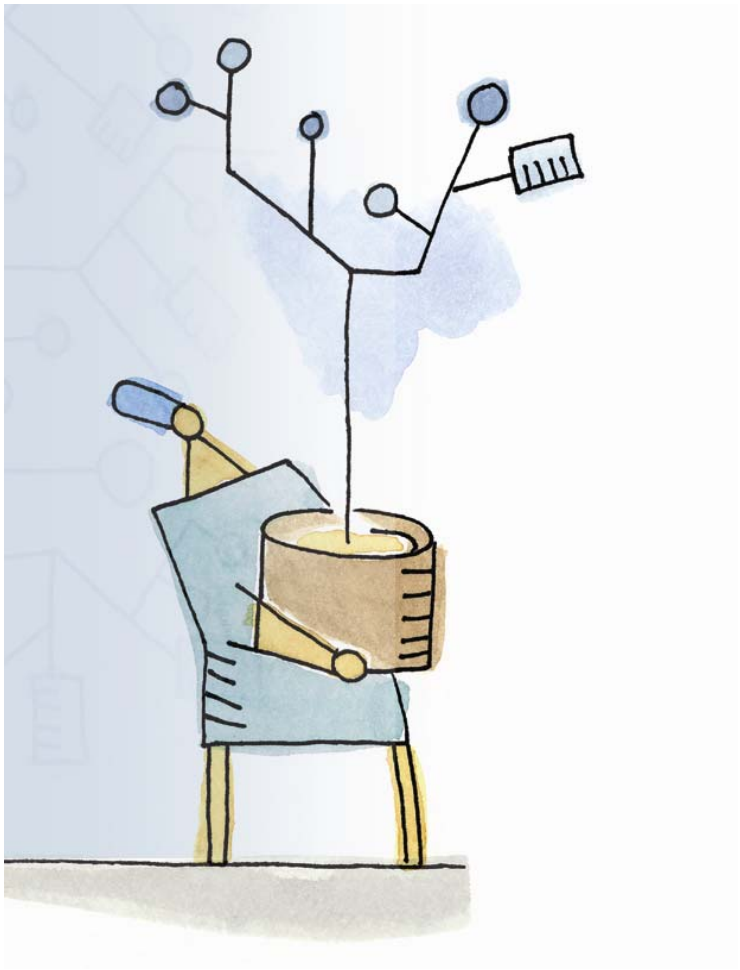
National Institutes of Health
Office of Technology Transfer



Biomarker-related Technologies Available for Licensing

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INTRODUCTION

NIH has an extensive intellectual property portfolio of early-stage technologies[1] and also invests substantially in their development. Roughly 10 percent of the annual NIH budget is dedicated to intramural research and development activities -- resulting in inventions that form the basis of a variety of new medical technology and therapies in the areas of medical devices, software, vaccines, diagnostics, and reagents. Similar to university research, commercial partners are needed to make sure that the long hours at the lab bench and the public investment pay off in the end in marketed products.

NIH believes that the future development of its innovative, early stage research lies largely with innovative, early stage companies. While the increasingly consolidated pharmaceutical industry remains a steady customer of research reagents and clinical collaborations with NIH, the more exciting therapeutic developments increasingly seem to come from NIH licenses signed with small and medium-sized life science companies early in their growth phase.

To further attract such early-stage concerns and start-ups, NIH affords favorable treatment to small firms and tries to provide IP agreements that facilitate new areas of product development based upon NIH research. For example, financially-burdened smaller companies can benefit from flexibility on patent costs and license execution fees in license agreements. Of particular note for venture-backed firms is that companies do not give up equity or management control nor are their future development or marketing rights compromised by signing NIH license agreements. Finally, once the product is in development, NIH is often able to assist with clinical trials, follow-on research collaborations, and even eventual purchase of the product as a customer.

We have collected some medical technologies your company might be interested in for further discussion with our licensing specialists.

Once you have picked the technology of interest, we urge you to apply for a License. A copy of the License Application template can be found at the NIH OTT website at: http://www.ott.nih.gov/forms_model_agreements/forms_model_agreements.html#LAP.

[1] *The NIH Office of Technology Transfer cannot guarantee that the listed technologies are still available for licensing. Please contact the Technology Licensing Specialist (listed under each technology) for the current status and for other complementary technologies.*

TABLE OF CONTENTS

GENE THERAPY

A Gene Therapy to Treat Lung Cancer

Description of Invention:
This invention relates to the identification of a new tumor suppressor gene named Caliban from Drosophila melanogaster and Serologically determined colon cancer antigen gene 1 (Sdccag1) from humans. Sdccag1 is inactive in human lung cancer cells but active in normal lung cells. When full length Caliban or Sdccag1 is expressed in human lung cancer cells they lose their tumorigenicity. This suggests that Caliban/Sdccag1 could be used as both a therapeutic and diagnostic for cancer.

Applications:
- Using gene therapy to replace the inactive gene with full length Caliban/Sdccag1 to treat cancer(s).
- A diagnostic assay that can determine whether the tumor suppressor Caliban/Sdccag1 gene product is functioning in cells.

Advantages:
- Caliban/Sdccag1 can be easily adopted into already standard gene therapy applications.
- Provides a novel therapeutic and diagnostic target for cancer.

Benefits:
It is estimated that there will be approximately 160,000 deaths caused by lung cancer in 2007. This technology will help in improving the quality of life of lung cancer patients as well as other cancers. Additionally, the gene therapy market is now a multi-million dollar industry.

Inventors:
Mark A. Mortin (NICHD)
Xiaolin Bi (NCI)

Patent Status:
DHHS Reference No. E-118-2005/0 --
Pending PCT Application PCT/US2006/022180, published as WO 2006/13316

Licensing Status:
Available for licensing.

Collaborative Research Opportunity:
The National Institute of Child Health and Human Development is seeking statements of capability or interest from parties interested in collaborative research to obtain pre-

clinical data to be used to further develop, evaluate, or commercialize Caliban/Sdccag1 as a novel therapeutic and diagnostic target for cancer and other diseases. Please contact John D. Hewes, Ph.D. at 301-435-3121 or hewesj@mail.nih.gov for more information.

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A Gene Expression Profile that Predicts Ovarian Cancer Patient Response to Chemotherapy

Description of Invention:
Ovarian cancer is a poor prognosis disease that remains the most lethal of all gynecologic malignancies. Warning symptoms do not occur until the tumor has already spread beyond the ovary, resulting in diagnosis at an advanced stage. As a result, there is a poor patient prognosis with only fifteen percent of women possessing advanced stage disease surviving for five years. Despite an initial clinical response of 80% to surgery and chemotherapy, most patients experience tumor recurrence within two years of treatment. The overwhelming majority of these patients will eventually develop chemoresistant disease and die.

Available for licensing are two gene signatures. One gene signature can predict whether a patient will initially respond to standard platinum-paclitaxel chemotherapy, but will relapse within six months of completing treatment. A second gene signature identifies patients who will show no response to therapy. This methodology may enable clinicians to identify patients who may be candidates for additional and/or novel chemotherapy drugs, and effectively choose appropriate cancer treatment. A unique feature of this signature is its derivation from pure, microdissected isolates of ovarian tumor cells, rather than undissected tissue. By utilizing this approach, the resulting gene list is specific to the cell type that causes the disease.

Applications:

- Method to detect if an ovarian cancer patient is sensitive to treatment with chemotherapeutic agents
- Method to evaluate ovarian cancer patient chemoresponsiveness
- Diagnostic tool to aid clinicians in determining appropriate cancer treatment
- Methods to treat ovarian cancer identified by chemoresistant biomarkers compositions

Market:

- Ovarian cancer is the fourth most common form of cancer in the U.S.
- Ovarian cancer is three times more lethal than breast cancer
- 15,310 deaths in the U.S. in 2006

Development Status:
The technology is currently in the pre-clinical stage of development.

Inventors:
Michael J. Birrer (NCI) et al.

Patent Status:
DHHS Reference No. E-060-2007/0

U.S. Provisional Application No. 60/899,942 filed 06 Feb 2007

Relevant Publication:
SC Mok et al. Biomarker discovery in epithelial ovarian cancer by genomic approaches. Adv Cancer Res. 2007;96:1-22. [PubMed abs]

Licensing Status:
Available for exclusive or non-exclusive licensing.

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Neural Crest-Melanocyte cDNA Based Microarray Analysis for Human Skin Pigmentation Research

Description of Invention:

Microarrays have wide applications in basic research and are used for the discovery of candidate genes as markers for disease and for therapeutic intervention. This invention pertains to the identification of a set of neural crest-melanocyte (NC-M) genes through microarray analysis and informatic analysis. Utilizing the extensive sequence information in the expressed sequence tag database (dbEST), the specific set of cDNA sequence was identified for microarray analysis of melanocyte function and diseases. This integrated technique of sequencing with bioinformatics led to the discovery of novel genes. The cDNA sequences selected in this invention are differently expressed in neural crest melanocyte derivates relative to non-neural derived samples. Given that many of the neural-crest melanocyte genes are expressed at embryonic stages of neural crest-melanocyte development, the gene set identified in this invention should provide a useful tool for the analysis of patterns of transcriptional regulation of NC-M development**.** Thus, this technology will be useful for the characterization of altered expression patterns in diseases such as melanoma. Further, this new microarray research tool has been developed using the set of genes that are likely to be involved in the control of human skin pigmentation. The microarray system utilizing these genes is of significant importance in identifying small molecules that may modulate their activity leading to alterations in human skin pigmentation. Therefore, this invention is significantly useful to the researchers to study alterations in human skin pigment amount and type.

Inventors:

William Pavan and Stacie K. Loftus (NHGRI)

Patent Status:

DHHS Reference No. E-014-2002/0 -- Research Tool

Licensing Status:

Available for licensing under a Biological Materials License.

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Methods of Determining the Prognosis of Hepatocellular Carcinoma

Description of Invention:

Hepatocellular carcinoma (HCC) represents an extremely poor prognostic cancer that remains one of the most common and aggressive malignancies worldwide. A major hallmark of HCC is intrahepatic metastasis and post-surgical reoccurrence. With current diagnostic methods, HCC patients are often diagnosed with end-stage cancer and have poor survival. Thus, there is a need for an accurate method to identify HCC and its proclivity for metastases/relapse, particularly at early stages of this disease.

The inventors have discovered a unique set of microRNA (miRNA) biomarkers that are associated with HCC metastasis/recurrence. This miRNA signature was validated in an independent cohort of 110 HCC samples as an independent predictor of HCC prognosis and likelihood of metastasis and relapse. In particular, the inventors provide evidence that these miRNA markers can predict HCC metastasis in the early stages of cancer. This methodology may enable clinicians to effectively stratify patients for appropriate cancer treatment and prioritize liver transplantation candidates.

Applications:

- Method to prognose HCC, patient survival and likelihood of HCC metastasis/relapse
- Diagnostic tool to aid clinicians in determining appropriate cancer treatment
- Compositions that inhibit miRNA HCC biomarkers such as siRNA
- Method to treatment HCC patients with inhibitory miRNA compositions

Market:

- Primary liver cancer accounts for about 2% of cancers in the U.S., but up to half of all cancers in some undeveloped countries
- Post-operative five year survival rate of HCC patients is 30-40%

Development Status:

This technology is currently in the pre-clinical stage of development.

Inventors:

Xin Wei Wang et al. (NCI)

Patent Status:

DHHS Reference No. E-050-2007/0 --
U.S. Provisional Application No. 60/884,052 filed 09 Jan 2007

Relevant Publication:

Budhu et al. A Unique Metastasis-related MicroRNA Expression Signature Predicts Survival and Recurrence in Hepatocellular Carcinoma, manuscript in preparation.

Licensing Status:
Available for exclusive or non-exclusive licensing.

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Genes For Niemann-Pick Type C Disease

Description of Invention:

Niemann-Pick disease is a class of inherited lipid storage diseases. Niemann-Pick Type C disease is an autosomal recessive neurovisceral lipid storage disorder which leads to systemic and neurological abnormalities including ataxia, seizures, and loss of speech. Patients with the disease typically die as children. The biochemical hallmark of Niemann-Pick Type C cells is the abnormal accumulation of unesterified cholesterol in lysosomes, which results in the delayed homeostatic regulation of both uptake and esterification of low density lipoprotein (LDL) cholesterol. Niemann-Pick Type C is characterized by phenotypic variability. The disease appears at random in families that have no history of the disorder, making diagnosis problematic. This invention provides the human gene for Niemann-Pick Type C disease and the nucleic acid sequences corresponding to the human gene for Niemann-Pick Type C disease. Also provided is the mouse homolog of the human gene. The invention could lead to improved diagnosis and the design of therapies for the disease and improved means of detection of carriers of the gene. In addition, this invention may contribute to the understanding and development of treatments for atherosclerosis, a more common disorder associated with cholesterol buildup that involves the accumulation of fatty tissue inside arteries that blocks blood flow, leading to heart disease and stroke. The invention may also lead to additional discoveries concerning how cholesterol is processed in the body.

Inventors:

Eugene D. Carstea (NINDS) et al.

Patent Status:

DHHS Reference No. E-122-1997/0 --
U.S. Patent No. 6,426,198 issued 30 Jul 2002
U.S. Patent No. 7,045,675 issued 16 May 2006

Relevant Publication:

1. S.K. Loftus et al., "Murine model of Niemann-Pick C disease: Mutation in a cholesterol homeostasis gene," Science 277(5323):232-235, 1997.
2. S.K. Loftus et al., "Rescue of neurodegeneration in Niemann Pick-C mice by a prion-promoter driven Npc1 cDNA transgene," Human Molec. Genet. 11(24):3107-14, 2002.

Licensing Status:

Licensees sought.

Also, the NHGRI Genetic Disease Research Branch is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize Niemann-Pick Type C disease diagnostics and therapies as well as potential applications of the Niemann-Pick Type C gene related to atherosclerosis and cholesterol processing. Please contact Claire T. Driscoll for more information (telephone:

301/594-2235; email: cdriscol@mail.nih.gov).

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Cytonectin, Cytonectin Gene and Cytonectin Inhibitors and Binding Ligands and Their Use in the Diagnosis and Treatment of Disease

Description of Invention:

Cytonectin is a 35K molecular weight protein that displays ion-independent adherence properties, is expressed in a variety of organs and tissues and is evolutionarily conserved from human to rodent and avian species. Within the body it is thought to serve the function of "super glue" contributing to cell-cell interactions and 3-dimensional tissue structure and a physiologic "do not attack" signal molecule that prevents tissue destruction by cells of monocyte lineage including odontoclasts in secondary teeth. It also plays an important role in the pathology associated with cancer, arthritis, Alzheimer's and Parkinson's disease.

The present invention relates to cytonectin, to polynucleotides that encode cytonectin, to inhibitors and antibodies that bind to cytonectin and to the use of compositions in the diagnosis and treatment of cytonectin-related diseases and conditions.

Potential Area of Application:

Research and drug development in cell adhesion based diseases

Inventors:

Soni J. Anderson et al. (NCI)

Patent Status:

DHHS Reference No. E-128-2004/0-US-01 filed 18 Mar 2004 (U.S. Provisional Application No. 60/553,977:
DHHS Reference No. E-128-2004/1-US-01 filed 09 Jun 2004 (U.S. Provisional Application No. 60/578,068)

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LMNA Gene and Its Involvement in Hutchinson-Gilford Progeria Syndrome (HGPS) and Arteriosclerosis

Description of Invention:

Hutchinson-Gilford Progeria Syndrome (HGPS) is a very rare progressive childhood disorder characterized by premature aging (progeria). The most common cause of death is from arteriosclerosis and few children affected by HGPS live beyond their teens. The invention identifies point mutations in the *LMNA* gene, a gene which encodes a nuclear lamin protein, as the cause of HGPS. These mutations activate a cryptic splice site within the *LMNA* gene which leads to the excision of a portion of an exon and the subsequent generation of a Lamin A protein with an internal deletion of fifty (50) amino acids. The identification of mutations associated with HGPS could lead to breakthroughs in detection, diagnosis, and treatment of HGPS and related or similar conditions, including arteriosclerosis and aging. See also Eriksson, M. et al "Recurrent *de novo* point mutations in lamin A cause Hutchinson-Gilford progeria syndrome" *Nature* 423, 293-298 (2003).

Inventors:

B. Maria H. Eriksson and Francis S. Collins (NHGRI)

Patent Status:

DHHS Reference No. E-020-2003/0 --
U.S. Provisional Application No. 60/419,541 filed 18 Oct 2002

DHHS Reference No. E-131-2003/0 --
U.S. Provisional Application No. 60/463,084 filed 14 Apr 2003

DHHS Reference No. E-020-2003/1 --
PCT Application No. PCT/US03/33058 filed 17 Oct 2003, which published as WO 2004/035753 on 29 Apr 2004
U.S. Patent Application No. 10/943,400 filed 17 Sep 2004

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Maxp1, A New Tumor Suppressor Regulated by Ras

Description of Invention:

The subject invention is directed to the cDNA sequence and the deduced amino acid sequence of the human Maxp1 gene. Maxp1 is frequently down-regulated in primary human tumors. Accordingly, a vector comprising the cDNA sequence, a host cell comprising such a vector, a method of using the vector, such as one comprising a cDNA sequence in which the C-terminal Ras binding site has been mutated or deleted, or the polypeptide (or fragment thereof, such as one in which the C-terminal Ras binding site has been mutated or deleted) in the prophylactic and therapeutic treatment of cancer, a method of assaying small molecules for the ability to stimulate Maxp1 growth inhibitory function in cancer cells that remain positive for Maxp1 expression, and the assessment of the levels of Maxp1 mRNA or protein in the diagnosis, characterization and prognosis of cancer are additional, non-limiting embodiments of the invention.

Further embodiments include: a) diagnosis and prediction of tumor characteristics, b) gene therapy to restore Nore1/Maxp1 function in tumor cells which have lost protein expression, c) the use of small molecules to simulate Nore1/Maxp1 growth inhibitory function in tumor cells which remain positive for Nore1/Maxp1 expression, d) the use of protein fragments/small molecules based on Nore1/Maxp1 structure to bind and inhibit the function of mutant Ras oncoproteins, and e) a specific polyclonal antibody that orks in westerns and in immunohistochemistry.

Inventors:

Geoffrey J. Clark (NCI)
Michelle Vos (NCI)

Patent Status:

DHHS Reference No. E-165-2001/0 --
U.S. Provisional Application No. 60/323,274 filed 19 Sep 2001
PCT Application No. PCT/US02/29643 filed 18 Sep 2002, which published as WO 03/025143 on 27 Mar 2003
U.S. Patent Application No. 10/489,906 filed 18 Mar 2004

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The Ovachip: A Clinically Useful cDNA Array for Differential Diagnosis of Ovarian Cancer

Description of Invention:
The present invention describes a specialized microarray that exclusively contains genes that are differentially expressed in ovarian cancer. The invention also provides for methods of generating an expression profile of multiple genes that are differentially expressed in ovarian cancer, methods of determining treatment for an ovarian tumor, and methods of identifying clusters of coordinately regulated genes that are differentially expressed in ovarian cancer.

Benefits of this invention include methods of predicting the response of a mammal to an anti-ovarian cancer therapeutic regimen, methods of monitoring cancer progression, methods of determining the efficacy of anti-cancer drugs, and methods of screening candidate anti-ovarian drugs for efficacy. All these applications hinge on the use of these ovarian cancer gene microarrays in generating gene expression profiles under various conditions and comparing them to each other and to standards.

Inventors: Morin et al. (NIA)

Patent Status:
DHHS Reference No. E-344-01/0 filed 06 Mar 2002

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NAG-1: A Non-Steroidal Anti-Inflammatory Drug Related Gene Which Has Anti-Tumorigenic Properties

Description of Invention:

Non-steroidal anti-inflammatory drugs (NSAIDs) are widely used in the treatment of inflammatory disease, and their anti-inflammatory effects are believed to result from their ability to inhibit the formation of prostaglandins by prostaglandin H synthase (COX). Two forms of prostaglandin H have been identified, COX-1 and COX-2. The former seems to be constitutively expressed in a variety of tissues while the high expression of the latter has been reported in colorectal tumors. NSAIDs have been shown to be effective in reducing human colorectal cancers and possibly breast and lung cancers. While the exact mechanism(s) by which NSAIDs function has not been elucidated, they could potentially play a critical role in detecting, diagnosing and treating inflammatory diseases as well as cancer. The present invention relates to screening methods for the identification of agonistic and/or antagonistic agents for the activation of the promoter region of NAG-1. Additional claims are directed to 1) the DNA sequence of NAG-1, 2) compositions containing the NAG-1 sequence and 3) methods for treating cancer patients using NAG-1.

Inventors:

Thomas E. Eling, Seung Joon Baek (NIEHS)

Patent Status:

DHHS Reference No. E-170-2000/0 --
U.S. Provisional Application No. 60/231,246 filed 08 Sep 2000
PCT Application No. PCT/US01/27544 filed 06 Sep 2001, which published as WO 02/20759 on 14 Mar 2002
U.S. Patent Application No. 10/363,514 filed 15 Aug 2003

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Genetic System in Yeast for Functional Identification of Human p53 Mutations

Description of Invention:

The tumor suppressor gene p53, a key regulator of cellular mechanisms that maintain genome integrity, is the most commonly inactivated gene target associated with neoplastic transformation. About 50% of all human tumors express a mutated form of p53 and more than 80% of these mutations are missense, leading to single amino acid changes. This invention relates to human p53 mutants and identification methods using screening assays in the yeast Saccharomyces cerevisiae to functionally categorize expressed p53 mutant proteins. Additionally, the invention relates to methods of detecting or generating novel human p53 mutations with properties that can include toxicity in yeast and growth suppression in human cells, enhanced or reduced transactivation relative to wild type p53, altered promoter selectivity, and reactivation of common tumor mutations for the transactivation function of major p53 downstream genes. The invention also provides for screening of genetic factors, peptides and chemicals that mimic the toxic or supertransactivating mutations or inhibit p53 function.

Inventors:

Michael A. Resnick and Alberto Inga (NIEHS)

Patent Status:

DHHS Reference No. E-183-1999/0 --
U.S. Provisional Application No. 60/146,634 filed 30 Jul 1999
PCT Application No. PCT/US00/20538 filed 28 Jul 2000, which published as WO 01/09325 on 08 Feb 2001
U.S. Patent Application No. 10/048,502 filed 12 Jun 2002

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Colon Mucosa Gene Having Down-Regulated Expression In Colon Adenomas And Adenocarcinomas

Description of Invention:

Tumor suppressor genes that are down-regulated in colon adenomas and adenocarcinomas have been identified and isolated that may be valuable for the study and treatment of these disorders as well as for detecting and identifying other tumor suppressor genes. Colorectal cancer is a significant problem in the U.S., with 130,000 new cases per year and more than 65,000 deaths per year. Colorectal cancer is a multistep process involving the loss of function of so-called tumor suppressor genes as well as the activation of oncogenes. Studies in cell cultures have shown that the transfer of wild-type tumor suppressor genes to colon cancer cells lacking this gene suppresses tumorigenicity. cDNAs encoding an mRNA that is down-regulated in adenocarcinomas and adenomas of the colon have been isolated and cloned. The mRNA encodes a polypeptide of about 84,500 daltons. This down-regulated in adenoma (DRA) gene maps to chromosome 7, in which abnormalities have previously been linked to colorectal carcinomas. The polypeptide product of the cDNA may be used for studying the process of tumorigenesis and suppression. In addition, the DRA gene and/or polypeptide may be valuable as therapy for colon cancer or for staging colon tumors. Finally, this invention includes nucleotide probes for detecting and isolating other tumor suppressor genes.

Inventors:

CW Schweinfest
TS Papas (NCI)

Patent Status:

Serial No. 08/424,567 filed 17 Apr 1995
U.S. Patent 5,569,755 issued 29 Oct 1996

Serial No. 08/711,928 filed 11 Sep 1996
U.S. Patent 5,831,015 issued 03 Nov 1998

Serial No. 09/184,937 filed 02 Nov 1998

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INFECTIOUS DISEASES

Human and Avian Influenza Whole Genome Phage Display Libraries

Description of Invention:
Available for use in developing research reagents, therapeutics or diagnostics are recombinant bacteriophage display libraries for identifying influenza viral gene products in preparation for pandemic threats the cross-reactivity and long-term protection of interpandemic influenza vaccines. Influenza vaccines predominantly include haemagglutinin (HA) and Neuraminidase (NA) antigens that characterize annual circulating influenza types A and type B. Analyses of the immune responses against new candidate vaccines is required in order to identify the best correlate of protection against seasonal human influenza strains and potential pandemic strains.

These "Whole Viral Genome Phage Display Libraries" express complete sets of protein fragments encoded by several Human and Avian Influenza strains including HlN1, H3N2, H5N1 and H7N7 and can be used for in depth analyses of plasma samples from: a) individuals exposed to human influenza; b) individuals exposed to avian influenza; c) individuals vaccinated with traditional influenza vaccines; d) individuals vaccinated with new generation vaccines against human and bird influenza viruses.

Applications:

- Serological assays for surveillance of pandemic influenza outbreaks
- Serological assays for distinguishing between exposure to human and bird influenza strains
- Serological assays for diagnosing true infections in previously vaccinated individuals
- Rapid analyses of immune sera from pre-clinical and clinical trials of novel influenza vaccines
- Mapping of monoclonal and polyclonal antibodies against different influenza gene products
- Identification of highly conserved "protective" epitopes for inclusion in future broadly-reactive influenza vaccines (against either inter-pandemic or pandemic influenza strains)
- Studies of viral protein-protein, viral RNA-protein and viral-host protein interactions (viral pathogenesis studies)

Market:
Influenza diagnostics and vaccines

Development Status:
Materials available as research tools

Scientific Contact:

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Inventors:
Hana Golding and Surender Khurana (FDA)

Patent Status:
DHHS Reference No. E-031-2007/0 – Research Tool

Licensing Status:
Available for licensing as a biological material.

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A Sensitive, High Throughput Pseudovirus-Based Papillomavirus Neutralization Assay for HPV 16 and HPV 18

Description of Invention:
This invention is a research tool for measuring protective antibody responses against Human Papilloma Viruses (HPV). Sensitive high-throughput neutralization assays, based upon pseudoviruses carrying a secreted alkaline phosphatase (SEAP) reporter gene, were developed and validated by the inventors for HPV 16, HPV 18, and bovine papillomavirus 1 (BPV1). In a 96-well plate format, the assay was reproducible and appears to be as sensitive as, but more type-specific than, a standard papillomavirus-like particle (VLP)-based enzyme-linked immunosorbent assay (ELISA). The SEAP pseudovirus-based neutralization assay should be a practical method for quantifying potentially protective antibody responses in HPV natural history and prophylactic vaccine studies.

Inventors:
John T. Schiller (NCI)
Douglas R. Lowy (NCI)
Christopher Buck (NCI)
Diana V. Pastrana (NCI)
et al.

Patent Status:
DHHS Reference No. E-137-2004/0 -- Research Material

Relevant Publication:
The assay is further described in Pastrana et al., "Reactivity of human sera in a sensitive, high-throughput pseudovirus-based papillomavirus neutralization assay for HPV16 and HPV18," Virology. 2004 Apr 10;321(2):205-216. [PubMed abs]

Licensing Status:
This assay is available nonexclusively through a biological materials license.

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Rapid Universal and/or Type-Specific Assay for Clostridium Botulinum

Description of Invention:
The urgent need for a rapid diagnostic test capable of detecting all serotypes of C. botulinum is well known. Botulinum neurotoxins (BoNTs) are the most potent biological toxins known and are categorized as category A biodefense agents because of lethality and ease of production. Current diagnostic methods include clinical observation of symptoms that could be mistaken for other neurological conditions and a mouse protection bioassay that takes as long as four days and has a number of disadvantages. The subject technology utilizes unique PCR primers for the detection of the non-toxin non-hemaglutinin (NTNH) gene of C. botulinum; this gene is highly conserved in all C. botulinum toxin types and subtypes. Thus, samples that contain botulinum can be determined regardless of serotype involved, providing a universal means of diagnosis. Further, the technology describes different PCR primers and flurogenic probes for a BoNT-specific assay. The type-specific assay can be used independently or in conjunction with the universal assay described above. The universal and type-specific assays were successfully used first to identify positively botulinum DNA samples in a test of botulinum and non-botulinum clostridia species then to determine the toxin type. The diagnostic testing described by the subject technology requires significantly less time than the current gold standard diagnostic test.

Applications:

- Universal diagnostic test for C. botulinum
- Diagnostic test for C. botulinum capable of detecting all seven toxin types
- Combination diagnostic

Development Status:
Fully developed

Inventors:
Daniel C. Douek (VRC/NIAID) et al.

Patent Status:
DHHS Reference No. E-046-2007/0 --
U.S. Provisional Application No. 60/884,539 filed 11 Jan 2007

Licensing Status:
Available for non-exclusive or exclusive licensing.

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HSV-2 Diagnostic

Description of Invention:
The present invention relates to novel diagnostic methods for Herpes Simplex Virus Type 2 (HSV-2). HSV-2 infects approximately one fifth of adults in the United States and is the most common cause of genital ulceration. The invention relates to the detection of HSV-2 based on a transforming nucleic acid sequence and its protein product. This DNA sequence harbors the potential to induce the tumorigenic transformation of normal cells in in vitro and in vivo assays and thus will be useful as a means of prognostic evaluation in predicting the development of genital or cervical cancer. Current HSV-2 diagnostic tests relying on tedious viral culture and/or immunoassays that do not have the sensitivity and the specificity essential for diagnosis. Using PCR, the current invention will provide a superior method for viral detection and subtyping.

Application:
HSV-2 diagnostic

Inventors:
Joseph A. DiPaolo (NCI) et al.

Patent Status:
DHHS Reference No. E-091-1999/0 --
U.S. Patent 6,617,103 issued 09 Sep 2003
CA Application 2,259,657 filed 30 Jun 1997

Licensing Status:
Available for non-exclusive or exclusive licensing.

Collaborative Research Opportunity:
The NCI Division of Basic Science is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize HSV-2 Diagnostic. Please contact Betty Tong, Ph.D. at 301-594-4263 or tongb@mail.nih.gov for more information.

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Multiplex Microarray for Simultaneous Detection of Hepatitis C Virus, Hepatitis B Virus, and Human Immunodeficiency Virus Type-1

Description of Invention:

Available for licensing and commercial development are patent rights that cover a specific and sensitive microarray (TTD -V-1) and multiplex assay for the simultaneous detection and discrimination of Hepatitis C Virus (HCV), Hepatitis B Virus (HBV) and Human Immunodeficiency Virus Type-1 (HIV-1), which include both RNA and DNA genomes. Four specific probes (30-45 bp oligonucleotides) for each of these three viruses as well as the two internal controls were designed. Totally, each microarray consists of 20 probes immobilized on silylated glass slides. The single-stranded Cy5-labeled samples for microarray hybridization were obtained from labeling the amplicons using primer extension thermocycling. The multiplex microarray assay was able to detect and discriminate as low as 3 copies of genotypes A, B, C, D, and 10 copies of genotype E of HBV, 10 copies of HCV (genotype 1b), and 20 copies of HIV-1 (group M, subtype B) in a single multiplex reaction. The microarray assay could also detect the coexistence of two or three of these viruses and discriminate them simultaneously. The results of this study demonstrated the feasibility and performance of microarray-based multiplex detection of the three viruses, HCV, HBV, and HIV-1 in comparison with conventional individual PCR and gel electrophoresis technique.

Inventors:

Chu Chieh Xia (FDA)
Gerardo Kaplan (FDA)
Hira Nakhasi (FDA)
Amy Yang (FDA)
Raj Puri (FDA)

Patent Status:

DHHS Reference No. E-077-2006/0 --
U.S. Provisional Application No. 60/759,214 filed 17 Jan 2006

Licensing Status:

Available for non-exclusive or exclusive licensing.

Collaborative Research Opportunity:

The Food and Drug Administration's Center for Biologics Evaluation and Research (CBER) is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize this technology. Please contact Beatrice Droke, Technology Development Coordinator, FDA, (301) 827-7008 for more information.

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Novel Methods and Compositions for Diagnosing AIDS and Other Diseases Involving Immune System Activation

Description of Invention:

Available for licensing and commercial development are methods and compositions suitable for monitoring the progression of AIDS and other diseases whose progression involves immune system activation in mammals, such as cancer, atherosclerosis, Alzheimer's disease, inflammation, autoimmune disorder, allergic asthma, Crohn's disease, Grave's disease, lupus, multiple sclerosis, Parkinson's disease, allograft transplant rejection, and graft vs. host disease.

In particular, the invention relates to the use of the TRAIL (TNF-related apoptosis-inducing ligand) and TRAIL compounds to monitor the progression of AIDS, and such other diseases. This is accomplished by assessing the presence or concentration of TRAIL, especially mTRAIL, sTRAIL, the TRAIL DR5 receptor molecule, and biological molecules that activate TRAIL or its receptor. These biological molecules include p53, alpha- and beta-interferon, as well as additional compounds such as CD69 and HLA-DR. Also claimed are kits for immunoassays to determine the presence or concentration of a TRAIL compound in a biological fluid, suitable for determining whether the mammal suffers from any of the above diseases.

TRAIL can be used as a new surrogate biomarker to monitor the progression of HIV infection and other conditions and diseases associated with immune system activation. In the case of HIV infection, measuring levels of this biomarker can distinguish among infected individuals with high viral load, infected individuals with low viral load, and uninfected individuals. Only two surrogate markers are currently recognized by the Food and Drug Administration as clinically relevant to HIV progression, HIV viral load and the absolute number of peripheral CD4+ T cells. Tests for assessing HIV viral load employ PCR, the use of which has drawbacks, including cross-contamination. TRAIL has mechanistic implications for HIV-1 pathogenesis and directly correlates to viral load but not necessarily inversely with CD4+ T cell count. Other surrogate markers have been proposed but do not consistently reflect AIDS progression in all individuals or may result in overlooking possible treatments that may affect disease progression but do not affect the chosen marker. Therefore, use of this new biomarker to assess disease progression in infected individuals and to evaluate the effectiveness of various treatment regimens has several advantages over currently used methods, since TRAIL is a death molecule involved in CD4+ T cell depletion in HIV/AIDS. TRAIL, its receptor, and activating molecules can all be used as sensitive markers for CD4 T cell activation and apoptosis.

Inventors:

Gene M. Shearer and Jean-Philippe Herbeuval (NCI)

Patent Status:

DHHS Reference No. E-045-2004/0 --
U.S. Provisional Application No. 60/564,588 filed 23 Apr 2004

DHHS Reference No. E-045-2004/1 --
U.S. Provisional Application No. 60/634,255 filed 12 Dec 2004

DHHS Reference No. E-045-2004/2 --
PCT Application No. PCT/US2005/13554 filed 21 Apr 2005

Relevant Publication:

1. Herbeuval JP, Hardy AW, Boasso A, Anderson SA, Dolan MJ, Dy M, Shearer GM. Regulation of TNF-related apoptosis-inducing ligand on primary CD4+ T cells by HIV-1: role of type I IFN-producing plasmacytoid dendritic cells. Proc Natl Acad Sci U S A. 2005 Sep 27;102(39):13974-9.
2. Herbeuval JP, Grivel JC, Boasso A, Hardy AW, Chougnet C, Dolan MJ, Yagita H, Lifson JD, Shearer GM "CD4+ T-cell death induced by infectious and noninfectious HIV-1: role of type 1 interferon-dependent, TRAIL/DR5-mediated apoptosis" Blood. 2005 Nov 15;106(10):3524-31.
3. Herbeuval JP, Boasso A, Grivel JC, Hardy AW, Anderson SA, Dolan MJ, Chougnet C, Lifson JD, Shearer GM "TNF-related apoptosis-inducing ligand (TRAIL) in HIV-1-infected patients and its in vitro production by antigen-presenting cells" Blood. 2005 Mar 15;105(6):2458-64.

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Novel Methods and Compositions for Diagnosing AIDS and Other Diseases Involving Immune System Activation

Description of Invention:

Available for licensing and commercial development are methods and compositions suitable for monitoring the progression of AIDS and other diseases whose progression involves immune system activation in mammals, such as cancer, atherosclerosis, Alzheimer's disease, inflammation, autoimmune disorder, allergic asthma, Crohn's disease, Grave's disease, lupus, multiple sclerosis, Parkinson's disease, allograft transplant rejection, and graft vs. host disease.

In particular, the invention relates to the use of the TRAIL (TNF-related apoptosis-inducing ligand) and TRAIL compounds to monitor the progression of AIDS, and such other diseases. This is accomplished by assessing the presence or concentration of TRAIL, especially mTRAIL, sTRAIL, the TRAIL DR5 receptor molecule, and biological molecules that activate TRAIL or its receptor. These biological molecules include p53, alpha- and beta-interferon, as well as additional compounds such as CD69 and HLA-DR. Also claimed are kits for immunoassays to determine the presence or concentration of a TRAIL compound in a biological fluid, suitable for determining whether the mammal suffers from any of the above diseases.

TRAIL can be used as a new surrogate biomarker to monitor the progression of HIV infection and other conditions and diseases associated with immune system activation. In the case of HIV infection, measuring levels of this biomarker can distinguish among infected individuals with high viral load, infected individuals with low viral load, and uninfected individuals. Only two surrogate markers are currently recognized by the Food and Drug Administration as clinically relevant to HIV progression, HIV viral load and the absolute number of peripheral CD4+ T cells. Tests for assessing HIV viral load employ PCR, the use of which has drawbacks, including cross-contamination. TRAIL has mechanistic implications for HIV-1 pathogenesis and directly correlates to viral load but not necessarily inversely with CD4+ T cell count. Other surrogate markers have been proposed but do not consistently reflect AIDS progression in all individuals or may result in overlooking possible treatments that may affect disease progression but do not affect the chosen marker. Therefore, use of this new biomarker to assess disease progression in infected individuals and to evaluate the effectiveness of various treatment regimens has several advantages over currently used methods, since TRAIL is a death molecule involved in CD4+ T cell depletion in HIV/AIDS. TRAIL, its receptor, and activating molecules can all be used as sensitive markers for CD4 T cell activation and apoptosis.

Inventors:

Gene M. Shearer and Jean-Philippe Herbeuval (NCI)

Patent Status:

DHHS Reference No. E-045-2004/0 --
U.S. Provisional Application No. 60/564,588 filed 23 Apr 2004

DHHS Reference No. E-045-2004/1 --
U.S. Provisional Application No. 60/634,255 filed 12 Dec 2004

DHHS Reference No. E-045-2004/2 --
PCT Application No. PCT/US2005/13554 filed 21 Apr 2005

Relevant Publication:

1. Herbeuval JP, Hardy AW, Boasso A, Anderson SA, Dolan MJ, Dy M, Shearer GM. Regulation of TNF-related apoptosis-inducing ligand on primary CD4+ T cells by HIV-1: role of type I IFN-producing plasmacytoid dendritic cells. Proc Natl Acad Sci U S A. 2005 Sep 27;102(39):13974-9.
2. Herbeuval JP, Grivel JC, Boasso A, Hardy AW, Chougnet C, Dolan MJ, Yagita H, Lifson JD, Shearer GM "CD4+ T-cell death induced by infectious and noninfectious HIV-1: role of type 1 interferon-dependent, TRAIL/DR5-mediated apoptosis" Blood. 2005 Nov 15;106(10):3524-31.
3. Herbeuval JP, Boasso A, Grivel JC, Hardy AW, Anderson SA, Dolan MJ, Chougnet C, Lifson JD, Shearer GM "TNF-related apoptosis-inducing ligand (TRAIL) in HIV-1-infected patients and its in vitro production by antigen-presenting cells" Blood. 2005 Mar 15;105(6):2458-64.

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Methods for High-Efficiency Single Genome Sequencing of HIV

Description of Invention:
The invention is directed to a method for efficiently obtaining single genome sequences (SGS) of HIV from a biological sample. The invention has the following advantages over the current commercial genotyping in use: 1) It might improve the sensitivity of diagnosis of drug resistant HIV in newly infected HIV patients; 2) It might provide a more affordable diagnostic tool for early detection of drug resistance since the invention is adaptable to an automated approach for the high-throughput processing of a large number of patient sample; 3) It might improve patient outcome since SGS has the ability to identify low level mutation and will permit a more comprehensive evaluation of resistance in patients and might potentially change the clinical approach to treating resistant virus. In summary, this invention might be a new important diagnostic tool for AIDS patients.

Inventors:
John Coffin (NCI)
Mary Kearney (NCI)
Frank Maldarelli (NCI)
Sarah E. Palmer (NCI)
et al.

Patent Status:
DHHS Reference No. E-022-2005/0-US-01 -- U.S. Provisional Application filed 25 Jan 2005

Relevant Publication: Sarah Palmer et al., "Multiple, Linked Human Immunodeficiency Virus Type 1 Drug Resistance Mutations in Treatment-Experienced Patients are Missed by Standard Genotype Analysis," J. Clin. Microbiol. (Jan 2005) 43(1):406-413.

Licensing Status: In addition to licensing, the technology is available for further development through collaborative research opportunities with the inventors.

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Antibodies Against the Amino Terminus Region of Circumsporozoite Protein Prevent the Onset of Malaria

Description of Invention:
Malaria is one of the 5 major diseases of the world and a leading cause of childhood death in sub-Saharan Africa. Furthermore, the economic devastation of the disease is measured in the billions of dollars of lost wages and lowered productivity for the endemic areas of the world. In the US, it is a concern of travelers as well the military having to serve in those parts of the world. To date, there is no vaccine and one is not expected for another decade.

The invention presented here focuses on the ability of the malarial sporozoite to infect liver cells. Previous vaccines have focused on the carboxyl end of the circumsporozoite (CSP) protein and have few successes to show. This invention utilizes the finding that the amino terminal portion of the CSP protein is required for hepatic entry. The invention includes several CSP polypeptides and constructs encoding such polypeptides that have been shown to be required for hepatic entry for vaccine development, prevention and treatment are also claimed. Methods and kit claims are included for the detection of the CSP protein in biological samples as well as for the detection of circulating antibodies of the CSP protein are also included.

Inventors:
Dharmendar Rathore and Thomas McCutchan (NIAID)

Patent Status:
DHHS Reference No. E-176-2003/0 --
U.S. Provisional Application No. 60/532,676 filed 23 Dec 2003
PCT Application No. PCT/US04/43269 filed 20 Dec 2004
Licensing Status: In addition to licensing, the technology is available for further development through collaborative research opportunities with the inventors.

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Human Monoclonal Antibodies Against Hendra and Nipah Viruses

Description of Invention:
Available for licensing are neutralizing human monoclonal antibodies against the envelope proteins (Envs) of Hendra virus (HeV) and Nipah virus (NiV) for uses in immunotherapy, vaccine development and as diagnostic or research reagents. Monoclonal antibody variable region fragments (Fabs and scFvs) have been isolated from screening a human phage display library against the Envs. The phage display library (DHHS Ref. No. E-005-2005) is useful for screening other viral or cancer antigens and can be licensed from DHHS under a biological materials license.

