Licensing Contacts

• Uri Reichman, PhD, MBA; 301–435–4616; *UR7a@nih.gov*.

• John Stansberry, PhD; 301–435–5236; *Stansbej@mail.nih.gov*.

Meningococcal and Pneumococcal Conjugate Vaccine and Method of Using Same

Description of Invention: Pneumococcal diseases are a major public health problem all over the world. The etiological agent, *Streptococcus pneumoniae* (the pneumococcus) is surrounded by a polysaccharide capsule. Differences in the composition of this capsule permit serological differentiation between about 90 capsular types, some of which are frequently associated with pneumococcal disease, others rarely. Invasive pneumococcal infections include pneumonia, meningitis and febrile bacteremia; among the common non-invasive manifestations are otitis media, sinusitis and bronchitis. At least 1 million children die of pneumococcal disease every year, most of these being young children in developing countries. Vaccination is the only available tool to prevent pneumococcal disease. The recent development of widespread microbial resistance to essential antibiotics underlines the urgent need for more efficient pneumococcal vaccines.

Meningococcal disease is a contagious bacterial disease caused by the meningococcus (*Neisseria meningitidis*). It is spread by person-to-person contact through respiratory droplets of infected people. There are 3 main clinical forms of the disease: the meningeal syndrome, the septic form and pneumonia. The onset of symptoms is sudden and death can follow within hours. In as many as 10–15% of survivors, there are persistent neurological defects, including hearing loss, speech disorders, loss of limbs, mental retardation and paralysis. Up to 5–10% of a population may be asymptomatic carriers. These carriers are crucial to the spread of the disease as most cases are acquired through exposure to asymptomatic carriers. Waning immunity among the population against a particular strain favors epidemics, as do overcrowding and climatic conditions such as dry seasons or prolonged drought and dust storms. The disease mainly affects young children, but is also common in older children and young adults. The disease occurs sporadically throughout the world with seasonal variations and accounts for a proportion of endemic bacterial meningitis. However, the highest burden of the disease is due to the cyclic epidemics occurring in the African meningitis belt.

With the burden of *S. pneumoniae* and *N. meningitidis* infection on the public health system at a global scale, it is desirable to have a single vaccine that is effective to prevent disease resulting from the infection of both pathogens. This application claims immunogenic compositions for inducing an immune response to two different microorganisms, *S. pneumoniae* and *N. meningitidis.* The application also claims conjugate vaccines comprising at least one *N. meningitidis* capsular polysaccharide conjugated to a recombinant pneumococcal protein.

Applications: Conjugate vaccine for the prevention and/or therapy of meningococcal and pneumococcal infections.

Advantages

• Rapid production time.

• Higher-yielding manufacturing method.

• Low manufacturing cost.

Development Status: Preclinical studies have been conducted by the inventors.

Inventors

• Stanley S. Tai (Howard University).

• Che-Hung Robert Lee (FDA).

Patent Status: HHS Reference No. E–030–2010/0—

• U.S. Patent Application No. 12/425,232 filed 16 Apr 2009.

• PCT/US2010/031083 filed 14 Apr 2010.

Licensing Status: Available for licensing.

Licensing Contact: Daniel G. McCabe; Associate General Counsel for Business Transactions; Howard University, Office of the General Counsel; 2400 6th Street, NW., Suite 321; Washington, DC 20059; Office: (202) 806–2650; Fax: (202) 806–6357; E-mail: *dmccabe@howard.edu*.

Dated: February 16, 2011.

Richard U. Rodriguez,

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

[FR Doc. 2011–4171 Filed 2–23–11; 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.

Terahertz Spatial Light Modulator System for Adaptive Near-Field Imaging

Description of Technology: The invention offered for licensing is in the field of imaging microscopes and relates to a terahertz light modulator system, and in particular to a terahertz spatial light modulator system for adaptive near-field imaging.

More specifically, the invention relates to a spatial light modulator system for adaptive near-field imaging having an optical source for transmitting an optical beam through a filter which is controlled to convert the optical light beam into a filtered optical light beam to define one or more transmission pathways through a photoconductive material. The system further includes a terahertz light source for transmitting a terahertz beam through one or more transmission pathways defined by the filtered optical light beam through the photoconductive material for illuminating and scanning the sample without the use of moving structural components. The device would allow micron-scale spatial resolution, would remove the need to mechanically scan a sample, and would allow automatic adjustment of image resolution and transmitted terahertz power. The near-field terahertz microscope of the invention could have a compact, fiber-coupled sensor head with no moving parts—ideal for scientific, medical, and industrial applications like crystal growth optimization, skin cancer diagnosis, and semiconductor chip inspection. In one application, such as "one-cut" surgery, the compact sensor

head of the terahertz imaging system has the capability of distinguishing healthy cells from cancerous cells with micron-scale spatial resolution by immediately identifying a skin cancer margin without the need for laboratory work or additional surgery. In another application, the terahertz imaging system may be used in nondestructive semiconductor chip inspection since the terahertz imaging system provides micron-scale spatial resolution.

