Advantages: The advent of multiphoton microscopy (MPM) provided several advantages in comparison to single-photon confocal microscopy. In particular the nonlinear optics used with this technology, combined with the elimination of a confocal pinhole aperture, led to direct sectioning and the use of lower energy photons. This approach preserves the integrity of the observed object (i.e. tissue) thus improving imaging results. The technology presented here further enhances the capabilities of MPM by providing the following advantages:

- Increased signal-to-noise ratio.
- Enhanced image resolution due to SNR.
- Improved analytical capabilities.
- Non-contact.
- May readily be adaptable to commercial microscopes.

Development Status: The invention is fully developed. Prototype microscope has been built. May need further validation by rigorous in vivo testing under a variety of different conditions. Also need to build the smaller prototype that could screw into normal objective turrets. Alternative realizations with 'integrated optic' structures are also planned.

Market: Multiphoton microscopy (MPM) has found a niche in the world of biological imaging as the best noninvasive means of fluorescence microscopy in tissue explants and living animals. Coupled with transgenic mouse models of disease and 'smart' genetically encoded fluorescent indicators, its use is now increasing exponentially. Properly applied, it is capable of measuring calcium transients 500 μm deep in a mouse brain, or quantifying blood flow by imaging shadows of blood cells as they race through capillaries. One of the great advantages of optical microscopy is its ability to let scientists peek beneath the tissue surface and study cellular processes at work. Over the last two decades, the use of multiphoton microscopy has spread to all major areas of biological research. As researchers are finding more and more applications for this powerful technique the need for enhanced performance and enhanced capabilities is also increasing. The improvements provided in the present technology are simply added to existing MPM and therefore present excellent commercial opportunities.

Inventors: Jay R. Knutson (NHLBI).

Related Publications

1. U.S. Patent Application Publication US–2008–0063345 A1, March 13, 2008.

2. Presentation, 7th EBSA European Biophysics Congress, July 11–15, 2009, Genova, Italy (*http://EBSA2009.org*).

3. CA Combs, AV Smirnov, JD Riley, AH Gandjbakhche, JR Knutson, RS Balaban. Optimization of multiphoton excitation microscopy by total emission detection using a parabolic light reflector. J Micros. 2007 Dec;228(Pt3):330–337.

Patent Status: U.S. Provisional Application No. 61/224,772 filed 10 Jul 2009 (HHS Reference No. E–236–2009/0–US–01).

Related Technology: U.S. Patent Application No. 11/979,600 filed 06 Nov 2007, now allowed (HHS Reference No. E–257–2005/0–US–04).

Licensing Status: Available for licensing.

Licensing Contacts: Uri Reichman, PhD, MBA; 301–435–4616; *UR7a@nih.gov;* or Michael Shmilovich, JD; 301–435–5019; *shmilovm@mail.nih.gov.*

Collaborative Research Opportunity: The NHLBI Laboratory of Molecular Biophysics is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize an enhanced method of multiphoton microscopy that is suitable for the spectral imaging of biological samples. Please contact Brian W. Bailey, PhD at *bbailey@mail.nih.gov* for more information.

Dated: December 24, 2009.

Richard U. Rodriguez,

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

[FR Doc. E9–31074 Filed 12–30–09; 8:45 am]

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.

ADDRESSES: 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.

Device and Method for Direct Measurement of Isotopes of Expired Gases: Application in Research of Metabolism and Metabolic Disorders, and in Medical Screening and Diagnostics

Description of Technology: The technology offered for licensing and for further development concerns a novel device for intervallic collection of expired gas from subjects and subsequent measurement of the isotopic content of such expired gases. The device is specifically designed for medical research and clinical applications, and in particular in the area of metabolic disorders. The device may facilitate the development and testing of new therapies for such disorders and may be used for medical screening and diagnostics of metabolic diseases. The unique design of the device includes a constant volume respiratory chamber equipped with a series of valves and stopcocks to allow precise and repetitive removal of expired gases, and addition of air or other gas to maintain the chamber at a constant volume. Also included is a vacuum tube adapter linked to a port on a three-way stopcock to allow facile transfer of the chamber gases to vacuum tubes for subsequent chemical analyses. The device also includes gas sensors operably linked to detectors and inserted to the chamber through airtight ports; this allows the operator to independently and directly measure the carbon dioxide production rate and oxygen consumption of the test subject while the expired gases are removed for study.

