[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.

Arsenical Compounds as Therapeutics for Inflammatory Diseases

Description of Technology: FDA approved Arsenic trioxide (Trisenox or As_2O_3) and other arsenical compounds for treatment of acute inflammatory conditions have been shown to be anti-inflammasome therapies. Inflammasomes are large cytoplasmic multi-protein complexes that form in response to intracellular danger signals and play a key role in many infections by controlling the innate immune response. Inflammasome activation has been implicated in metabolic disorders, such as diabetes, and inflammatory diseases, such as gout, arthritis, and cholesterol-associated atherosclerosis. The technology relates to arsenical compounds that inhibit a number of inflammasomes, including the Nlrpl, Nlrp3 and Naip5/Nlrc4, primarily by acting as an inhibitor of caspase-1 activity in innate immune cells (macrophages). It was shown that arsenical compounds induce a cellular condition which inhibits both the autoproteolytic activity of caspase-1, as well as its ability to cleave cytokine substrates. Further, it was shown that the inhibition does not occur through direct modification or inhibition of the caspase-1 enzyme, but rather through induction of a cellular environment inhibitory to its activity. Efficacy in inhibiting immune cell recruitment in a mouse model of gout has been demonstrated. The arsenicals have potential as treatment for a variety of inflammatory conditions.

Potential Commercial Applications: Therapeutics for rheumatoid arthritis, gout, colitis and various inflammatory skin diseases.

Competitive Advantages: These FDA-approved compounds have potential off-target use for treatment of acute inflammatory conditions shown to be responsive to anti-inflammasome therapies.

Development Stage:

• Early-stage

• Pre-clinical

• In vitro data available

• In vivo data available (animal)

Inventors: Mahtab Moayeri, Nolan K. Maier, Stephen H. Leppla (all of NIAID)

Intellectual Property: HHS Reference No. E-112-2013/0 – US Provisional Application No. 61/784,138 filed March 14, 2013

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

A Novel HIV-1 Drug Resistant Integrase Inhibitor

Description of Technology: The subject invention describes a novel and highly potent inhibitor of HIV-1 integrase (IN) that has high efficacy against the major forms of Raltegravir-resistant mutant forms of IN. Thus, this IN inhibitor can be developed as a therapeutic for patients who have developed resistance to current IN inhibitors, such as Raltegravir and Elvitegravir.

Potential Commercial Applications: HIV therapeutic.

Competitive Advantages:

• High efficacy against the major forms of Raltegravir-resistant mutant forms of IN in *in vitro* and whole cell assays.

• An HIV therapeutic for patients resistant to current IN inhibitors.

Development Stage:

• Early-stage

• In vitro data available

Inventors: Xue Zhi Zhao, Steven Smith, Mathieu Metifiot, Barry Johnson, Christophe Marchand, Stephen Hughes, Yves Pommier, Terrence Burke (all of NCI)

Publications:

1. Marchand C, et al. HIV-1 IN inhibitors: 2010 update and perspectives. Curr Top Med Chem. 2009;9(11):1016-37. [PMID 19747122]

2. Liao C, et al. Authentic HIV-1 integrase inhibitors. Future Med. Chem. 2010 Jul;2(7):1107-22. [PMID 21426159]

Intellectual Property: HHS Reference No. E-093-2013/0 – US Provisional Patent Application No. 61/824,306 filed May 16, 2013

Related Technology: PCT, WO2008010964 (A1), Merck

Licensing Contact: Sally Hu, Ph.D., MBA; 301-435-5606; hus@mail.nih.gov

Potent and Selective Analogues of Modafinil and Uses Thereof

Description of Technology: This invention describes novel analogues of modafinil, a wake-promoting agent that has been used to treat narcolepsy and other sleep disorders.

Modafinil has attracted attention for the treatment of cognitive dysfunction in disorders such as attention-deficit/hyperactivity disorder (ADHD) as well as cocaine and methamphetamine dependence. However, modafinil has relatively low affinity for binding to the dopamine transporter (DAT) to block dopamine reuptake, and is water-insoluble, thus requiring large doses to achieve pharmacological effects.

Investigators at the National Institute of Drug Abuse have synthesized a series of modafinil analogues that have higher affinity for the dopamine (DAT), serotonin (SERT) and/or norepinephrine (NET) transporters and improved water solubility. These novel analogues present the advantage of higher potency, which may translate into lower effective doses and better bioavailability over modafinil.

