Associated Virus of serotype 5 (AAV5). The particular target cells identified include the alveolar cells of the lung and cerebellar and ependymal cells of the brain. The methods described herein may be useful in carrying out gene therapy related to diseases of the brain or central nervous system and the respiratory tract.

This work has been published, in part, at Davidson BL, *et al.* PNAS, USA 97(7):3428–32 (March 28, 2000) and Zabner J, *et al.* J Virol. 74(8):3852–8 (April 2000).

In addition to this patent application, PHS owns additional intellectual property related to this technology. The patent application has been published as WO 99/61601 on December 2, 1999 and the research corresponding thereto has been published at Chiorini JA, *et al.* J. Virol. 73(5): 4293–98 (May 1999) and Chiorini JA, *et al.* J. Virol. 73(2): 1309–19 (Feb. 1999).

AAV4 Vector and Uses Thereof

JA Chiorini (NHLBI/NIDCR), RM Kotin, B Safer (both of NHLBI)
Serial No. 09/532,594 filed 22 Mar 2000

The invention described and claimed in this patent application relates to the delivery of heterologous nucleic acids or genes to particular target cells. In particular, the application relates to methods of delivering a heterologous nucleic acid or gene of interest to particular target cells using Adeno-Associated Virus of serotype 4 (AAV4). The particular target cells identified are the ependymal cells of the brain. The methods described herein may be useful in carrying out gene therapy for diseases of the brain or central nervous system.

This work has been published in part at Davidson, BL, *et al.* ''Recombinant adeno-associated virus type 2, 4, and 5 vectors: transduction of variant cell types and regions in the mammalian central nervous system'' PNAS USA 97(7):3428–32 (March 28, 2000).

In addition, PHS owns additional intellectual property related to this technology describing an AAV4-based vector system. The material contained in the patent application has been published as WO 98/11244 (March 19, 1998) and the research corresponding thereto has been published in J. Virology 71(9): 6823–33 (Sept 1997).

A Novel Pro-Apoptotic Protein, ARTS

S Larisch-Bloch, SJ Kim, RJ Lechleider, AB Roberts and Y Yi (all of NCI)
Serial No. 60/178,866 filed 29 Jan 2000

This application relates to the field of apoptosis, in particular the application relates to a novel gene product which is associated with induction of apoptosis by Transforming Growth Factor Beta (TGF–β). Apoptosis is a critical event in developmental processes and homeostasis; its dysregulation is often central to pathogenic mechanisms. Apoptotic aberrations contribute to the development of the transformed phenotype; both metastatic potential and tumor aggressiveness are associated with increased resistance to apoptosis. Certain chemotherapeutic agents act by increasing the sensitivity of cells to apoptosis and patients with mutations in genes regulating apoptosis are known to have a poor prognosis.

The application describes the cloning of a gene which encodes a splice variant of the known gene designated H5/PNUTL2/CDCrel–2a/2b and the isolation and characterization of its protein product. The newly identified protein, designated ARTS (*A*poptosis *R*elated *P*rotein in the *T*GF–β *S*ignaling Pathway), is a member of the septin family of proteins. It is localized to mitochondria and translocates to the nucleus where ARTS induces apoptosis in response to TGF–β. ARTS is the first septin shown to be essential for mediating *T*GF–β dependent apoptosis. Antisense ARTS nucleic acids are also contemplated. Because of its role in regulating the sensitivity of cells to TGF–β induced apoptosis ARTS derived products may provide a means for treating conditions where increased TGF–β induced apoptosis is desired (*e.g.,* cancer) and where decreased TGF–β induced apoptosis is desired (*e.g.,* neurodegenerative diseases).

This work has been published in part at Larisch-Bloch S *et al.* ''Selective loss of the transforming growth factor-beta apoptotic signaling pathway in mutant NRP–154 rat prostatic epithelial cells'' Cell Growth Differ 11(1):1–10 (Jan 2000).

