4. Publishing research results.

Selection criteria for choosing the CRADA Collaborator may include, but not be limited to:

1. The ability to collaborate with NCI on further research and development of this Technology. This ability can be demonstrated through experience and expertise in this or related areas of Technology indicating the ability to contribute intellectually to ongoing research and development.

2. The ability to collaborate with NCI on further research and development of this Technology. This ability can be demonstrated through experience and expertise in this or related areas of Technology indicating the ability to contribute intellectually to ongoing research and development.

3. The demonstration of adequate resources to perform the research, development and commercialization of this technology (e.g. facilities, personnel and expertise) and accomplish objectives according to an appropriate timetable to be outlined in the CRADA Collaborator's proposal.

4. The willingness to commit best effort and demonstrated resources to the research, development and commercialization of this Technology.

5. The demonstration of expertise in the commercial development, production, marketing and sales of products related to this area of Technology.

6. The level of financial support the CRADA Collaborator will provide for CRADA-related Government activities.

7. The willingness to cooperate with the National Cancer Institute in the timely publication of research results.

8. The agreement to be bound by the appropriate DHHS regulations relating to human subjects, and all PHS policies relating to the use and care of laboratory animals.

9. The willingness to accept the legal provisions and language of the CRADA with only minor modifications, if any. These provisions govern the equitable distribution of patent rights to CRADA inventions. Generally, the rights of ownership are retained by the organization that is the employer of the inventor, with (1) the grant of a license for research and other Government purposes to the Government when the CRADA Collaborator's employee is the sole inventor, or (2) the grant of an option to elect an exclusive or nonexclusive license to the CRADA Collaborator when the Government employee is the sole inventor.

Dated: October 8, 1998.

Kathleen Sybert,

Acting Director, Technology Development and Commercialization Branch, National Cancer Institute, National Institutes of Health.

[FR Doc. 98–27963 Filed 10–16–98; 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.

Agents That Bind To and Inhibit Cytochrome P450 2A6

HV Gelboin, FJ Gonzalez (NCI)
Serial No. 60/093,936 filed 23 Jul 98
Licensing Contact: Dennis Penn, 301/496–7056 ext. 211

The cytochrome P450 family of enzymes is primarily responsible for the metabolism of xenobiotics such as drugs, carcinogens and environmental chemicals, as well as several classes of endobiotics such as steroids and prostiglandins. Members of the cytochrome P450 family are present in varying levels and their expression and activities are controlled by variables such as chemical environment, sex, developmental stage, nutrition and age.

There are multiple forms of these P450 and each of the individual forms exhibit degrees of specificity towards individual chemicals of the above classes. Genetic polymorphisms of cytochrome P450 2A6 result in phenotypically distinct deficient subpopulations that differ in their ability to perform biotransformations of a particular drug and other chemical compounds.

This invention describes monoclonal antibody Mab 151–45–4, which is highly specific for human cytochrome P450 2A6 and does not cross react with 12 other human P450s. The inhibitory and immunoblotting monoclonal antibody that are described in this invention report is unique and is the only known inhibitory monoclonal antibody to human P450 2A6. Its inhibitory activity P450 2A6 is greater than 90%. This monoclonal antibody may be used as a diagnostic probe identifying the distribution of 2A6 in populations and thus identifying enzyme deficient individuals that are sensitive to 2A6 metabolized drugs. This Mab will also identify those drugs that are currently used and in the process of drug development which are substrates for 2A6. Metabolism of partner drugs by P450 2A6 may be the basis for drug-drug toxicity.

Agents That Bind To and Inhibit Human Cytochrome P450 1A2

HV Gelboin, FJ Gonzalez, TJ Yang (NCI)
Serial No. 60/093,913 filed 23 Jun 98
Licensing Contact: Dennis Penn, 301/466–7056 ext. 211

The cytochrome P450 family of enzymes is primarily responsible for the metabolism of xenobiotics such as drugs, food pyrolysate, carcinogens and environmental chemicals, as well as several classes of endobiotics such as steroids and prostaglandins. Members of the cytochrome P450 family are present in varying levels in human tissue.