Inventors:
Dimiter S. Dimitrov et al. (NCI)

Patent Status:
DHHS Reference No. E-004-2005/0-US-01 -- U.S. Provisional Application No. 60/624,247 filed 01 Nov 2004

Related Technologies: DHHS Reference No. E-005-2005/0 -- Research Tool (Phage Display Library)

Licensing Status: In addition to licensing, the technology is available for further development through collaborative research opportunities with the inventors.

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HIV-1 Infection Detection Assay for Seroconverted HIV-1 Vaccine Recipients

Description of Invention:
Available for licensing and commercial distribution is an assay method and kit having diagnostic peptide fragments derived from human immunodeficiency virus-1 (HIV-1). The new serology assay includes HIV-1 peptide fragments epitopes that map to HIV-1 GAG-p6, and gp41 genes. These epitopes are broadly reactive with early sera from HIV infected individuals, do not illicit protective antibodies, do not illicit immunologic cytotoxicity and are readily removable from current and future HIV-1 candidates. The assay is advantageous in detecting HIV-1 early breakthrough infections in seroconverted vaccine recipients while being able to distinguish between individuals with bonafide breakthrough infections versus non-HIV infected vaccine recipients presenting only vaccine borne antibodies. For example, 90% of vaccine recipients receiving a Canarypox construct expressing a plurality of HIV antigens (Env, Gag, Pol, HIV Protease, Nef) followed by an envelope protein boost, scored positive in FDA licensed enzyme immunoassay, rapid test, and Western blot (Marta-Louise Ackers et al., J Infect Dis. 187:879 (2003)). Such seroconversion has a negative impact on phase III efficacy trials of prophylactic HIV vaccines that require early detection of breakthrough infections and also exclude non-HIV infected vaccine recipients from the pool of potential blood donors.

Inventors:
Hana Golding and Surender Khurana (FDA/CBER)

Patent Status:
DHHS Reference No. E-259-2004/0 --
U.S. Provisional Application No. 60/607,579 filed 08 Sep 2004

DHHS Reference No. E-259-2004/1 --
U.S. Provisional Application No. 60/769,310 filed 03 May 2005
PCT filed

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Anti-Plasmodium Compositions and Methods of Use

Description of Invention:

This invention describes methods and compositions of peptides that inhibit the binding of *Plasmodium falciparum* (*P. falciparum*) to erythrocytes. Malarial parasites enter the red blood cell through several erythrocyte receptors, each being specific for a given species of *Plasmodia*. For *P. falciparum*, the erythrocyte binding antigen (EBA-175) is the ligand of the plasmodia merozoites that interacts with the receptor glycophorin A on the surface of red blood cells. Inhibiting this ligand/receptor interaction is one method of preventing further malarial attacks and is an active area of vaccine research.

This invention describes another specific peptide and antibodies that inhibit this ligand/receptor binding, thus is a potential source for vaccine development. The peptide described herein is a paralogue of EBA-175, identified as EBP2. Further, the invention includes antibodies and peptides that are specific for the claimed paralogue. Claims include the development of vaccines to the EBA-175 and EBP2. In addition, these antibodies and peptides can be developed as diagnostic and analytical reagents as well. Methods include the use of the peptides and the antibodies for the diagnosis, prevention and potential treatment of malaria. Further claims include their use in detection of *P. falciparum* in biological samples and culture methods.

Inventors:

David Narum (NIAID) et al.

Patent Status:

DHHS Reference No. E-049-2004/0 --
U.S. Patent Application No. 09/924,154 filed 07 Aug 2001, claiming priority to 07 Aug 2000
U.S. Patent Application No. 10/630,629 filed 29 Jul 2003

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Enhanced Sensitivity ELISA for SARS Diagnostic

Description of Invention:
Reagents and protocols for extremely sensitive ELISA for use as a SARS diagnostic are described. The ELISA uses recombinant-expressed nucleoprotein (N) or spike (S) glycoprotein from the SARS coronavirus as capture antigens. As little as five (5) days after onset, detection of antibody response is possible. The ELISA described herein is more sensitive than existing technology because of the N and S proteins; existing ELISAs use formalin-inactivated whole virus or peptides.

E-334-2003/1-US-01 also describes DNA Vaccines (CMV/R-SARS-S plasmid) including a nucleic acid encoding the peptide of SARS Spike glycoprotein, the RSV enhancer, the mouse ubiquitin enhancer (mUBB), and the CMV enhancer (Xu et al. 1998 Nature Med. 4: 37-42). Optionally the HTLV-1 R region (Takebe et al. 1988 Mol Cell Biol 8: 466-472) is also included.

Inventors:
Gary Nabel et al. (NIAID)

Patent Status:
DHHS Reference No. E-334-2003/0 --
U.S. Provisional Application No. 60/503,508 filed 15 Sep 2003

DHHS Reference No. E-334-2003/1 --
U.S. Provisional Application No. 60/550,317 filed 08 Mar 2004

DHHS Reference No. E-334-2003/2 --
PCT Application No. PCT/US2004/29999 filed 14 Apr 2004, which published as WO 2005/027963 on 31 Mar 2005

Related Technologies: DHHS Reference No. E-165-2004 -- SARS Coronavirus MVA Vaccines and Therapy

DHHS Reference No. E-278-2003 -- Interferon-Alpha SARS Treatment

DHHS Reference No. E-228-2003 -- Soluble SARS Coronavirus Spike Protein (S Protein)

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Methods and Compositions to Detect Nucleic Acid

Description of Invention:

This technology involves the isolation and identification of *Helicobacter* within fecal matter. The technology provides for the methods and nucleic acid primer reagents and sequences specific for *H. pylori*. Specifically, it addresses the identification of the common human species of *H. pylori*. *H. pylori* is a major infectious agent of the human gastric intestinal tract, affecting about 50% of the world population with various degrees of severity. *H. pylori* infection is associated with 95% of duodenal ulcers and 80% of gastric ulcers. Without treatment, 80% of duodenal ulcers will return. Further, gastric ulcers have been linked as precursors to the more life-threatening gastric cancers.

Current diagnostics are expensive, invasive, or require the patient to ingest radioactive substances. The technology presented provides for a quick, specific, inexpensive, non-invasive method for diagnosis of *H. pylori* infection as well the ability to repeat such tests for patient follow up on treatment effectiveness. Also included is the ability to develop kits for commercial purposes.

Inventors:

Dougbeh C. Nyan et al. (NIDDK)

Patent Status:

DHHS Reference No. E-146-2002/0 --
U.S. Provisional Application No. 60/468,341 filed 06 May 2003
PCT Application No. PCT/US2004/14374 filed 06 May 2004, which published as WO 2005/001109 on 06 Jan 2005

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C-C Chemokines That Inhibit Retrovirus Infection

Description of Invention:

This invention concerns three members of the human C-C chemokine family, RANTES, macrophage inflammatory protein 1alpha (MIP-1alpha) and macrophage inflammatory protein 1beta (MIP-1beta), which are produced and secreted by several cell types, including CD8-positive T lymphocytes, and which act in vitro as HIV suppressive factors. These factors and their respective genes may be used in the diagnosis, prognosis, treatment and prevention of AIDS and other retrovirus-induced diseases**.** The invention provides a therapeutic preparation, methods for therapeutic and prophylactic treatment of retroviral infection, and a method of prognosis for retroviral infection**.** The technology was reported in Science 270(8):1560-1561 (December 8, 1995).

Inventors:

Paolo Lusso
Robert C. Gallo
Fiorenza Cocchi
Anthony L. De Vico
Alfredo Garzino-Demo (NCI)

Patent Status:

DHHS Reference No. E-008-1996/0 --
PCT Application No. PCT/US96/18993 filed 27 Nov 1996
U.S. Patent Application No. 09/077,614 filed 29 May 1998, with priority to 30 Nov 1995

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Novel Receptor for Pathogenic Fungi

Description of Invention:

A specific receptor for pathogenic fungi has been isolated and substantially purified for the first time, and a method of using the receptor to prevent adhesion of pathogenic fungi to host cells has been developed. A kit for detecting the presence of certain fungi was also described. These products make possible the detection and removal of two important pathogenic fungi, Candida albicans and Cryptococcus neoformans, and may be useful in preventing yeast diseases.

Inventors:

Victor Jimenez (EM)
Victor Ginsburg (NIDDK)
Howard Krivan (NIDDK)

Patent Status:

DHHS Reference No. E-145-1989/0-US-01 (U.S. Patent 5,242,800 issued on 07 Sep 1993)

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HIV-Dependent Expression Vector

Description of Invention:

This invention provides a DNA construct that can be useful for both diagnostics and AIDS therapeutics. The construct can be incorporated into a retrovirus or into a cell line. This construct mediates the expression of a selected gene in the presence of HIV replication, but is silent in the absence of HIV. The cell line with the incorporated construct can be used as an indicator line for the presence of replication-competent HIV. The virus containing the construct can be used to co-infect a population of HIV-infected cells. If the construct-encoded gene is a reporter, it would specifically identify cells that are infected with HIV. If the construct-encoded gene is a cytotoxin, it would specifically kill cells that are HIV-infected**.** This invention may offer a novel approach to HIV elimination, as well as detection of HIV infected cells or the presence of cell-free infectious HIV.

Inventors:

Drs. Jon Marsh and Yuntao Wu (NIMH)

Patent Status:

DHHS Reference No. E-276-2003/0-US-01 filed 28 Sep 2003 (U.S. Provisional Application No. 60/507,034)

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Factors That Bind Intestinal Toxins

Description of Invention:

This invention discloses and covers polyphenolic compounds that will bind bacterial toxins, methods for the treatment of such infections, specifically Stx-1 toxins from STEC strains of *E. coli*.

Bacterial infections not only cause disease by their presence but also upon the release of toxins. The common enteric bacteria, *E. coli* O157:H7 releases such toxins (Stx-1) upon treatment with antibiotics. These toxins, when released into the lumen of the intestinal tract, will cause cellular damage thus increasing the severity of the infection. Thus not only does the patient become sick by the infection, but treatment can exacerbate the condition and clinical picture. Further, the indiscriminate use of antibiotics has lead to an increase in the number of resistant strains thus limiting the effectiveness of therapy as well.

The disclosed invention uses an extract from the bracts of *Humulus lupulus* that binds the toxins thus eliminating them as a source of cellular damage. The enclosed methods and devices to isolate such polyphenolic components, the methods to use such components in the detection of such bacteria in biological samples and potential therapies based on the isolated components.

Inventors:

Joel Moss (NHLBI)
Masatoshi Noda (EM)

Patent Status:

DHHS Reference No. E-223-2002/0 --
U.S. Provisional Application No. 60/409,742 filed 10 Sep 2002
PCT Application No. PCT/US03/28282 filed 09 Sep 2003, which published as WO 2004/024070 on 25 Mar 2004
U.S. Patent Application No. 10/526,820 filed 03 Mar 2005

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Molecular Diagnosis of Disseminated *Candida albicans* Infection Using Hemoglobin-Response Gene

Description of Invention:

Three hemoglobin-response genes from *Candida albicans* have been isolated. These genes are induced when the organism initiates systemic infections, coming into contact with hemoglobin. Further, the methods and composition of the included nucleic acid sequences and encoded proteins can be used in the development of reagents and kits used to discriminate between commensal colonization and the more life threatening disseminated infection.

Inventors:

David D. Roberts (NCI)
Sizhuang Yan (CC)

Patent Status:

DHHS Reference No. E-086-1999/0 --
U.S. Patent No. 6,875,855 issued 05 Apr 2005

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Hepatitis A Virus Receptor And Methods Of Use

Description of Invention:
This invention describes the discovery and isolation of HAVcr-1, a simian cellular receptor for the hepatitis A virus (HAV). Cells nonpermissive to HAV infection transfected with HAVcr-1 cDNA, a novel cell surface mucin-like glycoprotein, gain susceptibility to HAV infection. The invention claims nucleic acids encoding cellular receptors to HAV that hybridize with HAVcr-1 probes, including the human homologs of HAVcr-1 (hHAVcr-1). The invention also claims peptides encoded by the above-mentioned HAV receptor nucleic acid, antibodies against HAVcr-1 receptors, and ligands to HAVcr-1 receptors.

The human homolog of HAVcr-1 (hHAVcr-1) has been shown to be a marker of renal injury (given the alias of kidney injury molecule 1 or KIM-1) and kidney cancer as well as a putative asthma determinant gene and modulator of T cell helper responses (given the alias of T-cell immunoglobulin mucin 1 or TIM-1). Use of HAVcr-1 nucleic acids and derived peptides, antibodies, ligands, etc. for diagnosis and therapy are also covered in this patent.

Potential areas of application include use of HAVcr-1 receptors and homologs for diagnostics; use of HAVcr-1 receptors for treatment of patients; development of therapeutic compounds capable of interacting with HAVcr-1receptors that could block or activate these receptors, development of transgenic animals carrying HAVcr-1 receptors or portions of the receptors that could be used for vaccine production and testing and other applications.

HAVcr-1 has been molecularly cloned and its cDNA is available for further development.

Inventors:
Gerardo Kaplan and Stephen M. Feinstone (FDA)

Patent Status:
DHHS Reference No. E-150-1994/0-US-01 (U.S. Patent 5,622,861 issued 22 Apr 1997)
Licensing Status: This invention is available for licensing on an exclusive or nonexclusive basis.

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Recombinant Proteins of the Swine Hepatitis E Virus and Their Uses as a Vaccine and Diagnostic Reagents for Medical and Veterinary Applications

Description of Invention:

This invention is based on the discovery of the swine hepatitis E virus (swine HEV), the first animal strain of HEV identified and characterized, and its ability to infect across species. The inventors have found that the swine HEV is widespread in the general pig population in the United States and other countries and that swine HEV can infect non-human primates. The inventors have amplified and sequenced the complete genome of swine HEV. The capsid gene (ORF2) of swine HEV has been cloned and expressed in a baculovirus expression system.

The possibility that swine HEV may infect humans raises a potential public health concern for zoonosis or xenozoonosis in the United States and perhaps other countries. Therefore, it is likely that a vaccine based on the recombinant capsid protein of swine HEV will protect humans against zoonotic, as well as other, HEV infections and pigs against infection with the swine HEV. Also, diagnostic reagents based on these recombinant proteins of swine HEV will be very useful in screening donor pigs used in xenotransplantation and in detecting swine HEV or similar virus infection in humans. The diagnostic reagents may also be useful for veterinary studies and monitoring pig herds in general.

Inventors:

Xiang-Jin Meng (NIAID)
Robert H. Purcell (NIAID)
Suzanne U. Emerson (NIAID)

Patent Status:

DHHS Reference No. E-304-1998/0 --
U.S. Provisional Application No. 60/289,200 filed 07 May 2001
PCT Application No. PCT/US02/14100 filed 02 May 2002, which published as WO 02/089733 on 14 Nov 2002
U.S. Patent Application No. 10/476,777 filed 05 Nov 2003

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Adhesion Molecules (Carbohydrate Receptors) For Pathogenic Bacteria And Fungi

Description of Invention:
The ability of pathogenic organisms including bacteria and fungi to cause disease depends, at least initially, on the ability to bind to and enter target cells of the host. A wide variety of cellular molecules are involved in this interaction. The structure of the cell receptors involved in the initial binding of the bacteria or yeast can be very complex. Receptors involved in bacteria-animal cell interactions is the technology claimed in these inventions. Receptors identified in bacterial interactions are complex carbohydrate compounds whereas the receptor involved in the fungal interaction is a glycolipid. A variety of pathogenic bacteria are able to bind to the purified receptor including: Streptococcus pneumoniae, Staphylococcus aureus, Haemophilus influenzae and parainfluenzae, Klebsiella pneumoniae, Pseudomonas aeruginosa, cepacia, and maltophilia, some isolates of Escherichia coli, and Mycoplasma hominus and pneumoniae. Several species of fungi were shown to bind to a glycosphingolipid receptor including: Cryptococcus neoformans, Candida albicans, Histoplasma capsulatum, Sporotrichum schenckii, and Saccharomyces cerevisae. The technology claimed in these patents has potential diagnostic and therapeutic applications for both bacteria and fungi. Diagnostic kits are claimed allowing for the detection of certain microorganisms. These kits are comprised of either immobilized receptors on an insoluble substrate or a suspension of the purified compound. Binding of the bacteria is then detected by the use of either a labeled reagent specific for the suspected bacteria or by the presence of a perceptible agglutination reaction. Potential therapeutic applications relate to the administration of pharmaceutical compositions of the receptor to treat patients infected with the pathogen and as an immunization to prevent infection.

Inventors:
V Ginsburg
HC Krivan
DD Roberts (NIDDK)

Patent Status:
DHHS Reference No. E-127-1988
U.S. Patent 5,529,904 issued 25 Jun 1996

Related Technologies: U.S. Patent No. 5,225,330 issued 06 Jul 1993 U.S. Patent No. 5,242,800 issued 07 Sep 1993 U.S. Patent No. 5,217,715 issued 08 Jun 1993 U.S. Patent No. 5,389,521 issued 14 Feb 1995 U.S. Patent No. 5,386,027 issued 31 Jan 1995 U.S. Patent No. 5,089,479 issued 18 Feb 1992

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Method of Diagnosing Multidrug Resistant Tuberculosis

Description of Invention:

The invention relates to the discovery that a putative gene of *Mycobacterium tuberculosis* (MTb) with no previously identified function is responsible for the ability of the bacteria to activate a class of second line thioamide drugs used for MTb infections. The gene, termed "etaA", codes for the synthesis of a monooxigenase, the enzyme responsible for the oxidative activation of the drugs. Mutation in the etaA gene leads to the expression of mutated, inactivated enzyme, thus resulting in thioamide drug-resistant bacteria. The significance of this discovery is that now, resistance to the class of thioamide drugs in clinical isolates can be identified in a relatively short time, eliminating the need to perform lengthy culturing procedures. The invention claims test methods for determining resistance to thioamide drugs by detecting gene mutation. These include (a) amplifying the etaA gene or a portion of it containing the mutation, with a set of primers which provide amplified product, and sequencing the amplified product to compare the sequence with a known sequence of the wild-type etaA. A difference in sequence patterns indicate mutation, (b) subjecting the amplified gene product to digestion by restriction enzymes and comparing the cleaved DNA gel pattern to the one obtained from digestion of the wild type etaA gene. A difference indicates mutation in etaA, and (c) detecting the mutations by probe hybridization techniques, where the amplified product hybridizes to a nucleic acid of known sequence under stringent conditions, and the hybridized product is detected. In addition to the above, the invention proposes other detection methods such as commonly used for SNPs. Other methods claimed in the invention are immunoassay (i.e. ELISA) for the etaA gene product or mutated versions of it, or immunoassay and chemical analysis of the drug metabolites, whereby the absence of the metabolites indicates gene mutation and impaired activating ability.

Inventors:

Clifton E. Barry III (NIAID)
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Khisimuzi Mdluli (NIAID) et al.

Patent Status:

DHHS Reference No. E-093-2000/0 --
U.S. Patent No. 6,905,822 issued 14 Jun 2005
U.S. Patent Application No. 11/058,484 filed 14 Feb 2005

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Human Monoclonal Antibodies to HIV-1 Envelope Glycoprotein gp120

Description of Invention:

The human immunodeficiency virus (HIV) is the causative agent of acquired immunodeficiency syndrome (AIDS). Drug-resistance is a critical factor contributing to the gradual loss of clinical benefit to treatments for HIV infection. Accordingly, combination therapies have further evolved to address the mutating resistance of HIV. However, there has been great concern regarding the apparent growing resistance of HIV strains to current therapies. The present invention relates to human monoclonal antibodies to type 1 human immunodeficiency virus (HIV-1) envelope glycoprotein gp120, to phage display libraries, and to diagnostic methods and pharmaceutical compositions which employ these antibodies therapeutically and prophylactically.

Inventors:

Brynmor A. Watkins and Marvin S. Reitz
Jr. (NCI)

Patent Status:

Serial No. 60/141,701 filed 30 Jun 1999

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Identification Of A Region Of The Major Surface Glycoprotein (MSG) Gene Of Human Pneumocystis carinii

Description of Invention:

Pneumocystis carinii is an important life-threatening opportunistic pathogen of immuno-compromised patients, especially for those with human immunodeficiency virus (HIV) infection and acquired immunodeficiency syndrome (AIDS). The present invention provides for methods and kits for detecting Pneumocystis carinii infection in humans. More specifically, nucleic acid amplification (for example, polymerase chain reaction (PCR) amplification) of human Pneumocystis carinii MSG-encoding genes (approximately 100 copies of which are present per genome), may provide a particularly sensitive and specific technique for the detection of Pneumocystis carinii and the diagnosis of Pneumocystis carinii pneumonia (PNP).

Inventors:

Joseph Kovacs et al. (CC)

Patent Status:

Serial No. 60/096,805 filed 17 Aug 1998 PCT/US99/18750 filed 17 Aug 1999

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Probe To Identify Enteroinvasive E. coli And Shigella Species

Description of Invention:

Standard means for detecting pathogenic organisms in food or clinical specimens rely on animals or large DNA fragments, such as the 17 kb EcoRI fragment of Boileau. These methods are expensive, time-consuming, difficult to use, and have not been able to distinguish between nonvirulent enteroinvasive E. coli and Shigella. This invention describes DNA probes for enteroinvasive E. coli and Shigella species, including the sequence of the 2.5 kb fragment (SmaII and Falkow's) on which the probe is based. The probe is more reliable, more sensitive, and less expensive than methods now in use.

Inventors:

KA Lampel
JA Jagow (FDA)

Patent Status:

Serial No. 07/266,038 filed 02 Nov 1988
U.S. Patent 5,041,372 issued 20 Aug 1991

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Chemokine Variants And Methods Of Use

Description of Invention:

This invention relates to a nucleotide and amino acid sequence of truncated RANTES (3-68) which is different from the wild type RANTES in two amino acid positions. CD26 is a leukocyte activation marker that possesses dipeptidyl peptidase IV (DPPIV) activity but whose natural substrates and immunological functions had not been previously defined. Several chemokines, including RANTES (regulated on activation, normal T expressed and secreted) are provided, which are substrates for human CD26. RANTES (3-68) retains the ability to stimulate CCR5 receptors and to inhibit the cytopathic effects of HIV-1. The invention provides methods for identifying compounds that affect DPPIV-mediated chemokine cleavage, methods for inhibiting HIV infection and treating individuals having or at risk of having HIV infection, methods for diagnosis and/or prognosis of individuals having a chemokine-associated disorder and methods for accelerating wound healing and angiogenesis, all based on the discovery of DPPIV-mediated cleavage of chemokines.

Inventors:

T Oravecz
MA Norcross (FDA)

Patent Status:

Serial No. 60/067,033 filed 01 Dec 1997 PCT/US98/25492 filed 01 Dec 1998

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Recombinant Proteins Of A Pakistani Strain Of Hepatitis E And Their Use In Diagnostic Methods And Vaccines

Description of Invention:

A strain of hepatitis E virus from Pakistan (SAR-55) implicated in an epidemic of enterically transmitted non-A, non-B hepatitis, now called hepatitis E, is disclosed. The invention relates to the expression of the whole structural region of SAR-55, designated open reading frame 2 (ORF-2), in a eukaryotic expression system. The expressed protein is capable of forming HEV virus-like particles which can serve as an antigen in diagnostic immunoassays and as an immunogen or vaccine to protect against infection by hepatitis E.

Inventors:

SA Tsarev
SU Emerson
RH Purcell (NIAID)

Patent Status:

Serial No. 08/809,523 filed 28 Jun 1997

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Stromal Cell Derived Factor-1 (SDF-1) And Method Of Use For Diagnostic And Prognostic Indicator Or AIDS Pathogenesis

Description of Invention:

Stromal cell derived factor-1 (SDF-1) is the principal ligand for CXCR4 (a 7-transmembrane G-coupled receptor) which, with CD4, provides an entry port for T-tropic HIV-1, a variety that frequently develops in AIDS patients just prior to T-lymphocyte depletion. This invention is based on the discovery of a correlation between the presence of a mutation at one nucleotide position of the 3'untranslated region of the SDF1 gene and delayed progression to AIDS and death due to HIV infection. Based on this discovery, it is the object of the present invention to provide diagnostic and therapeutic approaches to treating HIV infection by diagnosing the mutation and down regulating the CXCR4 receptor with native or synthetic SDF-1.

Inventors:

C Winkler
S O'Brien (NCI)

Patent Status:

Serial No. 60/063,832 filed 30 Oct 1997 PCT/US98/25578 filed 23 Oct 1998

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Nucleotide, Deduced Amino Acid Sequence, Isolation And Purification Of Heat-Shock Chlamydial Proteins

Description of Invention:

This invention concerns the discovery of a novel gene that encodes the HSP60 protein from Chlamydia trachomatis, referred to as HypB in the application. This immunodominant protein is a major target for Chlamydia trachomatis vaccine development and diagnostics. This gene and protein, or fragments thereof, are useful in the development of both recombinant protein and DNA based vaccines. The recombinant protein or DNA sequences also have potential for the development of diagnostic tests for C. trachomatis. The three patent properties claim different aspects of the invention. The issued patent claims monoclonal antibodies reactive against C. trachomatis HSP60 protein. Serial No. 07/841,323 claims the HSP60 protein and its use as a vaccine. Serial No. 09/071,506 claims DNA sequences, and protein fragments thereof, encoding HSP60. This DNA sequence would be useful in a DNA vaccine, alone or with the MOMP DNA sequences claimed in Serial No. 07/853,359. No foreign patent rights exist.

Inventors:

RB Morrison
HD Caldwell (NIAID)

Patent Status:

Serial No. 07/531,317 filed 31 May 1990
U.S. Patent 5,071,962 issued 10 Dec 1991

Serial No. 07/841,323 filed 25 Feb 1992 (divisional of 07/531,317)

Serial No. 09/071,506 filed 01 May 1998 (divisional of 07/841,323)

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Nucleotide And Amino Acid Sequences Of The Four Variable Domains Of The Major Outer Membrane Proteins Of Chlamydia Trachomatis

Description of Invention:

Chlamydia trachomatis is the leading sexually transmitted infectious agent in the United States, causing about 10 million new cases per year. It is a major cause of involuntary infertility in women. This invention claims the DNA sequences, and their encoded amino acid sequences, of the four variable domains from the major outer membrane protein (MOMP) of Chlamydia trachomatis, from the serovars Ba, D, E, F, G, H, I, J, K and L3. Serovars D, E, F, G, H, I, J, and K are the most common serovars associated with Chlamydia trachomatis caused sexually transmitted diseases. The claimed variable domains of MOMP contain the major antigen targets of protective immunity including neutralizing antibodies capable of preventing chlamydial infection. Thus, these sequences are useful for the development of recombinant protein, peptide, and DNA based vaccines against C. trachomatis caused sexually transmitted diseases. The variable domains also represent the primary serotyping antigenic determinants of C. trachomatis organisms making these variable domain sequences potential useful targets for the development of DNA or antibody based diagnostic assays for C. trachomatis. The invention is described further in Ying et al., Infection & Immunity 57, 1040-1049, 1989. Zhang et al., J. Infect. Dis. 176, 1035 - 1040, 1997 describes DNA vaccines utilizing MOMP DNA.

Inventors:

H Caldwell et al. (NIAID)

Patent Status:

Serial No. 07/853,359 filed 16 Mar 1992 (with priority to 17 Mar 1989)
U.S. Patent 5,869,608 issued 09 Feb 1999

Serial No. 09/247,137 filed 09 Feb 1999

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Delayed Progression To AIDS By A Missense Allele Of The CCR2 Gene

Description of Invention:

A specific variant of chemokine receptor CCR2, which appears to be a co-receptor for HIV-1, has been identified. This variant, CCR2-64I, is associated with delayed progression to AIDS in individuals infected with HIV-1, and is the result of a conservative amino acid substitution within the first transmembrane receptor region of CCR2. CCR2-64I is independent of but additive with CCR5-d32, an allele of chemokine receptor CCR5 which is also associated with delayed progression to AIDS. Together, these two polymorphisms are present in nearly 40% of individuals in all ethnic groups; CCR2-64I alone occurs at an allele frequency of 10 - 29% in all ethnic groups. Polynucleotides and polypeptides are provided by the invention. Therapeutic approaches and pharmaceutical compositions are claimed, as are research uses, diagnostic uses, and screening methods.

Inventors:

M Dean
SJ O'Brien
M Carrington
MW Smith (NCI)

Patent Status:

Serial No. 60/055,569 filed 14 Aug 1997
Serial No. 09/131,827 filed 10 Aug 1998 PCT/US98/16523

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Versatile Reagent For Detecting Murine Leukemia Viruses

Description of Invention:

Monoclonal antibodies directed at the proteins of murine leukemia viruses (MuLVs) have some value as immunological reagents, but differ greatly in their applicability. The kit described in this invention uses a monoclonal antibody designated 83A25, which identifies almost all ecotropic, xenotropic, polytropic, and amphotropic MuLVs. It can be used in a wide variety of procedures, including focal immunofluorescence assays on live or fixed monolayers, immunoblotting, immunoprecipitation, immunohistochemical, and flow cytometric procedures. This kit overcomes some of the problems associated with prior methods, which may not efficiently precipitate proteins or react in immunoblots, are not capable of detecting MuLVs belonging to all classes with a single reagent, and may not efficiently neutralize all MuLVs.

Inventors:

LH Evans
WJ Britt (NIAID)

Patent Status:

Serial No. 08/046,352 filed 08 Apr 1993

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Antigenic Protein Of Borrelia Burgdorferi

Description of Invention:

This patent application describes a 39 kDa protein (P39) that is species-specific and expressed by all North American and European B. burgdorferi isolates. The discovery includes the cloning and expression of the gene for P39 in E. coli and the use of P39 as a diagnostic antigen for the serodiagnosis of Lyme borreliosis. The P39 described in this invention report has been found not only to be species-specific, but reactive only with human Lyme borreliosis sera. This suggests that any patient's serum that is shown to react to P39, irrespective of the patient's clinical picture, can be diagnosed as having or having had Lyme borreliosis**.**

Inventors:

WJ Simpson
TG Schwan (NIAID)

Patent Status:

Serial No. 08/020,245 filed 19 Feb 1993
U.S. Patent 5,470,712 issued 28 Nov 1995

Serial No. 08/396,957 filed 01 Mar 1995
U.S. Patent 5,780,041 issued 14 Jul 1998

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Parvovirus B19 Receptor And Parvovirus B19 Detection

Description of Invention:

The claimed invention provides a method of detecting the presence of a parvovirus in a sample. Parvoviruses infect animals and man. In man, the only known pathogenic member of this family is parvovirus B19. The inventors have identified the parvovirus B19 receptor which provides for a method to diagnose, prevent, and treat parvovirus infection utilizing the binding affinity for the receptor.

Inventors:

N Young
K Brown (NHLBI)

Patent Status:

Serial No. 08/034,132 filed 22 Mar 1993
U.S. Patent 5,449,608 issued 12 Sep 1995

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Monoclonal and Polyclonal Antibodies to 14-3-3 Proteins

Description of Invention:
The inventions are biological materials that can be used to detect 14-3-3 proteins in biological samples. One (E-054-1997) is a monoclonal antibody produced from partially-purified proteins of sheep pineal gland. It is specific for the 33 kD isoform of 14-3-3 and is designated **8C3**.

The other invention (E-055-1997) is a polyclonal antibody raised in rabbits using a synthetic peptide corresponding to a sequence conserved among 14-3-3 proteins. It reacts with both the 33 kD and 30 kD isoforms of 14-3-3 and is designated **274A**.

Potential Area of Application:

- Development of assays for Bovine Spongiform Encephalopathy (BSE) and Creutzfeldt Jakob Disease (CJD).
- In basic research studies of prion diseases.

Main Advantage of Invention:

- Antibodies are well-characterized and immediately available for use.

Inventors:
E-054-1997 -- M. Namboodiri
D. Klein
P. Roseboom
and J. Moffett (NICHD)
E-055-1997 -- P. Roseboom
D. Klein
F. Thomas
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Patent Status:
DHHS Reference No. E-054-1997/0 -- Research Material
DHHS Reference No. E-055-1997/0 -- Research Material

Relevant Publication: P. Roseboom, J. Weller, T. Babila, A. Aitken, L. Sellers, J. Moffett, M. Namboodiri and D. Klein, "Cloning and Characterization of the epsilon and zeta Isoforms of the 14-3-3 Proteins," DNA and Cell Biology 1994 June 13(6):629-640.

Licensing Status: Available for non-exclusive licensing

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Human B Lymphotropic Virus (HBLV) Isolation And Products

Description of Invention:

This invention concerns the isolation of a new human virus, originally called Human B Lymphotropic Virus (HBLV), now known as Human Herpes Virus Type 6 (HHV-6). HHV-6 causes the common childhood disease roseola. It has been linked to other diseases in persons in an immune deficient state, including those who are HIV infected. Recently it has been linked to multiple sclerosis. The claims cover the virus itself, nucleic acid sequences from the virus and proteins they encode, cell cultures infected with the virus, and detection of the virus by DNA hybridization and immunoassay means. The application was foreign filed, PCT/US87/01815, and has been granted in Europe.

Inventors:

SZ Salahuddin
DV Ablashi
SF Josephs
WC Saxinger
F Wong-Staal
RC Gallo (NCI)

Patent Status:

Serial No. 08/392,674 filed 22 Feb 1995
U.S. Patent 5,604,093 issued 18 Feb 1997

Serial No. 08/774,118 filed 23 Dec 1996
U.S. Patent 6,054,283 issued 25 Apr 2000

Serial No. 09/000,854 filed 30 Dec 1997
U.S. Patent 6,018,027 issued 25 Jan 2000

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Nucleotide And Deduced Amino Acid Sequences Of The Envelope-1 And Core Genes Of Isolates Of Hepatitis C Virus And Methods Of Use

Description of Invention:
This invention describes the complete nucleotide and deduced amino acid sequences of the envelope-1 (E1) and core genes of hepatitis C virus (HCV) isolates from around the world and the grouping of these isolates into fourteen distinct HCV genotypes. Specifically the invention relates to oligonucleotides, peptides, and recombinant proteins derived from the envelope-1 and core gene sequences of the HCV isolates and to diagnostic methods and vaccines which employ these reagents. Envelope polynucleotide sequences from 51 isolates and core sequences from 52 isolates were analyzed, along with their derived amino acid sequences. The invention is partially described in Proc. Natl. Acad. Sci. USA 89, 4942-4946 (1992), Proc. Natl. Acad. Sci. USA 90, 8234-8238 (1993), and Seminars in Liver Disease 15, 41-63 (1995).

Inventors:
J Bukh (NIAID)
R Miller (NIAID)
R Purcell (NIAID)

Patent Status:
U.S. Patent 5,882,852 issued 16 Mar 1999 (DHHS Reference No. E-032-1994/0-US-01)

U.S. Patent Application No. 09/084,691 filed 26 May 1998 (DHHS Reference No. E-032-1994/0-US-02)

Related Technologies: U.S. Patent 6,110,465 issued 29 Aug 2000 (DHHS Reference No. E-032-1994/1-US-01)

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Hepatitis C Virus Core Peptide For Stimulation Of Cytotoxic T Lymphocytes

Description of Invention:

The invention covers a series of peptide fragments of hepatitis C virus core protein and their use as activators of cytotoxic T lymphocytes. The peptides can be used as vaccines or components of vaccines to prevent hepatitis C. **Besides the peptide fragments, pharmaceutical compositions and methods of immunization and diagnostics are also claimed.**

Inventors:

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Patent Status:

Serial No. 08/224,973 filed 08 Apr 1994

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Production Of Complementary DNA Representing Hepatitis A Viral Sequences By Recombinant DNA Methods And Uses Therefor

Description of Invention:

A method for the production and use of single- and double-stranded (ds) cDNA representing hepatitis A virus (HAV) sequences has been discovered, including an infectious, full-length cDNA clone of wild-type HAV. Large quantitites of the novel HAV cDNA can be harvested at a relatively low cost via insertion of the cDNA molecules into a recombinant DNA vector and subsequent transformation in appropriate cells; modification of bacteria by genetic engineering permits for the production of ds HAV cDNA. The cDNA molecules hold substantial diagnostic potential because they are highly specific and very sensitive to HAV; they can also be used in the production of either HAV antigen or antibodies to HAV antigen for possible vaccine development. Currently, no vaccine is available for protection against HAV infection.

Inventors:

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SM Feinstone
RH Purcell
VR Racaniello
BM Baroudy
SU Emerson (NIAID)

Patent Status:

Serial No. 07/788,262 filed 06 Nov 1991
U.S. Patent 5,516,630 issued 14 May 1996

Serial No. 08/468,926 filed 06 Jun 1995
U.S. Patent 5,849,562 issued 15 Dec 1998

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Method For Immune Capture And Primary Isolation Of Borrelia Burgdorferi

Description of Invention:

This invention relates to novel antigens associated with Borrelia burgdorferi which are exported (or shed) in vivo and whose detection is a means of diagnosing Lyme disease. The antigens are extracellular membrane vesicles and other bioproducts including the major extracellular protein. The invention further provides antibodies, monoclonal and/or polyclonal, labeled and/or unlabeled, that react with the antigens. The invention is also directed to a method of diagnosing Lyme disease by detecting the antigens in a biological sample taken from a host using the antibodies in conventional immunoassay formats. The invention further relates to kits, for the diagnosis of Lyme disease, comprising the antibodies and ancillary reagents. The advantage of the antibodies used in the invention is that they react with the antigens from geographically diverse strains of Borrelia burgdorferi, but do not react with antigens from related Borrelia spirochetes.

Inventors:

DW Dorward
TG Schwan
CF Garon (NIAID)

Patent Status:

Serial No. 07/929,172 filed 11 Aug 1992
U.S. Patent 5,403,718 issued 04 Apr 1995

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Screening Test for Reverse Transcriptase Containing Virus such as Non-A, Non-B Hepatitis, NANBH

Description of Invention:

The invention covers a screening test for detecting the presence of contaminating or infectious agents causing non-A, non-B hepatitis or AIDS in a blood donor setting. A kit for detecting contaminating agents belongs to retrovirus is also disclosed. Screening blood or blood related products so as to prevent spreading of infection or contamination due to retroviruses is now possible by the present invention.

Inventors:

BP Seto
RJ Gerety
WG Coleman (FDA)

Patent Status:

Serial No. 06/665,400 filed 26 Oct 1984
U.S. Patent 4,707,439 issued 17 Nov 1987

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Specific And Sensitive Diagnostic Test For Lyme Disease

Description of Invention:

This patent application describes species-specific DNA sequences in the pathogenic bacterium Borrelia burgdorferi. It includes the use of these sequences, other related sequences obtained from the bacteria, and similar DNA sequences generated by recombinant techniques, as DNA probes for the identification of B. burgdorferi. The target sequences have been found in multiple locations and are associated with plasmid molecules. Thus, the natural amplification of these target sequences may create a sensitivity advantage over other single-site DNA probe targets.

Inventors:

WJ Simpson
T Schwan
C Garon (NIAID)

Patent Status:

Serial No. 08/173,718 filed 27 Dec 1993
U.S. Patent 5,489,511 issued 06 Feb 1996

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Self-Assembling Recombinant Papillomavirus Capsid Proteins

Description of Invention:
This invention is an enzyme-linked immunosorbent assay (ELISA) to detect humoral immunity response to papillomavirus infection in humans and other vertebrates. Assays have thus far been produced based upon serum immunoglobulin recognition of conformational epitopes of papillomavirus virion proteins on purified virus-like particles for HPV16, which is the HPV type most frequently found in cervical cancer. Assays for other high-risk cervical cancer HPV types (HPV18, HPV31, and HPV45) and for low-risk genital HPV types (HPV6 and HPV11) are under development using the same technology. The ELISA test for the genital HPV types may be useful as an adjunct to the Papanicolaou (PAP) test for identifying women with an increased risk of developing cervical cancer.

Inventors:
Douglas R. Lowy (NCI)
John T. Schiller (NCI)
Reinhard Kirnbauer (NCI)

Patent Status:
U.S. Patent 5,437,951 issued 01 Aug 1995 (DHHS Reference No. E-253-1993/0-US-01)
U.S. Patent 5,756,284 issued 26 May 1998 (DHHS Reference No. E-253-1993/0-US-02)
U.S. Patent 5,709,996 issued 20 Jan 1998 (DHHS Reference No. E-253-1993/0-US-03)
U.S. Patent 5,871,998 issued 16 Feb 1999 (DHHS Reference No. E-253-1993/0-US-04)
U.S. Patent 5,744,142 issued 28 Apr 1998 (DHHS Reference No. E-253-1993/0-US-05)
U.S. Patent 5,716,620 issued 10 Feb 1998 (DHHS Reference No. E-253-1993/0-US-06)
U.S. Patent 5,985,610 issued 16 Nov 1999 (DHHS Reference No. E-253-1993/0-US-07)
U.S. Patent Application No. 09/316,487 filed 21 May 1999 (DHHS Reference No. E-253-1993/0-US-08)
U.S. Patent Application No. 10/371,846 filed 21 Feb 2003 (DHHS Reference No. E-253-1993/0-US-10)

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Microarray for Detection and Subtyping of Human Influenza Viruses

Description of Invention:

Available for licensing and commercial development are a novel influenza virus microarray and methods for using the microarray for the identification of existing and new types and subtypes of human influenza viruses. There are three types of influenza viruses, type A, B and C. Influenza types A or B viruses cause epidemics of disease almost every winter, with type A causes major pandemic periodically. Influenza type A viruses are further divided into subtypes based on two proteins on the surface of the virus. These proteins are called hemagglutinin (H) and neuraminidase (N). There are 16 known HA subtypes and 9 known NA subtypes of influenza A viruses. Each subtype may have different combination of H and N proteins. Although there are only three known A subtypes of influenza viruses (H1N1, H1N2, and H3N2) currently circulating among humans, many other different strains are circulating among birds and other animals and these viruses do spread to humans occasionally. There is a requirement for sensitive and rapid diagnostic techniques in order to improve both the diagnosis of infections and the quality of surveillance systems. This microarray platform tiles the genomes of all types/subtypes of influenza viruses, and is capable of correctly identifying all 3 types/subtypes of influenza viruses from an influenza vaccine sample.

More specifically, the invention consists of: 1) microarrays comprising a solid support with a plurality of n-mer influenza viral nucleotide segments of influenza Types A, B and C, including each respective subtypes, and 2) methods of detecting and identifying known and unknown influenza viral types and subtypes by: a) using hybridization microarrays to known influenza viral nucleotide sequences, b) sequencing the nucleotides which hybridize to the microarrays and c) analyzing the hybridized sequences using existing databases, thus identifying existing or new subtypes of influenza viruses.

Applications:

- Detection and identification of human influenza viruses
- Efficient discovery of new subtypes of influenza viruses
- Diagnosis of influenza outbreaks

Development Status:

This microarray platform was capable of correctly identifying all 3 types/subtypes of influenza viruses from an influenza vaccine sample.

Inventors:

Xiaolin Wu (NCI)
Cassio S. Baptista (NCI)
Elizabeth Shannon (NCI)
David J. Munroe (NCI)

Patent Status:

DHHS Reference No. E-208-2006/0 --

U.S. Provisional Application No. 60/857,695 filed 07 Nov 2006

Licensing Status:
Available for non-exclusive or exclusive licensing.

