FDA received 146,274 mandatory reports to CDRH during 2007. Based on this experience, FDA estimates that CDRH will receive 146,274 mandatory reports annually from 1,665 users of the electronic reporting system (a group comprised of facilities, importers, and manufacturers). FDA estimates the maximum reporting burden for a mandatory report to be 1 hour, for a total burden of 146,274 hours (146,274 reports x 1 hour = 146,274 hours) or a minimum burden of 99,466 hours with ((146,274 reports x 80% x 0.60 hour) + (146,274 reports x 20% x 1 hour) = 99,466.32 hours). FDA received 5,000 voluntary reports to CFSAN during 2007. Based on this experience, FDA estimates that CFSAN will receive 5,000 voluntary reports annually from 5,000 users of the electronic reporting system. FDA estimates the reporting burden for a voluntary report to be 0.6 hours, for a total burden of 3,000 hours (5,000 reports x 0.6 hours = 3,000 hours).

FDA received 214 mandatory dietary supplement reports to CFSAN from January 1, 2008, to April 15, 2008. Based on this experience, FDA estimates that CFSAN will receive 856 mandatory reports annually from 150 users of the electronic reporting system. FDA estimates the maximum reporting burden for a mandatory report to be 1 hour, for a total burden of 856 hours (856 reports x 1 hour = 856 hours) or a minimum burden of 582 hours with ((856 reports x 80% x 0.60 hour) + (856 reports x 20% x 1 hour) = 582.08 hours).

FDA received 163 voluntary reports to CVM during 2007. Based on this experience, FDA estimates that CVM will receive 163 voluntary reports annually from 163 users of the electronic reporting system. FDA estimates the reporting burden for a voluntary report to be 0.6 hours for a total burden of 98 hours (163 reports x 0.6 hours = 97.8 hours).

FDA received 35,765 mandatory reports to CVM during 2007. Based on this experience, FDA estimates that CVM will receive 35,765 mandatory reports annually from 808 users of the electronic reporting system. FDA estimates the maximum reporting burden for a mandatory report to be 1 hour, for a total burden of 35,765 hours (35,765 reports x 1 hour = 35,765 hours) or a minimum burden of 24,320 hours with ((35,765 reports x 80% x 0.6 hour) + (35,765 reports x 20% x 1 hour) = 24,320.20 hours).

FDA received 5,000 voluntary reports to ORA during 2007. Based on this experience, FDA estimates that ORA will receive 5,000 voluntary reports annually from 5,000 users of the electronic reporting system. FDA estimates the reporting burden for a voluntary report to be 0.6 hours, for a total burden of 3,000 hours (5,000 reports x 0.6 hours = 3,000 hours). ORA does not receive mandatory reports.

FDAAA, Section 1005, the Reportable Food Registry, established new electronic mandatory and voluntary reporting requirements for instances of ''reportable'' food, meaning an article of food (other than infant formula) for which there is a reasonable probability that the use of, or exposure to, such article of food will cause serious adverse health consequences or death to humans or animals. FDA received 625 voluntary food complaints leading to adverse events from January 1, 2008, to June 30, 2008, and there were 206 and 182 Class 1 Recalls for human food in Fiscal Years 2006 and 2007, respectively. Based on these experiences, FDA estimates that FDA could receive 200 to 1,200 ''reportable'' food reports annually from 200 to 1,200 mandatory and voluntary users of the electronic reporting system. FDA will utilize the upper-bound estimate of 1,200 for these calculations. FDA estimates the reporting burden for a mandatory ''reportable'' food report to be 0.6 hours, for a total burden of 720 hours (1,200 reports x 0.6 hours = 720 hours). FDA estimates the reporting burden for a voluntary ''reportable'' food report to be 0.6 hours, for a total burden of 720 hours (1,200 reports x 0.6 hours = 720 hours).

FDAAA, Section 1002, Early Warning Recall, mandated FDA establish a system to receive voluntary pet food complaint reports and provide an Early Warning Recall system for the public. FDA received 270 voluntary pet food reports from January 1, 2008, to June 30, 2008. FDA received 10,740 and 99 pet food complaints in FY 2007 and 2006, respectively. Based on these experiences, FDA estimates that FDA could receive 540 voluntary pet food reports annually from 540 users of the electronic reporting system. FDA estimates the reporting burden for a voluntary ''Early Warning Recall'' report to be 0.6 hours, for a total burden of 324 hours (540 reports x 0.6 hours = 324 hours).

