[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.

Intrathecal (IT) Administration of Rituximab to Treat Multiple Sclerosis (MS)

Description of Technology: Multiple sclerosis (MS) is a chronic, neurological, autoimmune, demyelinating disease. The pathology of MS is characterized by an abnormal immune response directed against the central nervous system. In particular, T-lymphocytes are activated against the myelin sheath of the neurons of the central nervous system causing demyelination. Secondary-progressive multiple sclerosis (SP-MS) is the chronic phase of MS. The majority of people who have relapsing-remitting MS eventually develop SP-MS. There are currently no effective treatments for SP-MS patients who do not have evidence for focal brain inflammation measured by contrast enhancing lesions (CEL) on brain MRI. NIH investigators have proposed that intrathecal administration of Rituximab, a monoclonal antibody (Ab) that depletes B cells and effectively decreases CEL in relapsing-remitting MS (RR-MS) but does not affect progression of disability in progressive MS, may deplete B cells from the intrathecal compartment leading to inhibition of T cell activation within intrathecal compartment, and thereby provide a novel therapeutic approach to treat SP-MS. A Clinical trial is in progress to evaluate this novel approach.

Potential Commercial Applications: Improved therapeutics to treat or prevent Secondary-progressive multiple sclerosis (SP-MS).

Competitive Advantages: This technology would provide the first effective therapy for Secondary-progressive multiple sclerosis patients lacking contrast enhancing lesions.

Development Stage:

• Clinical

• In vivo data available (animal)

Inventor: Bibiana Bielekova (NINDS)

Publication: Double Blind Combination of Rituximab by Intravenous and Intrathecal Injection Versus Placebo in Patients With Low-Inflammatory Secondary Progressive Multiple Sclerosis (RIVITaLISe). ClinicalTrials.gov Identifier: NCT01212094 (http://clinicaltrials.gov/ct2/show/NCT01212094)

Intellectual Property: HHS Reference No. E-249-2011/0 — U.S. Provisional Application No. 61/539,870 filed 27 Sep 2011

Licensing Contact: Suryanarayana (Sury) Vepa, Ph.D., J.D.; 301-435-5020; vepas@mail.nih.gov

miR126 for the Mobilization of Hematopoietic Stem/Progenitor Cells (HSPCs) into Peripheral Blood

Description of Technology: The NIH inventors have discovered that a micro RNA, miR126, mobilizes hematopoietic stem/progenitor cells (HSPCs) from the bone marrow into blood. These mobilized HSPCs can be easily collected from blood and used for reconstitution of ablated or functionally-impaired bone marrow. miR126 may also facilitate mobilization of bone-resident cancer cells into the circulation where they could be more easily targeted by cancer therapeutics. This discovery could replace bone marrow transplantation as we do it today. Rather than using the current non-selective agent G-CSF (which preferentially mobilizes mature myeloid cells rather than stem/progenitor cells), miR126 could be used for selective mobilization of the HSPCs needed for hematopoietic cell transplantation. Additionally, miR126 could be used to

mobilize malignant cells from the bone marrow and render them more easy targets for therapy. It was previously shown that the bone marrow cavity promotes the survival of many cells including tumor cells, and that such cells may easily die when removed from the bone marrow niche and moved to the blood. Therefore, this discovery could also change treatment of many cancers that arise within the bone marrow or metastasize to the bone. Since the mechanism by which miR126 promotes HSPCs/tumor cell mobilization is attributable to the inhibition of VCAM-1 expression, miR126 could be used to treat inflammatory states where the expression of VCAM1 provides an anchor for inflammatory cells at sites of inflammation.

Potential Commercial Applications:

• Method of mobilizing hematopoietic stem/progenitor cells (HSPCs) from the bone marrow to the blood

• Use in hematopoietic cell transplantation and treatment of hematopoietic deficiency, hematological failure, and cancer treatments

• To mobilize cancer cells from the bone marrow and thus serve as adjuvant cancer therapy

• As an anti-inflammatory agent to reduce inflammatory cell infiltrates at sites of inflammation

Competitive Advantages: Mobilization of HSPCs yielding high-level, selective and rapid mobilization of HSPCs to the peripheral blood.

Development Stage:

• Pre-clinical

• In vivo data available (animal)

Inventors: Giovanna Tosato and Ombretta Salvucci (NCI)

Publication: Salvucci O, et al. MicroRNA126 contributes to G-CSF-induced hematopoietic progenitor cell mobilization by reducing VCAM-1 expression. Haematologica. 2012 Jan 22; Epub ahead of print. [PMID 22271895]

Intellectual Property: HHS Reference No. E-197-2011/0 — U.S. Provisional Application No. 61/542,468 filed 02 Oct 2011

Licensing Contact: Whitney Hastings; 301-451-7337; hastingw@mail.nih.gov

Collaborative Research Opportunity: The National Cancer Institute is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize miR126 and Mobilization of Hematopoietic Stem/Progenitor Cells. For collaboration opportunities, please contact John Hewes, Ph.D. at hewesj@mail.nih.gov.