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Oligo Microarray for Detection of All Known Mammalian and Avian Pathogenic Viruses

Description of Invention:

The spectrum of pathogenic viruses of importance in human disease, agriculture and biology is not only large and diverse, but continually evolving. The identification or isolation of viral pathogens, in correlation with the presence of specific disease phenotypes, is of paramount importance both to diagnosis of disease and the subsequent management or treatment of viral infection. The limitations of current viral detection methods, such as PCR and immunoassays, led to the development of a novel microarray system for specific detection of viruses. The technology offered here for licensing provides a method for high-throughput screening of known pathogenic viruses along with identification of "new" disease-associated viruses.

The novel method is based on a viral microarray containing 10,000 immobilized DNA oligonucleotide features, representing all known mammalian and avian pathogenic viruses (approximately 600). Software was also developed to analyze the viral microarray results. The oligonucleotide features in this system are 60-mer long and distributed across both conserved and non-conserved regions of known viral sequences. This design serves the dual purpose of: (1) facilitating validation via redundant signals associated with each represented virus and (2) allowing for the discovery of new viruses, which arise due to recombination. In addition, positive and negative controls against human and mouse housekeeping genes are included along with software for analysis of virus microarray results.

Further advantages of the viral microarray include: (a) the use of sample inputs as little as 10ng of either total DNA or RNA extracted from virus infected cells, representing as few as 20 viral particles; (b) detection of viruses of both DNA and RNA classes; (c) a capacity for high-throughput screening of various sample types including serum, saliva and biopsy tissues; and (d) analysis of a large number of samples in parallel on identical arrays.

The detection of viral DNA is unique to this technology, as other available technologies only detect viral genomic RNA or viral mRNA transcripts. Additionally, the viral chip was found to be highly specific and sensitive for detecting different viral genomic sequences in cell lines and multiple viral constructs co-infection in cultured cells.

Applications:

- Detection and identification of viruses that cause disease
- Efficient discovery of new pathogenic viruses
- Diagnosis of human and animal disease outbreaks
- Identification of viral agents used in bioterrorism.

Development Status:

- The pre-clinical performance of the viral microarray was evaluated by application of four virally positive infected cell lines (JSC-1-harboring EBV and KSHV, BCBL-1 harboring KSHV, HeLa- harboring HPV18, Cem X 174 harboring SIV).
- Clinical performance was tested and validated through analysis of total RNA from cold (swab), Japanese Encephalitis, Dengue, Ebola and West Nile virus samples.

Inventors:
Cassio S. Baptista (NCI)
Xiaolin Wu (NCI)
David J. Munroe (NCI)

Patent Status:
DHHS Reference No. E-206-2006/0 --
U.S. Provisional Application No 60/797,334 filed 02 May 2006

Licensing Status:
Available for non-exclusive or exclusive licensing.

Collaborative Research Opportunity:
The NCI-Laboratory of Molecular Technology is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize this oligo microarray for identification and detection of all known mammalian and avian pathogenic viruses. Please contact Betty Tong, Ph.D. at 301-594-4263 or tongb@mail.nih.gov for more information.

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A Novel Amplification Method Permits Pathogens to be Detected with Microarrays

Description of Invention:

Available for licensing and commercial development is a high throughput, microarray-based multiplex method of detecting target nucleic acids in a sample. In particular, PCR is coupled with microarrays for the qualitative identification of multiple target nucleic acids, with primers specific for a target sequence, and used to detect genomic nucleic acids of pathogens of interest, or transcripts derived therefrom. Also claimed are oligonucleotide microarrays for use in such methods.

The present method is distinguished from other multiplex PCR assays by the additional steps to ensure specificity and sensitivity, so that a larger number of probes can be detected simultaneously in each single reaction. An important application of this method, for which it was developed, is the detection of multiple "Category A List" agents for the purpose of differential diagnosis in case of bioterrorism attacks. The method comprises: a) screening the genomes of the desired infectious agents to find sequences specific for each of them and distinct from human sequences; b) designing 60 base long oligonucleotide targets, to print on microarrays; and c) including in the microarrays both sense and antisense versions of each, as well multiple targets per virus, to increase reliability.

Other methods, such as PCR amplification followed by separation and characterization of DNA products by gel electrophoresis, are simple and sensitive, but they have a number of inherent shortcomings. Highly sensitive PCR amplification tends to generate nonspecific DNA products, which complicate interpretation of the results. Additionally, in a typical method for detecting pathogens in a sample, PCR reactions for each pathogen must be run separately from one another due to differences in amplification conditions. Furthermore, in cases where multiplex PCR coupled with a microarray is used for the qualitative detection of several pathogens, the generation of nonspecific DNA products can be a significant problem. The current method is a rapid, high-throughput method for qualitative identification of multiple target nucleic acids that is sensitive, highly discriminating and robust.

Inventors:

Michael J. Brownstein (NIMH)
Charles Xiang (NIMH)
and Zhi-Qing Qi (NIMH)

Patent Status:

DHHS Reference No. E-184-2004/0-US-01 -- U.S. Provisional Application No. 60/635,239 filed 09 Dec 2004

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Detection and Identification of Mycobacterium Using SecA

Description of Invention:

This invention relates to a method of detecting a wide variety of Mycobacterium and Nocardia species in a sample. The method involves hybridizing an amplified Mycobacterium/Nocardia genus-specific secA nucleic acid to a Mycobacterium/Nocardia species-specific secA probe oligonucleotide, wherein the amplification utilizes at least two Mycobacterium/Nocardia genus-specific primers, and detecting hybridization of the Mycobacterium/Nocardia–specific secA nucleic acid. The Mycobacterium/Nocardia genus-specific primers bind within a conserved region of the nucleic acid sequence encoding a Mycobacterium/Nocardia bi-genus-specific secA protein, wherein the conserved region is in the 5' half of the Mycobacterium/Nocardia secA gene and includes a substrate specificity domain.

The approach for detection of Mycobacterium/Nocardia species in clinical materials could potentially be used as a universal system for detection of any member of the genus Mycobacterium and the genus Nocardia and identification at the species or complex level. The system currently identifies all mycobacteria tested to date. With a few modifications, we believe it will also detect all Nocardia species of clinical significance. Contrary to commercial methods based on 16S rRNA and ITS, the SecA method will detect both Mycobacterium and Nocardia species. The region targeted has sufficient sequence variation for discrimination at the species or complex level.

Based on the information available to date, the SecA approach could be potentially used to replace acid-fast smears (AFB) and modified acid-fast smears, could provide definitive detection and identification of a large variety of Mycobacterium and Nocardia species present in clinical materials, and could be used as a single confirmation and species identification system for suspected positive Mycobacterium or Nocardia cultures. The invention also contemplates devices, including arrays, and kits for detecting Mycobacterium or Nocardia species in a sample.

This technology is related to Dr. Fischer's other technology, E-278-1999/0, "Multiplex Hybridization System for the Identification of Pathogenic Mycobacterium and Method of Use" (published in the Federal Register on September 7, 2002, 65 FR 54288). The distinguishing feature in the current invention that makes it a vast improvement over E-278-1999/0 is the ability to detect all 29 Mycobacterium species tested to date and potentially all Nocardia species in a clinical sample.

Inventors:

Steven H. Fischer and Adrian M. Zelazny (CC)

Patent Status:

DHHS Reference No. E-238-2003/0 --
U.S. Provisional Application No. 60/548,371 filed 27 Feb 2004
PCT Application No. PCT/US05/06609 filed 28 Feb 2005

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CENTRAL NERVOUS SYSTEM

Latrophilin 3, a Gene Involved in Attention Deficit Hyperactivity Disorder

Description of Invention:
Attention Deficit Hyperactivity Disorder (ADHD) is the most common behavioral disorder in childhood, and is estimated to affect three to five percent of people in the United States, both children and adults. Treatment typically involves a combination of behavior modification, educational interventions, and medication. There are a variety of medications available for treatment of ADHD; the most frequently prescribed drugs are stimulants or antidepressants. However, currently there is no way to tell in advance which medication will be most helpful for a particular individual.

The inventors have identified haplotypes of latrophilin 3 (LPHN3) that increase susceptibility for development of ADHD. LPHN3 is a G-protein coupled receptor that is specifically expressed in the brain's mesolimbic system, which is associated with ADHD. The invention describes methods of identifying LPHN3 haplotypes in an individual for determining susceptibility for development of ADHD. Identification of LPHN3 haplotypes in an ADHD-affected individual may also make possible individualized drug treatment plans.

Applications:

- Identify individuals with enhanced susceptibility for ADHD
- Use LPHN3 haplotype information to design individualized treatments

Inventors:
Maximillian Muenke (NHGRI)
Mauricio Arcos-Burgos (NHGRI)
F. Xavier Castellanos (NIMH)

Patent Status:
DHHS Reference No. E-312-2006/0 --
U.S. Provisional Application No. 60/850,972 filed 11 Oct 2006

Licensing Status:
Available for exclusive or nonexclusive licensing.

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Use of Cripto-1 as a Biomarker for Neurodegenerative Disease and Method of Inhibiting Progression Thereof

Description of Invention:
Cripto-1 is a gene that is currently thought to play an important role in several cancers, and is being developed in clinical trials as a cancer therapeutic. Presented in this invention is another use of Cripto-1 as a biomarker and possible therapeutic target for a variety of neurodegenerative diseases, including NeuroAIDS, Alzheimer's disease (AD), multiple sclerosis (MS), amyotrophic lateral sclerosis (ALS), Parkinson's disease (PD) and encephalitis. Cripto-1 and concomitant protein expression appears to be overexpressed by 20-fold or more in the brains of macaque monkeys and humans afflicted with NeuroAIDS. This expression is confined to neurons related to neurodegeneration. Inhibition of Cripto-1 may be associated with inhibiting the progression of these diseases via a disclosed method for inhibiting the expression or downstream signaling pathways mediated by Cripto-1. This inhibition can be achieved through the expression of various inhibitory oligonucleotides. Additionally, the development of antibodies against Cripto-1 has already been achieved for the detection of Cripto-1 in human pathological specimens.

It is estimated that by 2050, 14 million Americans will suffer from AD, representing national annual costs for caring and due to productivity lost of approximately $160 billion. Despite active research in this area, there remains urgent need to identify differentially expressed genes in and to develop methods for detecting neurodegenerative disease through assaying expression levels of specific genes. Currently, there are no drugs directed at inhibiting Cripto-1 as a therapeutic agent for AD or other neurodegenerative diseases. This invention holds the promise of market opportunities through pursuing development of Cripto-1 as a biomarker for diagnosis of and possible target for therapeutic intervention of these diseases.

Inventors:
David S. Salomon (NCI) et al.

Patent Status:
DHHS Reference No. E-075-2003/0 --
U.S. Provisional Application No. 60/508,750 filed 03 Oct 2003
PCT Application No. PCT/US04/32649 filed 01 Oct 2004, which published as WO 2005/033341 on 14 Apr 2005

Relevant Publication:

1. CL Parish et al., "Cripto as a target for improving embryonic stem cell-based therapy in Parkinson's disease," Stem Cells 2005 Apr; 23(4):471-476. [PubMed abs.]

2. HB Adkins et al., "Antibody blockade of the Cripto CFC domain suppresses tumor cell growth in vivo," J Clin Invest. 2003 Aug 15; 112(4): 575-587 [PubMed abs.]

Licensing Status:
Available for non-exclusive or exclusive licensing.

Collaborative Research Opportunity:
The National Cancer Institute, Mammary Biology and Tumorigenesis Laboratory, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize this technology. Please contact Jeffrey Hildesheim, Ph.D. at (301) 435-1569 or hildesheimj@mail.nih.gov for more information.

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Novel Methods and Compositions for Diagnosing AIDS and Other Diseases Involving Immune System Activation

Description of Invention:

Available for licensing and commercial development are methods and compositions suitable for monitoring the progression of AIDS and other diseases whose progression involves immune system activation in mammals, such as cancer, atherosclerosis, Alzheimer's disease, inflammation, autoimmune disorder, allergic asthma, Crohn's disease, Grave's disease, lupus, multiple sclerosis, Parkinson's disease, allograft transplant rejection, and graft vs. host disease.

In particular, the invention relates to the use of the TRAIL (TNF-related apoptosis-inducing ligand) and TRAIL compounds to monitor the progression of AIDS, and such other diseases. This is accomplished by assessing the presence or concentration of TRAIL, especially mTRAIL, sTRAIL, the TRAIL DR5 receptor molecule, and biological molecules that activate TRAIL or its receptor. These biological molecules include p53, alpha- and beta-interferon, as well as additional compounds such as CD69 and HLA-DR. Also claimed are kits for immunoassays to determine the presence or concentration of a TRAIL compound in a biological fluid, suitable for determining whether the mammal suffers from any of the above diseases.

TRAIL can be used as a new surrogate biomarker to monitor the progression of HIV infection and other conditions and diseases associated with immune system activation. In the case of HIV infection, measuring levels of this biomarker can distinguish among infected individuals with high viral load, infected individuals with low viral load, and uninfected individuals. Only two surrogate markers are currently recognized by the Food and Drug Administration as clinically relevant to HIV progression, HIV viral load and the absolute number of peripheral CD4+ T cells. Tests for assessing HIV viral load employ PCR, the use of which has drawbacks, including cross-contamination. TRAIL has mechanistic implications for HIV-1 pathogenesis and directly correlates to viral load but not necessarily inversely with CD4+ T cell count. Other surrogate markers have been proposed but do not consistently reflect AIDS progression in all individuals or may result in overlooking possible treatments that may affect disease progression but do not affect the chosen marker. Therefore, use of this new biomarker to assess disease progression in infected individuals and to evaluate the effectiveness of various treatment regimens has several advantages over currently used methods, since TRAIL is a death molecule involved in CD4+ T cell depletion in HIV/AIDS. TRAIL, its receptor, and activating molecules can all be used as sensitive markers for CD4 T cell activation and apoptosis.

Inventors:

Gene M. Shearer and Jean-Philippe Herbeuval (NCI)

Patent Status:

DHHS Reference No. E-045-2004/0 --
U.S. Provisional Application No. 60/564,588 filed 23 Apr 2004

DHHS Reference No. E-045-2004/1 --
U.S. Provisional Application No. 60/634,255 filed 12 Dec 2004

DHHS Reference No. E-045-2004/2 --
PCT Application No. PCT/US2005/13554 filed 21 Apr 2005

Relevant Publication:

1. Herbeuval JP, Hardy AW, Boasso A, Anderson SA, Dolan MJ, Dy M, Shearer GM. Regulation of TNF-related apoptosis-inducing ligand on primary CD4+ T cells by HIV-1: role of type I IFN-producing plasmacytoid dendritic cells. Proc Natl Acad Sci U S A. 2005 Sep 27;102(39):13974-9.
2. Herbeuval JP, Grivel JC, Boasso A, Hardy AW, Chougnet C, Dolan MJ, Yagita H, Lifson JD, Shearer GM "CD4+ T-cell death induced by infectious and noninfectious HIV-1: role of type 1 interferon-dependent, TRAIL/DR5-mediated apoptosis" Blood. 2005 Nov 15;106(10):3524-31.
3. Herbeuval JP, Boasso A, Grivel JC, Hardy AW, Anderson SA, Dolan MJ, Chougnet C, Lifson JD, Shearer GM "TNF-related apoptosis-inducing ligand (TRAIL) in HIV-1-infected patients and its in vitro production by antigen-presenting cells" Blood. 2005 Mar 15;105(6):2458-64.

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Impaired Neuregulin1-stimulated B Lymphoblast Migration as Diagnostic for Schizophrenia

Description of Invention:
Schizophrenia may be a neurodevelopmental disorder (Weinberger D.R. and Marenco S. in Schizophrenia as a neurodevelopmental disorder, Hirsch S., Weinberger D.R. (eds) Schizophrenia, 2nd ed., Blackwell Science: Oxford, UK, 2003 pp 326-348). Neuregulin1 (NRG1) plays a critical role in neuronal migration and maturation by interacting with ErbB tyrosine kinase receptors and linkage studies and genetically engineered animals have implicated NRG1-mediated signaling in the neuropathogenesis of schizophrenia. Although no technique is available to assess NRG1/ErbB mediated neural migration in living human brain, there is increasing recognition that neuronal cells and immune cells share many cellular and molecular mechanisms for cell migration and motility. These inventors showed NRG1 mediated chemotactic responses of B lymphocytes from schizophrenic patients are significantly decreased compared to controls. If aberrant ErbB function during development is a cause of schizophrenia, and that aberrant ErbB function is expressed in peripheral blood cells throughout life, the assay should predict susceptibility to schizophrenia even before clinical symptoms are apparent.

Inventors:
Daniel Weinberger et al. (NIMH)

Patent Status:
DHHS Reference No. E-181-2005/1 --
U.S. Provisional Application No. 60/735,353 filed 10 Nov 2005

Licensing Status:
Available for non-exclusive or exclusive licensing.

In addition, the NIMH Clinical Brain Disorders Branch is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize the above technology. Please contact Suzanne L. Winfield at winfiels@mail.nih.gov for more information.

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Genes For Niemann-Pick Type C Disease

Description of Invention:
Niemann-Pick disease is a class of inherited lipid storage diseases. Niemann-Pick Type C disease is an autosomal recessive neurovisceral lipid storage disorder which leads to systemic and neurological abnormalities including ataxia, seizures, and loss of speech. Patients with the disease typically die as children. The biochemical hallmark of Niemann-Pick Type C cells is the abnormal accumulation of unesterified cholesterol in lysosomes, which results in the delayed homeostatic regulation of both uptake and esterification of low density lipoprotein (LDL) cholesterol. Niemann-Pick Type C is characterized by phenotypic variability. The disease appears at random in families that have no history of the disorder, making diagnosis problematic. This invention provides the human gene for Niemann-Pick Type C disease and the nucleic acid sequences corresponding to the human gene for Niemann-Pick Type C disease. Also provided is the mouse homolog of the human gene. The invention could lead to improved diagnosis and the design of therapies for the disease and improved means of detection of carriers of the gene. In addition, this invention may contribute to the understanding and development of treatments for atherosclerosis, a more common disorder associated with cholesterol buildup that involves the accumulation of fatty tissue inside arteries that blocks blood flow, leading to heart disease and stroke. The invention may also lead to additional discoveries concerning how cholesterol is processed in the body.

Inventors:
Eugene D. Carstea (NINDS) et al.

Patent Status:
DHHS Reference No. E-122-1997/0 --
U.S. Patent No. 6,426,198 issued 30 Jul 2002
U.S. Patent No. 7,045,675 issued 16 May 2006

Relevant Publication:

3. S.K. Loftus et al., "Murine model of Niemann-Pick C disease: Mutation in a cholesterol homeostasis gene," Science 277(5323):232-235, 1997.
4. S.K. Loftus et al., "Rescue of neurodegeneration in Niemann Pick-C mice by a prion-promoter driven Npc1 cDNA transgene," Human Molec. Genet. 11(24):3107-14, 2002.

Licensing Status:
Licensees sought.

Also, the NHGRI Genetic Disease Research Branch is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize Niemann-Pick Type C disease diagnostics and therapies as well as potential applications of the Niemann-Pick Type C gene related to atherosclerosis and cholesterol processing. Please contact Claire T. Driscoll for more information (telephone:

301/594-2235; email: cdriscol@mail.nih.gov).

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Methods of Diagnosing and Treating Schizophrenia

Description of Invention:
Neurotrophins promote survival of neurons from both the central nervous system and peripheral nervous system in cell culture. More recently it has been shown that neurotrophins may serve as a new class of neuromodulators that mediate activity-dependent modifications of neuronal connectivity and synaptic efficacy. Brain derived neurotrophic factor (BDNF) is a neurotrophin that mediates LTP and hippocampus-related spatial memory. Schizophrenia and other mental disorders appear to involve deficits in verbal memory and reduced hippocampal-acetyl aspartate (NAA), a measure of hippocampal neuronal integrity. BDNF may thus play a role in memory function and human diseases of the hippocampus such as schizophrenia.

The human BDNF gene contains one known non-conservative SNP, producing a met66val substitution. The invention is related to the discovery that a met66val polymorphism in the gene for BDNF is correlated with verbal memory and risk for schizophrenia. The invention provides methods and kits for diagnosing and modulating verbal memory and risk for schizophrenia in an individual by determining the individual's BDNF genotype, and associating a met allele with impaired verbal memory and risk for schizophrenia and a val allele with enhanced verbal memory and protection from schizophrenia. The invention also provides methods of finding and using compounds which modulate BDNF function in order to treat human diseases of the hippocampus such as memory disorders and schizophrenia.

Inventors:
Daniel R. Weinberger et al. (NIMH)

Patent Status:
DHHS Reference No. E-247-2001/0 --
U.S. Provisional Application No. 60/316,736 filed 31 Aug 2001
PCT Application No. PCT/US02/28086 filed 30 Aug 2002, which published as WO 03/018847 on 06 Mar 2003
U.S. Patent Application No. 10/789,169 filed 27 Feb 2004

Relevant Publication: MF Egan et al., "The BDNF val66met polymorphism affects activity-dependent secretion of BDNF and human memory and hippocampal function," Cell 2003 Jan 24;112(2):257-269.

AR Hariri et al., "Brain-derived neurotrophic factor val66met polymorphism affects human memory-related hippocampal activity and predicts memory performance," J. Neurosci. 2003 Jul 30;23(17):6690-6694.

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Effect of COMT Genotype on Frontal Lobe Function

Description of Invention:

Abnormalities of prefrontal cortical function are prominent features of schizophrenia and have been associated with genetic risk, suggesting that susceptibility genes for schizophrenia may impact on the molecular mechanisms of prefrontal function. A potential susceptibility mechanism involves regulation of prefrontal dopamine, which modulates the response of prefrontal neurons during working memory. The Catechol-o-methyltranferase (COMT) gene contains a G to A mutation which causes a substitution of methionine for valine at codon 158. The met allele has a four fold reduction in enzyme activity which leads to an increase in prefrontal cortical dopamine levels. NIH investigators observed that the functional polymorphism in the gene encoding COMT is associated with variations in executive function and efficiency of working memory in normal controls and schizophrenic patients.

The invention provides a method of detecting impaired prefrontal cognitive function in a subject individual comprising determining the individual's COMT genotype and associating a high activity val allele with impaired prefrontal cognitive function and a low activity met allele with enhanced prefrontal cognitive function. The COMT genotype can be determined using a relatively simple restriction fragment length polymorphism analysis after PCR amplification of the polymorphic region of exon four since the met substitution introduces an NlaIII restriction site into the allele. Clinical medical tests to determine prognosis in schizophrenia and other conditions associated with the polymorphism would thus be possible. The invention also provides for treating patients with COMT inhibitors after tests that predict the response of a patient with schizophrenia, other neurological disorders or aging related declines in cognition to administration of a COMT inhibitor.

Inventors:

Daniel R. Weinberger (NIMH)
Michael F. Egan (NIMH)
Terry E. Goldberg (NIMH)
David Goldman (NIAAA)
Joseph H. Callicott (NIMH)

Patent Status:

DHHS Reference No. E-174-2000/0 --
U.S. Provisional Application No. 60/290,565 filed 11 May 2001
U.S. Patent Application No. 10/144,000 filed 10 May 2002
U.S. Patent Application No. 11/395,043 filed 31 Mar 2006

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Polymorphic Human $GABA_A$ Receptor α-6 Subunit

Description of Invention:

Gamma-aminobutyric acid (GABA) is a key inhibitory neurotransmitter in the mammalian central nervous system. Evidence indicates that GABA receptors are associated with various neuropsychiatric disorders. Currently, there are no reliable and sensitive markers on the market for the molecular diagnosis of alcoholism or anxiety disorders, although both groups of disorders are thought to involve GABA function. Alcohol modulates GABA function and shows cross-tolerance with benzodiazepines. Anxiety disorders are treated with benzodiazepines. Also, there are no molecular predictors of interindividual variation in response to the commonly used benzodiazepine drugs (such as valium) which act through $GABA_A$ receptors. The -6 subunit of $GABA_A$ receptors is sensitive to alcohol and in a rat genetic model a genetic variant of the -6 subunit had been directly related to sensitivity to alcohol and benzodiazepine drugs. This invention pertains to a particular polymorphism in the human -6 subunit gene. This relatively common human sequence variant predicts sensitivity to both benzodiazepine drugs and ethanol. In children of alcoholics this substitution also correlates with susceptibility to alcoholism. Thus, this invention presents commercial opportunities both as a diagnostic screening tool in alcoholism, anxiety disorders and other neuropsychiatric diseases, and as a predictive tool for therapeutic and pathological responses to commonly administered benzodiazepine drugs.

Inventors:

David Goldman (NIAAA)
Nakao Iwata (NIAAA)
Mark Shuckit

Patent Status:

DHHS Reference No. E-061-1998/0 --
U.S. Patent No. 6,762,294 issued 13 Jul 2004

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Cloning Of A Gene Mutation For Parkinson's Disease

Description of Invention:

Parkinson's Disease (PD) affects between 500,000 to one million persons in the United States alone. The disease is most common in persons over the age of 70. However, one form of PD appears to be hereditary and is probably responsible for early on-set PD, wherein the symptoms occur before the age of 60. The newly discovered gene mutation appears to be linked to the early on-set form of PD. The mutation, a threonine for alanine substitution, at amino acid position 53 of the human alpha-synuclein protein effects the secondary structure of the protein and causes an aggregation of Lewy bodies in the brain. This new mutation is considered to be a valuable tool in predicting a person's susceptibility to early on-set PD. Assays developed from this mutation can also be used for diagnostic purposes.

Inventors:

MH Polymeropoulos (NHGRI)
C Lavedan (NHGRI)

Patent Status:

DHHS Reference No. E-190-1997/0 --
U.S. Patent No. 7,001,720 issued 21 Feb 2006

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A Method For Imaging Nicotinic Acetylcholinergic Receptors In The Brain Using Radiolabeled Pyridyl 7-Azabicycloheptanes

Description of Invention:

The current invention embodies the use of radiolabeled analogs of epibatidine to noninvasively image and quantify levels of nicotinic acetylcholine receptors in a living mammalian brain, using Positron Emission Tomography or other nuclear medicine methods. As nicotinic acetylcholine receptors have been implicated in various neuropathological and physiological disorders, including Alzheimer's disease, the invention may represent a powerful new method for the noninvasive diagnosis of Alzheimer's disease and other disorders. In addition, the method embodied in the invention may prove valuable for use in monitoring the progression of various disorders and in determining the efficacy of drug therapy protocols used in the treatment of these disorders.

Inventors:

ED London
AS Kimes
A Horti
RF Dannals
M Kassiou (NIDA)

Patent Status:

Serial No. 08/642,636 filed 06 May 1996
U.S. Patent 5,726,189 issued 10 Mar 1998

Serial No. 08/980,606 filed 01 Dec 1997
U.S. Patent 5,969,144 issued 19 Oct 1999

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Differential Expression of Molecules Associated with Intra-Cerebral Hemorrhage

Description of Invention:
Stroke affects 15 million people worldwide each year, and is the number three leading cause of morbidity in the United States. Although most forms of stroke are ischemic in nature, approximately 10-15% of strokes are hemorrhagic. At present, clinical applications for distinguishing between these two forms of stroke do not exist.

The present invention describes a highly predictive, cost-effective diagnostic assay capable of detecting whether an individual has suffered from an intracerebral hemorrhagic stroke and the likelihood of neurological recovery. It comprises a rapid screening device for measuring differential expression patterns of nucleic acid molecules or proteins of at least four hemorrhagic stroke-related genes. Accurate prediction of hemorrhagic stroke will improve rapid diagnosis and aid in determining early treatment regimens.

Applications:

- Gene expression profile assay for determining hemorrhagic stroke victims.
- Means of differentiating between hemorrhagic stroke and ischemic stroke thereby optimizing patient response to stroke therapies.

Market:

- Annually, fifteen billion people suffer from strokes worldwide, and an estimated 700,000 individuals have first-time or recurrent strokes each year in the United States alone.
- Almost three-fourth of all strokes occur in individuals over 65 years of age.
- In 2006, the projected indirect and direct costs of stroke are $57.9 billion.

Development Status:
This technology requires clinical validation studies.

Inventors:
Alison Baird (NINDS) et al.

Patent Status:
DHHS Reference No. E-197-2006/0 --
U.S. Provisional Application No. 60/807,027 filed 11 Jul 2006

Licensing Status:
Available for non-exclusive or exclusive licensing.

Collaborative Research Opportunity:
NINDS is also seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize this assay for

determining hemorrhagic stroke victims. For additional information, please contact: Heather Gunas, J.D., M.P.H; NINDS c/o NCI TTB; 6120 Executive Blvd., Suite 450, Rockville, MD 20852; Phone: 301-451-3944; Fax: 301-402-2117; Email: gunash@mail.nih.gov

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In Vivo Non-Invasive Diagnostic Method Using Magnetic Resonance Spectroscopy of Aspartate Transaminase

Description of Invention:

This invention describes a method for non-invasively diagnosing various diseases using magnetic resonance spectroscopy of aspartate transaminase (AST). The diagnostic market is a multi-billion dollar market, with a need for more efficient non-invasive techniques, markers and methods of diagnosis.

In particular, this is a novel non-invasive method for using carbon-13 magnetization transfer effects to determine and evaluate in vivo aspartate transaminase (AST) activity and levels in an organ, including the brain, as a biomarker of disease and certain neurological disorders. This comprises performing in vivo magnetization transfer spectroscopy, and determining the change in magnetic resonance signal intensity of reactants in AST catalyzed reaction.

AST activity is known to change as a result of tissue damage and necrosis in a variety of diseases. AST activity is routinely assessed in serum of patients as a non-invasive means of identifying and following up on disease progression. Furthermore, brain levels of AST are altered in certain diseases such as Huntington's Disease, olivopontocerebellar atrophy and epilepsy, but the blood-brain barrier prevents AST from entering serum and being readily measured. Brain AST levels in living patients can be measured by brain biopsies, which are expensive and dangerous. This invention overcomes this problem by measuring AST activity in the brain by using magnetization transfer effect. This can help diagnose or follow up on the progress of a variety of diseases, including Huntington's Disease, olivopontocerebellar atrophy, epilepsy, schizophrenia, as well as hepatitis, cirrhosis, cholangitis, Gilbert's diseases, muscular dystrophy, leukemia, kidney inflammation, cardiac infarction, or the presence of a tumor. Thus, tissue AST activity may become a novel marker of brain disorders which has been inaccessible using current clinical technologies.

Applications:

Diagnosis and monitoring disease status in a variety of diseases, including Huntington's Disease, olivopontocerebellar atrophy, epilepsy, schizophrenia, as well as hepatitis, cirrhosis, cholangitis, Gilbert's diseases, muscular dystrophy, leukemia, kidney inflammation, cardiac infarction, or the presence of a tumor.

Market:

The diagnostic market is a multi-billion dollar market, with a need for more efficient non-invasive techniques, markers and new methods of diagnosis.

Inventors:

Jun Shen (NIMH)

Patent Status:

DHHS Reference No. E-231-2005/0 --

U.S. Patent Application No. 11/356,214 filed 21 Feb 2006

Relevant Publication:
J Shen. In vivo carbon-13 magnetization transfer effect: detection of aspartate aminotransferase reaction. Magn Reson Med. 2005 Dec; 54(6):1321-1326. [PubMed abs]

Licensing Status:
Available for exclusive or non-exclusive licensing.

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INTERNAL MEDICINE

Methods and Materials for Identifying Polymorphic Variants, Diagnosing Susceptibilities, and Treating Disease

Description of Invention:
This invention relates to materials and methods associated with polymorphic variants in two enzymes involved in folate-dependent and one-carbon metabolic pathways important in pregnancy-related complications and neural tube birth defects: MTHFD1 (5,10-methylenetrahydrofolate dehydrogenase, 5,10-methenyltetrahydrofolate cyclohydrolase, 10-formyltetrahydrofolate synthase) and methylenetetrahydrofolate dehydrogenase (NADP+ dependent) 1-like (MTHFD1L). These enzymes are extremely important in the promotion of DNA synthesis, a process that is critical for normal placental and fetal development.

Recently, the inventors have discovered that a MTHFD1 polymorphism is also a maternal genetic risk factor for placental abruption, premature separation of a normally implanted placenta. This polymorphism may also be a risk factor for first and second trimester miscarriages. Diagnostic and therapeutic methods are provided in this invention involving the correlation of polymorphic variants in MTHFD1 and MTHFD1L and other genes with relative susceptibility for various pregnancy-related and other complications such as cancer, cardiovascular disease, developmental anomalies and psychiatric illnesses. Both nutrient status and genetic background are independent yet interacting risk factors for impaired folate metabolism. However, the mechanisms that lead to pathology or the mechanisms whereby folate prevents these disorders are unknown. Therefore, a diagnostic and therapeutic invention of this kind would significantly improve the detection and treatment of disorders associated with folate metabolism.

Inventors:
Lawrence C. Brody (NHGRI) et al.

Patent Status:
DHHS Reference No. E-149-2005/0 --
International Application No. PCT/US2005/21288 filed 16 Jun 2005, which published as WO 2007/001259 on 04 Jan 2007

Relevant Publication:

1. A Parle-McDermott et al. MTHFD1 R653Q polymorphism is a maternal genetic risk factor for severe abruptio placentae. Am J Med Genet A. 2005 Feb 1;132(4):365-368. [PubMed abs]
2. A Parle-McDermott et al. A polymorphism in the MTHFD1 gene increases a mother's risk of having an unexplained second trimester pregnancy loss. Mol Hum Reprod. 2005 Jul;11(7):477-480. [PubMed abs]

3. A Parle-McDermott et al. Confirmation of the R653Q polymorphism of the trifunctional C1-synthase enzyme as a maternal risk for neural tube defects in the Irish population. Eur J Hum Genet. 2006 Jun;14(6):768-772. [PubMed abs]
4. B Kempisty et al. MTHFD 1958G>A and MTR 2756A>G polymorphisms are associated with bipolar disorder and schizophrenia. Psychiatr Genet. 2007 Jun;17(3):177-181. [PubMed abs]

Licensing Status:
Available for exclusive or non-exclusive licensing.

Collaborative Research Opportunity:
The National Human Genome Research Institute is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize this technology. Please contact Claire Driscoll at 301-402-2537 or cdriscol@mail.nih.gov for more information.

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Zscan4: A Gene Critical for Early Embryonic Development

Description of Invention:
Activation of transcription from the embryonic genome, known as zygotic genome activation (ZGA), marks the key switch from maternal to embryonic control of development and establishes gene expression patterns required for continued development of the embryo. Genes expressed during ZGA may be important for assisted reproductive technologies, and in stem cell research and development.

The inventors have identified Zscan4, a gene expressed solely in late 2-cell stage embryos and in embryonic stem cells. Inhibition of Zscan4 expression using siRNA techniques delays progression from the 2-cell stage to the 4-cell stage, and produces blastocysts that fail to implant in the mouse embryo. Thus, Zscan4 plays an essential role in early embryonic development, with potential applications for the development of stem cell therapeutics. The invention discloses methods of promoting blastocyst outgrowth of embryonic stem cells. Also disclosed are Zscan4 expression vectors and methods of identifying a subpopulation of stem cells expressing Zscan4.

Applications:

- Development of stem cell therapeutics
- Assisted reproduction technologies and studies of early embryonic development

Market:
State and federal funding for stem cell research is predicted to reach $10 billion by 2018.

Development Status:
Early stage

Inventors:
Minoru S. Ko et al. (NIA)

Patent Status:
DHHS Reference No. E-088-2007/0 --
U.S. Provisional Application No. 60/920,215 filed 26 Mar 2007

Relevant Publication:
Geppino Falco et al. Zscan4: A novel gene expressed exclusively in late 2-cell embryos and embryonic stem cells. Dev Biol., in press.

Licensing Status:
Available for exclusive or non-exclusive licensing.

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TMC1, a Deafness-Related Gene

Description of Invention:

Hearing loss is a common communication disorder affecting nearly 1 in 1,000 children in the United States alone, and nearly 50% of adults by the age of eighty. Hearing loss can be caused by environmental and disease-related factors; however, hearing loss due to genetic factors accounts for approximately 50% of cases.

The NIH announces the isolation of two novel genes involved in hearing; TMC1, short for transmembrane channel-like gene 1. The inventors have discovered that dominant and recessive mutations in TMC1 underlie two forms of hereditary deafness, known as DFNA36 and DFNB7/11. TMC1 encodes a protein required for normal function of the mammalian hair cell, which plays a critical role within the hearing pathway that detects sound in the inner ear.

The invention discloses TMC1 nucleic acids, vectors, and cells. Also disclosed are methods of detecting hearing loss, or a predisposition to hearing loss, due to a mutation in TMC1, as well as methods for identifying agents that interact with the TMC1 gene in a cell. Nucleic acids and methods of use for TMC2, a gene closely related to TMC1, are also disclosed.

Applications:

- Development of a genetic diagnostic test for hearing loss
- Development of pharmaceuticals to treat hearing loss

Market:

Hearing loss with a genetic component accounts for 50% of all cases of hearing loss.

Development Status:

Early stage

Inventors:

Andrew J. Griffith et al. (NIDCD)

Patent Status:

DHHS Reference No. E-168-2001/0 --
U.S. Provisional Application No. 60/323,275 filed 19 Sep 2001
PCT Application No. PCT/US02/29614 filed 19 Sep 2002, which published as WO 03/025140 on 27 Mar 2003
U.S. Patent No. 7,192,705 issued 20 Mar 2007
U.S. Patent Application No. 11/615,250 filed 22 Dec 2006
Foreign counterparts in Australia, Canada, Europe, and Japan

DHHS Reference No. E-168-2001/1 --
U.S. Patent No. 7,116,433 issued 23 Jan 2007

Foreign counterparts in Australia and Canada

Relevant Publication:
K Kurima et al. Dominant and recessive deafness caused by mutations of a novel gene, TMC1, required for cochlear hair-cell function. Nat Genet. 2002 Mar;30(3):277-284. [PubMed abs]

Licensing Status:
Available for non-exclusive licensing.

Collaborative Research Opportunity:
The NIDCD Otolaryngology Branch is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize this technology as well as collaborate on further pre-clinical and clinical studies with the TMC2 gene mutations. Please contact Ms. Marianne Lynch at 301-402-5579 or via email at lynchm@nhlbi.nih.gov for more information.

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Neural Crest-Melanocyte cDNA Based Microarray Analysis for Human Skin Pigmentation Research

Description of Invention:

Microarrays have wide applications in basic research and are used for the discovery of candidate genes as markers for disease and for therapeutic intervention. This invention pertains to the identification of a set of neural crest-melanocyte (NC-M) genes through microarray analysis and informatic analysis. Utilizing the extensive sequence information in the expressed sequence tag database (dbEST), the specific set of cDNA sequence was identified for microarray analysis of melanocyte function and diseases. This integrated technique of sequencing with bioinformatics led to the discovery of novel genes. The cDNA sequences selected in this invention are differently expressed in neural crest melanocyte derivates relative to non-neural derived samples. Given that many of the neural-crest melanocyte genes are expressed at embryonic stages of neural crest-melanocyte development, the gene set identified in this invention should provide a useful tool for the analysis of patterns of transcriptional regulation of NC-M development**.** Thus, this technology will be useful for the characterization of altered expression patterns in diseases such as melanoma. Further, this new microarray research tool has been developed using the set of genes that are likely to be involved in the control of human skin pigmentation. The microarray system utilizing these genes is of significant importance in identifying small molecules that may modulate their activity leading to alterations in human skin pigmentation. Therefore, this invention is significantly useful to the researchers to study alterations in human skin pigment amount and type.

Inventors:

William Pavan and Stacie K. Loftus (NHGRI)

Patent Status:

DHHS Reference No. E-014-2002/0 -- Research Tool

Licensing Status:

Available for licensing under a Biological Materials License.

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Method for Promoting Stem Cell Proliferation and Survival

Description of Invention:

This technology describes a method to promote stem cell survival and proliferation by manipulating the phosphorylation state of Stat3 protein. This method has been shown to enhance survival and proliferation in stem cell cultures in vitro, and also in neuronal precursor cells in vivo. The methods include use of a Notch ligand and growth factors such as FGF-2 or insulin to promote neural stem cell survival and proliferation. The technology is also directed to a population of stem cells expressing STAT3 phosphorylated at serine 727.

Applications:

Clinical treatment for stroke and other neurodegenerative diseases by administration of agents that promote stem cell survival and proliferation.
Increased generation of stem cells *in vitro*.
Screening assays for agents that promote proliferation of stem cells or inhibit proliferation of cancer cells.
Diagnostic assay for cancer to determine the phosphorylation state of the protein in tumors.

Market:

Prognostic marker to help determine response of individuals with cancer.
Commercial suppliers or large-scale users of stem cells.
Development Status:
A method of increasing proliferation and survival of stem cells or precursor cells in vitro has been developed. The cells produced by this method have been described in an article in Nature 2006 Aug 17;442(7104):823-826.
The method of increasing proliferation and survival of stem cells is efficacious in in vivo rodent models of Parkinson's disease and stroke.

Inventors:

Andreas Androutsellis-Theotokis and Ronald D.G. McKay (NINDS)

Patent Status:

DHHS Reference No. E-239-2005/0 --
U.S. Provisional Application No. 60/715,935 filed 08 Sep 2005
PCT Application No. PCT/US2006/034988 filed 07 Sep 2006, which published as WO 2007/030693 on 15 Mar 2007

Relevant Publication:

A Androutsellis-Theotokis et al. Notch signalling regulates stem cell numbers in vitro and in vivo. Nature 2006 Aug 17;442(7104):823-826. [PubMed abs]

Licensing Status:

Available for non-exclusive or exclusive licensing.

Collaborative Research Opportunity:
The National Institute of Neurological Disorders and Stroke, Laboratory of Molecular Biology, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize agents that inhibit or induce phosphorylation of STAT3 protein and survival of stem cells and precursor cells. Please contact Martha Lubet at 301/435-3120 or lubetm@mail.nih.gov.

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Genetic Markers for Body Size in Dogs

Description of Invention:
Dogs exhibit the greatest diversity in body size of any mammalian species. To explore the genetic basis for size variation among dogs, the inventors compared the DNA of various small dog breeds to larger dog breeds. They found that variation in one gene, IGF-1, which codes for the protein hormone insulin-like growth factor 1, is very strongly associated with small stature across all dog breeds studied. An important determinant of body size in mammals, IGF-1 induces cell growth and differentiation and is a potent inhibitor of apoptosis. Analysis of DNA from over 3,000 dogs and 143 breeds revealed a specific IGF-1 gene sequence variant, or haplotype, associated with small size in the canine genetic code.

The invention discloses markers defining chromosomal haplotypes associated with adult body size in dogs. Also claimed are methods and kits for predicting adult body size in dogs using these markers. A genetic test based on this invention would be of use to breeders wishing to predict a dog's size, and thus its conformance to the breed standard, at adulthood.

Applications:
Canine genetic test to predict adult body size.

Market:
In 2006, over 1.7 million purebred dogs competed in American Kennel Club-sanctioned conformance shows in the United States.

