

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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## 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.

#### **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 Wetzels (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 Repola (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

the discovery that neuronal spike trains can be described using order statistics. The device has applications in the direct control of prosthetic limbs by neuronal signals originating from electrodes placed in the brain. The method allows for decoding neuronal responses by monitoring sequences of potentials from neurons while specific motor tasks are carried out. The sequences are then characterized using the innovative technique of applying order statistics to the spike train, such that subsequent action potentials representing unidentified motor tasks can be decoded to determine the unknown task. The invention is of substantial importance because it appears to have achieved a closed form interpretation of neuronal responses upon which a motor prosthetic device might be based.

#### **Expression Vectors Able to Elicit Improved Immune Response and Methods of Using Same**

Pavlakakis et al. (NCI)

DHHS Reference No. E-308-00/0 filed 01 Nov 2000

Licensing Contact: Carol Salata; 301/496-7735 ext. 232; e-mail: salatac@od.nih.gov

Cellular immune responses against human immunodeficiency virus type 1 (HIV-1) and the related simian immunodeficiency virus (SIV) have been shown to play an important role in controlling HIV-1 and SIV infection and in delaying disease progression. This invention relates to nucleic acids (such as DNA immunization plasmids), encoding fusion proteins containing a destabilizing amino acid sequence which increases their immunogenicity. In order to make HIV gag or env more immunogenic, several signals for proteasomal degradation were selected and linked to the proteins. One of these destabilizing amino acid sequences was found to be particularly effective. The DNA construct expressing the HIV-1 gag fusion protein was more immunogenic in mice than the HIV gag protein. Compared with gag alone, the DNA expressing the gag fusion protein evoked much higher HIV-specific proliferative responses, elevated CTL response and a high level of CD8+ IFN $\gamma$ -secreting cells.

Dated: March 28, 2001.

**Jack Spiegel,**

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

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BILLING CODE 4140-01-P

## **DEPARTMENT OF HEALTH AND HUMAN SERVICES**

### **National Institutes of Health**

#### **National Cancer Institute, 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 Cancer Institute Special Emphasis Panel, Four U01 Family Registry Supplements and One R24 Family Registry Application.

*Date:* April 16, 2001.

*Time:* 8 a.m. to 5 p.m.

*Agenda:* To review and evaluate grant applications.

*Place:* National Cancer Institute, Executive Plaza North, Conference Room E and F, 6130 Executive Boulevard, Rockville, MD 20852.

*Contact Person:* Sherwood Githens, PhD, Scientific Review Administrator, National Institutes of Health, National Cancer Institute, Special Review, Referral and Resources Branch, 6116 Executive Boulevard, Room 8068, Bethesda, MD 20892, (301) 435-1822.

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.

Any interested person may file written comments with the committee by forwarding the statement to the Contact Person listed on this notice. The statement should include the name, address, telephone number and when applicable, the business or professional affiliation of the interested person.

(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: March 27, 2001.

**LaVerne Y. Stringfield,**

*Director, Office of Federal Advisory Committee Policy.*

[FR Doc. 01-8364 Filed 4-4-01; 8:45 am]

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## **DEPARTMENT OF HEALTH AND HUMAN SERVICES**

### **National Institutes of Health**

#### **National Cancer Institute**

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 Cancer Institute Special Emphasis Panel, P01 Program Project Grant Application.

*Date:* April 18, 2001.

*Time:* 1 p.m. to 6 PM.

*Agenda:* To review and evaluate grant applications.

*Place:* National Cancer Institute, Division of Extramural Activities, Grants Review Branch, 6116 Executive Boulevard, 8th Floor, Rockville, MD 20852, (Telephone Conference Call).

*Contact Person:* Virginia P. Wray, PhD, Scientific Review Administrator, Grants Review Branch, Division of Extramural Activities, National Cancer Institute, National Institutes of Health, 6116 Executive Boulevard, Room 8125, Rockville, MD 20892-7405, 301/496-9236.

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.

Any interested person may file written comments with the committee by forwarding the statement to the Contact Person listed on this notice. The statement should include the name, address, telephone number and when applicable, the business or professional affiliation of the interested person.

(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: March 27, 2001.

**LaVerne Y. Stringfield,**

*Director, Office of Federal Advisory Committee Policy.*

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