DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Prospective Grant of Exclusive License: The Use of IL13–PE38 for the Treatment of Asthma and Pulmonary Fibrosis

AGENCY: National Institutes of Health, Public Health Service, HHS.

ACTION: Notice.

SUMMARY: This is notice, in accordance with 35 U.S.C. 209(c)(1) and 37 CFR part 404.7(a)(1)(i), that the National Institutes of Health (NIH), Department of Health and Human Services (HHS), is contemplating the grant of an exclusive patent license to practice the inventions embodied in U.S. Patent Application No. 60/337,179 filed December 4, 2001, entitled ''IL–13 Receptor-Targeted Immunotoxins Ameliorates Symptoms of Asthma and of Allergy'' [HHS Reference No. E–296–2001/0–US–01], PCT Application No. PCT/US02/00616 filed February 28, 2002, entitled ''Alleviating Symptoms of TH2-Like Cytokine Mediated Disorders by Reducing IL–13 Receptor-Expressing Cells in the Respiratory Tract'' [HHS Reference No. E–296–2001/0–PCT–02], U.S. Patent Application No. 10/497,804 filed June 4, 2004, entitled ''Alleviating Symptoms of TH2-Like Cytokine Mediated Disorders by Reducing IL–13 Receptor-Expressing Cells in the Respiratory Tract'' [HHS Reference No. E–296–2001/0–US–03], Australian Patent Application No. 2002258011 filed June 8, 2004, entitled ''Alleviating Symptoms of TH2-Like Cytokine Mediated Disorders by Reducing IL–13 Receptor-Expressing Cells in the Respiratory Tract'' [HHS Reference No. E–296–2001/0–AU–04], Canadian Patent Application No. 2469082 filed February 28, 2002, entitled ''Chimeric Molecule for the Treatment of TH2-Like Cytokine Mediated Disorders'' [HHS Reference No. E–296–2001/0–CA–05], and European Patent Application No. 02727815.9 filed June 29, 2004 entitled ''Alleviating Symptoms of TH2-Like Cytokine Mediated Disorders by Reducing IL–13 Receptor-Expressing Cells in the Respiratory Tract'' [HHS Reference No. E–296–2001/0–EP–06], including background patent rights to U.S. Patent No. 4,892,827, issued on January 9, 1990, entitled ''Recombinant Pseudomonas Exotoxins: Construction of an Active Immunotoxin with Low Side Effects'' [HHS Reference No. E–385–1986/0–US–01], U.S. Patent No. 5,919,456, issued on July 6, 1999, entitled ''IL–13 Receptor Specific Chimeric Proteins'' [HHS Reference No. E–266–1994/0–US–07], U.S. Patent 6,518,061, issued on February 11, 2003, entitled ''IL–13 Receptor Specific Chimeric Proteins and Uses Thereof'' [HHS Reference No. E–266–1994/0–US–08], to NeoPharm, Inc., which has offices in Waukegan, Illinois. The patent rights in these inventions have been assigned and/or exclusively licensed to the Government of the United States of America.

The prospective exclusive license territory may be worldwide, and the field of use may be limited to the treatment of asthma and pulmonary fibrosis with IL13–PE38.

ADDRESSES: Requests for copies of the patent application, inquiries, comments, and other materials relating to the contemplated exclusive license should be directed to: David A. Lambertson, Ph.D., Technology Licensing Specialist, Office of Technology Transfer, National Institutes of Health, 6011 Executive Boulevard, Suite 325, Rockville, MD 20852–3804; Telephone: (301) 435–4632; Facsimile: (301) 402–0220; E-mail: *lambertsond@od.nih.gov*.

SUPPLEMENTARY INFORMATION: The technology relates to the treatment of asthma and pulmonary fibrosis. When airway inflammation occurs (*e.g.*, during an asthmatic attack or a response to an allergen), the number of cells that produce the receptor for IL–13 increases in the lungs. When IL–13 interacts with the receptor, an inflammatory response is induced; when this occurs in the lungs, it leads to the symptom of constricted breathing. Blocking the interaction between IL–13 and its receptors on the cells has been shown to reduce the inflammatory response.

