[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.

Axon Regeneration After Brain or Spinal Cord Injury

Description of Technology: The invention is directed to modification of a particular sugar by the enzyme arylsulfatase B (ARSB), which results in axon regeneration.

Following traumatic brain or spinal cord injury, glial scars prevent regeneration of axons. Chondroitin sulfate proteoglycans (CSPGs) are major components of glial scars. CSPGs are made of a protein core containing glycosaminoglycan (GAG) sugar side chains, which, when sulfated, are responsible for the inhibitory activity of glial scars. Specifically, NIH researchers have shown that the 4-sulfate unit on a certain sugar on GAG is responsible for inhibiting axon regrowth and, when the 4-sulfate unit is reduced, axon regrowth is observed. Moreover, removal of this 4-sulfate unit by the ARSB enzyme promotes axon regrowth.

As a potential therapy for spinal cord injuries, researchers developed a vector expressing ARSB and demonstrated that this vector promotes axon regeneration when injected into the spinal cord of a mouse.

Potential Commercial Applications:

• Treatment of brain and spinal cord injury

• Treatment of other CNS injuries, including stroke

• Treatment of heart attack

Competitive Advantages:

• There are no existing products for treatment of traumatic spinal cord injury

• ARSB is already approved for treatment of Mucopolysaccharoidosis VI, a lysosomal storage disease

Development Stage:

• Early-stage

• In vitro data available

• In vivo data available (animal)

Inventors: Herbert M. Geller and Yasuhiro Katagiri (NHLBI)

Publication: Wang H, et al. Chondroitin-4-sulfation negatively regulates axonal guidance and growth. J Cell Sci. 2008 Sep 15;121(Pt 18):3083-91. [PMID 18768934]

Intellectual Property: HHS Reference No. E-214-2012/0 — U.S. Provisional Application No. 61/705,555 filed 25 Sept 2012

Licensing Contact: Lauren Nguyen-Antczak, Ph.D., J.D.; 301-435-4074; Lauren.Nguyen-antczak@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 the use of ARSB in axonal regeneration after brain or spinal cord injury using animal models. For collaboration opportunities, please contact Denise Crooks, Ph.D. at 301-435-0103 or crooksd@mail.nih.gov.

Nitric Oxide-Releasing Polyvinylpyrrolidone-Based Polymers for Wound Healing and Related Applications

Description of Technology: Novel nitric oxide-releasing polyvinylpyrrolidone-based polymers, their compositions, and use in treating wounds. The disclosed polymers appear to be stable, biocompatible and bioabsorbable, while providing for extended nitric oxide release at therapeutic levels. The invention also encompasses medical devices,

such as wound dressings and bandages, which include the polymers and are capable of releasing nitric oxide when in use. These devices may be used to treat a wound, various infections, and dermatological conditions.

The therapeutic efficacy of nitric oxide has been demonstrated for many indications, including wound healing. As wounds are deficient in nitric oxide, its application has been shown to have beneficial effects on wound healing by promoting angiogenesis and tissue remodeling.

Potential Commercial Applications: Wound healing, infections, and dermatological conditions.

Competitive Advantages: The claimed nitric oxide-releasing polymers are bioabsorbable and release greater amounts of nitric oxide over a greater period of time than other NO-releasing polymers.

Development Stage:

• Early-stage

• Pre-clinical

Inventors: Joseph A. Hrabie and Larry K. Keefer (NCI)

Intellectual Property: HHS Reference No. E-157-2012/0 — US Provisional Application No. 61/672,486 filed 17 Jul 2012

Licensing Contact: Betty B. Tong, Ph.D.; 301-594-6565; tongb@mail.nih.gov

Gag-Based DNA Vaccines Against HIV

Description of Technology: Novel DNA vaccine constructs against HIV that express highly conserved elements (CE) within the HIV Gag protein and elicit strong,

cross-clade cellular and humoral responses. The DNA vaccine vectors were engineered to express CEs for protection against different clades of HIV and prevention of immunodominance, two issues associated with current HIV vaccine candidates.

In vivo studies of Rhesus macaques vaccinated with variants of these constructs expressing seven highly CEs covering >99 of all known Gag sequences elicited strong, cellular T-cell and humoral antibody immune responses. The Gag-specific antibody responses were high titer and cross-clade. Cross-clade protection is important given the sequence diversity of HIV as is the absence of immunodominant epitopes that generate antibodies which are not protective against HIV.

