[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.

FOR FURTHER INFORMATION: 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

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.

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

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: NYESO-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 — US 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

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.

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 — US Provisional Application No. 61/647,101 filed 15 May 2012

Licensing Contact: Jaime M. Greene, M.S.; 301-435-5559; 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.

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.

June 29, 2012
Date

Richard U. Rodriguez,
Director
Division of Technology Development and Transfer
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