There are multiple forms of these P450 and each of the individual forms exhibit metabolic activity, often overlapping, towards individual chemicals of the above classes. Genetic polymorphisms of cytochrome P450 2A6 result in phenotypically distinct subpopulations that differ in their ability to perform biotransformations of a particular drug and other chemical compounds.

This invention describes monoclonal antibodies Mab 26–7–5, Mab 951–5–1 and Mab 1812–2–4, which are highly specific for human cytochrome P450 1A2 and do not cross react with 11 other human P450s. These Mabs exhibit strong immunoblotting activity and enzyme inhibitory activity greater than 85%. The inhibitory and immunoblotting monoclonal antibody that are described in this invention report is unique and is the only known inhibitory monoclonal antibody to

human P450 1A2. Thus these Mabs may be used to identify drugs, carcinogens and other xenobiotics metabolized by P450 1A2 in human liver. The inhibitory properties can determine the quantitative metabolic contribution of P450 1A2 in human liver relative to that of other P450s that may also metabolize 1A2 substrates. These Mabs can identify drugs currently in use and in the process of drug development which are substrates for 1A2. The Mab can also identify partner drugs metabolized by 1A2 that may be a basis of drug-drug toxicity. The Mabs are also diagnostic probes identifying the distribution of 1A2 in populations and thus identifying enzyme deficient individuals that are sensitive to 1A2 metabolized drugs.

AAV5 Vector and Uses Thereof

JA Chiorini (NHLBI)
Serial No. 60/087,029 filed 28 May 98
Licensing Contact: Susan S. Rucker, 301/496–7056 ext. 245

The invention described and claimed in this patent application provides for novel vectors and viral particles which comprise adeno-associated virus serotype 5 (AAV5). AAV5 is a single-stranded DNA virus of either plus or minus polarity which, like other AAV serotypes (AAV4, AAV2) requires a helper virus for replication. AAV type 2 has the interesting and potentially useful ability to integrate into human chromosome 19 q 13.3-q ter. This activity is dependent on the non-structural, Rep, proteins of AAV2. The Rep proteins of AAV types 2 and 5 are dissimilar and are not able to substitute in DNA replication of the heterologous serotype. Based on preliminary fluorescent in situ hybridization (FISH) results, the integration of AAV type 5 occurs specifically, but at a different genetic locus to that of AAV type 2.

AAV5 offers several advantages which make it attractive for use in gene therapy: 1. increased production (10–50 fold greater than AAV2); 2. distinct integration locus when compared to AAV2; 3. Rep protein and ITR regions do not complement other AAV serotypes; 4. appears to utilize different cell surface attachment molecules than those of AAV type 2.

Variant Peptide Ligands That Selectively Induce Apoptosis

MJ Lenardo, RN Germain, B Combadiere, C Reis e Sousa (NIAID)
Serial No. 60/072,952 filed 29 Jan 98
Licensing Contact: Jaconda Wagner, 301/496–7735 ext. 284

This invention relates to selective modulation of specific T cell responses. Variant peptide ligands for the T cell receptor have been identified and characterized. These variant peptide ligands act as partial agonists. Specifically, the ligands induce apoptosis in T cells without the concomitant production and release of non-death inducing cytokines. These variant peptide ligands can be used to treat or prevent T cell associated disorders such as autoimmune diseases, allergic disorders, graft rejection and graft versus host disease by selectively eliminating specific T cell populations.

Method For Synthesizing 9-(2,3-Dideoxy-2-fluoro-β-D-threo-pentofuranosyl)adenine (β-Fdda)

VE Marquez, MA Siddiqui, JS Driscoll (NCI)
Serial No. 60/067,765 filed 10 Dec 97
Licensing Contact: J. Peter Kim, 301/496–7056 ext. 264

AIDS (acquired immunodeficiency syndrome), first reported in the United States in 1981, has become a worldwide epidemic, crossing all geographic and demographic boundaries. More than 475,000 cases of AIDS have been reported in the United States since 1981 and more than 295,000 deaths have resulted in the U.S. from AIDS. Over 1.5 million Americans are thought to be infected with HIV (human immunodeficiency virus),the causative agent of AIDS. One clinically useful anti-HIV nucleoside is 9-(2,3-Dideoxy-2-fluoro-β-D-threo-pentofuranosyl)adenine (β-Fdda.)

