

promoting innovative therapies and helping to bring to market critical products for patients. When PDUFA was originally authorized in 1992, it had a 5-year term. The PDUFA program has been reauthorized every 5 years, with the most recent reauthorization occurring in 2007 for FYs 2008–2012. As directed by Congress in preparing for reauthorization of PDUFA for a new 5-year period, FDA conducted negotiations with regulated industry and conducted regular consultations with public stakeholders, including patient advocates, consumer advocates, and health care professionals between July 2010 and May 2011. Following these discussions, related public meetings, and Agency requests for public comment, FDA transmitted proposed PDUFA V recommendations to Congress for FYs 2013–2017 on January 13, 2012. If enacted into law, FDA's proposed PDUFA V recommendations will include an FDA commitment to implement a new review program for NME NDAs and original BLAs to enhance review transparency and communication between FDA and applicants on these complex applications.

## II. PDUFA V NME NDA and Original BLA Review Program

FDA's existing review performance goals for priority and standard applications, 6 and 10 months respectively, were established more than 15 years ago. Since that time, additional requirements in the drug review process and scientific advances in drug development have made those goals increasingly challenging to meet, particularly for more complex applications like NME NDAs and original BLAs that generally are discussed in an FDA advisory committee meeting. FDA further recognizes that increasing communication between the Agency and applicants during FDA's review has the potential to increase efficiency in the review process.

To promote greater transparency and improve communication between the FDA review team and the applicant, FDA has proposed a new review model for NME NDAs and original BLAs in PDUFA V. The Program provides opportunities for increased communication by building in mid-cycle communications and late-cycle meetings between FDA and applicants. To accommodate this increased interaction during regulatory review and to address the need for additional time to review these complex applications, FDA's review clock will begin after the 60-day administrative filing review

period for applications reviewed under the Program. The Program will apply to all NME NDAs and original BLAs received from October 1, 2012, through September 30, 2017. The goal of the Program is to improve the efficiency and effectiveness of the first-cycle review process by increasing communication with sponsors before application submission to improve the quality and completeness of submissions, and by increasing communications during application review. This will provide sponsors with opportunities to clarify previous submissions and provide additional data and analyses that are readily available, potentially avoiding the need for an additional review cycle when FDA's concerns about an application can be promptly resolved, but without compromising FDA's traditional high standards for approval. An efficient and effective review process that allows for timely responses to FDA questions can help ensure timely patient access to safe, effective, and high quality new drugs and biologics. To understand the Program's effect on the review of these applications, interim and final assessments by an independent contractor are key components of the Program. The performance commitments state that the statement of work for this effort will be published for public comment before beginning the assessment (section II.B). Because the assessment needs to commence at the beginning of PDUFA V on October 1, 2012, if the program is reauthorized, FDA must publish the statement of work for public comment in advance of that reauthorization to be able to begin the assessment on October 1, 2012. Accordingly, FDA is seeking public comment now on the proposed statement of work for the assessment of the Program, available at <http://www.fda.gov/downloads/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm304793.pdf>.

## III. Comments

Interested persons may submit to the Division of Dockets Management (see **ADDRESSES**) either electronic or written comments regarding this document. It is only necessary to send one set of comments. Identify comments with the docket number found in brackets in the heading of this document. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

Dated: June 29, 2012.

**Leslie Kux,**

*Assistant Commissioner for Policy.*

[FR Doc. 2012–16529 Filed 7–5–12; 8:45 am]

**BILLING CODE 4160–01–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.

**FOR FURTHER INFORMATION CONTACT:** 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.

#### Exposing T Cells to Fas Ligand (FasL)-Fas Receptor (FasR) Antagonists Withholds Differentiation and Increases Expansion Making T Cells More Suitable for Use in Cancer Immunotherapy

*Description of Technology:* NIH scientists have developed methods to make a better immunotherapy by exposing T cells to Fas ligand (FasL) or Fas receptor (FasR) antagonists and agonists. Researchers have found that FasL–FasR antagonists suppress T cell differentiation leaving them in a naïve state. These T cells are a more ideal cell type for adoptive cell transfer therapies since they have not exhausted their effector functions and demonstrate greater proliferation, enhanced persistence and survival, and better activity against their target antigen when infused in vivo to treat cancer. Also, the prevention of T cell differentiation/effector function in vivo

has implications for autoimmune diseases and syndromes. FasL–FasR agonists enhance T cell differentiation towards more effector-like cells. Enhancing the differentiation of T cells is expected to be useful in treating cell proliferation disorders, such as leukemias, lymphomas, or Wiskott-Aldrich syndrome.

