proteases: cruzain, rhodesain, and TbCatB. J Med Chem. 2010 Jan 14;53(1):52–60. [PubMed: 19908842]

Patent Status: PCT Application No. PCT/US2009/063078 filed 03 Nov 2009, which published as WO 2010/059418 on 27 May 2010 (HHS Reference No. E–267–2008/0–PCT–02)

Licensing Status: Available for licensing.

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

Collaborative Research Opportunity: The NIH Chemical Genomics Center (NCGC) is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize appropriate lead compounds described in the patent application. Please contact Dr. Craig J. Thomas (*craigt@nhgri.nih.gov*) or Claire Driscoll (*cdriscol@mail.nih.gov*), Director of the NHGRI Technology Transfer Office, for more information.

A Novel, Inhibitory Platelet Surface Protein (TREM Like Transcript, TLT–1): New Target for the Treatment of Cancer, Infectious Diseases, Cardiac Diseases, and Platelet-Associated Disorders

Description of Technology: Triggering Receptors in Myeloid Cells (TREM) recently were discovered to modulate innate and adaptive immunity. Specifically, TREM1 amplifies the response to sepsis in innate immunity by activating neutrophils and other leukocytes; and TREM2 potentiates dendritic cell maturation in adaptive immunity.

This invention describes a novel, inhibitory platelet surface protein known as TREM like Transcript (TLT–1). TLT–1 is the first inhibitory receptor discovered to reside within the TREM gene locus. Structurally, TLT–1 also possesses inhibitory domains that indicate this regulatory function. TLT–1 is highly expressed in peripheral blood platelets and may modulate many other types of myeloid cells. Additionally, the invention describes specific, human, single chain antibodies (scFvs) that recognize TLT–1.

Applications

- This discovery implies the receptor has an important regulatory role in both innate and adaptive immunity.
- TLT–1 is a potential therapeutic target for thrombosis and other platelet-associated disorders, as well as immune disorders, cancer, septic shock, infectious disease, stroke, heart disease, myocardial infarction, vascular disorders.
- Detection of soluble TLT–1 in patient plasma suggests the protein is a marker of ongoing coagulopathies.
- Defective platelet aggregation in TLT–1 null mice confirms a role for the protein in regulation of thrombosis associated with inflammation.

Advantages

- *In vitro* proof of concept data available—Three of the anti-TLT–1 scFvs inhibit thrombin-induced aggregation of human platelets in a dose-dependent manner.
- Complete human origin of these antibodies suggests negligible immunogenicity and minimizes the problem of adverse immune responses in human therapy.
- Target validation is complete. TLT–1 null mice demonstrate defects in platelet aggregation with no gross bleeding defect.

Development Status: In vitro experiments completed. Target validation with null mice completed. *In vivo* animal studies with scFv are currently ongoing.

Inventors: Toshiyuki Mori *et al.* (NCI)

Related Publication: Giomarelli B, Washington VA, Chisholm MM, Quigley L, McMahon JB, Mori T, McVicar DW. Inhibition of thrombin-induced platelet aggregation using human single-chain Fv antibodies specific for TREM-like transcript-1. Thromb Haemost. 2007 Jun;97(6):955–963. [PubMed: 17549298]

Patent Status: U.S. Patent No. 7,553,936 issued on 30 Jun 2009 (HHS Reference No. E–177–2006/0–US–01)

Licensing Status: Available for licensing.

Licensing Contact: Betty B. Tong, PhD; 301–594–6565; *tongb@mail.nih.gov*.

Collaborative Research Opportunity: The National Cancer Institute's Molecular Targets Development Program is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize antibodies that react specifically with TLT–1. Please contact John D. Hewes, PhD at 301–435–3121 or *hewesj@mail.nih.gov* for more information.

Dated: December 21, 2010.

Richard U. Rodriguez,

Director, Division of Technology Development and Transfer, Office of Technology Transfer, National Institutes of Health.

[FR Doc. 2010–32629 Filed 12–27–10; 8:45 am]

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.

ADDRESSES: 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.

