Dated: June 27, 2008.

Richard U. Rodriguez,

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

[FR Doc. E8–15178 Filed 7–2–08; 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.

A Prophylactic and Therapeutic for Preventing and Treating Tularemia by Rapid Activation of Host Cells and Antigen Recognition

Description of Technology: The invention is a composition and method for prophylactic and therapeutic treatment of tularemia caused by *Francisella tularensis* comprised of Cationic Liposome DNA Complexes (CLDC) complexed with noncoding DNA and membrane antigens isolated from *F. tularensis* strain LVS (MPF). *F. tularensis* is category A pathogen (as designated by the NIH) that was previously weaponized by both the former Soviet Union and the United States of America and is currently a potential bioweapon and bioterrorism threat. Furthermore, tularemia is endemic to the U.S. (majority of the cases occurring in the Midwest) and Europe. The prophylactic and therapeutic activities of this invention rely in part on rapid activation of host cells and recognition of bacterial antigens. *In vivo* studies in mice show that CLDC + MPF elicit protective immunity against pneumonic tularemia when administered shortly (days) prior to exposure to aerosols of virulent *F. tularensis.* The method can be applicable for eliciting immune response in other infectious diseases.

Applications:

Prophylactic and therapeutic for Tularemia.

Biodefense agent.

Method is applicable to other infectious diseases, particularly for pathogens that are enveloped or encapsulated (i.e. *Pseudomonas aeruginosa, Neisseria meningiditis, Yersinia pestis* and Influenza).

Advantages:

Rapid induction of protective immunity against *F. tularensis.*

Avoids antibiotic resistance associated with current therapies.

Development Status: In vitro and *in vivo* data are available.

Market:

Prophylactic and treatment for tularemia and other infectious diseases.

Biodefense.

Inventors: Catherine M. Bosio (NIAID).

Publication: PowerPoint slide presentation of invention can be provided upon request.

Patent Status: U.S. Provisional Application No. 61/030,984 filed 24 Feb 2008 (HHS Reference No. E–095–2008/0–US–01).

Licensing Status: This invention is available for exclusive or non-exclusive licensing.

Licensing Contact: Sally Hu, PhD.; 301–435–5606, *HuS@mail.nih.gov.*

A New Method for Screening of Anti-tumor Agents

Description of Technology: Astrocytomas and glioblastoma multiforme are the most common forms of malignant brain cancer, and are often unresponsive to surgical removal and pharmacological therapy. The 5 year survival rate of glioblastoma is 5%, thus, making it necessary for the identification of more effective anti-tumor agents. Individuals with the familial cancer syndrome neurofibromatosis type 1 are predisposed to developing multiple tumors including astrocytoma and glioblastoma.

Scientists at NCI have discovered a new technology that will help screen multiple anti-tumor and anti-neurofibromatosis agents in a high throughput assay by using an astrocytoma cell line (KR158) that expresses the luciferase gene under the influence of dual promoters, E2F and CMV.

This new technology distinguishes between cytostatic and cytotoxic compounds, thereby significantly reducing the time and cost required to screen anti-tumor agents.

Advantages:

Quantifiable.

Can be used in high throughput assays.

Distinguishes between cytostatic and cytotoxic activity of compounds.

Applications:

Cancer therapeutics.

Gene therapy.

Screening of anti-tumor agents.

Screening of anti-neurofibromatosis agents.

Pharmacology of drugs.

Market: Neurofibromatoses is inherited by many affected individuals and occurs in 1 in 3500 individuals. In addition, between 30 and 50 percent of new cases arise spontaneously through mutation in an individual's genes which can then be passed on to succeeding generations, leading to increased tumor risk. Astrocytomas and glioblastoma multiforme are the most common malignant brain tumor in adults with very poor prognosis.

Development Status: Late-stage.

Inventors: Jessica J. Hawes and Karlyne M. Reilly (NCI).

Patent Status: HHS Reference No. E–038–2008/0—Research Tool. Patent protection is not being sought for this technology.

Licensing Status: Available for non-exclusive licensing.

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

Collaborative Research Opportunity: The National Cancer Institute Mouse Cancer Genetics Program is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize anti-astrocytoma or anti-neurofibromatosis therapy. Please contact John D. Hewes, PhD., at 301–435–3121 or *hewesj@mail.nih.gov* for more information.