Replication Deficient Retroviral Vector System and Methods of Using

WJ Ramsey (NHGRI)

Serial No. 60/101,425 filed 22 Sep 1998; PCT/US99/21393

The technology described and claimed in this application relates to the field of gene therapy. More particularly, the technology described and claimed in the application relates to a method for producing replication deficient, but infectious, retroviral vectors. This method of producing replication deficient retroviral vectors for gene therapy yields virus in high titer and is readily adaptable to large scale production. In the methods described herein a producer cell is transformed with an integrating proviral sequence which includes a pair of retroviral LTRs, a retroviral packaging signal and the gene of interest. A second viral vector, containing trans complementing functions, such as the gag, pol, and env genes, is then used to infect/transform the cells containing the integrated proviral sequence enabling the generation of a replication deficient vector. This second viral vector may be chimeric, *e.g.,* have an adenoviral backbone and retroviral trans complementing functions. Producer cells, which now contain the trans complementing vector and the integrated proviral vector are then cultured to obtain the replication deficient viral vector from the medium.

The PCT application has been published as WO 00/17736 (March 30, 2000). Related technology describing chimeric vectors for gene therapy is also available for licensing. It is described in USSN 09/058,686 filed 10 Apr 1998 (published as WO 98/46778 (Oct. 22, 1998).

Dated: July 19, 2000.

Jack Spiegel,

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

[FR Doc. 00–19150 Filed 7–27–00; 8:45 am]

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.

V1 Knockout Mice for Screening New Vaccines Against Streptococcus Pneumoniae

Qing-Sheng Mi, James J. Kenny, Dan L. Longo (NIA)

DHHS Reference No. E–140–00/0

Licensing Contact: Uri Reichman; 301/496–7056 ext. 240; e-mail: reichmau@od.nih.gov

Streptococcus pneumonia (SP) is a bacterial agent found in both mild mucosa and severe systemic infection; it is also often responsible for pneumonia, a disease that takes over one million lives a year. Recent SP strains prove resistant to Penicillin and other antibiotics, making the development of a Pneumococcal vaccine crucial. The existing vaccine is only about eighty percent effective at preventing SP infection in adults, but is much less effective in infants, aged, or immune deficient patients. Antibodies to phosphocholine (PC), an immunodominant epitope in the cell wall of Streptococcus pneumoniae, protect mice from lethal pneumococcal infection. The heavy chain of the PC protecting antibody is encoded by the V1 segment of the S107 V_H gene family. The V1 knockout mice which are available for licensing, cannot produce protective antibodies against the PC epitope of Streptococcus pneumonia. They are however, capable of producing normal antibodies to other cell wall proteins following bacteria immunization and get partial protection against lethal pneumococcal infection. Thus, the V1 knockout mice can facilitate the screening of protective antigens other than PC. This may result in new vaccine candidates against Streptococcus pneumonia. Screening for new vaccine candidates can be done as follows: The V1 knockout mice can be immunized with avirulent SP bacteria. The immune serum will be utilized to detect and isolate the antigenic cell wall proteins, using standard affinity binding procedures. The antigenic proteins will then be cloned, sequenced and purified. Normal mice will be immunized with these proteins and then challenged with virulent SP bacteria to determine whether these proteins have protective function.

Methods and Compositions for Co-Stimulation of Immunological Responses to Peptide Antigens

Samir Khleif, Jay Berzofsky (NCI)

DHHS Reference No. E–128–00/0 filed 15 Mar 2000

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

This invention relates to peptide vaccines comprising administering a peptide comprising at least one T cell epitope coordinately with a non-viral vector comprising a polynucleotide encoding a T cell co-stimulatory molecule useful for eliciting cellular immune responses. The inventors have found that intradermal vaccination of mice with a DNA vector carrying the mouse co-stimulatory immunoglobulin B7.1 (CD80) in combination with a Human Papilloma Virus (HPV) E7 peptide significantly enhances the E7 specific cytotoxic lymphocyte response. Delivery of the B7.1 molecule as non-replicating DNA with antigenic peptides overcomes the problems of low antigenicity associated with some viral vectors as well as the instability, exogenous presentation and conformational maintenance problems associated with the delivery of full-length protein delivery. Furthermore, polynucleotides encoding the B7.1 construct can potentially be used along with any other form of antigen vaccine delivery systems, including peptides, full proteins and naked DNA antigens and are inexpensive to produce.

