[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, 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. 209

and 37 CFR Part 404 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.

Chimeric Antigen Receptors to ALK for Treating Neuroblastoma and Other Solid Tumors

Description of Technology: Chimeric antigen receptors (CARs) are hybrid proteins consisting of an antibody binding fragment fused to protein signaling domains that cause T-cells which express the CAR to become cytotoxic. Once activated, these cytotoxic T-cells can selectively eliminate the cells which they recognize via the antibody binding fragment of the CAR. By engineering a T-cell to express a CAR that is specific for a certain cell surface protein, it is possible to selectively target those cells for destruction. This is a promising new therapeutic approach known as adoptive cell therapy.

Anaplastic lymphoma kinase (ALK, CD246) is a tumor-associated antigen that is expressed on the cell surface of pediatric neuroblastomas and some non-small cell lung carcinomas (NSCLC). This technology concerns the development of four (4) CARs, each comprising a different antibody binding fragment to ALK. The CARs, known individually as ALKCAR15, ALKCAR48, ALKCAR53 and ALKCAR58, can be used in adoptive cell therapy treatment for neuroblastoma and other solid tumors which overexpress ALK or variants thereof.

Potential Commercial Applications:

• Treatment of cancers associated with expression of ALK or variants thereof.

• Specific cancers include neuroblastoma, NSCLC and other solid tumors.

Competitive Advantages:

• High affinity of the ALKCAR15, ALKCAR48, ALKCAR53 and ALKCAR58 increases the likelihood of successful targeting.

• Targeted therapy decreases non-specific killing of healthy, essential cells, resulting in fewer non-specific side-effects and healthier patients.

Development Stage:

• Early-stage

• In vitro data available

• In vivo data available (animal)

Inventors: Rimas J. Orentas and Crystal L. Mackall (NCI)

Publication: Orentas RJ, et al. ALK (anaplastic lymphoma kinase, CD246)-specific CARs: new immunotherapeutic agents for the treatment of pediatric solid tumors. J Immunother Cancer. 2013 Nov 7;1(Suppl 1):P27. [doi:10.1186/2051-1426-1-S1-P27] (Poster presentation)

Intellectual Property: HHS Reference No. E-007-2014/0 – US Provisional Patent Application No. 61/865,845 filed 06 November 2013

Related Technologies:

• HHS Reference No. E-104-2013/0 – US Provisional Patent Application No. 61/805,001 filed 25 March 2013 ("Anti-CD276 Polypeptides, Proteins, and Chimeric Antigen Receptors," Orentas RJ, et al.)

• HHS Reference No. E-291-2012/0 – International Patent Application No. PCT/US2013/060332 filed 18 September 2013 ("M971 Chimeric Antigen Receptors," Orentas RJ, et al.)

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

Collaborative Research Opportunity: The Pediatric Oncology Branch, CCR, NCI, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize CAR (chimeric antigen receptor) T cells specific for the ALK tumor-associated antigen. For collaboration opportunities, please contact John D. Hewes, Ph.D. at hewesj@mail.nih.gov.

Acid-Resistant, Attenuated Microbial Vector for Improved Oral Delivery of Multiple Targeted Antigens

Description of Technology: Ty21a, the licensed oral live, attenuated bacterial vaccine for *Salmonella typhi* (the causative agent of typhoid fever), has been engineered to stably express a variety of target LPS (lipopolysaccharides) and protein antigens to protect against shigellosis, anthrax, and plague. Ty21a induces mucosal, humoral, and cellular immunity and can be utilized as a multivalent vaccine vector that is inexpensive to produce. Salmonella species encode inducible acid tolerance, but this genus does not survive well below pH 4. Shigella and enterohemorrhagic *E. coli* isolates have more effective acid resistance systems than Salmonella and can survive an extreme acid challenge of pH 1-2 (the acidity of the human stomach when full).

This application claims an engineered Ty21a vector that can survive a very low pH for two to three hours (i.e.. normal transit time through a full stomach), allowing for a final delivery format for Ty21a as a rapidly dissolvable wafer, instead of the large bullet-size enteric-coated capsule, which small children cannot swallow. This formulation

enhances the ability of the immunogenic composition and/or vaccine to stimulate immune responses sublingually and throughout the intestinal tract.