A Novel Therapeutic Strategy for the Treatment of Hyperpigmentation and Melanoma

Description of Technology: The present invention describes that the transcription factor SOX9 is expressed by normal human melanocytes *in vitro* and in the skin *in vivo*, and that over-expression of SOX9 decreases the proliferation of mouse and human melanoma cell lines via several pathways. Furthermore, SOX9 (or its

bioactive derivatives) appears to be potentially useful in inducing skin pigmentation, may inhibit the proliferation of melanoma cells and increase their sensitivity to retinoic acid, which could be used to treat melanoma.

Advantages and Applications:

SOX9 (or its bioactive derivative) might be useful in increasing skin pigmentation in acquired hypopigmentary disorders such as vitiligo (1–2% of world population) or post-inflammatory hypopigmentation.

A novel gene therapy based treatment for Melanoma: Experimental results show that cells over-expressing SOX9 do not form tumors in human skin reconstructs or in mice as do wild type or GFP-transduced melanoma cells.

SOX–9 therapy in combination with retinoic acid can be an effective therapeutic strategy for treating melanoma.

Development Status: The technology is currently in the pre-clinical stage of development. Animal studies have been performed and the inventors are currently pursuing gene therapy approaches with SOX9 which may be useful in the treatment of melanoma.

Inventors: Vincent J. Hearing and Thierry Passeron (NCI).

Patent Status: U.S. Provisional Application No. 60/963,280 filed 03 Aug 2007 (HHS Reference No. E–150–2007/0–US–01).

Licensing Status: Available for exclusive and non-exclusive licensing.

Licensing Contact: Whitney Hastings, Ph.D.; 301–451–7337; *hastingw@mail.nih.gov.*

Collaborative Research Opportunity: The National Cancer Institute Laboratory of Cell Biology is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize the regulation of SOX9 function as a strategy to treat melanoma, modulate skin pigmentation and/or ameliorate skin pigmentary disorders. Please contact John D. Hewes, Ph.D. at 301–435–3121 or *hewesj@mail.nih.gov* for more information.

Method for Predicting and Detecting Tumor Metastasis

Description of Technology: Detecting cancer prior to metastasis greatly increases the efficacy of treatment and the chances of patient survival. Although numerous biomarkers have been reported to identify aggressive tumor types and predict prognosis, each biomarker is specific for a particular type of cancer, and no universal marker that can predict metastasis in a number of cancers has been identified. In addition, due to a lack of reliability, several markers are typically required to determine the prognosis and course of therapy.

Available for licensing are carboxypeptidase E (CPE) inhibitor compositions and methods to prognose and treat cancer as well as methods to determine the stage of cancer. The inventors discovered that CPE expression levels increase according to the presence of cancer and metastasis wherein CPE is upregulated in tumors and CPE levels are further increased in metastatic cancer. This data has been demonstrated both in vitro and in vivo experiments and in liver, breast, prostate, colon, and head and neck cancers. Metastatic liver cells treated with CPE siRNA reversed the cells from being metastatic and arrested cells from further metastasis. Thus, CPE as a biomarker for predicting metastasis and its inhibitors have an enormous potential to increase patient survival.

Applications:

Method to prognose multiple types of cancer and determine likelihood of metastasis.

Compositions that inhibit CPE such as siRNA.

Method to prevent and treat cancer with CPE inhibitors.

Market:

An estimated 1,437,180 new cases and 565,650 deaths from cancer are projected to occur in the U.S. in 2008;

Global cancer market is worth more than eight percent of total global pharmaceutical sales;

Cancer industry is predicted to expand to $85.3 billion by 2010.

Development Status: The technology is currently in the pre-clinical stage of development.

Inventors: Y. Peng Loh (NICHD) *et al.*

Publication: Manuscript in preparation.

Patent Status: PCT Application No. PCT/US2008/051438 filed 18 Jan 2008, claiming priority to 19 Jan 2007 (HHS Reference No. E–096–2007/3–PCT–01).

Licensing Status: Available for exclusive or non-exclusive licensing.

Licensing Contact: Jennifer Wong; 301–435–4633; *wongje@mail.nih.gov.*

Collaborative Research Opportunity: The National Institute for Child Health and Human Development, Section on Cellular Neurobiology, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize CPE as a biomarker for predicting metastasis. Please contact John D. Hewes, Ph.D. at 301–435–3121 or *hewesj@mail.nih.gov* for more information.

