specific mutations in HIV–1 Env on humoral and cellular immune responses after DNA vaccination has been investigated. The modifications of Env enhance antibody production to this viral protein that may facilitate the generation of broadly neutralizing antibodies to HIV. In addition, the immune response to HIV–1 Gag and Pol after plasmid DNA immunization with Rev-independent expression vectors encoding various forms of these proteins has been examined. The Gag-Pol fusion protein induced the most broad and potent CTL responses to Gag and Pol in DNA-vaccinated mice. These DNA sequences and proteins may be important immunogens for the treatment and prevention of HIV infection.

Mucosal Cytotoxic T Lymphocyte Responses

Jay A. Berzofsky (NCI), Igor M. Belyakov (NCI), Michael A. Derby (NCI), Brian L. Kelsall (NIAID), Warren Strober (NIAID)
Serial Number 09/508,552 filed June 12, 2000; DHHS Reference No. E–268–97/4 filed January 10, 2001
Licensing Contact: Peter Soukas; 301/496–7056, ext. 268; e-mail: soukasp@od.nih.gov

This invention claims methods and compositions for inducing a protective mucosal cytotoxic T lymphocyte (CTL) response in a mammal involving administering a soluble antigen or a soluble antigen with one or more active agents such as a cytokine or co-stimulatory molecule to a mucosal surface or tissue. As a preferred embodiment, the invention contemplates intrarectal administration of the peptide vaccine because the inventors have shown that there is a greater CTL response through intrarectal administration rather than intranasal administration. The synthetic peptide vaccines utilized in the invention to elicit protective immune responses after mucosal infection comprise a multideterminant helper peptide containing a cluster of overlapping helper epitopes (a PCLUS or cluster peptide) colinearly synthesized with a peptide epitope target for neutralizing antibodies and CTL. The inventors have generated data showing that an intrarectally administered synthetic multiepitope HIV/SIV peptide vaccine administered to macaques in conjunction with mutant E. coli heat labile enterotoxin as an adjuvant induces mucosal CTL responses that provide better protection against intrarectal SHIV infection when compared to a subcutaneously administered vaccine comprising the same peptides inducing as high or higher systemic CTL responses. The invention is further described in Belyakov et al., Proc. Natl. Acad. Sci. USA 1998 Feb 17;95(4):1709–14 and Belyakov et al., J. Clin. Invest. 102: 2072–2081, 1998.

A Novel Chimeric Protein for Prevention and Treatment of HIV Infection

Edward A. Berger (NIAID), Christie M. Del Castillo
Serial No. 60/124,681 filed 16 Mar 1999 and PCT/US00/06946 filed 16 Mar 2000
Licensing Specialist: Peter Soukas; 301/496–7056 ext. 268; e-mail: soukasp@od.nih.gov

This invention relates to bispecific fusion proteins effective in viral neutralization. Specifically, the invention is a genetically engineered chimeric protein containing a soluble extracellular region of human CD4 attached via a flexible polypeptide linker to a single chain human monoclonal antibody directed against a CD4-induced, highly conserved HIV gp120 determinant involved in coreceptor interaction. Binding of the sCD4 moiety to gp120 induces a conformational change that enables the antibody moiety to bind, thereby blocking Env function and virus entry. This novel bispecific protein displays neutralizing activity against genetically diverse primary HIV–1 isolates, with potency at least 10-fold greater than the best described HIV–1 neutralizing monoclonal antibodies. The agent has considerable potential for prevention of HIV–1 infection, both as a topical microbicide and as a systemic agent to protect during and after acute exposure (e.g. vertical transmission; post-exposure prophylaxis). It also has potential utility for treatment of chronic infection. Such proteins, nucleic acid molecules encoding them, and their production and use in preventing or treating viral infections are claimed.