The subject invention relates to methods and compounds for a highly effective synthesis of clinically useful anti-HIV active nucleosides such as 9-(2,3-Dideoxy-2-fluoro-β-D-threo-pentofuranosyl) adenine (β-FddA), and analogues and prodrugs thereof.

Single-Shot Spiral Scanning Magnetic Resonance Imaging Using Trapezoidal Gradients

JH Duyn (CC)
Serial No. 60/067,670 filed 05 Dec 97
Licensing Contact: John Fahner-Vihtelic, 301/496–7735 ext. 270

The present application describes a magnetic resonance imaging (MRI) apparatus which employs trapezoidal gradients. This apparatus allows for fast MRI scanning with excellent signal to noise ratio that is relatively insensitive to motion. Single-shot spiral scanning places high demands on gradient hardware which creates a need for carefully designed gradient waveforms. Use of the trapezoidal wave forms embodied in this invention overcome problems such as large heat load to the pulse-width modulators. The present technology applies to cardiac imaging as well as functional neuroimaging using fMRI based on blood oxygenation (BOLD) dependent contrast.

Methods of Using CR3 and CR4 Ligands for Inhibiting IL–12 To Treat Autoimmune Disease

B Kelsall, W Strober, I Fuss, T Marth (NIAID)
Serial No. 60/066,238 filed 20 Nov 97
Licensing Contact: Jaconda Wagner, 301/496–7735 ext. 284

This invention provides a novel approach to downregulating the production of IL–12. Specifically, Marth and Kelsall have shown that IL–12 production can be modulated via the complement receptors CR3 and CR4. By binding a ligand, such as an antibody, to the complement receptors, an IL–12 induced inflammatory response can be modulated. This method can be used to treat various autoimmune diseases.

Real-Time Monitoring of Electrocardiogram During Magnetic Resonance Scanning

A Berson (NHLBI)
Serial No. 08/965,869 filed 07 Nov 97
Licensing Contact: John Fahner-Vihtelic, 301/496–7735 ext. 270

The present application describes an apparatus and method for monitoring an electrocardiogram (ECG) during magnetic resonance (MR) scanning. This device consists of a unique electrode system that allows the ECG to be obtained by a series of potential measurements between certain of the placed electrodes. Monitoring the ECG in patients undergoing MR scanning can be extremely important if the subject of the MR scan is a cardiac patient or is being stressed at the time of the scan. Interference of ECG by the magnetic field associated with MR scanning, gradient fields, RF sampling fields, and magnetohydrodynamics incidental to blood flow, can be overcome with this invention.

A Swine Hepatitis E Virus and Uses Thereof

Serial No. 60/053,069 filed 18 Jul 97; PCT/US98/14665 X–J Meng, RH Purcell, SU Emerson (NIAID)
Licensing Contact: Carol Salata, 301/496–7735 ext. 232

This invention is directed to a novel swine hepatitis E virus (swine HEV) and its partial sequence. This swine HEV is unique from other previously-described HEV strains but is both genetically and serologically related to human HEV. The putative capsid protein of HEV strains, when expressed as a recombinant protein in insect cells, is highly useful in the evaluation of infection of swine

as well as of humans with HEV. The recombinant HEV capsid protein may also be useful in the vaccination of humans and animals against infection with HEV strains.

Oligonucleotides Which Specifically Bind Retroviral Nucleocapsid Proteins

A Rein, J Casas-Finet, R Fisher, M Fivash, LE Henderson (NCI)
PCT/US97/08936 filed 19 May 97 (claiming priority of USSN 60/017,128 filed 20 May 96)
Licensing Contact: J. Peter Kim, 301/496–7056 ext. 264

The human immunodeficiency virus (HIV) is the causative agent of acquired immunodeficiency syndrome (AIDS). A retroviral protein species, the gag polyprotein, is involved in the assembly of retrovirus particles and capable of specific interactions with nucleic acids. After the virion is released from the cell, the polyprotein is cleaved by the virus-encoded protease. One of the cleaved products, the nucleocapsid (NC) protein, then binds to genomic RNA, forming the ribonucleoprotein core of the mature particle. The interaction between gag and genomic RNA is known to involve the NC domain of the polyprotein.

