effective upon its delivery by the Secretary to the United States Court of Federal Claims (formerly known as the United States Claims Court). Such notice was delivered to the Court on January 27, 1999.

Dated: March 1, 1999.

Claude Earl Fox,

Administrator.

[FR Doc. 99–5466 Filed 3–4–99; 8:45 am]

BILLING CODE 4160–15–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Notice of Establishment

Pursuant to the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2), the Director, National Institutes of Health (NIH), announces the establishment of the Cancer Advisory Panel for Complementary and Alternative Medicine (Panel).

This Panel will advise the Director, National Center for Complementary and Alternative Medicine, the Director, National Cancer Institute, and the Director, NIH, regarding the review and assessment of summaries of evidence for complementary and alternative medicine cancer intervention clinical trials submitted by practitioners, to evaluate whether and how these interventions should be followed up, develop a means of communication of the results of these studies, and to identify future alternative and complementary cancer clinical trials initiatives.

Unless renewed by appropriate action prior to its expiration, the Charter for the Cancer Advisory Panel for Complementary and Alternative Medicine will expire two years from the date of establishment.

Dated: March 1, 1999.

Harold Varmus,

Director, National Institutes of Health.

[FR Doc. 99–5479 Filed 3–4–99; 8:45 am]

BILLING CODE 4140–01–M

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.

Identification of Polymorphisms of the PCTG–4 Gene

RA Philibert, EI Ginns (NIMH)
Provisional U.S. Patent Application No. 60/083,465 filed 29 Apr 98
Licensing Contact: Leopold J. Luberecki, Jr.; 301/496–7735 ext. 223; e-mail: 1187a@nih.gov

Mental retardation affects approximately 1–3% of the U.S. population and results in at least $10 billion in annual treatment costs. Mutations in the X-chromosome may cause 30–50% of all cases of mental retardation. This technology is directed to the identification of an X-linked polymorphism that appears to convey a five-fold increase in the relative risk for mental retardation and is markedly enriched in individuals suffering from autism. The various polymorphisms will likely enable further studies aimed at eliciting the underlying mechanisms of these diseases and may provide a model system for the development of new drugs. It may also have a role as a prognostic indicator.

Combination Therapy with VIP Antagonists

Illana Gozes (Tel Aviv University), Terry W. Moody (NCI), Douglas C. Brenneman (NICHD), Mati Fridkin (Weizman Institute of Science), Edgar Gelber (Tel Aviv University) and Albert Levy (Tel Aviv University)
Serial No. 60/104,472 filed 16 Oct 98 and Serial No. 60/104,907 filed 20 Oct 98
Licensing Contact: Dennis Penn; 301/496–7056 ext. 211; e-mail: dp144q@nih.gov

This invention relates generally to cancer treatment. More particularly, the present invention relates to combination therapy using a polypeptide which is an antagonist of the vasoactive intestinal polypeptide (VIP) and a chemotherapeutic agent, preferably in a pharmaceutical composition.

Vasoactive intestinal polypeptide (VIP) is a widely distributed peptide hormone which mediates a variety of physiological responses including gastrointestinal secretion, relaxation of gastrointestinal vascular and respiratory smooth muscle, lipolysis in adipocytes, pituitary hormone secretion, and excitation and hyperthermia after injection into the central nervous system. Vasoactive intestinal peptide is a 28 amino acid peptide with an amidated C-terminus, the peptide results from post translational processing of a hormone composed of 170 amino acid residues. The VIP peptide has been shown to contain at least two functional regions, a region involved in receptor specific binding and a region involved in biological activity (Gozes and Brenneman, Molecular Neurobiology, 3:201–236 (1989)).

Gozes, et al. have developed a VIP antagonist that has proven useful for altering the function of the vasoactive intestinal peptide. (See, U.S. Patent No. 5,217,953 issued to Gozes, et al. (1993)). This VIP antagonist was designed to retain the binding properties of VIP for its receptor, but to lack the amino acid sequence necessary for biological activity. Studies have shown that this VIP antagonist effectively antagonizes VIP-associated activity. It has been reported that this VIP antagonist inhibits the growth of VIP receptor bearing tumor cells such as, for example, lung tumor cells (i.e., non-small cell lung cancer cells). (See, U.S. Patent No. 5,217,953.)