Potential Commercial Applications: HIV vaccines

Competitive Advantages: Addresses two key hurdles faced by current HIV vaccines: sequence diversity of HIV and immunodominance.

Development Stage:

• Early-stage

• Pre-clinical

• In vitro data available

• In vivo data available (animal)

Inventors: George N. Pavlakis (NCI), Barbara K. Felber (NCI), James Mullins (University of Washington)

Intellectual Property: HHS Reference No. E-132-2012/0 — U.S. Provisional Application No. 61/606,265 filed 02 Mar 2012

Related Technology: HHS Reference No. E-308-2000/0 — Patent family filed in the U.S., Canada, Australia, Europe, and Japan

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

Diagnostic Test and Therapeutic Target for Sjogren's Syndrome

Description of Technology: Sjögren's syndrome is an autoimmune disease that attacks salivary glands resulting in chronic dry mouth and dry eyes. Currently, there is no single diagnostic test to confirm the presence of Sjögren's. Physicians presently reach diagnosis after conducting a series of blood and functional tests for tear and salivary production. Diagnosis is further complicated as Sjögren's symptoms frequently mimic those of other autoimmune diseases (e.g., lupus, rheumatoid arthritis, etc.) and is often overlooked as dryness associated with medications being taken by the patient.

Researchers at NIDCR have identified overexpression of a growth factor, bone morphogenetic protein 6 (BMP6), in patients with Sjögren's. By detecting BMP6 expression and/or activity, this invention potentially presents a singular confirmation to diagnose those suffering and those at risk for developing Sjögren's. BMP6 also presents a potential therapeutic target for Sjögren's, a disease for which there is presently no cure.

Researchers have also discovered unique expression profiles for two other genes (XIST and MECP2) in male Sjögren's patients. Detecting aberrant expression and/or activity of these genes also offer a potential singular test for diagnosing Sjögren's in male subjects.

Potential Applications:

- Singular diagnostic test to diagnose Sjögren's
- Therapeutic target to develop treatment for Sjögren's

Competitive Advantages:

• Currently no single test available to diagnose Sjögren's

• Currently there is no cure for Sjögren's; present palliative treatments only reduce symptoms (e.g., moisture replacement therapy for eyes and mouth, and systemic anti-inflammatory or immunosuppressive agents for more advanced forms of disease)

Development Stage:

• Pre-clinical

• In vitro data available

• In vivo data available (animal)

• In vivo data available (human)

Inventor: John Chiorini (NIDCR)

Publication: Dix DJ, et al. Targeted gene disruption of Hsp70-2 results in failed meiosis, germ cell apoptosis, and male infertility. Proc Natl Acad Sci USA. 1996 Apr 16;93(8):3264-8. [PMID 8622925]

Intellectual Property: HHS Reference No. E-232-2011/0-US-01 — U.S. Provisional Application No. 61/540,364 filed 28 Sep 2011

Licensing Contact: Lauren Nguyen-Antczak, Ph.D., J.D.; 301-435-4074; Lauren.Nguyen-antczak@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 BMP6 Based Diagnosis and Treatment of Sjögren's. For collaboration opportunities, please contact David W. Bradley, Ph.D. at bradleyda@nidcr.nih.gov.

Use of PAMP (proadrenomedullin N-terminal 20 peptide) and PAMP Inhibitors for the Treatment of Cancer, Cardiovascular Disease, and Other Angiogenesis-related Diseases

Description of Technology: This technology details the use of PAMP or PAMP derivatives as a means to induce angiogenesis in tissue, as well as the use of PAMP inhibitors to inhibit angiogenesis.

PAMP (Proadrenomedullin N-terminal 20 peptide) is a 20 amino-acid molecule originating from the post-translational processing of pre-proadrenomedullin. PAMP is known as a potent hypotensive and vasodilatory agent; however, in addition to these properties, the inventors have discovered that PAMP also functions as a potent angiogenic factor. The inventors have also shown that an inhibitory fragment of PAMP, PAMP (12-20), is able to delay tumor growth in xenograft models of tumor progression. The ability to promote angiogenesis can be used as a means to increase vascularization in specific tissue areas or to treat patients with ischemic diseases. In contrast, the ability to inhibit this process can be used to limit growth of solid tumors and as a therapy for retinopathies, endometriosis, or arthritis.