Antimicrobial Magainin Peptides

Michael A. Zasloff, Hao-Chia Chen, Judith H. Brown, John L. Morell, Charng-Ming Huang (NICHD)
Serial No. 07/280,363 filed 12/06/1988, now U.S. Patent 5,221,732; Serial No. 07/021,493 filed 03/04/1987, now U.S. Patent 4,810,777; Serial No. 07/834,992 filed 02/14/1992, now U.S. Patent 5,567,681; Serial No. 07/963,007 filed 10/19/1992, now U.S. Patent 5,643,876
Licensing Contact: Peter Soukas; 301/496–7056 ext. 268; e-mail: soukasp@od.nih.gov

First isolated from the skin of the African clawed frog *Xenopus laevis*, magainin peptides have been shown by the inventors to have broad-spectrum antimicrobial properties. Both synthetic and natural magainin peptides are active against many species of bacteria and fungi and induce osmotic lysis of protozoa. Magainin peptides are water soluble, nonhemolytic at effective antimicrobial concentrations, have molecular weights of 2500 or less and are amphiphilic. Compositions and methods for their use are claimed in the patents. These inventions are available for nonexclusive or exclusive licensing. The inventions are further described in Zasloff et al., P.N.A.S. USA 1987 Aug.;84(15):5449–53; Marion et al., FEBS Lett. 1988 Jan.18;227(1):21–6; Soravia et al., FEBS Lett. 1988 Feb. 15;228(2):337–40; Westerhoff et al., P.N.A.S. USA 1989 Sep.;86(17):6597–601; and Gwadz et al., Infect. Immun. 1989 Sep.; 57(9):2628–33.

Dated: February 15, 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

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.

Plasmids Expressing START Domains of StAR and MLN64

Dr. Yosuke Tsujishita and Dr. James Hurley (NIDDK)
DHHS Reference No. E–020–01/0
Licensing Contact: Marlene Shinn; 301/496–7056 ext. 285; e-mail: shinnm@od.nih.gov

Steroidogenic acute regulatory protein (StAR) manages acute steroidogenesis in the adrenal cortex and gonads by promoting the translocation of cholesterol to the mitochondrial inner membrane where initial steroid biosynthesis is catalyzed. Within StAR are StAR related lipid transfer (START) domains which are 200–210 amino acid motifs that occur in a remarkably wide range of proteins involved in diverse cell functions such as lipid transport and metabolism, signal transduction and transcription regulation. The closest homolog to StAR is MLN64, with 35% sequence identity between their START domains.

The technology embodied in this invention encompasses plasmids expressing START domains of StAR and MLN64. These fragments enable expression of proteins for many biochemical studies and specifically towards cholesterol transfer in acute steroidegenesis. Possible commercial applications include targets for cancer treatment to known over expressed MLN64 in breast carcinoma.

Macromolecular Enzyme Substrates

Glen L. Hortin (CC)
DHHS Reference No. E–233–99/0 filed 31 Jul 2000
Licensing Contact: Dennis Penn; 301/496–7056 ext. 211; e-mail: pennd@od.nih.gov

This invention discloses a new class of reagents used to measure the activity of enzymes. The inventor discovered that connecting a small reagent molecule onto a polymer that serves as a large carrier molecule confers advantages in the measurement of enzyme activity. Advantages of the new class of reagents are: (1) Better modeling of the size of natural targets (substrates) of many biologically important enzymes, (2) improved specificity of measurements, (3) ability to measure the influence of substrates size on enzyme activity (carrier group size can be varied over a wide range), (4) improved substrate solubility, and (5) the potential for easier methods of synthesis and purification of some enzyme substrates. Reagents of this class can be used to measure the activity of components forming and breaking down blood clots, of digestive components, of components of the complement system, and of many other components with essential biological functions.