Development Status:
Early stage

Inventors:
Elaine A. Ostrander and Nathaniel B. Sutter (NHGRI)

Patent Status:
DHHS Reference No. E-009-2007/0 --
U.S. Provisional Application No. 60/856,411 filed 02 Nov 2006

Relevant Publication:
N Sutter et al. A single IGF1 allele is a major determinant of small size in dogs. Science 2007 Apr 6;316(5821):112-115, doi: 10.1126/science.1137045. [PubMed abs]

Licensing Status:
Available for non-exclusive licensing.

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RAB38, a Target for Treatment of Melanoma and Pigmentation Disorders

Description of Invention:
Melanocytes are specialized pigment-producing cells that are responsible for coloration of skin, eyes and hair. Using cDNA microarray expression profiling, the inventors have identified *RAB38*, a small GTP-binding protein, as an important gene involved in melanocyte function. Human *RAB38* was localized to the mouse chocolate (*cht*) locus, and mutation of this gene in mice changes hair color from black to brown, similar to OCAIII mice, which have a mutation in *TYRP1*, another melanosomal gene, and are used as a model for oculocutaneous albinism.

The inventors have demonstrated that RAB38 is important for trafficking of the TYRP1 protein; thus, *RAB38* mutant mice are genocopies of *TYRP1* mutant mice. Modulation of RAB38 activity, such as by pharmacologic intervention, might alter pigmentation in human skin. Recently, RAB38 has also been identified as a melanocyte differentiation antigen that is strongly immunogenic, leading to spontaneous antibody responses in a significant proportion of melanoma patients. Thus, *RAB38* may also have applications for melanoma diagnostics and treatment.

This invention discloses *RAB38* nucleic acids and protein, and methods for detecting mutations in *RAB38*. Also disclosed are methods for screening for agents to modulate RAB38 activity, and for modulating pigmentation through modulation of RAB38 activity.

Applications:

- Marker protein and target for antigen-specific immunotherapy in patients with malignant melanoma.
- Therapeutics and diagnostics for melanin-related disorders.

Development Status:
Early stage

Inventors:
William J. Pavan and Stacie K. Loftus (NHGRI)

Patent Status:
DHHS Reference No. E-315-2001/0 --
U.S. National Stage Application No. 10/501,611 filed 20 Nov 2005, claiming priority to 18 Jan 2002
Foreign counterparts pending in Australia, Canada, Europe, and Japan

Relevant Publication:
Stacie K. Loftus, Denise M. Larson, Laura L. Baxter, Anthony Antonellis, Yidong Chen, Xufeng Wu, Yuan Jiang, Michael Bittner, John A. Hammer III, and William J. Pavan. Mutation of melanosome protein RAB38 in *chocolate* mice. Proc Natl Acad Sci U.S.A.

2002 Apr 2;99(7):4471-4476. [PubMed abs]

Licensing Status:
Available for exclusive or non-exclusive licensing.

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GDF15, a Marker and Cause of Morbidity in Thalassemia

Description of Invention:

The invention includes methods for the measurement of Growth Differentiation Factor 15 (GDF15, also known as MIC-1 or NAG-1) levels in order to diagnose or predict disease severity in patients with thalassemia and with related complications, as well as methods for treating thalassemia by administration of a GDF15 antagonist. Also disclosed is a method to reduce hepcidin levels by administration of GDF15, a GDF15 substitute, or GDF15 agonist.

GDF15 is a member of the TGF-Beta superfamily of proteins, which are known to control cell proliferation, differentiation, and apoptosis in numerous cell types. The inventors are additionally interested in investigating the role of GDF15 in other disorders characterized by ineffective erythropoiesis, as well as the role of GDF15 in the regulation of iron metabolism.

Thalassemia consists of a group of inherited diseases of the red blood cells, arising from deficient or absent production of globin chains. In beta-thalassemia, also known as Cooley's anemia or Mediterranean anemia, defective globin production reduces the number and viability of red blood cells, causing anemia and subsequent expansion of bone marrow. As a result of marrow expansion distorted bone formation ensues. Beta thalassemia, the most severe form of thalassemia, also results in iron overload, which is the major cause of beta-thalassemia mortality worldwide. As a result of iron overload, the patient may develop hypropituitarism, hypothyroidism, hypoparathyrodism, diabetes, arthropathy, cirrhosis and cardiopulmonary disease. Treatment of beta-thalassemia involves frequent blood transfusions and chelation therapy to remove excess iron from the blood.

In thalassemia, the patient's hepcidin expression is pathologically suppressed. Hepcidin is a protein synthesized in the liver, which reduces iron absorption in the body. The inventors have identified GDF-15 as a hepcidin-suppressing cytokine that is overexpressed in thalassemia. GDF15 levels in blood plasma have been found to be dramatically elevated in beta-thalassemia patients compared to healthy donors and patients with hereditary hemochromatosis, another form of iron overload disease.

Applications:

- Diagnostic test to detect increased risk for thalassemia-related complications.
- Treatment of thalassemia by administration of a GDF15 antagonist.
- Treatment of iron-dysregulated diseases.
- Treatment of ineffective erythropoiesis.
- Treatment of anemia of chronic disease.

Market:

Thalassemia is a growing global public health problem. It is estimated that seven percent of the world's population are carriers, with about 400,000 affected babies born each year.

Approximately 1,000 people in the United States currently have beta-thalassemia; however, the number of patients is expected to grow. Prevalence of the disease is higher in those of Mediterranean descent and those from China, India and other Asian countries. The U.S. Food and Drug Administration classifies thalassemia as a rare or orphan disease.

Development Status:
Early stage

Inventors:
Jeffery L. Miller and Toshihiko Tanno (NIDDK)

Patent Status:
DHHS Reference No. E-022-2007/0 --
U.S. Provisional Application No. 60/864,705 filed 07 Nov 2006

Relevant Publication:
In Review

Licensing Status:
Available for exclusive or nonexclusive licensing.

Collaborative Research Opportunity:
The NIDDK's Molecular Medicine Branch is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize the role of GDF-15 in other disorders characterized by ineffective erythropoiesis, as well as the role of GDF15 in the regulation of iron metabolism. Please contact Dr. Jeffery L. Miller at Jeff.Miller1@nih.hhs.gov or 301/402-2373 for more information.

For Additional Information Please Contact:
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Fax: (301)402-0220

Latrophilin 3, a Gene Involved in Attention Deficit Hyperactivity Disorder

Description of Invention:

Attention Deficit Hyperactivity Disorder (ADHD) is the most common behavioral disorder in childhood, and is estimated to affect three to five percent of people in the United States, both children and adults. Treatment typically involves a combination of behavior modification, educational interventions, and medication. There are a variety of medications available for treatment of ADHD; the most frequently prescribed drugs are stimulants or antidepressants. However, currently there is no way to tell in advance which medication will be most helpful for a particular individual.

The inventors have identified haplotypes of latrophilin 3 (LPHN3) that increase susceptibility for development of ADHD. LPHN3 is a G-protein coupled receptor that is specifically expressed in the brain's mesolimbic system, which is associated with ADHD. The invention describes methods of identifying LPHN3 haplotypes in an individual for determining susceptibility for development of ADHD. Identification of LPHN3 haplotypes in an ADHD-affected individual may also make possible individualized drug treatment plans.

Applications:

- Identify individuals with enhanced susceptibility for ADHD
- Use LPHN3 haplotype information to design individualized treatments

Inventors:

Maximillian Muenke (NHGRI)
Mauricio Arcos-Burgos (NHGRI)
F. Xavier Castellanos (NIMH)

Patent Status:

DHHS Reference No. E-312-2006/0 --
U.S. Provisional Application No. 60/850,972 filed 11 Oct 2006

Licensing Status:

Available for exclusive or nonexclusive licensing.

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A Fertility Test to Detect Ovarian Autoimmune Disease Using Human Recombinant MATER Protein

Description of Invention:

The inventors have identified *MATER*, a gene that plays an important role in fertility, and have shown that antibodies against MATER protein are detected at higher frequencies in women experiencing infertility and irregular menstrual periods than in healthy women. The discovery of MATER as an important factor in autoimmune-mediated ovarian dysfunction will facilitate diagnosis and treatment of these disorders. In addition to its critical role in ovarian autoimmunity, the inventors have also discovered that the *MATER* gene plays an essential role in embryonic development.

The invention discloses the *MATER* gene, MATER protein and MATER-specific antibodies. Also disclosed are methods and kits for evaluating female infertility through detection of an abnormal autoimmune response, an abnormal *MATER* gene, or abnormal MATER protein expression.

Applications:

- Diagnostic test for women suffering from infertility or irregular menstrual periods
- Tool for the study of early embryonic development
- Tool for the development of *MATER*-based contraceptives.

Market:

Approximately 10% of women of reproductive age experience infertility, and approximately 5% per year experience menstrual irregularity.

Development Status:

Established research test, ready for additional clinical research and commercial development.

Inventors:

Lawrence Nelson and Zhi-bin Tong (NICHD)

Patent Status:

DHHS Reference No. E-239-2000/0 --
PCT Application No. PCT/US01/10981 filed 04 Apr 2001, which published as WO 02/32955 on 25 Apr 2002
U.S. Patent Application No. 10/399,443 filed 16 Apr 2003 (allowed)
U.S. Patent Application No. 11/586,160 filed 24 Oct 2006
U.S. Patent Application No. 11/586,075 filed 24 Oct 2006
Foreign counterparts pending in Australia, Canada, Europe, and Japan

DHHS Reference No. E-239-2000/1 --
U.S. Patent Application No. 10/677,943 filed 01 Oct 2003 (allowed)
Foreign counterparts pending in Australia, Canada, Europe, and Japan

Relevant Publication:

1. Zhi-Bin Tong et al. A mouse gene encoding an oocyte antigen associated with autoimmune premature ovarian failure. Endocrinology. 1999 Aug;140(8):3720-3726. [PubMed abs]
2. Zhi-Bin Tong et al. Developmental expression and subcellular localization of mouse MATER, an oocyte-specific protein essential for early development. Endocrinology. 2004 Mar;145(3):1427-1434. [PubMed abs]
3. Zhi-Bin Tong et al. A human homologue of mouse Mater, a maternal effect gene essential for early embryonic development. Hum Reprod. 2002 Apr; 17(4):903-911. [PubMed abs]
4. Zhi-Bin Tong et al. Mater, a maternal effect gene required for early embryonic development in mice. Nat Genet. 2000 Nov;26(3):267-268. [PubMed abs]

Licensing Status:
Available for exclusive or non-exclusive licensing.

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Diagnostics and Therapeutics for Hydrocephalus

Description of Invention:

Congenital hydrocephalus is a significant public health problem, affecting approximately one in 500 live births in the United States. Congenital hydrocephalus has an adverse effect on developing brain and may persist as neurological defects in children and adults. Some of these defects may manifest as mental retardation, cerebral palsy, epilepsy and visual disabilities. Improved diagnostics are needed for assessing the risks of developing this debilitating disease.

The inventors have shown that RFX4_v3, a splice variant of the Regulatory Factor X4 (RFX4) transcription factor, is associated with the development of neurological structures. The reduction or absence of RFX4_v3 promotes the development of congenital hydrocephalus. This invention describes RFX4_v3 polypeptides and nucleic acids, as well as methods for detection of RFX4_v3 polymorphisms associated with congenital hydrocephalus. Also described are treatment methods including the RFX4_v3 polypeptide and RFX4_v3 transgenic animals and antibodies.

Applications:

- Prenatal diagnostic assay for identifying children at risk for congenital hydrocephalus
- Genotyping assay for congenital hydrocephalus

Market:

In the United States, the health care costs for congenital hydrocephalus are estimated at $100 million per year.

Development Status:

In vitro data are available.

Inventors:

Perry J. Blackshear (NIEHS)
Darryl C. Zeldin (NIEHS)
Joan P. Graves (NIEHS)
Deborah J. Stumpo (NIEHS)

Patent Status:

DHHS Reference No. E-163-2002/2 --
PCT Application No. PCT/US03/12348 filed 18 Apr 2003, which published as WO 03/088919 on 30 Oct 2003
U.S. Patent Application No. 10/511,362 filed 15 Oct 2004, which published as US 2005/0181369 on 18 Aug 2005

Relevant Publication:

1. Perry J. Blackshear et al. Graded phenotypic response to partial and complete deficiency of a brain-specific transcript variant of the winged helix transcription factor RFX4. Development. 2003 Oct;130(19):4539-4552. [PubMed abs]
2. Donghui Zhang et al. Identification of potential target genes for RFX4_v3, a transcription factor critical for brain development. J Neurochem. 2006 Aug;98(3):860-875. [PubMed abs]
3. Donghui Zhang et al. Regulatory factor X4 variant 3 (RFX4_v3): a transcription factor involved in brain development and disease. Submitted for publication, Journal of Neuroscience Research.

Licensing Status:
Available for exclusive or nonexclusive licensing.

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Methods for Enhancing Beta Cell Function in Diabetes

Description of Invention:

Diabetes results when beta cell performance is compromised through loss of cells or by reduced cell function. Anti-diabetic drugs that stimulate insulin production, such as sulfonylureas and meglitinides, have limited efficacy when beta cell responsiveness is deficient. There exists a critical need, therefore, for new diagnostics and therapeutics that focus on beta cell responsiveness in diabetes.

This technology describes methods for improving pancreatic endocrine function and delaying the onset of diabetes by enhancing beta cell function using ligands and/or regulators of Notch receptors. These methods are directed not only to mature beta cells, but to immature beta cells and to beta cells formed from differentiation of stem cells. This technology also describes isolated pancreatic progenitor cells, and offers an effective method for identifying and isolating these cells using Notch receptor markers.

Applications:

- Treatment for diabetes that enhances beta cell function or replaces lost beta cells
- Isolation and expansion of pancreatic progenitor cells for diabetes therapy
- Diagnostic test to monitor beta cell function

Market:

- Over 20 million people suffer from diabetes in the United States, and approximately 170 million people are affected worldwide.
- There are an estimated 6.2 million undiagnosed cases of diabetes in the United States.

Development Status:

Pre-clinical data are available.

Inventors:

Josephine M. Egan et al. (NIA)

Patent Status:

DHHS Reference No. E-262-2003/0 --
U.S. Provisional Application No. 60/590,281 filed 22 Jul 2004
PCT Application No. PCT/US2005/026207 filed 22 Jul 2005, which published as WO 2006/023209 on 02 Mar 2006

Licensing Status:

Available for exclusive or non-exclusive licensing.

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Complement Regulatory Gene Variants as Predictive Tests for Age-related Macular Degeneration (AMD)

Description of Invention:

Age-related macular degeneration (AMD) is a complex multigenic disorder that affects the central region of the retina (macula) and is the leading cause of legal blindness in developed countries. Age, lifestyle (e.g. smoking, diet) and genetic predisposition are major risk factors for AMD and 1.75 million adults over 40 are affected by advanced AMD in the United States with a further 7 million considered to be at risk (defined by the presence of large retinal deposits or drusen, which are the hallmark of this disease). A variety of immune-associated molecules including immunoglobulins, complement components, activators and regulators, etc. are associated with drusen and evidence suggests that AMD, like other age-related diseases such as Alzheimer's disease and atherosclerosis, involves a major inflammatory component. Several disease-susceptibility genes have been identified in family studies of macular degeneration and in patient cohorts by several groups including NIH researchers and their collaborators, and variants in the factor H gene (*CFH*), a major inhibitor of the alternative complement pathway, have been associated with the risk for developing AMD.

NIH researchers and their collaborators have now extended this work to two other regulatory genes of this pathway, Factor B (*BF*) and complement component 2 (*C2*). These genes were screened for genetic variation in two independent cohorts comprised of ~900 AMD cases and ~400 matched controls. Haplotype analyses revealed a significant common risk haplotype (H1) and two protective haplotypes (H7 and H10). Combined analysis of the *C2/BF* haplotypes and *CFH* variants shows that variation in the two loci can predict the clinical outcome in 74% of the cases and 56% of the controls (Nature Genetics (2006) 38, 458). This suggests that these variants can be used as predictive genetic tests in combination with other potential risk factors.

Available for licensing are methods for identifying a subject at increased risk for developing AMD by determining the presence of protective genotypes at either the BF/C2 locus and at the CFH locus. Microarrays and kits are also provided. The complex and polygenic nature of AMD suggests that the protective and risk haplotypes claimed here can be of great value not only to companies targeting Macular Degeneration but perhaps more broadly to those involved in complement-mediated inflammatory disorders.

Inventors:

Michael Dean (NCI)
Bert Gold (NCI)
et al.

Patent Status:

DHHS Reference No. E-042-2006/0 --
U.S. Provisional Application No. 60/772,989 filed 13 Feb 2006

Licensing Status:

Available for non-exclusive or exclusive licensing.

Collaborative Research Opportunity:
The NCI Laboratory of Genomic Diversity is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize functional or genetic tests on complement genes and proteins. Please contact Kathleen Higinbotham at 301-846-5465 for more information.

For Additional Information Please Contact:
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Predictive Test for Age-Related Macular Degeneration in Asymptomatic Individuals

Description of Invention:

Age-related macular degeneration (ARMD) is the leading cause of severe, irreversible vision loss for those over the age of fifty in the United States and in other developed countries. Thirteen million Americans over the age of forty have ARMD. ARMD is caused by the deterioration of the central area of the retina, or macula, resulting in a loss of central vision. This disease is believed to be a multigenic disorder, and is triggered by environmental factors such as smoking, age or diet in genetically susceptible individuals.

The present invention describes a highly predictive genetic test for universal practical clinical use to identify individuals at increased risk for ARMD. It comprises a rapid, accurate and affordable genetic screen, utilizing DNA microarray technology on a single chip. Sixteen genes are screened for 90 mutations/polymorphisms associated with ARMD, with a high predictive power (up to 92.7%) to identify asymptomatic carriers at risk. Accurate prediction of genetic susceptibility to this disorder will allow interventions to protect at-risk individuals.

Applications:

- Diagnostic kit to identify asymptomatic individuals at risk for age-related macular degeneration
- Make possible the identification of genetic factors in an affected individual, aiding in the development of a tailored therapeutic plan
- Provide genetic epidemiologic data to elucidate the role of genetic factors in the progression of the disease

Market:

- Individuals at risk for age-related macular degeneration.
- There are an estimated 15 million cases of age-related macular degeneration in the United States, and 50 million cases worldwide.

Development Status:

This technology requires analytic validation before commercialization.

Inventors:

Cigdem F. Dogulu (NICHD)
Owen M. Rennert (NICHD)
Wai-Yee Chan (NICHD)

Patent Status:

DHHS Reference No. E-023-2006/0 --
U.S. Provisional Application No. 60/733,042 filed 02 Nov 2005

Licensing Status:

Available for non-exclusive or exclusive licensing.

Collaborative Research Opportunity:
The NICHD Laboratory of Clinical Genomics is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize Method Evolved for Recognition and Testing of Age-Related Macular Degeneration (MERT-ARMD). Please contact Kenneth J. Rose, Esq, Ph.D., at 301/496-0477 or rosek@mail.nih.gov for more information.

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Novel Glycated Peptides and Proteins as Biomarkers for Diabetes Control

Description of Invention:

A primary goal of diabetes therapy is to improve control of blood glucose levels (known as glycemic control) in patients. Prospective studies of both Type 1 and Type 2 diabetes indicate that careful glycemic control significantly reduces the risk of microvascular, neurological, and cardiovascular complications of diabetes.

The current method to monitor glycemic control is by measurement of the relative concentration of glycated red-cell hemoglobin (HbA1C). However, levels of HbA1C, an intracellular protein, reflect glycemic control over a timeframe of several months. They are also susceptible to a variety of perturbing factors such as hematologic disorders, kidney disease, aspirin or penicillin use, or alcohol intake.

This technology describes a family of novel glycated peptide and protein biomarkers for glycemic control, as well as a method to monitor glycemic control in diabetic patients. In contrast to HbA1C, which is an intracellular protein, the glycated proteins described in this invention are found in blood plasma, and might reflect changes in glycemic control more rapidly, and with more sensitivity. A test developed using this technology could be envisioned to supplement or replace current monitoring of glycemic control by HbA1C. Also described are methods for making antibodies and aptamers that bind the described glycated peptides and proteins, and a database listing glycated peptide concentrations in diabetic and control samples.

Applications:

- Diagnostic tool to monitor glycemic control in diabetic or at-risk individuals
- Markers to track development of diabetes complications

Development Status:

Early stage

Inventors:

Perry J. Blackshear (NIEHS)

Patent Status:

DHHS Reference No. E-057-2005/0 --
U.S. Provisional Application No. 60/779,710 filed 06 Mar 2006

Licensing Status:

This technology is available for exclusive, co-exclusive, or nonexclusive licensing.

Collaborative Research Opportunity:

The National Institute of Environmental Health Sciences, Office of Clinical Research, is seeking statements of capability or interest from parties interested in collaborative

research to further develop, evaluate, or commercialize this technology. Please contact John S. Penta, Ph.D. at 919-541-3696 or penta@niehs.nih.gov for more information.

For Additional Information Please Contact:

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Antibodies That Specifically Recognize S100A15, A Protein Involved in Epidermal Differentiation and Inflammation

Description of Invention:
This technology describes rabbit polyclonal antibodies that recognize the human and mouse S100A15 proteins. S100A15 is involved in epidermal differentiation and inflammation, and is dysregulated in skin tumors and inflammatory psoriasis.

Applications:

- Diagnostic tool for evaluation of agents that alter skin pathology
- Research tool to probe the role of S100A15 during epidermal maturation, skin carcinogenesis, and inflammation
- Diagnostic tool for the clinical evaluation of skin tumors and inflammatory diseases such as psoriasis

Development Status:
Early stage

Inventors:
Ronald Wolf (NCI)
Stuart H. Yuspa (NCI)
Paul Goldsmith (NCI)
Christopher J. Voscopoulos (NCI)

Patent Status:
DHHS Reference No. E-145-2006/0 -- Research Tool

Relevant Publication:
R Wolf et al., "The mouse S100A15 ortholog parallels genomic organization, structure, gene expression, and protein-processing pattern of the human S100A7/A15 subfamily during epidermal maturation," *J Invest Dermatol* advance online publication 09 March 2006, doi: 10.1038/sj.jid.5700210.

Licensing Status:
Available for non-exclusive licensing under a Biological Materials License.

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Immunogenic T Cell Targets in Autoimmune Hepatitis and Methods of Use

Description of Invention:

Available for licensing and commercial development are new methods of diagnosing and monitoring the progression or response to therapy of subjects with autoimmune hepatitis (AIH) by quantitating the frequency and determining the function of autoantigen-specific CD4+ T cells in the peripheral blood with HLA-DRB1*0301 tetramers that display the autoepitopes. The invention identifies the immunogenic peptide regions that are targets of the T-cell immune response in two types of autoimmune hepatitis: (1) anti-SLA (soluble liver antigen)-positive autoimmune hepatitis type 3 and (2) anti-LKM (liver kidney microsomal antigen)-positive autoimmune hepatitis type 2. Upon mapping the immunogenic regions within SLA and P450 2D6 using short, overlapping peptides, the inventors discovered at least four immunogenic peptides within SLA and at least one peptide within P450 2D6 that were recognized by HLA-DRB*0301-restricted T cells. The technology is partially described in Hepatology 2005; 42: 291A-292A.

Inventors:

Barbara Rehermann (NIDDK) et al.

Patent Status:

DHHS Reference No. E-263-2003/0 --
U.S. Provisional Application No. 60/659,513 filed 07 Mar 2005

Licensing Status:

In addition to licensing, the technology is available for further development through collaborative research opportunities with the inventors.

For Additional Information Please Contact:

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Genes For Niemann-Pick Type C Disease

Description of Invention:
Niemann-Pick disease is a class of inherited lipid storage diseases. Niemann-Pick Type C disease is an autosomal recessive neurovisceral lipid storage disorder which leads to systemic and neurological abnormalities including ataxia, seizures, and loss of speech. Patients with the disease typically die as children. The biochemical hallmark of Niemann-Pick Type C cells is the abnormal accumulation of unesterified cholesterol in lysosomes, which results in the delayed homeostatic regulation of both uptake and esterification of low density lipoprotein (LDL) cholesterol. Niemann-Pick Type C is characterized by phenotypic variability. The disease appears at random in families that have no history of the disorder, making diagnosis problematic. This invention provides the human gene for Niemann-Pick Type C disease and the nucleic acid sequences corresponding to the human gene for Niemann-Pick Type C disease. Also provided is the mouse homolog of the human gene. The invention could lead to improved diagnosis and the design of therapies for the disease and improved means of detection of carriers of the gene. In addition, this invention may contribute to the understanding and development of treatments for atherosclerosis, a more common disorder associated with cholesterol buildup that involves the accumulation of fatty tissue inside arteries that blocks blood flow, leading to heart disease and stroke. The invention may also lead to additional discoveries concerning how cholesterol is processed in the body.

Inventors:
Eugene D. Carstea (NINDS) et al.

Patent Status:
DHHS Reference No. E-122-1997/0 --
U.S. Patent No. 6,426,198 issued 30 Jul 2002
U.S. Patent No. 7,045,675 issued 16 May 2006

Relevant Publication:

5. S.K. Loftus et al., "Murine model of Niemann-Pick C disease: Mutation in a cholesterol homeostasis gene," Science 277(5323):232-235, 1997.
6. S.K. Loftus et al., "Rescue of neurodegeneration in Niemann Pick-C mice by a prion-promoter driven Npc1 cDNA transgene," Human Molec. Genet. 11(24):3107-14, 2002.

Licensing Status:
Licensees sought.

Also, the NHGRI Genetic Disease Research Branch is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize Niemann-Pick Type C disease diagnostics and therapies as well as potential applications of the Niemann-Pick Type C gene related to atherosclerosis and cholesterol processing. Please contact Claire T. Driscoll for more information (telephone:

301/594-2235; email: cdriscol@mail.nih.gov).

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Anti-Marinobufagenin Antibodies and Methods for Their Use

Description of Invention:

Pre-eclampsia is associated with increased blood levels of marinobufagenin (MBG), a steroid that increases blood pressure by inhibiting a membrane enzyme, Na/K ATPase, in the vascular wall. Pre-eclampsia complicates up to 10% of pregnancies in the U.S. and is a significant factor in causing maternal and fetal mortality and morbidity worldwide.

The present invention relates to compositions and methods for detecting the presence of MBG in a biological sample. It also relates to methods for the use of monoclonal antibodies or antigen binding fragments as prophylactic, therapeutic, and diagnostic agents for the detection, inhibition and treatment of hypertension.

Inventors:

Alexei Bagrov et al. (NIA)

Patent Status:

DHHS Reference No. E-092-2004/0 --
U.S. Provisional Application No. 60/694,733 filed 27 Jun 2005
PCT Application No. PCT/US2006/024918 filed 26 Jun 2006

Licensing Status:

In addition to licensing, the technology is available for further development through collaborative research opportunities with the inventors.

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Proteomic Profiles Associated with Aging

Description of Invention:

This invention relates to proteomic profiles associated with normal aging. Biological markers (Biomarkers) that characterize the state of "normal aging" could provide a useful comparison for biomarkers of age-associated diseases (cardiovascular, cancer, arthritis). The profiles could then be used to develop markers linked with other diseases.

The proteins identified could either be included in elisa or multiplex assays, or incorporated into a protein-based chip. These products would be of utility to characterize research subjects for clinical trials. Specific proteins or groups of proteins could be used as potential therapeutic targets to prevent or attenuate disease development or help to improve the normal aging process.

Inventors:

Dr. Shari M. Ling (NIA)

Patent Status:

DHHS Reference No. E-354-2004/1 -- Research Tool

Licensing Status:

In addition to licensing, the technology is available for further development through collaborative research opportunities with the inventors.

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Identification of Molecular Markers for Endometriosis in Blood Lymphocytes Using DNA Microarrays

Description of Invention:

Endometriosis is a common, non-malignant gynecological disease that affects up to 20% of women during their reproductive years. Endometriosis is characterized by the growth of endometrial tissue outside the uterus. This growth of tissue causes recurring severe pain and can lead to infertility. As the current procedure used for diagnosis is invasive and not entirely accurate, there is a need for a fast, accurate, and minimally invasive test to test for endometriosis.

Using DNA microarray analysis of blood lymphocytes, the inventors have identified two gene markers expressed in blood that are able to discriminate between those women who have endometriosis and those that don't. The two gene markers identified are interleukin-2 receptor gamma (IL-2RG, a component of cytokine receptors) and lysyl oxidase-like 1 (LOXL1, which plays an important role in collagen synthesis and has also been implicated as a growth regulatory gene). Other genes identified in the same manner and which also represent potential biomarkers for endometriosis await further validation studies.

The test would be minimally invasive and quick using a blood sample from the patient. Currently, patients must undergo a laparoscopy with the diagnosis dependent upon the expertise of the surgeon performing the procedure.

Inventors:

Idhaliz Flores (NHGRI) et al.

Patent Status:

DHHS Reference No. E-068-2005/0 --
U.S. Provisional Application No. 60/654,331 filed 18 Feb 2005
PCT Application No. PCT/US2005/044723 filed 09 Dec 2005

Licensing Status:

In addition to licensing, the technology is available for further development through collaborative research opportunities with the inventors.

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Methods for the Selection of Subjects for Multiple Sclerosis Therapy

Description of Invention:

Multiple Sclerosis (MS) is a life-long chronic autoimmune disease diagnosed primarily in young adults who have a virtually normal life expectancy. Estimates place the annual costs of MS in the United States in excess of $2.5 billion. There are approximately 250,000 to 400,000 persons in the United States with MS, and approximately 2.5 million persons worldwide suffer from MS. A variety of therapies are used to treat MS, but there is no single therapy that can be used to treat all patients. Furthermore, therapies that are currently approved for MS are only moderately effective, and in some patients they have no effect at all. The invention provides a method to determine if a patient with MS will respond to a therapeutic protocol by analyzing the expression of genes expressed by the immune system. For example, a single gene can be assessed, or an expression profile of a patient can be created using an array comprising gene sequences and analyzed to determine if the patient will respond to one or more therapeutic protocols. A cDNA probe constructed from mRNA of lymphocytes isolated from a patient can hybridize with a microarray, and the extent of hybridization of the probes to each gene on the microarray can be determined. The microarray can include nucleic acid sequences encoding, for example, IL-8, Bcl-2-interacting protein, dihydrofolate reductase, gyanylate-binding protein 1, interferon-induced 17 kDa protein, 2’5’ OAS, plakoglobin, interferon inducible proteinkinase, and STAT-1, among others.

Inventors:

Roland Martin et al. (NINDS)

Patent Status:

DHHS Reference No. E-005-2004/0-PCT-01 -- International Application No. PCT/US04/10584 filed 05 Apr 2004

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Modulating P38 Kinase Activity

Description of Invention:

Protein kinases are involved in various cellular responses to extracellular signals. The protein kinase termed p38 is also known as cytokine suppressive anti-inflammatory drug binding protein (CSBP) and RK. It is believed that p38 has a role in mediating cellular response to inflammatory stimuli, such as leukocyte accumulation, macrophage/monocyte activation, tissue resorption, fever, acute phase responses and neutrophilia. In addition, p38 has been implicated in cancer, thrombin-induced platelet aggregation, immunodeficiency disorders, autoimmune diseases, cell death, allergies, osteoporosis and neurodegenerative disorders.

This invention includes compositions and methods for controlling the activity of p38 specifically in T cells through an alternate activation pathway. By controlling p38 activity through interference with this alternate pathway, the T cells themselves can be controlled which in turn can be a treatment for conditions or diseases characterized by T cell activation such as autoimmune diseases, transplant rejection, graft-versus-host disease, systemic lupus erythematosus, and viral infections such as HIV infections. One major benefit for this invention is the development of small molecular inhibitors of the alternative p38 activation pathway (i.e. Gadd45a-mimetics). The inventors have found that Gadd45a specifically inhibits the activity of p38 phosphorylated on Tyr-323. p38 activated by MKK6 (which phosphorylates Thr-180/Tyr-182) is found not to be inhibited by Gadd45a. This emphasizes the specific nature of the activating modification and its regulation by Gadd45a, including its suitability as a tissue-specific molecular target.

Inventors:

Jonathan D. Ashwell et al. (NCI)

Patent Status:

DHHS Reference No. E-010-2004/2 -- Research Materials

Relevant Publication:

1. JM Salvador et al. The autoimmune suppressor Gadd45alpha inhibits the T cell alternative p38 activation pathway. Nat Immunol. 2005 Apr;6(4):396-402. Epub 27 Feb 2005, doi:10.1038/ni1176 [PubMed abs]
2. JM Salvador et al. Alternative p38 activation pathway medicated by T cell receptor-proximal tyrosine kinases. Nat. Immunol. 2005 Apr;6(4):390-395. Epub 27 Feb 2005, doi:10.1038/ni1177. [PubMed abs]

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Multi-Domain Amphipathic Helical Peptides and Methods of Their Use

Description of Invention:

Mutations in the ABCA1 transporter lead to diseases characterized by the accumulation of excess cellular cholesterol, low levels of HDL and an increased risk for cardiovascular disease. Currently, there are a wide variety of treatments for dyslipidemia, which include, but are not limited to, pharmacologic regimens (mostly statins), partial ileal bypass surgery, portacaval shunt, liver transplantation, and removal of atherogenic lipoproteins by one of several apheresis procedures.

The present invention relates to the composition of peptides or peptide analogs with multiple amphipathic alpha-helical domains that promote lipid efflux from cells. It further relates to methods for identifying non-cytotoxic peptides that promote lipid efflux from cells that are useful in the treatment and prevention of dyslipidemic and vascular disorders. Dyslipidemic and vascular disorders amenable to treatment with the isolated multi-domain peptides include, but are not limited to, hyperlipidemia, hyperlipoproteinemia, hypercholesterolemia, hypertriglyceridemia, HDL deficiency, apoA-I deficiency, coronary artery disease, atherosclerosis, thrombotic stroke, peripheral vascular disease, restenosis, acute coronary syndrome, and reperfusion myocardial injury.

Inventors:

Alan Remaley et al. (NHLBI)

Patent Status:

DHHS Reference No. E-114-2004/0 --
U.S. Provisional Application No. 60/619,392 filed 15 Oct 2004
PCT Application No. PCT/US2005/036933 filed 14 Oct 2005, which published as WO 2006/044596 on 27 Apr 2006

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The UBE2G2 Binding Domain in the Ubiquitin Ligase GP78 and Methods of Use Thereof

Description of Invention:

Cytosolic and nuclear proteins are targeted for proteosomal degradation by the addition of multiubiquitin chains. The specificity of this process is largely conferred by ubiquitin protein ligases (E3s) that interact with specific ubiquitin conjugating enzymes (E2s). One important role for ubiquitylation is in quality control in the secretory pathway, targeting proteins for degradation through a set of processes known as endoplasmic reticulum (ER) -associated degradation (ERAD). ERAD is important in many diseases including cystic fibrosis, neurodegenerative disorders, alpha-1 antitrypsin deficiency, tyrosinase deficiency and cancer. ERAD is also important in controlling levels of cell surface receptors and in regulation crucial enzymes involved in cholesterol metabolism. gp78, also known as the autocrine motility factor receptor, is an E3 implicated in ERAD. This invention relates to the identification of a discrete domain within gp78 that encodes a binding site specific for gp78's cognate E2, Ube2g2. Ube2g2 is the most widely implicated E2 in ERAD. Expression of the Ube2g2 binding region provides a means of blocking ERAD by preventing interactions between gp78 and Ube2g2 and has the potential to provide diagnostic and therapeutic methods of intervening in modulating ERAD with consequences for disease processes and for generating recombinant secreted proteins in mammalian cells.

Inventors:

Allan Weissman et al. (NCI)

Patent Status:

DHHS Reference No. E-244-2004/0-US-01 filed 26 Jun 2004 (U.S. Provisional Application No. 60/583,263)

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Methods for Diagnosis of Atherosclerosis

Description of Invention:

In industrialized countries coronary heart disease and stroke due to atherosclerosis are the leading causes of morbidity and mortality. Coronary heart disease is the single largest cause of death in the U.S.A. and will cost approximately $133.2 billion according to the 2004 American Heart Association statistics update.

The identification of more sensitive and specific markers of atherosclerosis that are non-invasive and cost-effective may have profound impacts on public health. One such strategy involves the detection of marker genes or their products in blood or serum. Such markers may help identify high-risk patients with subclinical atherosclerosis who may benefit from intensive primary prevention or they may help determine the activity of established disease for monitoring response to treatment, resulting in more targeted secondary prevention.

The present invention relates to methods for detecting atherosclerosis using highly reactive biomarkers (FOS and/or DUSP1) expressed in blood cells or released into serum. Because these markers are also involved in pathogenesis, they may serve as potential targets for drug discovery and for intervention to modify disease progression.

Inventors:

Paul Hwang et al. (NHLBI)

Patent Status:

DHHS Reference No. E-276-2004/0-US-01 -- U.S. Provisional Application No. 60/607,031 filed 03 Sep 2004

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Genetic Fingerprint of Acute Stroke

Description of Invention:

Stroke is the third leading cause of death and the leading cause of adult disability in developed countries. Despite the prevalence and burden of this disease, stroke precipitants and pathophysiological mechanisms in individual patients are often unknown. It is also difficult to accurately predict whether a stroke will lead to only minor neurological sequelae or more serious medical consequences. Although animal experiments in focally ischemic brain tissue have indicated that there are alterations in gene expression following a stroke, gene expression profiling has not yet been applied to clinical human stroke, primarily because brain tissue samples are inaccessible and rarely justified.

The present provisional patent application discloses methods of determining whether a subject had an ischemic stroke, methods of determining the prognosis of a subject who had an ischemic stroke, as well as methods of determining an appropriate treatment regimen for a subject who had an ischemic stroke.

Inventors:

Alison E. Baird (NINDS)

Patent Status:

DHHS Reference No. E-306-2003/0 --
U.S. Provisional Application No. 60/575,279 filed 27 May 2004
PCT Application No. PCT/US2005/18744 filed 27 May 2005, which published as WO 2005/116268 on 08 Dec 2005

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Evaluative Means For Detecting Inflammatory Reactivity

Description of Invention:

Dysregulations of neuroendocrine stress responses have profound effects on the immune system that are associated with various autoimmune/inflammatory disorders such as rheumatoid arthritis (RA) and psychiatric conditions such as depression and post traumatic stress disorder (PTSD). Inventors from NIMH had previously found that the hypothalamic pituitary adrenal (HPA) hormonal axis, which acts as a regulatory checkpoint between the neuroendocrine and the immune system, is dysregulated in such disorders. Further research now shows that in particular, dysregulation in the secretion of corticotropin releasing hormone (CRH) from the hypothalamus contributes to these conditions. Therefore, the HPA axis, CRH and CRH receptors can serve as major targets for drug development and diagnosis of these diseases.

This patent covers the development of therapeutics and diagnostics for autoimmune/inflammatory diseases that affect millions of people. The patent proposes the use of a wide variety of classes of HPA axis active agents to treat inflammatory illnesses. The patent claims specifically predict that an HPA agonist can be used to treat arthritis. The usefulness and applicability of the patent also extends to the CRH receptor antagonists (e.g., CRH R1 antagonist, Antalarmin) that are now being developed for the treatment of depression and PTSD. Diagnostically, this invention can be used to identify individual susceptibility to autoimmune/inflammatory diseases. Testing of the HPA axis to predict and select responders and non-responders to HPA agonists and CRH receptor antagonists could provide an approach for safe application of such therapeutic agents to a larger proportion of the target population. For example a subject found to have a low HPA axis responsiveness based upon the methods as described in the patent, would be predicted to have a greater risk of developing adrenal insufficiency while being treated with this new class of drugs. Such individuals could then be treated accordingly to prevent adverse events while on CRH antagonist therapy.

Currently, such predictive approaches are not used routinely in clinical settings. The potential of this invention to diagnose and treat certain diseases in a predictive fashion makes it an excellent candidate for simultaneously developing therapeutics and the associated diagnostics. Antalarmin – which is being developed through an NIH initiative - has passed preliminary assessment at the FDA and will soon be in phase I human trials. The inventors found Antalarmin to be effective in reducing clinical arthritis score in rats by 50%, possibly through its blockade of CRH’s peripheral pro-inflammatory effects.

Given that an estimated 43 million people in the United States alone have arthritis or other rheumatic conditions, and that this number is expected to reach 60 million by 2020, this patent holds great potential in further development of therapeutics and diagnostics for autoimmune/inflammatory diseases.

Inventors:

Esther M. Sternberg et al. (NIMH)

Patent Status:
DHHS Reference No. E-289-1988/2 --
U.S. Patent 5,209,920 issued 11 May 1993

Relevant Publication:

1. F. Eskandari et al., "Neural immune pathways and their connection to inflammatory diseases," Arthritis Res. Ther. 2003, 5(6):251-265.
2. E.L. Webster et al., "Corticotropin releasing hormone (CRH) antagonist attenuates adjuvant induced arthritis: Role of CRH in peripheral inflammation," J. Rheumatol. 2002 Jun 29(6):1252-1261.
3. J.I. Webster et al., "Neuroendocrine regulation of immunity," Annu. Rev. Immunol. 2002 20:125-163.

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Human UGRP1 (Uteroglobin-Related Protein 1) Promoter and Its Use

Description of Invention:

Asthma is a genetically complex, multi-factorial disease affecting more than 17 million people in the United States alone and costing approximately US$6 billion to treat annually. Identification, mapping and linkage analyses of Single Nucleotide Polymorphisms (SNPs) have been increasingly used both to study the genetic etiology of asthma and to detect genetic loci contributing to asthma susceptibility. Researchers from the National Cancer Institute have described a novel gene, located in an asthma-susceptibility gene loci 5q31-34, named UGRP1 (uteroglobin-related protein 1) and an associated polymorphism that is significantly associated with asthma (Nimi et al. (2002) *Am. J. Hum. Genet.* 70: 718-725).

UGRP1 is a homodimeric secretory protein of ~10 kDA and is expressed only in lung and trachea. The -112G/A polymorphism was identified in the human UGRP1 gene promoter and is responsible for a 24% reduction in the promoter activity in relation to the -112G allele, as examined by transfection analysis. In a case-control study using 169 Japanese individuals (84 with asthma and 85 unrelated healthy controls) those with a -112A allele (G/A or A/A) were 4.1 times more likely to have asthma than were those with the wild-type allele(G/G).

The invention describes the -112G/A polymorphism and the UGRP1 promoter region as well as methods for detecting polymorphisms present in the UGRP1 promoter which can be used as indicators for diagnosing or for predicting a predisposition to develop a respiratory disorder. The complex and polygenic nature of asthma suggests that this potential asthma susceptibility allele can be of great value not only to companies targeting respiratory diseases such as asthma but also to those more broadly involved in gene discovery, gene mapping, association-based candidate polymorphism testing, pharmacogenetics, diagnostics and risk profiling.

