[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.

Small interfering RNA Knock-down of Cannabinoid-1 Receptor (CB1R) for the Treatment or Prevention of Type-2 Diabetes

Description of Technology: Endocannabinoids (EC) are lipid signaling molecules that act on the same cannabinoid receptors that recognize and mediate the effects of marijuana. Activation of the EC receptor CB1R has been shown to play a key role in the development of obesity and its metabolic consequences, including insulin resistance and type 2 diabetes. Researchers at NIH have now demonstrated in the Zucker diabetic fatty (ZDF) rat model of type-2 diabetes that beta-cell loss is caused by the CB1R-mediated activation of a macrophage-mediated inflammatory response. They have further demonstrated that treatment of ZDF rats with a peripheral CB1R antagonist restores normoglycemia and preserves beta-cell function and that similar results were seen following selective *in vivo* knockdown of macrophage CB1R by daily treatment of ZDF rats with D-glucan-encapsulated CB1R Small interfering RNA (siRNA). Therefore, knock-down of CB1R with siRNA may represent a new method of treating type-2 diabetes or preventing the progression of insulin resistance to overt diabetes.

Potential Commercial Applications: Treatment of obesity, insulin resistance, and diabetes.

Competitive Advantages: A new means of inhibiting the endocannabinoid receptor CB1R.

Development Stage: In vivo data available (animal).

Inventors: George Kunos (NIAAA), Tony Jourdan (NIAAA), Michael P. Czech (UMass Medical School), Myriam Aouadi (UMass Medical School).

Intellectual Property: HHS Reference No. E-103-2013/0 – US Application No. 61/839,239 filed June 25, 2013.

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

Methods for the Treatment of AIDS and Other Retroviral Diseases Using Plant-derived Compounds

Description of Technology: Human immunodeficiency virus-1 (HIV-1) affects 1.4 million patients in the US and over 33 million worldwide. While highly active antiretroviral therapy (HAART), the current standard of care, is effective in suppressing retroviral activity, cure has not been achieved due to the persistence of latently infected T cells in treated patients. An agent capable of sensitizing this T cell subpopulation concordant with HAART may add significant benefit to individuals with retroviral diseases.

Researchers at the NIH have identified Englerin A and its derivatives as potent and specific activators of viral replication in infected T cells. Use of these compounds in conjunction with existing antiviral therapies has been described for the treatment of AIDS, adult T cell leukemia/lymphoma and other retroviral diseases.

Intellectual property assets available for license include novel compositions of Englerin A along with methods of their use in the treatment of retroviral diseases.

Potential Commercial Applications:

• Novel adjuvant therapy for the treatment of retroviral diseases such as AIDS or HTLV-induced leukemia/lymphoma.

• Therapeutic for the management of T lymphocytopenia.

Competitive Advantages:

• Englerin A and its derivatives are potent and selective activator of protein kinase C theta in immune cells.

• Compounds are anticipated to have fewer off-target toxicities relative to currently available PKC activators (e.g., interleukins-2 and 7).

• Compounds are optimized for use in combination with clinically available antiviral agents.

Development Stage:

• Pre-clinical.

• In vitro data available.

• In vivo data available (animal).

Inventors: Leonard Neckers, Marston Lineham, Carole Sourbier, Jane Trepel, Min-jung Lee, Bradley Scroggins, John Beutler (all of NCI).

Publications:

1. Ratnayake R, et al. Englerin A, a selective inhibitor of renal cancer cell growth, from Phyllanthus engleri. Org Lett. 2009 Jan 1;11(1):57-60. [PMID 19061394].

2. Li Z et al. A brief synthesis of (-)-englerin A. J Am Chem Soc. 2011 May 4;133(17):6553-6. [PMID 21476574].

3. Akee R, et al. Chlorinated englerins with selective inhibition of renal cancer cell growth. J Nat Prod. 2012 Mar 23;75(3):459-63. [PMID 22280462].

4. Sourbier C, et al. Englerin A stimulates PKC theta to inhibit insulin signaling and to simultaneously activate HSF1: pharmacologically induced synthetic lethality. Cancer Cell. 2013 Feb 11;23(2):228-37. [PMID 23352416].

Intellectual Property: HHS Reference No. E-201-2012/0 – US Application No. 61/726,975 filed November 15, 2012.

Related Technologies:

• HHS Reference No. E-064-2008 – "Englerin A: A Novel Renal Cancer Therapeutic Isolated from an African Plant."

• HHS Reference No. E-042-2012 – "Use of Englerin A for the Treatment of Diabetes, Obesity and Other Diseases."

Licensing Contact: Surekha Vathyam, Ph.D.; 301-435-4076; vathyams@mail.nih.gov.

Collaborative Research Opportunity: The National Cancer Institute Molecular Targets Development Program is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize epoxy-guaiane derivatives for retroviral therapy. For collaboration opportunities, please contact John D. Hewes, Ph.D. at hewesj@mail.nih.gov.

Development of Immune System Tolerance for the Treatment of Autoimmune Disease

Description of Technology: The present invention provides a therapeutic method for the treatment of autoimmune or autoinflammatory diseases by first breaking down the dysregulated immune system and then reprogramming the immune system to

restore tolerance to the patient's self-antigens by induction of antigen specific regulatory T cells. The inventors have shown that only with the combination of apoptosis, phagocytes, and antigen can antigen-specific regulatory T cells (T_{reg}) cells be optimally generated to develop long-term immune tolerance. This strategy for developing immune tolerance can be applied to the treatment of autoimmune diseases.

Potential Commercial Applications: Treatment of autoimmune disease.

Competitive Advantages: This technology represents a novel means of treating autoimmune disease.

Development Stage:

• Early-stage.

• In vivo data available (animal).

Inventors: Wanjun Chen (NIDCR), Shimpei Kassagi, Pin Zhang.

Intellectual Property: HHS Reference No. E-186-2009/0 – US Provisional Application No. 61/844,564 filed July 10, 2013.

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

Dated: September 19, 2013. _____

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National Institutes of Health.

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