orally or in writing, on issues pending before the committee. Written submissions may be made to the contact person by August 22, 1997. Oral presentations from the public will be scheduled between approximately 8:30 a.m. to 9 a.m., and between approximately 1 p.m. to 2 p.m. on September 4, 1997. Time allotted for each presentation may be limited. Those desiring to make formal oral presentations should notify the contact person before August 22, 1997, and submit a brief statement of the general nature of the evidence or arguments they wish to present, the names and addresses of proposed participants, and an indication of the approximate time requested to make their presentation. The agency encourages investigators, academicians, members of the pharmaceutical industry, consumer groups, and others with information relevant to the topic to respond to the contact person.

Notice of this meeting is given under the Federal Advisory Committee Act (5 U.S.C. app. 2).

Dated: August 7, 1997.

William B. Schultz,

Acting Lead Deputy Commissioner.

[FR Doc. 97–21434 Filed 8–12–97; 8:45 am]

BILLING CODE 4160–01–F

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

Advisory Committee; Notice of Meeting

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

This notice announces a forthcoming meeting of a public advisory committee of the Food and Drug Administration (FDA). At least one portion of the meeting will be closed to the public.

Name of Committee: Hematology and Pathology Devices Panel of the Medical Devices Advisory Committee.

General Function of the Committee: To provide advice and recommendations to the agency on FDA regulatory issues.

Date and Time: The meeting will be held on September 5, 1997, 10 a.m. to 5 p.m.

Location: Corporate Bldg., conference room 020B, 9200 Corporate Blvd., Rockville, MD.

Contact Person: Veronica J. Calvin, Center for Devices and Radiological Health (HFZ–440), Food and Drug Administration, 2098 Gaither Rd., Rockville, MD 20850, 301–594–1243, or FDA Advisory Committee Information Line, 1–800–741–8138 (301–443–0572 in the Washington, DC area), code 12515. Please call the Information Line for up-to-date information on this meeting.

Agenda: The committee will discuss quality control issues for home-use prothrombin time devices.

Procedure: On September 5, 1997, from 10:30 a.m. to 5 p.m., the meeting is open to the public. Interested persons may present data, information, or views, orally or in writing, on issues pending before the committee. Written submissions may be made to the contact person by August 22, 1997. Oral presentations from the public will be scheduled between approximately 11 a.m. and 12:15 p.m. Time allotted for each presentation may be limited. Those desiring to make formal oral presentations should notify the contact person before August 22, 1997, and submit a brief statement of the general nature of the evidence or arguments they wish to present, the names and addresses of proposed participants, and an indication of the approximate time requested to make their presentation.

Closed committee deliberations. On September 5, 1997, from 10 a.m. to 10:30 a.m., the meeting will be closed to permit discussion and review of trade secret and/or confidential information. (5 U.S.C. 552b(c)(4)). FDA staff will present trade secret and/or confidential commercial information regarding present or future issues.

Notice of this meeting is given under the Federal Advisory Committee Act (5 U.S.C. app. 2).

Dated: August 11, 1997.

Michael A. Friedman,

Deputy Commissioner for Operations.

[FR Doc. 97–21552 Filed 8–12–97; 8:45 am]

BILLING CODE 4160–01–F

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Government-Owned Inventions; Availability for Licensing

AGENCY: National Institutes of Health.

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 U.S. 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.

Dvl1-Deficient Mice

AJ Wynshaw-Boris, N Lijam, D Sussman, R Paylor, J Crawley (NHGRI)

OTT Reference No. E–100–97/0

Licensing Contact: David Sadowski; *phone:* 301/496–7735 ext. 288; *e-mail:* DS27A@NIH.GOV

Genetic factors are important modifiers of a variety of simple and complex behaviors in virtually all organisms. Genetic effects have been inferred from inbred strain analysis in rodents and from linkage analysis in rodents and humans. More recently, genes influencing specific behaviors have been identified by analyzing behavioral abnormalities in mice with targeted gene disruption.