Engineered Biological Pacemakers

Description of Technology: A common symptom of many heart diseases is an abnormal heart rhythm or arrhythmia. While effectively improving the lives of many patients, implantable pacemakers have significant limitations such as limited power sources, risk of infections, potential for interference from other devices, and absence of autonomic rate modulation.

The technology consists of biological pacemakers engineered to generate normal heart rhythm. The biological pacemakers include cardiac cells or cardiac-like cells derived from embryonic stem cells or mesenchymal stem cells. The biological pacemakers naturally integrate into the heart. Their generation of rhythmic electric impulses involves coupling factors, such as cAMP-dependent PKA and Ca^{2+} -dependent CaMK II, which are regulatory proteins capable of modulating/enhancing interactions (*i.e.* coupling) of the sarcoplasmic reticulum-based, intracellular Ca^{2+} clock and the surface membrane voltage clock, thereby converting irregularly or rarely spontaneously active cells into pacemakers generating rhythmic excitations.

Applications: This technology can be utilized in heart disease characterized by arrhythmia or situations requiring an implantable cardiac pacemaker.

Advantages: In contrast to current implantable cardiac pacemaker technology, this technology is not externally powered, has a lower risk of infection, has decreased potential for interference from other devices, and has full autonomic rate modulation.

Development Status: Early stage.

Inventors: Victor A. Maltsev *et al.* (NIA)

Publications:

1. VA Maltsev and EG Lakatta. Synergism of coupled subsarcolemmal Ca^{2+} clocks and sarcolemmal voltage clocks confers robust and flexible pacemaker function in a novel pacemaker cell model. Am J Physiol Heart Circ Physiol. 2009 Mar;296(3):H594–H615. [PubMed: 19136600]

2. VA Maltsev and EG Lakatta. Dynamic interactions of an intracellular Ca^{2+} clock and membrane ion channel clock underlie robust initiation and regulation of cardiac pacemaker function. Cardiovasc Res. 2008 Jan 15;77(2):274–284. [PubMed: 18006441]

Patent Status: PCT Application No. PCT/US2010/035823 filed 21 May 2010 (HHS Reference No. E–134–2009/0–PCT–02).

Licensing Status: Available for licensing.

Licensing Contact: Fatima Sayyid, M.H.P.M.; 301–435–4521; *Fatima.Sayyid@nih.hhs.gov.*

Collaborative Research Opportunity: The National Institute on Aging, Cellular Biophysics Section, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize this technology. Please contact Vio Conley at 301–496–0477 or *conleyv@mail.nih.gov* for more information.

Method of Detecting and Quantifying Contaminants in Heparin Preparations

Description of Technology: Heparin is a naturally occurring acidic carbohydrate produced commercially from extracts of animal tissues (such as bovine lung or porcine intestine) and is used in the treatment of a wide range of diseases in addition to their classic anticoagulant activity. Heparin is also used to coat many medical devices, such as catheters, syringes, stents and filters. Recently, certain lots of heparin were associated with serious side effects and adverse events. Recalls were issued in multiple countries and it became evident that there was an extensive problem with heparin manufacture.

Traditional tests may not be able to determine the presence of contaminant(s) without lyophilizing and concentrating each sample and may not be suitable for testing finished medical devices. Therefore, there is a demonstrated need to develop other assay methods for detecting contaminating oversulfated compounds of any source in heparin and heparin derived products.

This technology relates to methods for detecting and/or quantifying oversulfated glycosaminoglycans based on inhibition of nucleic acid polymerases and resistance to enzymatic degradation. It also relates to the use of these methods to screen and quantify pharmaceutical preparations such as heparin preparations for oversulfated contaminants.

Potential Applications: Robust, simple and effective method for detecting and optionally quantifying oversulfated contaminants in heparin preparations.

Development Status: The method has been developed and qualified for sensitivity and identity, but full validation and commercialization have not been undertaken.