Applications:

• Biomedical research applications (living tissues have distinctive terahertz absorption signals)

• Clinical applications like diagnostics of skin cancer (skin cancer and normal skin reflect terahertz radiation differently)

• Industrial applications like crystal growth optimization

• Industrial applications like semiconductor chip inspection.

Advantages: The system provides micron-scale spatial resolution, while removing any need to mechanically scan samples (it is equipped with a fiber-coupled sensor head), and at the same time allows automatic adjustment of image resolution and transmitted terahertz power.

Development Status: In development. Prototype is being built.

Inventors: Hari Shroff et al. (NIBIB).

*Relevant Publication*s:

1. Mair S, Gompf B, Dressel M. Microspectroscopy and imaging in the THz range using coherent CW radiation. Phys Med Biol. 2002 Nov 7;47(21):3719–3725. [PubMed: 12452559]

2. Chen Q, Jiang Z, Xu GX, Zhang XC. Near-field terahertz imaging with a dynamic aperture. Opt Lett. 2000 Aug 1;25(15):1122–1124. [PubMed: 18064291]

3. Wallace VP, Fitzgerald AJ, Shankar S, Flanagan N, Pye R, Cluff J, Arnone DD. Terahertz pulsed imaging of basal cell carcinoma ex vivo and in vivo. Br J Dermatol. 2004 Aug;151(2):424–432. [PubMed: 15327550]

4. Hu BB, Nuss MC. Imaging with terahertz waves. Opt Lett. 1995 Aug 15;20(16):1716–1718.

Patent Status: U.S. Provisional Application No. 61/425,007 filed 20 Dec 2010 (HHS Reference No. E–243–2010/0–US–01).

Licensing Status: Available for licensing.

Licensing Contact:

• Uri Reichman, PhD, MBA; 301–435–4616; *UR7a@nih.gov.*

• Michael Shmilovich, Esq.; 301–435–5019; *ShmilovichM@mail.nih.gov.*

Collaborative Research Opportunity: The National Institute of Biomedical Imaging and Bioengineering is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize this technology. Please contact Hari Shroff at *hari.shroff@nih.gov* or 301–435–1995 for more information.

Versatile Melanoma Antigen Family A3 (MAGE–A3) Specific Human T Cell Receptors To Treat Cancer That Also Recognize Other MAGE–A Antigen Superfamily Members

Description of Technology: Current approaches for treating cancer can also generate harsh side effects in patients and many cancer patients do not respond to generalized chemotherapy and radiation. New and improved therapeutic strategies need to be characterized by reduced side-effects and enhancements in specific anti-tumor activity in individual patients. Adoptive immunotherapy is a promising new approach to cancer treatment that engineers an individual's innate and adaptive immune system to fight against specific diseases, such as cancer. Scientists are aiming to improve cell transfer therapies by targeting an increasing collection of tumor antigens with more effective immune cell cultures.

T cell receptors (TCRs) are specialized proteins that recognize antigens in the context of infected or transformed cells and activate T cells to mediate an immune response and destroy abnormal cells. TCRs consist of a variable domain that recognizes the antigen and a constant region that anchors the TCR to the membrane and transmits recognition signals by interacting with other proteins. When a TCR is activated by recognizing its antigen, such as a tumor antigen, signaling pathways are triggered in the cell to produce cytokines that mediate the immune response.

Scientists at the National Institutes of Health (NIH) have developed T cells genetically engineered to recognize melanoma antigen family A3 (MAGE–A3) peptide antigens. MAGE–A superfamily antigens, including MAGE–A3, are expressed primarily by tumor cells from a variety of cancers. Other than germ cells of the testis, normal cells do not express MAGE–A3 and other MAGE–A proteins, which makes these antigens ideal targets for developing cancer immunotherapies. There are twelve (12) known MAGE–A genes designated A1–A12. The normal function of MAGE–A3 is not completely known, but in cancerous cells it appears to mediate fibronectin-controlled tumor growth and spreading. MAGE–A3 is one of the most widely expressed cancer testis antigens (CTAs) on human tumors and its expression increases as the cancer progresses to more advanced stages. The T cell receptors (TCRs) developed by these NIH scientists have specificity for MAGE–A3 and MAGE–A12 and deliver a robust immune response when they encounter tumor cells expressing these antigens. These TCRs also recognize MAGE–A2 and/or MAGE–A6, but to a lesser extent that MAGE–A3 and MAGE–A12. The ability to recognize antigens from multiple MAGE–A family members could allow these TCRs to be utilized in the treatment of multiple types of cancer in a wide array of cancer patients. Infusing cancer patients with MAGE–A3 specific T cells via adoptive immunotherapy could prove to be a powerful approach for selectively attacking tumors without generating toxicity against noncancerous cells.