In the present invention, mice completely deficient for Dvl1, a mouse homolog of the Drosophila segment polarity gene Dishevelled, were created by gene targeting. These mice demonstrate that Dvl1 participates in complex behaviors in mammals. Dvl1-deficient mice exhibit reduced social interaction, including differences in whisker-trimming, deficits in nest-building, less huddling contact during home cage sleeping, and subordinate responses in a social dominance test. In addition, Dvl1-deficient mice display striking abnormalities in sensorimotor gating, as indicated by attenuation of prepulse startle inhibition in the mutant mice. Prepulse inhibition is abnormal in several human neuropsychiatric disorders including schizophrenia, schizotypal personality disorders, obsessive-compulsive disorders, Huntington's disease, and Tourette syndrome. In addition, many of these disorders (as well as autism) are characterized by abnormal social interaction. Hence, Dvl1-deficient mice provide a genetic animal model of aspects of several human psychiatric disorders and serve as a useful model for screening drugs that modify

abnormal social interaction and sensorimotor gating.

Transgenic and Chimeric Viral Delivery Systems

WJ Ramsey, RM Blaese (NHGRI)

OTT Reference No. E–011–97/0 filed 11 Apr 97

Licensing Contact: Larry Tiffany; *phone:* 301/496–7056 ext. 206; *e-mail:* LT10X@NIH.GOV

The development of eukaryotic viral vectors has generally focused on delivery of one or more heterologous genes to target cells, particularly for gene therapy. Such development has primarily involved vector systems utilizing retrovirus, adenovirus, herpes virus, vaccinia virus, and adeno-associated virus particles. However, each of these viral vector systems has presented one or more of several obstacles including low viral titers, induced host immune responses, inefficient transduction, and transient expression of the desired heterologous gene. This invention addresses the need for improved eukaryotic viral vectors for diagnostic applications and for delivering heterologous genes to cells *in vitro*, *ex vivo*, and *in vivo*.

The present invention provides a system for the production of viral vectors (secondary viruses) whose genome is encoded within another virus with a different life cycle and biologic characteristics (primary virus). For example, chimeric primary viruses with high transduction efficiencies (adenoviruses) can be used to direct the production of secondary viruses (retroviruses) in a wide range of producer cell types. Thus single (or panels of) secondary viral vectors containing identical secondary vector genomes can easily and rapidly be produced in retroviral vector packaging cells containing different envelope targeting components with the additional advantage that there will be little chance for vector rearrangement or recombination. Secondary viruses also can be readily produced in cells obtained from the eventual gene therapy target species so that enveloped viruses will contain membrane constituents from the same, rather than a xenogeneic species, lessening the chance for neutralizing immune responses to the vectors. Similarly, serum complement-mediated lysis of retroviral vectors may be eliminated by the ability to easily use vector producer cells from the same species as the species to be treated by gene therapy. Such secondary viruses may comprise an expression cassette constituting a nucleic acid encoding a heterologous protein and/or an antisense nuclei acid. Hence, this invention overcomes obstacles occurring with the *in vitro*, *ex vivo*, and *in vivo* use of common viral vector systems. In addition, these chimeric primary viruses can be used to rescue unknown viral genomes from host cells for use in the development of diagnostic tests or in the development of novel viral vector systems.

MEN1, The Gene For Multiple Endocrine Neoplasia Type 1

SC Chandrasekharappa (NHGRI), AM Spiegel (NIDDK), LA Liotta (NCI) et al.

