

• U.S. Provisional Application No. 61/004,940 filed 30 Nov 2007 (HHS Reference No. E-042-2007/0-US-01).
• PCT Application No. PCT/US2008/012064 filed 22 Oct 2008, which published as WO 2009/073068 on 11 Jun 2009 (HHS Reference No. E-042-2007/0-PCT-02).

Licensing Status: Available for licensing.

Licensing Contact: Charlene Sydnor, PhD; 301-435-4689; sydnorc@mail.nih.gov.

Collaborative Research Opportunity: The National Institute of Dental and Craniofacial Research, Craniofacial and Skeletal Diseases Branch, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize this technology. Please contact David W. Bradley, PhD at 301-402-0540 or bradleyda@nidcr.nih.gov for more information.

Gamma Substituted Peptide Nucleic Acids

Description of Invention: PNAs are nuclease/protease resistant synthetic nucleic acid analogs capable of forming very stable and highly sequence-specific complexes with DNA. Scientists at the NIH have developed novel peptide nucleic acids (PNAs) that contain a unique sidechain that can attach any small ligand, peptide, or carbohydrate to complementary DNA for rapid optimization. This invention could revolutionize the way in which multivalent display is used in research as well as help develop new medications.

Applications:

- Controlled interactions ensure only a single stoichiometry is attained.
- Simple access to a wide range of multivalent platforms.

Development Status: Early stage.

Inventors: Daniel Appella (NIDDK)

Patent Status: U.S. Provisional

Application No. 61/162,175 filed 20 Mar 2009 (HHS Reference No. E-151-2009/0-US-01).

Licensing Status: Available for licensing.

Licensing Contact: Charlene Sydnor, PhD; 301-435-4689; sydnorc@mail.nih.gov.

Collaborative Research Opportunity: The National Institute of Diabetes and Digestive and Kidney Diseases, Laboratory of Bioorganic Chemistry, Drug-Receptor Interactions Section, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize this technology. Please contact Dr. Daniel

Appella at appellad@niddk.nih.gov for more information.

Use of Modified Peptide Nucleic Acids for Visualizing DNA

Description of Technology: The compounds described in this technology may be useful in the development of nucleic acid detection kits for various pathogens.

Technologies for genomic detection most commonly use DNA probes to hybridize to target sequences, and require the use of Polymerase Chain Reaction (PCR) to amplify target sequences. Replacing the DNA probe with peptide nucleic acid (PNA) can greatly eliminate the need for PCR because the binding strength of PNAs to complementary DNA is stronger than DNA binding to complementary DNA. In addition, PNAs are nuclease and protease resistant, and form very stable and highly sequence-specific complexes with DNA.

This technology describes a method of making pure enantiomers of trans-tert-butyl-2-aminocyclopentylcarbamate (tcycp) and methods of modifying PNAs by incorporating tcycp compounds into the PNA. This technology may also be practical for detecting infectious agents such as anthrax, avian flu, tuberculosis (TB), severe acute respiratory syndrome (SARS), human papilloma virus (HPV) and human immunodeficiency virus (HIV).

Applications:

- Very stable diagnostic method to detect nucleic acids without using Polymerase Chain Reaction (PCR).
- Binding to complementary DNA can be seen by eye.
- Visual detection of anthrax has been shown.
- Useful for outside of a laboratory environment.

Development Status: Early stage.

Inventors: Daniel Appella *et al.* (NIDDK).

Patent Status: U.S. Patent Application No. 12/441,925 filed 19 Mar 2009 (HHS Reference No. E-308-2006/2-US-02).

Licensing Status: Available for licensing.

Licensing Contact: Charlene Sydnor, PhD; 301-435-4689; sydnorc@mail.nih.gov.

Collaborative Research Opportunity: The National Institute of Diabetes and Digestive and Kidney Diseases, Laboratory of Bioorganic Chemistry, Drug-Receptor Interactions Section, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize this technology. Please contact Dr. Daniel

Appella at appellad@niddk.nih.gov for more information.