Efficient Generation of Midbrain Neurons From Mouse Embryonic Stem Cells

Sang-Hun Lee, Nadya Lumelsky, Lorenz Studer and Ronald McKay (NINDS)
DHHS Reference No. E–291–99/0 filed May 1, 2000
Licensing Contact: Norbert Pontzer; 301/496–7735, ext. 284; e-mail: pontzern@od.nih.gov

Parkinson's disease is a progressive neurological disorder affecting an estimated one million patients in the United States. Parkinson's disease occurs when dopamine producing cells in the central nervous system degenerate. Currently patients receive medications to treat the symptoms, but not cure or stop the progression of the disease. As the disease progresses the medications usually become less effective. One encouraging new form of therapy replaces the lost dopamine producing neurons with transplanted cells. A major obstacle to cell replacement therapy has been obtaining sufficient dopamine producing cells. Therapeutic or ethical problems exit for all presently available sources of cells for transplantation.

This invention provides a method for efficiently generating dopaminergic neurons from embryonic stem cells. Embryonic cells are totipotent cells which can proliferate indefinitely in the undifferentiated state. A method of generating specific differentiated cells from embryonic stem cells thus provides a potentially unlimited source of those cells. A sequence of culturing steps involving exposure to specific neurotrophic factors and other agents produces a high percentage of cultured dopaminergic neurons. An unlimited supply of dopaminergic neurons which may be suitable for transplantation is thus provided. Details of some aspects of this invention can be found in Nature Biotechnology Vol. 18, pages 675–679, June 2000.

Methods for Delivering Biologically Active Molecules Into Cells

Jeffrey L. Miller, Urszula Wojda, Paul K. Goldsmith (NIDDK)
DHHS Reference Nos. E–174–98/0 filed 15 Jan 1999 and E–174–98/1 filed 14 Jan 2000
Licensing Contact: Dennis Penn; 301/496–7056 ext. 211; e-mail: pennd@od.nih.gov

The appropriate gene therapy delivery system depends greatly on the cells being targeted and the means by which delivery is anticipated. Numerous clinical trials are currently ongoing for gene therapy, each typically usually a different mode of delivery. It is still too early to determine which mode will be approved and which will be the most effective. The polyethylenimineDNA (PEI–DNA) complex is known to be an effective system for delivery of DNA. In vitro models of a new delivery system based on the cationic properties of PEI have found that the cellular incorporation is significantly enhanced using an Avidin-PEI–DNA complex. Experiments have shown that there is, at a minimum, a 3x to 10x increase in the cellular uptake of the DNA. It is believed that this gene delivery system can be targeted to any cell of interest. It was demonstrated that the transfection can be targeted to native and biotinylated cells. For cells, with a known surface phenotype, biotinylated monoclonal antibodies can be attached to specific sites and the Avidin-PEI–DNA complex then binds and enters the cell via endocytosis.

Alternatively, cells without a known surface phenotype, biotin can be covalently attached to the cell surface and the Avidin-PEI–DNA complex is then able to bind and carry the DNA into the cells. This system appears to be not only applicable to gene therapy, but to the diagnostic market and to the delivery of other anionic materials into cells. This Avidin-PEI–DNA system may find a niche market or it may become utilitarian, such that it can be effectively utilized in more than one gene therapy treatment. This technology is available for immediate licensing and independent commercialization and/or a Cooperative and Development Research Agreement can be considered.

Dated: February 15, 2001.

Jack Spiegel,

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

[FR Doc. 01–4617 Filed 2–23–01; 8:45 am]

BILLING CODE 4140–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Prospective Grant of Co-Exclusive License: Homogeneous Tests for Sequentially Determining Lipoprotein Fractions

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

ACTION: Notice.

SUMMARY: This is 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 (NIH), Department of Health and Human Services, is contemplating the grant of a co-exclusive worldwide to practice the inventions embodied in US Patent Application Serial Number (60/136,709 (PCT/US00/14827) entitled ''Homogeneous Tests for Sequentially Determining Lipoprotein Fractions'', provisionally filed May 28, 1999 and PCT filed May 26, 2000, to Genzyme Diagnostics, having a place of business