Potential Commercial Applications:

• Shigella vaccines

• Biodefense vaccines

• Diagnostics

Competitive Advantages:

• Ease of manufacture

• Inexpensive to manufacture

• Ease of administration

• Known live attenuated bacterial vector

Development Stage:

• Pre-clinical

• In vitro data available

• In vivo data available (animal)

Inventors: Madushini N. Dharmasena and Dennis J. Kopecko (FDA/CBER)

Intellectual Property: HHS Reference No. E-535-2013/0 – US Provisional Application No. 61/862,815 filed 06 August 2013

Licensing Contact: Peter Soukas; 301-435-4646; ps193c@nih.gov

Collaborative Research Opportunity: The Food and Drug Administration, Center for Biologics Evaluation and Research, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or

commercialize acid-resistant Shigellosis vaccines. For collaboration opportunities, please contact Alice Welch, Ph.D. at 301-796-8449 or alice.welch@fda.hhs.gov.

Assay to Screen Anti-metastatic Drugs

Description of Technology: Scientists at the NIH have developed a research tool, a murine cell line model (JygMC(A)) with a reporter construct, of spontaneous metastatic mammary carcinoma that resembles the human breast cancer metastatic process in a triple negative mammary tumor. The assay is useful for screening compounds that specifically inhibit pathways involved in mammary carcinoma and can improve clinical management of triple negative breast cancer which are greatly refractory to conventional chemo and radiotherapy. The key feature of the cell line is that when introduced orthotopically into the mammary gland of immunocompromised mice it produces murine mammary tumors that rapidly metastasize to distant sites, such as lungs, lymph nodes, liver and kidneys. This allows for precise tracking of tumor growth and metastasis.

Potential Commercial Applications:

• Laboratory tool to investigate molecular mechanisms and/or signaling pathways involved in tumorigenesis, angiogenesis and metastasis of breast cancer and its response to therapy (in vivo and in vitro).

• Research tool for high through-put screening of libraries for compounds that specifically inhibit mechanisms and/or signaling pathways involved in metastatic triple negative breast cancer.

• Research tool to optimize therapeutic regimens.

Competitive Advantages: Dual report construct: enhanced green fluorescent protein (eGFP) or a fusion of firefly luciferase and eGFP (ffLuc2-eFGP) and mouse Cripto-1 promoter sequence cloned into a vector for reporter assays and/or visualization of molecular mechanisms involved in tumorigenesis of metastatic breast cancer cells.

Development Stage:

• Pre-clinical

• In vitro data available

• In vivo data available (animal)

Inventors: Nadia P. Castro, David S. Salomon, Frank F. Cuttitta (all of NCI)

Publications:

1. Castro, Nadia P. "Role of the Notch signaling in the metastasis of a murine breast cancer model." Abstract presented at the Mammary Gland Biology Gordon Research Conference, Lucca (Barga) Italy, June 10-15, 2012.

2. Castro, Nadia P. "Notch pathway in an experimental model of breast cancer metastasis." Abstract presented at the Sixth AACR Special Conference on Advances in Breast Cancer Research, San Francisco, California, October 12-15, 2011.

Intellectual Property: HHS Reference No. E-088-2013/0 – Research Tool. Patent protection is not being pursued for this technology.

Licensing Contact: Surekha Vathyam, Ph.D.; 301-435-4076; vathyams@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 mechanism of tumor growth and lung

metastasis. For collaboration opportunities, please contact John D. Hewes, Ph.D. at hewesj@mail.nih.gov.

Mouse Model for the Preclinical Study of Metastatic Disease

Description of Technology: The successful development of new cancer therapeutics requires reliable preclinical data that are obtained from mouse models for cancer. Human tumor xenografts, which require transplantation of human tumor cells into an immune compromised mouse, represent the current standard mouse model for cancer. Since the immune system plays an important role in tumor growth, progression and metastasis, the current standard mouse model is not ideal for accurate prediction of therapeutic effectiveness in patients. This may contribute to increased failure in later phases of clinical trials, as appropriate tumor-host interactions are not preserved.

This technology establishes a system for producing mouse cancer models where the model is not immune compromised, providing an environment which is more akin to the disease state of cancer patients. To establish the model, a tumor is (a) developed in tissue that has been propagated by serial transplantation (rather than cell culture), (b) labeled (using lentiviral vectors) with bioimaging markers (e.g., green fluorescent protein (GFP) and luciferase), and (c) transplanted into immunocompetent mice. Once established, the model can be used to monitor tumor growth, progression and metastasis through standard imaging techniques. The effectiveness of a given therapeutic approach can also be monitored using the same techniques.