Full-Length Infectious cDNA Clones of Tick Borne Flavivirus

Alexander Pletnev, Robert M. Chanock (NIAID)

DHHS Reference No. E–281–98/0 filed 10 Feb 2000

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

The tick-borne encephalitis virus complex of flavivirus family includes tick-borne encephalitis (TBEV), Kyasanur forest disease, Langat, Louping ill, Negishi, Omsk hemorrhagic fever and Povassan viruses. These viruses are endemic throughout most of the Northern Hemisphere and except for Langat, cause human disease of varying severity that can have mortality as high as 20 to 30%. Tick-borne encephalitis remains a pressing public health problem in Eastern Europe and Russia, where 9,000 to 12,000 patients are diagnosed annually and there is a need for a vaccine which can prevent this disease. This invention relates to an infectious full length Langat virus cDNA which has been successfully constructed and can be used to further attenuate this naturally attenuated tick-borne flavivirus. This full length Langat virus can be used as a live attenuated virus vaccine for the prevention of severe, often fatal disease caused by its more virulent tick-borne flavivirus relatives such as tick-borne encephalitis virus.

Polypeptides That Bind HIV gp120 and Related Nucleic Acids, Antibodies, Compositions, and Methods of Use

Carl Saxinger (NCI)

DHHS Reference No. E–245–99/0 filed 27 Aug 1999

Licensing Contact: J.P. Kim; 301/496–7056 ext. 264; e-mail: kimj@od.nih.gov

The presence of chemokines has been observed to have an inhibitory effect on HIV–1 attachment to, and infection of, susceptible cells. The interaction between gp120 and CD4, or at least one chemokine receptor is obligatory for HIV–1 infection. Reagents which interfere with the binding of gp120 to chemokine receptors and to CD4 are used in the biological and medical arts; however, there remains a need for additional reagents that can compete with one or more proteins of the gp120-CD4-chemokine-receptor complex to assist in the development of HIV therapeutics.

The present invention relates to such polypeptides with homology to domains of the human chemokine receptors CCR5, CXCR4, and STRL33, as well as domains of CD4 that bind with human immunodeficiency virus (HIV), in particular the HIV–1 glycoprotein 120 (gp120) envelope protein. These receptor polypeptides were identified through the application of a recent technological advance in the design and synthesis of synthetic peptide arrays (see Saxinger, WC: An automated peptide design and synthesis; U.S. Patent 6,031,074 issued 29 Feb 2000). The binding of gp120 to receptor peptide arrays was highly linearly correlated with structure/activity relationships between biological receptors and HIV infectivity in vitro ($r=>95\%$, $p<=0.03$). The binding of gp120 by active receptor polypeptides was unrestricted by viral or receptor strain or subtype suggesting that the polypeptides participated in an early stage of infection common to multiple virus strains, thus potentially addressing problems of virus variation and multiple virus strains. The invention further provides for nucleic acids encoding such polypeptides, antibodies, compositions comprising such polypeptides, nucleic acids or antibodies, and methods of use thereof, such as in therapeutics and vaccine design.

System and Method for Simulating a Two-Dimensional Radiation Intensity Distribution of Photon or Electron Beams

J van de Geijn, H Xie (NCI)

Serial No. 08/368,589 filed 06 Jan 1995; U.S. Patent No. 5,526,395 issued 11 Jun 1996

Licensing Contact: NIHOTT@od.nih.gov

The present invention provides a method for computer-assisted, interactive 3-dimensional radiation treatment planning and optimization. The computerized system is capable of processing and analyzing data obtained from x-ray, CT, MRI, PET, SPECT, and gammacamera devices. Hence, the system can be used as a training device, alleviating the need for training centers to purchase each of these devices. The computerized system comprises a fast, versatile, and user-friendly software package and computer components which are commercially available and which can be used without significant modification. Because the hardware costs of this system are much lower than the cost of systems of comparable ability, this invention ought to be particularly attractive to smaller radiation oncology facilities which seek a powerful treatment planning system. The low cost of the system is also particularly advantageous for medical training facilities, including medical schools. The invention also has potential use as a monitor for clinical quality assurance.