FasL (or cluster of differentiation 95L) is a transmembrane protein in the tumor necrosis factor (TNF) family. FasR (or apoptosis antigen 1, CD95, or TNF receptor superfamily member 6) is a transmembrane protein belonging to the TNF receptor/nerve growth factor receptor superfamily. Normally, when FasL binds to FasR, a cell death signal is triggered in the cell. Antagonists of FasL–FasR interaction may include caspase inhibitors, mutated FasL/FasR, RNAi, or FasL/FasR antibodies. Agonists may include FasL/FasR encoding nucleotides.

#### Potential Commercial Applications

- Immunotherapy for cancer and other diseases or disorders using FasL/FasR antagonist exposed T cells.
- Methods for generating better T cells to utilize for infusion into patients in adoptive cell transfer therapies.
- Therapeutic to prevent T cell mediated toxicity in vivo (i.e. autoimmunity like lupus, Crohn's disease, MS, vitiligo, etc.).
- Components of a combination therapy to increase or suppress T cell differentiation and activity in patients.

#### Competitive Advantages

- Some patients do not respond to T cell immunotherapy due to lack of cell persistence, survival, or activity or other reasons. Administering a FasL/FasR antagonist to a patient's T cells before immunotherapy should increase the success rate of treatment by increasing the persistence and survival of the infused cells.
- Differentiation and effector function of T cells can be suppressed by an antibody (molecular product) rather than a drug (chemical product) like rapamycin.

#### Development Stage

- Pre-clinical.
- In vitro data available.
- In vivo data available (animal).

*Inventors:* Anthony J. Leonardi, Christopher A. Klebanoff, Luca Gattinoni, Nicholas P. Restifo (all of NCI).

*Intellectual Property:* HHS Reference No. E–142–2012/0—U.S. Provisional Application No. 61/623,733 filed 13 Apr 2012.

*Related Technology:* HHS Reference No. E–069–2010/0—PCT Application

No. PCT/US2011/63375 filed 08 Dec 2010.

*Licensing Contact:* Samuel E. Bish, Ph.D.; 301–435–5282; [bishse@mail.nih.gov](mailto:bishse@mail.nih.gov).

*Collaborative Research Opportunity:* The Surgery Branch of the NCI is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize the prevention of T cell differentiation and effector function as part of Immunotherapy. For collaboration opportunities, please contact Steven A. Rosenberg, M.D., Ph.D. at [sar@nih.gov](mailto:sar@nih.gov).

#### Benign Tissue or Malignant Tumors? Using CpG Dinucleotide Methylation Patterns To Diagnose Cancer in the Adrenal Glands and Adrenal Cortex

*Description of Technology:* Scientists at the National Institutes of Health (NIH) have developed new methods to distinguish malignant adrenocortical tumors from benign tumors and normal tissue in the adrenal glands/cortex using the methylation patterns of cytosine-phosphate-guanine dinucleotide (CpG) sequences. A biopsy or other noninvasive means of tissue or fluid collection to obtain patient nucleic acid can allow clinicians to test an individual's CpG methylation patterns to diagnose if the individual's sample is malignant and if a malignancy is a primary or metastatic adrenocortical tumor. Different CpG methylation patterns comparing normal/benign and malignant tissues may also serve as target sites for developing adrenocortical cancer therapies. Genes where increased CpG methylation is predictive of malignancy include KCTD12, KIRREL, SYNGR1, and NTGN2, as well as other secondary sequences.

Adrenal glands sit atop the kidneys and release stress response hormones. The CpG methylation patterns of 5-methylcytosines at CpG sites can alter gene expression, which can impact if a tumor will develop benign or malignant properties and influence its metastatic potential. Effective diagnosis of these tumors will improve adrenal cancer therapy and help avoid unnecessary surgery or chemotherapy for patients with benign tumors.

#### Potential Commercial Applications

- Nucleic acid-based diagnostic tests or kits to identify malignant adrenocortical tumors and distinguish them from common benign tumors or normal adrenocortical tissue.
- Identify CpG methylation sequences and patterns that could serve as targets for nonsurgical therapeutic

interventions against adrenocortical tumors.

- Companion diagnostic test for candidate demethylation agent therapies for treating adrenocortical malignancies.

#### Competitive Advantages

• Removal of adrenal malignancies is currently the only cure, but most patients are not candidates for surgery. Benign adrenal tumors are common, but treated by clinicians as a precaution, mainly with harsh chemotherapy. Now, malignant adrenocortical tumors can be differentiated from benign tumors, so that individuals with benign tumors are not treated unnecessarily.

