Comments Due Date

Comments regarding this information collection are best assured of having their full effect if received on or before June 4, 2001.

Dated: March 19, 2001.

Carol Tippery,

Acting Director, OPERA, NIH.

[FR Doc. 01–8354 Filed 4–4–01; 8:45 am]

BILLING CODE 4140–01–M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Government-Owned Inventions; Availability for Licensing

AGENCY: National Institutes of Heath, 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 contacting Sally Hu, Ph.D., Technology Licensing Specialist, Office of Technology Transfer, National Institutes of Health, 6011 Executive Boulevard, Suite 325, Rockville, Maryland 20852–3804; telephone: 301/496–7056 ext. 265; fax: 301/402–0220; e-mail: hus@od.nih.gov. A signed Confidential Disclosure Agreement will be required to receive copies of the patent applications.

A Method of Inhibiting Viral Replication Targeting the Nucleocapsid Protein

Robert H. Shoemaker, Robert J. Fisher, and Judy A. Mikovits (NCI) DHHS Reference No. E–276–00/0 filed 05 Feb 2001

This invention concerns novel compounds that inhibit replication of retroviruses, such as HIV. These compounds act in a mechanistically distinct way from any other anti-HIV compound and appear to be relatively non-toxic. The compounds exert anti-HIV activity through inhibition of a key step in the viral replication cycle, specifically, the interaction of the nucleocapsid with nucleic acid. Clinical experience in chemotherapy of patients with AIDS has clearly shown that use of combinations of drugs acting through different mechanisms is essential for control of virus replication. Consequently, these compounds are believed to have the potential to substantially enhance anti-HIV therapy by introduction of agents acting by this novel mechanism.

Method of Preparing a Production Intermediate for HIV Protease Inhibitors

Guangyang Wang, Michael A. Eissenstat, and Tatiana Guerassina (NCI) DHHS Reference No. E–188–00/0 filed 24 Jan 2000

The invention describes a novel process amenable for the large-scale practical synthesis of cis-tetrahydro-furo[2,3-b]furan-3-one. This compound is useful as a key intermediate for the synthesis of highly potent and resistance-repellent HIV protease inhibitors that share a common component called bis-tetrahydrofuran (bis-THF). Specifically, the invention provides a method of preparing these precursors by modification of reaction temperatures, conditions and reagents leading to increased yields and purity of the desired intermediates. Such modifications would be useful in the large-scale preparation of highly potent and resistance-repellent HIV protease inhibitors currently under development as antiviral agents useful in treating AIDS.

Dated: March 29, 2001.

Jack Spiegel,

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

[FR Doc. 01–8374 Filed 4–4–01; 8:45 am]

BILLING CODE 4140–01–P

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Enhanced Homologous Recombination Mediated by Lambda Recombination Proteins

Drs. E. Lee, N. Copeland, N. Jenkins, and D. Court (NCI)

DHHS Reference No. E–077–01/0 filed 26 Feb 2001

The present invention concerns methods to enhance homologous recombination in bacterial and eukaryotic cells using recombination proteins derived from bacteriophage lambda. It also concerns methods for promoting homologous recombination using other recombination proteins. Concerted use of restriction endonucleases and DNA ligases allows in vitro recombination of DNA sequences. The recombinant DNA generated by restriction and ligation may be amplified in an appropriate microorganism such as *E. coli*, and used for diverse purposes including gene therapy. However, practical limitations imposed by this system generally results in DNA fragments with an upper limit of approximately 20 kilobases. The present invention utilizes homologous recombination instead of restriction enzymes to build DNA constructs. These DNA constructs may be several hundreds of kilobases in size. Using this invention, small linear fragments of DNA (such as a gene of interest) may be inserted efficiently and precisely into very large cloned fragments of DNA. These DNA constructs may be used for a variety of purposes, including generation of transgenic animals in which appropriate tissue specific regulation of gene expression is maintained.

Biologically Active FLAG–Epitope-Tagged Transforming Growth Factor Beta (TGF-beta) Protein

Lawrence A. Wolfraim, John J. Letterio, Kathleen Flanders, Lalage Wakefield, Anita B. Roberts (NCI)