The experimental subject (*e.g.* mammal) is first contacted with a substrate (*e.g.* amino acid, fatty acid, organic acid) containing an isotope (*e.g.* ^{13}C) and placed in the chamber. The unique design allows easy gas removal and addition while maintaining a constant chamber volume. Precisely measured air samples are collected from the chamber by the syringe and subsequently transferred to a self-sealing vacuum tube which is then removed for analysis. Subsequent sampling is accomplished in the exact

same manner, after an equivalent volume of ambient air, or other gas such as pure oxygen, is reinjected in the chamber to maintain pressure and volume. Air samples from the chamber are collected periodically and the content of the isotope (^{13}C) accumulated in the chamber gas due to metabolism and the formation of $^{13}CO_2$ is measured (*e.g. via* Isotope Ratio Mass Spectroscopy (IRMS)) from the collected samples. The rate of the metabolite's development (*i.e.* $^{13}CO_2$) can thus be determined and can thus provide information on the metabolic status of the subject, such as the rate and extent of oxidation of the administered isotope. Furthermore, results of such analysis can provide fundamental information on the ability of the subject to metabolize a compound, quantitate the effectiveness of an experimental therapy (*i.e.* enzyme replacement, gene therapy, hormone administration, etc.) and thus facilitate progress in the development of interventional therapies.

Applications:

- Research in the area of metabolic disorders.
- Development of therapies (including enzyme replacement and gene therapy) for metabolic disorders.
- Potential applications in screening and diagnostics of metabolic disorders.
- Assessment of non-invasive breath tests to study metabolism.

Advantages:

- The device of this invention is uniquely designed for precise periodic collection of expired gas samples from a test subject and their transfer for analytical processing while the carbon dioxide production rate and oxygen consumption rate are independently and simultaneously measured.
- The unique configuration of the device and the manner in which the valves and stopcocks are attached to the main chamber facilitates the performance of repetitive measurements in a seamless, precise and reliable fashion.
- The technique and device uses stable isotopes, so treated animals can be returned to the cage after study with no concerns of radioactive contamination. This also allows animals that are difficult and expensive to create, such as genetically engineered rodents, to be repeatedly studied, pre- and post-intervention(s) and with various compounds at different times.
- The device can be readily fabricated in a relatively inexpensive manner and operated with simple instructions.

Development Status: The invention is fully developed. A prototype functioning device was fabricated.

Market: Metabolic disorders affect millions of people worldwide. Thousands of metabolic diseases, including inborn errors of metabolism and endocrinopathies, have been identified in humans. Apart for affecting the life quality of people afflicted with these diseases, some of them are responsible for large numbers of morbidity and mortality. The World Health Organization (WHO) estimates that type 2 diabetes affects 135 million people worldwide and that 300 million people meet the criteria for obesity. Dyslipidemia is another major metabolic disorder, affecting approximately 300 million people in the United States, Japan, and Western Europe. These three disorders alone—type 2 diabetes, obesity, and dyslipidemia (high blood cholesterol and triglycerides is lipid disorder)—are highly prevalent and lead to significant morbidity and mortality. Many other known metabolic disorders such as polycystic ovarian syndrome (PCOS), and non-alcoholic steatohepatitis (NASH) are common in the population, and although they may be less severe, still account for significant morbidity and mortality, especially in the pediatric population. A large group of metabolic diseases have received extensive attention due to the implementation of population newborn screening are caused by the body's inability to break down certain proteins and fats and the undesirable buildup of amino and organic acids in the blood. Examples include amino acid disorders such as phenylketonuria (PKU) and maple syrup urine disease (MSUD); fatty acid oxidation defects such as medium- and long-chain acyl-CoA dehydrogenase deficiencies (VLCADD and MCADD), and organic acidemias including methylmalonic, propionic and isovaleric acidemia. Most states in the USA are now testing every baby for these, and other conditions as part of routine newborn screening. These diseases are caused by genetic defects and are inherited; for example MMA (Methylmalonic Acidemia) is estimated to occur in 1 in 25,000–48,000 babies. Similarly, Propionic Acidemia, caused by a deficiency of the enzyme propionyl-CoA carboxylase, affects 1 in 100,000 new born babies in the U.S. and even more than that in other countries. While the disorders are individually infrequent, collectively, they occur at an incidence of approximately 1 in 6000 births. The device of this invention is particularly suitable for research in this area of diseases and an example related to its application in MMA is provided in the patent application and a recent publication (RJ Chandler and CP Venditti. Long-term rescue of a lethal murine model of methylmalonic acidemia using adeno-associated viral gene therapy. Mol Ther 2009 Oct 27. Epub ahead of print, PMID: 19861951).