OTT Reference No. E–094–97/0 filed 05 Mar 97

Licensing Contact: Ken Hemby; *phone:* 301/496–7735 ext. 265; *e-mail:* JH259B@NIH.GOV

Multiple endocrine neoplasia type 1 (MEN1) is an autosomal dominant familial cancer syndrome characterized by occurrence of tumors in parathryroids, enteropancreatic endocrine tissues, the anterior pituitary, and occasionally other sites. The present invention provides an isolated DNA sequence encoding a gene which when mutated in the germline is associated with the development of MEN1. This invention also comprises polyclonal and monoclonal antibodies which selectively bind to menin, the protein encoded by MEN1. In addition, the present invention provides methods for immunological detection of menin in biological samples as well as methods for detecting the presence, alteration, or absence of MEN1 DNA or RNA. This research has been published in Science 276: 404–407 (1997).

Potential areas of application of this invention include sporadic and familial MEN1 diagnostics using immunoassays and nucleic acid hybridizations, and gene therapy.

Invaginated Liposome Delivery System

N Smyth-Templeton, GN Pavlakis (NCI)

Serial No. 60/024,386 Filed 19 Aug 96

Licensing Contact: Larry Tiffany; *phone:* 301/496–7056 ext. 206; *e-mail:* LT10X@NIH.GOV

Liposome formulations for in vivo delivery are valuable alternatives to viral vectors and avoid the inherent problems associated with modifying viral genomes to create expression vehicles. Previous liposome formulations limited therapeutic efficacy due to generally low expression of the DNA being delivered. In contrast, these novel liposomes are able to transfect a broad host range and express the encoded proteins at high titers.

The present technology involves highly efficient cationic liposomes for increased in vivo delivery of biologically active agents. These extruded DOTAP:cholesterol complexes allow gene expression to be improved up to 150-fold over previous liposomes. This improvement is due to the novel morphology of the DNA:liposome complexes. The complexes are vaselike structures which invaginate and condense DNA between two protective lipid bilayers. Because the outside of the DNA:liposome complexes is substantially free of DNA, targeting ligands may be placed on the outside of the complexes, without compromising the effect of the targeting ligand or the ability of DNA to be delivered and expressed.

The present technology may be used for: systematic or site-specific delivery and expression of nucleic acid products; production of kits capable of carrying any biologically active agent; delivery of reagents for human gene therapy in the treatment of disease; and providing a method for long term expression of a gene product from a non-integrated nucleic acid.

Licensees are currently being sought for all therapeutic applications.

In Vitro Determination Of CD4+ T Cell Depletion In HIV–1 Seropositive Subjects as a Predictor of Future CD4+ T Cell Decline In Vivo

D Zella, A Riva, M Reitz (NCI)

OTT Reference No. E–061–96/0

Licensing Contact: George Keller; *phone:* 301/496–7735 ext. 246; *e-mail:* GK40J@NIH.GOV

The current invention embodies a prognostic method for determining whether an asymptomatic HIV–1 seropositive individual is a progressor or a non-progressor to AIDS. The inventors have discovered that in HIV–1 seropositive persons in the asymptomatic stage of the disease, peripheral blood mononuclear cells (PBMCs) respond in one of two ways when isolated and subsequently activated in vitro by IL–2. Either (1) the CD3+CD4+ cell number increases in culture (non-progressor subjects) or (2) the CD3+CD4+ number does not increase or decreases in culture (progressor subjects). This analysis was performed by an automated flow cytometer. This method, when developed as a commercially-available test, may represent an economical and accurate assay to determine when detrimental changes for the immune system occur in asymptomatic HIV–1 seropositive subjects, and for this reason to predict whether an individual is

progressing to AIDS. This assay may therefore be a valuable tool to use in determining the appropriate course of therapy to target not only HIV–1 replication but also to monitor the effects of therapeutic drugs on the host immune system response.

Avian Based Retrovirus Vectors

E Barsov, SH Hughes (NCI)

Serial No. 08/445,462 filed 22 May 95

Licensing Contact: Larry Tiffany; *phone:* 301/496–7056 ext. 206; *e-mail:* LT10X@NIH.GOV

Recombinant retrovirus vectors based on the Rous sarcoma virus (RSV) are valuable alternatives to murine based or replication-defective vectors because they do not require a packaging or helper cell line. Previous RSV vectors limited efficacy due to their inability to infect a broad range of mammalian species. In contrast, these novel vectors are able to infect a wider range of host at high titers while remaining inherently defective in mammalian cells.