Potential Commercial Applications:

• PAMP and derivatives may be used as treatments for ischemic disease or coronary artery disease and to promote vascularization in graft tissues.

• PAMP inhibitors may be used as treatments to limit growth of solid tumors or other angiogenesis-related disease.

Competitive Advantages:

• PAMP exhibits a potent angiogenic potential at femtomolar concentrations, as opposed to nanomolar concentrations of other growth factors such as bFGF and VEGF.

• PAMP and PAMP inhibitors provide a new mechanism for modulation of angiogenesis and treatment of angiogenesis-related diseases.

Development Stage:

• Early-stage

• In vitro data available

• In vivo data available (animal)

Inventor: Frank F Cuttitta (NCI)

Publication: Martinez A, et al. Proadrenomedullin NH2-terminal 20 peptide is a potent angiogenic factor, and its inhibition results in reduction of tumor growth. Cancer Res. 2004 Sep 15;64(18):6489-94. [PMID 15374959]

Intellectual Property: HHS Reference No. E-294-2002/0 —

• US Patent No. 7,462,593, Issued 09 Dec 2008

• US Patent No. 7,862,815, Issued 04 Jan 2011

• Foreign counterparts in Australia, Canada, and Japan

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

Methods for Measuring Adrenomedullin and Monitoring and Treating Adrenomedullin-mediated Diseases, Such as Diabetes and Cancer

Description of Technology: The technology includes methods for utilizing purified adrenomedullin (AM)-binding proteins, or functional portions thereof, to diagnose, treat, and monitor AM-related diseases such as diabetes and cancer. Antibodies

and small-molecule antagonists, which can down-regulate the function of AM, Complement Factor-H (CFH), and the AM-CFH complex, have also been isolated.

AM is a ubiquitously-expressed peptide that functions as a universal autocrine growth factor. AM drives cell proliferation, acts as a vasodilator, can protect cells against oxidative stress in hypoxic injury, and acts as a dose-dependent inhibitor of insulin secretion. Methods for measuring *in vivo* levels of AM accurately and regulating the activity of available AM may be critically important in diagnosis and treatment of many conditions, such as heart disease, pulmonary disease, cirrhosis, cancer, diabetes, sepsis, and inflammation.

This technology centers on the observation that AM binds to CFH *in vivo*. Without a means to determine the amount of AM that is bound to CFH, measurements of AM are inaccurate. Furthermore, therapies focused on the AM-CFH complex may have advantages over therapies focused on AM alone.

Potential Commercial Applications:

• Methods for diagnosis and treatment of conditions, such as cancer, diabetes, or other conditions influenced by AM levels.

• AM-specific antibodies could be used in a diagnostic assay to measure levels of AM.

Competitive Advantages:

• More accurate measurements of serum adrenomedullin than current tests

• Targeting AM-CFH decrease bioavailable AM, provides an additional pathway for modulating angiogenesis

Development Stage:

• Pre-clinical

• In vitro data available

• In vivo data available (animal)

Inventor: Frank F Cuttitta (NCI)

Publications:

1. Martínez A, et al. Mapping of the adrenomedullin-binding domains in human complement factor H. Hypertens Res. 2003 Feb;26 Suppl:S55-9. [PMID 12630812]

2. Pio R, et al. Complement factor H is a serum-binding protein for adrenomedullin, and the resulting complex modulates the bioactivities of both partners. J Biol Chem. 2001 Apr 13;276(15):12292-300. [PMID 11116141]

3. Miller MJ, et al. Adrenomedullin expression in human tumor cell lines. Its potential role as an autocrine growth factor. J Biol Chem. 1996 Sep 20;271(38):23345-51. [PMID 8798536]

Intellectual Property: HHS Reference No. E-256-1999/0 —

• PCT Application No. PCT/US00/24722 filed 08 Sep 2000

• US Patent No. 7,659,081 issued 09 Feb 2010

• US Patent No. 7,993,857 issued 09 Aug 2011

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

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Date

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