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:


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.

**Development Stage:**
- In vivo data available (animal).
- In vivo data available (human).

License 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 immature lamellar bone at 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 mineralization 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; Gsf1/f mice model discovered that the antagonists of the Hedgehog pathway prevent formation of HO. The inventors also observed that Prx1-cre; Gsf1/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-dihydroxyacrylaflavin 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.

**Intellectual Property:**

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

**Inventors:**
- Charles P. Venditti
- Liccjie G. Biesecker
- Jennifer L. Sloan
- Jennifer J. Johnston
- Eirini Manoli
- Randy J. Chandler

**Application No.**
- 61/504,030 filed 01 Jul 2011
- 61/504,041 filed 01 Jul 2011
- E–209–2011/0—U.S. Provisional Application No. 61/504,030 filed 01 Jul 2011
- E–116–2011/0—U.S. Provisional Application No. 61/504,041 filed 01 Jul 2011

**Antagonists of the Hedgehog Pathway for Treatment of 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.

**Intellectual Property:**

License Contact: Claire T. Driscoll at 301–594–2235 or cdriscoll@mail.nih.gov.

**Collaborative Research Opportunity:**
The NIH Office of Technology Development 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.
target PSAC or other parasite-specific transporters. For collaboration opportunities, please contact Dana Hsu at 301–496–2644.


Richard U. Rodriguez,
Director, Division of Technology Development and Transfer, Office of Technology Transfer, National Institutes of Health.

[FR Doc. 2012–3824 Filed 2–16–12; 8:45 am]
BILLING CODE 4140–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Institute on Aging; Notice of Closed Meetings

Pursuant to section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. App.), notice is hereby given of the following meetings.

The meetings will be closed to the public in accordance with the provisions set forth in sections 552b(c)(4) and 552b(c)(6), Title 5 U.S.C., as amended. The grant applications and the discussions could disclose confidential trade secrets or commercial property such as patentable material, and personal information concerning individuals associated with the grant applications, the disclosure of which would constitute a clearly unwarranted invasion of personal privacy.

Name of Committee: National Institute on Aging Special Emphasis Panel; Alzheimer’s Prevention.

Date: March 1, 2012.

Time: 5 p.m. to 8 p.m.

Agenda: To review and evaluate grant applications.

Place: Embassy Suites, Chevy Chase Pavilion, 4300 Military Road NW., Washington, DC 20005.

Contact Person: William Cruce, Ph.D., Scientific Review Officer, National Institute on Aging, Gateway Building 2C–212, 7201 Wisconsin Ave., Bethesda, MD 20814, 301–402–7704, crusew@nia.nih.gov.

This notice is being published less than 15 days prior to the meeting due to the timing limitations imposed by the review and funding cycle.

Name of Committee: National Institute on Aging Special Emphasis Panel; Contract ABC.

Date: March 9, 2012.

Time: 12 p.m. to 1:30 p.m.

Agenda: To review and evaluate contract proposals.

Place: National Institute on Aging, Gateway Building, 7201 Wisconsin Avenue, Suite 2C212, Bethesda, MD 20892, (Telephone Conference Call).

Contact Person: Alicia L. Markowsa, Ph.D., DSc, Scientific Review Branch, National Institute on Aging, 7201 Wisconsin Avenue, Suite 2C212, Bethesda, MD 20892, markowsa@nia.nih.gov.

Name of Committee: National Institute on Aging Special Emphasis Panel; Datasets in Alzheimer’s Research.

Date: April 2–3, 2012.

Time: 9 a.m. to 2 p.m.

Agenda: To review and evaluate grant applications.

Place: Doubletree Hotel, 8120 Wisconsin Avenue, Bethesda, MD 20814.

Contact Person: Rebecca J. Ferrell, Ph.D., Scientific Review Officer, National Institute on Aging, Gateway Building 2C212, 7201 Wisconsin Avenue, Bethesda, MD 20892, 301–402–7703, ferrellry@mail.nih.gov.