Huge efforts have been made by many pharmaceutical companies to develop and market drugs for the treatment of metabolic diseases, and many commercial opportunities exist in this area. The magnitude of the potential market can be further exemplified by the following data published in commercial market research analyses:

- The global market for prescription endocrine and metabolic disease drugs was $66.2 billion in 2005 and $72.3 billion in 2006. At a compounded annual growth rate (CAGR) of 5.2%, the market will reach $96.4 billion by 2011.
- Drugs for hypercholesterolemia dominated the highest share of the market, worth almost $37.1 billion in 2006, a 51.3% share. By 2011 its share will drop slightly to 47.2% ($45.5 billion of the total market), though it will remain the largest sector of the market.
- Obesity drugs and treatment have the highest growth potential throughout the forecast period. A relatively small market, its growth however is booming at a CAGR of 23.8%. By 2011 the sector will be worth more than $4.0 billion.
- 2007 sales of the recombinant enzyme replacement therapies (ERT) reached a record level of US$ 2.3 billion shared predominantly by three companies (Genzyme, Shire and Biomarin Pharmaceuticals) for a total of seven different products. Companies are working to extending the market by developing novel ERTs for further human genetic diseases as well as by profiling small molecule therapies for enhancement of enzymatic activities. Porcine-derived extracts containing pancrelipase (a mixture of lipase, amylase and protease among others) recently were forced by the FDA to undergo regulatory review of an NDA. Now these products are exposed to upcoming competition with enzymes produced by recombinant DNA technology which intent to capture a part or maintain existing sales of exocrine enzyme replacement therapies (2007 sales > US$ 300 million).

The huge market for drugs and diagnostics for metabolic diseases and the need to develop newer treatments increase the demand for new tools to facilitate and accelerate research in this area. The present invention therefore presents a favorable commercial opportunity.

Inventors: Randy Chandler and Charles P. Venditti (NHGRI)

Related Publications:

1. CP Venditti, E Manoli, RJ Chandler. A Method To Determine The In Vivo Oxidative Capacity For 13C Isotopomers In Mice: Use To Study Intermediary Metabolism And To Monitor Transgene Activity. Presented at the American Society of Gene Therapy 12th Annual Meeting, May 2009.

2. RJ Chandler and CP Venditti. Long-term rescue of a lethal murine model of methylmalonic acidemia using adeno-associated viral gene therapy. Mol Ther. 2009 Oct 27; Epub ahead of print.

Patent Status: U.S. Patent Application No. 12/418,795 filed 09 Apr 2009 (HHS Reference No. E–099–2009/0–US–01).

Licensing Status: Available for licensing.

Licensing Contacts: Uri Reichman, PhD, MBA; 301–435–4616; *UR7a@nih.gov;* Michael Shmilovich, Esq.; 301–435–5019; *shmilovm@mail.nih.gov.*

Collaborative Research Opportunity: The Organic Acid Research Section, Genetic and Molecular Biology Branch, 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 this technology or related laboratory interests. Please contact Claire T. Driscoll at *cdriscol@mail.nih.gov* for more information.

Vaccines Against Malarial Diseases

Description of Technology: The invention offered for licensing is in the field of use of vaccines for malaria. The invention provides gene sequences encoding an erythrocyte binding protein of a malaria pathogen for the expression of the erythrocyte binding protein. The codon composition of the synthetic gene sequences approximates the mammalian codon composition. The synthetic gene sequences are useful for incorporation into DNA vaccine vectors, for the incorporation into various expression vectors for production of malaria proteins, or both. The synthetic genes may be modified to avoid post-translational modification of the encoded protein in other hosts. Administration of the synthetic gene sequences, or the encoded protein, as an immunization agent is useful for induction of immunity against malaria, treatment of malaria, or both. The approach presented in this invention, i.e. vaccine that may block the binding of the malaria parasite and subsequent erythrocyte invasion, may work independently or in combination with other vaccines which are based on different mechanisms.

Applications: Vaccines compositions against Malaria in the form of DNA vaccines or as protein immunogens.

Advantage: Due to the complex nature of the malaria parasite, multiple approaches have been attempted to develop malaria vaccines. In particular, due to the diversity attributed to the different life cycle stages of the parasite, there are several sites that can be used as vaccine targets. The approach offered in the present invention, i.e. blockage of the binding to blood erythrocyte, may work independently or in combination with other vaccines based on different mechanisms to create an effective vaccine against malaria.

Development Status: Proof of concept demonstrated.

Market: Malaria is a major public health problem in more than 90 countries, inhabited by more than 2.4 billion people—40% of the world's population. The disease is estimated to kill approximately one (1.0) million people a year, and to cause up to 600 million new infections worldwide annually. Although the disease is mostly prevalent in developing countries and in particular in Sub-Saharan Africa, it also presents a significant health problem for the developed countries due to the extensive travelling between continents at this age of global economy.

