[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.

Selective Inhibitors of Polo-like Kinase 1 (PLK1) Polo-box Domains as Potential Anticancer Agents

Description of Technology: PLK1 is a regulator of cell growth that represents a new target for anticancer therapeutic development. High expression of PLK1 has been associated with several types of cancer (e.g., breast cancer, prostate cancer, ovarian cancer, non-small cell lung carcinoma). Inhibiting PLK1 could be an effective treatment for cancer patients without significant side-effects. Available for licensing are synthetic peptides with the ability to bind to polo-like kinase 1 (PLK1) polo-box domains (PBDs) with selectivity and nanomolar affinity and induce apoptosis in cancer cells. By inhibiting the functions of PLK1, these peptides could serve as potential anti-cancer therapies. This technology is related to and an extension of HHS technology reference E-181-2009.

Potential Commercial Applications:

• New anticancer therapies that specifically target PLK1.

• Platform for the development of further improved PLK1 inhibitors.

Competitive Advantages:

• High PBD binding affinity

• High binding selectivity

Development Stage: Early-stage

Inventors: Terrence R. Burke, Jr. (NCI), et al.

Publications:

1. Liu F, et al. Serendipitous alkylation of a Plk1 ligand uncovers a new binding channel. Nat Chem Biol. 2011 Jul 17;7(9):595-601. [PMID 21765407]

2. Qian W, et al. Investigation of unanticipated alkylation at the N(pi) position of a histidyl residue under Mitsunobu conditions and synthesis of orthogonally protected histidine analogues. J Org Chem. 2011 Nov 4;76(21):8885-8890. [PMID 21950469]

Intellectual Property: HHS Reference No. E-053-2012/0 — U.S. Provisional Application No. 61/588,470 filed 19 Jan 2012

Related Technology: HHS Reference No. E-181-2009/3 — U.S. Provisional Application No. 61/474,621 filed 12 Apr 2011

Licensing Contact: Patrick McCue, Ph.D.; 301-435-5560; mccuepat@mail.nih.gov

Influenza Vaccine

Description of Technology: It has been shown that the fusion peptide, a sequence comprised of fourteen amino acids at the N-terminal of the influenza hemagglutinin 2 protein is conserved among A and B influenza viruses. Monoclonal antibodies against this peptide are capable of binding all influenza virus HA proteins and inhibit viral growth by impeding the fusion process between the virus and the target cell. This application claims immunogenic conjugates comprising the fusion peptide region linked to a carrier protein. In preclinical studies, these conjugates were immunogenic and induced booster responses. The induced antibodies bound to the recombinant HA protein. This methodology of linking the highly conserved fusion peptide region to a carrier protein can broaden the protective immune response to include influenza A and B virus strains. This would eliminate the need for annual influenza vaccination.

Potential Commercial Applications:

• Influenza vaccines

• Influenza diagnostics

• Research tools

Competitive Advantages:

• Universal influenza vaccine

• Efficient manufacturing process

• May eliminate need for yearly influenza vaccination

Development Stage:

• Pre-clinical

• In vitro data available

• In vivo data available (animal)

Inventors: Joanna Kubler-Kielb, Jerry M. Keith, Rachel Schneerson (NICHD)

Intellectual Property: HHS Reference No. E-271-2011/0 — U.S. Provisional Application No. 61/541,942 filed 30 Sep 2011

Licensing Contact: Peter A. Soukas, J.D.; 301-435-4646; ps193c@nih.gov

Collaborative Research Opportunity: The NICHD is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize conjugate influenza vaccines comprising fusion peptide region. For collaboration opportunities, please contact Joseph Conrad, Ph.D., J.D. at 301-435-3107 or jmconrad@mail.nih.gov.

ACSF3-based Diagnostics and Therapeutics for Combined Malonic and Methylmalonic Aciduria (CMAMMA) and Other Metabolic Disorders

Description of Technology: Combined malonic and methylmalonic aciduria (CMAMMA) is a metabolic disorder in which malonic acid and methylmalonic acid, key intermediates in fatty acid metabolism, accumulate in the blood and urine. This disorder is often undetected until symptoms manifest, which can include developmental delays and a failure to thrive in children, and psychiatric and neurological disorders in adults. Once thought to be a very rare disease, CMAMMA is now thought to be one of the most common forms of methylmalonic acidemia, and perhaps one of the most common inborn errors of metabolism, with a predicted incidence of one in 30,000.

Investigators at the National Human Genome Research Institute (NHGRI) have identified the genetic cause of CMAMMA, an enzyme encoded by the ACSF3 (Acyl-CoA Synthetase Family Member 3) gene. This enzyme is located in the mitochondrion, and appears to be a methylmalonyl-CoA and malonyl-CoA synthetase, which catalyzes the first step of intra-mitochondrial fatty acid synthesis. As such, this discovery may not only be critical for the development of diagnostic tools and treatments for CMAMMA, but also holds promise for the treatment of other related metabolic disorders.

Potential Commercial Applications:

• Diagnosis of CMAMMA or other metabolic diseases

• Therapies for CMAMMA or other metabolic diseases, such as lipoic acid administration, gene therapy or enzyme replacement therapy

Competitive Advantages:

• Mutation of ACSF3 has been shown to be the genetic cause of CMAMMA, and there are no existing methods to diagnose this disorder.