U.S. Patent No. 5,565,424, which issued to Gozes, et al. on October 15, 1996, discloses another family of polypeptides which are antagonists of the vasoactive intestinal polypeptide. The VIP antagonists disclosed therein are 10–1000 times more efficacious, i.e., more potent in inhibiting VIP-associated activity than previous VIP antagonists. These superactive VIP antagonists were shown to inhibit cancer growth in lung and gioblastoma cells. Examples of superactive VIP antagonists include amino acid sequences referred to as the ''norleucine-hybrid VIP antagonist'', the ''stearyl-norleucine-hybrid VIP antagonist'' and the ''stearyl-hybrid VIP antagonist''.

The present invention relates to a pharmaceutical composition comprising a vasoactive intestinal polypeptide (VIP) antagonist, a chemotherapeutic agent

(such as platinum coordination compounds, topoisomerase inhibitors, antibiotics, antimitotic alkaloids, antimicrotubules, and difluoronucleosides) and a pharmaceutically acceptable carrier. Certain combinations of a VIP antagonist plus a chemotherapeutic agent resulted in a synergistic reduction in the IC50 of 2–7 fold. This synergistic affect was observed in a non-small cell lung cancer, breast cancer, pancreatic cancer, glioblastoma, ovarian, and prostate cancer cell lines.

A Test for Both Sensitivity to and Resistance to Warfarin and Other Drugs Metabolized by CYP2C9 and CYP2A6

Frank J. Gonzalez (NCI) and Jeffery R. Idle (University of Newcastle)
Serial No. 08/750,703 filed 07 Apr 97
Licensing Contact: Dennis Penn; 301/496–7056 ext. 211; e-mail: dp144q@nih.gov

It is well known that genetic polymorphisms in drug metabolizing genes give rise to a variety of phenotypes. This information has been used to advantage in the past for developing genetic assays that predict phenotype and thus predict an individual's ability to metabolize a given drug. The information is of particular volume in determining the likely side effects and therapeutic failures of various drugs.

Drug metabolism is carried out by the cytochrome P450 family of enzymes. For example, the cytochrome P450 isozyme gene, CYP2C9 encodes a high affinity hepatic [S]-warfarin 7-hydroxylase which appears to be principally responsible for the metabolic clearance of the most potent enantiomer of warfarin. Similarly, the cytochrome P450 isozyme gene, CYP2A6, encodes a protein that metabolizes nicotine and coumarin and activates the tobacco-specific nitrosamine 4-(methyinitrosamino)-1-(3-pyridyl)-1-butanone) (NNK). The above gene products are also known to metabolize other substrates, for example, the CYP2C9 gene product is also know to metabolize Tolbutamide, Phenytoin, Ibuprofen, Naproxen, Tienilic acid, Diclofenac and Tetrahydrocannabinol. It follows that genetic polymorphisms or mutations in either of the two aforementioned genes can lead to an impairment in metabolism of at least the aforementioned drugs.

The present invention relates to novel variant alleles incytochrome P450 genes, which express ezymes involved in the metabolism of particular drugs and/or chemical carcinogens. The present invention describes a new mutant or variant CYP2A6 allele wherein the human gene is characterized. This variant allele is designated CYP2A6v2 and its cDNA and genomic sequence are provided in the present invention. Another new gene related to CYP2A6 has been discovered and is designated CYP2A13 and its cDNA and genomic sequence are included.

The objective of this invention is to provide the genetic material, a method, and a kit which enable genotyping of the CYP2C9 and CYP2A65 gene with a view to providing phenotyping information concerning drug metabolism for use in screening and evaluating side effects and therapeutic failures. In addition, the method may be used to screen patients for a predisposition to cancers related to excessive nitrosamine activation, which are associated with mutations within the CYP2A6 gene locus. Further, the method may be used to screen patients for sensitivity to chemical carcinogens, based upon the genotype of the CYP2A6 and/or CYP2C9 alleles.