Inventors:

Shioko Kimura and Tomoaki Nimi (NCI)

Patent Status:

DHHS Reference No. E-058-2001/0-PCT-02 filed 18 Jun 2002 (PCT Application No. PCT/US02/19456, which published as W0 03/000111 on 03 Jan 2003)

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Method for the Diagnosis and Treatment of Vascular Disease

Description of Invention:

Cardiovascular disease is a major health risk throughout the industrialized world. Atherosclerosis, the most prevalent of cardiovascular diseases, is the principal cause of heart attack, stroke, and gangrene of the extremities. It is also the principal cause of death in the United States.

This invention portrays a method for diagnosing decreased vascular function, detecting increased cardiovascular risk and diagnosing atherosclerosis. An embodiment includes assaying the number of endothelial progenitor cells and treating a subject with decreased vascular function by administering a therapeutically effective amount of endothelial progenitor cells.

Inventors:

Toren Finkel et al. (NHLBI)

Patent Status:

DHHS Reference No. E-037-2003/0 --
U.S. Provisional Application No. 60/426,545 filed 15 Nov 2002

DHHS Reference No. E-125-2003/0 --
U.S. Provisional Application No. 60/445,417 filed 05 Feb 2003

DHHS Reference No. E-037-2003/1 --
PCT Application No. PCT/US03/36317 filed 12 Nov 2003, which published as WO 2004/045517 on 03 Jun 2004
U.S. Patent Application No. 10/534,626 filed 11 May 2005

Relevant Publication:

J.M. Hill, G. Zalos, J.P.J. Halcox, W.H. Schenke, M.A. Waclawiw, A.A. Quyyumi, and T. Finkel. Circulating endothelial progenitor cells, vascular function, and cardiovascular risk. New Eng. J. Med. 348:593-600, Feb 13, 2003.

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PTH2 and PTH1 Receptor Ligands

Description of Invention:

Parathyroid hormone receptors found on osteoblasts in bone and renal tubule cells in kidney elevate blood calcium levels when stimulated by parathyroid hormone (PTH) and PTH-related protein (PTHrP). Excessive secretion of PTH from the parathyroid gland results in primary hyperparathyroidism. Production of PTHrP by various tumors results in humoral hypercalcemia of malignancy. In both of these conditions, excessive blood calcium levels lead to clinically significant morbidity. A parathyroid hormone antagonist could therefore have therapeutic value. Until now, no effective antagonists for the classical parathyroid hormone receptor (PTH1 receptor) were known. This invention describes a peptide which binds with high affinity (Kd = 1.3 +/- 0.1 nM, dissociation T1/2 = 14 min.) and acts as purely competitive antagonist at the PTH1 receptor. This novel peptide is related to tuberoinfundibular peptides of 39 residues (TIP39), also described in this invention, which binds to a related receptor. Deletion of amino acids from the N-terminus of TIP39 resulted in the high affinity PTH1 receptor antagonist peptide described here. This peptide may be used therapeutically to treat excessive blood calcium caused by PTH or PTHrP, other pathology caused by PTHrP, to demonstrate the utility of parathyroid hormone receptor antagonism in the treatment of hypercalcemia or other conditions, or to help screen for other antagonists at the parathyroid hormone receptor.

Inventors:

Ted B. Usdin and Samuel R. Hoare (NIMH)

Patent Status:

DHHS Reference No. E-123-1999/0 --
U.S. Provisional Application No. 60/139,335 filed 15 Jun 1999
PCT Application No. PCT/US00/16776 filed 15 Jun 2000
U.S. Patent Application No. 10/014,162 filed 11 Dec 2001

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Use and Targeting of CD98 Light-Chain Proteins in Therapies for Thyroid Hormone Disorders

Description of Invention:

Thyroid hormone disorders are among the most common problems in the Western world. These include hypo- and hyper-thyroidism (including goiter), as well as obesity and developmental abnormalities caused by excess or deficient levels of thyroid hormones during pregnancy. The NIH announces the discovery of a protein, which is a member of the CD98 light-chain permease family, which acts as a thyroid hormone transporter across vertebrate cell membranes. This protein provides a missing link in the chain by which thyroid hormones in the blood reach the cell nucleus. By utilizing the cDNA of this protein, genomic libraries can be screened for sequences capable of being used as primers for use in diagnostics. Also, by targeting this protein through drug discovery, new treatments for thyroid disorders may be found and developed.

Inventors:

Yun-Bo Shi (NICHD)

Patent Status:

DHHS Reference No. E-054-2000/0 --
U.S. Provisional Application No. 60/215,414 filed 30 Jun 2000
PCT Application No. PCT/US01/20843 filed 28 Jun 2001
U.S. Patent Application No. 10/307,063 filed 27 Nov 2002

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Methods and Compositions for Correlating CCR5 Expression with Essential Hypertension

Description of Invention:

Hypertension is a disease which afflicts as many as 1 in 5 persons in the United States and is the most common cause of visits to physicians. Once diagnosed with hypertension, treatment of the disease is lifelong. There is mounting evidence that lifestyle changes can prevent the usual rise in blood pressure with age, but for patients whose hypertension cannot be adequately treated by lifestyle changes, drug therapy must be instigated which can be difficult to control and have adverse side affects.

The present invention demonstrates that there is a link between a naturally occurring mutation in the CC-chemokine receptor 5 (CCR5) gene and an increased risk of developing hypertension. This technology will allow for the screening of individuals for the presence of the CCR5-D32/D32 genotype which correlates with an increased risk of developing hypertension and possibly prevent its occurrence through adequate antihypertensive therapy.

This technology may lead to a method of treating or preventing hypertension through the administration of: 1) an effective amount of a CCR5 expression enhancing agent; 2) CCR5 activity enhancing agent; 3) an effective amount of CCR5; or 4) an effective amount of a nucleic acid encoding CCR5. Also, this technology can be employed as a method of identifying an agent that could be used to treat or prevent hypertension through the above-identified processes.

Inventors:

Dr. Thomas O'Brien (NCI)

Patent Status:

DHHS Reference No. E-257-1999/0 --
U.S. Provisional Application No. 60/159,688 filed 14 Oct 1999
PCT Application No. PCT/US00/41051 filed 02 Oct 2000, which published as WO 01/27334 on 19 Apr 2001
U.S. Patent Application No. 10/110,519 filed 11 Apr 2002

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Evaluative Means for Detecting Inflammatory Disease

Description of Invention:

A new diagnostic tool for screening for resistance, or susceptibility to certain forms of inflammatory disease (including Alzheimer's, Systemic Lupus Erythematosis, Sarcoidosis, Scleroderma, and Arthritis) was identified using a mutation of the Angiotensin Converting Enzyme (ACE) gene. The mutation in the ACE cDNA was associated with a high level of ACE activity and resistance to exudative inflammation. Related mutations could confer or predict susceptibility to these diseases. Drugs designed to interact with the enzyme, or at the active site near the mutation could be used to treat such illnesses. This could have important implications in the study of human populations with related inflammatory diseases and may be linked to a variety of autoimmune and inflammatory diseases. It is available for immediate licensing, and research collaborations via Cooperative Research and Development Agreements (CRADAs) will be considered.

Inventors:

Esther M. Sternberg
Ruth M. Barrientos
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Mehrnaz J. Tehrani (NIMH)

Patent Status:

Serial No. 60/132,921 filed 06 Apr 1999

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Monoclonal Antibodies Specific And Inhibitory To Human Cytochrome P450 2C8, 2C9, 2C18 And 2C19 - New Avenues For Drug Discovery

Description of Invention:
The cytochrome P450 family of enzymes has primary responsibility for the metabolism of xenobiotic drugs and non-drug carcinogens and environmental chemicals, as well as some endobiotics. This laboratory has isolated monoclonal antibodies (MAbs) that are specific to and inhibit the ten major human cytochrome P450s (CYPs) that are responsible for the metabolism of most drugs. The MAb based analytic system identifies the P450s responsible for metabolism of a drug and is thus an entirely new system for Drug Discovery. Drug-drug toxicity can be due to drug partners competing for an individual P450 and be a cause of drug toxicity. Certain drugs given to genetically polymorphic individuals that are defective in a specific P450 can cause serious toxicity to the defective individual. In one case 6-10% of the world population is missing an important P450 (2D6).

The 2C family of cytochrome P450s metabolizes a very large and extensive number of drugs which include tolbutamide, S-Warfarin, mephenytoin, diazepam and taxol. The invention reports the production of inhibitory MAbs to the P450 2C family. The invention describes MAb 5-1-5 and 281-1-1 that specifically inhibit CYP 2C8, MAb 292-2-3 that specifically inhibits CYP 2C9, and MAb 592-2-5 that specifically inhibits both CYP 2C9 and 2C18. MAb 5-7-5 specifically inhibits CYP 2C9, 2C18, and 2C19. In addition MAb 1-68-11 previously reported specifically inhibits all four members of the 2C family, 2C8, 2C9, 2C18 and 2C19. The MAbs may be used as diagnostic probes identifying the single or several P450s responsible for a drugs metabolism and also yield important information on inter-individual differences. The MAb system identifies and characterizes the P450 based metabolism of drugs currently in use and drugs in the screening and development stages of Drug Discovery.

Inventors:
Harry V. Gelboin (NCI)
Frank J. Gonzalez (NCI)
Kristopher W. Krausz (NCI)

Patent Status:
DHHS Reference No. E-077-1999/0 --
U.S. Patent No. 6,623,960 issued 23 Sep 2003
U.S. Patent Application No. 10/616,760 filed 09 Jul 2003

Related Technologies:
See Monoclonal Antibodies (MAbs) Define Human Cytochrome P450 Drug Metabolism

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Method and Composition for Detecting Dihydropyrimidine Dehydrogenase Splicing Mutations

Description of Invention:

Dihydropyrimidine dehydrogenase (DPD) is the first and rate limiting enzyme in the three step metabolic pathway of the catabolism of thymidine and uracil. In mammals, this pathway is the route for synthesis of beta-alanine. DPD can be considered an enzyme that is expressed in most cells, but has been studied extensively in liver, lymphocytes, and the CNS. DPD is responsible for the metabolism of fluoropyrimidine drugs, such as the much used chemotherapeutic agent 5-fluorouracil. The invention covers isolated nucleic acids that code for DP. It also includes nucleic acids that code for a DPD polypeptide that specifically binds to an antibody generated against an immunogen consisting of DPD polypeptide and its amino acid sequence. Also claimed are methods for determining whether a cancer patient is at risk of a toxic reaction to 5-fluorouracil. The methods involve analyzing DPD DNA or mRNA a sample from the patient to determine the amount of intact DPD nucleic acid.

Inventors:

Frank J. Gonzalez
Pedro Fernandez-Salguero (NCI)

Patent Status:

DHHS Reference No. E-157-94/1 filed 20 Mar 1996

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A Mitochondrial-Specific ATP-Binding Transporter Gene (ABC7) Is An Iron Transporter In An Inherited Ataxia-Anemia Syndrome

Description of Invention:

The gene responsible for the rare genetic disease, X-linked siderblastic anemia and ataxia (XLSA/A) has been identified and linked to a mutation of the ATP-binding transporter gene (ABC7). Two sequence changes which correspond to amino acid changes at positions 50 and 396 were detected. This gene may prove useful as a diagnostic for XLSA/A carriers or as a means to rule out XLSA/A from other siderblastic anemias. ABC7, an iron transporter, may prove to be a valuable tool for studying the function and regulation of muscle cells and the loss of motor function associated with many diseases with faulty iron metabolism, i.e. neuromuscular disease, cardiac disorders and neurological disorders.

Inventors:

MC Dean
R Allikmets
AA Hutchinson (NCI)

Patent Status:

Serial No. 60/105,497 filed 23 Oct 1998

Serial No. 09/422,840 filed 21 Oct 1999

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Methods And Compositions For Inhibiting Inflammation And Angiogenesis

Description of Invention:

The invention provides compositions and methods directed to isolated alpha subunits of the 7TM protein CD97. CD97 is a heterodimer existing in three isoforms, namely three forms of alpha subunit and one invariant beta subunit. The invention provides compositions and methods for detecting a subunit of CD97, a T-cell protein which is upregulated in activated T-cells and is involved in the onset and maintenance of inflammation and angiogenesis. The invention provides an isolated protein comprising a soluble CD97 alpha subunit, and an isolated nucleic acid encoding a soluble CD97 alpha subunit protein. The invention also provides methods for identifying compounds which inhibit soluble CD97 alpha subunit expression. The invention may be used to inhibit angiogenesis associated with chronic inflammation in a mammal by administering a therapeutically effective amount of a CD97 antagonist. Another application includes determining the degree of inflammation at a site in a mammal with an antibody composition specifically reactive to a soluble CD97 alpha subunit. Further, it should be noted that these compositions and methods further have in vitro utility in the construction of proteins and subsequences thereof for the construction of antibodies, and nucleic acids and subsequences thereof for use as probes.

Inventors:

K Kelly (NCI)

Patent Status:

DHHS Reference No. E-009-1996/0 --
U.S. Patent No. 6,365,712 issued 02 Apr 2002
U.S. Patent No. 6,846,911 issued 25 Jan 2005

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Rapid Method For Diagnosing The Various Forms Of Alpha-Thalassemia

Description of Invention:

The present invention is directed to a simple, inexpensive, and rapid method for detecting thalassemias. The present invention provides for the identification of nucleic acid primers capable of detecting and distinguishing between the various forms of alpha-thalassemia using any biological material (dry or fluid) containing nucleic acid material. The invention further provides for a method and diagnostic kit for the detection and quantitation of hemoglobin (Hb) alpha gene(s) in alpha-thalassemia patients, a method and kit for screening for carriers of this genetic disorder, a sensitive non-radioisotopic test capable of differentiating between the various forms of thalassemia, and a means to identify persons who are at risk of having offspring with homozygous alpha-thalassemia.

Inventors:

GP Rodgers (NIDDK)
DC Tang (NIDDK)

Patent Status:

DHHS Reference No. E-156-1996/0 --
U.S. Patent 6,322,981 issued 27 Nov 2001

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Identification Of The Gene Causing Familial Mediterranean Fever

Description of Invention:
The invention identifies the gene (MEFV) encoding the protein (pyrin) that is associated with familial Mediterranean fever (FMF). FMF, a recessive inherited disorder, is characterized by episodes of fever, inflammation, and unexplained arthritis, pleurisy, or abdominal pain. Pyrin is thought to a play a role in keeping inflammation under control, whereas mutated forms lead to a malfunctioning protein and uncontrolled inflammation. Mutated forms of MEFV were isolated and correlated to FMF disease. It is anticipated that the immediate use of the pyrin gene and its mutations will be to aid in the diagnosis of FMF. It may also prove useful for evaluating FMF as a possible cause of currently unexplained fevers or abdominal pain. The normal gene and its mutations may also be useful for studying and controlling inflammation.

Inventors:
D Kastner (NIAMS) et al.

Patent Status:
DHHS Reference No. E-257-1997/0 --
U.S. Patent 6,627,745 issued 30 Sep 2003

Relevant Publication: The International FMF Consortium. Ancient Missense Mutations in a New Member of the *RoRet* Gene Family Are Likely to Cause Familial Mediterranean Fever. Cell 1997 Aug 22;90(4):797-807, 1997.

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Materials And Methods For Detection And Treatment Of Insulin Dependent Diabetes

Description of Invention:

Insulin-dependent diabetes mellitus (IDDM) affects close to one million people in the United States. It is an autoimmune disease in which the immune system produces antibodies that attack the body's own insulin-manufacturing cells in the pancreas. Patients require daily injections of insulin to regulate blood sugar levels. The invention identified two proteins, named IA-2 and IA-2beta, that are important markers for type I (juvenile, insulin-dependent) diabetes. IA-2/IA-2beta, when used in diagnostic tests, recognized autoantibodies in 70 percent of IDDM patients. Combining IA-2/IA-2beta with other known markers increased the level of identification to 90 percent of individuals with IDDM. Moreover, the presence of autoantibodies to IA-2/IA-2beta in otherwise normal individuals was highly predictive in identifying those at risk of ultimately developing clinical disease. It is now possible to develop a rapid and effective test that can screen large populations for IDDM. In addition, IA-2/IA-2beta are candidates for immune tolerance and prevention of disease development.

Inventors:

AL Notkins (NIDCR) et al.

Patent Status:

DHHS Reference No. E-184-1995/0 --
U.S. Patent No. 6,391,651 issued 21 May 2002

DHHS Reference No. E-184-1995/1 --
U.S. Patent 5,989,551 issued 23 Nov 1999

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Macrophage Stimulating Protein

Description of Invention:

Macrophage stimulating protein (MSP), a relative of the hepatocyte growth factor (HGF), is a component of human and animal (mammalian) blood plasma which accelerates the movement and increases the activity of macrophages. Macrophages, when activated, cankill foreign microorganisms and tumor cells. This invention describes the preparation of highly purified MSP and the production of antibodies to the purified MSP. These methods overcome the primary problem with natural MSP, i.e., that its concentration in the plasma is too low for purification by conventional techniques and for use as an effective therapeutic agent. The highly purified MSP and/or its antibodies can be used as a diagnostic and therapeutic agent and a basic research tool for diseases characterized by macrophage-mediated inflammation. The invention also describes a bioassay for the detection of antibodies to that bind MSP.

Inventors:

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AH Skeel (NCI)
T Yoshimura (NCI)
E Appella (NCI)
S Showalter (NCI)
S Tanaka (NCI)

Patent Status:

DHHS Reference No. E-083-1990/0 --
U.S. Patent No. 5,219,991 issued 15 Jun 1993
U.S. Patent No. 5,527,685 issued 18 Jun 1996

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Soluble Interleukin-2 Receptor As A Disease Indicator And A Method Of Assaying The Same

Description of Invention:

Soluble IL-2 receptor is produced in response to immune activation and by some malignant cells. For instance, elevated levels of IL-2 have been detected in patients with adult T-cell leukemia, Sezary syndrome, Hodgkin's disease, chronic lymphocytic leukemia, multiple myeloma, and solid tumors. The systemic level of IL-2 receptor is also relevant in the diagnosis and treatment of such diseases as rheumatoid arthritis and systemic lupus erythematosis and may be used to titrate immunosuppressive therapy in such applications as graft rejection. The invention disclosed in the patent is a sandwich immunoassay useful for determining the amount of IL-2 receptor in a sample. The invention also discloses a method of detecting such disturbed or abnormal conditions in humans which release soluble IL-2 receptor in bodily fluids.

Inventors:

D Nelson
W Biddison
L Rubin
W Greene
W Leonard
R Yarchoan (NCI)

Patent Status:

Serial No. 06/724,897 filed 19 Apr 1985
U.S. Patent No. 4,707,443 issued 17 Nov 1987

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Methods for Diagnoses and Treatment of XSCID

Description of Invention:
The invention provides a method of diagnosing X-linked severe combined immunodeficiency (XSCID) in males or determining whether females are carriers. This method is based upon the presence of either a mutated or truncated IL-2Rg gene. The invention also discloses a method of treating XSCID as well as a method for monitoring the therapy. Lastly, the invention provides a promoter which regulates the expression of IL-2Rg, a vector comprising a DNA molecule operably linked to the promoter, a cell host that has been transformed with the vector, and a transgenic mouse comprising the promoter or a mutant IL-2Rg.

Potential Area of Application:

- diagnosing XSCID
- identifying a carrier
- treating XSCID
- monitoring effectiveness of therapy for XSCID
- research reagent

Main Advantage of Invention:

- diagnostic test is only way of definitively diagnosing XSCID
- process for diagnosis is completely developed

Further Development Required:

- testing of methods for treatment
- clinical trials

Inventors:
Warren J. Leonard (NHLBI)
Masayuki Noguchi (NHLBI)
Wesley McBride (NCI)

Patent Status:
USSN 08/031,143 entitled "Methods for Diagnosis of XSCID and Kits Thereof" filed 12 Mar 1993, issued as U.S. Patent No. 5,518,880 on 21 May 1996 USSN 08/424,224 entitled "A Transgenic Murine Model for XSCID" filed 19 Apr 1995, issued as U.S. Patent No. 5,912,173 on 15 Jun 1999 No foreign rights

Relevant Publication: * Leonard WJ. Dysfunctional cytokine receptor signaling in severe combined immunodeficiency. J Investig Med 1996 Aug;44(6):304-11 * Leonard WJ. The molecular basis of X-linked severe combined immunodeficiency: defective cytokine receptor signaling. Annu Rev Med 1996;47:229-39 * Qazilbash MH, Walsh CE,

Russell SM, Noguchi M, Mann MM, Leonard WJ, Liu JM. Retroviral vector for gene therapy of X-linked sever combined immunodeficiency syndrome. J. Hematotherapy, 4, 91-98, 1995. * Leonard WJ; Noguchi M; Russell SM; McBride OW. The molecular basis of X-linked severe combined immunodeficiency: the role of the interleukin-2 receptor gamma chain as a common gamma chain, gamma c. Immunol Rev 1994 Apr;138:61-86 * Noguchi M, Yi H, Rosenblatt HM, Filipovich AH, Adelstein S, Modi WS, McBride OW, Leonard WJ. Interleukin-2 receptor g chain mutation results in X-linked severe combined immunodeficiency in humans. Cell, 73, 147-157, 1993

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Method for Non-Invasive Identification of Individuals at Risk for Diabetes

Description of Invention:

The invention is a non-invasive technique for the detection of ocular pathologies, including molecular changes associated with diabetes. Raman spectra emitted from an eye that is subject to a laser probe provides information regarding early markers of diabetes or diabetes-induced ocular pathologies. The invention compares spectra taken from the subject under study to spectra from a normal subject. Multivariate statistical methods are used to obtain predictive information based on the detected spectra, and to diagnose or predict the onset or stage of progression of diabetes-induced ocular pathology.

Inventors:

Anthony J. Durkin (FDA)
Marwood N. Ediger (FDA)
Michelle V. Chenault (FDA)

Patent Status:

DHHS Reference No. E-091-1998/0 --
U.S. Provisional Application No. 60/109,257 filed 19 Nov 1998
PCT Application No. PCT/US99/27360 filed 18 Nov 1999, which published as WO 00/28891 on 25 May 2000
U.S. Patent Application No. 09/856,186 filed 20 Mar 2002, which issued as U.S. Patent 6,721,583 on 13 Apr 2004

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Diagnosis and Prognosis of Fabry Disease by Detecting Neuronal Apoptosis Inhibitor Protein (NAIP) Expression

Description of Invention:

Fabry disease is a severe metabolic disorder that affects the vascular system of multiple tissues and organs. An estimated 1 in 40,000 individuals inherit this rare disease, and suffer from various complications including stroke, renal failure, and cardiac arrest. At present, molecular markers that directly measure cellular dysfunction to not exist, thus, prognosis for Fabry disease therapy can not be assessed.

Available for licensing and commercial development is a rapid diagnostic assay to identify individuals with Fabry disease and an effective mechanism of evaluating enzyme replacement therapy. It provides a quick, inexpensive device for determining expression patterns of the neuronal apoptosis inhibitor protein (NAIP). Peripheral blood white cells of Fabry disease patients are analyzed for elevated levels of the marker NAIP, which is over-expressed in patients suffering from acute strokes. These elevated levels have been found in children with Fabry disease and point to the need for preventive therapies. Additionally, this test can be routinely utilized for evaluation of specific and non-specific therapies that aid in minimizing the complications associated with Fabry disease.

Applications:

- Rapid diagnostic test to identify person at risk for Fabry disease.
- Reliable diagnostic test to identify subject response to Fabry disease therapy.

Market:

Individuals genetically susceptible to Fabry disease.

Development Status:

This technology requires analytic validation.

Inventors:

Raphael Schiffmann (NINDS) et al.

Patent Status:

DHHS Reference No. E-196-2006/0 --
U.S. Provisional Application No. 60/806,295 filed 30 Jun 2006

Relevant Publication:

1. DF Moore, H Li, N Jeffries, V Wright, RA Cooper Jr, A Elkahloun, MP Gelderman, E Zudaire, G Blevins, H Yu, E Goldin, AE Baird. Using peripheral blood mononuclear cells to determine a gene expression profile of acute ischemic stroke: a pilot investigation. Circulation. 2005 Jan 18; 111(2):212-221. [PubMed abs]

2. Y Okada, H Sakai, E Kohiki, E Suga, Y Yanagisawa, K Tanaka, S Hadano, H Osuga, JE Ikeda. A dopamine D4 receptor antagonist attenuates ischemia-induced neuronal cell damage via upregulation of neuronal apoptosis inhibitory protein. J Cereb Blood Flow Metab. 2005 Jul; 25(7):794-806. [PubMed abs]
3. N Inohara, M Chamaillard, C McDonald, G Nunez. NOD-LRR proteins: role in host-microbial interactions and inflammatory disease. Annu Rev Biochem. 2005 Jul; 74:355-383.

Licensing Status:
Available for non-exclusive or exclusive licensing.

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CANCER

Serum Autoantibody for Cancer Diagnostics

Description of Invention:
The invention demonstrates that the approach of autoantibody analysis provides a valuable approach for cancer diagnosis. Detecting serum autoantibodies against extracellular form of protein kinase A (ECPKA) can effectively diagnose cancer.

The technology describes compositions and methods for detecting autoantibodies against an ECPKA for the diagnosis of cancer. Because ECPKA is secreted from cancer cells at higher rate than normal cells, the formation of serum autoantibodies to ECPKA in cancer patients is greater. A highly sensitive enzyme immunoassay that measures the presence of anti-ECPKA autoantibody in serum of of cancer patients can therefore be used for cancer diagnosis.

Application:
ECPKA-autoantibody-based immunoassay method provides an important diagnostic procedure applicable for the detection of various cancers.

Advantages:

- Highly sensitive and specific immunoassay developed for anti-ECPKA antibody is more sensitive and specific than results from other current assays that detect only antigen activity
- High statistical corelation betweeen the presence of serum-autoantibody directed against ECPKA and presence of cancer

Benefits:
Early detection of cancer and this technology can contribute significantly to improving the clinical management of cancer and thus the quality of life for people suffering from the disease. Furthermore, the cancer diagnostic market is estimated to grow to almost $ 10 billion dollars in the next 5 years, providing a significant financial opportunity.

Inventors:
Yoon S. Cho-Chung (NCI)

Patent Status:
DHHS Reference No. E-081-2004/2 --
U.S. Patent Application No. 10/592,040
Foreign Rights are also available

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Diagnostic and Therapeutic Methods of Detecting and Treating Cancers of Reproductive Tissues

Description of Invention:

PAGE-4 is a human X-linked gene that is strongly expressed in prostate and prostate cancer, and is also expressed in other male and female reproductive tissue (e.g., testis, fallopian tube, placenta, uterus, and uterine cancer). PAGE-4 shows similarity with the GAGE protein family, but it diverges significantly from members of the family so that it appears to belong to a separate family. This, and the existence of another gene, PAGE-2, that share more homology with PAGE-4 than with members of the GAGE family indicates that the PAGE-4 protein belongs to a separate protein family.

The specific detection of PAGE-4 might be valuable for the diagnosis of prostate and testicular tumors, as well as uterine tumors. There are sufficient differences between PAGE-4 and other members of the PAGE and MAGE proteins to produce specific antibodies. Analyses with such antibodies are needed to confirm by immunohistology the expression specificity that is seen in database and mRNA analyses, and to evaluate whether anti-PAGE-4 immunotherapy could be a promising therapeutic approach. One possibility of eliminating PAGE-4 expressing cells could be to use it as cancer vaccine. Among the many possible approaches to vaccination, one method is direct vaccination with plasmid DNA. In fact, Dr. Pastan's laboratory has been able to obtain good expression of the PAGE-4 protein with mammalian expression plasmids, and has demonstrated that DNA-immunization with such expression constructs leads to good immune responses. Hence, this method may generate anti-PAGE-4 responses, and allow us to analyze if "PAGE-4-vaccination" can eliminate PAGE-4 expressing cells, as a therapeutic approach towards neoplasms of the prostate, testis, and uterus.

Inventors:

Ira H. Pastan (NCI)
Ulrich Brinkmann (NCI)
George Vasmatzis (NCI)
Byungkook Lee (NCI)

Patent Status:

DHHS Reference No. E-028-1999/0 --
U.S. Patent Application No. 11/704,714 filed 09 Feb 2007, claiming priority to 01 Sep 1998, entitled "PAGE-4, An X-Linked GAGE-Like Gene Expressed in Normal and Neoplastic Prostate, Testis and Uterus, and Uses Therefor"

Related Technologies:

DHHS Reference No. E-104-2006/0 --
PCT Application No. PCT/US2007/004603 filed 21 Feb 2007, claiming priority to 24 Feb 2006, entitled "Immunogenic Peptides and Methods of Use"

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Methods for Determining Hepatocellular Carcinoma Subtype and Detecting Hepatic Cancer Stem Cells

Description of Invention:

Hepatocellular carcinoma (HCC) is the third leading cause of cancer death worldwide, and it is very heterogeneous in terms of its clinical presentation as well as genomic and transcriptomic patterns. HCC can originate from both adult hepatocytes and hepatic progenitor cells. The extent of progenitor cell activation and the direction of differentiation are correlated with the severity of the disease. HCC patient variability indicates that HCC comprises several biologically distinct subtypes. This heterogeneity and the lack of appropriate biomarkers have hampered patient prognosis and treatment stratification.

Available for licensing are microRNA biomarkers that are associated with four HCC subtypes: hepatic stem cell-like, bile duct epithelium-like, hepatocytic progenitor-like, and mature hepatocyte-like. One unique profile is associated with HCC with features of liver stem cells and poor patient prognosis. It has both diagnostic and therapeutic value in the management of HCC patients.

Applications:

- A diagnostic assay where HCC treatment can be individualized according to patient HCC subtype
- An assay for HCC to prognose patient survival
- Therapeutic compositions that target subtype specific HCC

Market:

- HCC is the third leading cause of cancer death worldwide
- HCC is the fifth most common cancer in the world
- Post-operative five year survival rate of HCC patients is 30-40%

Development Status:

The technology is currently in the pre-clinical stage of development.

Inventors:

Xin Wei Wang (NCI) et al.

Patent Status:

DHHS Reference No. E-215-2007/0 --
U.S. Provisional Application No. 60/942,833 filed 08 Jun 2007

Relevant Publication:

1. Presented at Keystone Symposia on MicroRNA and Cancer in June 2007.

2. R Garzon et al. MicroRNA expression and function in cancer. Trends Mol Med. 2006 Dec;12(12):580-587. [PubMed abs]

Licensing Status:
Available for exclusive or non-exclusive licensing.

Collaborative Research Opportunity:
The National Cancer Institute, Laboratory of Human Carcinogenesis, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize this technology. Please contact John D. Hewes, Ph.D. at 301-435-3121 or hewesj@mail.nih.gov for more information.

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Potential Serum Bio-Markers for Alpha-fetoprotein (AFP) Negative Hepatocellular Carcinoma

Description of Invention:

This technology relates to improved methods of detecting hepatocellular carcinoma (HCC) by using new biomarkers. The overexpression of Gpc3, Mdk, SerpinI1, PEG-10 and QP-C correlates with the presence of HCC, even in small tumors. By comparing the expression levels of at least three of these markers in subject samples with their expression levels in control samples, the presence of HCC can be diagnosed. The method can also be used to monitor the progression, and regression of HCC.

HCC is a common and aggressive cancer with a high mortality rate. The high mortality rate stems from an inability to diagnose the cancer at an early stage in patients, due to the lack of available biomarkers for HCC. Currently, HCC is diagnosed by measuring the levels of serum alpha-fetoprotein (AFP); however, AFP is not always present in HCC tumors, especially small tumors.

Applications:

- Protein markers useful for screening HCC more accurately and with increased sensitivity.
- The proteins can also serve as prognostic and therapeutic response biomarkers.

Advantages:

- Highly sensitive, secretory markers that can be easily identified in patient serum.
- Markers can identify HCC in patients with small tumors that would previously go undetected.

Benefits:

HCC affects 20,000 people in U.S. or over half a million worldwide every year and 90% of them die of the disease. Improving the quality of life and duration of life for people suffering from this disease will depend a lot on early detection of the disease and this technology can contribute significantly to that social cause. Furthermore, the cancer diagnostic market is estimated to grow to almost $ 10 billion dollars in the next 5 years.

Inventors:

Xin Wei Wang (NCI) et al.

Patent Status:

DHHS Reference No. E-333-2005/0 --
Pending PCT Application PCT/US2006/042591, published as WO 2007/053659

Licensing Status:

Licensees sought.

Collaborative Research Opportunity:
The National Cancer Institute, Laboratory of Human Carcinogenesis, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize new biomarkers for hepatocellular carcinoma (HCC). Please contact John D. Hewes, Ph.D. at 301-435-3121 or hewesj@mail.nih.gov for more information.

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A Gene Therapy to Treat Lung Cancer

Description of Invention:
This invention relates to the identification of a new tumor suppressor gene named Caliban from Drosophila melanogaster and Serologically determined colon cancer antigen gene 1 (Sdccag1) from humans. Sdccag1 is inactive in human lung cancer cells but active in normal lung cells. When full length Caliban or Sdccag1 is expressed in human lung cancer cells they lose their tumorigenicity. This suggests that Caliban/Sdccag1 could be used as both a therapeutic and diagnostic for cancer.

Applications:

- Using gene therapy to replace the inactive gene with full length Caliban/Sdccag1 to treat cancer(s).
- A diagnostic assay that can determine whether the tumor suppressor Caliban/Sdccag1 gene product is functioning in cells.

Advantages:

- Caliban/Sdccag1 can be easily adopted into already standard gene therapy applications.
- Provides a novel therapeutic and diagnostic target for cancer.

Benefits:
It is estimated that there will be approximately 160,000 deaths caused by lung cancer in 2007. This technology will help in improving the quality of life of lung cancer patients as well as other cancers. Additionally, the gene therapy market is now a multi-million dollar industry.

Inventors:
Mark A. Mortin (NICHD)
Xiaolin Bi (NCI)

Patent Status:
DHHS Reference No. E-118-2005/0 --
Pending PCT Application PCT/US2006/022180, published as WO 2006/13316

Licensing Status:
Available for licensing.

Collaborative Research Opportunity:
The National Institute of Child Health and Human Development is seeking statements of capability or interest from parties interested in collaborative research to obtain pre-clinical data to be used to further develop, evaluate, or commercialize Caliban/Sdccag1 as a novel therapeutic and diagnostic target for cancer and other diseases. Please contact John D. Hewes, Ph.D. at 301-435-3121 or hewesj@mail.nih.gov for more information.

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Identification of Ovarian Cancer Tumor Markers and Therapeutic Agents

Description of Invention:

Germline mutations of BRCA1 and BRCA2 tumor suppressor genes are responsible for 5%–10% of all epithelial ovarian cancers. However, little is known about the molecular mechanisms involved in BRCA1 and/or BRCA2 mutation-associated (termed BRCA-linked) ovarian carcinogenesis. To elucidate their pathways, microarrays were used to compare gene expression patterns in ovarian cancers associated with BRCA1 or BRCA2 mutations with gene expression patterns in sporadic epithelial ovarian cancers to identify patterns common to both hereditary and sporadic tumors. As a result of this analysis, genes that are upregulated in ovarian cancer were identified. Approximately two-thirds of the sequences identified were previously known genes, while approximately one-third were expressed sequence tags, representing sequences that are cloned and identified but not yet characterized. Eighty-three genes were over-expressed in 50% of all tumors and these over-expressed sequences may be used as markers for ovarian cancer and/or targets for therapy.

Applications:

- Method to diagnose ovarian cancer
- Method to treat ovarian cancer with therapeutics that target ovarian biomarkers
- Ovarian cancer therapeutics that inhibit ovarian cancer markers such as siRNA

Market:

- Ovarian cancer is the fourth most common form of cancer in the U.S.
- Ovarian cancer is three times more lethal than breast cancer
- 22,430 new cases of ovarian cancer expected in 2007
- 15,280 ovarian cancer deaths in the U.S. in 2007

Development Status:

The technology is currently in the pre-clinical stage of development.

Inventors:

Amir Jazaeri (NCI)
Edison T. Liu (NCI)
et al.

Patent Status:

DHHS Reference No. E-310-2001/0 --
U.S. Provisional Application No. 60/357,031 filed 13 Feb 2002
PCT Application No. PCT/US03/04688 filed 13 Feb 2003, which published as WO 03/068054 on 21 Aug 2003
U.S. Patent Application No. 10/505,680 filed 12 Aug 2004

Relevant Publication:

1. AA Jazaeri et al. BRCA1-mediated repression of select X chromosome genes. J Transl Med. 2004 Sep 21;2(1):32. [PubMed abs]
2. AA Jazaeri et al. Molecular determinants of tumor differentiation in papillary serous ovarian carcinoma. Mol Carcinog. 2003 Feb;36(2):53-59. [PubMed abs]
3. AA Jazaeri et al. Gene expression profiles of BRCA1-linked, BRCA2-linked, and sporadic ovarian cancers. J Natl Cancer Inst. 2002 Jul 3;94(13):990-1000. [PubMed abs]

Licensing Status:
Available for exclusive or non-exclusive licensing.

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Tumor Markers in Ovarian Cancer

Description of Invention:
Ovarian cancer is one of the most common forms of neoplasia in women. Although advanced ovarian cancer has only a 20-30% survival rate, an estimated 90% of cases are effectively treated when detected early. However, few symptoms are associated with early ovarian cancer, and approximately 25% of ovarian cancer cases are diagnosed before it metastasizes. Utilizing SAGE analysis, a unique set of ovarian cancer biomarkers has been identified that are highly expressed in ovarian epithelial tumor cells in comparison to normal ovarian epithelial cells. A better knowledge of the mechanisms underlying ovarian tumorigenesis will likely result in the development of novel approaches for the diagnosis and therapy of this deadly disease.

Applications:

- Method to diagnose ovarian cancer
- Methods to treat patients with compositions that inhibit ovarian biomarkers such as siRNA

Market:

- Ovarian cancer is the fourth most common form of cancer in the U.S.
- Ovarian cancer is three times more lethal than breast cancer
- 22,430 new cases of ovarian cancer expected in 2007
- 15,280 ovarian cancer deaths in the U.S. in 2007

Development Status:
The technology is currently in the pre-clinical stage of development.

Inventors:
Patrice J. Morin et al. (NIA)

Patent Status:
DHHS Reference No. E-138-2000/0 --
U.S. Provisional Application No. 60/194,336 filed 03 Apr 2000
PCT Patent Application No. PCT/US2001/10947 filed 03 Apr 2001, which published as WO 01/75177 on 11 Oct 2001
U.S. Patent Application No. 10/257,021 filed 03 Oct 2002

Relevant Publication:

1. KJ Hewitt, R Agarwal, PJ Morin. The claudin gene family: expression in normal and neoplastic tissues. BMC Cancer. 2006 Jul 12;6:186. [PubMed abs]
2. PJ Morin. Claudin proteins in human cancer: promising new targets for diagnosis and therapy. Cancer Res. 2005 Nov 1;65(21):9603-9606. [PubMed abs]

3. R Agarwal, T D'Souza, PJ Morin. Claudin-3 and claudin-4 expression in ovarian epithelial cells enhances invasion and is associated with increased matrix metalloproteinase-2 activity. Cancer Res. 2005 Aug 15;65(16):7378-7385. [PubMed abs]
4. CD Hough, CA Sherman-Baust, ES Pizer, PJ Morin. Use of SAGE to study gene expression in ovarian cancer. American Association for Cancer Research, 9th Annual Meeting, April 10-14, 1999, Philadelphia, Pennsylvania.

Licensing Status:
Available for exclusive or non-exclusive licensing.

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DLC-1 Gene Deleted in Cancers

Description of Invention:

Chromosomal regions that are frequently deleted in cancer cells are thought to be the loci of tumor suppressor genes, which restrict cell proliferation. Recurrent deletions on the short arm of human chromosome 8 in liver, breast, lung and prostate cancers have raised the possibility of the presence of tumor suppressor genes in this location.

The inventors have discovered the deletion of human DLC-1 gene in hepatocellular cancer (HCC) cells. They have performed in vitro experiments demonstrating the deletion in over 40% of human primary HCC and in 90% of HCC cell lines. The DLC-1 gene is located on human chromosome 8p21.3-22, a region frequently deleted in many types of human cancer. DLC-1 mRNA is expressed in all normal tissues tested, but it has either no or low expression in a high percentage of several types of human cancer, such as liver, breast, lung, prostate cancers. Through in vitro and in vivo tumor suppression experiments, the inventors further demonstrated that DLC-1 acts as a new tumor suppressor gene for different types of human cancer.

Applications:

- Method to diagnose HCC
- Method to treat HCC patients with DLC-1 compositions
- Transgenic model to study HCC and other types of human cancer
- DLC-1 compositions

Market:

- Primary liver cancer accounts for about 2% of cancers in the U.S., but up to half of all cancers in some undeveloped countries.
- 251,000 new cases are reported annually.
- Post-operative five year survival rate of HCC patients is 30-40%.

Development Status:

The technology is currently in the pre-clinical stage of development.

Inventors:

Bao-Zhu Yuan (NCI)
Snorri S. Thorgeirsson (NCI)
Nicholas Popescu (NCI)

Patent Status:

DHHS Reference No. E-042-1998/0 --
U.S. Patent No. 6,897,018 issued 24 May 2005

Relevant Publication:

1. BZ Yuan et al. DLC-1 operates as a tumor suppressor gene in human non-small cell lung carcinomas. Oncogene. 2004 Feb 19;23(7):1405-1411. [PubMed abs]
2. BZ Yuan et al. DLC-1 gene inhibits human breast cancer cell growth and in vitro tumorigenicity. Oncogene. 2003 Jan 23;22(3):445-450. [PubMed abs]
3. BZ Yuan et al. Promoter hypermethylation of DLC-1, a candidate tumor suppressor gene, in several common human cancers. Cancer Genet Cytogenet. 2003 Jan 15;140(2):113-117. [PubMed abs]
4. BZ Yuan et al. Cloning, characterization, and chromosomal localization of a gene frequently deleted in human liver cancer (DLC-1) homologous to rat RhoGAP. Cancer Res. 1998 May15;58(10):2196–2199. [PubMed abs]

Licensing Status:
Available for exclusive or non-exclusive licensing.

Collaborative Research Opportunity:
The National Cancer Institute, Laboratory of Experimental Carcinogenesis, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize diagnostics based on tumor suppressor genes. Please contact John D. Hewes, Ph.D., at 301/435-3121 or hewesj@mail.nih.gov for more information.

For Additional Information Please Contact:
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Diagnostic and Therapeutic Use of Brother of the Regulator of Imprinted Sites (BORIS) Alternative Splice Forms

Description of Invention:

This technology identifies twenty five (25) new alternatively spliced transcripts of the BORIS gene. The transcripts lead to the expression of seventeen different protein isoforms with variable N- and C-termini encoded by BORIS gene locus. Differential expression levels of BORIS isoforms were observed in different cancers. While some BORIS alternative splice variants were expressed at different levels in all types of cancers, other expressed forms are specific to particular cancer(s).

Advantages and Applications:

- Simple, rapid, RT-PCR based diagnostic test to detect BORIS isoforms in cancer patients.
- Profiling of BORIS splice variants can be useful as a diagnostic tool for the detection of cancers.
- BORIS can be a therapeutic target antigen for immunotherapeutic and/or siRNA based treatments for cancer.
- BORIS can be used in combination with other established immunogens for immunotherapeutic treatment of several cancers.