A chimeric molecule was developed that comprised both an IL–13 domain (capable of interacting with its cognate receptor) and a toxin domain. This molecule has the capacity to interact with and kill IL–13 receptor expressing cells. The invention relates to a method of treating asthma or pulmonary fibrosis by administering a chimeric molecule comprising a toxin linked to an IL–13 targeting moiety (*e.g.*, IL13–PE38). By administering the toxin in this form, cells involved in airway inflammation can be selectively targeted and killed, thereby alleviating the symptom of constricted breathing.

The prospective exclusive license will be royalty bearing and will comply with the terms and conditions of 35 U.S.C. 209 and 37 CFR part 404.7. The prospective exclusive license may be granted unless within sixty (60) days from the date of this published notice, the NIH receives written evidence and argument that establishes that the grant of the license would not be consistent with the requirements of 35 U.S.C. 209 and 37 CFR part 404.7.

Applications for a license in the field of use filed in response to this notice will be treated as objections to the grant of the contemplated exclusive license. Comments and objections submitted to this notice will not be made available for public inspection and, to the extent permitted by law, will not be released under the Freedom of Information Act, 5 U.S.C. 552.

Dated: February 27, 2006.

Steven M. Ferguson,

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

[FR Doc. 06–2096 Filed 3–3–06; 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.

Method for Determining Redox Status of a Tissue

James B. Mitchell et al. (NCI).
U.S. Provisional Application No. 60/707,518 filed August 11, 2005 (HHS Reference No. E–258–2005/0-US–01).
Licensing Contact: Chekesha Clingman; 301/435–5018; *clingmac@mail.nih.gov.*

This invention describes methods for diagnosis and therapy of cancer and other pathologies associated with oxidative stress by administering a nitroxyl contrast agent and employing magnetic resonance imaging (MRI). Tumor tissues exhibit viable but hypoxic regions that allow them to reduce nitroxide compounds more efficiently than normal tissue. The paramagnetic relaxivity of nitroxide compounds makes it possible to use standard MRI scanners to determine the redox status of tissue in vivo. By determining the redox status of a tumor it is possible to not only diagnose a tumor due to its enhanced reduction of intracellular nitroxide contrast agent, but also to determine appropriate radiation treatment fields spatially to deliver therapeutic doses of radiation, and to determine appropriate timing sequences after the administration of a nitroxide contrast agent such that the maximum difference between normal and tumor tissue with respect to the radioprotective form of the nitroxide is present in the normal tissue, thereby limiting collateral damage to the normal tissue.

In addition to licensing, the technology is available for further development through collaborative research opportunities with the inventors.

Susceptibility-Matched Multiwell Plates for High-Throughput Screening by Magnetic Resonance Imaging and Spectroscopy

Kenneth W. Fishbein (NIA).
U.S. Provisional Application No. 60/725,299 filed October 12, 2005 (HHS Reference No. E–243–2005/0-US–01).
Licensing Contact: Chekesha Clingman; 301/435–5018; *clingmac@mail.nih.gov.*

This invention describes the development of a multi-well assay plate for high-throughput screening by magnetic resonance imaging (MRI) and nuclear magnetic resonance (NMR) spectroscopy. Multi-well plates are used in a wide variety of high-throughput measurements in clinical chemistry and immunology, as well as in drug discovery and other research applications. Magnetic resonance imaging (MRI) of multi-well plates offers the possibility of performing new kinds of high-throughput assays, including the detection of magnetic nanoparticles attached to or within cells. Moreover, MRI-guided localized nuclear magnetic resonance (NMR) spectroscopy could be used to perform detailed chemical analysis of complex mixtures of metabolites not possible by any other common analytical technique. Best of all, conventional MRI techniques exist which would permit all samples in one or more multi-well plate(s) to be analyzed simultaneously. Unfortunately, conventional multi-well plates typically give poor performance for MRI-based assays since they provide inadequate matching of magnetic susceptibility between the plate, the sample and their surroundings. This results in distortion of the magnetic field within the scanner and thus reduces the sensitivity for detecting magnetic particles and the resolution of NMR spectra. This invention relates to a new multi-well plate design incorporating one-piece polyetherimide plastic construction for improved magnetic susceptibility matching for aqueous samples. This design can easily be extended to non-aqueous samples by the selection of an appropriate, commercially-available plastic resin or resin blend. Further enhancement in susceptibility matching can be accomplished by combining the new plate design with plugs for each well constructed from the same plastic as the plate. These plugs would allow the entire thickness of each sample to be scanned in chemical analyses, improving signal-to-noise ratio and sensitivity. These plugs can be integrated into a single ''cap mat'' so that the entire assembly can be filled and manipulated by standard robotic laboratory equipment already in wide use in the pharmaceutical industry. Alternatively, spherical wells, accessed by narrow fill holes, may be molded into a solid plate, eliminating the need for individual plugs to seal each well. The new multi-well plate/plug design reduces magnetic field distortions and should dramatically improve spectral resolution and sensitivity for NMR and MRI-based high-throughput screening.