- A minimally invasive biopsy or tissue collection to measure DNA methylation could avoid unnecessary invasive surgery/harsh chemotherapy and lead to more assured treatment of malignant tumors.

#### Development Stage

- Pre-clinical.
- In vitro data available.

*Inventors:* Electron Kebebew, Nesrin S. Rechache, Paul S. Meltzer, Yonghong Wang (all of NCI).

*Publication:* Rechache N, *et al.* DNA methylation profiling identifies global methylation differences and markers of adrenocortical tumors. *J Clin Endocrinol Metab.* 2012 Jun;97(6):E1004–13. [PMID 22472567]

*Intellectual Property:* HHS Reference No. E–135–2012/0—U.S. Provisional Application No. 61/615,869 filed 26 Mar 2012.

*Related Technology:* HHS Reference No. E–026–2011/0—PCT Application No. PCT/US2011/040648 filed 16 Jun 2011.

*Licensing Contact:* Samuel E. Bish, Ph.D.; 301–435–5282; [bishse@mail.nih.gov](mailto:bishse@mail.nih.gov).

#### Mouse-Derived T Cell Receptor for Use in Immunotherapy That Recognizes NY–ESO–1, a Cancer Testis Antigen Expressed by Many Human Cancers

*Description of Technology:* Scientists at the National Institutes of Health have developed a T cell receptor (TCR) derived from mouse T cells (i.e. murine TCR) that can be expressed in human T cells to recognize the cancer testis antigen (CTA), NY–ESO–1, with high specificity. This anti-NY–ESO–1 TCR has murine variable regions that recognize the NY–ESO–1 epitope and murine constant regions. The inventors performed in vitro studies comparing this murine NY–ESO–1 TCR with a previously developed human NY–ESO–1 TCR counterpart, which yielded promising clinical outcomes in patients with a variety of cancers. The murine

TCR functioned similarly to the human counterpart in their ability to recognize and react to NY-ESO-1 tumor targets.

NY-ESO-1 is a CTA, which is expressed only on tumor cells and germline cells of the testis and placenta. CTAs are ideal targets for developing cancer immunotherapeutics, such as anti-CTA TCRs, since these TCRs are expected to target cancer cells without harming normal tissues and thereby minimize the harsh side effects associated with other types of cancer treatment. NY-ESO-1 is expressed on a wide variety of cancers, including but not limited to breast, lung, prostate, thyroid, and ovarian cancers, melanoma, and synovial sarcomas, so this technology should be applicable in adoptive cell transfer therapies for many types of cancer.

#### Potential Commercial Applications

- Personalized immunotherapy with high probability for mediating tumor regression in patients with a variety of cancers expressing NY-ESO-1.
- Component of a combination immunotherapy regimen consisting of a variety of immune receptors and other immune molecules (cytokines, etc.) targeting multiple tumor antigens.
- A research tool to investigate the progression and metastasis of NY-ESO-1 expressing cancers in mouse models.
- An in vitro diagnostic tool to identify cancer tissues that express the NY-ESO-1 cancer testis antigen.

#### Competitive Advantages

- Predicted high probability of clinical success: Murine TCRs from this invention exhibited similar in vitro properties to a human NY-ESO-1 TCR that has mediated tumor regression in many patients in a recent clinical trial.
- Lower toxicity than other cancer treatments: NY-ESO-1 is overexpressed on a wide variety of cancers, but not on any normal human tissues that could be reactive with an engineered TCR. TCRs engineered to recognize NY-ESO-1 could be utilized as an immunotherapy to treat many different cancer types.

#### Development Stage

- Pre-clinical.
- In vitro data available.

*Inventors:* Maria R. Parkhurst, Richard A. Morgan, Steven A. Rosenberg (all of NCI).

*Intellectual Property:* HHS Reference No. E-105-2012/0—U.S. Provisional Patent Application No. 61/650,020 filed 22 May 2012.

#### Related Technologies

- HHS Reference No. E-304-2006/0.
- HHS Reference No. E-312-2007/1.

*Licensing Contact:* Samuel E. Bish, Ph.D.; 301-435-5282; [bishse@mail.nih.gov](mailto:bishse@mail.nih.gov).

*Collaborative Research Opportunity:* The NCI Surgery Branch is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize this murine NY-ESO-1 reactive TCR. For collaboration opportunities, please contact Steven A. Rosenberg, M.D., Ph.D. at [sar@nih.gov](mailto:sar@nih.gov).