The present technology involves recombinant avian sarcoma leukosis virus (ASLV) derived retroviral vectors having an expanded host range. Specifically, the ASLV envelope gene is replaced by the env region derived from a virus capable of infecting both mammalian and avian cells. This improvement allows the vectors to produce high titer stock in avian cells and the resulting virus can infect both avian and mammalian species efficiently.

The present technology may be used for in vitro and in vivo delivery of nucleic acid sequences to avian or mammalian cells and for treatment or prevention of diseases involving transfer by recombinant retroviral vectors.

Licensees are currently being sought for all therapeutic applications.

Nucleotide and Deduced Amino Acid Sequences of a New Tumor Gene, Int6

R Callahan, A Marchetti, F Buttitta, G Smith (NCI)

OTT Reference Nos. E–265–94/0 and E–265–94/1

Licensing Contact: Ken Hemby; *phone:* 301/496–7735 ext. 265; *e-mail:* JH259B@NIH.GOV

Murine retroviruses have been useful in the identification of mammalian genes involved in tumor development. Five loci have been previously identified as integration sites for one specific retrovirus, mouse mammary tumor virus (MMTV). This work describes a sixth site of integration for MMTV, the Int6 gene. The Int6 gene is highly conserved among vertebrate species, including humans. This invention embodies a series of reagents derived from the nucleic acid and amino acid sequences of the Int6 gene and the use of these reagents in diagnostic methods, immunotherapy, gene therapy, and as vaccines.

N-(1-thienylcycloalkyl)alkenyl-amines For Treatment Of Neurotoxic Injury

KC Rice, AE Jacobson, A Thurkauf, MV Mattson, TL O'Donohue, PC Contreras, NM Gray (NIDDK)

Serial No. 08/344,433 Filed 23 November 94; U.S. Patent 5,604,255 issued 18 February 97

Licensing Contact: Leopold Luberecki, Jr.; *phone:* 301/496–7735 ext. 223; *e-mail:* LL87A@NIH.GOV

This invention describes compounds, compositions, and methods for neuroprotective purposes such as controlling brain damage which occurs during periods of anoxia, or ischemia associated with stroke, cardiac arrest or perinatal asphyxia. The treatment includes administration of an N-(1-thienylcycloalkyl) alkylamine compound as an antagonist to inhibit excitotoxic actions at major neuronal excitatory amino acid receptor sites. Compounds of most interest are described in detail.

Brain tissue is particularly sensitive to deprivation of oxygen or energy; permanent damage to neurons can occur during brief periods of hypoxia, anoxia or ischemia. Neurotoxic injury is known to be caused or accelerated by certain excitatory amino acids (EAA) found naturally in the central nervous system. Neurons, which have EEA receptors on their dendritic or somal surface, undergo acute excitotoxic degeneration when these receptors are excessively activated by glutamate. Thus agents which selectively block or antagonize the action of glutamate at the EAA synaptic receptors of central neurons can prevent neurotoxic injury associated with anoxia, hypoxia or ischemia caused by stroke, cardiac arrest or perinatal asphyxia.

The method embodied in the invention may prove valuable for the control of neuropathological processes and the neurodengenerative consequences thereof in mammals by treating a mammal susceptible to neurotoxic injury with an anti-excitotoxic effective amount of a compound of a class described herein.

