[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.

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.

Treatment of Viral Infection by Blocking Interleukin-21

Description of Technology: Blocking interleukin (IL-21) may be an effective method to treat or prevent various viral infections. In the course of an immune response to a virus, IL-21, produced primarily by $CD4^+$ T cells, can inhibit or stimulate (regulate), immune cell function (B cells, T cells, natural killer cells, dendritic cells). IL-21 regulation may be either protective or pathological; autoimmune disease pathology has been associated with IL-21 promoted inflammation (in: type 1 diabetes, lupus, and multiple sclerosis). This technology describes methods of blocking IL-21 that may reduce damaging inflammatory responses during certain viral infections. Specifically, the absence of IL-21 during respiratory viral infection such as pneumonia virus infection actually prevents some of the pathogenic effects that may be promoted by IL-21. Methods for controlling IL-21 signaling may be used to treat to prevent many pathological effects of pneumonia viruses, and other viral infections.

Potential Commercial Applications: Prevention and treatment of many pathological effects of viral infections, including pneumonia.

Competitive Advantages: New method for treating viral infection pathology.

Development Stage:

• Early-stage

• Pre-clinical

• In vivo data available (animal)

Inventors: Warren J. Leonard and Rosanne Spolski (NHLBI)

Publication: Spolski R, et al. IL-21 promotes the pathologic immune response to pneumovirus infection. J Immunol. 2012 Feb 15;188(4):1924-32. [PMID 22238461]

Intellectual Property: HHS Reference No. E-017-2012/0 — U.S. Provisional Application No. 61/579,801 filed 23 Dec 2011

Licensing Contact: Tedd Fenn; 301-435-5031; Tedd.Fenn.nih.gov

Collaborative Research Opportunity: The NHLBI is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize treatment of viral infection by blocking Interleukin-21 (E-017-2012). For collaboration opportunities, please contact Vincent Kolesnitchenko, Ph.D. at kolesniv@nhlbi.nih.gov.

Transgenic ZP2 Mouse Model Produces Eggs That Bind to Human Sperm Protein

Description of Technology: Fertilizing sperm bind to an extracellular coat surrounding mammalian eggs called zona pellucida. Depending on the species, the zona pellucida is composed of ZP1, ZP2, ZP3, and/or ZP4 proteins. Recent studies show that sperm successfully adhere to the zona pellucida surface when ZP2 is intact. In contrast, when ZP2 has been proteolytically cleaved, sperm binding is disrupted.

To further study the effect of ZP2 cleavage in sperm-egg recognition, researchers at NIDDK have developed a transgenic mouse expressing human ZP2. Prior attempts using ZP2 knockout mice were unsuccessful because the produced eggs were not fertile in vivo. Transgenic ZP2 mice produced humanized zonae pellucida, and produced fertile eggs to which human sperm successfully and specifically bound. This mouse model contradicts previous notions that production of human transgenic ZP2 would adversely change the specificity of sperm binding.

Potential Commercial Applications:

• Transgenic eggs can be used in diagnostic functional assays to assess human sperm viability for reproductive technologies.

• Diagnostic assay can be extended to determine presence of male infertility in a variety of mammals, including pets, farm livestock, and zoological mammals.

Competitive Advantages:

• This ZP2 mice model produces eggs containing transgenic mammalian zona pellucida, which can successfully and specifically be fertilized with the corresponding mammalian sperm.

• Use in human infertility studies spares the use of a human egg for binding studies.

Development Stage:

• Prototype

• Early-stage

• In vitro data available

• In vivo data available (animal)

Inventors: Tracy L. Rankin, Jenell S. Coleman, Olga Epifano, Tanya Hoodbhoy, Scott Turner, Jurrien Dean (all of NIDDK)

Publications:

1. Rankin TL, et al. Fertility and taxon-specific sperm binding persist after replacement of mouse sperm receptors with human homologs. Dev Cell. 2003 Jul;5(1):33-43. [PMID 12852850]

2. Gahlay G, et al. Gamete recognition in mice depends on the cleavage status of an egg's zona pellucida protein. Science. 2010 Jul 9;329(5988):216-9. [PMID 20616279]

Intellectual Property: HHS Reference No. E-288-2011/0 — Research Tool. Patent protection is not being pursued for this technology.

Related Technology: HHS Reference No. E-162-2011/0 — Research Tool. Patent protection is not being pursued for this technology.

Licensing Contact: Lauren Nguyen-Antczak, Ph.D., J.D.; 301-435-4074; Lauren.Nguyen-antczak@nih.gov

Englerin A: A Novel Renal Cancer Therapeutic Isolated from an African Plant

Description of Technology: Renal cell cancer of the kidney accounts for 13 thousand deaths per year, largely due to the ineffective treatment methods available. The current standard of care is limited to surgical resection of the diseased tissue and to date chemotherapy/radiation intervention has been of limited effectiveness.

Researchers at the NIH have isolated a series of novel natural compounds from the African plant *Phyllanthus engleri* that display potent anti-cancer properties, particularly in renal cancer cell lines. Englerin A displays renal cancer cell line growth inhibition *in vitro* and efficacy against renal and prostate cancer cell lines *in vivo*. The compound can be efficiently extracted from the plant, and recent work has described methods for the synthesis of Englerin A and novel analogs.

Further preclinical studies have yielded an optimized formulation for parenteral drug administration, the establishment of a method for measuring bioavailability, and modeling studies suggestive that Englerin A should be orally bioavailable.

Potential Commercial Applications: The new chemical entities can be potential cancer therapeutics, especially for renal cancer.

Competitive Advantages:

• Isolated compounds are specifically toxic to renal cancer cells, a disease with limited current chemotherapeutic options

• Compounds are effective in vivo and have potential applications to other disease states

• There is reasonable yield and recovery of the compounds from the natural product extracts.

• Recent work has identified efficient routes for synthesis of Englerin A

Development Status:

• Pre-clinical

• In vitro data available

• In vivo data available (animal)

Inventors: John A. Beutler et al. (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]

Intellectual Property: HHS Reference No. E-064-2008/2 — U.S. Patent Application No. 12/811,245 filed 29 Jul 2010

Related Technology: HHS Reference No. E-042-2012/0 — U.S. Provisional Application No. 61/584,526 filed 09 Jan 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 cancer inhibitors. Please contact John D. Hewes, Ph.D. at 301-435-3121 or hewesj@mail.nih.gov for more information.

June 5, 2012
Date

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

[FR Doc. 2012-14038 Filed 06/08/2012 at 8:45 am; Publication Date: 06/11/2012]