[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.

ADDRESS: 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.

Genetically Engineered Mouse Model for Use as an Alternative Screening Method for Evaluating P-glycoprotein (P-gp) Substrate Toxicity in Avermectin-sensitive Dogs

Description of Technology: A pitfall to avermectins is central nervous system (CNS) toxicities in herding dogs. As a result, all new avermectins must be tested in a "Collie Safety Study" to determine the degree of CNS toxicity. The toxicity is due to a 4 base pair mutation in the ATP-binding cassette, sub-family B member 1 (ABCB1) gene. This gene encodes for the P-glycoprotein (P-gp) that affects absorption, distribution and elimination of certain drugs. Researchers at FDA have developed an alternate animal model that includes two transgenic mouse models, one containing the mutant form of the canine ABCB1 gene (Yancy 1 line) and the other containing the canine wild-type gene (Yancy 2 line). The paired mouse system can be utilized to assess the safety of avermectins and other canine drugs by determining the toxicity to canines with the mutated form of the ABCB1 gene. Ivermectin, a derivative of the avermectin family of heartworm drugs used to treat and control parasitic infections, was used to verify this mouse model. This technology will enhance the population predictions derived from clinical safety data and serve to reduce the use of dogs in avermectin derivative safety studies that are part of the Investigational New Animal Drug (INAD) approval process.

Potential Commercial Applications: Drug screening technology to assess the toxicity of canine drugs to canines with the mutated form of the ABCB1 gene.

Competitive Advantages: Use as an alternative in vivo model to canines for assessment of drug safety in the presence of the ABCB1 mutation.

Development Stage: In vivo data available (animal)

Inventor: Haile F. Yancy (FDA)

Publication: Orzechowski K, et al., in press Am J Vet Res.

Intellectual Property: HHS Reference No. E-292-2011/0 – Research Tool. Patent protection is not being pursued for this technology.

Licensing Contact: Jaime Greene; 301-435-5559; greenejaime@mail.nih.gov

Collaborative Research Opportunity: The FDA Center for Veterinary Medicine is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize this alternative mouse model. For collaboration opportunities, please contact Haile F. Yancy at haile.yancy@fda.hhs.gov or 301-210-4096.

Treatment of Tuberculosis — Adjuvant Therapies to Increase the Efficiency of Antibiotic Treatments

Description of Technology: There is growing evidence that resistance to *Mycobacterium tuberculosis* infection is governed in large part by the regulation of host cell death. Lipid mediators called eicosanoids are thought to play a central role in this process. The subject invention is a novel method of enhancing the efficacy of antibiotic treatments for *Mycobacterium tuberculosis* infection by co-administering an inhibitor of 5-lipoxygenase and a COX-2 dependent prostaglandin. Inhibition of 5-lipoxygenase and treatment with prostaglandin E2 results in alteration of the eicosanoid balance. The synergistic effects of altering the eicosanoid balance and treatment with antibiotics is believed to result in more efficient reduction of the bacterial burden and thus, the period

of antibiotic administration and antibiotic dosage could potentially be reduced. In vivo data from mouse models can be provided upon request.

Potential Commercial Applications: The subject invention can be used as an adjuvant therapy for existing antibiotic treatment regiments against tuberculosis.

Competitive Advantages: The disclosed method can be applied to increase the efficacy of existing antibiotic treatments for tuberculosis, potentially reducing both the duration and dosage of the antibiotic treatment.

Development Stage:

• Early-stage

• Pre-clinical

• In vitro data available

• In vivo data available (animal)

Inventors: Katrin D. Mayer, Bruno Bezerril D. Andrade, F. Alan Sher, and Daniel L. Barber (NIAID)

Intellectual Property:

• HHS Reference No. E-189-2011/0 — U.S. Provisional Patent Application No. 61/515,229 filed 04 Aug 2011

• HHS Reference No. E-189-2011/1 — U.S. Provisional Patent Application No. 61/515,237 filed 04 Aug 2011

Licensing Contact: Kevin W. Chang, Ph.D.; 301-435-5018; changke@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 adjuvant therapy for antibiotic treatment regiments against tuberculosis. For collaboration opportunities, please contact Katrin Mayer. Ph.D. at mayerk@niaid.nih.gov or 301-594-8061.