Novel O-GLcNAcase Inhibitor and Fluorogenic Substrate as a Tool for Diagnosing Type 2 Diabetes

Description of Technology: NIH researchers have synthesized a novel analogue of O-(2-acet-amido-2-deoxy-D-glycopyrano-sylidene)amino-N-phenylcarbamate (PUGNAc), which bears an extension on the N-acetyl moiety. This modified PUGNAc acts as a selective inhibitor of O-GlcNAcase; an enzyme that removes N-acetylglucosamine from nuclear and cytoplasmic proteins, and whose inhibition is associated with the development of Type 2 diabetes. The most desirable feature of this new compound is its ability to specifically inhibit O-GlcNAcase without targeting the related hexosaminidase A (HEX A) and hexoaminidase B (HEX B) enzymes. This unique property distinguishes it from the original PUGNAc and other compounds which inhibit O-GlcNAcase as well as other enzymes. It also has a smaller inhibitory effect on O-GlcNAcase compared to the original PUGNAc. These properties make the modified PUGNAc useful for diagnostic or therapeutic applications involving Type 2 diabetes.

A fluorescent derivative of the modified PUGNAc has also been developed. Modified PUGNAc, conjugated to a fluorescent moiety such as 4-methylumbelliferone, can serve as a substrate for O-GlcNAcase without inhibiting HEX A. This allows the fluorescently labeled compound to be used for measuring O-GlcNAcase enzyme activity, and thus provide a means of diagnosing Type 2 diabetes in human blood or tissue samples. Previous reagents have monitored other Type 2 diabetes related enzymes, but with much less specificity. Recent studies that link mutations of the MGEA5 gene (which codes for O-GlcNAcase) to Type 2 diabetes provide further support for the use of the fluorescent derivative as a potent tool for diagnosing the disease. The fluorogenic derivative may also be used as a novel imaging agent for assessing O-GlcNAcase function *in-vivo.*

Applications:

Diagnosis of type 2 diabetes.

In vivo imaging of O-GlcNAcase enzyme function.

Development Status: Early stage.

Inventors: John A. Hanover *et al.* (NIDDK).

Publication: Eun Ju Kim, Melissa Perreira, Craig J. Thomas, and John A. Hanover. An O-GlcNAcase-specific inhibitor and substrate engineered by the extension of the N-acetyl moiety. J. Am. Chem. Soc. 2006 Apr 5;128(13):4234–4235.

Patent Status: U.S. Patent Application No. 11/654,647 filed 18 Jan 2007 (HHS Reference No. E–229–2006/0–US–01).

Licensing Status: Available for exclusive or non-exclusive licensing.

Licensing Contact: Jasbir (Jesse) S. Kindra, J.D., M.S.; 301–435–5170; *kindraj@mail.nih.gov.*

Collaborative Research Opportunity: The NIDDK Laboratory of Cell Biochemistry and Biology is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize modified PUGNAc for prevention or treatment of Type 2 diabetes. Please contact Rochelle Blaustein at 301–451–3636 or *Rochelle.Blaustein@nih.gov* for more information.

Use of Human Gamma Satellite Insulator Sequences To Prevent Gene Silencing and Allow for Long Term Expression of Integrated Transgenes

Description of Technology: The lack of stable expression of transgenes in target cell lines remains a serious problem for gene therapy and cellular reprogramming approaches. Once integrated into chromosomes, the expression of these transgenes may be regulated by epigenetic effects of the surrounding chromatin. These position effects, which include transgene silencing and expression variegation, are often associated with changes in the chromatin structure, and are capable of inhibiting gene expression and neutralizing the intended effect of the inserted transgene.

Experimental results suggest that gene position effects can be partially overcome by flanking the transgene with regulatory elements called chromatin insulators which work by establishing defined domains of transcriptional activity within the eukaryotic genome. These insulators can partially overcome position effects by shielding the promoters from the influence of neighboring regulatory elements, or by preventing the spread of heterochromatin which can lead to subsequent gene silencing.

This invention discloses the use of gamma satellite DNA, residing in the pericentromeric region of human chromosomes, as highly efficient chromatin insulators. These insulators have a remarkable ability to overcome position effects and prevent the silencing of transgenes. When human chromosome 8 gamma satellite sequences were used as flanking DNA for eGFP (enhanced green fluorescent protein) gene expression in mouse erythroleukemia (MEL) cells, stable transgene expression was recorded for well over eight months. Until recently, no chromatin insulator sequences were known to completely prevent gene silencing on a long term basis in transfected cells. The human gamma-satellite sequences demonstrate a higher efficiency than any known chromatin insulator identified so far in intergenic regions, and may have invaluable applications in the fields of gene therapy, protein expression, and cellular reprogramming where adequate expression of the transgene is essential for long term therapeutic or developmental success.

Applications:

Gene therapy.