Dated: May 13, 2009.

Jeffrey Shuren,

Associate Commissioner for Policy and Planning.

[FR Doc. E9–11687 Filed 5–19–09; 8:45 am]

BILLING CODE 4160–01–S

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.

A549 Cells: A Well-Characterized Lung Carcinoma Cell Line Utilized for a Variety of Scientific Studies, Including Adenovirus Production and Testing

Description of Technology: Scientists at the National Institutes of Health have developed a cell line designated A549 that was derived from explanted cultures of human lung cancer tissue. The A549 cell line has been tested under the guidance of the United States Food and Drug Administration (FDA) so, under current Good Manufacturing Practices (GMP), these cells may be suitable for use in manufacturing constructs for use in clinical trials. The A549 cell line has also been found to be suitable for adenovirus production, most notably replicating adenovirus constructs that do not require complementation by the viral oncogene, early region 1A (E1A), which is responsible for viral gene transcription. This cell line is further utilized as a negative control in assays to measure the replication of adenoviruses that lack E1A and as a target cell line to detect replication competent adenoviruses (RCA). A549 cells have been well characterized through their use in a wide variety of molecular studies, such as anti-tumor drug permeability and

efficacy analysis, infection assays, respiratory immunotoxicity tests, cell senescence studies, and cytokine expression profiling. These cells can also be utilized to study a variety of molecular characteristics for human tumors in culture.

Application:

• Cell bank tested under cGMP-compliance regulations and used to produce adenoviruses for use in clinical trials.

• Research tool to analyze the efficacy of potential anti-cancer agents to devise better cancer treatments for malignancies, such as non-small cell lung cancer (NSCLC).

• Research tool to study the infectivity of viruses that cause asthma in order to develop better asthma treatments.

• Standard research tool to analyze a variety of molecular biology procedures, for example, cell senescence, cytokine induction, protein expression, apoptosis, and receptor-ligand interactions.

Advantages:

• A549 cells are a well-characterized standard among the human lung carcinoma/alveolar cell lines used in molecular biology.

• The A549 cells stored at the NIH were tested under the guidance of the FDA's cGMP regulations.

• The A549 cells stored at the NIH may be suitable for producing adenoviruses that can be used in clinical trials and analyzing adenoviral-based therapies and vaccine strategies.

Inventors: Wade P. Parks, Donald J. Giard, and Stuart Aaronson (all formerly NCI).

Publication: DJ Giard et al. In vitro cultivation of human tumors: Establishment of cell lines derived from a series of solid tumors. J Natl Cancer Inst. 1973 Nov; 51(5):1417–1423.

Patent Status: HHS Reference No. E–129–2009/0—Research Tool. Patent protection is not being pursued for this technology.

Licensing Status: Available for licensing under a Biological Materials License Agreement.

Licensing Contact: Samuel E. Bish, PhD; 301–435–5282; *bishse@mail.nih.gov*.

Mobilizing the Body to Fight Cancer: T Cell Receptors Specific for the Tumor Antigen Survivin

Description of Technology: A major drawback of current chemotherapy-based cancer treatments is the harsh side-effects associated with many cancer drugs. Thus, there is an urgent need to develop new therapeutic strategies combining fewer side-effects and more specific anti-tumor activity. Immunotherapy is a promising new cancer therapeutic approach that directs an individual's innate and adaptive immune system to fight against specific diseases, including cancer.

T cell receptors (TCRs) are proteins that recognize antigens in the context of infected or transformed cells and activate T cells to mediate an immune response and destroy abnormal cells. TCRs consist of two domains, one variable domain that recognizes the antigen and one constant region that helps the TCR anchor to the membrane and transmit recognition signals by interacting with other proteins.