Method for Detecting a Receptor-Ligand Complex Using a Cytochrome P450 Reporter Gene

Charles L. Crespi (Gentest), Bruce W. Pennman (Gentest), Frank J. Gonzalez (NCI), Harry V. Gelboin (NCI) and Talia Sher (NCI)
Serial No. 08/697,329 filed 22 Aug 96; U.S. Patent 5,726,041 issued 10 Mar 98
Licensing Contact: Dennis Penn; 301/496–7056 ext. 211; e-mail: dp144q@nih.gov

The use of reporter genes to measure the relative activity of a promoter sequence is well known. This invention is directed to methods and compositions for measuring the activity of a promoter sequence in a mammalian cell. The methods involve substituting a DNA sequence encoding a cytochrome P450 for a known reporter gene (e.g. CAT, luciferase) and measuring the relative activity of the expressed cytochrome P450 protein. In contrast to the reporter genes of the prior art, the claimed invention advantageously provides a method for measuring the activity of a promoter sequence in intact mammalian cells that contain a P450 catalysis system using real time light (fluorescence) measurements. Virtually all mammalian cells contain the requisite cytochrome P450 catalysis system. Thus, the invention eliminates the labor-intensive aspects (e.g., cell lysis and separation of cellular components) that are required to practice other methods for measuring the activity of a promoter sequence in a mammalian cell.

The invention also provides a method for detecting the formation of a receptor-ligand complex in a mammalian cell. The cell contains a reported cassette for detecting formation of the receptor-ligand complex and a cytochrome P450 catalysis system. The reporter cassette includes a DNA sequence encoding a cytochrome P450 with a polyadenylation signal sequence operatively coupled to a promoter sequence that is responsive to (i.e., binds to) a DNA binding element present in the receptor-ligand complex. According to one aspect of the invention, this method is useful for detecting the activation of PPARα by peroxisome proliferators.

Restenosis/Atherosclerosis Diagnosis, Prophylaxis, and Therapy

SE Epstein, T Finkel, EH Speir, Y Zhou, J Zhou, L Erdile, S Pincus (NHLBI)
Serial No. 08/796,101 filed 05 Feb 97
Licensing Contact: Manja Blazer; 301/496–7735 ext. 224; e-mail: mb379e@nih.gov

This technology relates to the compositions and methods for the diagnosis, prevention, and therapy of restenosis and atherosclerosis. It involves the use of an agent for decreasing viral load, preferably a vaccine, against cytomegalovirus (CMV) and p53, including a method for providing the therapy and administering the agent. This invention thus relates to stimulating an immune response, preferably a cellular immune response, directed against CMV and p53 inhibit or prevent restenosis, atherosclerosis, and smooth muscle proliferation. Such a response can cause cell death and thus inhibition of smooth muscle cell proliferation, atherosclerosis, and restenosis. Therefore, the technology offers methods for inducing cell death with the purpose of inhibiting smooth muscle proliferation as a means of preventing or treating restenosis and atherosclerosis.

The Use of Lecithin-Cholesterol Acyltransferase (LCAT) in the Treatment of Atherosclerosis

S Santamarina-Fojo, JM Hoeg, B Brewer Jr. (NHLBI)
DHHS Reference No. E–007–96/1 filed 11 Aug 96
Licensing Contact: Manja Blazer; 301/496–7735 ext. 224; e-mail: mb379e@nih.gov

This technology relates to methods for the preventive and therapeutic treatment of atherosclerosis and to diseases relating to a deficiency of

lecithin-cholesterol acyltransferase activity. The plasma protein enzyme lecithin-cholesterol acyltransferase (LCAT) catalyzes the transfer of fatty acid from the sn-2 position of lecithin to the free hydroxyl group of cholesterol. Various mutations of the LCAT gene are known. Individuals who are homozygous for a non-functional LCAT mutant have classic LCAT deficiency disease, characterized by clouding of the cornea, normochromic anemia and glomerulosclerosis. Mutations of the LCAT gene that result in some residual LCAT activity lead to Fish Eye disease, characterized by opacity of the cornea and hypoalphalipoproteinemia. Thus there is a need for compositions and methods for the prevention and therapeutic treatment of atherosclerosis and conditions associated with LCAT deficiency. This invention satisfies this need by providing compositions and methods for increasing the serum level of LCAT activity.

Dated: February 22, 1999.

Jack Spiegel,

Director, Division of Technology Development and Transfer, Office of Technology Transfer.

[FR Doc. 99–5419 Filed 3–4–99; 8:45 am]

BILLING CODE 4140–01–M

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 invention listed below is owned by an agency of the U.S. Government and is 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.

