[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 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.

Methods for Amelioration and Treatment of Pathogen-associated Inflammatory Response

Description of Technology: This CDC invention provides methods for preventing or treating inflammatory response-linked, infection induced pathologies, which are mediated by endogenous substance P. Substance P is a naturally-occurring and major pro-inflammatory neuromediator or neuromodulator, and elevated levels of substance P have been implicated in numerous inflammation-associated diseases. More specifically, this technology entails administration of anti-substance P antibodies or anti-substance P antibody fragments to a subject in need, thereby inhibiting the activity of endogenous substance P.

Small molecule anti-inflammatory agents currently employed to treat inflammation frequently cause adverse side effects, such as gastrointestinal discomfort and decreased blood clotting efficiency. Use of steroid-based anti-inflammatory drugs may result in reduced adrenal gland function and generalized immune system inhibition. This technology specifically targets and alleviates substance P-induced hyper-inflammatory diseases, potentially avoiding the complications associated with other anti-inflammatory compounds. Blocking the activity of endogenous substance P potentially can be employed to prevent or treat a wide variety of diseases or syndromes caused in whole or part by an inflammatory response mediated by substance P. These include, but are not limited to, virus-mediated bronchiolitis including that mediated by respiratory syncytial virus, bacterial colitis, inflammation associated with chlamydial diseases, lung injury associated with staphylococcal enterotoxin B, inflammation due to

cytomegalovirus or hepatitis B virus, sepsis, allergic diseases such as asthma, autoimmune diseases such as rheumatoid arthritis, pancreatitis, inflammatory bowel disease, inflammation associated with multiple sclerosis, and rejection of allografts and other transplanted tissues or organs.

Potential Commercial Applications:

• Treatment of pathogen induced inflammation, especially bronchiolitis

• Prevention or lessening of adverse effects associated with other anti-inflammatory agents

• Amelioration of pain

Competitive Advantages:

• Useful for management of numerous inflammatory-related viral and/or bacterial infections

• May reduce or circumvent adverse side effects associated with other small-molecule and/or steroid-based anti-inflammatory treatments

Development Stage:

• In vitro data available

• In vivo data available (animal)

Inventors: Ralph A. Tripp, Larry J. Anderson, Deborah D. Moore (all of CDC)

Publication: Tripp RA, et al. Respiratory syncytial virus infection and G and/or SH protein expression contribute to substance P, which mediates inflammation and enhanced pulmonary disease in BALB/c mice. J Virol. 2000 Feb;74(4):1614-22. [PMID 10644330]

Intellectual Property: HHS Reference No. E-236-2013/0 –

• PCT Application No. PCT/US2000/001032 filed 14 Jan 2000

• US Patent No. 7,101,547 issued 05 Sep 2006

• Various international patent applications pending or issued

Licensing Contact: Whitney Blair, J.D., M.P.H.; 301-435-4937; whitney.blair@nih.gov

Recombinant Sulfated HIV Envelope Protein and Methods for Making Protein

Description of Technology: This technology comprises sulfated recombinant gp120 proteins and peptides. Also included are methods for producing sulfated recombinant gp120 proteins. The focus of this technology is on sulfation of two tyrosines in the V2 loop of the HIV major envelope glycoprotein, gp120, which increase the stability of gp120 and promote the synthesis of gp120 protein in its native "closed" conformation. Gp120 in its native form is highly sulfated; however, recombinant gp120 produced for vaccines or structural analyses typically display low levels of V2 tyrosine sulfation. Sulfation of the V2 loop results in increased binding to trimer-recognizing anti-HIV antibodies specific to the V2 loop region of gp120 (PG9, PG16, CH01, PGT145) and decreased binding of CD4. The sulfation of recombinant gp120 is accomplished by over expression of a tyrosyl sulfotransferase in the producing cell line. Preliminary experiments indicate the recombinant sulfated gp120 proteins can be used to elicit the formation of HIV neutralizing antibodies in immunized animals.

Potential Commercial Applications:

• Design of HIV vaccines

• Production of HIV vaccines

• Induction of Neutralizing Antibodies

• HIV vaccine booster protein

Competitive Advantages:

• Consistent sulfation/production of gp120

• Gp120 vaccine component with improved stability and immunogenicity

• Recombinant gp120 vaccine component in native conformation

Development Stage:

• Early-stage

• In vitro data available

• In vivo data available (animal)

• Prototype

Inventors: Paolo Lusso and Raffaello Cimbro (NIAID)

Publication: Cimbro R, et al. Tyrosine sulfation in the second variable loop (V2) of HIV-1 gp120 stabilizes V2–V3 interaction and modulates neutralization sensitivity. Proc Natl Acad Sci USA. E-pub before print, 2014 Feb 03. [doi:10.1073/pnas.1314718111]

Intellectual Property: HHS Reference No. E-067-2012/0 – PCT Application No. PCT/US2013/074801, claiming priority to U.S. Provisional Application No. 61/736,350 filed 12 Dec 2012

Related Technology: Unpublished modifications to recombinant GP120.