#### Antagonists of Hyaluronan Signaling for Treatment of Airway Inflammation and Hyperresponsiveness

*Description of Technology:* Airway inflammation and hyperresponsiveness are hallmarks of airway disease. Investigators at NIEHS identified a new class of compounds that can block hyaluronan signaling and inhibit airway hyperresponsiveness and inflammation. Airway diseases, such as asthma and chronic obstructive airway disease, affect tens of millions of patients worldwide, and are chronic diseases with limited options for treatment (bronchodilators and inhaled steroids are the two classes of drugs currently in common use). Therefore, a novel class of treatment agents could have significant public health and market impact.

*Potential Commercial Applications:* Treatment of Airway Inflammation and Hyperresponsiveness.

*Competitive Advantages:* Potentially cost-effective treatment for widespread conditions.

*Development Stage:* In vitro data available.

*Inventors:* Stavros Garantziotis (NIEHS), John W. Hollingsworth, Bryan P. Toole, Jian Liu.

*Intellectual Property:* HHS Reference No. E-080-2012/0—U.S. Provisional Application No. 61/647,101 filed 15 May 2012.

*Licensing Contact:* Jaime M. Greene, M.S.; 301-435-5559; [greenejaime@mail.nih.gov](mailto:greenejaime@mail.nih.gov).

*Collaborative Research Opportunity:* The NIEHS is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize the use of hyaluronan antagonists to treat chronic respiratory diseases. For collaboration opportunities, please contact Elizabeth M. Denholm, Ph.D. at [denholme@niehs.nih.gov](mailto:denholme@niehs.nih.gov).

#### Individualized Cancer Therapy That Suppresses Tumor Progression and Metastasis Through Decreased Expression of TGF-Beta Receptor II in Bone Marrow Derived Cells

*Description of Technology:* Scientists at the NIH have developed a method of suppressing tumor progression and metastasis by targeting a pathway. This novel treatment method is an individualized therapy that first screens patients to determine if they are a candidate for the treatment, and then utilizes their own altered bone marrow to inhibit tumor progression.

Tumor inhibition is achieved through decreased expression of TGF-beta receptor II (TGFβ r2) in bone marrow derived myeloid cells, which is essential in tumor metastasis. The inventors have devised a patient selection method whereby the patient's blood is drawn and screened for TGFβ r2 expression, and those patients with above normal expression are candidates for treatment. After candidate screening the patient's bone marrow is harvested and divided into two parts: One part for cell culture and the other for storage and later use. The patient's cell culture bone marrow is treated to remove TGFβ r2 in myeloid cells through either virus, non viral particle, or nanoparticle. The patient is treated with total body radiation and then receives an infusion of the treated cell culture bone marrow. After tumor metastasis is suppressed, the altered bone marrow is removed, and the stored bone marrow is returned to the patient.

#### Potential Commercial Applications

- Novel immunotherapy for cancer.
- Treatment method to suppress tumor metastasis in patients overexpressing TGFβ r2 in myeloid cells.
- TGFβ r2 RNAi with specific myeloid cell promoters delivered by virus, non viral particle, or nanoparticle.

#### Competitive Advantages

- Specifically targets myeloid cells and not other host cells.
- Individualized therapy.
- Patient selection process; treatment is specific to eligible patients reducing cost.

#### Development Stage

- In vitro data available.
  - In vivo data available (animal).
- Inventor:* Li Yang (NCI).  
*Publication:* Abrogation of transforming growth factor β signaling in myeloid cells significantly inhibit tumor progression and metastasis; submitted.

*Intellectual Property:* HHS Reference No. E-151-2011/0—U.S. Patent Application No. 61/525,025 filed 18 August 2011.

*Licensing Contact:* Sabarni Chatterjee, Ph.D., MBA; 301-435-5587; chatterjeesa@mail.nih.gov.

*Collaborative Research Opportunity:* The National Cancer Institute is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize technologies including but not limited to RNAi viral particle or nanoparticle, or miRNA. For collaboration opportunities, please contact John Hewes, Ph.D. at hewesj@mail.nih.gov.

Dated: June 29, 2012.

**Richard U. Rodriguez,**

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

[FR Doc. 2012-16500 Filed 7-5-12; 8:45 am]

BILLING CODE 4140-01-P

## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### National Institutes of Health

#### National Institute of Environmental Health Sciences; Notice of Closed Meeting

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

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

*Name of Committee:* National Institute of Environmental Health Sciences Special Emphasis Panel, Immunotoxicity Studies for the National Toxicology Program.