In addition to licensing, the technology is available for further development through collaborative research opportunities with the inventors.

Measuring Fifteen Endogenous Estrogens Simultaneously in Human Urine by High-Performance Liquid Chromatography-Mass Spectrometry

Xia Xu, Timothy Veenstra, Larry Keefer, Regina Ziegler (NCI).
U.S. Provisional Application No. 60/688,160 filed June 7, 2005 (HHS Reference No. E–207–2005/0–US–01).
Licensing Contact: Michael Shmilovich; 301/435–5019; *shmilovm@mail.nih.gov.*

Available for licensing and commercial development is a patent-pending, validated high-performance liquid chromatography-electrospray ionization-tandem mass spectrometry method for measuring the absolute quantities of fifteen endogenous estrogens and their metabolites in human urine. The method is sensitive, specific, accurate, and precise. It requires a single hydrolysis/extraction/derivatization step and only 0.5 mL of urine, yet is capable of simultaneously quantifying estrone, its 2- and 4-methoxy derivatives, and its 2-, 4-, and 16α-hydroxy derivatives; estradiol, its 2- and 4-methoxy derivatives, and its 2- and 16α-hydroxy derivatives; 2-hydroxyestrone-3-methyl ether; 16-epiestriol; 17-epiestriol; and 16-ketoestradiol in premenopausal and postmenopausal women as well as men. Standard curves are linear over a 10^3-fold concentration range with the relative standard error of the estimate for the linear regression line ranging from 1.2 to 7.3%, respectively. The lower limit of quantitation for each estrogen is 0.02 ng per 0.5-mL urine sample (only 2 pg placed on column). The percent recovery of a known added amount of estrogen metabolite ranges from 96 to 107%. The overall precision, including the hydrolysis, extraction, and derivatization steps, is 1–5% relative standard deviation for samples prepared concurrently and 1–12% relative standard deviation for samples prepared in separate batches.

Immunogenic T Cell Targets in Autoimmune Hepatitis and Methods of Use

Barbara Rehermann (NIDDK) et al.
U.S. Provisional Application No. 60/659,513 filed March 7, 2005 (HHS Reference No. E–263–2003/0–US–01)
Licensing Contact: Cristina Thalhammer-Reyero; 301/435–4507; *thalhamc@mail.nih.gov.*

Available for licensing and commercial development are new methods of diagnosing and monitoring the progression or response to therapy of subjects with autoimmune hepatitis (AIH) by quantitating the frequency and determining the function of autoantigen-specific CD4+ T cells in the peripheral blood with HLA–DRB1*0301 tetramers that display the autoepitopes. The invention identifies the immunogenic peptide regions that are targets of the T-cell immune response in two types of autoimmune hepatitis: (1) Anti-SLA (soluble liver antigen)-positive autoimmune hepatitis type 3 and (2) anti-LKM (liver kidney microsomal antigen)-positive autoimmune hepatitis type 2. Upon mapping the immunogenic regions within SLA and P450 2D6 using short, overlapping peptides, the inventors discovered at least four immunogenic peptides within SLA and

at least one peptide within P450 2D6 that were recognized by HLA–DRB*0301-restricted T cells. The technology is partially described in Hepatology 2005; 42: 291A–292A.

In addition to licensing, the technology is available for further development through collaborative research opportunities with the inventors.

Methods for Rapid and Specific Fluorescent Staining of Biological Tissue for Laser Capture Microdissection

Robert A. Star (NIDDK), Hiroshi Murakami (NIDDK), Lance A. Liotta (NCI), Kenneth R. Spring (NHLBI)

U.S. Patent No. 6,790,636 issued 14 Sep 2004 (HHS Reference No. E–133–2000/0–US–02).