Dated: March 1, 2010.

Richard U. Rodriguez,

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

[FR Doc. 2010-4759 Filed 3-4-10; 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.

Methods To Increase Stability of Recombinant Vaccinia-Vectored Vaccines and Increase Expression of a Foreign Gene Inserted in Such Vaccines

Description of Invention: The technology offered for licensing is in the field of vaccinia-based recombinant vaccines. In particular the invention relates to methods of stabilizing the recombinant virus, thus resulting in efficient production of the vaccine and efficient expression of the inserted gene. Stabilization of the recombinant virus is achieved by the insertion of the exogenous gene into an intergenic region (IGR) of the viral genome (i.e. Modified Vaccinia Ankara, MVA), where the IGR is flanked by open reading frames of conserved poxvirus genes. Furthermore, the invention relates to plasmids vectors useful to

insert the exogenous DNA into the genome of a vaccinia virus. Stability can be further enhanced by incorporating silent mutations that decrease the lengths of homopolynucleotide runs in the foreign gene.

Applications:

- Efficient production of vaccinia-vectored vaccines for infectious diseases and other diseases such as cancer.
- Efficient production of therapeutic proteins from vaccinia-vectored exogenous genes.

Advantages:

- Enhancing stability of foreign genes in vaccinia-vectored constructs.
- Increasing efficiency of vaccine production and gene expression.

Development Status: The invention is fully developed.

Market: Vaccines development based on vaccinia (e.g. MVA) vector inserted with foreign gene of immunologic or therapeutic interest has become one of the most promising approaches for vaccine development. Several companies established vaccine development programs based on this approach and many research laboratories around the world conduct research in the area. Improvements in the production process and in production yields, such as provided by the subject invention, are therefore of great significance for successful accomplishments in this area. Commercial products for veterinary use already exist. Many applications for human use are now in various stages of clinical trials, in particular applications for HIV, HPV in the infectious disease area and as therapeutic vaccine in the cancer field. The market potential for the subject technology is therefore vast.

Inventors: Bernard Moss *et al.* (NIAID).

Related Publication: LS Wyatt, PL Earl, W Xiao, J Americo, C Cotter, J Vogt, B Moss. Elucidating and minimizing the loss by recombinant vaccinia virus of human immunodeficiency virus gene expression resulting from spontaneous mutations and positive selections. *J Virol.* 2009 Jul;83(14):7176–7184. [PubMed: 19420086].

Patent Status: U.S. Provisional Application No. 61/252,326 filed October 16, 2009, entitled “Plasmid Shuttle Vector for Insertion of Foreign Genes into Del III Site of Modified Vaccinia Ankara (MVA) to Increase Stability of Foreign Gene Expression in This Site” (HHS Reference No. E-018–2010/0–US-01).

Related Technologies:

- WO 2008/142479 A2 (PCT/IB2007/004575)—“Intergenic Sites between Conserved Genes In The Genome of

Modified Vaccinia Ankara (MVA) Vaccinia Virus,” Bernard Moss *et al.*

- US Patent 6,998,252; US Patent 7,015,024; US Patent 7,045,136; US Patent 7,045,313—“Recombinant Vaccinia Virus Containing a Chimeric Gene Having Foreign DNA Flanked by Vaccinia Regulatory DNA,” Bernard Moss *et al.*

Licensing Status: Available for licensing.

Licensing Contacts: Uri Reichman, PhD, MBA; 301–435–4616; UR7a@nih.gov; or John Stansberry, Ph.D.; 301–435–5236; stansbej@mail.nih.gov.