Market:

Approximately 600,000 deaths from cancer related diseases are estimated in 2007. The technology, involving a differential expression of BORIS isoforms in cancer, can be useful for the diagnostics and treatment of several cancers having a potential market of more than 7 billion U.S. dollars.

Development Status:

The technology is currently in the pre-clinical stage of development.

Inventors:

Victor V. Lobanenkov et al. (NIAID)

Patent Status:

DHHS Reference No. E-117-2006/0 --
U.S. Provisional Application No. 60/841,342 filed 31 Aug 2006

Licensing Status:

Available for exclusive and non-exclusive licensing.

Collaborative Research Opportunity:

The NIAID Laboratory of Immunopathology is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize methods of cancer diagnostics and treatment based on detection of BORIS isoforms. Please contact Cecilia Pazman at pazmance@niaid.nih.gov or (301) 451-3526

for more information.

For Additional Information Please Contact:

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A MicroRNA Profile for Androgen Responsive Prostate Cancer

Description of Invention:
This invention describes a microRNA gene expression profile in prostate cancers that correlates with androgen responsiveness. Most prostate cancers are androgen sensitive and can be treated with anti-androgen therapies. Tumors non-responsive to anti-androgen therapy are more aggressive and needs alternative therapeutic interventions. Additionally, the microRNAs discovered can also be potential targets for developing new prostate cancer drugs.

Applications:
MicroRNA expression profile can help physicians take informed treatment action on an individual basis.

Advantages:
In vitro proof-of-concept data available.

Inventors:
Dr. Chang Hee Kim et al. (NCI)

Patent Status:
DHHS Reference No. E-142-2007/0 --
U.S. Provisional Application No. 60/906,742 filed 12 Mar 2007

Relevant Publication:
A manuscript directly related to this technology will be available as soon as it is accepted for publication.

Licensing Status:
Available for exclusive and non-exclusive licensing.

Collaborative Research Opportunity:
The NCI/SAIC-Frederick, Advanced Technology Program, Laboratory for Molecular Technology, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize microRNA diagnostic markers in cancer. Please contact John D. Hewes, Ph.D. at 301-435-3121 or hewesj@mail.nih.gov for more information.

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A Gene Expression Signature Identifying Pro-Angiogenic Genes in Ovarian Tumor Endothelial Cell Isolates

Description of Invention:
Cancer is a heterogeneous disease that requires multimodality therapy. Most of the therapeutic approaches for ovarian cancer have focused on chemotherapy, which primarily targets proliferating tumor cells. Women with ovarian cancer are typically asymptomatic and they are often diagnosed at an advanced stage and have poor survival. Despite an 80% positive patient response rate to surgery and chemotherapy, most patients will experience tumor recurrence within two years. A majority of women who die of ovarian cancer will have ovarian epithelial carcinomas.

The inventors have discovered a unique proangiogenic biomarkers isolated from ovarian endothelial cells. By targeting tumor angiogenesis by inhibiting endothelial cells that support tumor growth, this technology provides methods to diagnose and ovarian cancer in its early stages.

Applications:

- Method to diagnose and treat ovarian cancer in its early stage.
- Novel early stage ovarian cancer biomarkers.
- Therapeutic targets and compositions that inhibit ovarian tumors such as siRNA.

Market:

- Ovarian cancer is the seventh most common cancer and the fifth leading cause of cancer death in the U.S.
- An estimated 15,310 deaths in the U.S. in 2006.

Development Status:
The technology is currently in the pre-clinical stage of development.

Inventors:
Michael J. Birrer (NCI) et al.

Patent Status:
DHHS Reference No. E-095-2007/0 --
U.S. Provisional Application No. 60/901,455 filed 14 Feb 2007

Relevant Publication:
C Lu et al. Gene alterations identified by expression profiling in tumor-associated endothelial cells from invasive ovarian carcinoma. Cancer Res. 2007 Feb 15;67(4):1757-1768. [PubMed abs]

Licensing Status:

Available for exclusive or non-exclusive licensing.

Collaborative Research Opportunity:
The National Cancer Institute's Cell and Cancer Biology Branch, Molecular Mechanisms Section, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize this technology. Please contact John D. Hewes, Ph.D., at 301/435-3121 or hewesj@mail.nih.gov for more information.

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A Gene Expression Profile that Predicts Ovarian Cancer Patient Response to Chemotherapy

Description of Invention:
Ovarian cancer is a poor prognosis disease that remains the most lethal of all gynecologic malignancies. Warning symptoms do not occur until the tumor has already spread beyond the ovary, resulting in diagnosis at an advanced stage. As a result, there is a poor patient prognosis with only fifteen percent of women possessing advanced stage disease surviving for five years. Despite an initial clinical response of 80% to surgery and chemotherapy, most patients experience tumor recurrence within two years of treatment. The overwhelming majority of these patients will eventually develop chemoresistant disease and die.

Available for licensing are two gene signatures. One gene signature can predict whether a patient will initially respond to standard platinum-paclitaxel chemotherapy, but will relapse within six months of completing treatment. A second gene signature identifies patients who will show no response to therapy. This methodology may enable clinicians to identify patients who may be candidates for additional and/or novel chemotherapy drugs, and effectively choose appropriate cancer treatment. A unique feature of this signature is its derivation from pure, microdissected isolates of ovarian tumor cells, rather than undissected tissue. By utilizing this approach, the resulting gene list is specific to the cell type that causes the disease.

Applications:

- Method to detect if an ovarian cancer patient is sensitive to treatment with chemotherapeutic agents
- Method to evaluate ovarian cancer patient chemoresponsiveness
- Diagnostic tool to aid clinicians in determining appropriate cancer treatment
- Methods to treat ovarian cancer identified by chemoresistant biomarkers compositions

Market:

- Ovarian cancer is the fourth most common form of cancer in the U.S.
- Ovarian cancer is three times more lethal than breast cancer
- 15,310 deaths in the U.S. in 2006

Development Status:
The technology is currently in the pre-clinical stage of development.

Inventors:
Michael J. Birrer (NCI) et al.

Patent Status:
DHHS Reference No. E-060-2007/0 --

U.S. Provisional Application No. 60/899,942 filed 06 Feb 2007

Relevant Publication:
SC Mok et al. Biomarker discovery in epithelial ovarian cancer by genomic approaches. Adv Cancer Res. 2007;96:1-22. [PubMed abs]

Licensing Status:
Available for exclusive or non-exclusive licensing.

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Diagnosing and Treating Cancer Using beta-Catenin Splice Variants

Description of Invention:

This application discloses and claims inventions which may be used alone or together. One group of inventions relates to early detection diagnostic, prognostic and patient monitoring methods ("Diagnostic Methods"). The other group of inventions relates to methods of treatment. Both groups of inventions have particular application with respect to esophageal squamous cell cancers (ESCC) or other types of adenocarcinomas and squamous cell carcinomas.

The Diagnostic Methods are useful in evaluating the status of preneoplastic lesions as well as tumor tissue. Because of this, the methods can be used to track the progression or regression of disease in many types of cell samples from normal to dysplasia to cancer.

The Diagnostic Methods involve measuring the level of one or more pairs of transcripts or the protein products of these pairs of transcripts or the cellular localization of the transcripts or proteins. The primary transcripts or protein products useful in this method are those of the beta-Catenin gene (CTNNB1). In particular, the levels of the 16A and 16B CTNNB1 transcripts or protein products are of importance in carrying out the methods of this patent application. Other gene transcripts or protein products that may be used in conjunction with CTNNB1 16A and 16B to provide additional information are WAF1 (p21) and cMYC.

The treatment methods include employing small interfering RNA molecules (siRNAs) as a means to alter the expression of one or more of these particular CTNNB1 transcripts. More specifically, preferred siRNA molecules can be used to alter the expression of the CTNNB1 transcripts 16A and/or 16B. These siRNA molecules may be single-stranded (ss) or double-stranded (ds) and may be delivered using a construct capable of producing the siRNA molecule upon delivery to the target cell.

Applications:

- Diagnostic or prognostic methods for squamous cell cancers and adenocarcinomas
- Monitoring therapeutic response during and after patient treatment
- Development of cancer treatments
- Basic research to further elucidate the role of beta catenin in signal transduction pathways and carcinogenesis

Development Stage:

The use of beta catenin transcripts to provide prognostic or diagnostic information remains the subject of research but early patient data is found in the article in Genes Chromosomes & Cancer listed below. Work related to the use of siRNA as a treatment strategy remains in its early stages of research and has not yet progressed to clinical trials.

Inventors:

Mark J. Roth and Konrad Huppi (NCI)

Patent Status:
DHHS Reference No. E-018-2005/2 --
PCT/US2006/05032 filed 10 Feb 2006 and published as WO 2006/086772 on 17 Aug 2006, currently pending, entitled "Method of Diagnosing and Treating Cancer Using Beta Catenin Splice Variants"

DHHS Reference No. E-018-2005/1 --
U.S. Provisional Application No. 60/667,084 filed 30 Mar 2005, now abandoned

DHHS Reference No. E-018-2005/0 --
U.S. Provisional Application No. 60/652,154 filed 10 Feb 2005, now abandoned

Relevant Publication:

1. The patent application has been published as WO 2006/086772 A2 on 17 August 2006.
2. MJ Roth et al. beta-Catenin splice variants and downstream targets as markers for neoplastic progression of esophageal cancer. Genes Chromosomes Cancer. 2005 Dec;44(4):423-428. [PubMed abs]
3. SE Martin et al. Multiplexing siRNAs to compress RNAi-based screen size in human cells. Nucleic Acids Res. 2007 Mar 28; E published ahead of print, doi:10.1093/nar/gkm141. [PubMed abs]
4. A Thiele et al. AU-rich elements and alternative splicing in the beta-Catenin 3' UTR can influence the human beta-Catenin mRNA stability. Exp Cell Res. 2006 Jul 15;312(12):2367-2378. [PubMed abs]

Licensing Status:
This application is available for licensing on a non-exclusive or exclusive basis.

Biological Materials Availability:
Biological materials related to this technology are available and include those referred to in the following publications as well as a series of recently established aptamers capable of specific binding to the CTNNB1 protein.

1. MJ Roth et al. Cytologic detection of esophageal squamous cell carcinoma and precursor lesions using balloon and sponge samplers in asymptomatic adults in Linxian, China. Cancer. 1997 Dec 1;80(11):2047-2059. [PubMed abs]
2. Q-J Pan et al. Cytologic detection of esophageal squamous cell carcinoma and its precursor lesions using balloon samplers and liquid-based cytology in asymptomatic adults in Linxian, China. ACTA Cytologica (In Press).
3. MJ Roth et al. A study of beta-catenin splice variants and associated downstream targets as markers for neoplastic progression of squamous cell carcinoma of the esophagus. Genes Chromosomes Cancer. 2005 Dec;44(4):423-428. [PubMed abs]

4. PJ Limburg et al. Randomized, placebo-controlled esphogeal squamous cell cancer chemoprevention trial of selenomethionine and celecoxib. Gastroenterology. 2005 Sept;129(3):863-873. [PubMed abs]

Collaborative Research Opportunity:
The National Cancer Institute, Division of Cancer Epidemiology and Genetics, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize a method of diagnosing and treating cancer using beta-Catenin splice variants. Please contact John D. Hewes, Ph.D. at 301-435-3121 or hewesj@mail.nih.gov for more information.

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Method for Predicting and Detecting Tumor Metastasis

Description of Invention:

Detecting cancer prior to metastasis greatly increases the efficacy of treatment and the chances of patient survival. Although numerous biomarkers have been reported to identify aggressive tumor types and predict prognosis, each biomarker is specific for a particular type of cancer, and no universal marker that can predict metastasis in a number of cancers have been identified. In addition, due to a lack of reliability, several markers are typically required to determine the prognosis and course of therapy.

Available for licensing are carboxypeptidase E (CPE) inhibitor compositions and methods to prognose and treat cancer as well as methods to determine the stage of cancer. The inventors discovered that CPE expression levels increase according to the presence of cancer and metastasis wherein CPE is upregulated in tumors and CPE levels are further increased in metastatic cancer. This data has been demonstrated both in vitro and in vivo experiments and in liver, breast, prostate, colon, and head and neck cancers. Metastatic liver cells treated with CPE siRNA reversed the cells from being metastatic and arrested cells from further metastasis. Thus, CPE as a biomarker for predicting metastasis and its inhibitors have an enormous potential to increase patient survival.

Applications:

- Method to prognose multiple types of cancer and determine likelihood of metastasis.
- Compositions that inhibit CPE such as siRNA.
- Method to prevent and treat cancer with CPE inhibitors.

Market:

- 600,000 cancer related deaths in 2006.
- Global cancer market is worth more than eight percent of total global pharmaceutical sales.
- Cancer industry is predicted to expand to $85.3 billion by 2010.

Development Status:

The technology is currently in the pre-clinical stage of development.

Inventors:

Y. Peng Loh (NICHD) et al.

Patent Status:

DHHS Reference No. E-096-2007/0 --
U.S. Provisional Application No. 60/885,809 filed 19 Jan 2007

DHHS Reference No. E-096-2007/1 --
U.S. Provisional Application No. 60/887,061 filed 29 Jan 2007

DHHS Reference No. E-096-2007/2 --
U.S. Provisional Application No. 60/895,912 filed 20 Mar 2007

Relevant Publication:
Manuscript in preparation.

Licensing Status:
Available for exclusive or non-exclusive licensing.

Collaborative Research Opportunity:
The National Institute for Child Health and Human Development, Section on Cellular Neurobiology, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize CPE as a biomarker for predicting metastasis. Please contact John D. Hewes, Ph.D. at 301-435-3121 or hewesj@mail.nih.gov for more information.

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Biomarkers for Tissue Status

Description of Invention:

Tissue regeneration and tumorigenesis are complex, adaptive processes controlled by cues from the tissue microenvironment. There are complex processes both characterized by cell proliferation, migration, and angiogenesis suggesting that wounds and cancer share a number of phenotypic similarities including cellular behavior, signaling molecules, and gene expression.

Utilizing the kidneys as a model to compare renal regeneration and repair (RRR) from ischemically-injured tissues and renal cellular carcinoma (RCC), the inventors have identified biomarkers which are differentially expressed. The invention relates to methods of quickly and accurately diagnosing RCC and monitoring renal tissue health as well as RCC treatment.

Applications:

- Method to accurately diagnose RCC
- RCC biomarker inhibitors such as siRNA
- Method to treat RCC
- Method to determine and monitor renal tissue health status
- Method for improving renal ischemia recovery without promoting RCC
- Biomarkers for immunotherapy, drug targeting and drug screening, for targeting tumors and not normal regenerating tissue
- Biomarkers for immunotherapy, drug targeting and drug screening, for targeting ischemic tissue and not tumors

Market:

- Kidney cancer is one of the top ten most prevalent cancers in the U.S. and it accounts for 12,200 deaths annually.
- Approximately 35,000 new cases of kidney cancer are diagnosed annually; 50% survival rate after five years of diagnosis.
- Renal cancer accounts for 3% of all adult male malignancies.

Development Status:

The technology is currently in the pre-clinical stage of development.

Inventors:

Joseph Riss (NCI) et al.

Patent Status:

DHHS Reference No. E-064-2005/0 --
U.S. Provisional Application No. 60/649,208 filed 01 Feb 2005
PCT Application No. PCT/US2006/003611 filed 01 Feb 2006

Relevant Publication:

1. Journal of Urology, May 2007, Vol. 177 No. 5, in press.
2. J Riss et al. Cancers as wounds that do not heal: differences and similarities between renal regeneration/repair and renal cell carcinoma. Cancer Res. 2006 July 15;66(14):7216-7224. [PubMed abs]

Licensing Status:
Available for exclusive or non-exclusive licensing.

Collaborative Research Opportunity:
The National Cancer Institute, Center for Cancer Research, Laboratory of Cancer Biology and Genetics, Wound Healing and Oncogenesis (NCI/CCR/LCBG), is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize topics of invention or related to cancer biology, metastasis, wound healing, bioinformatics, pharmacogenomics and therapeutic. Please contact John D. Hewes, Ph.D. at 301-435-3121 or hewesj@mail.nih.gov for more information.

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Novel Diagnostics and Therapeutics for Various Hematologic Malignancies: Monoclonal Antibodies to Members of Fc receptor-like (FCRL) Proteins

Description of Invention:

Fc receptor-like (FCRL) is a gene family homologous to Fc receptors (alternative names, FcRH, IRTA, IFGP, SPAP). FCRL1-6 genes are located on human chromosome 1, where translocations and other abnormalities are frequently observed in certain B-cell lymphoma and multiple myeloma. Previous studies suggests that the FCRL proteins are differently expressed on various malignant cells from B-linage cells as well as normal B cells in different stage of the differentiation in adaptive immunity. Although the natural ligands are not known, FCRL proteins likely play roles in regulation of immunity. The members of the immunoglobulin superfamily receptor translocation associated (IRTA) genes 1-6 encode proteins homologous to Fc receptors. Previous studies suggest that each IRTA may play a different role in B-cell differentiation and immune responses. FCRL1-6 proteins possess 3-9 extracellular immunoglobulin (Ig) domains, each of which exhibits a substantial homology to the same subtypes of Ig domains (up to 86% identity). Consequently there are some epitopes shared by FCRL1-6 extracellular domains evidenced by the presence of many cross-reactive monoclonal antibodies (MAbs) with FCRL1-6. The invention relates to the development of novel MAbs specific to each member of the FCRL proteins, which show no cross-reactivity with other FCRL members. These antibodies could be used for studies on detailed expression studies of FCRLs in different cancer cells and on potential therapeutic use for FCRL-expressing hematological malignancies.

Applications and Modality:

- Novel monoclonal antibodies to FCRL family members can help diagnose and treat B cell malignancies and RA.
- The antibodies can be used as research tools to detect cellular expression of FCRLs.

Advantage:

Monoclonal antibody clones are available that are specific to one member of the FCRL family with no cross-reactivity to other members.

Development Status:

The technology is in pre-clinical stage of development.

Inventors:

Ira Pastan (NCI) et al.

Patent Status:

DHHS Reference No. E-016-2006/0 --
U.S. Provisional Application No. 60/891,434, filed 23 Feb 2007, entitled "Antibodies That Specifically Bind IRTA and Methods of Use"

DHHS Reference No. E-287-2004/1 --
PCT Application No. PCT/US2005/034444 filed 22 Sep 2005, entitled "IRTA2 Antibodies and Methods of Use," which published as WO 2006/039238 on 25 Jan 2007
U.S. Patent Application No. 11/664,211 filed 28 Mar 2007, entitled "IRTA2 Antibodies and Methods of Use"

Relevant Publication:

1. A manuscript directly related to this technology will be available as soon as it is accepted for publication.
2. T Ise, H Maeda, K Santora, L Xiang, RJ Kreitman, I Pastan, S Nagata. Immunoglobulin superfamily receptor translocation associated 2 protein on lymphoma cell lines and hairy cell leukemia cells detected by novel monoclonal antibodies. Clin Cancer Res. 2005 Jan 1;11(1):87-96. [PubMed abs]
3. T Ise, RJ Kreitman, I Pastan, S Nagata. Sandwich ELISAs for soluble immunoglobulin superfamily receptor translocation-associated 2 (IRTA2)/FcRH5 (CD307) proteins in human sera. Clin Chem Lab Med. 2006;44(5):594-602. [PubMed abs]
4. T Ise, S Nagata, RJ Kreitman, WH Wilson, AS Wayne, M Stetler-Stevenson, MR Bishop, DA Scheinberg, L Rassenti, TJ Kipps, RA Kyle, DF Jelinek, I Pastan. Elevation of soluble CD307 (IRTA2/FcRH5) protein in the blood and expression on malignant cells of patients with multiple myeloma, chronic lymphocytic leukemia, and mantle cell lymphoma. Leukemia. 2007 Jan;21(1):169-174. Epub 2006 Oct 19. [PubMed abs]

Licensing Status:
Available for exclusive and non-exclusive licensing.

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Sipa-Gene and Sipa-1 Inhibitor for the Diagnosis and Treatment of Metastatic Cancer

Description of Invention:

This technology relates to methods and compositions of a new gene Sipa-1 that can identify and treat metastatic cancer. The inventors have identified the Sipa-1 gene as a possible metastasis modifying gene. Further analyses revealed that Sipa-1 expression levels correlate with metastasis. Inhibitors that modulate the Sipa-1 expression and reduce metastasis in animal models have been identified. Additionally, single nucleotide polymorphisms (SNPs) present in the mouse Sipa-1 gene have been identified that, if also present in humans, could serve as the basis for diagnosing cancer and metastasis.

Market Opportunity:

No screening markers are currently available in the market that can diagnose early metastasis, which causes majority of cancer related deaths. Opportunity for new diagnostic and therapeutic technologies exists as personalized medicine is taking a major role in the clinical management of cancer. This invention can provide the much needed new diagnostic marker for predicting early metastasis as well as a new therapy targeting metastasis causing factors.

Applications and Modality:

- Method for diagnosing early onset of metastasis with Sipa-1.
- Sipa-1 as a new therapeutic target for treatment of metastatic cancer.

Advantages:

- Simple PCR based assay for detecting single nucleotide polymorphisms (SNPs) within the Sipa-1 gene.
- Inhibitors of Sipa-1 are known in the art, they can be easily screened from existing small molecule libraries.

Current Development Status:

- The technology is currently in the pre-clinical stage of development.
- Proof of concept results show that inhibition of Sipa-1 reduces metastasis in mouse models.
- Laboratory data shows single nucleotide polymorphisms (SNPs) within the Sipa-1 gene linked to metastatic disease.

Inventors:

Kent Hunter et al. (NCI)

Patent Status:

DHHS Reference No. E-082-2005/0 --
U.S. Provisional Application No. 60/649,365 filed 02 Feb 2005

DHHS Reference No. E-082-2005/2 --
PCT Application No. PCT/US2006/003672 filed 02 Feb 2006

Related Technologies:
DHHS Reference No. E-216-2005/0 --
U.S. Provisional Application No. 60/695,024 filed 29 Jun 2005

Relevant Publication:

1. PCT Publication No. WO 2006084027, published October 8, 2006.
2. YG Park et al. Sipa1 is a candidate for underlying the metastasis efficiency modifier locus Mtes1. Nat Genet. 2005 Oct;37(10):1055-1062. Epub 2005 Sep 4. [PubMed abs]
3. NP Crawford et al. Germline polymorphisms in SIPA-1 are associated with metastasis and other indicators of poor prognosis in breast cancer. Breast Cancer Res. 2006;8(2):R16. Epub 2006 Mar 21. [PubMed abs]

Licensing Status:
Available for exclusive and non-exclusive licensing.

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Methods of Determining the Prognosis of an Adenocarcinoma

Description of Invention:
Available for licensing and commercial development is a novel method for determining the prognosis of a subject with adenocarcinoma in an organ, such as the lung, and to aid in the selection of a specific therapeutic regimen. Lung adenocarcinoma (AC) is the predominant histological subtype of lung cancer, which is the leading cause of cancer deaths worldwide. The risk of metastasis remains substantial in AC patients, even when a curative resection of early-stage AC is performed. The prognosis includes the determination of the likelihood of survival, the likelihood of metastasis, or both. The method includes quantization of the expression of a plurality of Th1 and Th2 cytokines of interest in the adenocarcinoma and in non-cancerous tissue in the organ. Altered expression of one or more of the Th1 and Th2 cytokines in the adenocarcinoma as compared to the non-cancerous tissue determines the prognosis for the subject. The method is capable of distinguishing patients with lymph node metastasis versus those with short term survival. Furthermore, methods are provided for evaluating the effectiveness of anti-cancer agents.

Applications:
Prognosis of adenocarcinoma, aid in the selection of specific therapeutic regimens and evaluation of the effectiveness of anti-cancer agents.

Development Status:
The technology is in early stage of development.

Inventors:
Curtis C. Harris (NCI)
Masahiro Seike (NCI)
Xin Wei Wang (NCI)

Patent Status:
DHHS Reference No. E-263-2006/0 --
U.S. Provisional Application No. 60/830,936 filed 14 Jul 2006

DHHS Reference No. E-085-2007/0 --
U.S. Provisional Application No. 60/885,101 filed 17 Jan 2007

Licensing Status:
Available for non-exclusive or exclusive licensing.

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RAB38, a Target for Treatment of Melanoma and Pigmentation Disorders

Description of Invention:
Melanocytes are specialized pigment-producing cells that are responsible for coloration of skin, eyes and hair. Using cDNA microarray expression profiling, the inventors have identified *RAB38*, a small GTP-binding protein, as an important gene involved in melanocyte function. Human *RAB38* was localized to the mouse chocolate (*cht*) locus, and mutation of this gene in mice changes hair color from black to brown, similar to OCAIII mice, which have a mutation in *TYRP1*, another melanosomal gene, and are used as a model for oculocutaneous albinism.

The inventors have demonstrated that RAB38 is important for trafficking of the TYRP1 protein; thus, *RAB38* mutant mice are genocopies of *TYRP1* mutant mice. Modulation of RAB38 activity, such as by pharmacologic intervention, might alter pigmentation in human skin. Recently, RAB38 has also been identified as a melanocyte differentiation antigen that is strongly immunogenic, leading to spontaneous antibody responses in a significant proportion of melanoma patients. Thus, *RAB38* may also have applications for melanoma diagnostics and treatment.

This invention discloses *RAB38* nucleic acids and protein, and methods for detecting mutations in *RAB38*. Also disclosed are methods for screening for agents to modulate RAB38 activity, and for modulating pigmentation through modulation of RAB38 activity.

Applications:

- Marker protein and target for antigen-specific immunotherapy in patients with malignant melanoma.
- Therapeutics and diagnostics for melanin-related disorders.

Development Status:
Early stage

Inventors:
William J. Pavan and Stacie K. Loftus (NHGRI)

Patent Status:
DHHS Reference No. E-315-2001/0 --
U.S. National Stage Application No. 10/501,611 filed 20 Nov 2005, claiming priority to 18 Jan 2002
Foreign counterparts pending in Australia, Canada, Europe, and Japan

Relevant Publication:
Stacie K. Loftus, Denise M. Larson, Laura L. Baxter, Anthony Antonellis, Yidong Chen, Xufeng Wu, Yuan Jiang, Michael Bittner, John A. Hammer III, and William J. Pavan. Mutation of melanosome protein RAB38 in *chocolate* mice. Proc Natl Acad Sci U.S.A.

2002 Apr 2;99(7):4471-4476. [PubMed abs]

Licensing Status:
Available for exclusive or non-exclusive licensing.

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A Novel, Clinically Validated, Efficient and Non-Invasive In Vitro Diagnostic and Prognostic Test for Cancer

Description of Invention:
Cripto-1 (CR1) is a member of the epidermal growth factor (EGF)-related families of peptides and is involved in the development and progression of various human carcinomas. In particular, CR1 overexpression has been detected in 50-90% of carcinomas of the colon, pancreas, stomach, gallbladder, breast, lung, endometrium and cervix. Current methodologies of cancer detection, e.g. immunohistochemistry, can be time consuming, inconvenient and oftentimes, inaccurate, and therefore, a need exists for more efficient, reliable and less time consuming methods of detection. The invention relates to such a method of detection. Thus, this test could be used to more effectively screen and perhaps stage cancers. Additionally, should particular tumor cells, e.g. breast tumor cells, express a sufficiently high level of CR1, it may be possible to use the disclosed assay to detect and measure CR1 in human serum and/or plasma and possibly other physiological fluids.

Applications:

- Antibody-mediated cancer therapeutics
- Method for the detection and quantification of cripto-1 human milk, serum, plasma and other biological fluids using an ELISA-based protocol

Inventors:
Caterina Bianco (NCI)
David S. Salomon (NCI)

Patent Status:
DHHS Reference No. E-290-2000/0 --
U.S. Patent No. 7,078,176 issued 18 Jul 2006

Relevant Publication:

1. C Bianco, C Wechselberger, A Ebert, NI Khan, Y Sun, DS Salomon. Identification of Cripto-1 in human milk. Breast Cancer Res Treat. 2001 Mar;66(1):1-7. [PubMed abs]
2. C Bianco, L Strizzi, M Mancino, A Rehman, S Hamada, K Watanabe, A De Luca, B Jones, G Balogh, J Russo, D Mailo, R Palaia, G D'Aiuto, G Botti, F Perrone, DS Salomon, N Normanno. Identification of cripto-1 as a novel serologic marker for breast and colon cancer. Clin Cancer Res. 2006 Sep 1;12(17):5158-5164. [PubMed abs]

Licensing Status:
This technology is available for non-exclusive licensing.

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Methods of Determining the Prognosis of Hepatocellular Carcinoma

Description of Invention:

Hepatocellular carcinoma (HCC) represents an extremely poor prognostic cancer that remains one of the most common and aggressive malignancies worldwide. A major hallmark of HCC is intrahepatic metastasis and post-surgical reoccurrence. With current diagnostic methods, HCC patients are often diagnosed with end-stage cancer and have poor survival. Thus, there is a need for an accurate method to identify HCC and its proclivity for metastases/relapse, particularly at early stages of this disease.

The inventors have discovered a unique set of microRNA (miRNA) biomarkers that are associated with HCC metastasis/recurrence. This miRNA signature was validated in an independent cohort of 110 HCC samples as an independent predictor of HCC prognosis and likelihood of metastasis and relapse. In particular, the inventors provide evidence that these miRNA markers can predict HCC metastasis in the early stages of cancer. This methodology may enable clinicians to effectively stratify patients for appropriate cancer treatment and prioritize liver transplantation candidates.

Applications:

- Method to prognose HCC, patient survival and likelihood of HCC metastasis/relapse
- Diagnostic tool to aid clinicians in determining appropriate cancer treatment
- Compositions that inhibit miRNA HCC biomarkers such as siRNA
- Method to treatment HCC patients with inhibitory miRNA compositions

Market:

- Primary liver cancer accounts for about 2% of cancers in the U.S., but up to half of all cancers in some undeveloped countries
- Post-operative five year survival rate of HCC patients is 30-40%

Development Status:

This technology is currently in the pre-clinical stage of development.

Inventors:

Xin Wei Wang et al. (NCI)

Patent Status:

DHHS Reference No. E-050-2007/0 --
U.S. Provisional Application No. 60/884,052 filed 09 Jan 2007

Relevant Publication:

Budhu et al. A Unique Metastasis-related MicroRNA Expression Signature Predicts Survival and Recurrence in Hepatocellular Carcinoma, manuscript in preparation.

Licensing Status:
Available for exclusive or non-exclusive licensing.

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New Tumor Endothelial Markers: Genes that Distinguish Physiological and Pathological Angiogenesis

Description of Invention:

Angiogenesis, the formation of new blood vessels, is associated with normal physiological processes such as wound healing, ovulation or menstruation as well as with many diseases. Presently, it is thought to be required for the progressive growth of solid tumors and age-related macular degeneration. Lack of disease-specific endothelial markers has hindered the development of cancer therapies targeted against angiogenesis.

This invention describes specific markers that can be used to identify tumor angiogenesis, separate from normal physiological angiogenesis. Several markers have been identified which may serve as potential targets for tumor vessels by using comparative gene expression analysis on various normal and tumor endothelial cells. Furthermore, the invention describes several organ-specific endothelial markers that can aid in the selective delivery of molecular medicine to specific sites. For example, brain endothelial markers (BEMs) and liver endothelial markers (LEMs) described herein could potentially be used to direct molecular medicine specifically to these tissues.

The novel tumor endothelial markers (TEMs) described in this invention also have potential diagnostic ability. These markers can be used to distinguish between normal and tumor tissues. Some of the secreted TEMs can serve as surrogate markers in the determination of the optimum biological dose (OBD) for the current anti-angiogenic drugs in clinical trials.

Applications and Modality:

- Novel therapeutic targets associated with tumor vessels
- New agents can be developed against these novel targets
- Novel endothelial markers that distinguish pathological angiogenesis from normal physiological angiogenesis
- Surrogate tumor endothelial markers that can be used to determine optimal biological dose (OBD) of anti-angiogenic drugs

Market:

- Sales of the first FDA approved anti-angiogenic drug Avastin™ has reached $600 million.
- Another promising anti-angiogenic molecule, Thalidomide™, has been approved as an anti-cancer agent and for other use in Europe and Australia.

Development Status:

The technology is currently in the pre-clinical stage of development.

Inventors:

Brad St. Croix and Steven Seaman (NCI)

Patent Status:
DHHS Reference No. E-285-2006/0 --
U.S. Provisional Application No. 60/858,068 filed 09 Nov 2006

Relevant Publication:
A Nanda and B St. Croix. Tumor endothelial markers: new targets for cancer therapy. Curr Opin Oncol. 2004 Jan;16(1):44-49. [PubMed abs]

Licensing Status:
Available for exclusive and non-exclusive licensing.

Collaborative Research Opportunity:
The NIH National Cancer Institute, Tumor Angiogenesis Section, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize specific biomarkers that can be used to identify tumor angiogenesis. Please contact John D. Hewes, Ph.D. at 301/435-3121 or hewesj@mail.nih.gov for more information.

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A New Method for Improving the Therapeutic Efficacy of L-Asparaginase in Multiple Types of Cancer

Description of Invention:

For the last several decades, L-asparaginase (L-ASP) has been widely used as a clinical treatment for leukemias. Studies show that cancer cells that contain less asparagine synthetase (ASNS) are more susceptible to L-ASP. The response to L-ASP therapy is often better when the expression of ASNS is limited.

The present invention describes a new method for enhancing L-ASP activity by combining it with antagonists of ASNS – such as siRNAs, antisense nucleotides, antibodies or small-molecule inhibitors – for treatment of cancers. Reducing or suppressing the expression of ASNS potentiates the growth inhibitory activity of L-ASP.

Additionally, the invention discloses a novel biomarker screening tool to identify leukemia, ovarian, and other cancer patients that would be most likely to respond to L-ASP treatment.

Applications and Modality:

- A new method for improving the therapeutic efficacy of L-asparaginase.
- ASNS antagonists such as siRNA, antibodies, antisense nucleotides, or small-molecule inhibitors can potentially be used in combination with L-ASP in the treatment of cancers.
- ASNS gene or protein expression can serve as a therapeutic response biomarker for personalization of cancer therapy with the aforementioned combinations.

Market:

- There were more than 500,000 deaths from cancer in 2006. The current technology has the potential of being used in conjunction with L-ASP in treating cancer patients.
- Oncaspar™, the PEG-derivitized L-ASP developed by Enzon Pharmaceuticals, registered annual sales of about $25 million in 2006, largely on the basis of treatment of acute lymphoblastic leukemia. The present invention may make L-ASP applicable to treatment of types of cancers that are much more common.

Development Status:

The technology is currently in the pre-clinical stage of development. With respect to L-ASP treatment of patients with solid tumors, Phase I clinical trials have been initiated (Principal Investigator Daniel D. Von Hoff, TGen, Inc.) at three institutions using L-ASP in combination with gemcitabine.

Inventors:

Philip L. Lorenzi (NCI)
John N. Weinstein (NCI)

Natasha J. Caplen (NCI)

Patent Status:
DHHS Reference No. E-132-2006/0 --
U.S. Provisional Application No. 60/779,143 filed 03 Mar 2006
U.S. Provisional Application No. 60/833,027 filed 25 Jul 2006

Relevant Publication:
PL Lorenzi et al. Asparagine synthetase as a causal, predictive biomarker for L-asparaginase activity in ovarian cancer cells. Mol Cancer Ther. Nov; 5(11):2613-2623. Epub 2006 Nov 6, doi 10.1158/1535-7163.MCT-06-0447. [PubMed abs]

Licensing Status:
Available for exclusive and non-exclusive licensing.

Collaborative Research Opportunity:
The National Cancer Institute's Genomics & Bioinformatics Group in the Laboratory of Molecular Pharmacology is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize the combination therapies described in this abstract. Please contact John D. Hewes, Ph.D. at 301/435-3121 or hewesj@mail.nih.gov for more information.

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Megakaryocyte Potentiation Factor as a New Serum Tumor Marker for Mesothelioma

Description of Invention:

Mesothelin is a glycoprotein, whose expression has been largely restricted to mesothelial cells in normal tissues, although epithelial cells of the trachea, tonsil, fallopian tube, and kidney have shown immunoreactivity. Mesothelin has been shown to be expressed in several cancers including mesothelioma, lung cancer, pancreatic carcinomas, gastric carcinomas and ovarian carcinomas, and has the potential of being used as a tumor marker and a novel target for the development of new treatments.

Mesothelin precursor protein is a 69 kDa protein that is proteolytically cleaved into two products, the megakaryocyte potentiation factor (MPF) and mesothelin. MPF is a 33 kDa soluble protein that is shed into the blood stream of patients with mesotheliomas and other tumors including ovarian and pancreatic and thus can be used as a serum marker for the diagnosis of mesothelin expressing cancers.

This invention describes the generation of monoclonal antibodies to MPF. The antibodies can be useful for diagnosing mesotheliomas and other cancers. Additionally, it can be used by the oncological research community as a research tool.

Applications:

- New monoclonal antibodies against MPF
- A new monoclonal antibody against MPF that can be used for diagnosis method for mesotheliomas and other cancers including ovarian and pancreatic by detecting MPF in serum of patients

Market:

- Cancer diagnostic market is projected to grow to approximately $8B in the next 5 years
- Potential as a research tool for oncology research market

Inventors:

Ira H. Pastan et al. (NCI)

Patent Status:

DHHS Reference No. E-293-2006/0 – Research Tool

Relevant Publication:

M Onda et al. Megakaryocyte potentiation factor cleaved from mesothelin precursor is a useful tumor marker in the serum of patients with mesothelioma. Clin Cancer Res. 2006 Jul 15;12 (14 Pt 1):4225-4231. [PubMed abs]

Licensing Status:

Available for licensing under a Biological Materials license.

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Extracellular Matrix/Metastasis Modifier Genes as a Method for Characterization and Prevention of Metastatic Tumor

Description of Invention:

To a large extent cancer mortality is due to metastatic disease than a primary tumor. Recent evidence suggests that metastatic disease can be an early event and in majority of patients metastasis starts by the time the disease is diagnosed. Thus there is a need for methods of characterizing the early metastatic process for better treatment of cancer.

This invention provides methods of characterizing the metastatic capacity of a tumor as well as inhibiting metastasis of a cancer cell. More specifically, this invention discloses an extracellular matrix (ECM) modifier protein named *Anakin*, detection of the *Anakin* protein as a marker for metastatic disease and use of *Anakin* as potential therapeutic target.

Applications and Modality:

- Method of diagnosis for early metastasis and therapeutic inhibition of metastasis
- Nucleic acid sequence of *Anakin* protein, an extracellular matrix (ECM) modifier gene
- SiRNA sequences that inhibit *Anakin* expression as therapeutics
- Purified antibodies that recognize *Anakin* protein as a research reagent and in diagnostics related products

Market:

600,000 deaths from cancer related diseases estimated in 2006.

Development Status:

The technology is currently in the pre-clinical stage of development.

Inventors:

Kent W. Hunter (NCI) et al.

Patent Status:

DHHS Reference No. E-125-2006/1 --
U.S. Provisional Application No. 60/778,463 filed 31 Mar 2006

Licensing Status:

Available for exclusive and non-exclusive licensing.

Collaborative Research Opportunity:

The NCI Laboratory of Population Genetics is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize the use of *Anakin* as a prognostic tool for diagnosing breast cancer outcome. Please contact John Hewes, Ph.D., at 301-435-3121 for more information.

For Additional Information Please Contact:

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Novel Monoclonal Antibody Microarray

Description of Invention:

Gene expression profiling at the mRNA level has proven to be a powerful and useful tool, however this approach suffers from inherent limitations: 1) the mRNA abundance does not typically correlate well with protein abundance and 2) protein structure, activity, and function can be altered and regulated by post-translational modifications. Thus, there is growing recognition that these approaches should be complemented by profiles of the gene products or proteins themselves. The present invention provides methods for constructing and using a novel Monoclonal Antibody Microarray which allows high-throughput determination of protein expression profiles from serum, tissue, and cultured cells.

The Monoclonal Antibody Microarray consists of more than 1000 different antibodies immobilized on a glass slide, which recognize antigens from several groups of proteins, including cytokines, kinases, apoptotic proteins, growth factor receptors, tumor suppressors, and oncoproteins. Protein samples to be identified and quantified are labeled with fluorescence and hybridized to the antibodies immobilized on the arrays. By differentially labeling two protein samples (dual-color labeling) and co-hybridizing to the same microarray, a direct comparative analysis of protein expression can be performed using as little as 100 ìg of total protein. This method allows a large number of samples to be screened in parallel on identical arrays.

Applications:

- High-throughput analysis of protein expression
- Direct measurement of protein expression at the gene product or post-translational levels

Development Status:

- The microarrays' performance was tested by proteomic profiling of two NCI-60 cancer cell lines (Renal UO-31 and Leukemia HL-60), demonstrating a high level of reproducibility.
- The microarrays' performance was further evaluated by analysis of the protein expression profiles of 12 Borderline ovarian and 9 Adenocarcinoma ovarian tumors using normal ovarian surface epithelial cells as a reference cell line. It was possible to detect 77 proteins that showed statistically significant ($p<0.05$) differences distinguishing Borderline tumors and Adenocarcinoma tumors, demonstrating that the novel microarrays described are useful tools for proteomics.

Inventors:

Cassio S. Baptista (NCI)
Lionel Best (NCI)
David J. Munroe (NCI)

Patent Status:
DHHS Reference No. E-207-2006/0 --
U.S. Provisional Application No. 60/797,301 filed 02 May 2006

Licensing Status:
Available for non-exclusive or exclusive licensing.

Collaborative Research Opportunity:
The NCI-Laboratory of Molecular Technology is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize this novel monoclonal antibody microarray. Please contact Betty Tong, Ph.D. at 301-594-4263 or tongb@mail.nih.gov for more information.

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Cancer Peptides of NY-ESO-1/CAG-3

Description of Invention:
The current invention embodies the identification, isolation and cloning of a gene encoding a novel tumor antigen, NY ESO-1/CAG-3, as well as cancer peptides thereof and antigenic cancer epitopes contained within the cancer peptides. This novel antigen is recognized by cytotoxic T lymphocyte clones derived from the TIL586 (tumor infiltrating lymphocyte) cell line in an HLA restricted manner.

The inventors believe that cancer peptides which are encoded by the NY ESO-1/CAG-3 gene represent potential cancer vaccines, protecting an individual from development of cancer by inhibiting the growth of cells or tumors which express the NY ESO-1/CAG-3 antigen. Also embodied in the invention are pharmaceutical compositions comprising the NY ESO-1/CAG-3 antigen, peptide, or an antigenic cancer epitope thereof in combination with one or more immunostimulatory molecules. These compositions represent potential anticancer therapeutics, stimulating NY ESO-1/CAG-3-specific T cells to elicit an anti-cancer immunogenic response and thereby eliminating or reducing the cancer. While these vaccines and pharmaceutical compositions may be developed for use against a variety of cancers, data obtained to date indicate that they may be of particular value for use against melanoma.