Use of Frizzled (Fzd) as a Biomarker for Cancer Patient Selection and Therapeutic Intervention

Description of Technology: Personalized medicine is becoming more important in the diagnosis and treatment of diseases, particularly cancer. One signaling pathway which has been demonstrated to be involved in cancer is the Wnt/beta catenin signaling pathway. The NIH scientists associated with this technology have identified a potential new biomarker for cancer based on their investigation of the role of the secreted frizzled related proteins, sFRP's, which are known to play a role in Wnt/beta catenin signaling. In particular, the scientists have determined that different Frizzled receptors (Fzd) have different and opposite roles in Wnt/beta catenin signaling with the expression of certain

Fzd receptors, e.g. Fzd5, being associated with an increase in Wnt/beta catenin signaling and the expression of other Fzd receptors, e.g., Fzd2, being associated with a decrease in Wnt/beta catenin signaling.

Potential Commercial Applications:

• As a diagnostic to identify patients for whom frizzled antagonists may be useful therapeutic agents.

• As an aid for determining the appropriate level of frizzled antagonist to be given to a patient.

• As an aid in drug discovery for the evaluation of Wnt/frizzled antagonists.

Competitive Advantages:

• Ability to stratify clinical trials by identifying patients whose tumor has the appropriate molecular signature

• Ability to provide an appropriate dosing regimen based on the specificity of the drug for a particular Fzd

• Tool for further characterizing cancer drugs which target the Wnt/beta catenin pathway providing for more well characterized and specific drugs

Development Stage:

• Early-stage

• In vitro data available

Inventors: Jeffrey S. Rubin, Charles P. Xavier, and Maria Melikova (all of NCI)

Intellectual Property:

• HHS Reference No. E-196-2011/0 — U.S. Provisional Application No. 61/497,513 filed 15 Jun 2011

• HHS Reference No. E-196-2011/1 — U.S. Provisional Application No. 61/499,684 filed 21 Jun 2011

Related Technologies: NIH also has other intellectual property (IP) related to sFRP which may be useful in conjunction with the use of the biomarker described above. The IP includes patents belonging to:

• HHS Reference No. E-160-1997/2 — U.S. Patents 6,479,255 and 7,183,377

• HHS Reference No. E-014-2000/0 — U.S. Patents 6,600,018, 7,223,853, and 7,947,651

• HHS Reference No. E-060-2000/1 — U.S. Patent 7,488,710; Foreign patent protection is also available (PCT/US02/00869, published as WO 02/055547)

Licensing Contact: Susan S. Rucker; 301-435-4478; ruckersu@mail.nih.gov

Collaborative Research Opportunity: The National Cancer Institute is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize Regulation of Wnt and Frizzled signaling by secreted Frizzled-related proteins. For collaboration opportunities, please contact John Hewes, Ph.D. at hewesj@mail.nih.gov.

A Highly Potent Human sRAGE Protein for Treating Vascular Disease, Injury, or Inflammation

Description of Technology: The receptor for advanced glycation end products (RAGE) is a cell surface protein that triggers signaling pathways leading to inflammation. RAGE-stimulated inflammation can contribute to adverse vascular conditions, such as atherosclerosis and restenosis. The soluble version of RAGE

(sRAGE) binds the same target molecules (advanced glycation end products), but cannot activate inflammatory signaling pathways. For this reason, sRAGE is thought to act as a decoy for RAGE. sRAGE reduces inflammation and pathogenic consequences associated with RAGE signaling. The administration of sRAGE has been used to treat atherosclerosis and arterial restenosis in animal models. The inventors established a way to produce human sRAGE with more than 1000-fold greater potency than current methods. Production of full length human sRAGE in cultured mammalian cells enables addition of mammalian post-translational modifications that dramatically enhance potency. This invention covers methods of production, the resulting modified sRAGE molecules, and methods of using this highly potent sRAGE for treating adverse vascular conditions.

Potential Commercial Applications:

• Atherosclerosis therapeutics

• Prevention of vascular inflammation

• Treating vascular injuries due to angioplasty or traumatic injury

• Treating vascular complications of Diabetes mellitus

• Alzheimer's Disease treatment based on amyloid-beta protein binding

Competitive Advantages:

• Greater than 1000-fold increased potency over sRAGE produced in insect cells

• Readily scalable production as a recombinant protein secreted from CHO cells

• Simple affinity purification method

Development Stage:

• Early-stage

• Pre-clinical

• In vitro data available

• In vivo data available (animal)

Inventors: Li Lin, Sungha Park, Wen Wei, Rui-ping Xiao, and Mark Talan (NIA)

Publication: Lin L, et al. RAGE signaling in inflammation and arterial aging. Front Biosci. 2009 Jan 1;14:1403-1413. [PMID 19273137]

Intellectual Property: HHS Reference No. E-165-2011/0 — U.S. Provisional Application No. 61/582,574 filed 03 Jan 2012

Related Technology: HHS Reference No. E-016-2009/0 — U.S. Patent Application No. 12/652,395 filed 05 Jan 2010

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

Collaborative Research Opportunity: The National Institute on Aging, Laboratory of Cardiovascular Science, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize sRAGE. For collaboration opportunities, please contact Vio Conley, M.S. at conleyv@mail.nih.gov.

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Date

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Richard U. Rodriguez, M.B.A.
Director
Division of Technology Development and Transfer
Office of Technology Transfer
National Institutes of Health

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