• Therapies based on ACSF3 may be applicable to a variety of metabolic disorders.

Development Stage:

• In vivo data available (animal)

• In vivo data available (human)

Inventors: Charles P. Venditti, Leslie G. Biesecker, Jennifer L. Sloan, Jennifer J. Johnston, Eirini Manoli, Randy J. Chandler (all of NHGRI)

Publication: Sloan JL, et al. Exome sequencing identifies ACSF3 as a cause of combined malonic and methylmalonic aciduria. Nat Genet. 2011 Aug 14;43(9):883-886. [PMID 21841779]

Intellectual Property: HHS Reference No. E-209-2011/0 — U.S. Provisional Application No. 61/504,030 filed 01 Jul 2011

Licensing Contact: Tara L. Kirby, Ph.D.; 301-435-4426; tarak@mail.nih.gov

Antagonists of the Hedgehog Pathway as Therapeutics for the Treatment of Heterotopic Ossification, Vascular Calcification, and Pathologic Mineralization

Description of Technology: Heterotopic ossification (HO) results from osteoid formation of mature lamellar bone in soft tissue sites outside the skeletal periosteum (skeletal system), most commonly around proximal limb joints. HO can also be caused by genetic diseases such as progressive osseous heteroplasia (POH) and fibrodysplasia

ossificans progressiva (FOP). Currently, all forms of HO lack adequate treatments and definite cure. Vascular calcification is a complex process that involves biomineralization and resembles osteogenesis. It is exacerbated during such conditions as diabetes, osteoporosis, menopause, hypertension, metabolic syndrome, chronic kidney disease, and end stage renal disease. In the present technology, the inventors describe novel methods for preventing or treating HO and vascular calcification using one or more antagonists of the Hedgehog pathway. The inventors, using both in vitro (limb culture experiments) and in vivo studies using Prx1-cre; Gsf/f mice model discovered that the antagonists of the Hedgehog pathway prevent formation of HO. The inventors also observed that Prx1-cre; Gsf/f mice developed calcification or mineralization around their blood vessels, and treatment with Hedgehog antagonists reduced mineralization throughout the body of these mice, including regions around the blood vessels, as observed by mineral staining. The antagonists that can be used to develop effective therapeutics include zerumbone epoxide, arcyriaflavin C, 5,6-dihyroxyarcyriaflavin A, physalin F, physalin B, arsenic trioxide (ATO), sodium arsenite, etc.

Potential Commercial Applications: Development of therapeutics for heterotopic ossification, vascular calcification, and pathologic mineralization.

Competitive Advantages: Several clinically tested and FDA-approved Hedgehog antagonists are currently available and these compounds will expedite the commercial development of this technology.

Development Stage:

- Early-stage
- Pre-clinical

• In vitro data available

• In vivo data available (animal)

Inventors: Yingzi Yang and Jean Regard (NHGRI)

Intellectual Property: HHS Reference No. E-116-2011/0 — U.S. Provisional Application No. 61/504,041 filed 01 Jul 2011

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

Collaborative Research Opportunity: The National Human Genome Research Institute (NHGRI) is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize antagonists of the Hedgehog pathway for treatment of ossification and calcification disorders. For collaboration opportunities, please contact Claire T. Driscoll at 301-594-2235 or cdriscoll@mail.nih.gov.

A Novel Treatment for Malarial Infections

Description of Technology: The inventions described herein are antimalarial small molecule inhibitors of the plasmodial surface anion channel (PSAC), an essential nutrient acquisition ion channel expressed on human erythrocytes infected with malaria parasites. These inhibitors were discovered by high-throughput screening of chemical libraries and analysis of their ability to kill malaria parasites in culture. Two separate classes of inhibitors were found to work synergistically in combination against PSAC and killed malaria cultures at markedly lower concentrations than separately. These inhibitors have high affinity and specificity for PSAC and have acceptable cytotoxicity

profiles. Preliminary *in vivo* testing of these compounds in a mouse malaria model is currently ongoing.

Potential Commercial Applications: Treatment of malarial infections

Competitive Advantages:

• Novel drug treatment for malarial infections

• Synergistic effect of these compounds on PSAC

Development Stage:

• In vitro data available

• In vivo data available (animal)

Inventor: Sanjay A. Desai (NIAID)

Publications:

1. Kang M, et al. Malaria parasites are rapidly killed by dantrolene derivatives specific for the plasmodial surface anion channel. Mol. Pharmacol. 2005 Jul;68(1):34-40. [PMID 15843600]

2. Desai SA, et al. A voltage-dependent channel involved in nutrient uptake by red blood cells infected with the malaria parasite. Nature. 2000 Aug 31;406(6799):1001-1005. [PMID 10984055]

Patent Status: HHS Reference No. E-202-2008/0 — U.S. Patent Application No. 13/055,104 filed 20 Jan 2011; various international patent applications

Licensing Contact: Kevin W. Chang, Ph.D.; 301-435-5018; changke@mail.nih.gov

Collaborative Research Opportunity: The NIAID Office of Technology Development is seeking statements of capability or interest from parties interested in

collaborative research to further develop, evaluate, or commercialize antimalarial drugs that target PSAC or other parasite-specific transporters. For collaboration opportunities, please contact Dana Hsu at 301-496-2644.

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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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