Methods for diagnosing cancer via the detection of NY ESO-1/CAG-3 are also embodied in the invention.

Inventors:
Steven A. Rosenberg (NCI) et al.

Patent Status:
DHHS Reference No. E-265-1997/0 --
U.S. Patent No. 7,084,239 issued 01 Aug 2006

Licensing Status:
Available for non-exclusive licensing or exclusive licensing.

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Methods of Identifying and Treating Tumors that Express Erythropoietin Receptor Protein (EPOR)

Description of Invention:
The inventors have discovered that EPO and EPOR are co-expressed in tumors of von Hippel-Lindau (VHL) patients and in tumors of sporadic renal tumor patients. Ligands that bind to EPOR but do not activate the receptor can target specific tumor cells with minimal detrimental effect on normal cells.

Applications:

- Treatment and diagnosis of renal tumors in sporadic and kidney dialysis patients
- Treatment and diagnosis of multiple tumors in different organs in patients with von Hippel-Landau patients
- Treatment and diagnosis of pheochromocytomas
- Treatment and diagnosis of eye and CNS hemangioblastomas

Inventors:
Zhengping Zhuang et al. (NINDS)

Patent Status:
DHHS Reference No. E-274-2004/0-US-01 --
U.S. Provisional Application No. 60/611,616 filed 20 Sep 2004
International Patent Application No. PCT/US2005/033850 filed 20 Sep 2005, which published as WO 2006/034354 on 30 Mar 2006

Licensing Status:
Available for non-exclusive or exclusive licensing.

Collaborative Research Opportunity:
In addition to licensing, the technology is available for further development through collaborative research opportunities with the inventors. For further information regarding collaborative research opportunities, please contact Dr. Martha Lubet at email: lubetm@mail.nih.gov or telephone: 301/435-3120.

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Diagnostic and Therapeutic Use of SPANX-N Genes in Cancer and Fertility

Description of Invention:

Cancer is the second leading cause of death in United States and it is estimated that there will be approximately 600,000 deaths caused by cancer in 2006. In spite of the success of cancer screening and early diagnosis cancer still remains a life threatening disease. There is a great need for the development of new markers and new therapeutic strategies that would more accurately predict the outcome of the disease and aid in the proper management of cancer. Antibody-based strategies have taken a lead among the new cancer therapeutic approaches.

This technology describes the identification of the link between expression of individual members of the SPANX-gene cluster and malignancies including prostate cancer. SPANX-genes consist of two subfamilies, SPANX-A/D and SPANX-N1/N5. The invention provides SPANX polypeptides, nucleic acids and antibodies that could be useful for detecting and treating prostate or other cancers. The SPANX-N genes are a family of related genes that are expressed in normal testis and in tumor cells in humans including melanoma, bladder carcinomas and myelomas. The SPANX cancer/testis antigens thus represent good candidates for diagnosis or treatment of several cancers. The present invention also describes a new approach for mutation screen of the SPANX gene cluster, including gene amplification, linking predisposition to prostate cancer with a specific architecture of the SPANX gene cluster. Additionally, due to the differential localization of SPANX-proteins in the spermatozoa, the mutational screen can be also used for diagnostics of infertility. Developed antibodies against SPANX-A/D and SPANX-N1/N5 proteins can be used for i) diagnostics of cancer, ii) diagnostics of infertility and iii) for the development of new contraceptives.

Applications:

- Novel antibodies to SPANX-A/D and SPANX-N1/N5
- New approach for mutation screen of SPANX gene cluster
- Antibodies can be used for diagnosis and development of immunotherapeutics for several cancers including prostate
- Compounds can also be used for the diagnosis of infertility and development of new contraceptives.

Market:

- 600,000 deaths from cancer related diseases estimated in 2006
- The technology platform involving novel antibodies for the diagnosis and therapeutics of several cancers has a potential market of more than 7 billion US dollars
- The technology platform has additional market in fertility related diagnostics and therapeutics.

Development Status:
The technology is currently in the pre-clinical stage of development.

Inventors:
Natalay Kouprina et al. (NCI)

Patent Status:
DHHS Reference No. E-212-2004/0 --
U.S. Provisional Application No. 60/636,811 filed 15 Dec 2004
PCT Application No. PCT/US2005/045317 filed 15 Dec 2005, which published a WO 2006/065938 on 22 Jun 2006

Relevant Publication:

1. N Kouprina et al. The SPANX gene family of cancer/testis-specific antigens: rapid evolution and amplification in African great apes and hominids. Proc Natl Acad Sci USA. 2004 Mar 2;101(9):3077-3082. Epub 2004 Feb 18, doi 10.1073/pnas.0308532100. [PubMed abs]
2. N Kouprina et al. Dynamic structure of the SPANX gene cluster mapped to the prostate cancer susceptibility locus HPCX at Xq27. Genome Res. 2005 Nov;15(11):1477-1486. [PubMed abs]
3. N Kouprina and V Larionov. TAR cloning: insights into gene function, long-range haplotypes, and genome structure and evolution. Nat Rev Genet. 2006 Oct;7(10):805-812. [PubMed abs]
4. N Kouprina et al. SPANX-N gene cluster at Xq27: a new group of cancer-testis antigen genes encoding acrosomal proteins. Submitted to Cancer Research, 2006.

Licensing Status:
Available for exclusive and non-exclusive licensing.

Collaborative Research Opportunity:
The National Cancer Institute Laboratory of Biosystems and Cancer is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize this new diagnostic marker for malignancy and infertility and new targets for immuno-cancer therapy. Please contact Betty Tong, Ph.D. at 301-594-4263 or tongb@mail.nih.gov for more information.

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Diagnostic and Therapeutic Strategies for Metastatic Hepatocellular Carcinoma by Targeting Osteopontin

Description of Invention:

Cancer is one of the leading causes of death in United States and it is estimated that there will be more than half a million deaths caused by cancer in 2006. For the last decade breast and prostate cancer survival rate has significantly increased thanks to contribution of screening, early detection and novel therapeutics. This success needs to be translated to other cancers as well, where there is a need of novel diagnostic and therapeutic strategies for successful disease management.

Osteopontin (OPN) is a well known serum prognostic marker for breast cancer. This technology identifies a 10 kD residue of OPN as a potential prognostic marker and therapeutic target for metastatic hepatocellular carcinoma (HCC). Mechanistically, OPN has been shown to be a novel substrate for MMP-9 and the 10kD fragment is demonstrated to be a mediator of cell invasion and metastasis. Short synthetic peptides against OPN have been shown to block OPN mediated cell invasion, providing a novel therapeutic approach targeting OPN. Finally, polyclonal antibodies against the 10kD fragment of OPN have been developed that can be used for detection of OPN in physiological fluids of HCC patients. This technology provides a novel therapeutic and diagnostic strategy for the management of HCC patients using OPN.

Development Status:

The technology is in the pre-clinical stage, animal studies are under way.

Inventors:

Vivian A. Takafuji (NCI) et al.

Patent Status:

DHHS Reference No. E-201-2006/0 --
U.S. Provisional Application No. 60/805,298 filed 20 Jun 2006

Relevant Publication:

1. A manuscript relating to this invention has been submitted for publication and will be available once accepted.
2. J Kim, SS Ki, SD Lee, CJ Han, YC Kim, SH Park, SY Cho, YJ Hong, HY Park, M Lee, HH Jung, KH Lee, SH Jeong. Elevated plasma osteopontin levels in patients with hepatocellular carcinoma. Am J Gastroenterol. 2006 Jul 18; Epub ahead of print, doi: 10.1111/j.1572-0241.2006.00679. [PubMed abs]
3. QH Ye, LX Qin, M Forgues, P He, JW Kim, AC Peng, R Simon, Y Li, AI Robles, Y Chen, ZC Ma, ZQ Wu, SL Ye, YK Liu, ZY Tang, XW Wang. Predicting hepatitis B virus-positive metastatic hepatocellular carcinomas using gene expression profiling and supervised machine learning. Nat Med. 2003 Apr; 9(4):416-423. [PubMed abs]

Licensing Status:
This technology is available for licensing under an exclusive or non-exclusive patent license.

Collaborative Research Opportunity:
The NCI Laboratory of Human Carcinogenesis is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize diagnostic and therapeutic strategies for metastatic hepatocellular carcinoma. Please contact Betty Tong at 301-594-4263 or tongb@mail.nih.gov for more information.

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ABCB1 Genotyping to Predict Paclitaxel Toxicity

Description of Invention:

Paclitaxel has been a frontline chemotherapeutic drug used for the treatment of various cancers including metastatic breast cancer and ovarian cancer. Its use has successfully prolonged patient survival. A major drawback of paclitaxel is the cytotoxic side-effects that are associated with it such as myologenic and neurogenic toxicities. The degree of such toxicities varies with individual patients. Predicting the extent of such toxicities following paclitaxel treatment will immensely help in defining optimal treatment schedules for each individual patient. Concurrently, it will significantly improve patient quality of life.

This technology describes the identification of three genetic markers in the ABCB1 (MDR-1, P-glycoprotein) gene that can be used to predict the degree of neutropenia and peripheral neuropathy that an individual will experience following paclitaxel treatment. These markers were identified using DNA from blood samples of cancer patients undergoing paclitaxel treatment. This technology can be developed into a routine blood test to identify patient subsets that are more susceptible to paclitaxel treatment associated neutropenia and neuropathy.

Applications:

- Three novel genetic markers that can predict extent of paclitaxel associated toxicities.
- A screening test based on ABCB1 genotype profiling using patient blood samples that predicts paclitaxel associated neutropenia and peripheral neuropathy.

Market:

The diagnostic market is worth about $3 billion by 2007 and estimated to grow further.

Development Status:

- The technology is a pilot study currently in the pre-clinical stage of development.
- A prospective ABCB1 genotype directed clinical trial is foreseen in the near future.

Inventors:

William D. Figg (NCI)
Alex Sparreboom (NCI)
Tristan M. Sissung (NCI)
Stephan Mielke (NCI)
et al.

Patent Status:

DHHS Reference No. E-237-2006/0 --
U.S. Provisional Application No. 60/807,453 filed 14 Jul 2006

Relevant Publication:
T. M Sissung et al. Association of ABCB1 genotypes with paclitaxel-mediated neutropenia and peripheral neuropathy, To be submitted to Clinical Pharmacology and Therapy.

Licensing Status:
Available for non-exclusive or exclusive licensing.

Collaborative Research Opportunity:
The NCI Medical Oncology Branch is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize ABCB1 genotyping to predict paclitaxel toxicity. Please contact Betty Tong, Ph.D. at 301-496-0477, tongb@mail.nih.gov for more information.

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Agonist Epitopes for Renal Cell Carcinoma

Description of Invention:

Approximately 30,000 patients are diagnosed with renal cell carcinoma (RCC) each year in the United States, and an estimated 12,000 patients die of this disease. Most patients are diagnosed with advanced local disease or metastatic disease. Metastatic RCC carries a poor prognosis with median survivals in the range of 10-12 months. Drugs that inhibit VEGF receptor tyrosine kinases such as Sorafenib and Sunitinib have recently been approved by the FDA to treat metastatic RCC. Although a significant percentage of patients will achieve a partial response or disease stabilization with these agents, complete responses are rare and disease progression eventually ensues. RCC is unusual among solid tumors as it appears to be susceptible to immunotherapy. Cytokines such as IL-2 and IFN-alpha nonspecifically stimulate the immune system resulting in disease regression. Unfortunately, these drugs achieve success in only a minority (15-20%) of the metastatic RCC patient population. Therefore, new methods are needed to improve on immune-based therapies and expand the curative potential of therapies for patients with RCC.

The present invention discloses peptides and antigen epitopes specific for RCC for use in the diagnosis, vaccination, or adoptive infusion of antigen specific T cells to treat patients with metastatic RCC. The immunogenic peptide, which binds to the HLA-A11 epitope, was identified in a patient with metastatic RCC that under went an investigational allogeneic hematopoietic stem cell transplant. Cancer regression occurred post-transplant consistent with a graft-vs-tumor effect. A T-cell line, expanded from the patient's blood cells at the time of tumor regression, was isolated and subsequently shown to kill the patients RCC cells in vitro. Expression and sequencing studies revealed that the patient's T-cells recognize an antigen epitope derived from a human endogenous retrovirus (HERV). Further, pre-clinical studies using quantitative real-time PCR found that this HERV was expressed in eight of 14 RCC tumor cell lines with no HERV expression in patient fibroblasts, hematopoietic cells or in c-DNAs analyzed from 48 different normal tissues. Plans are underway to investigate the immunogenic potential of this peptide to induce expansion of T-cells that are cytotoxic to RCC cells in vitro and in pre-clinical animal models.

Inventors:

Richard W. Childs et al. (NHLBI)

Patent Status:

DHHS Reference No. E-122-2006/0 --
U.S. Provisional Application No. 60/783,350 filed 17 Mar 2006

Relevant Publication:

1. I Espinoza-Delgado and RW Childs, "Nonmyeloablative transplantation for solid tumors: a new frontier for allogeneic immunotherapy," Expert Rev Anticancer Ther. 2004 Oct;4(5):865-75. [PubMed abs]

2. Y Takahashi and RW Childs, "Nonmyeloablative transplantation: an allogeneic-based immunotherapy for renal cell carcinoma," Clin Cancer Res. 2004 Sep 15;10(18 Pt 2):6353S-9S. [PubMed abs]
3. R Childs et al., "Regression of Metastatic Renal-Cell Carcinoma after Nonmyeloablative Allogeneic Peripheral-Blood Stem-Cell Transplantation," N Engl J Med. 2000 Sep 14;343(11):750-758. [PubMed abs]
4. Marco Bregni, Naoto T. Ueno, and Richard Childs. Meeting Report: The Second International Meeting on Allogeneic Transplantation in Solid Tumors (ATST). Bone Marrow Transplantation (Submitted 2006).

Licensing Status:
Available for non-exclusive or exclusive licensing.

Collaborative Research Opportunity:
The Hematology Branch of the NHLBI is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize therapeutic treatment approaches targeting this novel RCC antigen. Please contact Dr. Richard Childs at 301/594-8008 or childsr@nhlbi.nih.gov for more information.

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Identification of a Novel Folliculin Interacting Protein, FNIP-1

Description of Invention:

Renal cell carcinoma is an important health problem in the United States, affecting 32,000 individuals each year and resulting in 12,000 deaths annually. Several familial cancer disorders with a renal epithelial tumor phenotype have been well characterized and the causative genes have been identified including the Birt-Hogg-Dube (BHD) gene. The BHD gene encodes a protein called folliculin. Mutations in BHD lead to the development of Birt-Hogg Dube syndrome, a dermatologic disorder associated with an increased risk for developing renal cancer, spontaneous pneumothorax and lung cysts.

This invention describes the cloning and characterization of the first folliculin interacting protein FNIP-1 and purified antibodies that selectively bind to an epitope of FNIP-1. FNIP-1 interacts with subunits of AMP-dependent protein kinase (AMPK). The FNIP-1/AMPK interaction places FNIP-1 and folliculin as potential interactors in cellular pathways essential for regulating cell growth and cell size. FNIP-1 may play an important role in folliculin's function. Identification of the FNIP-1 cDNA sequence will enable evaluation of sporadic renal tumors, enable the development of cancer diagnostics and aid in the treatment of BHD skin lesions.

Inventors:

Laura S. Schmidt et al. (NCI)

Patent Status:

DHHS Reference No. E-139-2005/0 --
U.S. Provisional Application No. 60/689,749 filed 09 Jun 2005

Licensing Status:

Available for non-exclusive or exclusive licensing.

Collaborative Research Opportunity:

The National Cancer Institute, Center for Cancer Research, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize folliculin interacting protein FNIP-1 and purified antibodies. Please contact Kathy Higinbotham at 301-846-5465 or higinbok@mail.nih.gov for more information.

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Sensitive Antibody-based Assay for the Measurement of c-Met Concentration Shed in Bodily Fluids Useful in the Diagnosis and Prognosis of Cancer

Description of Invention:
This invention described and claimed in these patent applications provide for methods and assays which may be used to diagnose and follow the progression of cancers associated with c-Met expression. The data supporting this application suggests that c-Met expression may be an appropriate biomarker in certain types of cancer. In particular, the applications describe a sensitive assay useful for monitoring levels of c-Met shed in the urine or blood. The assay was developed using commercially available reagents. The applications contain data, derived from patient samples, supporting the clinical utility of the assay. In particular, the data shows the use of the assay to detect levels of shed c-Met in patients with bladder cancer, renal cancers and prostate cancer. Data showing the applicability of the assay for glioblastoma was derived using murine models of cancer for glioblastoma. Data showing the applicability of the assay for breast cancer, melanoma and prostate cancer was derived using various human cell line model systems.

HGF/met signaling has been most widely studied in settings related to cancer. It has been demonstrated to have a role in metastasis and angiogenesis. In addition to cancer, HGF activity has also been linked, through its role in apoptosis, to Alzheimer's disease and cardiovascular disease.

Inventors:
Donald Bottaro and Pathirage G. Dharmawardana (both of NCI)

Patent Status:
DHHS Reference No. E-261-2005/0 --
U.S. Provisional Application No. 60/734,993 filed 08 Nov 2005

DHHS Reference No. E-261-2005/1 --
U.S. Provisional Application No. 60/780,626 filed 09 Mar 2006

At this time only U.S. Patent protection has been sought for this technology. There are no foreign counterpart patent applications.

Relevant Publication:
These applications have not been published. The investigators presented their work in a poster session at the AACR Meeting April 16-20, 2005 (Abstract 2788). At this time there are no other publications related to this work.

Licensing Status:
Available for non-exclusive or exclusive licensing.

Collaborative Research Opportunity:
The National Cancer Institute, Urologic Oncology Branch, is seeking statements of capability or interest from parties interested in collaborative research to further develop,

evaluate, or commercialize HGF/c-Met signaling as it relates to tissue repair and regeneration, cancer, and other diseases. Please contact Brian W. Bailey, Ph.D. at (301) 451-2158 or bbailey@mail.nih.gov for more information.

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Antibodies That Specifically Recognize S100A15, A Protein Involved in Epidermal Differentiation and Inflammation

Description of Invention:
This technology describes rabbit polyclonal antibodies that recognize the human and mouse S100A15 proteins. S100A15 is involved in epidermal differentiation and inflammation, and is dysregulated in skin tumors and inflammatory psoriasis.

Applications:

- Diagnostic tool for evaluation of agents that alter skin pathology
- Research tool to probe the role of S100A15 during epidermal maturation, skin carcinogenesis, and inflammation
- Diagnostic tool for the clinical evaluation of skin tumors and inflammatory diseases such as psoriasis

Development Status:
Early stage

Inventors:
Ronald Wolf (NCI)
Stuart H. Yuspa (NCI)
Paul Goldsmith (NCI)
Christopher J. Voscopoulos (NCI)

Patent Status:
DHHS Reference No. E-145-2006/0 -- Research Tool

Relevant Publication:
R Wolf et al., "The mouse S100A15 ortholog parallels genomic organization, structure, gene expression, and protein-processing pattern of the human S100A7/A15 subfamily during epidermal maturation," *J Invest Dermatol* advance online publication 09 March 2006, doi: 10.1038/sj.jid.5700210.

Licensing Status:
Available for non-exclusive licensing under a Biological Materials License.

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Novel Methods and Compositions for Diagnosing AIDS and Other Diseases Involving Immune System Activation

Description of Invention:

Available for licensing and commercial development are methods and compositions suitable for monitoring the progression of AIDS and other diseases whose progression involves immune system activation in mammals, such as cancer, atherosclerosis, Alzheimer's disease, inflammation, autoimmune disorder, allergic asthma, Crohn's disease, Grave's disease, lupus, multiple sclerosis, Parkinson's disease, allograft transplant rejection, and graft vs. host disease.

In particular, the invention relates to the use of the TRAIL (TNF-related apoptosis-inducing ligand) and TRAIL compounds to monitor the progression of AIDS, and such other diseases. This is accomplished by assessing the presence or concentration of TRAIL, especially mTRAIL, sTRAIL, the TRAIL DR5 receptor molecule, and biological molecules that activate TRAIL or its receptor. These biological molecules include p53, alpha- and beta-interferon, as well as additional compounds such as CD69 and HLA-DR. Also claimed are kits for immunoassays to determine the presence or concentration of a TRAIL compound in a biological fluid, suitable for determining whether the mammal suffers from any of the above diseases.

TRAIL can be used as a new surrogate biomarker to monitor the progression of HIV infection and other conditions and diseases associated with immune system activation. In the case of HIV infection, measuring levels of this biomarker can distinguish among infected individuals with high viral load, infected individuals with low viral load, and uninfected individuals. Only two surrogate markers are currently recognized by the Food and Drug Administration as clinically relevant to HIV progression, HIV viral load and the absolute number of peripheral CD4+ T cells. Tests for assessing HIV viral load employ PCR, the use of which has drawbacks, including cross-contamination. TRAIL has mechanistic implications for HIV-1 pathogenesis and directly correlates to viral load but not necessarily inversely with CD4+ T cell count. Other surrogate markers have been proposed but do not consistently reflect AIDS progression in all individuals or may result in overlooking possible treatments that may affect disease progression but do not affect the chosen marker. Therefore, use of this new biomarker to assess disease progression in infected individuals and to evaluate the effectiveness of various treatment regimens has several advantages over currently used methods, since TRAIL is a death molecule involved in CD4+ T cell depletion in HIV/AIDS. TRAIL, its receptor, and activating molecules can all be used as sensitive markers for CD4 T cell activation and apoptosis.

Inventors:

Gene M. Shearer and Jean-Philippe Herbeuval (NCI)

Patent Status:

DHHS Reference No. E-045-2004/0 --
U.S. Provisional Application No. 60/564,588 filed 23 Apr 2004

DHHS Reference No. E-045-2004/1 --
U.S. Provisional Application No. 60/634,255 filed 12 Dec 2004

DHHS Reference No. E-045-2004/2 --
PCT Application No. PCT/US2005/13554 filed 21 Apr 2005

Relevant Publication:

4. Herbeuval JP, Hardy AW, Boasso A, Anderson SA, Dolan MJ, Dy M, Shearer GM. Regulation of TNF-related apoptosis-inducing ligand on primary CD4+ T cells by HIV-1: role of type I IFN-producing plasmacytoid dendritic cells. Proc Natl Acad Sci U S A. 2005 Sep 27;102(39):13974-9.
5. Herbeuval JP, Grivel JC, Boasso A, Hardy AW, Chougnet C, Dolan MJ, Yagita H, Lifson JD, Shearer GM "CD4+ T-cell death induced by infectious and noninfectious HIV-1: role of type 1 interferon-dependent, TRAIL/DR5-mediated apoptosis" Blood. 2005 Nov 15;106(10):3524-31.
6. Herbeuval JP, Boasso A, Grivel JC, Hardy AW, Anderson SA, Dolan MJ, Chougnet C, Lifson JD, Shearer GM "TNF-related apoptosis-inducing ligand (TRAIL) in HIV-1-infected patients and its in vitro production by antigen-presenting cells" Blood. 2005 Mar 15;105(6):2458-64.

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Use of CYP1B1*3 Genotyping to Predict Survival to Docetaxel Treatment in Androgen-Independent Prostate Cancer

Description of Invention:
Androgen-independent prostate cancer (AIPC) remains the second leading cause of cancer death in men in developed nations, and it is estimated that one in six men will be diagnosed with prostate cancer. The use of docetaxel has been shown to prolong survival rate and improve the quality of life in patients suffering from AIPC.

Scientists at NIH have identified a genetic marker called CYP1B1*3 (4326C>G; L432V) that can predict survival in patients with prostate cancer prior to treatment with docetaxel. In a study of 25 patients suffering from AIPC, patients that were homozygous or heterozygous wild-type for the 4326C>G transition had an increased mean survival time after docetaxel treatment when compared to patients carrying the homozygous variant. These patients showed a survival rate of 15.3 months compared to 7.5 months for those homozygous with the variant CYP1B1*3.

This genetic marker (CYP1B1*3) can be measured in DNA obtained from a blood sample. This technology can be potentially used as a diagnostic tool to predict the patient's propensity to respond to docetaxel treatment when being treated for AIPC.

Inventors:
William D. Figg et al. (NCI)

Patent Status:
DHHS Reference No. E-307-2005/0 --
U.S. Provisional Application No. 60/716,439 filed 12 Sep 2005
PCT Application No. PCT/US06/34769 filed 08 Sep 2006

Licensing Status:
In addition to licensing, the technology is available for further development through collaborative research opportunities with the inventors.

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Method for Determining Redox Status of a Tissue

Description of Invention:
This invention describes methods for diagnosis and therapy of cancer and other pathologies associated with oxidative stress by administering a nitroxyl contrast agent and employing magnetic resonance imaging (MRI). Tumor tissues exhibit viable but hypoxic regions that allow them to reduce nitroxide compounds more efficiently than normal tissue. The paramagnetic relaxivity of nitroxide compounds makes it possible to use standard MRI scanners to determine the redox status of tissue in vivo. By determining the redox status of a tumor it is possible to not only diagnose a tumor due to its enhanced reduction of intracellular nitroxide contrast agent, but also to determine appropriate radiation treatment fields spatially to deliver therapeutic doses of radiation, and to determine appropriate timing sequences after the administration of a nitroxide contrast agent such that the maximum difference between normal and tumor tissue with respect to the radioprotective form of the nitroxide is present in the normal tissue, thereby limiting collateral damage to the normal tissue.

Inventors:
James B. Mitchell et al. (NCI)

Patent Status:
DHHS Reference No. E-258-2005/0 --
U.S. Provisional Application No. 60/707,518 filed 11 Aug 2005

Licensing Status:
In addition to licensing, the technology is available for further development through collaborative research opportunities with the inventors.

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Autoantibody Screening for Cancer Diagnosis

Description of Invention:
There are a number of specific antigens, such as alpha-fetal protein (AFP), nonmucinous ovarian cancer antigen (CA125), vascular endothelial growth factor (VEGF), prostate-specific antigen (PSA), which are secreted into the serum of patients who have particular cancers. Kits for detecting these antigens are generally used as a means of diagnosing patients as having a specific cancer. However, the current methods suffer from a lack of sensitivity.

The instant technology provides a method for the early diagnosis of different cancers that does not suffer the drawbacks of the current assays. The inventors observed that auto-antibodies against the cancer marker antigens can be detected in the serum of patients with particular cancers. This new technology is designed to screen for the autoantibodies for a spectrum of secreted tumor antigens in a single assay (BBA, in press). This provides a highly sensitive assay for diagnosing cancer at an early stage, or when the tumor is of a very small size. Claims of the instant invention are drawn to methods and kits for performing this analysis as a means of diagnosing cancer.

Inventors:
Yoon S. Cho-Chung (NCI)

Patent Status:
DHHS Reference No. E-057-2006/0 --
U.S. Provisional Application No. 60/751,133 filed 16 Dec 2005

Licensing Status: In addition to licensing, the technology is available for further development through collaborative research opportunities with the inventors.

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ELISA Assay of Serum Soluble CD22 to Assess Tumor Burden/Relapse in Subjects with Leukemia and Lymphoma

Description of Invention:
Disclosed are methods of using previously unknown soluble forms of CD22 (sCD22) present in the serum of subjects with B-cell leukemias and lymphomas to assess tumor burden in the subjects. Also disclosed are methods of diagnosing or prognosing development or progression of a B-cell lymphoma or leukemia in a subject, including detecting sCD22 in a body fluid sample taken or derived from the subject, for instance serum. In some embodiments, soluble CD22 levels are quantified. By way of example, the B-cell lymphoma or leukemia can be hairy cell leukemia, chronic lymphocytic leukemia, or non-Hodgkin's lymphoma. Soluble CD22 in some embodiments is detected by a specific binding agent, and optionally, the specific binding agent can be detectably labeled.

Also disclosed are methods of selecting a B-cell lymphoma or leukemia therapy that include detecting an increase or decrease in sCD22 levels in a subject compared to a control, and, if such increase or decrease is identified, selecting a treatment to prevent or reduce B-cell lymphoma or leukemia or to delay the onset of B-cell lymphoma or leukemia.

Other embodiments are kits for measuring a soluble CD22 level, which kits include a specific binding molecule that selectively binds to the CD22, e.g. an antibody or antibody fragment that selectively binds CD22.

Further disclosed methods are methods for screening for a compound useful in treating, reducing, or preventing B-cell lymphomas or leukemias, or development or progression of B-cell lymphomas or leukemias, which methods include determining if application of a test compound lowers soluble CD22 levels in a subject, and selecting a compound that so lowers sCD22 levels.

Inventors:
Robert Kreitman et al. (NCI)

Patent Status:
DHHS Reference No. E-065-2002/0 --
U.S. Patent Application No. 10/514,910 filed 16 Nov 2004, with priority to 20 May 2002

Licensing Status: In addition to licensing, the technology is available for further development through collaborative research opportunities with the inventors.

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Identification of Biomarkers by Serum Protein Profiling

Description of Invention:

This invention describes serum features that distinguish colorectal carcinoma malignant patient samples versus healthy samples using surface-enhanced laser desorption ionization time-of-flight (SELDI-TOF) mass spectrometry. By comparing healthy versus malignant samples, the investigators were able to identify thirteen (13) serum features that have been validated using an independently collected, blinded validation set of 55 sera samples. The features are characterized by the mass to charge ratio (m/z ratio). The investigators have shown that SELDI-TOF based serum marker protein profiling enables minimally invasive detection of colon cancer with 96.7 percent sensitivity and 100 percent specificity.

Colorectal cancer is the third most common cancer and the third leading cause of cancer-related mortality in the United States. Current diagnostic methods for colorectal cancer have a large non-compliance rate because of discomfort, e.g., sigmoidoscopy or colonoscopy, or have a high rate of false positive results, e.g., fecal occult blood tests. The claimed invention has the potential to be a widely used, easy-to-use, and inexpensive diagnostic.

Inventors:

Thomas Ried and Jens Habermann (NCI)

Patent Status:

DHHS Reference No. E-106-2005/0 --
U.S. Provisional Application No. 60/664,681 filed 22 Mar 2005

Licensing Status: In addition to licensing, the technology is available for further development through collaborative research opportunities with the inventors.

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Mitotic Spindle ASPM as a Diagnostic Marker for Neoplasia and Uses Thereof

Description of Invention:

Cancer is responsible for approximately 23% of deaths in the United States of America. A high percentage of these deaths are caused by the lack of a precise diagnostic method that can detect malignancy in a particular tissue at an early stage. This invention provides for diagnostic methods, compositions, and kits that are useful for identifying neoplasia by measuring Abnormal Spindle-like Microcephaly associated (ASPM) expression in a patient sample. The ASPM gene is the human ortholog of the Drosophila melanogaster 'abnormal spindle' gene (asp), which is essential for normal mitotic spindle function in embryonic neuroblasts. By measuring ASPM expression levels one can also determine if a particular subject has a higher propensity to develop neoplasia. This invention is particularly useful in detecting neoplasia in hard to diagnose cancers like ovarian and uterine cancer.

Inventors:

Paul K. Goldsmith (NCI)
Vladmir Larionov (NCI)
Natalay Kouprina (NCI)
John I. Risinger (NCI)

Patent Status:

DHHS Reference No. E-210-2005/0 --
U.S. Provisional Application No. 60/696,212 filed 01 Jul 2005
Licensing Status: In addition to licensing, the technology is available for further development through collaborative research opportunities with the inventors.

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Quantitative Assay of the Angiogenic and Antiangiogenic Activity of a Test Molecule

Description of Invention:
The invention provides a method of measuring the angiogenic or antiangiogenic activity of a test molecule. The method comprises obtaining an embryonated fowl egg, creating a window in the shell of the fowl egg, such that the CAM membrane is exposed, providing to a test region of interest on the CAM a substrate, administering to a vessel located in the CAM a test molecule, administering to a vessel located in the CAM a fluorescent-labeled particle, such that the fluorescent-labeled particle travels through each vessel contained in the test region of interest, removing the substrate and the test region of interest from the fowl egg, capturing a three-dimensional image of the test region of interest, wherein the three-dimensional image comprises a plurality of pixels, such that a fluorescent vascular density (FVD) value can be assigned to the test region of interest, and comparing the FVD value of the test region of interest with the FVD value of a control region of interest that was prepared in the same manner as the test region of interest but without the administration of a test molecule, such that the angiogenic or antiangiogenic activity of the test molecule is measured. A lower FVD value of the test region of interest as compared to the FVD value of the control region of interest is indicative of the test molecule being useful as an inhibitor of angiogenesis. Conversely, a higher FVD value of the test region of interest as compared to the FVD value of the control region of interest is indicative of the test molecule being useful as a stimulator of angiogenesis.

Inventors:
Steven K. Libutti (NCI)

Patent Status:
DHHS Reference No. E-152-2002/0 --
U.S. Provisional Application No. 60/371,010 filed 09 Apr 2002
PCT Application No. PCT/US03/10932 filed 09 Apr 2003, which published as WO 03/086299 on 23 Oct 2003
U.S. Patent Application No. 10/510,652 filed 28 Oct 2004

DHHS Reference No. E-152-2002/1 --
U.S. Patent Application No. 11/014,472 filed 16 Dec 2004

Licensing Status: In addition to licensing, the technology is available for further development through collaborative research opportunities with the inventors.

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Minimally Immunogenic Variants of SDR-Grafted Humanized Antibody CC49 and Their Use

Description of Invention:

Tumor Associated Glycoprotein 72 (TAG)-72 is an oncofetal antigen expressed on a majority of human carcinomas, including colorectal, gastric, pancreatic, breast, lung, and ovarian. The murine monoclonal antibody (mAb) CC49 specifically recognizes TAG-72 and has a higher affinity for TAG-72 than its predecessor, B72.3.

The present invention relates to humanized monoclonal antibodies that have high binding affinity for the tumor-associated glycoprotein (TAG)-72 with minimal immunogenicity. This anti-TAG-72 antibody binds to the same epitope as the CC49 murine variant developed at the National Cancer Institute. The variants of CC49 described in this patent application have been shown to have a decreased immune response, with comparable binding affinity, than the parent murine antibodies.

These variants have potential benefits for use in the detection and/or treatment of a range of human carcinomas. Certain fields of use may not be available. Please contact OTT for information regarding the availability of specific fields of use.

Inventors:

Syed Kashmiri (NCI)
Jeffrey Schlom (NCI)
Eduardo Padlan (NIDDK)

Patent Status:

DHHS Reference No. E-323-2003/0 --
U.S. Provisional Application No. 60/493,903 filed 29 Aug 2003
PCT Application No. PCT/US04/28004 filed 27 Aug 2004

Relevant Publication: This variant was published in Kashmiri et al., “Minimizing Immunogenicity of the SDR-grafted Humanized Antibody CC49 by Genetic Manipulation of the Framework Residues,” Molecular Immunology, 40 (2003), 337-349.

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Autotaxin: Motility Stimulating Protein Useful in Cancer Diagnosis and Therapy

Description of Invention:
Cell motility plays an important role in embryonic events, adult tissue remodeling, wound healing and metastasis of tumor cells. Some tumor cells produce proteins termed "autocrine motility factors" that stimulate motility in tumor cells. This invention describes a novel tumor protein called Autotaxin ("ATX") that stimulates both random and directed migration of human A2058 melanoma cells. ATX is a member of the nucleotide phosphodiesterase and pyrophosphatase (NPP) family of proteins but is the only member of the family that stimulates motility. It is also the only member shown to possess lysophospholipase D activity.

This invention can provide a functional marker that can directly estimate the invasive potential of a particular human cancer. One could also use this invention as an assay for a particular secreted marker in body fluids, or in tissues. Other uses include the detection, diagnosis, and treatment of human malignancies, and other inflammatory, fibrotic, infectious and healing disorders.

Inventors:
Mary Stracke (NCI)
Lance Liotta (NCI)
Elliot Schiffman (NCI)
Jerry Krutzch (NCI)
and Jun Murata (NCI)

Patent Status:
DHHS Reference No. E-142-1990/2 --
U.S. Patent Application filed 16 Feb 2005
Licensing Status: In addition to licensing, the technology is available for further development through collaborative research opportunities with the inventors.

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Compositions and Methods for Diagnosis and Treatment of Chemotherapy-Resistant Neoplastic Disease

Description of Invention:

The present invention relates to compositions and methods for the treatment of a neoplastic disease state (i.e. tumors) using RNA interference-mediated down regulation of stathmin expression. This invention also discloses methods for determining the presence or predisposition to a neoplastic disease state.

Stathmin is a cytoplasmic protein that is highly expressed in many different types of tumors such as leukemias, lung cancers and brain tumors. Stathmin is believed to be involved in the regulation of the cell cycle via its interactions with microtubules. Lowering the expression of stathmin in tumor cells using RNA interference (RNAi) technology causes a decrease in tumor cell growth and also causes such cells to become more sensitive to the effects of standard chemotherapeutic agents.

Accordingly, the delivery of stathmin RNAi oligonucleotides either alone or in combination with standard chemotherapies may be used to treat patients with various tumors. For example, retroviruses or adeno-associated viruses containing stathmin RNAi oligonucleotides could be delivered to brain tumors in order to decrease cell growth and increase sensitivity to standard chemotherapies.

Inventors:

John Park (NINDS)

Patent Status:

DHHS Reference No. E-192-2004/0 --
U.S. Provisional Application No. 60/571,296 filed 15 May 2004
PCT Application No. PCT/US2005/016924 filed 13 May 2005, which published as WO 2005/120520 on 22 Dec 2005

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SH2 Domain Binding Inhibitors (E-262-2000)

Description of Invention:
Signal transduction processes underlie the transfer of extracellular information to the interior of the cell and ultimately to the nucleus. A variety of signal transduction processes are critical for normal cellular homeostasis, with protein-tyrosine kinases (PTKs) playing central roles in many of these pathways. Examples of such PTKs include the PDGF receptor, the FGF receptor, the HGF receptor, members of the EGF receptor family, such as the EGF receptor, erb-B2, erb-B3 and erb-B4, the src kinase family, Fak kinase and the Jak kinase family. Protein-tyrosine phosphorylation that results from the action of PTKs can modulate the activity of certain target enzymes as well as facilitate the formation of specific multi-protein signaling complexes through the actions of homologous protein modules termed Src homology 2 (SH2) domains, which recognize specific phosphotyrosyl containing sequences. A malfunction in this system through tyrosine kinase overexpression and/or deregulation can be manifested by various oncogenic and hyperproliferative disorders, including cancers, inflammation, autoimmune disease, hyperproliferative skin disorders, psoriasis and allergy/asthma, etc. The disclosed compounds, e.g. peptides, preferably, macrocyclic peptides, are Grb2 SH2 domain signaling antagonists with enhanced binding affinity. The claims of the current application are directed to compositions of matter and methods of use which provide for the diagnosis, testing and treatment of the aforementioned disease states.

Inventors:
Terrence R. Burke Jr. et al. (NCI)

Patent Status:
DHHS Reference No. E-262-2000/0 --
U.S. Patent No. 6,977,241 issued 20 Dec 2005

DHHS Reference No. E-262-2000/1 --
U.S. Patent Application No. 10/517,717 filed 17 Mar 2005, claiming priority to 28 Jun 2002

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Diagnostic Tool for Diagnosing Benign Versus Malignant Thyroid Lesions

Description of Invention:
The present invention relates to methods for the diagnosis and staging of thyroid cancer. The invention employs analysis of gene expression using microarrays or quantitative RT-PCR to distinguish between malignant and benign tumors. Primer and probe sequences are described that represent a six gene or ten gene model for diagnosing benign and malignant thyroid cancer. Analysis of the expression of these genes in thyroid lesions taken from patients could be used for molecular classification of the lesions. As analysis of thyroid lesions by traditional means, such as fine needle biopsy with cytologic examination, can result in indeterminate results, the current invention may provide a superior method for molecular diagnoses of thyroid cancer.

Inventors:
Steven Libutti et al. (NCI)

Patent Status:
DHHS Reference No. E-124-2004/0 --
U.S. Provisional Application No. 60/560,900 filed 09 Apr 2004

DHHS Reference No. E-124-2004/1 --
U.S. Provisional Application No. 60/622,643 filed 26 Oct 2004

DHHS Reference No. E-124-2004/2 --
PCT Patent Application No. PCT/US05/12289 filed 11 Apr 2005

Relevant Publication: This research is described, in part, in Mazzanti et al., "Using gene expression profiling to differentiate benign versus malignant thyroid tumors," Cancer Res. 2004 Apr 15 64(8):2898-2903.

Licensing Status: In addition to licensing, the technology is available for further development through collaborative research opportunities with the inventors.

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Methods for Detecting Progression of Low Grade Cervical Dysplasia

Description of Invention:

This invention describes a test that can be applied to Pap smears to differentiate low-grade dysplastic lesions that are likely to progress to higher-grade dysplasia and cervical cancer from those that are likely to regress. The differentiating factor is the presence of genetic gain on the long arm of chromosome 3. The inventors have shown that low grade Pap smears that progress already exhibit extra copies of 3q, while those that do not show the 3q gain spontaneously regress.

Around 10-15% of the 3 million Pap smears with low-grade dysplasia each year in the United States progress to higher-grade lesions. Currently, HPV testing is used to stratify these low-grade disease Pap smears, but as the majority of these Pap smears are already HPV infected, the test has very low specificity. The instant 3q test, which targets the human telomerase gene, TERC, is a significant improvement in sensitivity and specificity over the current methods used for the detection of progressing versus regressing lesions.

Inventors:

Thomas Ried et al. (NCI)

Patent Status:

DHHS Reference No. E-041-2005/0-US-01

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T-Cell Receptor Alternate Reading Frame Protein, (TARP) and Uses Thereof

Description of Invention:
This invention relates to a tumor-associated protein, TARP, which is expressed in breast and prostate cancer cells. This antigen target might be a useful tool for the diagnosis and treatment of breast and prostate cancer. TARP has shown efficacy in vivo as a potential therapeutic for the treatment of cancer. TARP has been the subject of several publications, including: J. Biol. Chem. (2004 Jun 4) 279(23):24561-24568, Epub 2004 Mar 29 as doi:10.1074/jbc.M402492200; Cancer Res. (2004 Apr 1) 64(7):2610-2618; Endocrinology (2003 Aug) 144(8):3433-40; Cancer Res. (2001 Nov 15) 61(22):8122-8126; Proc. Natl. Acad. Sci. USA (2000 Aug 15) 97(17):9437-9442.

Inventors:
Ira Pastan (NCI)
Magnus Essand (NCI)
Byungkook Lee (NCI)
George Vasmatzis (NCI)
Ulrich Brinkman (NCI)
Paul Duray (NCI)
and Curt Wolfgang (NCI)

Patent Status:
DHHS Reference No. E-104-1999/2 --
U.S. Patent Application No. 10/031,158 filed 11 Jan 2002, and multiple National Stage foreign filings

Licensing Status: In addition to licensing, the technology is available for further development through collaborative research opportunities with the inventors.