Protein expression.

Cellular reprogramming.

Development Status: Prolonged transgene expression attained in mouse erythroleukemia (MEL) cells.

Inventors: Vladimir L. Larionov, Jung-Hyun Kim, Tom Ebersole (NCI).

Publications:

1. G Felsenfeld, B Burgess-Beusse, C Farrell, M Gaszner, R Ghirlando, S Huang, C Jin, M Litt, F Magdinier, V Mutskov, Y Nakatani, H Tagami, A West, T Yusufzai. Chromatin boundaries and chromatin domains. Cold Spring Harb Symp Quant Biol. 2004;69:245–250.

2. T Ebersole, Y Okamoto, VN Noskov, N Kouprina, JH Kim, SH Leem, JC Barrett, H Masumoto, V Larionov. Rapid generation of long synthetic tandem repeats and its application for analysis in human artificial chromosome formation. Nucleic Acids Res. 2005 Sep 1;33(15):e130, doi:10.1093/nar/gni129.

Patent Status:

U.S. Provisional Application No. 60/890,176 filed 15 Feb 2007 (HHS Reference No. E–154–2006/0–US–01).

PCT Application No. PCT/US2008/054170 filed 15 Feb 2008 (HHS Reference No. E–154–2006/0–PCT–02).

Licensing Status: Available for exclusive or non-exclusive licensing.

Licensing Contact: Jasbir (Jesse) S. Kindra, J.D., M.S.; 301–435–5170; *kindraj@mail.nih.gov.*

Collaborative Research Opportunity: The National Cancer Institute Laboratory of Molecular Pharmacology is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize gamma-satellite DNA insulators for stable transgene expression in ectopic chromosomal sites and in Human Artificial Chromosomes (HACs). Please contact John D. Hewes, Ph.D. at 301–435–3121 or *hewesj@mail.nih.gov* for more information.

Single Nucleotide Polymorphism Detection by DNA Melting Analysis

Description of Technology: A Single Nucleotide Polymorphism (SNP) is defined as a single base pair difference occurring between members of the same species, or between paired chromosomes in an individual. Some SNPs have been associated with disease traits, and may predispose an individual to a disease or may influence that individual's response to therapeutic agents. There are several high-throughput methods that can detect SNPs of moderate to high abundance, where the polymorphism frequency is greater than ten percent. However, SNPs that alter gene expression or affect the structure of a gene product are often of much lower abundance, with allele frequency of around one percent. Thus, there is a need to devise high-throughput, inexpensive and efficient methods for their detection.

The patent discloses methods for accurately detecting nucleotide sequence variations, such as polymorphisms, deletions, insertions or inversions, by comparison of DNA melting profiles. Methods of detecting single nucleotide sequence variations within arrays are also disclosed, as are methods of detecting mutations correlated with genetic disease.

Applications:

Detection of SNPs and small insertions, deletions, and inversions in a DNA sequence.

Prediction of the etiology or prognosis of certain diseases, or determination of disease traits among individuals.

Advantages:

Useful for detecting rarely-occurring SNPs.

High throughput, simple method that measures DNA melting efficiently, without using intervening steps such as gels, columns etc.

Inventors: Robert H. Lipsky *et al.* (NIAAA)

Patent Status: U.S. Patent No. 7,273,699 issued 25 Sep 2007 (HHS Reference No. E–251–2001/0 US–02).

Licensing Status: Available for exclusive, co-exclusive, or non-exclusive licensing.

Licensing Contact: Jasbir (Jesse) S. Kindra, J.D., M.S.; 301–435–5170; *kindraj@mail.nih.gov.*

Collaborative Research Opportunity: The National Institute on Alcohol Abuse and Alcoholism Section on Molecular Genetics is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize single nucleotide polymorphism detection by melting

analysis. Please contact Dr. Robert Lipsky at 301/402–5591 or *rlipsky@mail.nih.gov* for more information.

Dated: June 26, 2008.

Richard U. Rodriguez,

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

[FR Doc. E8–15201 Filed 7–2–08; 8:45 am]

BILLING CODE 4140–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Public Teleconference Regarding Licensing and Collaborative Research Opportunities for: Methods and Compositions Relating to Detecting Dihydropyrimidine Dehydrogenase (DPD)

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

ACTION: Notice.

Technology Summary

This technology relates to a method of detecting DPD Splicing Mutations.

Technology Description

Scientists at the National Cancer Institute have discovered a method detecting DPD Splicing Mutations. This method can identify patients with such mutations, and thereby alert the health care provider that the patient will have an adverse reaction to the chemotherapeutic agent, 5–Fluorouracil.