Despite of the urgent need to find an effective cure against malaria, such cure has not been developed yet. Although several small molecule drugs have been used to alleviate the symptoms of the disease, a vaccine that can prevent the disease, or eradicate it altogether has not been developed yet, in spite of the many efforts to develop such a vaccine. The challenge in developing a malaria vaccine is due to the nature of the parasites that cause the disease, primarily the *Plasmodium falciparum* parasite. The parasite, which is transmitted to the human body via mosquito's bite, is quite complex and is characterized by structural diversity associated with the different stages of its life cycle.

The urgent public health need in a vaccine against malaria may present a substantial commercial opportunity to any vaccine or pharmaceutical company. The approach described and claimed in the present invention, i.e. blocking of the binding of the parasite to the blood erythrocytes, may therefore be an opportunity for vaccine developers. Furthermore, a vaccine of this invention may work effectively in combination with other malaria vaccines based on different mechanisms (i.e. RTS,S vaccine currently developed by GSK Biologicals and others).

Inventors: David Narum (NIAID) *et al.*

Related Publications:

1. H Liang and BK Sim. Conservation of structure and function of the erythrocyte-binding domain of Plasmodium falciparum EBA–175. Mol Biochem Parasitol. 1997 Feb;84(2):241–245.

2. DL Narum *et al.* Codon optimization of gene fragments encoding Plasmodium falciparum merzoite proteins enhances DNA vaccine protein expression and immunogenicity in mice. Infect Immun. 2001 Dec;69(12):7250–7253.

3. DL Narum *et al.* A novel Plasmodium falciparum erythrocyte binding protein-2 (EBP2/BAEBL) involved in erythrocyte receptor binding. Mol Biochem Parasitol. 2002 Feb;119(2):159–168.

Patent Status: U.S. Patent No. 7,078,507 issued 18 Jul 2006, entitled ''Synthetic genes for malarial proteins and methods of use'' (HHS Reference No. E–052–2004/0–US–02)

Licensing Status: Available for licensing.

Licensing Contacts: Uri Reichman, PhD, MBA; 301–435–4616; *UR7a@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 the erythrocyte binding protein as a malaria vaccine. Please contact Dana Hsu at 301–496–2644 for more information.

Novel Acylthiol Compositions and Methods of Making and Using Them Against HIV

Description of Technology: This invention provides a novel family of acylthiols and uses thereof. More specifically, this invention provides effective inhibitors of HIV that selectively target its highly conserved nucleocapsid protein (NCp7) by interacting with metal chelating structures of a zinc finger-containing protein. Because of the mutationally intolerant nature of NCp7, drug resistance is much less likely to occur with compounds attacking this target. In addition, these drugs should inactivate all types and strains of HIV and could also inactivate other retroviruses, since most retroviruses share one or two highly conserved zinc fingers that have the CCHC motif of the HIV Ncp7. Finally, this invention could be very useful for the large-scale practical synthesis of HIV inhibitors, because these compounds can be prepared by

using inexpensive starting materials and facile reactions. Thus, it opens the possibility that an effective drug treatment for HIV could be made available to much larger populations. These thioesters may also be used as an active component in topical applications that serve as a barrier to HIV infection.

Inventors: John K. Inman (NIAID), Atul Goel (NCI), Ettore Appella (NCI), James A. Turpin (NIAID), Marco Schito (NCI)

Publications:

1. ML Schito, A Goel, Y Song, JK Inman, RJ Fattah, WG Rice, JA Turpin, A Sher, E Appella. In vitro antiviral activity of novel human immunodeficiency virus type 1 nucleocapsid p7 zinc finger inhibitors in a transgenic murine model. AIDS Res Hum Retroviruses. 2003 Feb;19(2):91–101.

2. P Srivastava, M Schito, RJ Fattah, T Hara, T Hartman, RW Buckheit Jr, JA Turpin, JK Inman, E Appella. Optimization of unique, uncharged thioesters as inhibitors of HIV replication. Bioorg Med Chem. 2004 Dec 15;12(24):6437–6450.

3. LM Jenkins, JC Byrd, T Hara, P Srivastava, SJ Mazu, SJ Stahl, JK Inman, E Appella, JG Omichinski, P Legault. Studies on the mechanism of inactivation of the HIV–1 nucleocapsid protein NCp7 with 2-mercaptobenzamide thioesters. J Med Chem. 2005 Apr 21;48(8):2847–2858.

4. V Basrur, Y Song, SJ Mazur, Y Higashimoto, JA Turpin, WG Rice, JK Inman, E Appella. Inactivation of HIV–1 nucleocapsid protein P7 by pyridinioalkanoyl thioesters. Characterization of reaction products and proposed mechanism of action. J Biol Chem. 2000 May 19;275(20):14890–14897.

