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. 202 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 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 epsilon 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.

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...