Inventor: Daniela Verthelyi *et al.* (FDA)

Publication: C Tami, M Puig, JC Reepmeyer, H Ye, DA D'Avignon, L Buhse, D Verthelyi. Inhibition of Taq polymerase as a method for screening heparin for oversulfated contaminants. Biomaterials 2008 Dec;29(36):4808–4814. [PubMed: 18801571]

Patent Status: PCT Application No. PCT/US2009/056263 filed 08 Sep 2009, which published as WO 2010/030608 on 18 Mar 2010 (HHS Reference No. E–227–2008/0–PCT–02).

Licensing Status: Available for licensing.

Licensing Contact: Fatima Sayyid, M.H.P.M.; 301–435–4521; *Fatima.Sayyid@nih.hhs.gov.*

Collaborative Research Opportunity: The FDA, Division of Therapeutic Proteins, Laboratory of Immunology, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize this high throughput screening test for oversulfated glycosamineglycan contaminants in heparin. Please contact Daniela Verthelyi at *daniela.verthelyi@fda.hhs.gov* or Alice Welch at *alice.welch@fda.hhs.gov* for more information.

Method for the Diagnosis and Prognosis of Age-Related Cardiovascular Disorders

Description of Technology: NIH investigators have discovered a method for the diagnosis and prognosis of cardiovascular aging. Current methodologies include the measurement of patient lipid profiles or expression of up to two proteins. In contrast, this technology utilizes the expression levels of a panel of proteins not previously known to be related to cardiovascular aging and may prove to be a more accurate diagnostic or prognostic of cardiovascular aging than currently available tests or it may improve the accuracy of currently available tests when used in concert.

The technology relates to methods for determining susceptibility to having an extremely common age-associated vascular disorder. It also describes the subsequent use of these proteins as markers for disease. While the underlying cellular and molecular mechanisms of age-related vascular disease remain largely undefined, the expression levels of the genes described in this technology have been empirically determined to differ between healthy and age-inflamed arterial tissue. Further, this technology includes a companion mass spectroscopic-based methodology for reproducible quantification of specific expression levels of interest.

Application: Diagnosis of age-related vascular disorder.

Development Status: Early stage.

Inventors: Mingyi Wang *et al.* (NIA).

Patent Status: PCT Application No. PCT/US2010/024816 filed 19 Feb 2010, which published as WO 2010/096713 on 26 Aug 2010 (HHS Reference No. E–219–2008/0–PCT–02).

Licensing Status: Available for licensing.

Licensing Contact: Fatima Sayyid, MHPM; 301–435–4521; *Fatima.Sayyid@nih.hhs.gov.*

Collaborative Research Opportunity: The National Institute on Aging, Cardiovascular Biology Unit—Vascular Group, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize idea of how to assess and retard accelerated arterial aging and its attendant risks for atherosclerosis and hypertension. Please contact Vio Conley at 301–496–0477 or *conleyv@mail.nih.gov* for more information.

Identification of Subjects Likely To Benefit From Copper Treatment

Description of Technology: Menkes disease is an infantile onset X-linked recessive neurodegenerative disorder caused by deficiency or dysfunction of a copper-transporting ATPase, ATP7A. The clinical and pathologic features of this condition reflect decreased activities of enzymes that require copper as a cofactor, including dopamine-β-hydrolase, cytochrome c oxidase and lysyl oxidase. Recent studies indicate that ATP7A normally responds to N-methyl-D-aspartate receptor activation in the brain, and an impaired response probably contributes to the neuropathology of Menkes disease. Affected infants appear healthy at birth and develop normally for 6 to 8 weeks. Subsequently, hypotonia, seizures and failure to thrive occur and death by 3 years of age is typical. Occipital horn syndrome (OHS) is also caused by mutations in the copper transporting ATPase ATP7A, although its symptoms are milder than Menkes syndrome, including occipital horns and lax skin and joints.

Treatment with daily copper injections may improve the outcome in Menkes disease if commenced within days after birth; however, newborn screening for this disorder is not available and early detection is difficult because clinical abnormalities in affected newborns are absent or subtle. Moreover, the usual biochemical markers (low serum copper and ceruloplasmin) are unreliable predictors in the neonatal period, since levels in healthy newborns are low and overlap with those in infants with Menkes disease. Although molecular diagnosis is available, its use is complicated by the diversity of mutation types and the large size of ATP7A (about 140kb). Thus, there is a need for improved methods for early detection of infants with Menkes disease or OHS in order to improve outcomes.

