Dated: June 15, 2000.

Jack Spiegel,

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

[FR Doc. 00–16325 Filed 6–27–00; 8:45 am]

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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.

Gene Profiling Arrays

Ena Wang, Lance Miller, Francesco Marincola (NCI)

DHHS Reference No. E–086–00/0 filed 28 Mar 2000

Licensing Contact: Richard Rodriguez; 301/496–7056 ext. 287; e-mail: rr154z@nih.gov

The invention(s) embodied in this application, provides for ordered arrays of mixtures of nucleic acid molecules, which reflect the gene expression profile of one or more specimens, such as different cell types or tissues. In particular embodiments, complete mRNA mixtures (*i.e.* gene transcripts) or cDNA representatives from specimens are individually arrayed on a substrate. Such mixtures of nucleic acids can be derived from any specimen source, including animal, plant and/or microbial cells and can be assembled in any collection desired. The collections can, for instance, include nucleic acid mixtures from different cell types, different phenotypes, cells grown under different conditions, cells of different ages or developmental stages, and so forth. The nucleic acid arrays are provided in both macro- and micro-formats and are suitable for measuring the relative abundance of particular gene transcripts across a collection of complex nucleic acid mixtures.

Techniques are also disclosed for producing high-fidelity, amplified mixtures of nucleic acid molecules using a combination of RNA (sense or anti-sense) amplification and template-switching synthesis. Amplified mixtures produced using this method can, for instance, be applied to the disclosed arrays. The disclosed arrays allow high throughput analysis of differential gene expression in a specimen, such as a tumor, or a variety of specimens, such as a variety of tumors, and is suitable for automated preparation and analysis.

The Isolation of a New Gene, TRAG, Associated with TGF–Beta

Snorri S. Thorgeirsson, Sean R. Sanders (NCI)

DHHS Ref. No. E–047–00/0 filed 07 Mar 2000 and 60/187,848 filed 08 Mar 2000

Licensing Contact: Susan S. Rucker; 301/406–7056 ext. 245; e-mail: sr156v@nih.gov

A new gene has been isolated from a cell line resistant to a protein, TGF-beta, which can block the proliferation of cancer cells. This resistance endows the cell with cancer forming abilities. The protein encoded by the newly-discovered TRAG gene has been found at much higher levels in these cancer-forming cells than their non-cancerous ancestors. In addition, the TRAG protein is greatly elevated in many other rodent and human cancer cell lines and in primary mouse liver tumors, but not in surrounding non-tumorous tissue. This indicates a strong association between TRAG and cancer-forming potential. TRAG may be involved in the mechanism by which normal cells become cancerous. The TRAG gene could provide an excellent target for cancer or gene therapy. Abrogation of TRAG protein production using anti-sense oligonucleotides or antibodies could conceivably prevent, reduce, or destroy certain types of tumors.

Identification of a Novel Domain in the Tumor Necrosis Factor Receptor Ligand Family that Mediates Pre-Ligand Receptor Assembly and Function

MJ Lenardo, FK Chan, R Siegel (all of NIAID)

Serial No. 60/181,909 filed 11 Feb 2000

Licensing Contact: Susan S. Rucker; 301/496–7056 ext. 245; e-mail: sr156v@nih.gov

This application discloses the identification of a functional domain, which is essential for signaling involving receptors of the Tumor Necrosis Factor Superfamily (TFNR's) including TNFR–1 (p60), TNFR–2 (p80), Fas, TRAIL–R, LTβR, CD40, CD30, CD27, HVEM, OX40 and DR4. The functional domain, denoted the Pre-Ligand Assembly Domain (PLAD), can be isolated as functional polypeptides which can be useful in inhibiting the first step in TNFR mediated signaling, ligand-independent assembly of members of the TNFR Superfamily. The ability to inhibit TNFR signaling suggests that these PLAD polypeptides may be useful in developing new therapeutic molecules or as therapeutic molecules themselves for modulation of immune responses, apoptosis, and inflammation.

In addition to being available for license, the investigators who have developed this technology are also willing to consider entering into a CRADA relationship with companies interested in commercial development of this technology.

Transition Metal Complexes of N,N′,N″-trialkyl-cis,cis-1,3,5-triaminocyclohexane and Related Compositions and Methods

Martin W Brechbiel, Roy P. Planalp, Kim A. Deal (NCI)

DHHS Reference No. E–072–99/0 filed 10 Aug 1999

Licensing Specialist: Girish C. Barua; 301/496–7735 ext. 263; gb18t@nih.gov

The invention is directed to copper complexes of N,N′,N″-trimethyl-cis,cis-1,3,5-triaminocyclohexane and N,N′,N″-triethyl-cis,cis-1,3,5-triaminocyclohexane as well as methods of producing and using said complexes. These complexes are capable of cleaving DNA and RNA *in vitro* and could be used for the treatment of cancer or other disease states that are characterized by abnormal cellular proliferation. The complexes could also be used as delivery agents or as imaging-tracers. These complexes offer advantages over previously described cleaving methodologies, *e.g.*, oxidative or transesterification protocols. The disclosed copper-complexes act via hydrolytic reactions. These advantages could offer significant benefits over related therapeutic approaches to the aforementioned abnormal conditions.