Potential Commercial Applications:

• Improved mouse model for preclinical testing of drugs to treat metastatic disease

• Can be applied to any cancer where tumor cell lines can be developed without cell culture propagation

• Can be used to build preclinical models that require consistent disease tracking and normal immune context (e.g. bone marrow transplantation, stem cell therapy, tissue regeneration)

Competitive Advantages:

• Labeling markers are tolerized, allowing consistent expression in this mouse

• Increase in accurate prediction of drug effectiveness during preclinical stages; allows better prediction of success at later clinical stages

• Mice are not immunocompromised, and thereby more accurately representing in vivo disease states

• Labeling of tumors for transplantation allows tumors to be traced during growth, progression and metastasis in normal immune context

• Labeling also allows more efficient study of the effectiveness of treatments

Development Stage:

• Early-stage

• In vitro data available

• In vivo data available (animal)

Inventors: Chi-Ping Day and Glenn Merlino (NCI)

Publications:

1. Day CP, et al. Preclinical therapeutic response of residual metastatic disease is distinct from its primary tumor of origin. Int J Cancer. 2012 Jan 1;130(1):190-9. [PMID 21312195]

2. Day CP, et al. Immunological naturalization of immunocompetent host mice to luciferase-GFP for consistent tracking of transplanted tumors. Poster #1556, Annual Meeting 2013, American Association of Cancer Research, Washington D.C., April 6-10, 2013.

Intellectual Property: HHS Reference No. E-296-2012/0 – Biological Material/Research Tool. Patent protection is not being pursued for this technology.

Licensing Contact: David A. Lambertson, Ph.D.; 301-435-4632; lambertsond@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 preclinical models allowing consistent disease tracking in normal immune context. For collaboration opportunities, please contact John D. Hewes, Ph.D. at hewesj@mail.nih.gov.

Software for Evaluating Drug Induced Hepatotoxicity

Description of Technology: This invention pertains to a software tool for assisting differential medical diagnosis of drug-induced liver injury (hepatotoxicity) using clinical trial data. The software is capable of identifying a small subset of patients at risk for hepatotoxicity out of a pool of thousands of clinical trial participants. This software tool is the only one of its kind developed using SAS/IntrNet®.

Potential Commercial Applications:

• Hepatotoxicity detection

• Drug interactions

Competitive Advantages:

• Personalized predictions

• SAS/IntrNet® compatible

Development Stage: Prototype

Inventor: Ted J. Guo (FDA)

Publications:

1. Guo T, et al. A Tool to Help You Decide [detect potentially serious liver injury]. Silver Spring, Maryland: Presentation at the Annual Conference of the American Association for the Study of Liver Diseases, 2008.

2. Guo T, et al. How a SAS/IntrNet tool was created at the FDA for the detection of potential drug-induced liver injury using data with CDISC standard. San Diego, California: Proceedings of the Western Users of SAS Software Annual Conference, 2009.

3. Watkins PB, et al. Evaluation of drug-induced serious hepatotoxicity (eDISH): application of this data organization approach to phase III clinical trials of rivaroxaban after total hip or knee replacement surgery. Drug Saf. 2011 Mar 1;34(3):243-52. [PMID 21332248]

Intellectual Property: HHS Reference No. E-103-2012/0 – Software Tool. Patent protection is not being pursued for this technology.

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

Hexanucleotide Repeat in the C9orf72 Gene for the Diagnosis and Treatment of Amyotrophic Lateral Sclerosis and Frontotemporal Dementia

Description of Technology: This invention relates to the discovery of a pathogenic GGCCCC hexanucleotide repeat expansion in the first intron of the C9orf72 gene on chromosome 9p21 in patients exhibiting amyotrophic lateral sclerosis (ALS) and/or frontotemporal dementia (FTD). The inventors have previously identified a strong association signal in this genomic region and used this information to identify the underlying pathogenic mutation. The pathogenic repeat expansion accounts for up to 50% of familial ALS and familial FTD cases and up to 10% of sporadic ALS and sporadic FTD cases in European ancestry populations. The inventors represent that this finding will be the basis of diagnostic screening for ALS and/or FTD patients, as well as an important target in the development of therapeutics for ALS and/or FTD.

Potential Commercial Applications: Diagnosis and treatment of ALS and/or FTD.

Competitive Advantages: Improved diagnosis and treatment of ALS and/or FTD.

Development Stage: In vitro data available

Inventors: Stuart Pickering-Brown (The University of Manchester), Bryan Traynor (NIA), Andrew Singleton (NIA), Huw Morris (Cardiff University), Peter Heutink (Vu University Medical Center Amsterdam), John Hardy (University College London), Pentti Tienari (University of Helsinki)

Intellectual Property: HHS Reference No. E-275-2011/0 –

• US Provisional Application No. 61/529,531 filed 31 August 2011

• PCT Application No. PCT/GB2012/052140 filed 31 August 2012

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

greenejaime@mail.nih.gov

December 19, 2013   _____
Date   Richard U. Rodriguez,
     Director
     Division of Technology Development and Transfer
     Office of Technology Transfer
     National Institutes of Health

[FR Doc. 2013-30745 Filed 12/24/2013 at 8:45 am; Publication Date: 12/26/2013]