Applications:

• Immunotherapeutics to treat and/or prevent the recurrence of a variety of human cancers, including melanoma, lung cancers, head and neck cancers, liver cancers, and multiple myeloma, by adoptively transferring the gene-modified T cells into patients whose tumors express a MAGE–A family member protein recognized by this TCR.

• A drug component of a combination immunotherapy regimen aimed at targeting specific tumor-associated antigens, including MAGE–A3, MAGE–A12, and MAGE–A2 and/or MAGE–A6 expressed by cancer cells within individual patients.

• A research tool to investigate signaling pathways in MAGE–A antigen expressing cancer cells.

• An *in vitro* diagnostic tool to screen for cells expressing a MAGE–A antigens.

Advantages:

• *Selective toxicity for tumor cells*—MAGE–A3 and other MAGE–A proteins are only expressed on testis germ cells and tumor cells. Thus, infused cells expressing an anti-MAGE–A3 TCR should target MAGE–A3-expressing tumor cells with little or no toxicity to normal cells. Immunotherapy with these T cells should yield little or no harsh side effects to patients.

• *Ability to recognize multiple MAGE–A antigens*—Since these MAGE–A3 directed TCRs can also recognize up to three (3) additional MAGE–A antigens (MAGE–A12, A2, and A6), cells expressing these TCRs are expected to be able to fight a larger range of tumor types. During treatment, if an infused anti-MAGE–A3 T cell culture encounters tumor cells expressing other recognized MAGE–A antigens, these T cells would not only

be capable of eliminating the MAGE–A3 expressing tumor cells, but MAGE–A12, MAGE–A2, and MAGE–A6 expressing cells as well. This versatility should allow these TCRs to be utilized to treat a broader range of cancer patients.

• *Expression on a majority of tumors* —MAGE–A3 is one of the most highly expressed cancer testis antigens (CTAs) on human tumors. For example, over half of melanoma tumors and non-small cell lung cancer cells express MAGE–A3. A large spectrum of cancer patients should be eligible for treatment with these MAGE–A3 TCRs should they prove successful in clinical studies.

Development Status: This technology is in an early clinical stage of development.

Inventors: Richard A. Morgan, *et al.* (NCI).

Publications:

1. N Chinnasamy *et al.* A TCR Targeting the HLA–A*0201–Restricted Epitope of MAGE–A3 Recognizes Multiple Epitopes of the MAGE–A Antigen Superfamily in Several Types of Cancer. J Immunol. 2011 Jan 15;186(2):685–696. [PubMed: 21149604]

2. V Cesson et al. MAGE–A3 and MAGE–A4 specific CD4(+) T cells in head and neck cancer patients: Detection of naturally acquired responses and identification of new epitopes. Cancer Immunol Immunother. 2010 Sept. 21, E-pub ahead of print, doi: 10.1007/s00262–010–0916-z. [PubMed: 20857101]

Patent Status: U.S. Provisional Application No. 61/405,668 filed 22 October 2010 (HHS Reference No. E–236–2010/0–US–01).

Related Technologies: T cell receptor technologies developed against other CTAs: E–304–2006/0 and E–312–2007/1 (anti-NY–ESO–1) and E–269–2010/0 (anti-SSX–2).

Licensing Status: Available for licensing.

Licensing Contact: Samuel E. Bish, PhD; 301–435–5282; *bishse@mail.nih.gov.*

Collaborative Research Opportunity: The National Cancer Institute Surgery Branch is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize the use of anti-MAGE–A T-cell receptors for the adoptive immunotherapy of cancer. Please contact John Hewes, PhD at 301–435–3121 or *hewesj@mail.nih.gov* for more information.