ADDRESSES: Licensing information and a copy of the U.S. patent application referenced below may be obtained by contacting J.R. Dixon, Ph.D., at the Office of Technology Transfer, National Institutes of Health, 6011 Executive Boulevard, Suite 325, Rockville, Maryland 20852–3804 (telephone 301/496–7056 ext 206; fax 301/402–0220; E-Mail: jd212g@NIH.GOV). A signed Confidential Disclosure Agreement is required to receive a copy of any patent application.

Entitled: Transcription Factor Decoy and Tumor Growth Inhibitor.

Inventor: Dr. Yoon S. Cho-Chung (NCI) U.S.P.A. 08/977,643—Filed November 24, 1997.

Alteration of gene transcription by inhibition of specific transcriptional regulatory proteins has important therapeutic potential. Synthetic double-stranded phosphorothioate oligonucleotides with high affinity for a target transcription factor can be introduced into cells as decoy cis-elements to bind the factors and alter gene expression. The CRE (cyclic AMP response element)—transcription factor complex is a pleiotropic activator that participates in the induction of a wide variety of cellular and viral genes. Because the CRE cis-element, TGACGTCA, is palindromic, a synthetic single-stranded oligonucleotide composed of the CRE sequence self-hybridizes to form a duplex/hairpin. The CRE-palindromic oligonucleotide can penetrate into cells, compete with CRE enhancers for binding transcription factors, and specifically interfere with CRE- and AP-1-directed transcription in vivo. These oligonucleotides restrained tumor cell proliferation, without affecting the growth of noncancerous cells. This decoy oligonucleotide approach offers great promise as a tool for defining cellular regulatory processes and treating cancer and other diseases.

This research has been published in J. Biol. Chem. 274, 1573–1580 (1999).

This invention is available for licensing on an exclusive or non-exclusive basis.

Dated: February 24, 1999.

Jack Spiegel,

Director, Division of Technology Development and Transfer, Office of Technology Transfer.

[FR Doc. 99–5420 Filed 3–4–99; 8:45 am]

BILLING CODE 4140–01–M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Cancer Institute; Notice of Closed Meeting

Pursuant to section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2), notice is hereby given of the following meeting.

The meeting will be closed to the public in accordance with the provisions set forth in sections 552b(c)(4) and 552b(c)(6), Title 5 U.S.C., as amended. The grant applications and the discussions could disclose confidential trade secrets or commercial property such as patentable material, and personal information concerning individuals associated with the grant applications, the disclosure of which would constitute a clearly unwarranted invasion of personal privacy.

Name of Committee: National Cancer for Institute Initial Review Group, Subcommittee A—Cancer Centers.

Date: March 29–30, 1999.

Time: 7:30 am to 1:00 pm.

Agenda: To review and evaluate grant applications.

Place: Embassy Suites, Chevy Chase Pavilion, 4300 Military Rd., Wisconsin at Western Ave., Washington, DC 20015.

Contact Person: David E. Maslow, PhD, Scientific Review Administrator, Grants Review Branch, Division of Extramural Activities, National Cancer Institute, National Institutes of Health, 6130 Executive Boulevard—EPN 643A, Bethesda, MD 20892–7405, 301/496–2330.

(Catalogue of Federal Domestic Assistance Program Nos. 93.392, Cancer Construction; 93.393, Cancer Cause and Prevention Research; 93.394, Caner Detection and Diagnosis Research; 93.395, Cancer Treatment Research; 93.396, Cancer Biology Research; 93.397, Cancer Centers Support; 93.398, Cancer Research Manpower; 93.399, Cancer Control, National Institutes of Health, HHS)

Dated: February 26, 1999.

LaVerne Y. Stringfield,

Committee Management Officer, NIH.

[FR Doc. 99–5410 Filed 3–4–99; 8:45 am]

BILLING CODE 4140–01–M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Institute of General Medical Sciences; Notice of Closed Meeting

Pursuant to section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2), notice is hereby given of the following meeting.

The meeting will be closed to the public in accordance with the provisions set forth in sections 552b(c)(4) and 552b(c)(6), Title 5 U.S.C., as amended. The grant applications and the discussions could disclose confidential trade secrets or commercial property such as patentable material, and personal information concerning individuals associated with the grant applications, the disclosure of which would constitute a clearly unwarranted invasion of personal privacy.

Name of Committee: National Institute of General Medical Sciences Special Emphasis Panel, Pharmacology.

Date: March 26, 1999.

Time: 1:00 p.m. to 2:00 p.m.

Agenda: To review and evaluate grant applications.