Compounds That Interfere With the Androgen Receptor Complex: Use in Treating Prostate Cancer or Enlargements, Diabetes, and as Contraceptives

Description of Invention: Investigators at the National Institutes of Health (NIH) have discovered compounds that have potential as novel anti-androgen therapeutics. The immunophilin protein FKBP52 is part of a protein complex that helps fold the androgen receptor (AR) protein, a target for treating prostate cancer, and enhances its activity. Disruption of the FKBP52–AR interaction greatly reduces the activity of the AR. With the goal of finding potential therapeutic compounds that inhibit the FKBP52-mediated activation of AR, several small molecules were tested and found to be antagonists of FKBP52 and to inhibit AR activity in prostate cells. These compounds can serve as therapeutics for the treatment of prostate cancer and benign prostate enlargement. Moreover, FKBP52 is also implicated in the regulation of other hormone receptors so these compounds could be used to treat other hormone-dependent diseases such as diabetes or even used as contraceptives.

One of the standard treatments for prostate cancer makes use of anti-androgens, like bicalutamide, which compete for binding with the natural male hormones to AR and inhibit their proliferative activity. The problem with available anti-androgen drugs is that prostate tumors eventually become drug resistant resulting in so-called androgen-resistant prostate cancer. One cause of this is an increase in the levels of AR produced by the prostate cancer cells. A solution to this problem may lie in disrupting the protein folding of AR by interfering with its interaction with FKBP52 using these compounds.

Applications:

- Use of the compounds for treatment of prostate cancer and benign prostate enlargement

- Use of the compounds in treating insulin-independent diabetes

- Use of the compounds as male or female contraceptives

- Use in screening for compounds that inhibit of FKBP52-enhanced AR activity

Advantages:

- The compounds do not compete with androgens and specifically inhibit FKBP52-enhanced AR function
- Potential for synergistic use with conventional anti-androgens for treatment of androgen resistant prostate cancer

Development Status: Pre-clinical.

Market: Prostate cancer is the second most common type of cancer among men in the United States and is the second leading cause of cancer death in men. It was estimated that in 2009 there would be 192,280 new cases and 27,360 deaths from prostate cancer in the U.S. The prevalence of benign prostate enlargement is much greater as 50% men age 50 are affected and continues to increase with age.

Diabetes is a growing health problem in the U.S. and the world. The most recent estimate (2007 National Diabetes Fact Sheet) in the U.S. was that 7.8% of the population had diabetes and 1.6 million new cases per year would be diagnosed. In the population of people over 60 the prevalence of diabetes is even higher (23%).

Among the 64 million women of reproductive age in the U.S., the leading contraceptive method is hormonal contraceptives. Presently, there are no hormonal contraceptives to reversibly block fertility in men and there is a need for safe and effective hormonal methods as exist for women.

Inventors: Leonard M. Neckers (NCI), Marc Cox (UTEP) *et al.*

Relevant Publication: J Cheung-Flynn *et al.* Physiological role for the cochaperone FKBP52 in androgen receptor signaling. *Mol Endocrinol.* 2005 Jun;19(6):1654–1666. [PubMed: 15831525].

Patent Status: U.S. Provisional Application No. 61/242,541 filed 15 Sep 2009 (HHS Reference No. E-162–2009/0–US-01).

Licensing Status: Available for licensing.

Licensing Contact: Sabarni Chatterjee, Ph.D.; 301–435–5587; chatterjeesa@mail.nih.gov.

Collaborative Research Opportunity: The Center for Cancer Research, Urologic Oncology Branch, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize antagonists of FKBP52-dependent remodeling of the androgen

receptor. Please contact John D. Hewes, Ph.D. at 301-435-3121 or hewesj@mail.nih.gov for more information.

Radioprotectants and Tumor Radiosensitizers Targeting Thrombospondin-1 and CD47

Description of Invention: Radiation therapy not only damages cancer cells, but it also damages healthy cells and can cause serious side effects for patients. One effort to enhance the therapeutic potential of radiotherapy, while reducing its detrimental effects on normal tissue and maintaining tumor sensitivity, is centered upon the development of radioprotective agents.

NIH inventors previously discovered that when the secreted protein, thrombospondin-1 (TSP1) binds to its receptor CD47, this signaling pathway prevents nitric oxide from dilating blood vessels and increasing blood flow to organs and tissues. They found that blocking TSP1-CD47 interaction through the use of antisense morpholino oligonucleotides, peptides or antibodies has several therapeutic benefits; one of them being increased blood flow to ischemic tissues.