Selective 12–Human Lipoxygenase Inhibitors for the Treatment of Diabetes and Clotting

Description of Technology: This invention discloses small molecule inhibitors of human 12-lipoxygenase (12-hLO). 12-lipoxygenase expression, activation, and lipid metabolites have been implicated in type 1 and type 2 diabetes, cardiovascular disease, hypertension, Alzheimer's, and Parkinson's disease. The development of 12-hLO inhibitors may be a potent intracellular approach to decreasing the ability of platelets to form large clots in response to vessel injury or activation of the coagulation pathway. Thus, 12-hLO inhibition has the potential to attenuate platelet-mediated clot formation caused by diabetes and/or cardiovascular disease and significantly decrease the occurrence of myocardial infarction and death. Moreover, Type 1 and Type 2 diabetes are serious disorders that can lead to major complications and reduced lifespan. An unmet medical need is to identify new ways to protect beta cells in these metabolic disorders. A selective 12-hLO inhibitor could provide a new therapeutic approach to prevent or treat either form of diabetes.

Applications:

• Therapeutic developments (blood clots; Type 1 and Type 2 diabetes, cardiovascular disease, and neurodegenerative diseases)

• Inflammatory responses

Advantages:

• Small molecule (series of analogs can be derived in search of improved performances and/or different functions)

• Selective inhibitor of human 12-lipoxygenase

Market:

• Metabolic disorders

• Neurodegeneration

• Research tool—screening for 12-lipoxygenase-mediated responses in various human cell lines

Development Status: Pre-clinical; no animal data.

Inventors: David J Maloney (NHGRI); Ajit Jadhav (NHGRI); Ganesha Rai (NHGRI); Anton Simeonov (NHGRI); Theodore Holman (University California Santa Cruz); Jerry Nadler (Eastern Virginia Medical School); Michael Holinstat (Thomas Jefferson University).

Patent Status: U.S. Provisional Application No. 61/345,708 filled 18 May 2010 (HHS Reference No. E–134–2010/0–US–01).

Licensing Status: Available for licensing.

Licensing Contact: Steven H. Standley, PhD 301–435–4074; *sstand@mail.nih.gov*.

Gene Expressed in Prostate Cancer and Methods of Use

Description of Technology: Prostate cancer is the second leading cause of cancer-related deaths among males in the United States. There are approximately two hundred and fifteen thousand (215,000) newly diagnosed cases of prostate cancer and thirty thousand (30,000) prostate cancer-related deaths each year, underscoring the importance of addressing this deadly disease. Although there are diagnostic tests in place for identifying the potential for developing prostate cancer, even the most widely accepted diagnostic for detecting cancer (prostate-specific antigen or PSA) is capable of producing a false negative result. Furthermore, current treatments are invasive and may produce deleterious side-effects. Therefore, there is a clear need to identify and develop new and effective diagnostics and treatments for prostate cancer.

This technology concerns the identification of a novel protein that is specifically expressed on prostate tissue: Novel Gene Expressed in Prostate (NGEP). Because of its selective expression on prostate tissue, NGEP represents a potential target in the fight against prostate cancer. Monoclonal antibodies that specifically recognize NGEP have been developed in conjunction with the identification of the protein. These antibodies can be used as both diagnostic agents and therapeutic agents.

Applications:

• Antibodies to NGEP can be used as diagnostic agents to identify metastatic prostate tissue, either alone or in combination with other diagnostic antibodies

• Antibodies to NGEP can also be used therapeutically to specifically target cytotoxic agents to prostate cancer cells or to induce antibody-dependent cell-mediated cytotoxicity (ADCC)

• Antibodies to NGEP can be used as research reagents for identifying prostate tissue, including cancerous tissue

Advantages:

• The selective expression of NGEP allows the specific detection and recognition of prostate tissue, which is useful in both diagnostic and therapeutic applications

• Combining the detection of NGEP with other prostate cancer diagnostic agents may reduce the incidence of a false negative diagnosis

• The use of NGEP antibodies in targeted therapy can decrease the non-specific killing of non-cancerous cells, thereby decreasing side-effects

associated with current prostate cancer therapies

Development Status: Preclinical stage of development.

Inventors: Pastan (NCI) *et al.*

Patent Status:

• US Patent 7,816,087 (E–005–2002/0–US–03)—Issued

• US Patent Application 12/193,604 (E–005–2002/0–US–05)—Allowed

• EP Patent Application 02795643.2 (E–005–2002/0–EP–04)—Pending

For more information, see:

• Das *et al.* "Topology of NGEP, a prostate-specific cell:cell junction protein widely expressed in many cancers of different grade level." *Cancer Res.* 2008 Aug 1; 68(15):6306–12

• Das *et al.* "NGEP, a prostate-specific plasma membrane protein that promotes the association of LNCaP cells." *Cancer Res.* 2007 Feb 15; 67(4):1594–601

• Bera *et al.* "NGEP, a gene encoding a membrane protein detected only in prostate cancer and normal prostate." *Proc Natl Acad Sci U S A.* 2004 Mar 2; 101(9):3059–64.