The invention relates to methods and compositions that are useful for detecting deficiencies in DPD levels in mammals including humans. Cancer patients having a DPD deficiency are at risk of a severe toxic reaction to the commonly used anticancer agent 5-fluorouracil (5–FU). The technology encompasses DPD genes from human and pig, methods for detecting the level of nucleic acids that encode DPD in a patient, and nucleic acids that are useful as probes for this purpose.

Novel applications of the methods include:

- Screening of patients prior to the administration of the chemotherapeutic agent, 5–Fluorouracil.
- Diminishing and potentially eliminating the severe side effects of 5–Fluorauracil in patients.

Competitive Advantage of Our Technology

5–Fluorouracil (5–FU) is a therapeutic for the treatment of multiple cancers, including breast and colon cancers. In the United States, approximately 275,000 cancer patients receive 5–FU annually. It is estimated that three percent (3%) of those patients develop some degree of toxic reaction. Patients suffering toxic reactions are difficult and expensive to treat further. Approximately, 15% of those developing toxic reaction, will die as a result of exposure to 5–FU. Death is typically caused by cardiotoxicity. More than 1,300 patients in the United States die each year as a result of 5–FU toxicity. These deaths are all potentially avoidable if patients that are likely to get adverse reaction with 5–FU treatment are detected prior to treatment.

Patent Estate

This technology consists of the following patents and patent applications:

I. United States Patent Number 5,856,454 entitled ''cDNA for Human and Pig Dihydropyrimidine Dehydrogenase,'' issued January 5, 1999 (HHS Ref. No. E–157–1994/0–US–01);

II. United States Patent Number 6,015,673 entitled ''Cloning and Expression of cDNA for Human Dihydropyrimidine Dehydrogenase,'' issued January 18, 2000 (HHS Ref. No. E–157–1994/0–US–03);

III. United States Patent Number 6,787,306 entitled ''Methods and Compositions for Detecting Dihydropyrimidine Dehydrogenase Splicing Mutations,'' issued September 7, 2004 (HHS Ref. No. E–157–1994/1–US–01);

IV. United States Pre-Grant Publication number 2005/0136433A1 corresponding to application serial number 10/911237 entitled ''Methods and Compositions for Detecting Dihydropyrimidine Dehydrogenase Splicing Mutations,'' published June 23, 2005 (HHS Ref. No. E–157–1994/1–US–19) and all issued and pending counterparts in Europe, Canada, and Australia.

Next Step: Teleconference

There will be a teleconference where the principal investigator will explain this technology. Licensing and collaborative research opportunities will also be discussed. If you are interested in participating in this teleconference please call or e-mail Mojdeh Bahar; (301) 435–2950; *baharm@mail.nih.gov.* OTT will then e-mail you the date, time and number for the teleconference.

Dated: June 26, 2008.

Richard U. Rodriguez,

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

[FR Doc. E8–15182 Filed 7–2–08; 8:45 am]

BILLING CODE 4140–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Institute on Alcohol Abuse and Alcoholism; Notice of Closed Meeting

Pursuant to section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2), 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 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 Alcohol Abuse and Alcoholism Special Emphasis Panel; Deferred AA3 Applications.

Date: July 16, 2008.

Time: 1 to 3 p.m.

Agenda: To review and evaluate grant applications.

Place: National Institutes of Health, 5635 Fishers Lane, Room 3042, Rockville, MD 20852 (Telephone Conference Call).

Contact Person: Katrina L. Foster, PhD, Scientific Review Officer, National Institute on Alcohol Abuse and Alcoholism, National Institutes of Health, 5635 Fishers Lane, Room 3042, Rockville, MD 20852, 301–443–4032, *katrina@mail.nih.gov.*

The applications being reviewed in EEO2 were initially assigned to panel AA3. The appropriate expertise was not available in AA3; thus, these applications were removed and are being reviewed in a SEP meeting.

(Catalogue of Federal Domestic Assistance Program Nos. 93.271, Alcohol Research Career Development Awards for Scientists and Clinicians; 93.272, Alcohol National Research Service Awards for Research Training; 93.273, Alcohol Research Programs; 93.891, Alcohol Research Center Grants, National Institutes of Health, HHS)

Dated: June 25, 2008.

Jennifer Spaeth,

Director, Office of Federal Advisory Committee Policy.

[FR Doc. E8–14924 Filed 7–2–08; 8:45 am]

BILLING CODE 4140–01–M