In the present technology, the inventors discovered that hindlimb irradiated TSP1 and CD47 null mice have less hair loss, and decreased cell death in muscle and bone marrow than untreated TSP1 and CD47 null mice. They also discovered that when irradiated human vascular cells are treated with antibodies towards TSP1 or CD47, viability and proliferative capacity are preserved. Furthermore, the inventors determined that irradiation of wild type mice following treatment with CD47 antisense morpholino resulted in decreased apoptosis in irradiated tissues at 24 hours, preservation of hematopoietic stem cell proliferative capacity in irradiated bone marrow, and less alopecia, ulceration, and desquamation at the end of eight weeks. These results led the inventors to propose that antagonists of TSP1 and/or CD47 preserve cell viability and tissue function following radiation treatment, and these antagonists may be useful as radioprotective agents to reduce side effects associated with radiation therapy. Remarkably, the same treatment dramatically enhanced the delay in melanoma and squamous carcinoma tumor regrowth following irradiation. Thus, these agents are radioprotective agents for normal tissue but radiosensitizers for tumor tissue.

The present technology describes the use of morpholinos, peptides and antibodies that block the TSP1/CD47 signaling pathway as radioprotectants

for normal tissue, radioenhancers for tumor tissue, and methods of selectively protecting normal tissue from damage caused by radiation exposure by contacting the tissue with these agents.

Applications:

- Protect normal tissue from damage following radiation therapy.
- Enhance tumor responses to radiotherapy.
- Enable use of higher therapeutic doses for radiotherapy of cancer.
- Protect personnel from radiation injuries resulting from occupational exposure to ionizing radiation, military exposure, or terrorist acts.

Development Status: Mouse data available. In vitro data available in mouse, bovine, porcine, and human cells.

Inventors: Jeffery S. Isenberg, David D. Roberts, Justin B. Maxhimer (NCI)

Related Publications:

1. JB Maxhimer, DR Soto-Pantoja, LA Ridnour, HB Shih, WG DeGraff, M Tsokos, DA Wink, JS Isenberg, DD Roberts. Radioprotection in normal tissue and delayed tumor growth by blockade of CD47 signaling. *Sci Transl Med.* 21 October 2009; Vol 1, Issue 3, pg. 3ra7; DOI:10.1126/scitranslmed.3000139.

2. JS Isenberg, G Martin-Manso, JB Maxhimer, DD Roberts. Regulation of nitric oxide signaling by thrombospondin-1: implications for anti-angiogenic therapies. *Nat Rev Cancer.* 2009 Mar;9(3):182-194. [PubMed: 19194382]

3. JS Isenberg, JB Maxhimer, F Hyodo, ML Pendrak, LA Ridnour, WG DeGraff, M Tsokos, DA Wink, DD Roberts. Thrombospondin-1 and CD47 limit cell and tissue survival of radiation injury. *Am J Pathol.* 2008;173(4):1100-1112. [PubMed: 18787106]

Patent Status: PCT/US2009/052902 filed 05 Aug 2009 (HHS Reference No. E-153-2008/0-PCT-02).

Licensing Status: Available for licensing.

Licensing Contact: Charlene A. Sydnor, Ph.D.; 301-435-4689; sydnorc@mail.nih.gov.

Collaborative Research Opportunity:

The Center for Cancer Research, Laboratory of Pathology, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize CD47-targeting agents as radioprotectants and tumor sensitizers. Please contact John D. Hewes, Ph.D. at 301-435-3121 or hewesj@mail.nih.gov for more information.

Mouse Lacking the Chemokine Receptor CX3CR1

Description of Invention: This mouse has been generated by targeted gene

disruption. The mouse provides a model to investigate the function of the chemokine receptor CX3CR1, which is a proinflammatory receptor for the leukocyte chemoattractant CX3CL1 (aka fractalkine). As an example, the mouse is in use in the study of atherosclerosis. Further, the mouse may serve as a model study the role of the immune system during infection with pathogens as well as other immunologically mediated diseases and responses to tumors.