Licensing Contact: Cristina Thalhammer-Reyero, Ph.D., M.B.A.; 301-435-4507; thalhamc@mail.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 as a HIV vaccine component or a therapeutic for treating HIV. For collaboration opportunities, please contact Bill Ronnenberg at wronnenberg@niaid.nih.gov or 301-451-3522.

Novel Host Target for Treatment of Hepatitis C Virus Infection

Description of Technology: The subject technology is a newly discovered Interferon-lambda 4 (IFNL4) protein found through analysis of genomic data derived from primary human hepatocytes, molecular cloning and functional annotation. The IFNL4 protein is related to but distinct from other know IFNs and its expression is inducible in conditions that mimic viral infection. Preliminary studies indicate that this protein may play a role in impaired natural and treatment induced clearance of HCV. These findings suggest that the protein can potentially be a new target for treating HCV infection.

Potential Commercial Applications:

• Novel target for treatment of HCV infection.

• Diagnostics can be developed for detection of IFNL4 mRNA or protein.

• Existing biological reagents for detection of IFNL4 - expression assays, antibodies and protein.

Competitive Advantages: IFNL4 is created by a genetic variant *IFNL4-deltaG*, which is present only in a subset of individuals, suggesting that IFNL4 is not an essential protein and its functional inactivation may be well-tolerated.

Development Stage:

• Early-stage

• Pre-clinical

• In vitro data available

Inventors: Liudmila Prokunina (NCI), Thomas R. O'Brien (NCI), Brian P. Muchmore (NCI), Raymond P. Donnelly (FDA)

Publication: Prokunina-Olsson L, et al. A variant upstream of IFNL3 (IL28B) creating novel interferon gene IFNL4 is associated with impaired clearance of hepatitis C virus. Nat Genet. 2013 Feb;45(2):164-71. [PMID 23291588]

Intellectual Property: HHS Reference No. E-217-2011/1 –

• U.S. Provisional Patent Application No. 61/616,664 filed 28 Mar 2012

• International PCT Application No. PCT/US13/31624 filed 14 Mar 2013, which published as WO 2013/148272 on 03 Oct 2013

Related Technology: HHS Reference No. E-217-2011/0 –

• U.S. Provisional Patent Application No. 61/543,620 filed 05 Oct 2011

• International PCT Application No. PCT/US2012/59048 filed 05 Oct 2012, which published as WO 2013/052862 on 11 Apr 2013

Licensing Contact: Kevin W. Chang, Ph.D.; 301-435-5018; changke@mail.nih.gov

Collaborative Research Opportunity: The NCI Division of Cancer Epidemiology & Genetics, Laboratory of Translational Genomics, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize development of tools for detection of IFNL4 mRNA and protein and modulation of its function. For collaboration opportunities, please contact John Hewes, Ph.D. at hewesj@mail.nih.gov.

Knockout Mouse Models for Study of Cholesterol Biosynthesis and Metabolic Diseases

Description of Technology: The farnesoid X receptor (FXR), also known as the bile acid receptor (BAR), is expressed in high levels in the liver and intestine, and controls the synthesis and transport of bile acids, which are degradation products of cholesterol. As such, FXR is a potential drug target for a number of metabolic disorders, such as dyslipidemia, diabetes and atherosclerosis.

Available for licensing are mouse models with a total deletion of the FXR gene (FXR-null mouse), as well as mice with tissue-specific deletions of the FXR gene in the liver or in the intestine. These mice may be useful for the study of cholesterol and bile acid synthesis and their role in metabolic disease, as well as for the development of drugs targeting FXR.

Potential Commercial Applications:

• Development of FXR/BAR-based drugs for the treatment of cholesterol disorders and metabolic diseases including dyslipidemia, diabetes and atherosclerosis.

• Study of the role of FXR in cholesterol biosynthesis and metabolic disease.

Development Stage: Early-stage

Inventor: Frank J. Gonzalez (NCI)

Publications:

1. Sinal C, et al. Targeted disruption of the nuclear receptor FXR/BAR impairs bile acid and lipid homeostasis. Cell. 2000 Sep 15;102(6):731-44. [PMID 11030617]

2. Kim I, et al. Differential regulation of bile acid homeostasis by the farnesoid X receptor in liver and intestine. J Lipid Res. 2007 Dec;48(12):2664-72. [PMID 17720959]

Intellectual Property: Research Tools – Patent protection is not being pursued for this technology:

• HHS Reference No. E-323-2001/0 - a mouse line lacking the nuclear receptor FXR/BAR

• HHS Reference No. E-323-2001/1 - a mouse line lacking FXR/BAR expression in the liver

• HHS Reference No. E-323-2001/2 - a mouse line lacking FXR/BAR expression in the intestine

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

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Date

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