

desired. The compound is reconstituted when needed, and may then be used immediately without further filtration.

**Potential Applications of This Invention:** All researchers worldwide who utilize sterile, labile compounds will have an interest in this product, including governmental, university, institutional, and drug company laboratories. Most notably in need are investigators involved in drug-testing, which is normally done either in cell cultures, laboratory animals, or humans, and which requires sterility of many aliquots of many drugs. Additionally, this product will have a large market relating to basic research utilizing microbial, plant, or animal cell or organ cultures, to which sterile compounds such as growth factors are commonly added. Research in drugs, growth factors, etc., is expanding ever more rapidly, and generally requires a cell culture system in which to study such compounds. Most of these compounds are quite expensive. Loss of potency during storage and loss of material during filtration are widespread problems which may be overcome with this invention. Therefore, there exists a tremendous need and immense market for these multi-well plates.

Dated: August 14, 2003.

**Steven M. Ferguson,**

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

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## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### National Institutes of Health

#### Government-Owned Inventions; Availability for Licensing

**AGENCY:** National Institutes of Health, Public Health Service, DHHS.

**ACTION:** Notice.

**SUMMARY:** The inventions listed below are owned by agencies 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.

#### LMNA Gene and Its Involvement in Hutchinson-Gilford Progeria Syndrome (HGPS) and Arteriosclerosis

B. Maria H. Eriksson and Francis S. Collins (NHGRI). Serial No. 60/419,541 filed 18 Oct 2002 (DHHS Reference No. E-020-2003/0-US-01) and Serial No. 60/463,084 filed 14 Apr 2003 (DHHS Reference No. E-131-2003/0-US-01).

Licensing Contact: Fatima Sayyid; 301/435-4521; [sayyidf@mail.nih.gov](mailto:sayyidf@mail.nih.gov).

Hutchinson-Gilford Progeria Syndrome (HGPS) is a very rare progressive childhood disorder characterized by premature aging (progeria). The most common cause of death is from arteriosclerosis and few children affected by HGPS live beyond their teens. The invention identifies point mutations in the LMNA gene, a gene which encodes a nuclear lamin protein, as the cause of HGPS. These mutations activate a cryptic splice site within the LMNA gene which leads to the excision of a portion of an exon and the subsequent generation of a Lamin A protein with an internal deletion of fifty (50) amino acids. The identification of mutations associated with HGPS could lead to breakthroughs in detection, diagnosis, and treatment of HGPS and related or similar conditions, including arteriosclerosis and aging. See also Eriksson, M. et al "Recurrent de novo point mutations in lamin A cause Hutchinson-Gilford progeria syndrome" *Nature* 423, 293-298 (2003).

#### Synthesis of Proteins by Cell-Free Protein Expression

Deb K. Chatterjee (NCI). DHHS

Reference No. E-328-2002/0-US-01 filed 11 Mar 2003.

Licensing Contact: Fatima Sayyid; 301/435-4521; [sayyidf@mail.nih.gov](mailto:sayyidf@mail.nih.gov).

Cell-free protein expression is becoming a valuable tool for rapid and economical production of recombinant proteins. In conventional cell-free protein synthesis systems, the ATP (high energy) supply is accomplished by secondary energy regenerating sources containing high-energy phosphate bonds. The sources include glucose (G), glucose-6-phosphate (G-6P), phosphoenolpyruvate (PEP), acetyl phosphate (AP), creatine phosphate (CP) or pyruvate. However, for some of these systems (G, G-6P and pyruvate) require the addition of exogenous enzymatic

cofactors such as NAD/NADH, adding considerable expense to the system. In addition, the conventional systems (PEP, AP or CP) are also mired by unproductive enzymatic degradation of energy sources and unproductive consumption of ATP resulting in lower yields of protein.

The present invention offers a new ATP regeneration system for cell-free protein expression, using one of the early intermediates of the glycolytic pathway as the secondary energy source. The new energy source, costs only a fraction of the conventional substrates, provides chemical energy for protein synthesis without the addition of an exogenous enzymatic cofactor, thereby reducing the costs of the system. Moreover, the present system improves efficiency of protein synthesis by several folds by providing an improved energy regeneration system and protein-folding machinery.

#### Cyclooxygenase Inhibition With Nitroxyl

David A. Wink *et al.* (NCI). Serial No.