A Method for the Liposomal Delivery of Nucleic Acids

AR Thierry (NCI)

Serial No. 08/286,730 Filed 05 August 94 and Serial No. 08/522,246 Filed 04 September 95 (CIP of 08/286,730)

Licensing Contact: Larry Tiffany; *phone:* 301/496–7056 ext. 206; *e-mail:* LT10X@NIH.GOV

The present invention is directed to a liposomal preparation of nucleic acids or analogues and specific lipids which form liposomes. Liposome vesicles are prepared from a mixture of cationic lipopolyamine and a neutral lipid. Nucleic acids are associated with the liposomes in two ways: (1) Complex formation between the cationic lissome vesicle and negatively charged nucleic acid or (2) partial encapsulation and partial complex formation in and with the cationic liposome vesicle. Liposome-encapsulated nucleic acids have been shown to be more efficient in transducing cells in cell cultures. Sonication of liposome-complexed nucleic acids allow for more homogenized and smaller liposome particles, and consequently for the ability to circulate for longer periods in blood following systemic injection. Nucleic acids associated with the liposomal carrier are completely protected from enzymatic attack such as nucleases, and stability in circulating blood after administration can be achieved. The present invention provides for the highly efficient delivery of nucleic acids to cells *in vitro* or *in vivo.* Therefore, this invention provides a method for gene therapy. This liposome method does not have safety concerns associated with gene therapy based upon viral vectors. However, liposomal delivery in accordance with the present invention may be used for increasing recombinant retrovirus infection by enhancing the penetration and/or expression of the viral agents.

The patent application includes claims to liposome compositions and method of use. These materials and methods are useful in the delivery of nucleic acids to cells and tissues.

Nitrogen-Containing Cyclohetero Alkylamino Aryl Derivatives for CNS Disorders

BR De Costa, WD Bowen, X-S He, L Radesca, KC Rice (NIDDK)

Serial No. 08/261,796 Filed 20 June 94; U.S. Patent 5,571,832 Issued 05 Nov 96

Licensing Contact: Leopold Luberecki, Jr.; *phone:* 301/496–7735 ext. 223; *e-mail:* LL87A@NIH.GOV

This invention describes a class of therapeutically useful compounds

comprising a pyrrolidinyl ring, compositions and methods for treatment of Central Nervous System (CNS) dysfunctions, neurotoxic damage, or neurodegenerative diseases. These compounds are particularly useful for treating neurotoxic injury which follows periods of hypoxia, anoxia or ischemia associated with stroke, cardiac arrest or perinatal asphyxia. In addition these compounds are also useful as antipsychotics and anticonvulsives.

Unlike other tissues which can survive extended periods of hypoxia, brain tissue is particularly sensitive to deprivation of oxygen or energy. Permanent damage to neurons can occur during brief periods of hypoxia, anoxia or ischemia. Neurotoxic injury is known to be caused or accelerated by certain excitatory amino acids (EAA) found naturally in the CNS. Compounds as described herein block the action of EEA synaptic receptors and thus can prevent neurotoxic injury.

Treatment of CNS disorders and diseases such as cerebral ischemia, psychotic disorders, convulsions and parkinsonism, as well as prevention of neurotoxic damage and neurodegenerative diseases, may be accomplished by administration of a therapeutically-effective amount of a compound of a class described herein.

Severe Renal Glomerular Disease in Mice Homozygous for Targeted Disruption of Uteroglobin Gene: A Model for Human Hereditary Glomerulopathies

AB Mukherjee, Z Zhang (NICHD)

OTT Reference No. E–164–96/0

Licensing Contact: David Sadowski; *phone:* 301/496–7735 ext. 288; *e-mail:* DS27A@NIH.GOV

Uteroglobin (UG) is a protein fraction of pregnant uterine fluid which can induce and regulate blastocystic development and also possesses important anti-inflammatory properties. This invention describes a novel physiological function of UG, which is its role in preventing severe fibronectin (Fn) deposit-associated renal glomerular disease. Uteroglobin binds to Fn thereby inhibiting the formation of Fn-Fn aggregates and Fn-collagen aggregates, thus preventing the disease. Uteroglobin knockout mice (UG-/-) were generated by targeted disruption of the UG gene. These mice developed glomerular disease, became cachectic and died within 4–5 weeks after birth.