The present invention relates to retroviral proteins, such as NC and the gag precursor, and their ability to bind to specific nucleic acid sequences with high affinity. Accordingly, the invention provides for oligonucleotides which bind to nucleocapsids proteins with high affinity, molecular decoys for retroviral nucleocapsid proteins which inhibit viral replication, targeted molecules comprising high affinity oligonucleotides, assays for selecting molecules which inhibit the specific interaction between retroviral proteins and high affinity oligonucleotides, and related kits.

Compositions for the Prevention or Retardation Of Cataracts

JS Zigler Jr., P Russell, S Tumminia, C Qin, CM Krishna (NEI)
PCT/US97/01105 filed 24 Jan 97 (claiming priority of USSN 60/010,637 filed 26 Jan 96)
Licensing Contact: David Sadowski, 301/496–7735, ext. 288

Oxidative stress is becoming recognized as a major problem, and free radicals and activated oxygen species are recognized as agents of tissue damage associated with a number of conditions. Aging-related cataract is a disease of multifactorial origin involving many of the same processes which characterize the process of aging in other tissues. It appears that once cataractogenesis has begun, the process of cataract development may proceed via one or more common pathways or processes. The subject invention focuses on intervening at the level of these common pathways in hopes of stopping or slowing the progression of the disease process. The present invention provides methods and compositions for the prevention and treatment of cataract formation which comprise a nitroxide free radical compound or its hydroxylamine and a thiol reducing agent.

Methods for Enhancing Oral Tolerance and Treating Autoimmune Disease Using Inhibitors Of IL–12

W Strober, Brian Kelsall, T Marth (NIAID)
PCT/US96/16007 filed 11 Oct 96 designating AU, US, CA, JP (no rights in EPO); published as WO 98/16248 on 23 Apr 98
Licensing Contact: Jaconda Wagner, 301/496–7735 ext. 284

Oral tolerance is the immunologic mechanism by which the mucosal immune system maintains unresponsiveness to the myriad of antigens in the mucosal environment which might otherwise induce untoward immune responses. Recent studies have shown that it is mediated by several distinct, yet interacting mechanisms including the generation of suppressive T cells producing antigen nonspecific cytokines and the induction of clonal deletion and/or anergy. This invention provides two methods: 1) for enhancing oral tolerance to an antigen and 2) for treating an autoimmune disease. By orally administering an antigen associated with an autoimmune disease, allergic disease or graft versus host (GvH) disease along with an inhibitor of IL–12, oral tolerance can be enhanced. The diseases can also be treated using virtually the same method.

Method for Protecting Bone Marrow Against Chemotherapeutic Drugs Using Transforming Growth Factor Beta 1

JR Keller, FW Ruscetti, R Wiltrout (NCI)
U.S. Patent 5,278,145 issued 11 Jan 94
Licensing Contact: Jaconda Wagner, 301/496–7735 ext. 284

This invention provides a method for protecting hematopoietic stem cells from the myelotoxicity of chemotherapeutic drugs or radiation therapy. Chemotherapeutic agents destroy the body's ability to make granulocytes thereby exposing patients to potentially lethal microorganisms. Previous attempts to alleviate this problem focused on the use of growth factors to accelerate recovery from myelotoxicity. This invention details a method for administering TGF–β1 in conjunction with the administration of chemotherapeutic drugs in order to reduce the number of stem cells killed thereby reducing myelotoxicity which is an improvement to the previous method.

Dated: October 13, 1998.

Jack Spiegel, Ph.D.

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

[FR Doc. 98–27959 Filed 10–16–98; 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.

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Dimeric Naphthylisoquinoline Alkaloids and Synthesis Methods Thereof

G Bringmann, S Harmsen, MR Boyd (NCI)
Serial No. 08/279,339 filed 22 Jul 94 (U.S. Patent 5,571,919 issued 05 Nov 96) and Serial No. 08/674,359 filed 01 Jul 96 (U.S. Patent 5,789,594 issued 04 Aug 98)

This invention embodies the synthesis and novel compounds comprising homodimeric and heterodimeric napthylisoquinoline