Combination Therapies for Viral Infection

Lori *et al.* (NCI); Malley & Vila

Serial Nos. 08/065,814 filed 21 May 1993; 08/245,259 filed 17 May 1994; 08/169,253 filed 20 Dec 1993; 08/378,219 filed 25 Jan 1995; 08/401,488 filed 08 Mar 1995; 08/577,322 filed 22 Dec 1995; 08/617,421 filed 18 Mar 1996; 09/497,700 filed 03 Feb 2000

Licensing Contact: J.P. Kim; 301/496–7056 ext. 264; e-mail: kimj@od.nih.gov

The subject inventions provide for formulations and methods for inhibiting replication of reverse transcription dependent viruses in animals cells comprising administering a compound that depletes the intracellular pool of deoxyribonucleoside phosphate, and further comprising administering a compound that serves to inhibit replication of the virus by terminating DNA chain elongation.

Dated: July 19, 2000.

Jack Spiegel,

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

[FR Doc. 00–19151 Filed 7–27–00; 8:45 am]

BILLING CODE 4140–01–P

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National Institutes of Health

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Vessel Delineation in Magnetic Resonance Angiographic Images

Peter Yim (CC)

Serial No. 60/181,990 filed 11 Feb 2000

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

This invention relates to advances in magnetic resonance angiography (MRA) or the imaging of blood vessels in the body for the evaluation of vascular pathology. Presented are new methods for processing magnetic resonance angiographic images, or angiograms, to delineate certain vessels in an angiogram. These methods find particular utility in highly vascular regions of the body such as the cerebrum, heart, abdomen and extremities where there is extensive overlapping and variation in the size of the vessels. Current MRA methods are unable to generate high-resolution images of complex vessel geometries in these dynamic environments. The patent application for this invention covers algorithms and computer-implemented methods for tracking the paths of vessels in magnetic resonance angiography. Also covered are similar methods for digital image processing in alternative imaging technologies such as tomography and X-ray angiography.

Methods for Predicting the Biological, Chemical, and Physical Properties of Molecules From Their Spectral Properties

Dwight W. Miller *et al.* (FDA)

Serial No. 09/496,314 filed 01 Feb 2000

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

The number of known chemical compounds is enormous, and the number is constantly increasing. While there are a vast number of chemical compounds, only a relative few of those compounds may exhibit a particular desirable property, such as pharmaceutical activity. Random testing of known compounds to identify those compounds which show pharmaceutical activity is very expensive and time-consuming. Similarly, there is also a need to screen compounds for toxicity, so that rational decisions can be made regarding the use and regulation of compounds that have toxic potential. At present, only a fraction of known compounds have been thoroughly tested for their toxicological and potential therapeutic properties.

Scientists have developed methods which attempt to predict which compounds are likely to exhibit a particular property. The present invention provides a method for establishing a quantitative relationship between spectral properties of molecules and a biological, chemical, or physical endpoint of the molecules. The present invention further provides methods for rapidly screening isolated compounds or mixtures of compounds based upon their spectral data.

Molecules That Influence Pathogen Resistance

Gregory A. Taylor and George F. Vande Woude (NCI)

DHHS Reference No. E–068–00/0 filed 03 Jan 2000

Licensing Contact: J.P. Kim; 301/496–7056 ext. 264; e-mail: kimj@od.nih.gov

Interferon-gamma (IFN-γ) is an important cytokine for control of infectious agents and regulation of the immune system. IFN-γ is thought to exert its effects largely by activation of IFNγ-responsive genes. One recently identified IFNγ-regulated gene is IGTP. It has been found that the IGTP-family proteins mediate the immune response of mammals to various infectious pathogens. In particular, it has been noted that IGTP functions as a downstream mediator of IFN-γ and