*Date:* August 2, 2012.

*Time:* 10 a.m. to 5 p.m.

*Agenda:* To review and evaluate contract proposals.

*Place:* NIEHS/National Institutes of Health, Building 4401, East Campus, 79 T.W. Alexander Drive, Research Triangle Park, NC 27709 (Telephone Conference Call).

*Contact Person:* RoseAnne M McGee, Associate Scientific Review Officer, Scientific Review Branch, Division of Extramural Research and Training, Nat. Institute of Environmental Health Sciences,

P.O. Box 12233, MD EC-30 Research Triangle Park, NC 27709, (919) 541-0752, mcgee1@niehs.nih.gov.

(Catalogue of Federal Domestic Assistance Program Nos. 93.115, Biometry and Risk Estimation—Health Risks from Environmental Exposures; 93.142, NIEHS Hazardous Waste Worker Health and Safety Training; 93.143, NIEHS Superfund Hazardous Substances—Basic Research and Education; 93.894, Resources and Manpower Development in the Environmental Health Sciences; 93.113, Biological Response to Environmental Health Hazards; 93.114, Applied Toxicological Research and Testing, National Institutes of Health, HHS)

Dated: June 28, 2012.

**Jennifer S. Spaeth,**

Director, Office of Federal Advisory Committee Policy.

[FR Doc. 2012-16497 Filed 7-5-12; 8:45 am]

BILLING CODE 4140-01-P

## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### National Institutes of Health

#### Prospective Grant of Exclusive License: Use of the Citrus Flavanones Hesperetin, Hesperidin, and Naringenin in Nutrition for Endothelial Function, Vascular Health, Diabetes, and Insulin Resistance

**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, Department of Health and Human Services, is contemplating the grant of an exclusive patent license to BioActor B.V., a company having a place of business in Maastricht, Netherlands, to practice the inventions embodied in U.S. Provisional Patent Application No. 61/369,229, filed July 30, 2010 (HHS Ref. No. E-148-2010/0-US-01) and PCT Patent Application No. PCT/US2011/045898, filed July 29, 2011 (HHS Ref. No. E-148-2010/0-PCT-02), both entitled “Treatment of Metabolic Syndrome and Insulin Resistance with Citrus Flavanones.” The patent rights in these inventions have been assigned to the United States of America. The prospective exclusive license territory may be “worldwide”, and the field of use may be limited to “hesperidin, naringenin, and any derivatives thereof for use in nutrition relating to endothelial function, vascular health, diabetes, and insulin resistance, wherein the Licensed Products are marketed under an approved Health Claim or GRAS designation from the

FDA, under an approved Health Claim or Novel Food designation from the EFSA, or a foreign regulatory equivalent of the above.”

**DATE:** Only written comments and/or applications for a license which are received by the NIH Office of Technology Transfer on or before August 6, 2012 will be considered.

**FOR FURTHER INFORMATION CONTACT:** Requests for copies of the patent application(s), inquiries, and comments relating to the contemplated exclusive license should be directed to: Tara L. Kirby, Ph.D., Senior Licensing and Patenting Manager, Office of Technology Transfer, National Institutes of Health, 6011 Executive Boulevard, Suite 325, Rockville, MD 20852-3804; Telephone: (301) 435-4426; Facsimile: (301) 402-0220; Email: tarak@mail.nih.gov.

#### SUPPLEMENTARY INFORMATION:

Hesperidin is a flavonoid compound found in citrus fruits. Large epidemiological studies have linked increased consumption of flavonoid-rich foods, such as citrus, with reduced cardiovascular morbidity and mortality. Investigators from the National Center for Complementary and Alternative Medicine have demonstrated that administration of oral hesperidin to patients with metabolic syndrome attenuates biomarkers of inflammation and improves blood vessel relaxation, lipid cholesterol profiles, and insulin sensitivity when compared to controls. Thus, hesperidin and its active aglycone form, hesperetin, may be effective agents for the treatment of diabetes, obesity, metabolic syndrome, dyslipidemias, and their cardiovascular complications including hypertension, atherosclerosis, coronary heart disease, and stroke. This technology discloses methods for using a hesperetin or hesperidin composition to treat metabolic syndrome and insulin resistance. Also described is the use of the related citrus polyphenol, naringenin.

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 404.7. The prospective exclusive license may be granted unless within thirty (30) 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 404.7.

Only applications for a license in the field of use set forth in this notice and filed in response to this notice will be treated as objections to the grant of the