Licensing Status: Available for licensing

Licensing Contact: David A. Lambertson, PhD; 301–435–4632; *lambertsond@mail.nih.gov*.

Stem Cells That Transform To Beating Cardiomyocytes

Description of Technology: Many people die each year of congestive heart failure occurring from a variety of causes including cardiomyopathy, myocardial ischemia, congenital heart disease and valvular heart disease resulting in cardiac cell death and myocardial dysfunction. When cardiomyocytes are not replaced in adult myocardial tissue, physiologic demands on existing, healthy cardiomyocytes can lead to hypertrophy. Heart transplants have been the only recourse for patients in end-stage heart disease however this is complicated by lack of donors, tissue incompatibility and high cost.

An alternative approach to heart transplantation is to generate cardiomyocytes from stem cells *in vitro* that can be used in the treatment of cardiac diseases characterized by myocardial cell death or dysfunction.

This invention discloses a novel isolated population of stem cells, called spoc cells, isolated from skeletal muscle, that can be induced, either *in vivo* or *in vitro,* to differentiate into cardiomyocytes. Spoc cells may be differentiated and utilized for screening agents that affect cardiomyocytes and as therapeutic agents in the treatment of cardiac MI.

Potential Applications and Advantages: This invention is an alternative approach to heart transplantation which is typically complicated by lack of donors, tissue incompatibility and high cost.

Inventors: Neal D. Epstein (NHLBI), *et al.*

Related Publication: SO Winitsky, *et al.* Adult murine skeletal muscle contains cells that can differentiate into beating cardiomyocytes in vitro. PLoS Biol. 2005 Apr;3(4):e87, doi:10.1371/journal.pbio.0030087. [PubMed: 15757365]

Patent Status:

• Issued Australian Patent No. 2002337949 (HHS Ref. No. E–329–2001/0–AU–03)

• Issued Japanese Patent No. 4377690 (HHS Ref. No. E–329–2001/0–JP–04)

• Allowed Canadian Patent Appl. No. 2464088 (HHS Ref. No. E–329–2001/0–CA–05)

Licensing Status: Available for licensing.

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

Dated: February 16, 2011.

Richard U. Rodriguez,

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

[FR Doc. 2011–4170 Filed 2–23–11; 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.

Recombinant BoCPB: An Enzymatic Reagent for Removing Disordered, Positively Charged C-terminal Residues From Recombinant Proteins

Description of Technology: Affinity tags are commonly used to facilitate the purification of recombinant proteins, but concerns about the potential impact of the tags on the biological activity of the target proteins makes it necessary to remove them in most cases. Proteases with high sequence specificity, such as tobacco etch virus (TEV) protease, are typically used for this purpose. Affinity tags on the amino-terminus (N-terminal tag) can be cleaved by TEV protease to yield a recombinant protein product with only one nonnative residues on its C-terminus (usually G or S). In contrast, removal by TEV protease of tags added to the carboxy-terminus (C-terminal tag) of proteins has proven to be somewhat problematic, yielding a recombinant protein product with six nonnative residues on its C-terminus (ENLYFQ). Since C-terminal affinity tags are potentially very useful, particularly when used in combination with N-terminal tags in an "affinity sandwich" format, it would be very desirable to have a reagent to remove the C-terminal affinity tags without leaving extra nonnative residues behind.

Previously, the NIH inventors created a tagged version of a fungal carboxypeptidase from *Metarhizium anisopliae* (MeCPA) that is capable of removing histidine residues and many other types of amino acids from the C-termini of recombinant proteins. The only limitation of the MeCPA enzyme is that it does not remove positively charged residues (arginine and lysine). To overcome this drawback of MeCPA, the NIH inventors have now cloned, expressed and purified bovine carboxypeptidase B (BoCPB), which is specific for the removal of these positively charged residues. Like the genetically engineered MeCPA, the recombinant BoCPB has a C-terminal polyhistidine tag. This feature facilitates the purification of the enzyme, and, because this His-tag as been engineered to be immune to the action of MeCPA and BoCPB, it can be used to separate the enzymes from the products of a carboxypeptidase digest. By using a mixture of MeCPA and BoCPB, it should be possible to remove any short affinity tag along with disordered C-terminal residues of a recombinant protein with the exception of proline, which can be used as a "stop sign" to facilitate the