5. JA Turpin, Y Song, JK Inman, M Huang, A Wallqvist, A Maynard, DG Covell, WG Rice, E Appella. Synthesis and biological properties of novel pyridinioalkanoyl thiolesters (PATE) as anti-HIV–1 agents that target the viral nucleocapsid protein zinc fingers. J Med Chem. 1999 Jan 14;42(1):67–86.

Patent Status:

- U.S. Patent No. 7,528,274 issued 05 May 2009 (HHS Reference No. E–329–2000/0–US–06)
- U.S. Patent Application No. 12/414,321 filed 30 Mar 2009 (HHS Reference No. E–329–2000/0–US–07)

Licensing Status: Available for licensing.

Licensing Contact: Sally H. Hu, PhD, MBA; 301–435–5605; *hus@mail.nih.gov.*

Dated: December 23, 2009.

Richard U. Rodriguez,

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

[FR Doc. E9–31072 Filed 12–30–09; 8:45 am]

BILLING CODE 4140–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Library of Medicine; Notice of Meeting

Pursuant to section 10(a) 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 open to the public, with attendance limited to space available. Individuals who plan to attend and need special assistance, such as sign language interpretation or other reasonable accommodations, should notify the Contact Person listed below in advance of the meeting.

Name of Committee: National Library of Medicine Special Emphasis Panel.

Date: February 17, 2010.

Time: 12 p.m. to 2 p.m.

Agenda: To provide concept review of proposed grant applications.

Place: National Library of Medicine, 6705 Rockledge Drive, Bethesda, MD 20817. (Telephone Conference Call)

Contact Person: Zoe E. Huang, MD, Scientific Review Officer, Division of Extramural Programs, National Library of Medicine, National Institutes of Health, 6705 Rockledge Drive, Suite 301, MSC 7968, Bethesda, MD 20892–7968, 301–594–4937, *huangz©mail.nih.gov.*

(Catalogue of Federal Domestic Assistance Program Nos. 93.879, Medical Library Assistance, National Institutes of Health, HHS)

Dated: December 22, 2009.

Jennifer Spaeth,

Director, Office of Federal Advisory Committee Policy.

[FR Doc. E9–30949 Filed 12–30–09; 8:45 am]

BILLING CODE 4140–01–M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Agency for Healthcare Research and Quality

Notice of Meeting

In accordance with section 10(d) of the Federal Advisory Committee Act (5 U.S.C., Appendix 2), announcement is made of a Health Care Policy and Research Special Emphasis Panel (SEP) meeting.

A Special Emphasis Panel is a group of experts in fields related to health care research who are invited by the Agency for Healthcare Research and Quality (AHRQ), and agree to be available, to conduct on an as needed basis, scientific reviews of applications for AHRQ support. Individual members of the Panel do not attend regularly-scheduled meetings and do not serve for fixed terms or a long period of time. Rather, they are asked to participate in particular review meetings which require their type of expertise.

Substantial segments of the upcoming SEP meeting listed below will be closed to the public in accordance with the Federal Advisory Committee Act, section 10(d) of 5 U.S.C., Appendix 2 and 5 U.S.C. 552b(c)(6). Grant applications for the Accelerating Development of Methods for the Study of Complex Patients (R21) applications are to be reviewed and discussed at this meeting. These discussions are likely to reveal personal information concerning individuals associated with the applications. This information is exempt from mandatory disclosure under the above-cited statutes.

SEP Meeting on: AHRQ Developing Prospective Practice-based Comparative Effectiveness Research Clinical Registries: Orthopedic Devices, Drugs, and Procedures (P50).

Date: January 20, 2010 (Open on January 20 from 8 a.m. to 8:15 a.m. and closed for the remainder of the meeting).

Place: Marriott RIO, Conference Room TBD, 9751 Washingtonian Blvd., Gaithersburg, MD 20878.

Contact Person: Anyone wishing to obtain a roster of members, agenda or minutes of the nonconfidential portions of this meeting should contact Mrs. Bonnie Campbell, Committee Management Officer, Office of Extramural Research, Education and Priority Populations, AHRQ, 540 Gaither Road, Room 2038, Rockville, Maryland 20850, Telephone (301) 427–1554.

Agenda items for this meeting are subject to change as priorities dictate.

Dated: December 15, 2009.

Carolyn M. Clancy,

Director.

[FR Doc. E9–30956 Filed 12–30–09; 8:45 am]

BILLING CODE 4160–90–M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Institute on Drug Abuse; 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.