Inventors: Philip Murphy, Christopher Combadière, Ji-liang Gao (NIAID).

Related Publication: C Combadière *et al.* Decreased atherosclerotic lesion formation in CX3R1/ApoE double knockout mice. *Circulation* 2003 Feb 25;107(7):1009-1016. [PubMed: 12600915].

Patent Status: HHS Reference No. E-216-2003/0—Research Tool. Patent protection is not being pursued for this technology.

Licensing Status: Available for licensing under a biological materials license.

Licensing Contact: Susan Ano, Ph.D.; 301-435-5515; anos@mail.nih.gov.

Oligonucleotides Which Specifically Bind Retroviral Nucleocapsid Proteins

Description of Invention: The human immunodeficiency virus (HIV) is the causative agent of acquired immunodeficiency syndrome (AIDS). A retroviral protein species, the gag polyprotein, is involved in the assembly of retrovirus particles and capable of specific interactions with nucleic acids. After the virion is released from the cell, the polyprotein is cleaved by the virus-encoded protease. One of the cleaved products, the nucleocapsid (NC) protein, then binds to genomic RNA, forming the ribonucleoprotein core of the mature particle. The interaction between gag and genomic RNA is known to involve the NC domain of the polyprotein. In addition, the NC protein plays crucial roles in both the reverse transcription and integration steps in the viral life cycle.

The present invention relates to retroviral nucleocapsid proteins, such as NC and the gag precursor, and their ability to bind to specific nucleic acid sequences with high affinity. The high affinity of this interaction has potential applications in the design of new antiviral approaches and in sensitive detection of HIV particles. Accordingly, the invention provides for oligonucleotides which bind to nucleocapsid proteins with high affinity, molecular decoys for retroviral nucleocapsid proteins which inhibit viral replication, targeted molecules

comprising high affinity oligonucleotides, assays for selecting test compounds, and related kits.

Inventors: Alan R. Rein *et al.* (NCI).

Patent Status: U.S. Patent No.

6,316,190 issued 13 Nov 2001 (HHS Reference No. E-107-1996/0-US-06).

Licensing Status: Available for licensing.

Licensing Contact: Sally Hu, PhD; 301-435-5606; hus@mail.nih.gov.

Dated: March 1, 2010.

Richard U. Rodriguez,

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

[FR Doc. 2010-4757 Filed 3-4-10; 8:45 am]

BILLING CODE 4140-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Centers for Medicare & Medicaid Services

Notice of Opportunity for a Hearing on Compliance of Missouri State Plan Provisions Concerning Payments for Home Health Services With Title XIX (Medicaid) of the Social Security Act

AGENCY: Centers for Medicare & Medicaid Services (CMS), HHS.

ACTION: Notice of Opportunity for a Hearing; Compliance of Missouri Medicaid State Plan Home Health Benefit.

SUMMARY: This notice announces the opportunity for an administrative hearing to be held no later than 60 days following publication in the **Federal Register** at the CMS Kansas City Regional Office, 601 E. 12th Street, Kansas City, Missouri 64106, to consider whether Missouri State plan provisions concerning payments for home health services comply with the requirements of the Social Security Act as discussed in the February 26, 2010 letter sent to the State and published herein.

Closing Date: Requests to participate in the hearing as a party must be received by the presiding officer by April 5, 2010.

FOR FURTHER INFORMATION CONTACT: Benjamin R. Cohen, Presiding Officer, CMS, 2520 Lord Baltimore Drive, Suite L, Baltimore, Maryland 21244, Telephone: (410) 786-3169.