Scientists at the National Institutes of Health (NIH) have developed genetically modified T cells, which possess TCRs that specifically recognize human survivin, a tumor antigen expressed in many adult and pediatric cancers that is absent from most normal tissues. Non-human T cells that recognized human survivin peptides with high affinity in the context of human leukocyte antigen (HLA) alleles were identified. Then, using recombinant DNA technology, the survivin-specific TCRs from the non-human T cells were fused to human TCR backbones and expressed in human T cells. The resulting survivin-specific human T cells could prove to be powerful new immunotherapeutic tools for attacking survivin-expressing tumors after infusion into patients.

Applications:

• Immunotherapeutics to treat and/or prevent the reoccurrence of a variety of human cancers that overexpress human survivin by inserting survivin-specific TCR sequences into patient T cells

• A drug component of a combination immunotherapy regimen aimed at targeting the specific tumor-associated antigens expressed by cancer cells within individual patients.

Advantages:

• Survivin is overexpressed in virtually all cancers, including lung, colon, breast, pancreatic, stomach, liver, ovarian and prostate cancer, as well as in melanoma and hematopoietic malignancies, but this antigen is not expressed on normal cells. Thus, survivin is an ideal antigen for targeted treatment. Anti-survivin TCR immunotherapy could treat a host of cancer types while reducing the side-effects of treatment.

• The survivin-specific TCR sequences can be derived in non-human species in the context of a wide variety of HLA molecules and, thus, TCRs specific for each patient's HLA profile can be generated rapidly.

• The survivin-specific T cells should not be rejected by a patient's immune system since the survivin-specific TCR sequences are fused to a human TCR backbone.

Development Status: This technology is in the pre-clinical stage of development. The inventors plan to initiate a clinical trial in the next 6–12 months.

Market: Cancer continues to be a medical and financial burden on U.S. public health. According to U.S. estimates, cancer is the second leading cause of death with over 565,000 deaths reported in 2008 and almost 1.5 million new cases were reported (excluding some skin cancers) in 2008. In 2007, the NIH estimated that the overall cost of cancer was $219.2 billion dollars and $89 billion went to direct medical costs. Despite our increasing knowledge of oncology and cancer treatment methods, the fight against cancer will continue to benefit from the development of new therapeutics aimed at treating individual patients.

Inventors: Crystal L. Mackall *et al.* (NCI).

Publications:

1. Manuscript in preparation.

2. CJ Cohen et al. Recognition of fresh human tumor by human peripheral blood lymphocytes transduced with a bicistronic retroviral vector encoding a murine anti-p53 TCR. J Immunol. 2005 Nov 1;175(9):5799–5808. (Erratum in: J Immunol. 2006 Oct 15;177(8):5746.)

3. RA Morgan et al. Cancer regression in patients after transfer of genetically engineered lymphocytes. Science 2006 Oct 6;314(5796):126–129.

Patent Status: U.S. Provisional Application No. 61/140,338 filed 23 Dec 2008 (HHS Reference No. E–325–2008/0–US–01)

Licensing Status: Available for licensing.

Licensing Contact: Samuel E. Bish, PhD; 301–435–5282; *bishse@mail.nih.gov*.

Collaborative Research Opportunity: The National Cancer Institute Pediatric Oncology Branch is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize genetically engineered lymphocytes with specificity for human survivin. Please contact John D. Hewes, PhD at 301–435–3121 or *hewesj@mail.nih.gov* for more information.

Fused Azepinone Cyclin Dependent Kinase Inhibitors

Description of Technology: The invention describes a class of cyclin dependent kinase (CDK) inhibitors that have anti-proliferative activity in human tumor cell lines. CDKs are important in

the control of the cell cycle and alterations in CDK expression, function, or regulation and are associated with diseases characterized by cellular proliferation. Increasing CDK activity has been reported in many cancers. Likewise, the loss of inhibitory activity has been observed in a wide variety of primary human tumors and human tumor-derived cell lines, including lung, breast, brain, bone, skin, bladder, kidney, ovary, liver, colon, and pancreas as well as in leukemia. These compounds have also been found to potently inhibit GSK3beta activity which has recently been linked to a variety of cellular processes and several disparate areas of biology. In particular, GSK3beta activity has been strongly implicated in Alzheimer's as well as cardiac failure. Thus, the compounds of this invention offer unique opportunities for a variety of indications.

Applications: CDK/GSK3beta inhibitor therapeutics for the treatment of several indications including various cancers, neurodegenerative diseases, and cardiac conditions.