60/470,320 filed 13 May 2003 (DHHS Reference No. E-301-2002/0-US-01).

Licensing Contact: Fatima Sayyid; 301/435-4521; [sayyidf@mail.nih.gov](mailto:sayyidf@mail.nih.gov).

Inflammation is initiated and maintained by the overproduction of prostaglandins in injured cells. Cyclooxygenase (COX) regulates the production of prostaglandins. As the rate-limiting step for prostaglandin synthesis, the COX pathway is the primary target for anti-inflammatory drugs. Inhibition of COX accounts for the activity of the non-steroidal anti-inflammatory drugs (NSAIDs), such as aspirin, acetaminophen, ibuprofen, naproxen, indomethacin. However, these drugs are nonselective COX inhibitors. While they inhibit the activity of COX-2 in inflammation, they also interfere with the activity of COX-1 in non-inflamed cells. The inhibition of COX-1 produces undesirable side effects, such as gastrointestinal bleeding and renal failure. Therefore, agents that selectively inhibit COX-2 over COX-1 are desirable for the treatment of inflammation. Moreover, COX-2 inhibiting compounds have been reported to be useful in treating a variety of conditions, such as general pain, osteoarthritis, rheumatoid arthritis, menstrual pain associated with primary dysmenorrhea, cancers, Alzheimer's disease and diabetes.

The present invention relates to methods of using nitroxyl to selectively inhibit COX-2 activity. Also disclosed are methods of using nitroxyl to treat conditions that respond favorably to COX-2 inhibition. Nitroxyl-donating compounds include nitroxyl-donating

diazoniumdiolates such as IPA/NO ( $\text{Na}(\text{CH}_3)_2\text{C}(\text{H})\text{N}(\text{H})\text{N}(\text{O})\text{NO}$ ). Other embodiments include methods of screening candidate nitroxyl-donating compounds for COX-2 inhibition.

#### Nitroxyl Progenitors in the Treatment of Heart Failure

David Wink and Katrina Miranda (NCI). Serial No. 10/226,412 filed 21 Aug 2002 (DHHS Reference No. E-273-2002/0-US-01).

Licensing Contact: Fatima Sayyid; 301/435-4521; [sayyidf@mail.nih.gov](mailto:sayyidf@mail.nih.gov).

Congestive Heart Failure affects nearly 5 million Americans and approximately 550,000 new cases are diagnosed each year.

The present invention relates to the administration of nitroxyl donating compounds, such as Angeli's salt for increasing myocardial contractility while concomitantly lowering left ventricular preload in subjects experiencing heart failure. Moreover, administration of the nitroxyl donating compound, isopropylamine, surprisingly exhibits positive inotropic effects in subjects experiencing heart failure that were superior to those caused by Angeli's salt. Additionally, in contrast to the effects observed with nitric oxide donors, administration of a nitroxyl donating compound in combination with a positive inotropic agent does not impair the positive inotropic effect of the positive inotropic agent. Furthermore, nitroxyl donating compounds exert its positive inotropic effect independent of the adrenergic system, increasing contractility even in subjects receiving beta-antagonist therapy.

#### Vasopressor Peptide Derived From Adrenomedullin and Methods of Its Use

Frank Cuttitta *et al.* (NCI). Serial No. 60/416,291 filed 04 Oct 2002 (DHHS Reference No. E-293-2002/0-US-01).

Licensing Contact: Fatima Sayyid; 301/435-4521; [sayyidf@mail.nih.gov](mailto:sayyidf@mail.nih.gov).

Systemic hypertension is the most prevalent cardiovascular disorder in the United States, affecting over 60 million Americans. In spite of increasing public awareness and rapidly expanding array of antihypertensive medications, hypertension remains one of the leading causes of cardiovascular morbidity and mortality. On the other end of the spectrum are hypovolemic shock (often from acute hemorrhage), cardiogenic shock (from arrhythmia or heart failure) and vasodilatory shock (from cerebral trauma, drug intoxication, heat exposure or septic shock accompanying a gram negative bacterial infection). In view of the above, there exists a need for agents

that counteract aberrations in blood pressure, including hypertension and hypotension.

This invention discloses compounds that are useful as vasoconstrictors or vasodilators and their methods of use. Specific embodiments include administration of AM (II-22) to reverse vasodilation and administration of an inhibitor of MMP-2 to reverse vasoconstriction.

