a higher detection sensitivity and higher silencing efficiencies of targeted genes than conventional siRNAs. This technology has significant therapeutic potential against multiple disease types, including cancer and viral infections.

Potential Commercial Applications:

• Treatment for various diseases

• Clinical research

• Basic research

Competitive Advantages:

• More sensitivity

• Higher efficiency

• Low cytotoxicity

• Multiple functionality

• Multiple targets

• Visualization

• Controlled activation

Development Stage:

• In vitro data available

• In vivo data available

Inventors: Bruce A. Shapiro, Kirill A. Afonin, Angelica N. Martins, Mathias D. Viard (all of NCI)

Intellectual Property: HHS Reference No. E-765-2013/0 - US Provisional Application No. 61/878,758 filed 17 Sep 2013

Related Technologies:

• HHS Reference No. E-039-2012

• HHS Reference No. E-156-2014

Licensing Contact: John Stansberry, Ph.D.; 301-435-5236; stansbej@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 scaling up, animal models, multiple targets, delivery. For collaboration opportunities, please contact John D. Hewes, Ph.D. at hewesj@mail.nih.gov.

Nucleic Acid Nanoparticles for Triggering RNA Interference

Description of Technology: RNA interference (RNAi) is a naturally occurring cellular post-transcriptional gene regulation process that utilizes small double-stranded RNAs to trigger and guide gene silencing. By introducing synthetic RNA duplexes called small-interfering RNAs (siRNAs), we can harness the RNAi machinery for therapeutic gene control and the treatment of various diseases.

The present invention discloses RNA, RNA-DNA, DNA-RNA, hybrid nanocubes consisting of a DNA or RNA core (composed of six strands) with attached RNA or DNA hybrid duplexes. The nanocubes can induce the reassociation of the RNA duplexes, which can then be processed by the human recombinant Dicer enzyme, thus activating RNAi. This technology opens a new route for the development of "smart" nucleic acid based nanoparticles for a wide range of biomedical applications. Immune responses can be controlled by altering the composition of the particles.

Potential Commercial Applications:

• Treatment for various diseases

• Clinical research

• Basic research

Competitive Advantages:

• Low cytotoxicity

• Chemical stability

• More specificity

• Controlled activation

• Multiple targets

• Visualization

Development Stage: In vitro data available

Inventors: Bruce A. Shapiro, Kirill A. Afonin, Mathias D. Viard (all of NCI)

Publications:

1. Afonin KA, et al. Computational and experimental characterization of RNA cubic nanoscaffolds. Methods. 2014 May 15;67(2):256-65. [PMID 24189588]

2. Afonin KA, et al. In vitro assembly of cubic RNA-based scaffolds designed in silico. Nat Nanotechnol. 2010 Sep;5(9):676-82. [PMID 20802494]

Intellectual Property: HHS Reference No. E-156-2014/0 - US Provisional Application 61/989,520 filed 06 May 2014

Related Technologies:

• HHS Reference No. E-765-2013

• HHS Reference No. E-039-2012

Licensing Contact: John Stansberry, Ph.D.; 301-435-5236; stansbej@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 scaling up, animal models, multiple targets, delivery. For collaboration opportunities, please contact John D. Hewes, Ph.D. at hewesj@mail.nih.gov.

Dated: July 9, 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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