DPEP1 and TPX2 as Prognostic Biomarkers for Pancreatic Ductal Adenocarcinoma

Description of Technology: Scientists at NIH have developed prognostic biomarkers and a candidate therapeutic target for pancreatic ductal adenocarcinoma (PDAC). PDAC is a devastating cancer, and patients have an average survival of six months. The 5-year survival for PDAC patients is only 6%. This high lethality in pancreatic cancer is due to the late diagnosis and lack of any effective treatment. Greater than 80% of patients are diagnosed in an advanced stage of the disease. The instant invention is a discovery of biomarkers to make prognostic conclusions about the progression of PDAC by measuring the expression of DPEP1 and TPX2. Patients with decreased DPEP1 and increased TPX2 expression have poorer outcome. Furthermore, DPEP1 and TPX2 are controlled by the MAPK pathway. A MAPK inhibitor can be used as a treatment because it can lead to increased DPEP1 and decreased TPX2 expression, which is associated with better survival.

Potential Commercial Applications:

• Prognostic biomarker to identify high-risk patients

• Identification of MAPK inhibitor(s) altering DPEP1 and TPX2 expression

Competitive Advantages:

• Combination of measuring DPEP1 and TPX2 expression levels results in improved prognosis prediction

• Development of expression level patterns during tumorigenesis that are representative of PDAC

Development Stage: In vivo data available (human)

Inventors: Syed P. Hussain and Geng Zhang (NCI)

Publication: DPEP1 and TPX2 as Independent Predictors of Cancer-Specific Mortality in Pancreatic Ductal Adenocarcinoma, submitted April 2011.

Intellectual Property: HHS Reference No. E-171-2011/0 — U.S. Patent Application No. 61/512,302 filed 27 July 2011

Licensing Contact: Uri Reichman, Ph.D., MBA; 301-435-4616; reichmau@mail.nih.gov

AAV Mediated CTLA-4 Gene Transfer to Treat Sjögren's Syndrome

Description of Technology: Sjögren's syndrome is an autoimmune disease that affects over 2 million Americans, primarily over the age of 40. One of the major outcomes of Sjögren's syndrome is xerostomia (dry mouth) that is caused by immune system attack on moisture producing salivary glands. Researchers at the National Institute of Dental and Craniofacial Research have developed a therapy that alleviates xerostomia in a murine model of Sjögren's syndrome. This technology consists of a local delivery of adeno-associated virus (AAV) mediated cytotoxic T-lymphocyte antigen 4 Immunoglobulin-G (CTLA4IgG) fusion protein to salivary glands. The system effectively blocks CTLA4 ligand interactions with T cell surface receptors, resulting in immune suppression and reversal of autoimmune-related xerostomia. Targeted delivery

of the AAV-CTLA4-IgG system makes this invention a novel therapeutic for the prevention of xerostomia-associated pain and discomfort caused by Sjögren's syndrome.

Potential Commercial Applications: Prevention of salivary gland destruction and xerostomia development in patients with Sjögren's syndrome.

Competitive Advantages:

• Current treatments temporarily reduce the discomfort of xerostomia but do not prevent the deleterious effects of this disorder.

• AAV gene transfer to salivary glands is highly efficient.

• AAV therapy is safe and noninflammatory.

Development Stage:

• In vitro data available

• In vivo data available (animal)

Inventors: Hongen Yin and John Chiorini (NIDCR)

Publications:

1. Zheng C, et al. Assessment of the safety and biodistribution of a regulated AAV2 gene transfer vector after delivery to murine submandibular glands. Toxicol Sci. 2011 Sep;123(1):247-255. [PMID: 21625005]

2. Kanaya K, et al. Combined gene therapy with adenovirus vectors containing CTLA4Ig and CD40Ig prolongs survival of composite tissue allografts in rat model. Transplantation. 2003 Feb 15;75(3):275-281. [PMID: 12589145]

3. Genovese MC, et al. Abatacept for rheumatoid arthritis refractory to tumor necrosis factor alpha inhibition. N Engl J Med. 2005 Sep 15;353(11):1114-1123. [PMID: 16162882]

Intellectual Property: HHS Reference No. E-087-2011/0 — U.S. Provisional Application No. 61/476,168 filed 15 April 2011

Licensing Contact: Jaime Greene; 301-435-5559; greenejaime@mail.nih.gov

Collaborative Research Opportunity: The NIDCR 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 David Bradley at bradleyda@nidcr.nih.gov.

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Date

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