Potential Commercial Applications:

• Therapeutic agent for substance abuse (such as nicotine, cocaine, methamphetamine, opioids)

• Therapeutic agent for attention/cognitive disorders (such as ADHD)

• Therapeutic agent for sleep disorders

Competitive Advantages:

• Higher affinity for monoamine transporters (DAT, SERT, and NET)

• Lower effective doses

• Better bioavailability,

• Improved water solubility

Development Stage: Early-stage

Inventors: Amy H. Newman, Oluyomi M. Okunola-Bakare, Jianjing Cao, Jonathan Katz (all of NIDA)

Intellectual Property: HHS Reference No. E-073-2013/0 – US Provisional Application No. 61/774,878 filed March 8, 2013

Related Technologies:

• HHS Reference No. E-251-2002 – US Provisional Application No. 60/410,715

• HHS Reference No. E-128-2006 – PCT Application No. PCT/US2007/071412

Licensing Contact: Charlene Sydnor, Ph.D.; 301-435-4689; sydnorc@mail.nih.gov

Collaborative Research Opportunity: The National Institute on Drug Abuse is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize Potent and Selective Analogues of Modafinil and Uses Thereof. For collaboration opportunities, please contact Michelle Kim Leff, MD, MBA at mleff@mail.nih.gov.

Translocator Protein 18 kDa PET Radioligands with High Affinities Regardless of Genotype

Description of Technology: This technology relates to a group of Translocator protein 18 kDa (TSPO) radioligands for Positron Emission Tomography (PET) that are specific and accurate, regardless of genotype. TSPO is a mitochondrial protein expressed in inflammatory cells, which is a marker for neuroinflammation. Neuroinflammation is symptomatic of many neuropsychiatric and neurodegenerative disorders, such as multiple sclerosis, stroke, epilepsy, dementia, and traumatic brain injuries. Monitoring and quantifying TSPO 18 kDa with radioligands in PET may have clinical application in understanding, diagnosing and treating many neuropsychiatric disorders. However,

current TSPO 18 kDa radioligands either lack specificity or, due to TSPO polymorphisms, have highly variable inter-subject sensitivities depending on genotype. These new ligands are specific and accurate, regardless of genotype, allowing simplified interpretation and quantification of the binding signal.

Potential Commercial Applications: Biomarker or diagnostic for neuroinflammation

Competitive Advantages: Specific and accurate, regardless of genotype

Development Stage:

• Early-stage

• Pre-clinical

• In vivo data available (animal)

Inventors: Robert B. Innis, Victor W. Pike, Sam S. Zoghbi, Yi Zhang (NIMH); Sabrina Castellano (University of Salerno, Italy); Giorgio Stefancich (University of Trieste, Italy); Sabrina Talia, Federico Da Settimo, Claudia Martini (University of Pisa, Italy)

Publications:

1. Oh U, et al. Translocator protein PET imaging for glial activation in multiple sclerosis. J Neuroimmune Pharmacol. 2011 Sep;6(3):354-61. [PMID 20872081]

2. Kreisl WC, et al. Stroke incidentally identified using improved positron emission tomography for microglial activation. Arch Neurol. 2009 Oct;66(1):1288-9. [PMID 19822787]

3. Hirvonen J, et al. Increased in vivo expression of an inflammatory marker in temporal lobe epilepsy. J Nucl Med. 2012 Feb;53(2):234-40. [PMID 22238156]

4. Kreisl WC, et al. In vivo radioligand binding to translocator protein correlates with severity of Alzheimer's disease. Brain. 2013 Jul;136(Pt 7):2228-38. [PMID 23775979]

Intellectual Property: HHS Reference No. E-262-2012/0 – U.S. Provisional Patent Application No. 61/777,542 filed March 12, 2013

Licensing Contact: Edward (Tedd) Fenn, J.D.; 424-500-2005; Tedd.fenn@nih.gov

Collaborative Research Opportunity: The National Institute of Mental Health is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize TSPO radioligands for monitoring inflammation. For collaboration opportunities, please contact Suzanne Winfield at winfiels@mail.nih.gov.

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Date

Richard U. Rodriguez, M.B.A.
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