This research is described, in part, in J. Lopez & A. Martinez, "Cell and Molecular Biology of the Multifunctional Peptide, Adrenomedullin," *Int. Rev. Cytol.* 2002, 221:1-92.

#### Foamy Virus Mutant Reverse Transcriptase

Stephen H. Hughes *et al.* (NCI). Serial No. 60/292,994 filed 22 May 2001 (DHHS Reference No. E-152-2001/0-US-01) and PCT/US02/16528 filed 22 May 2002 (DHHS Reference No. E-152-2001/0-PCT-02).

Licensing Contact: Fatima Sayyid; 301/435-4521; [sayyidf@mail.nih.gov](mailto:sayyidf@mail.nih.gov).

The present invention provides a recombinant reverse transcriptase (RT) obtained from a mutant Foamy Virus (FV), which has highly active and highly processive reverse transcriptase activity and substantially reduced protease activity. In particular, the FV protease-reverse transcriptase has been mutated to functionally inactivate the protease activity. The FV RT has better polymerase activity than other commercially available products (MLV, AMV, HIV).

The invention discloses the production of the mutant FV RT, vectors and plasmids comprising nucleic acids that encode the FV RT and recombinant host cells. The invention also encompasses kits for the production of cDNA from RNA comprising the FV RT.

This research is described, in part, in Rinke *et al.*, *J. Virol.* 76:7560, 2002.

Dated: August 14, 2003.

Steven M. Ferguson,

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

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## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### National Institutes of Health

#### National Cancer Institute; Notice of Meeting

Pursuant to section 10(d) of the Federal Advisory Committee Act, as

amended (5 U.S.C. Appendix 2), notice is hereby given of the meeting of the National Cancer Advisory Board.

The meeting will be open to the public as indicated below, with attendance limited to space available. Individuals who plan to attend and need special assistance, such as sign language interpretation or other reasonable accommodations, should notify the contact person listed below in advance of the meeting.

A portion of the meeting will be closed to the public in accordance with the provisions set forth in sections 552b(c)(4), and 552b(c)(6), as amended. The grant applications and the discussions could disclose confidential trade secrets or commercial property such as patentable material, and personal information concerning individuals associated with the grant applications, the disclosure of which would constitute a clearly unwarranted invasion of personal privacy.

*Name of Committee:* National Cancer Advisory Board, Subcommittee on Planning and Budget.

*Closed:* September 8, 2003, 7 p.m. to 8:30 p.m.

*Agenda:* The subcommittee will be establishing a funding policy for scoring large unfunded R01 grants applications.

*Place:* Bethesda Hyatt Hotel, 1 Metro Place, Bethesda, MD 20892.

*Contact Person:* Ms. Kathie Reed, Acting Executive Secretary, National Cancer Institute, National Institutes of Health, 9000 Rockville Pike, Building 31, Room 11A03, Bethesda, MD 20892. (301) 496-5515.

*Name of Committee:* National Cancer Advisory Board.

*Open:* September 9, 2003, 8:30 a.m. to 4:20 p.m.

*Agenda:* Program reports and presentations; business of the Board.

*Place:* National Cancer Institute, 9000 Rockville Pike, Building 31, C Wing, 6th Floor, Conference Room 10, Bethesda, MD 20892.

*Contact Person:* Dr. Paulette S. Gray, Executive Secretary, National Cancer Institute, National Institutes of Health, 6116 Executive Boulevard, 8th Floor, Room 8141, Bethesda, MD 20892-8327. (301) 496-4218.

*Name of Committee:* National Cancer Advisory Board.

*Closed:* September 9, 2003, 4:20 p.m. to recess.

*Agenda:* Review of grant applications.

*Contact Person:* Dr. Paulette S. Gray, Executive Secretary, National Cancer Institute, National Institutes of Health, 6116 Executive Boulevard, 8th Floor, Room 8141, Bethesda, MD 20892-8327. (301) 496-4218.

*Name of Committee:* National Cancer Advisory Board.

*Open:* September 10, 2003, 8:30 a.m. to adjournment.

*Agenda:* Program reports and presentations; business of the Board.

*Contact Person:* Dr. Paulette S. Gray, Executive Secretary, National Cancer