[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.

Monoclonal Antibodies That Recognize the Human Type I Interferon Receptor and Block Interferon Signaling

Description of Technology: Type I interferons play a critical role in both innate and adaptive immunity through the stimulation of the IFNAR1 which initiates interferon signaling in response to viral and bacterial infections. However, abnormal interferon signaling is associated with human diseases, such as lupus. The present invention discloses six hybridomas that produce mouse monoclonal antibodies specific for the extracellular domain of human IFNAR1. Two of the monoclonal antibodies are able to bind IFNAR1 and reduce interferon signaling. As such, they can be utilized as a research tool for studying the expression of IFNAR1 and the inhibition of IFNAR1 function in humans or possibly as therapeutic reagents for human diseases.

Potential Commercial Applications:

• Research reagents for studying the expression and signaling of IFNAR1.

• A potential therapeutic reagent.

Competitive Advantages:

• Specific for the extracellular domain of human IFNAR1. Can therefore specifically recognize receptor expressed on the cell surface.

• Bind IFNAR1 and reduce interferon signaling

Development Stage:

• Pilot

• In vitro data available

Inventors: Sonja M. Best, Kirk Lubick, Shelly J. Robertson (NIAID)

Publications:

1. Goldman LA, et al. Characterization of antihuman IFNAR-1 monoclonal antibodies: epitope localization and functional analysis. J Interferon Cytokine Res. 1999 Jan;19(1):15-26. [PMID 10048764]

2. Benoit P, et al. A monoclonal antibody to recombinant human IFN-alpha receptor inhibits biologic activity of several species of human IFN-alpha, IFN-beta, and IFN-omega. Detection of heterogeneity of the cellular type I IFN receptor. J Immunol. 1993 Feb 1;150(3):707-16. [PMID 8423335]

Intellectual Property: HHS Reference No. E-527-2013/0 – Research Material. Patent protection is not being pursued for this technology.

Licensing Contact: Susan Ano, Ph.D.; 301-435-5515; anos@mail.nih.gov

Collaborative Research Opportunity: The National Institute of Allergy and Infectious Diseases (NIAID) is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize human type I interferon receptor antibodies. For collaboration opportunities, please contact Alicia Evangelista at alicia.evangelista@nih.gov or 301-594-1673.

Anthrax Fusion Toxins with Improved Ability to Penetrate Cells

Description of Technology: Available for licensing are novel conjugated or fusion proteins comprised of anthrax toxin lethal factor cytolethal distending toxin subunit B. Several human tumor cell lines have been found to be highly sensitive to these toxins with LD50 values in the pM range. *In vivo* studies in mice have revealed that these toxins selectively treat tumors and have very low systemic toxicity.

Potential Commercial Applications:

• Pharmaceutical compositions to selectively treat cancer

• Applications to treat or prevent growth of undesirable cells

Competitive Advantages:

• Selective with low systemic toxicity

• Potent (pM LD50 values)

Development Stage:

• Early-stage

• In vitro data available

• In vivo data available (animal)

Inventors: Christopher Bachran and Stephen Leppla (NIAID)

Intellectual Property: HHS Reference No. E-120-2013/0 – US Application No. 61/837,428 filed June 20, 2013

Licensing Contact: Patrick McCue, Ph.D.; 301-435-5560; mccuepat@mail.nih.gov

Method and Platform for Selectively Labeling RNA

Description of Technology: The invention pertains to a three step initiation, elongation and termination method and platform for synthesizing selectively labeled RNA molecules by first polymerizing a first liquid phase RNA molecule from a solid phased DNA template fixed onto a solid phase. The method includes the steps of incubating the solid and liquid phases at appropriate elongation temperatures and then terminating elongation by a separation stage where the phases are incubated at near 0

degrees Celsius where it selectively terminates RNA elongation. The steps can be repeated by the number bases (rNTPs) in the final RNA molecule wherein in each iterative stage a new rNTP can be added that is selectively labeled. The DNA may have a density of 30-80% on the solid substrate, and the solid substrate may be a bead. The bead may comprise a gel, glass, or a synthetic polymer. The bead may have a diameter of 5-100 mm. The concentration of DNA may be 30 mm-1 nm. The concentration of rNTP may be 1-100 times the DNA concentration. The RNA polymerase may be a T7 RNA polymerase. The label may be $^{13}C/^{5}N$, ^{2}H, Cy3, Cy5, a fluorophore, a heavy atom, or a chemical modification.