This technology relates to methods of identifying individuals who may benefit from treatment with copper, particularly those having Menkes disease or Occipital Horn Syndrome.

Inventor: Stephen G. Kaler (NICHD).

Publication: SG Kaler, CS Holmes, DS Goldstein, JR Tang, SC Godwin, A Donsante, CJ Liew, S Sato, N Patronas. Neonatal diagnosis and treatment of Menkes disease. N Engl J Med. 2008 Feb 7;358(6):605–614. [PubMed: 18256395]

Patent Status: PCT Application No. PCT/US2008/078966 filed 06 Oct 2008, which published as WO 2010/042102 on 15 Apr 2010 (HHS Reference No. E–186–2008/0–PCT–01).

Licensing Status: Available for licensing.

Licensing Contact: Fatima Sayyid, M.H.P.M.; 301–435–4521; *Fatima.Sayyid@nih.hhs.gov.*

Collaborative Research Opportunity: The National Institute of Child Health and Human Development, Division of Intramural Research, Molecular Medicine Program, Unit on Pediatric Genetics, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize population-based newborn screening for Menkes disease and related disorders of copper transport in order to identify subjects likely to benefit from copper injections and other treatments. Please contact Alan Hubbs, PhD at 301–594–4263 or *hubbsa@mail.nih.gov* for more information.

Dated: December 21, 2010.

Richard U. Rodriguez,

Director, Division of Technology Development and Transfer, Office of Technology Transfer, National Institutes of Health.

[FR Doc. 2010–32669 Filed 12–27–10; 8:45 am]

BILLING CODE 4140–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

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AGENCY: National Institutes of Health, Public Health Service, HHS.

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A New Class of Antibiotics: Natural Inhibitors of Bacterial Cytoskeletal Protein FtsZ to Fight Drug-susceptible and Multi-drug Resistant Bacteria

Description of Technology: The risk of infectious diseases epidemic has been alarming in recent decades. This is not only because of the increase incident of so-called "super bugs," but also because of the scarce number of potential antibiotics in the pipeline. Currently, the need for new antibiotics is greater than ever! The present invention by the National Institute of Diabetes and Digestive and Kidney Disease (NIDDK), part of the National Institute of Health (NIH), address this urgent need. The invention is a new class of chrysophaentin antibiotics that inhibit the growth of broad-spectrum, drug-susceptible, and drug-resistant bacteria.

Derived from the yellow algae *Chrysophaeum taylori,* the inventor has extracted 8 small molecules of natural products and tested for antimicrobial activity against drug resistant bacteria, methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *Enterococcus faecalis* (VRE), as well as other drug susceptible strains. Structurally, the molecules represent a new class of antibiotic that also likely work through a distinct mechanism of action from that of current antibiotics, which is key for the further development of antibiotics that inhibit drug-resistant strains.

The bacterial cytoskeletal protein FtsZ is a GTPase and has structural homology to the eukaryotic cytoskeletal protein tubulin, but lacks significant sequence similarity. FtsZ is essential for bacterial cell division. It is responsible for Z-ring assembly in bacteria, which leads to bacterial cell division. Experiments show that the disclosed compounds are competitive inhibitors of GTP binding to FtsZ, and must bind in the GTP-binding site of FtsZ. Inhibition of FtsZ stops bacterial cell division and is a validated target for new antimicrobials. FtsZ is highly conserved among all bacteria, making it a very attractive antimicrobial target.

Applications:

- Therapeutic potential for curing bacterial infections in vivo, including for clinical and veterinary applications.
- Antiseptics in hospital settings.
- Since FtsZ is structurally similar, but does not share sequence homology to eukaryotic cytoskeletal protein tubulin, these compounds may have antitumor properties against some cancer types or cell lines.

Advantages: