

of the receptor, thereby modulating the uptake of HDL by cells expressing the receptor on the cell surface.

HDL has anti-atherogenic properties and is known to inhibit oxidation of low density lipoprotein (LDL). Transgenic animals having elevated levels of HDL are resistant to high cholesterol diet-induced atherosclerosis. Therefore, understanding factors which influence plasma levels of HDL, such as mechanisms of HDL metabolism, is of major importance.

The present invention makes a significant contribution to the art by providing an HDL holoparticle uptake receptor comprising a complex of proteins and screening methods for identifying substances that modulate the activity and/or expression of the receptor.

Modified HCV Peptide Vaccine

Jay A. Berzofsky (NCI), Pablo Sarobe (NCI), CD Pendleton (NCI), Stephen M. Feinstone (FDA)

Serila No. 60/-97,446 filed 21 Aug 98
Licensing Contact: J. Peter Kim; 301/496-7056 ext. 264; e-mail: jk141n@nih.gov

Hepatitis C virus (HCV) is a single stranded RNA virus responsible for the majority of non-A non-B hepatitis. Hepatitis C virus (HCV) has a worldwide distribution and is a major cause of liver cirrhosis and hepatocellular carcinoma in the U.S., Europe, and Japan. For this reason, development of a vaccine against hepatitis C is of great importance.

The present invention provides immunogenic peptides of HCV core protein which elicit an enhanced immune response, methods for making these peptides, and methods for using these peptides for a variety of therapeutic, diagnostic, and prognostic applications, including a vaccine. More specifically, the present invention provides an isolated peptide, and isolated HCV core polypeptide, a fragment of an HCV core polypeptide and nucleic acids which encode the peptides and polypeptides of this invention. The invention provides a modified HCV core peptide that is more immunogenic than the corresponding natural core peptide for eliciting human cytotoxic T lymphocytes.

Conformationally Locked Nucleoside Analogues

Inventors: Victor E. Marquez, Juan B. Rodriguez, Marc C. Nicklaus, Joseph J. Barchi, Jr., Maqbool A. Siddiqui (NCI)
U.S. Patent Numbers: 5,869,666 (filed March 14, 1997); 5,629,454 (filed September 23, 1994, with priority back to September 24, 1993)

Foreign Filing: PCT/US94/10794 (issued as European Patent Number 0720604 and Australian Patent Number 677441)

Conformationally Locked Nucleoside Analogues As Antiherpetic Agents

Inventors: Victor E. Marquez, Juan B. Rodriguez, Marc C. Nicklaus, Joseph J. Barchi, Jr., Maqbool A. Siddiqui (NCI)
U.S. Patent Number: 5,840,728 (filed August 7, 1997, with priority back to August 7, 1996)

Licensing Contact: Peter Soukas; 301/496-7056 ext. 268; e-mail: ps193c@nih.gov

The compounds of the present invention represent the first examples of carbocyclic dideoxynucleosides that in solution exist locked in a defined N-geometry (C3'-endo) conformation typical of conventional nucleosides. These analogues exhibit increased stability due to the substitution of carbon for oxygen in the ribose ring. The invention includes 4'-6'-cyclopropane fused carbocyclic dideoxynucleosides, 2'-deoxynucleosides and ribonucleosides as well as oligonucleotides derived from these analogues; the preferred embodiment of the invention is carbocyclic-4'-6'-cyclopropane-fused analogues of dideoxypurines, dideoxypyrimidines, deoxypurines, deoxypyrimidines, purine ribonucleosides and pyrimidine ribonucleosides. In addition, oligonucleotides derived from one or more of the nucleosides in combination with the naturally occurring nucleosides are within the scope of the present invention.

The second invention discloses a method for the treatment of herpes virus infections by the administration of cyclopropanated carbocyclic 2'-deoxynucleosides to an affected individual. This invention is a method of administration of the compounds described above. The compounds of this invention are particularly efficacious against herpes simplex viruses 1 and 2 (HSV-1 and HSV-2), Epstein-Barr Virus (EBV) and human cytomegalovirus (CMV), although the nucleoside analogues of the invention may be used to treat any condition caused by a herpes virus. Specifically, the N-methanocarba-T (Thymidine) analogue has been shown to exhibit strong activity against HSV-1 and HSV-2, and moderate to strong activity against EBV. Significantly, the anti-HSV activity of the Thymidine analogue is stronger than that of Acyclovir (shown in a plaque reduction assay), a widely used anti-HSV therapeutic. Furthermore, the Thymidine analogue is also non-toxic against stationary cells and is potent against rapidly dividing cells. Dosage

amounts for the compounds are similar to those of Acyclovir.

Descriptions of the inventions may be found in Rodriguez et al., J. Medicinal Chemistry 37:3389-3399 (1994) and Marquez et al., J. Medicinal Chemistry 39:3739-3747 (1996).

Dated: May 28, 1999.

Jack Spiegel,

Director, Division of Technology Development and Transfer, Office of Technology Transfer.

[FR Doc. 99-14377 Filed 6-4-99; 8:45 am]

BILLING CODE 4140-01-M

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.

The meeting will be closed to the public in accordance with the provisions set forth in sections 552b(c)(4) and 552b(c)(6), Title 5 U.S.C. Code and Section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2). The grant applications and/or contract proposals 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 and/or contract proposals, the disclosure of which would constitute a clearly unwarranted invasion of personal privacy.

Name of Committee: National Cancer Advisory Board.

Date: June 8, 1999.

Open: June 8, 1999, 8:30 a.m. to 4:00 p.m.

Agenda: Report of the Director, NCI; Reports and Presentations Related to NCI Administrative and Program Developments; Presentations and Discussions Related to Special Populations and Quality of Care Issues; NCI Clinical Research Opportunities; NCAB Subcommittee Meeting and NCAB Working Group Report; Legislative and National Cancer Statistic Updates.

Place: Building 31, C Wing, 6 Floor, Conference Room 10, National Institutes of Health, 3100 Center Drive, Bethesda, MD 20892.

Closed: June 8, 1999, 4:15 p.m. to 5:30 p.m.
Agenda: To review and evaluate grant applications.

Place: Building 31, C Wing, 6 Floor, Conference Room 10, National Institutes of Health, 3100 Center Drive, Bethesda, MD 20892.

Contact Person: Dr. Marvin R. Kalt, Executive Secretary, Director, Division of Extramural Activities, National Cancer Institute, National Institutes of Health, Executive Plaza North, Suite 600, 6130 Executive Boulevard, Rockville, MD 20892, (301) 496-5147.

This notice is being published less than 15 days prior to the meeting due to the timing limitations imposed by the review and funding cycle.

(Catalogue of Federal Domestic Assistance Program Nos. 93.392, Cancer Construction; 93.393, Cancer Cause and Prevention Research; 93.394, Cancer Detection and Diagnosis Research; 93.395, Cancer Treatment Research; 93.396, Cancer Biology Research; 93.397, Cancer Centers Support; 93.398, Cancer Research Manpower; 93.399, Cancer Control, National Institutes of Health, HHS)

Dated: June 1, 1999.

LaVerne Y. Stringfield,

Committee Management Officer, NIH.

[FR Doc. 99-14374 Filed 6-4-99; 8:45 am]

BILLING CODE 4140-01-M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Institute of Neurological Disorders and Stroke; Notice of Closed 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 following meeting.

The meeting will be closed to the public in accordance with the provisions set forth in sections 552b(c)(4) and 552b(c)(6), Title 5 U.S.C., 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 Institute of Neurological Disorders and Stroke Special Emphasis Panel.

Date: June 21-22, 1999.

Time: 8:30 am to 5:00 pm.

Agenda: To review and evaluate grant applications.

Place: Madison Hotel, Fifteenth & M Streets NW, Washington, DC 20005.

Contact Person: Alan Willard, PHD, PHD, Scientific Review Administrator, Scientific

Review Branch, NINDS/NIH/DHHS, Neuroscience Center, 6001 Executive Blvd, Suite 3208, MSC 9529, Bethesda, MD 20892-9529, 301-496-9223.

(Catalogue of Federal Domestic Assistance Program Nos. 93.853, Clinical Research Related to Neurological Disorders; 93.854, Biological Basis Research in the Neurosciences, National Institutes of Health, HHS)

Dated: June 1, 1999.

LaVerne Y. Stringfield,

Committee Management Officer, NIH.