Development: Pre-clinical stage of development.

Inventors: Daniel W. Zaharevitz *et al.* (NCI).

Publication: DW Zaharevitz et al. Discovery and initial characterization of the paullones, a novel class of small-molecule inhibitors of cyclin-dependent kinases. Cancer Res. 1999 Jun 1;59(11):2566–2569.

Patent Status: HHS Reference No. E–025–1998/0—

- U.S. Patent No. 6,610,684, issued August 26, 2003;
- Australian Patent Nos. 780528 and 778735, issued March 24, 2005 and December 16, 2004;
- Canada Patent Application No. 2335115, filed June 16, 1999;
- Japanese Patent Application No. 2000–554735, filed June 16, 1999;
- United Kingdom Patent No. 1086105, validated March 01, 2006 ((E–025–1998/0–GB–09);
- French Patent No. 1086105, validated March 01, 2006 (E–025–1998/0–FR–10); and
- German Patent No. 69930120.3, validated March 16, 2006 (E–025–1998/0–DE–11).

Licensing Status: Available for licensing.

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

Dated: May 13, 2009.

Richard U. Rodriguez,

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

[FR Doc. E9–11706 Filed 5–19–09; 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.

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Antibody and Immunotoxin Treatments for Mesothelin-Expressing Cancers

Description of Technology: Mesothelin is a cell surface protein that is highly expressed in aggressive cancers such as malignant mesothelioma, ovarian cancer and pancreatic cancer. As a result, mesothelin is an excellent candidate for tumor targeted immunotherapeutics. However, the antibodies against mesothelin that are available for clinical trials are of murine origin. These antibodies have the potential to elicit immune responses in patients, which may adversely affect the ability to provide patients with repeated doses. Thus, the clinical application of the antibodies may be limited.

In order to address the issue of immunogenicity in patients, NIH inventors have generated anti-mesothelin antibody variable fragments (Fv) of human origin. These antibody fragments (HN1 and HN2) have the ability to efficiently recognize mesothelin on the surface of numerous cancer cells. As a result, these antibody fragments represent an attractive therapeutic alternative to the murine anti-mesothelin antibodies currently being tested in clinical trials.

Application:

- Use as an antibody therapeutic for mesotheliomas, pancreatic tumors and ovarian tumors.
- Use in an immunotoxin therapeutic for mesotheliomas, pancreatic tumors and ovarian tumors.
- Diagnostic for the detection of mesothelin positive tumors.
- Research agent for the detection of mesothelin.

Advantages:

- Fully human antibody reduces potential immunogenicity, thereby allowing repeated dosing.
- Antibody specificity improves the therapeutic efficacy of the agent.

Development Status: Preclinical stage of development with some pre-clinical data available.

Inventors: Mitchell Ho *et al.* (NCI).

Patent Status: U.S. Provisional Application No. 61/162,778, filed 24 Mar 2009 (HHS Reference E–091–2009/0–US–01)

Related Technologies/Publications:

- U.S. Patent 6,083,502 entitled ''Mesothelium Antigen and Methods and Kits For Targeting It.''
- PCT Application PCT/US97/0224 entitled ''Mesothelium Antigen and Methods and Kits For Targeting It.''
- U.S. Patent 6,809,184 entitled ''Antibodies, Including Fv Molecules, and Immunoconjugates Having High Binding Affinity for Mesothelin and Methods for Their Use.''
- PCT Application PCT/US98/25270 entitled ''Antibodies, Including Fv Molecules, and Immunoconjugates Having High Binding Affinity for Mesothelin and Methods for Their Use.''
- U.S. Patent 7,081,518 entitled ''Anti-mesothelin antibodies having high binding affinity.''
- PCT Application PCT/US00/14829 entitled ''Immunoconjugates Having High Binding Affinity Improvement of scFVsr Ab's with Higher Affinity for Mesothelin.''

Licensing Status: Available for licensing.

Licensing Contact: David A. Lambertson, Ph.D.; 301–435–4632; *lambertsond@mail.nih.gov*.

Collaborative Research Opportunity: The National Cancer Institute Laboratory of Molecular Biology is seeking statements of capability or interest from parties interested in collaborative research to further