This mouse could potentially be a valuable model system for the study and treatment of glomerular disease.

A description of this research may be found in Science, vol. 276, pp. 1408–1412, 1997.

A Method for Producing Retrovirus RNA Packaging Cassettes Amplified in the Cytoplasm by Autocatalytic Togavirus Vectors

R Morgan, J Wahlfors, K Xanthopoulos (NHGRI)

OTT Reference No. E–135–96/0 filed 25 Sep 96

Licensing Contact: Larry Tiffany; *phone:* 301/496–7056 ext. 206; *e-mail:* LT10X@NIH.GOV

Retroviral vectors are currently the most advanced system available for mammalian gene therapy. The major obstacle with the previous methods is that the transfer of complex or large genomic elements is virtually impossible. This technology obviates the need for the retrovirus DNA provirus stage of the life cycle via retroviral RNA vectors. Specifically, this invention utilizes Togaviruses, especially the Semliki Forest virus (SFV), to produce recombinant retroviral vector RNA in the cytoplasm of a retrovirus packaging cell. Using the SFV system, a retroviral cassette with a heterologous gene is cloned into an SFV expression vector. This in vitro transcribed RNA vector is used to transduce packaging cells. The retroviral RNA vector is amplified in the cytoplasm using the SFV system, and packaged into infectious viral particles. This system represents a means by which large fragments of viral RNA, or complex gene structures, can be transferred via retroviral vectors. An additional advantage is that by using the SFV production system, it is able to produce high titers of retrovirus particles, due to its self-amplification capabilities.

Potential areas of application include: *ex vivo* and *in vivo gene* therapy for infectious (e.g., HIV) and noninfectious (e.g., cancer, birth defects) disease; untranslated genomic regions of DNA may be important for regulation of gene expression.

Dated: August 5, 1997.

Barbara M. McGarey,

Deputy Director, Office of Technology Transfer.

[FR Doc. 97–21401 Filed 8–12–97; 8:45 am]

BILLING CODE 4140–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Eye Institute

Notice of the meeting of the National Advisory Eye Council Pursuant to Pub. L. 92–463, notice is hereby given of the meeting of the National Advisory Eye Council (NAEC) on September 11–12, 1997, Executive Plaza North, Conference Room G, 6130 Executive Boulevard, Bethesda, Maryland.

The NAEC meeting will be open to the public on September 11, from 8:30 a.m. until approximately 11:30 a.m. Following opening remarks by the Director, NEI, there will be presentations by the staff of the Institute and discussions concerning Institute programs and policies. Attendance by the public at the open session will be limited to space available.

In accordance with provisions set forth in sec. 552b(c)(4) and 552b(c)(6), Title 5, U.S.C. and sec. 10(d) of Pub. L. 92–463, the meeting of the NAEC will be closed to the public on September 11 from approximately 11:30 a.m. until adjournment at approximately 5:00 p.m. for the review, discussion, and evaluation of individual grant applications. These applications and the discussions could reveal confidential trade secrets or commercial property such as patentable material, and personal information concerning individuals associated with the applications, the disclosure of which would constitute a clearly unwarranted invasion of personal privacy.

Ms. Lois DeNinno, Council Assistant, National Eye Institute, EPS, Suite 350, 6120 Executive Boulevard, MSC–7164, Bethesda, Maryland 20892–7164, (301) 496–9110, will provide a summary of the meeting, roster of committee members, and substantive program information upon request. Individuals who plan to attend and need special assistance, such as sign language interpretation or other reasonable accommodations, should contact Ms. DeNinno in advance of the meeting.

(Catalog of Federal Domestic Assistant Program No. 93.867, Vision Research: National Institutes of Health)

Dated: August 7, 1997.

LaVerne Y. Stringfield,

Committee Management Officer, NIH.

[FR Doc. 97–21423 Filed 8–12–97; 8:45 am]

BILLING CODE 4140–01–M