[FR Doc. 99-14373 Filed 6-4-99; 8:45 am]

BILLING CODE 4140-01-M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Prospective Grant of Exclusive License: Drug and Method for the Therapeutic Treatment of Lymphomas and Leukemias

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

ACTION: Notice.

SUMMARY: This notice in accordance with 35 U.S.C. 209(c)(1) and 37 CFR 404.7(a)(1)(I) that the National Institutes of Health, Department of Health and Human Services, is contemplating the grant of an exclusive world-wide license to U.S. Patents and Patent Applications USPA SN: 60/041,437, entitled: "Recombinant Antibodies and Immunoconjugates Targeted to CD-22 Bearing Cells and Tumors"; USPN 4,892,827, entitled, "Recombinant *Pseudomonas* Exotoxin: Construction of an Active Immunotoxin with Low Side Effects"—excluding any foreign equivalents corresponding to 4,892,927 (= USSN 06/911,227); USPN 5,747,654, entitled, "Recombinant Disulfide-Stabilized Polypeptide Fragments Having Binding Specificity"; USPA SN: 09/002,753, entitled: "Recombinant Disulfide-Stabilized Polypeptide Fragments Having Binding Specificity"; USPA SN: 07/865,722; entitled: "Recombinant Antibody-Toxin Fusion Protein"; USPN 5,863,745, entitled: "Recombinant Antibody-Toxin Fusion Protein"; USPN 5,696,237, entitled: "Recombinant Antibody-Toxin Fusion Protein"; and USPA SN: 06/005,388, entitled: "Immunotoxin Containing a Disulfide-Stabilized Antibody Fragment Joined to a *Pseudomonas* Exotoxin that does not Require Proteolytic Activation" and corresponding foreign patent applications to AlbaPharm, inc. having an address in Ann Arbor, Michigan. The United States of America is an assignee of the patent rights in these inventions

and the contemplated exclusive license may be limited to the use of RFB4 (dsFv)—PE38 [also known as BL22] immunotoxin and relevant patents and patent applications for the therapeutic treatment of Lymphomas and Leukemias which express the CD22 surface antigen.

DATES: Only written comments and/or applications for a license which are received by NIH on or before August 6, 1999 will be considered.

ADDRESSES: Requests for copies of the patent applications, inquiries, comments and other materials relating to this contemplated exclusive license should be directed to: J.R. Dixon, Ph.D., Technology Licensing Specialist, Office of Technology Transfer, National Institutes of Health, 6011 Executive Boulevard, Suite 325, Rockville, Maryland 20852-3804. Telephone: (301) 496-7735 ext. 206; Facsimile: (301) 402-0220, E-Mail: DixonJ@OD.NIH.GOV. A signed Confidentiality Agreement will be required to receive copies of any patent applications.

SUPPLEMENTARY INFORMATION: The technology is directed to a RFB4 (dsFv)—PE38 (also known as: BL22) immunotoxin and to methods and DNA sequences to produce disulfide-stabilized (ds) recombinant polypeptide fragments to construct the aforementioned immunotoxin. RFB4 is a disulfide-linked recombinant immunotoxin fused to PE38, a mutant form of *Pseudomonas* Exotoxin, that binds to CD22—a 135kDa phosphoglycoprotein adhesion molecule present on the surface of B-cells. RFB4 is a mouse monoclonal antibody that recognizes an external epitope on the CD22 cell surface antigen and has no detectable cross-reactivity with any other normal cell types. CD22 is a lineage-restricted B-cell antigen that belongs to the Ig superfamily and is displayed on chronic B-Lymphocytic Leukemia cells and B-cell Non-Hodgkins Lymphoma cells. To kill CD22-positive cells, the RFB4 antibody was used to make a recombinant immunotoxin. To construct the recombinant PE immunotoxin, the variable portions of the heavy and light chains of RFB4 were cloned and the Fv fragments linked together by a disulfide bond to form a disulfide stabilized (ds) construct. The construct was combined by gene fusion with PE38, a truncated version of PE, to form RFB4 (dsFv)—PE38, or BL22.

The prospective exclusive license will be royalty-bearing and will comply with the terms and conditions of 35 U.S.C. 209 and 37 CFR 404.7. The prospective