SUPPLEMENTARY INFORMATION: This notice announces the opportunity for an administrative hearing concerning the finding of the Administrator of the Centers for Medicare & Medicaid Services (CMS) that the approved State plan under title XIX (Medicaid) of the

Social Security Act (the Act) for the State of Missouri is not in compliance with the provisions of sections 1902(a) of the Act and the proposed withholding of Federal financial participation for a portion of Missouri's expenditures for home health services. In particular, CMS has found that the State plan does not provide for home health services for Medicaid beneficiaries who are not "confined to the home." As a result of this "homebound" requirement, certain Medicaid beneficiaries are not receiving the full benefit package required under the Act and applicable regulations. Consequently, Federal payments for a portion of the Federal funding for home health services will be withheld, subject to the opportunity for a hearing described below. This notice is being provided pursuant to the requirements of section 1904 of the Act, as implemented at 42 CFR 430.35 and 42 CFR part 430, subpart D.

Section 1902(a)(10)(D) requires that State plans provide for the coverage of home health services for any individual who, under the State plan, is entitled to nursing facility services. Nursing facility services are a required service for categorically needy populations under section 1902(a)(10)(A), as defined in section 1905(a)(4)(A). Under CMS regulations, a service included as a covered benefit under a State plan must be "sufficient in amount, duration and scope to reasonably achieve its purpose" (42 CFR 440.230(b)) and, for required services, cannot be denied or reduced to an eligible beneficiary "solely because of the diagnosis, type of illness, or condition" (42 CFR 440.230(c)). It is not consistent with these requirements to deny home health services to eligible individuals who need such services on the basis that they are not "homebound."

The CMS provided interpretive guidance indicating that these statutory requirements preclude denial of home health services to eligible individuals because they are not "homebound." On July 25, 2000, CMS, then the Health Care Financing Administration, issued Olmstead Update #3 which clarified that the Medicare rule for home health services requiring an individual to be "homebound" did not apply to the receipt of Medicaid home health services. Specifically, Olmstead Update #3 states that the "homebound" requirement violates Federal regulatory requirements at 42 CFR section 440.230(c) and section 440.240(b).

The "homebound" requirement in Missouri was raised during the review of Missouri State plan amendment (SPA) 05-09. At that time, Missouri chose to withdraw the page containing

the "homebound" language but did not reverse the policy. Since that time, there have been numerous discussions between CMS and Missouri regarding this issue. On October 30, 2009, CMS provided Missouri with notice of the preliminary determination that it appeared to be out of compliance with Federal Medicaid requirements. In addition, CMS requested that Missouri submit a SPA to remove the "homebound" requirement.

In its response dated December 31, 2009, Missouri indicated that it was operating under its approved State plan and that the requirements of Missouri's home health program are the same as those of the Federal Medicare program. The State did not submit a SPA. CMS believes that Missouri has had numerous opportunities to come into compliance with Federal requirements.

The notice to Missouri, dated February 26, 2010, containing the details concerning the compliance issue, the proposed withhold, and the opportunity for an administrative hearing reads as follows:

CERTIFIED MAIL—RETURN RECEIPT REQUESTED

Mr. Ronald J. Levy, Director,
Department of Social Services,
Broadway State Office Building,
Jefferson City, MO 65102.

Dear Mr. Levy: This letter provides notice that the Centers for Medicare & Medicaid Services (CMS) has found that Missouri is not providing all Medicaid beneficiaries with home health benefits that are required under title XIX of the Social Security Act (the Act) and that until this deficiency is corrected (by making home health services available to all beneficiaries entitled to such services), a portion of the Federal funding for home health services will be withheld, subject to the opportunity for a hearing. The details of the finding, proposed withholding, and opportunity for a hearing are described in detail below.

Specifically, CMS has found that the approved Missouri State plan under title XIX (Medicaid) of the Act is not in compliance with the provisions of section 1902(a) of the Act with respect to the home health benefit. In particular, CMS has found that the State plan does not provide for home health services for Medicaid beneficiaries who are not "confined to the home." As a result of this "homebound" requirement, certain Medicaid beneficiaries are not receiving the full benefit package required under section 1902(a)(10) of the Act, which in subparagraph (D) provides for the inclusion of home health services in the standard Medicaid benefit package.