[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 CONTACT: 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.

Novel Benztropine Analogs for Treatment of Cocaine Abuse and Other Mental Disorders

Description of Technology: Dopamine is a neurotransmitter that exerts important effects on locomotor activity, motivation and reward, and cognition. The dopamine transporter (DAT) is expressed on the plasma membrane of dopamine synthesizing neurons, and is responsible for clearing dopamine released into the extra-cellular space, thereby regulating neurotransmission. The dopamine transporter plays a significant role in neurotoxicity and human diseases, such as Parkinson's disease, drug abuse (especially cocaine addiction), Attention Deficit Disorder/Attention Deficit Hyperactivity Disorder (ADD/ADHD), and a number of other CNS disorders. Therefore, the dopamine transporter is a strong target for research and the discovery of potential therapeutics for the treatment of these indications.

This invention discloses novel benztropine analogs and methods of using these analogs for treatment of mental and conduct disorders such as cocaine abuse, narcolepsy, ADHD, obesity and nicotine abuse. The disclosed analogs are highly selective and potent inhibitors of DAT, but without an apparent cocaine-like behavioral profile. In addition to their use as a treatment for cocaine abuse, these compounds have also shown efficacy in animal models of ADHD and nicotine abuse, and have also been shown to

reduce food intake in animals. They may also be useful medications for other indications where dopamine-related behavior is compromised, such as alcohol addiction, tobacco addiction, and Parkinson's disease.

Potential Commercial Applications:

• Drug leads for treatment of cocaine abuse, ADHD, nicotine abuse, obesity, and other dopamine-related disorders

• Imaging probes for dopamine transporter binding sites

Development Stage: Early-stage; In vitro data available

Inventors: Amy H. Newman, Mu-fa Zou, Jonathan L. Katz (all of NIDA)

Intellectual Property: HHS Reference No. E-234-2005/1 - US Patent No. 8,383,817 issued February 26, 2013

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

Collaborative Research Opportunity: The National Institute on Drug Abuse, Medicinal Chemistry and Psychobiology Sections, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize medications to treat cocaine abuse and addiction. For collaboration opportunities please contact John D. Hewes, Ph.D. at john.hewes@nih.gov.

Novel Dopamine Receptor Ligands as Therapeutics for Central Nervous System Disorders

Description of Technology: The dopamine D3 receptor subtype is a member of the dopamine D2 subclass of receptors. These receptors have been implicated in a number of CNS disorders, including psychostimulant abuse, psychosis and Parkinson's

disease. Compounds that bind with high affinity and selectivity to D3 receptors can not only provide important tools with which to study the structure and function of this receptor subtype, but may also have therapeutic potential in the treatment of numerous psychiatric and neurologic disorders.

The 4-phenylpiperazine derivatives are an important class of dopamine D3 selective ligands. However, due to their highly lipophilic nature, these compounds suffer from solubility problems in aqueous media and reduced bioavailability. To address this problem, a process was designed to introduce functionality into the carbon chain linker of these compounds. Compared to currently available dopamine D3 receptor ligands, the resulting compounds show improved pharmacological properties and D3 selectivities but due to their more hydrophilic nature, these derivatives are predicted to have improved water solubility and bioavailability.

Potential Commercial Applications:

• Therapeutics for a variety of psychiatric and neurologic disorders

• Research tools to study D3 receptor structure and function

Competitive Advantages:

• Improved pharmacological properties and selectivity over existing dopamine D3 receptor ligands

• Hydrophilic nature likely to lead to improved water solubility and bioavailability

Development Stage: Early-stage; In vitro data available

Inventors: Amy H. Newman (NIDA), Peter Grundt (NIDA), Jianjing Cao (NIDA), Robert Luedtke

Intellectual Property: HHS Reference No. E-128-2006/0 - US Patent No. 8,748,608 issued June 10, 2014

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

Collaborative Research Opportunity: The National Institute on Drug Abuse, Medications Discovery Research Branch, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize 4-phenylpiperazine derivatives as dopamine D3 selective ligands. For collaboration opportunities, please contact Vio Conley, M.S. at 240-276-5531 or conleyv@mail.nih.gov.

Genome Wide DNase I Hypersensitive Sites Detection in Formalin-Fixed Paraffin-Embedded Single Cells

Description of Technology: A method of detecting DNase I hypersensitive sites ((DHS) in a single cell or very small number of cells, including cells recovered from formalin-fixed paraffin-embedded (FFPE) tissue slides of patient samples. DHS has revealed a large number of potential regulatory elements for transcriptional regulation in various cell types. The application of DNase-Seq techniques to patient samples can elucidate pathophysiological mechanisms of gene function in a variety of diseases as well as provide potentially important diagnostic and prognostic information. Unfortunately, the current DNase-Seq techniques require large number of cells and are applicable only to larger biopsies and surgical specimens. This technique, called Pico-Seq, allows detection when only very small population of cells are available, such as rare primary tumor cells and circulating-tumor-cells, isolated by a variety of methods. Pico-Seq uses

conditions capable of restoring the DNase I sensitivity, similar to native/fresh cells, in tissue/cells from slides processed by extremely harsh conditions, such as in FFPE tissues.

Potential Commercial Applications:

• Diagnostic and prognostic kits

• Research kits

Competitive Advantages:

• Applicable to very small number of cells down to a single cell.

• Capable of using cells isolated by any of the available methods, including flow cytometry, biopsies, laser capture microdissection, and even cells recovered from formalin-fixed paraffin-embedded tissue slides of patient samples.

Development Stage: Early-stage; In vitro data available

Inventors: Keji Zhao and Tang Qingsong (NHLBI)

Intellectual Property: HHS Reference No. E-254-2014/0 - US Provisional Application No. 62/118,574 filed February 20, 2015

Licensing Contact: Cristina Thalhammer-Reyero, Ph.D., M.B.A.; 301-435-4507; ThalhamC@mail.nih.gov

Dated: August 18, 2015.

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Richard U. Rodriguez,
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National Institutes of Health.

[FR Doc. 2015-20694 Filed: 8/20/2015 08:45 am; Publication Date: 8/21/2015]