DHHS Reference No. E–149–00/0 filed 20 Oct 2000

The current invention discloses an epitope-tagged TGF-beta that can be expressed in mammalian cells while still maintaining complete biological activity. An epitope is a region of a protein that can be recognized by an antibody. Although there are currently TGF-beta antibodies available, their usefulness is limited by cross reactivity amongst all members of the TGF family, as well as by an inability to distinguish between endogenous and exogenous TGFs. The current invention provides a means for distinguishing between these variations by epitope tagging of TGF-beta. The tag of this invention is the FLAG tag, an 8 amino acid sequence consisting of DYKDDDDK (D=aspartate, Y=tyrosine, K=lysine). Two FLAG tagged TGF constructs have been generated: the first inserts the tag at the amino terminus of the mature polypeptide and the second inserts the tag between amino acids 11 and 12 of the mature polypeptide. The core of the invention is that the insertion of the tag into these specific regions of the TGF molecule still allows for the retention of complete biological activity. Thus the tagged TGF may be monitored and distinguished by various biochemical means (through the FLAG epitope) from endogenous TGFs while at the same time the physiological effects of the tagged TGF may be analyzed as though it were a natural TGF. The TGF of the current invention may also be used to study TGF receptor expression levels, the loss of which has been correlated with various disease states, including cancers and autoimmune diseases. In addition, in the future the FLAG tag may permit the development of therapeutic compounds which could be used to ''ferry'' the TGFs to target tissues, thereby reducing side effects associated with systemic administration of TGF family proteins.

Dated: March 29, 2001.

Jack Spiegel,

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

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Methods and Compositions for Inhibiting HIV–Coreceptor Interactions

Oleg Chertov (NCI), Joost J. Oppenheim (NCI), Xin Chen (NCI), Connor McGrath (NCI), Raymond C. Sowder II (NCI), Jacek Lubkowski (NCI), Michele Wetzel (EM), and Thomas J. Rogers (EM)

DHHS Reference No. E–190–00/0 filed 15 Feb 2001

Licensing Contact: Sally Hu; 301/496–7056 ext. 265; e-mail: hus@od.nih.gov

This invention provides peptides that might be potent inhibitors of HIV replication, in both macrophages and T lymphocytes. Specifically, the inventors have identified peptides, from the HIV–1 gp120 envelope protein, that share structural similarities with chemokines and are shown to block ''docking'' interactions between the HIV–1 envelope protein gp120 and chemokine receptors that function as ''coreceptors'' for HIV entry on the surface of target cells (macrophages and T lymphocytes). The inventors synthesized two peptides (designated 15K and 15D) based on this information and showed that both were effective in competing with chemokines for binding to CCR5- and CXCR4-expressing cells. These peptides efficiently inhibited infection of human monocyte derived macrophages and peripheral blood mononuclear cells by different strains of HIV. The synthesized peptides also inhibited chemotaxis of CCR5 expressing transfected cells stimulated by the chemokine RANTES. Thus, these peptides and other molecules based on their structure can be potentially used as inhibitors of HIV. Moreover, these peptides could also have anti-inflammatory and anti-tumor activity. Further, it has been determined that these peptides are multi-tropic in their effects (blocking HIV interactions with multiple co-receptors) for blocking both T cell tropic (lymphotropic) and macrophage tropic (m-tropic) HIV strains.

Identification of New Small RNAs and ORFs

Susan Gottesman (NCI), Gisela Storz (NICHD), Karen Wassarman (NICHD), Francis Repoila (NCI), Carsten Rosenow (EM)

DHHS Reference No. E–072–01/0 filed 01 Feb 2001

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

The inventors have isolated a number of previously unknown sRNAs found in E. coli. Previous scientific publications by the inventors and others regarding sRNAs have shown these sRNAs to serve important regulatory roles in the cell, such as regulators of virulence and survival in host cells. Prediction of the presence of genes encoding sRNAs was accomplished by combining sequence information from highly conserved intergenic regions with information about the expected transcription of neighboring genes. Microarray analysis also was used to identify likely candidates. Northern blot analyses were then carried out to demonstrate the presence of the sRNAs. Three of the sRNAs claimed in the invention regulate (candidates 12 and 14, negatively and candidate 31, positively) expression of RpoS, a major transcription factor in bacteria that is important in many pathogens because it regulates (amongst other things) virulence. The inventors' data show that these sRNAs are highly conserved among closely related bacterial species, including Salmonella and Klebsiella presenting a unique opportunity to develop both specific and broad-based antibiotic therapeutics. The invention contemplates a number of uses for the sRNAs, including, but not limited to, inhibition by antisense, manipulation of gene expression, and possible vaccine candidates.

Decoding Algorithm for Neuronal Responses

Barry J. Richmond, Matthew C. Wiener (NIMH)

DHHS Reference No. E–038–01/0 filed 12 Jan 2001

Licensing Contact: Dale Berkley; 301/496–7735 ext. 223; e-mail: berkleyd@od.nih.gov

The invention is a new algorithm for decoding neuronal responses based on