Potential Commercial Applications: Differentially labeled diagnostics

Competitive Advantages: Multiple use detection method

Development Stage:

• Prototype

• In vitro data available

Inventors: Yun-Xing Wang (NCI), Liu Yu (NCI), Ping Yu (NCI), Rui Sousa (Univ. Texas Health Science Ctr)

Publications:

1. Guajardo R, Sousa R. A model for the mechanism of polymerase translocation. J Mol Biol. 1997 Jan 10;265(1):8-19. [PMID 8995520]

2. Guo Q, et al. (2005). Major conformational changes during T7RNAP transcription initiation coincide with, and are required for, promoter release. J Mol Biol. 2005 Oct 21;353(2):256-70. [PMID 16169559]

3. Mukherjee S, et al. Structural transitions mediating transcription initiation by T7 RNA polymerase. Cell. 2002 Jul 12;110(1):81-91. [PMID 12150999]

4. Mentesana PE, et al. Characterization of halted T7 RNA polymerase elongation complexes reveals multiple factors that contribute to stability. J Mol Biol. 2000 Oct 6;302(5):1049-62. [PMID 11183774]

Intellectual Property: HHS Reference No. E-119-2013/0 – US Provisional Patent Application No. 61/843,864 filed July 8, 2013

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

Blood-Based Assay for the Diagnosis and Monitoring of Hyposialylation Disorders

Description of Technology: Sialic acid, a monosaccharide widely distributed in glycoproteins and glycolipids, plays an important role in biological processes such as cellular adhesion, cellular communication and signal transduction. Reduced levels of sialic acid in tissues (also known as hyposialylation) affect the function of muscle, kidney, and other organ systems, and are found in a number of disorders, such as hereditary inclusion body myopathy (HIBM, also known as GNE myopathy), renal hyposialylation disorders, and congenital disorders of glycosylation.

The inventors have developed a sensitive, reliable assay for the diagnosis of hyposialylation disorders that detects a novel glycoprotein biomarker in a patient blood sample. This assay has been validated using samples from patients with GNE myopathy and other hyposialylation disorders. A distinct advantage of this assay is that it is minimally invasive, unlike many currently-available methods for diagnosing

hyposialylation disorders, which typically require a tissue biopsy. In particular, this biomarker represents the first non-invasive method for diagnosis of renal hyposialylation.

Potential Commercial Applications:

• Diagnostic assay to detect hyposialylation

• Monitoring tool to track patient response to sialylation-increasing therapy

Competitive Advantages: A blood-based assay based on this technology would be less invasive, time-consuming, and costly than a tissue biopsy, which is the current diagnostic standard for hyposialylation disorders, particularly kidney disorders.

Development Stage:

• Early-stage

• In vitro data available

Inventors: Marjan Huizing (NHGRI), William Gahl (NHGRI), Nuria Carrillo-Carrasco (NCATS)

Intellectual Property: HHS Reference No. E-056-2013/0 – U.S. Application No. 61/785,094 filed 14 Mar 2013

Related Technologies:

• HHS Reference No. E-217-2007/0 – N-Acetyl Mannosamine as a Therapeutic Agent

• HHS Reference No. E-270-2011/0 – Encapsulated N-Acetylmannosamine or N-Acetylneuraminic Acid to Increase Sialylation

Licensing Contact: Tara Kirby, Ph.D.; 301-435-4426; tarak@mail.nih.gov

Vaccine Adjuvant for Inducing Th17 Focused Response

Description of Technology: Adjuvant selection can be critical to a vaccine's effectiveness. Ideally, an adjuvant will target and activate specific immune pathways to increase the magnitude of a response to the vaccine. A limited range of adjuvants are presently available for human clinical use; these primarily affect T helper cells 1 and 2 (Th1 and Th2). Currently, no adjuvants are approved for human use which primarily affect IL-17-producing T helper cells (Th17) cells. Th17 focused adjuvants may prove critical for developing operative vaccines against pathogens where Th17 activity is essential for protection. This technology relates to novel adjuvants activating either caspase-associated recruitment domain protein 9 (CARD9) or caspase 1 pathways, or a combination of the two; and methods for using these adjuvants for stimulating an immune response. These adjuvants induce Th17 focused stimulation, which may prove essential to development of effective vaccines against a range of pathogens including bacteria and fungi.

Potential Commercial Applications: Vaccine

Competitive Advantages: Th17 skewing adjuvant

Development Stage: Early-stage

Inventors: Alan Sher (NIAID), Kevin Shenderov (NIAID), Vincenzo Cerundolo (University of Oxford, U.K.), Gurdyal Besra (University of Birmingham, U.K.)

Publication: Shenderov K, et al. Cord factor and peptidoglycan recapitulate the Th17-promoting adjuvant activity of mycobacteria through mincle/CARD9 signaling and the inflammasome. J Immunol. 2013 Jun 1;190(11):5722-30. [PMID 23630357]

Intellectual Property: HHS Reference No. E-089-2012/0 – U.S. Provisional Patent Application No. 61/709,713 filed October 4, 2012

Licensing Contact: Edward (Tedd) Fenn, J.D.; 424-500-2005; Tedd.fenn@nih.gov

Collaborative Research Opportunity: The National Institute of Allergy and Infectious Diseases is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize this technology. For collaboration opportunities, please contact Richard Kitei at 301-496-2644.

August 22, 2013
Date

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

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