(Catalogue of Federal Domestic Assistance Program Nos. 93.866, Aging Research, National Institutes of Health, HHS)


Jennifer S. Spaeth,
Director, Office of Federal Advisory Committee Policy.

[FR Doc. 2012–3824 Filed 2–16–12; 8:45 am]
BILLING CODE 4140–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Heart, Lung, and Blood Institute; Notice of Closed Meetings

Pursuant to section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. App.), notice is hereby given of the following meetings.

The meetings will be closed to the public in accordance with the provisions set forth in sections 552b(c)(4) and 552b(c)(6), Title 5 U.S.C., as amended. The grant applications and the discussions could disclose confidential trade secrets or commercial property such as patentable material, and personal information concerning individuals associated with the grant applications, the disclosure of which would constitute a clearly unwarranted invasion of personal privacy.

Name of Committee: National Heart, Lung, and Blood Institute Special Emphasis Panel; Novel Technologies for Powering Ventricular Assist Devices.

Date: March 8, 2012.

Time: 9 a.m. to 5 p.m.

Agenda: To review and evaluate grant applications.

Place: Bethesda Marriott Suites, 6711 Democracy Boulevard, Bethesda, MD 20817.

Contact Person: Stephanie J Webb, Ph.D., Scientific Review Officer, Review Branch/DERA, National Heart, Lung, and Blood Institute, 6701 Rockledge Drive, Room 7196, Bethesda, MD 20892, 301–435–0291, stephanie.webb@nih.gov.

Name of Committee: National Heart, Lung, and Blood Institute Special Emphasis Panel; Pulmonary Vascular—Right Ventricular Axis Research Program.

Date: March 9, 2012.

Time: 8:30 a.m. to 5 p.m.

Agenda: To review and evaluate grant applications.

Place: Hilton Garden Inn, 7301 Waverly Street, Bethesda, MD 20814.

Contact Person: YingYing Li-Smerin, MD, Ph.D., Scientific Review Officer, Office of Scientific Review/DERA, National Heart, Lung, and Blood Institute, 6701 Rockledge Drive, Room 7184, Bethesda, MD 20892–7924, 301–435–0277, lismerin@nihlibi.nih.gov.

(Catalogue of Federal Domestic Assistance Program Nos. 93.233, National Center for Sleep Disorders Research; 93.837, Heart and Vascular Diseases Research; 93.838, Lung Diseases Research; 93.839, Blood Diseases and Resources Research, National Institutes of Health, HHS)


Jennifer S. Spaeth,
Director, Office of Federal Advisory Committee Policy.

[FR Doc. 2012–3826 Filed 2–16–12; 8:45 am]
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DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Institute of Diabetes and Digestive and Kidney Diseases; Notice of Closed Meeting

Pursuant to section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. App.), notice is hereby given of the following meeting.

The meeting will be closed to the public in accordance with the provisions set forth in sections 552b(c)(4) and 552b(c)(6), Title 5 U.S.C., as amended. The contract proposals and the discussions could disclose confidential trade secrets or commercial property such as patentable material, and personal information concerning individuals associated with the contract proposals, the disclosure of which would constitute a clearly unwarranted invasion of personal privacy.

Name of Committee: National Institute of Diabetes and Digestive and Kidney Diseases Special Emphasis Panel; NIDDK UDA Contract Proposal Review.

Date: March 16, 2012.

Time: 2:30 p.m. to 4 p.m.

Agenda: To review and evaluate contract proposals.

Place: National Institutes of Health, Two Democracy Plaza, 6707 Democracy Boulevard, Bethesda, MD 20892, (Telephone Conference Call).

Contact Person: Xiaodu Guo, MD, Ph.D., Scientific Review Officer, Review Branch, DIA, NIDDK, National Institutes of Health, Room 761, 6707 Democracy Boulevard, Bethesda, MD 20892–5452, (301) 594–4719, guox@extra.niddk.nih.gov.