Licensing Contact: Michael Shmilovich; 301–435–5019; *shmilovm@mail.nih.gov.*

Available for licensing and commercial development are methods for rapid and specific fluorescent staining of biological tissue samples that substantially preserve biological molecules such as mRNA. Also within the scope of the invention are methods for microdissecting tissue to obtain pure populations of cells or tissue structures based upon identifying and excising cells or tissue structures that are labeled with fluorescent specific binding agents. A laser capture microdissection (LCM) apparatus useful for identifying and isolating cells and tissue structures following rapid immunofluorescent staining is also disclosed. Other LCM devices are available for purchase from Arcturus Engineering.

Dated: February 27, 2006.

Steven M. Ferguson,

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

[FR Doc. 06–2097 Filed 3–3–06; 8:45 am]

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Deoxyhypusine Hydroxylase

Myung Hee Park et al. (NIDCR)

U.S. Provisional Application No. 60/748,879 filed 09 Dec 2005 (HHS Reference No. E–051–2006/0–US–01).

Licensing Contact: John Stansberry; 301/435–5236; *stansbej@mail.nih.gov.*

Translation initiation factor eIF5A is a highly conserved eukaryotic protein. One of its lysine residues is enzymatically modified, using spermidine, to form an unusual amino acid, hypusine, a posttranslational modification unique to eIF–5A. This eukaryotic initiation factor (eIF5A) and its hypusine modification are essential for mammalian cell proliferation. Inventors at the National Institutes of Health have recently cloned and characterized the enzyme deoxyhypusine hydroxylase (DOHH) that catalyzes the final step in the modification of eIF5A. The inventors have characterized and cloned both the yeast and human recombinant versions of this enzyme.

Studies have shown that metal chelating compounds like deferiprone and ciclopirox olamine that inhibit DOHH activity in cells also inhibit HIV–1 replication in cell culture. These findings suggest potential utility of DOHH as a novel target for anti-cancer and anti-retroviral therapy. These advances could also conceivably lead to the development of small molecule inhibitors that bind to specific sites in the enzyme.

In addition to licensing, the technology is available for further development through collaborative research opportunities with the inventors.

Methods of Treating Cancer Using Pyridine Carboxaldehyde Pyridine Thiosemicarbazone Radiosensitizing Agents

Philip J. Tofilon et al. (NCI)

U.S. Provisional Application No. 60/718,172 filed 16 Sep 2005 (HHS Ref. No. E–319–2005/0–US–01).

Licensing Contact: George G. Pipia; 301/435–5560; *pipiag@mail.nih.gov.*

Ribonucleotide reductase is the rate-limiting enzyme of de novo DNA synthesis. The enzyme is composed of two homodimer subunits, hRRM1 and hRRM2. Hydroxyurea, a ribonucleotide reductase inhibitor, is commonly used in conjunction with radiotherapy but it its efficacy as shown in many chemoradiation trials is limited. Triapine (2-carboxyaldehyde pyridine thiosemicarbazone), a novel ribonucleotide reductase inhibitor, exhibits sensitivity to the subunit hRRM2 and inhibits ribonucleotide reductase more effectively when compared to hydroxyurea, thus imparting a radiosensitizing effect.

This present invention provides methods of preventing DNA synthesis and DNA repair after exposing cells to ionizing radiation. The present invention further provides methods of treating cancer and other tumors by coadministration of a radiosensitizing amount of Triapine and ionizing radiation.

Methods and Compositions for Treating FUS1 Related Disorders

Michael I. Lerman *et al.* (NCI)

U.S. Provisional Application No. 60/697,596 filed 07 Jul 2005 (HHS Reference No. E–137–2005/0–US–01).

Licensing Contact: Thomas Clouse; 301/435–4076; *clousetp@mail.nih.gov.*

The FUS1 gene residing in the 3p21.3 chromosome region may function as a tumor suppressor gene. Results show that FUS1 null mutants show consistent changes in NK cells and secreted antibodies, suggesting that FUS1 plays an important role in the development and activation of the mammalian immune system. The invention relates to methods, systems and transgenic animals useful for screening, diagnosing and treating FUS1 related disorders. Interestingly, targeted disruption of FUS1 gene in mice resulted in a viable and fertile phenotype.

Possible uses of this invention include using the FUS1 protein to modulate and boost the immune system in diseases like cancer and AIDS. Also, the cDNA and the corresponding protein are small and the applications could include gene therapy with