Dated: June 15, 2000.

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

Government-Owned Inventions; Availability for Licensing: Novel Multiple Peptide Conjugate System

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.

This novel multiple peptide conjugate system is described in DHHS Reference Nos. E–208–99/0, E–280–99/0, and E–114–00/0—all now incorporated under a PCT application, DHHS Reference No. E–208–99/1.

ADDRESSES: Licensing information and copies of the U.S. patent applications listed below may be obtained by Carol Salata, Ph.D., at the Office of Technology Transfer, National Institutes of Health, 6011 Executive Boulevard, Suite 325, Rockville, Maryland 20852–3804; telephone: 301/496–7735 ext. 232; fax: 301/402–0220; e-mail: SalataC@od.nih.gov. A signed Confidential Disclosure Agreement will be required to receive copies of the patent applications.

Novel Multiple Peptide Conjugate System

I. Pathogenic TAT Peptides

Subhash Dhawan, Robert A. Boykins, Kenneth M. Yamada (FDA)

Infection with HIV, the causative agent of Acquired Immune Deficiency Syndrome (AIDS), is responsible for a large number of deaths annually and represents a significant threat to human health. Accordingly, an extensive effort has been mounted to characterize the HIV virus and to identify potential targets for therapeutics. The present invention relates to the identification of functional domains within the HIV Tat protein which are capable of mediating many of the effects of the full length Tat protein. In particular, this invention describes the use of peptides comprising functional domains to induce an immune response against the HIV Tat protein and the identification of dominant-negative mutants and chimeras of these functional domains which may be used as therapeutics. Another aspect of the present invention relates to the use of these functional domains as reagents for elucidating the biochemical mechanisms of HIV gene expression. This invention is described further in Boykins *et al.* July 1999, J. Immunol. 163:15–20.

II. Multiple Peptide Conjugates

Robert A. Boykins, Manju B. Joshi, Chiang Syin, Subhash Dhawan, Hira Nakhasi (FDA)

This invention describes the design and synthesis of a multi-peptide conjugate (MPC) system containing antigens from the human malaria parasite (Plasmodium falciparium) and the Tat protein of HIV type-1 (HIV–1–Tat) for use as a subunit vaccine. Prior multiple antigen peptides (MAPs) prepared by the classical solid phase synthesis led to heterogeneity, due in part to the aggregation and steric hindrance of the growing peptide chains during synthesis. Aggregation of the peptide chain may be a factor in the formation of intra-chain hydrogen bonding by the peptide backbone, causing the formation of beta sheets or other secondary structures. The current multiple peptide conjugates (MPCs) have distinct advantages over prior MAPs because only two adjacent peptide branches are elongated on the solid phase at either the alpha or epsilon amino groups thereby allowing maximum spacing between the resin bound peptide chains. Cysteine is inserted at the respective position in the sequence thus permitting the thiol groups to be used in the formation of stable thioether bonds with haloacetyl peptides coupled through solution chemistry. A modification to the coupling solvent and key amino acid derivatives are used in the sequence to minimize peptide chain aggregation. Furthermore, the elongation of only two peptide chains at the alpha or epilson groups of opposite lysine residues yields a dimeric or base peptide. These modifications of the solid phase methodology for the traditional MAP plus a coupling solvent modification, and the addition of key amino acid derivatives for amide bond protection allow the synthesis of base peptides on the solid phase greater than 7500kDa. These peptides are then reacted with high performance liquid chromatography purified haloacetyl peptides to generate multiple peptide conjugates with molecular masses of 10 to 13 kDa. This invention is described further in Boykins *et al.,* Peptides Jan 2000;21(1):9–17.

III. HIV–1–Tat-Multiple Peptide Conjugate: A Potential Synthetic AIDS Vaccine Candidate

Subhash Dhawan and Robert A. Boykins (FDA)

The present invention is directed to a novel highly immunogenic synthetic multiple peptide conjugate constituting three Tat functional domains. Vaccination of mice with this HIV–1–Tat multiple peptide conjugate induces an effective immune response to three Tat functional domains. Anti-HIV–1–Tat multiple peptide conjugate antibodies efficiently inhibit Tat-induced viral activation in monocytes infected with HIVBa–L as well as with various clinical HIV–1 isolates, and reduce Tat-mediated cytopathicity in infected cells by greater than 75%. The results indicate that anti-HIV–1–Tat multiple peptide conjugate antibodies inhibit viral pathogenesis, possibly by blocking functional determinants of Tat and disrupting autocrine and paracrine actions of secreted Tat protein. This epitope-specific synthetic Tat construct provides a subunit AIDS vaccine for inducing and effective immunoprophylaxis response to reduce progression of HIV infection.

Dated: June 15, 2000.

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

Substance Abuse and Mental Health Services Administration (SAMHSA)

Notice of Meetings

Pursuant to Public Law 92–463, notice is hereby given of the following meetings of SAMHSA Special Emphasis Panels I in July, August and September 2000.

A summary of the meetings and a roster of the members may be obtained from: Ms. Coral Sweeney, Review Specialist, SAMHSA, Office of Policy and Program Coordination, Division of Extramural Activities, Policy, and