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Composition and Methods for Diagnosis and Treatment of Metastatic Disease

Description of Invention:
Liver cancer, particularly hepatocellular carcinoma (HCC), is a leading cause of cancer deaths worldwide. In spite of recent progress in therapeutic strategies, prognosis of patients with advanced HCC remains very poor. Although routine screening of individuals at risk for developing HCC may extend the life of some patients, many are still diagnosed with advanced HCC and have little chance of survival. A small subset of HCC patients qualifies for surgical intervention, but the consequent improvement in long-term survival is only modest. The extremely poor prognosis of HCC is largely the result of a high rate of recurrence after surgery or of intra-hepatic metastases that develop through invasion of the portal vein or spread to other parts of the liver; extra-hepatic metastases are less common.

The present invention describes tools to determine a unique gene expression profile present in either liver parenchyma through needle biopsy or blood that can aid diagnosis or prognosis of HCC patients with or without metastatic potential. This method also provides a signature-derived polymerase chain reaction or serological screening method to identify drug candidates to treat metastatic or recurrent HCC.

Inventors:
Xin Wei Wang and Anuradha Budhu (NCI)

Patent Status:
DHHS Reference No. E-127-2005/0-US-01 -- U.S. Provisional Application filed 09 Mar 2005
Licensing Status: In addition to licensing, the technology is available for further development through collaborative research opportunities with the inventors.

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Identification of Novel Birt-Hogg-Dubé (BHD) Gene

Description of Invention:

Birt-Hogg-Dubé (BHD) syndrome is an inherited autosomal dominant neoplasia syndrome characterized by benign hair follicle tumors and is associated with a higher risk for developing renal cancer, spontaneous pneumothorax and /or lung cysts.

The present invention describes identification of the BHD syndrome associated germline mutations in a novel human gene, herein called BHD gene. This gene encodes for the protein, folliculin, functions of which remain currently unknown.

This discovery makes possible the development of a diagnostic method for BHD syndrome using a simple blood test. The test is particularly useful in detecting BHD mutations in asymptomatic carriers within BHD families.

Patients with kidney tumors can be evaluated for BHD gene mutations using a similar genetic diagnostic test, which will allow for a more accurate diagnosis of a kidney cancer and improved patient prognosis. The BHD encoding sequence is the third gene found to be responsible for inherited kidney cancer, and mutation testing allows for a correct diagnosis and initiation of the proper treatment, which is different for each of the types of kidney cancer caused by the three genes. Since BHD is the first gene found to be associated with chromophobe renal cancer or renal oncocytoma, this invention will enable the development of specific treatments or therapies for these particular histologic types of kidney cancer.

Methods of using BHD encoding sequence also allows for a differential genetic diagnosis of spontaneous pneumothorax, or collapsed lung. Since collapsed lung can be caused by several factors, a BHD diagnostic test allows a physician to determine predisposition to and possible recurrence of additional spontaneous pneumothoraces due to mutation(s) in the BHD gene.

The discovery should also lead to the development of novel pharmaceutical products and methods for treating BHD skin lesions using creams containing the BHD gene product, folliculin. Such products and methods of treatment are expected to reduce the size and appearance of the benign hair follicle tumors.

The disclosed technology will provide new and exciting methodologies to correctly diagnose BHD syndrome and should lead to the development of novel pharmaceutical reagents for treatment of BHD skin lesions as well as other skin diseases.

Inventors:

Laura S. Schmidt (NCI)

Patent Status:

DHHS Reference No. E-190-2002/2 --
U.S. Patent Application No. 10/514,744 filed 16 Nov 2004

Relevant Publication:

1. MB Warren et al., "Expression of Birt-Hogg-Dubé gene mRNA in normal and neoplastic human tissues," Mod Pathol. (2004 Aug) 17(8):998-1011.
2. ML Nickerson et al., "Mutations in a novel gene lead to kidney tumors, lung wall defects, and benign tumors of the hair follicle in patients with the Birt-Hogg-Dubé syndrome," Cancer Cell (2002 Aug) 2(2):157-164.
3. B Zbar et al., "Risk of renal and colonic neoplasms and spontaneous pneumothorax in the Birt-Hogg-Dubé syndrome," Cancer Epidem. Bio. Prev. (2002 Apr) 11(4):393-400.
4. LS Schmidt et al., "Birt-Hogg-Dubé syndrome, a genodermatosis associated with spontaneous pneumothorax and kidney neoplasia, maps to chromosome 17p11.2," Am. J. Hum. Genet. (2001 Oct) 69(4):876-882.
5. JR Toro et al., "Birt-Hogg-Dubé syndrome: a novel marker of kidney neoplasia," Arch. Dermatol. (1999 Oct) 135(10): 1195-1202.

Licensing Status: In addition to licensing, the technology is available for further development through collaborative research opportunities with the inventors.

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Methods for Identifying, Diagnosing, and Predicting Survival of Lymphomas

Description of Invention:
Human lymphomas and leukemias are a diverse set of cancers. Many of these cancers, while expressing a similar phenotype between different individuals, have a diverse underlying genetic basis for the disease. This diverse genetic basis has implications on the effective treatment of the various phenotypes of lymphoma. For example, a drug that was effective against one individual's phenotype of lymphoma will not be effective against a similar lymphoma in another individual. An invention that helps clinicians classify a lymphoproliferative disorder would provide the basis for a "pharmacogenomic" method for treating such cancers.

The present invention discloses a novel microarray for obtaining gene expression profile data to be used in identifying lymphoma types and predicting survival in a lymphoma patient. The present invention further discloses a variety of methods for analyzing gene expression data obtained from a lymphoma sample, and specific algorithms for predicting survival and clinical outcome in a subject suffering from a lymphoma. The gene expression profile data set was established using a human genome gene chip set measuring the expression of over 27,000 genes in more than 500 lymphoproliferative tumor samples collected from patients at numerous healthcare institutions worldwide.

This invention could be developed into a useful pharmacogenomic, diagnostic product. The number of genes required for an accurate prognosis is reduced almost ten-fold from the human genome gene chip, allowing for lower density microarray technology and alternative gene expression measuring platforms. The choice of the gene set in this invention is optimized to provide an all in one method for the diagnosis of all lymphomas.

Inventors:
Louis M. Staudt et al. (NCI)

Patent Status:
DHHS Reference No. E-234-2003/0 --
U.S. Provisional Application No. 60/506,377 filed 03 Sep 2003
PCT Application No. PCT/US2004/029041 filed 03 Sep 2004

DHHS Reference No. E-108-2004/0 --
U.S. Patent Application No. 10/934,930 filed 03 Sep 2004

Licensing Status: In addition to licensing, the technology is available for further development through collaborative research with the inventors via a Cooperative Research and Development Agreement (CRADA).

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Antibodies and Polypeptides to AAMP-1 for Use in Diagnosis and Therapy of AAMP-1-Expressing Cancers

Description of Invention:

Angio-associated migratory cell protein (AAMP-1) was first isolated from a human melanoma cell line as a motility-associated cell protein. AAMP-1 contains two immunoglobin domains, six WD40 repeats, and a heparin-binding domain. In vitro, over expression of AAMP-1 promotes tumor cell invasion and metastasis as well as angiogenesis. AAMP-1 was later found to be over expressed in endothelial cells, cytotrophoblasts, and poorly differentiated colon adenocarcinoma cells found in lymphatics. In addition, gene expression studies have shown that AAMP-1 is over expressed in breast and gastrointestinal tumors.

The issued patents claim proteins, polypeptides, and recombinant polyclonal antibodies specific to AAMP-1 and their use in diagnostic and therapeutic applications. The antibodies are specific and can detect formalin-fixed antigen and SDS-denatured antigen.

These antibodies can be used for detailed expression studies of AAMP-1 in different cancer cell lines. The antibodies could also be used to promote cell adhesion to a substrate, promote tissue acceptance of prostheses, and promote wound healing. The antibodies could also be used to detect AAMP-1 in patient's sera as a useful diagnostic marker for multiple carcinomas including high nuclear grade ductal carcinoma in situ (Clinical Cancer Research Dec 2002 8:3788-95).

Inventors:

Lance Liotta et al. (NCI)

Patent Status:

DHHS Reference No. E-084-1991/1-US-01 -- U.S. Patent No. 6,274,134 issued 14 Aug 2001
DHHS Reference No. E-084-1991/1-AU-05 -- Australian Patent No. 684806 issued 23 Apr 1998

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Use of Anti-Parafibromin Antibodies to Diagnose Hyperparathyroidism-Jaw Tumor Syndrome (HPT-JT) and Parathyroid Cancer

Description of Invention:
This technology relates to methods of diagnosing cancer using antibodies that specifically bind to parafibromin. Parafibromin appears to be a tumor suppressor. Mutations in the coding sequence, specifically truncations or deletions, might be indicative of cancer or increased susceptibility to cancer. Antibodies targeting this tumor suppressor protein might have utility as a cancer diagnostic or prognostic, either alone, or as part of a kit.

Inventors:
William Simonds (NIDDK)
Jian-hua Zhang (NIDDK)
Geoffrey Woodard (NIDDK)

Patent Status:
DHHS Reference No. E-032-2004/0 --
U.S. Provisional Application No. 60/531,875 filed 22 Dec 2003

PCT Application No. PCT/US2004/43512 filed 22 Dec 2004, which published as WO 2005/064346 on 14 Jul 2005

Relevant Publication: This technology is described, in part, in GE Woodard et al., "Parafibromin, product of the hyperparathyroidism-jaw tumor syndrome gene HRPT2, regulates cyclin D1/PRAD1 expression." Oncogene 2004 Dec 06 (e-pub ahead of print, doi:10.1038/sj.onc.1208274).

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Composition for Detecting the Response of Rectal Adenocarcinomas to Radiochemotherapy

Description of Invention:

Rectal adenocarcinomas are among the most frequent malignant tumors. Surgery, including total mesorectal resection, is the primary treatment. Radiation or combined radiochemotherapy can be necessary before or after resection of the primary tumor. However, the response of individual tumors to radiochemotherapy is not uniform, and patients with radiochemotherapy resistant tumors are needlessly exposed to radiation, chemotherapy drugs, and the associated side effects thereof. The invention discloses the identification of genes and gene products, e.g., molecular markers or molecular signatures that are differentially expressed in responders and non-responders to radiochemotherapy treatment of rectal adenocarcinoma. The detection of differential expression levels of these genes can serve as a basis for diagnostic assays to predict the response to radiochemotherapy and can be used to identify the appropriate agent to be administered to enhance the effectiveness of the radiochemotherapy.

Inventors:

Thomas Ried et al. (NCI)

Patent Status:

DHHS Reference No. E-269-2003/0-US-01 filed 12 Jan 2004 (U.S. Provisional Application No. 60/535,491)

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Recombinant Immunotoxin and Use in Treating Tumors

Description of Invention:

The current invention relates to the 8H9 monoclonal antibody (MAb), which is highly reactive with a cell surface glycoprotein expressed on human breast cancers, childhood sarcomas, and neuroblastomas but is not reactive with the cell surface of normal human tissues. This specific reactivity suggests that this antibody could be useful as a diagnostic, or as a therapeutic molecule to treat breast cancer, osteosarcoma, and neuroblastoma. The PCT application claims the 8H9 protein, 8H9 antibodies, 8H9 immunotoxins, pharmaceutical compositions, and methods of use.

Inventors:

Ira Pastan (NCI)
Masanori Onda (NCI)
Nai-Kong Cheung (EM)

Patent Status:

DHHS Reference No. E-051-2003/0 --
PCT Application No. PCT/US03/38227 filed 01 Dec 2003, which published as WO 2004/050849 on 17 Jun 2004
U.S. Patent Application No. 10/537,061 filed 01 Jun 2005

Relevant Publication: M. Onda et al., "In vitro and in vivo cytotoxic activities of recombinant immunotoxin 8H9(Fv)-PE38 against breast cancer, osteosarcoma, and neuroblastoma," Cancer Res. 2004 Feb 15;64(4):1419-1424.

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Mabs to IRTA2 for Use in Diagnosis and Therapy of IRTA-Expressing Cancers

Description of Invention:
Immunoglobulin superfamily receptor translocation associated 2 (IRTA2) is a cell surface receptor that is normally expressed in mature B cells. ITRA2 expression is deregulated in multiple myeloma and Burkitt lymphoma cell lines. The invention discloses monoclonal antibodies specific for the extracellular domain of IRTA2 and their use in diagnostic and therapeutic applications. The antibodies can detect ITRA2 expression on non-Hodgkin's B-cell lymphoma cell lines and can detect hairy cell leukemia cells in blood samples taken from patients. The antibodies are specific for IRTA2, and can detect formalin-fixed antigen and SDS-denatured antigen.

These antibodies could be used for detailed expression studies of IRTA2 in different cancer cells lines. The antibodies could be also be used to treat B cell malignancies. In a diagnostic application the antibodies could be employed to investigate the presence of a residual number of malignant cells following a therapeutic regimen. The IRTA2 gene is known to produce alternative spliced products that encode soluble forms of IRTA2. The antibodies could be used to construct immunoassays to detect soluble IRTA2s in patients' sera as an useful diagnostic maker for B-cell malignancies.

Inventors:
Ira Pastan (NCI)

Patent Status:
DHHS Reference No. E-287-2004/0 --
U.S. Provisional Application No. 60/615,406 filed 30 Sep 2004

DHHS Reference No. E-287-2004/1 --
PCT Application No. PCT/US2005/034444 filed 22 Sep 2005, which published as WO 2006/039238 on 25 Jan 2007

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Glioma-Selective Polypeptides, Alone or Coupled to a Therapeutic/Diagnostic Agent, Compositions Comprising Same, and Uses Thereof

Description of Invention:

Primary brain tumors are an important cause of cancer mortality in the U.S., representing the leading cause of cancer-related death in children and the fourth leading cause of cancer-related death in young adults. Progress in the treatment of these tumors has been slow, since the demonstration of more than 20 years ago that fractionated radiotherapy could significantly extend survival. Although improved neurosurgical techniques have lessened the morbidity of extensive resections, the impact of such procedures on the overall survival of patients with the most malignant gliomas remains modest, at best, given the diffuse infiltrative nature of the tumor. Chemotherapy recently has been demonstrated to have some activity for specific subtypes of malignant gliomas, such as oligodendrogliomas and anaplastic astrocytomas. The effectiveness, however, of standard chemotherapy for the most common and malignant of the gliomas, glioblastoma, is marginal at best. Clearly, novel therapeutic approaches and novel drug targets are needed. In view of the foregoing, it is an object of the present invention to provide new agents and compositions that can be used in the diagnosis and treatment of glioma. This and other objects and advantages of the present invention, as well as additional inventive features, will be apparent from the detailed description provided in the patent application.

The present invention relates to glioma-selective polypeptides, which can be used alone or coupled to a therapeutic or diagnostic agent, in the diagnosis and therapy of glioma. Also provided by the present invention is a composition comprising the above-described polypeptide, desirably coupled to a diagnostic agent or a therapeutic agent, and a carrier.

Additionally, a method of diagnosing glioma in an animal is provided. The method comprises administering to the animal a polypeptide coupled to a diagnostic agent as described above, or a composition comprising same and a carrier therefore, and assaying for the presence of the diagnostic agent in the central nervous system (CNS). The presence of the diagnostic agent in the CNS is indicative of the presence of glioma in the animal.

A method of inhibiting the proliferation of a glioma cell in an animal having a glioma is also provided. The method comprises administering to the animal in an amount sufficient to inhibit the proliferation of the glioma cell in the animal a polypeptide coupled to a therapeutic agent as described above, or a composition comprising the same and a carrier, whereupon the proliferation of the glioma cell in the animal is inhibited.

Inventors:

Howard A. Fine (NCI)
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Patent Status:

DHHS Reference No. E-244-2002/0-US-01 filed 08 Oct 2003 (U.S. Provisional

Application No. 60/509,737)

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Interference with *c-maf* Function in Multiple Myeloma Retards Tumor Adherence and Progression and Decreases Expression of Integrin beta7, C-C Chemokine Receptor 1, and Cyclin D2

Description of Invention:
Multiple myeloma (MM) is an incurable malignancy of the plasma cell that accounts for 20% of all hematologic malignancies. It has been shown that there are recurrent genetic lesions associated with the disease. One of the recurrent lesions, occurring in approximately 5-10% of the cases, is a translocation involving the *c-maf* gene which results in overexpression of the *c-maf* gene.

Unexpectedly, the inventors have found that overexpression of the *c-maf* gene is more frequent than the occurrence of the genetic lesion, with approximately 50 % of MM samples showing overexpression of *c-maf*. Additionally, the inventors have shown that the interference with *c-maf* function markedly decreases expression of integrin beta7, C-C chemokine receptor1, and cyclin D2. The inventors have also demonstrated that decreased expression of integrin beta7 markedly decreases the ability of tumor cells to bind to bone marrow stroma and that the proliferation of myeloma cells was slowed significantly by the inhibition of *c-maf* expression. Therefore, *c-maf* appears to play a central role in regulating the proliferation and survival of tumor cells in MM.

Inventors:
Louis Staudt et al. (NCI)

Patent Status:
DHHS Reference No. E-173-2003/0 --
PCT Application No. PCT/US03/03316 filed 17 Oct 2003, which published as WO 2005/046731 on 26 May 2005
Licensing Status: The above-mentioned invention is available for licensing on an exclusive or a non-exclusive basis.

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Met Proto-Oncogene and a Method for Predicting Breast Cancer Progression

Description of Invention:

The invention described and claimed in this patent is generally applicable to assessing the prognosis of cancer. In particular, the invention is useful in assessing the whether or not breast cancer is likely undergoing metastasis. The met proto-oncogene is located on the long arm of chromosome 7 at 7q31. Its activity has been linked to the invasive/metastatic phenotype of several cancers in addition to breast cancer, e.g. prostate, stomach.

According to this invention the likelihood of metastasis of breast cancer is assessed by measuring the amount of (a) protein produced by the met proto-oncogene, (b) levels of the met proto-oncogene itself, or (c) levels of mRNA produced by the met proto-oncogene in breast tumor tissue and comparing it with the amount present in normal ductal tissue of the breast. The methodology of this invention may be carried out, for example, using antibody-based assays (ELISA or Western Blot), PCR, or Northern Blots.

Inventors:

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James H. Resau (NCI)
Iafa Keydar (NCI)
Donna Faletto (NCI)
George F. Vande Woude (NCI)

Patent Status:

DHHS Reference No. E-046-1991/3 --
U.S. Patent 6,673,559 issued 06 Jan 2004
Foreign patent protection is not available

Relevant Publication:

1. I Tsarfaty et al. The met proto-oncogene receptor and lumen formation. Science 1992 Aug 28;257(5074):1258-1261. [PubMed abs]
2. I Tsarfaty et al. Alteration of Met protooncogene product expression and prognosis in breast carcinomas. Anal Quant Cytol Histol. 1999 Oct;21(5):397-408. [PubMed abs]
3. R Hay et al. Grappling with metastatic risk: bringing molecular imaging of Met expression toward clinical use. J Cell Biochem Suppl. 2002;39:184-193. [PubMed abs]

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Brother of the Regulator of Imprinted Sites (BORIS)

Description of Invention:
The subject application discloses an isolated or purified nucleic acid molecule consisting essentially of a nucleotide sequence encoding a human or a non-human BORIS, or a fragment of either of the foregoing; an isolated or purified nucleic acid molecule consisting essentially of a nucleotide sequence that is complementary to a nucleotide sequence encoding a human or a non-human BORIS, or a fragment of either of the following; a vector comprising such an isolated or purified polypeptide molecule consisting essentially of an amino acid sequence encoding a human or a non-human BORIS, or a fragment or either of the foregoing; a cell line that produces a monoclonal antibody that is specific for an aforementioned isolated or purified polypeptide molecule; and the monoclonal antibody produced by the cell line; methods of diagnosing a cancer or a predisposition to a cancer in a male or female mammal; a method of prognosticating a cancer in a mammal; a method of assessing the effectiveness of treatment of a cancer in a mammal; a method of treating a mammal prophylactically or therapeutically for a cancer; and a composition comprising a carrier and an inhibitor of BORIS.

Inventors:
Victor Lobanenkov et al. (NIAID)

Patent Status:
DHHS Reference No. E-227-2001/0 --
U.S. Provisional Application No. 60/358,889 filed 22 Feb 2002
PCT Application No. PCT/US03/05186 filed 21 Feb 2003, which published as WO 03/072799 on 04 Sep 2003
U.S. Patent Application No. 10/505,377 filed on 20 Oct 2004

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Methods and Composition for the Diagnosis of Neuroendocrine Lung Cancer

Description of Invention:

The technology relates to the use of cDNA microarrays to facilitate the identification of pulmonary neuroendocrine tumors. In order to identify molecular markers that could be used to classify pulmonary tumors, the inventors examined the gene expression profiles of clinical samples from patients with small cell lung cancer (SCLC), large cell neuroendocrine carcinoma (LCNEC), and typical carcinoma (TC) tumors by cDNA microarray analysis to detect hybridization between cDNA from tumor cells and DNA from a panel of 8,897 human genes. Gene expression was found to be nonrandom and to exhibit highly significant clustering that divided the tumors into their assigned World Health Organization (WH0) classification with 100% accuracy. The inventors concluded that pulmonary neuroendocrine tumors could be classified based on the genome-wide expression profile of the clinical samples without further manipulations.

Inventors:

Curtis Harris (NCI)

Patent Status:

DHHS Reference No. E-248-2002/0-US-01 filed 04 Nov 2002 (U.S. Provisional Application No. 60/423,380)

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Methods of Diagnosis of Colorectal Cancer, Compositions and Methods of Screening for Modulators of Colorectal Cancer

Description of Invention:
Oncogene activation by gene amplification is a major pathogenetic mechanism in human cancer. Comparative genomic hybridization and DNA microarray expression profiling was used to examine the expression of over 2000 genes that were identified as residing on chromosome arms that were amplified in metastatic colon cancer cancers i.e. 7p, 8q, 13q, and 20q. The results indicated that amplified genes that also demonstrate increased expression levels are quite rare. However, the results also identified 93 genes, which reside on the chromosome arms in question, which showed an increased expression level concomitant with amplification. Some of these genes could provide targets for therapy.

As a result of the above findings, the inventors contemplate methods of diagnosing colon cancer through detection of the increased expression of one or more of the identified 93 genes. Aspects of this work have been published as follows: Platzer et al., 2002, Silence of Chromosomal Amplifications in Colon Cancer, *Cancer Research* 62:1134-1138.

Inventors:
Thomas Ried and Madhvi Upender (NCI)

Patent Status:
DHHS Reference No. E-206-2003/0-US-01 filed 13 Dec 2001 (U.S. Provisional Application No. 60/340,124)
DHHS Reference No. E-206-2003/0-US-02 filed 12 Dec 2002 (U.S. Patent Application No. 10/318,578)
Licensing Status: This technology is available for licensing on an exclusive or a non-exclusive basis.

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Zap70 Protein Expression as a Marker for Chronic Lymphocytic Leukemia (CLL)

Description of Invention:
The presence or absence of somatic mutations in the expressed immunoglobulin heavy chain variable regions (IgVH) of chronic lymphocytic leukemia (CLL) cells provides prognostic information. Patients whose leukemic cells express unmutated IgVH regions (Ig-unmutated CLL) often have progressive disease whereas patients whose leukemic cells express mutated IgVH regions (Ig-mutated CLL) more often have an indolent disease. Given the difficulty in performing IgVH sequencing in a routine diagnostic laboratory, this prognostic distinction is currently unavailable to most patients.

The present invention relates to the discovery that ZAP-70 expression also distinguishes the two CLL subtypes. Ig-unmutated CLL expressed ZAP-70 5.54-fold more highly than Ig-mutated CLL. ZAP-70 expression correctly predicted IgVH mutation status in 93% of patients, and ZAP-70 expression and IgVH mutation status were comparable in their ability to predict time to treatment requirement following diagnosis. Clinically applicable RNA and protein-based assays for ZAP-70 expression have been developed. These assays would yield important prognostic information for CLL patients.

Inventors:
Louis M. Staudt et al. (NCI)

Patent Status:
DHHS Reference No. E-091-2002/0-US-01 -- U.S. Provisional Application No. 60/375,966 filed 25 Apr 2002
DHHS Reference No. E-091-2002/0-US-02 -- U.S. Patent Application No. 10/309,548 filed 03 Dec 2002
Licensing Status: The above-mentioned invention is available for licensing on a non-exclusive basis only.

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Method of Distinguishing Epithelioid Melanoma from Fibroblastoid Melanoma

Description of Invention:

The incidence of primary cutaneous malignant melanoma is increasing such that, at the beginning of this century, the lifetime risk for developing melanoma approached one in 75 in the United States. In addition, the death rate from melanoma has doubled over the last 50 years.

Melanoma in humans can have epithelioid or fibroblastoid morphology. The fibroblastoid morphology has been associated with resistance to treatment and escape mechanisms. Therefore, there is a need for a method of distinguishing epithelioid and fibroblastoid melanoma. The ability to distinguish epithelioid and fibroblastoid melanoma would be useful in diagnosis and determining treatment protocols. It is an object of the present invention to provide such a method.

The present invention provides a method of distinguishing epithelioid melanoma from fibroblastoid melanoma. The method comprises assaying a sample of melanoma cells for retinyl ester synthesis. Retinyl ester synthesis is indicative of the melanoma cells being epithelioid, whereas the absence of retinyl ester synthesis is indicative of the melanoma cells being fibroblastoid.

Inventors:

Denise Simmons (NCI)

Patent Status:

DHHS Reference No. E-233-2002 filed 31 Oct 2002

Relevant Publication: This research is described, in part, in Simmons et al., Carcinogenesis, Vol. 23 No. 11, pp 1821-1830, November 2002.

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Use of Semenogelin in the Diagnosis, Prognosis, and Treatment of Cancer

Description of Invention:
The invention provides a method of diagnosing cancer in a male mammal wherein the cancer is other than prostate cancer. The method comprises: (a) obtaining a test sample from the male mammal, and (b) assaying the test sample for an increased level of semenogelin, wherein the increased level of semenogelin in the test sample is diagnostic for the cancer. The test sample can be assayed for an increased level of semenogelin in (b) by comparing the level of semenogelin in the test sample to the level of semenogelin in a control sample obtained form one or more cancer-free male mammals of the same species, wherein an increase in the level of semenogelin in the test sample as compared to the control sample obtained is diagnostic for the cancer. Alternatively, the level of semenogelin in the test sample can be compared to an already determined range of semenogelin for cancer-free male mammals of the same species.

In addition, the invention provides a method of diagnosing cancer in a female mammal. The method comprises: (a) obtaining a test sample from the female mammal, and (b) assaying the test sample for the presence of semenogelin, wherein the presence of semenogelin in the test sample is diagnostic for the cancer.

Inventors:
David Roberts and Henry Krutzsch (NCI)

Patent Status:
DHHS Reference No. E-138-2001/0 --
U.S. Provisional Application No. 60/281,994 filed 06 Apr 2001

PCT Application No. PCT/US02/10535 filed 03 Apr 2002, which published as WO 02/081630 A2 on 17 Oct 2002

U.S. Patent Application No. 10/474,213 filed 06 Oct 2003

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Methods of Screening for Risk of Cancer Using Human Lactoferrin DNA Probe or Primer

Description of Invention:
While normal breast ductal epithelium and neutrophilic granulocytes contain lactoferrin, their malignant counterparts frequently do not. The NIH announces primers or probes corresponding to the human lactoferrin gene, its promoter region, and its protein product, obtained from human breast tissue. The lactoferrin primer or probes can be used to screen for malignancy arising from tissues that normally secrete lactoferrin, or as a test to check the recovery of a patient from a malignancy

Inventors:
Christina Teng and Timothy Panella (NIEHS)

Patent Status:
DHHS Reference No. E-003-1991 --
U.S. Patent 5,948,613 issued 07 Sep 1999

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gp100 Cancer Antigens

Description of Invention:
DHHS announces the availability of select gp100 cancer antigens for licensing. These antigens are composed of a class that fall under the following definition:
gp100 P Core Peptide(s), meaning any gp100 peptide of nine (9) to fifteen (15) amino acids in length which is capable of eliciting an HLA-A2.1-restricted cytotoxic T cell response, and which comprises the formula $X_1X_2X_3PGPX_5TX_4$, where X_1 is any naturally occurring amino acid, X_2 is any hydrophobic aliphatic amino acid; X_3 is any naturally occurring amino acid; X_4 is any hydrophobic aliphatic amino acid, and X_5 is the amino acid V, C, I, L, or M.

gp100 is a tumor specific melanoma antigen. gp100 has been shown to be successful in stimulating the immune response to melanoma in humans.

Inventors:
Yutaka Kawakami (NCI)
Steven A. Rosenberg (NCI)

Patent Status:
U.S. Patent 5,844,075 issued 01 Dec 1998 (DHHS Reference No. E-057-1994/2-US-01)
U.S. Patent 6,537,560 issued 25 Mar 2003 (DHHS Reference No. E-057-1994/2-US-02)

Related Technologies: U.S. Patent 5,874,560 issued 23 Feb 1999 (DHHS Reference No. E-057-1994/0-US-01)
U.S. Patent 5,994,523 issued 30 Nov 1999 (DHHS Reference No. E-057-1994/0-US-02)

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Humanized Anti-TAG 72 CC49 for Diagnosis and Therapy of Human Carcinomas

Description of Invention:

Tumor associated glycoprotein (TAG-72) is expressed on the cells of a majority of human carcinomas, including colorectal, gastric, pancreatic, breast, lung, and ovarian. The murine monoclonal antibody (mAb) CC49 specifically recognizes TAG-72 and has a higher affinity for TAG-72 than its predecessor, B72.3.

The present invention discloses new humanized variants of CC49 that have a higher binding affinity to TAG-72 than previous humanized variants. Identified as HuCC49V15 and HuCC49V14, these variants also retain low immunogenicity of variable regions using sera of patients vaccinated with murine CC49.

These variants have potential benefits for use in the detection and/or treatment of a range of human carcinomas. Certain fields of use may not be available. Please contact OTT for information regarding the availability of specific fields of use.

Inventors:

Syed V. Kashmiri (NCI)
Jeffrey Schlom (NCI)
Eduardo Padlan (NIDDK)

Patent Status:

DHHS Reference No. E-013-2002/0 --
U.S. Provisional Application No. 60/393,077 filed 28 Jun 2002
PCT Application No. PCT/US03/20367 filed 26 Jun 2003, which published as WO 2004/003155 on 08 Jan 2004
U.S. Patent Application No. 10/519,580 filed 11 Jul 2005

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Pyrimidine Phosphorylase as a Target for Imaging and Therapy

Description of Invention:

The present invention describes methods to diagnose and monitor the treatment of tumors with high expression of thymidine phosphorylase (TP). Overexpression of TP has been shown to correlate with angiogenesis, and this fact can be used, via TP's enzyme function, to preferentially label angiogenic cells through the introduction of relevant precursors. These precursors consist of labeled thymine analogues which are converted by TP into retained cell-components. This can allow for the non-invasive imaging of tumors with high angiogenic activity. The technique can also be used to kill tumor cells by providing the analogues in higher concentrations or with therapeutic isotopes so as to be toxic to cells with high TP levels.

Inventors:

Raymond W. Klecker and Jerry M. Collins (FDA)

Patent Status:

DHHS Reference No. E-156-1999/0 --
U.S. Provisional Application No. 60/262,414 filed 19 Jan 2001
PCT Application No. PCT/US02/01216 filed 18 Jan 2002, which published as WO 02/057239 on 19 Jul 2002
U.S. Patent Application No. 10/466,423 filed 16 Jul 2003

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A Metastasis Suppressor Gene on Human Chromosome 8 and Its Use in the Diagnosis, Prognosis, and Treatment of Cancer

Description of Invention:
The subject technology is directed to a gene on human chromosome 8 that suppresses metastasis of prostate cancer. The gene has been shown to suppress the metastatic ability of rat prostate cancer and is down-regulated in human prostate cancers from metastatic foci. Embodiments of the technology include gene therapy to prevent the metastasis of human cancer, in particular prostate cancer, use of the gene as a clinical marker in the diagnosis and prognosis of cancer, in particular prostate cancer, and the development of small molecules that mimic the effect of the gene product.

The present invention provides an isolated or purified nucleic acid molecule consisting essentially of a nucleotide sequence encoding the metastasis suppressor gene located at p21-p12 on human chromosome 8, which has been named Tey 1, or a fragment thereof comprising at least 455 contiguous nucleotides.

Inventors:
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Vladimir Larionov (NCI)

Patent Status:
DHHS Reference No. E-238-2001/0 --
U.S. Provisional Application No. 60/345,109 filed 21 Dec 2001
PCT Application No. PCT/US02/40998 filed 20 Dec 2002, which published as WO 03/060074 on 24 Jul 2003
U.S. Patent Application No. 10/499,515 filed 21 Jun 2004

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New Gene Expressed in Prostate Cancer and Methods of Use

Description of Invention:

A new polypeptide is described in this invention that is specifically detected in the cells of the prostate. This polypeptide has been termed Novel Gene Expressed In Prostate (NGEP). There are potential claims to the NGEP gene, polynucleotides encoding NGEP, antibodies to NGEP, methods for using an NGEP polypeptide, polynucleotide, or antibody, and pharmaceutical compositions containing any of the above NGEP-related molecules. This invention might be useful in prostate cancer diagnostics, such as an assay to detect prostate cancer, or as a therapeutic directed towards prostate cancer.

Inventors:

Ira Pastan (NCI)

Patent Status:

DHHS Reference No. E-005-2002/0 --
U.S. Provisional Application No. 60/336,308 filed 14 Nov 2001
PCT Application No. PCT/US02/36648 filed 13 Nov 2002, which published as WO 03/042370 on 22 May 2003
U.S. Patent Application No. 10/495,663 filed 12 May 2004

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Use of Interferon-Inducible 2',5'-Oligoadenylate-Dependent RNase in the Diagnosis, Prognosis, and Treatment of Prostate Cancer

Description of Invention:

This invention pertains to the use of interferon-inducible 2',5'-oligoadenlyate-dependent RNase L in the diagnosis, prognosis and treatment of cancer, particularly prostate cancer. The inventors have identified a potential prostate cancer susceptibility locus, which has been designated HPC1 due to its putative link to hereditary prostate cancer. HPC1 may lead to an early, sensitive and accurate method for detecting cancer or a predisposition to cancer, especially prostate cancer, in a mammal. In addition, such claimed methods can be used to monitor onset and progression of cancer, as well as a patient's response to a particular treatment.

Inventors:

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Patent Status:

DHHS Reference No. E-196-2001/0 --
PCT Application PCT/US02/19516 filed 20 Jun 2002, which published as WO 03/000112 on 21 Dec 2002, claiming priority to a U.S. Provisional Patent Application filed on 20 Jun 2001

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Use of Mx GTPases in the Prognosis and Treatment of Cancer

Description of Invention:
The present invention describes novel approaches in the diagnosis, reduction of progression and treatment of cancer using Mx GTPases (Mxs) and Mx-encoding nucleic acids. The diagnostic benefits of this invention include methods of assessing the metastatic potential of cancer cells by determining the level of an Mx or Mx-encoding nucleic acid present in the cells. This invention also provides a method for administration of an Mx or expression of a nucleic acid encoding an Mx at, in, or near cancer cells, as well as a method for systemic induction of an Mx protein to reduce cancer progression in both solid tumors and hematologic malignancies.

Inventors:
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Patent Status:
DHHS Reference No. E-292-2001/0 -- U.S. Provisional Application No. 60/329,740 filed 18 Oct 2001

Related Technologies: DHHS Reference No. E-292-2001/1 --
PCT Application No. PCT/US02/33232 filed 18 Oct 2002, which published as WO 03/033667 on 24 Apr 2003;
U.S. Patent Application No. 10/492,396 filed 12 Apr 2004

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New Tumor Suppressor Gene, p28ING5

Description of Invention:

This technology pertains to the discovery of a new member of the ING (**in**hibitor **g**rowth) family of putative tumor suppressor genes, p28ING5. p28ING5 was identified by homology to the tumor suppressor gene p33ING1. Over-expression of the ING5 protein causes cell cycle arrest in human cancer cell lines and ING5 expression varies between cancer cell lines. Detection of ING5 gene or protein expression could potentially be used for cancer diagnosis and ING5 could be used as a medicant.

Inventors:

Dr. Curtis C. Harris et al. (NCI)

Patent Status:

DHHS Reference No. E-300-2001/0 --
U.S. Provisional Application No. 60/351,504 filed 23 Jan 2002
PCT Application No. PCT/US03/02174 filed 23 Jan 2003, which published as WO 03/062398 on 23 Jul 2003
U.S. Patent Application No. 10/502,431 filed 22 Jul 2004

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MRP8, A Member of the ABC Transporter Superfamily Highly Expressed in Breast Cancer, and Uses Thereof

Description of Invention:

MRP8 encodes an ATP-binding cassette transporter protein. Current data shows that it is expressed in a restrictive manner, and that it is highly expressed in breast cancer cells. This expression pattern makes it suitable as a molecular target, and MRP8-specific antibodies could be used to target MRP8-expressing cancer cells. Additionally, the MRP8-protein, immunogenic portions of said protein or nucleic acids encoding the protein, or immunogenic portions of said protein, could be used as immunogens to stimulate or to augment immune responses to MRP8-expressing cancer cells.

Inventors:

Ira Pastan et al. (NCI)

Patent Status:

DHHS Reference No. E-225-2001/0 --
U.S. Provisional Application No. 60/305,251 filed 12 Jul 2001

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Tumor Antigen Homologous to Poly(A) Polymerase

Description of Invention:

Poly(A) polymerase (PAP) activity has long been linked to cancer, and several forms of PAP have been identified to date by various researchers. PAP is an enzyme that is required for the processing and stability of nascent RNA transcripts. The current invention embodies the identification of a new human tumor associated antigen, neo-poly(A) polymerase (neo-PAP), which shares approximately 70% amino acid and 61% nucleic acid sequence similarity with classic PAP.

Neo-PAP is overexpressed in all tumor cell lines tested, including human prostate cancers, colon cancers, and melanomas. It is expressed at low levels in normal human testis tissue as well, but is expressed only at very low levels or not at all in other normal human tissues. Thus, neo-PAP appears to be a "cancer-testis" antigen, which is a category of tumor-associated antigens that are recognized by cytotoxic and helper T lymphocytes as well as serum immunoglobulins. Members of this tumor antigen category, including NY-ESO-1 and MAGE-3, and currently in clinical testing as cancer vaccines. Neo-PAP therefore could represent a potential immunotherapeutic vaccine for use against cancers of various types, and could also be useful in the diagnosis/prognosis of cancer.

Inventors:

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J. Manley
S. Kaneko

Patent Status:

DHHS Reference No. E-002-01/0 filed 16 May 2001

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Histone Deacetylase Inhibitors in Diagnosis and Treatment of Thyroid Neoplasms

Description of Invention:

The invention disclosed is novel approaches to thyroid cancer therapy. These approaches include methods to enhance thyroid specific gene expression, for example methods to enhance expression of thyroglobulin and/or the Na/I symporter in thyroid cancer cells. Enhanced expression of thyroid-specific genes promotes cellular differentiation and reduces biologically aggressive behavior such as invasion and metastasis. In addition, enhanced expression of thyroglobulin and/or the Na/I symporter increases the ability of thyroid cancer cells to concentrate iodine, thereby making the cells more susceptible to radioactive iodine therapy. Also disclosed are methods for detecting thyroid neoplasms in a subject, by administering a therapeutically effective amount of a histone deacetylase inhibitor, administering a detectable agent whose uptake or concentration in thyroid cells is increased by administration of the histone deacetylase inhibitor, and detecting the detectable agent.

Inventors:

Tito A. Fojo (NCI)
Susan Bates (NCI)

Patent Status:

DHHS Reference No. E-286-2000/0 --
U.S. Provisional Application No. 60/260,733 filed 10 Jan 2001
PCT Application No. PCT/US02/00714 filed 09 Jan 2002, which published as WO 02/055688 on 18 Jul 2002
U.S. Patent Application No. 10/250,320 filed 26 Jun 2003

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XAGE-1, A Gene Expressed in Multiple Cancers and Uses Thereof

Description of Invention:

The XAGE-1 gene is a human X-linked gene that is strongly expressed in breast cancer, lung cancer and several other cancers as well as normal testes. The largest open reading frame of the XAGE-1 transcript encodes a putative protein of 16.3 kD (p16) with a potential transmembrane domain at the amino terminus. In addition, the XAGE-1 transcript contains a second ATG in the reading frame corresponding to residue 66, which would encode a 9 kD protein (p9). In vitro transfection experiments using 293 T cells have revealed a 9 kD protein. However, the size of the endogenously expressed protein is not yet known. XAGE-1 shares homology with GAGE/PAGE proteins in the C-terminal end.

The invention relates to the fact that the XAGE-1 gene is expressed in a number of human cancers, specifically: breast, lung, prostate, pancreatic, and ovarian cancers. The proteins p9 and p16, immunogenic fragments thereof, analogs of these proteins, and nucleic acids encoding these proteins, fragments, or analogs, can be administered to persons with XAGE-1 expressing cancers to raise or augment an immune response to the cancer. The invention further provides nucleic acid sequences encoding the protein, as well as expression vectors, host cells, and antibodies to the proteins. Further, the invention provides immunoconjugates that comprise an antibody to p16 or to p9, and an effector molecule, such as a label, a radioisotope, or a toxin. The invention also provides methods of inhibiting the growth of XAGE-1 expressing cells by contacting them with immunoconjugates of an anti-p9 or p16 antibody and a toxic moiety. The invention also provides kits for the detection of p9 or p16 proteins in a sample. The XAGE-1 gene and encoded protein could be of value in the development of a cancer diagnostic and/or a cancer immunotherapy.

Inventors:

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Xiu F. Liu (NCI)
Byungkook Lee (NCI)
Lee J. Helman (NCI)

Patent Status:

DHHS Reference No. E-161-2000/0 --
U.S. Provisional Application No. 60/229,684 filed 01 Sep 2000
PCT Application No. PCT/US01/27258 filed 31 Aug 2001, which published as WO 02/18584 on 07 Mar 2002
U.S. Patent Application No. 10/363,233 filed 18 Jul 2003

Licensing Status:

Available for licensing on an exclusive or non-exclusive basis.

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Imaging of Extracellular Proteases in Cells Using Mutant Anthrax Toxin Protective Antigens

Description of Invention:

The claimed invention provides highly specific and sensitive methods for in vivo, in vitro, or ex vivo imaging of specific extracellular protease activity using an anthrax binary toxin system. The system targets cells that express extracellular proteases of interest. Such a system would be highly useful since various studies have demonstrated a positive correlation between the activity of extracellular proteases and various diseases and undesirable physiological conditions. For example, breakdown of the extracellular matrix by extracellular proteases is a prerequisite for the invasive growth of malignant cells, metastatic spread of tumors, and other pathological remodeling of tissue. In this case, methods are provided for the imaging of a specific extracellular protease by contacting a cell with: 1) a mutant anthrax toxin protective antigen (mPrAg) that binds to a cell surface receptor of a cell expressing an extracellular protease and is cleaved by a specific extracellular protease expressed by the cell and 2) a ligand that specifically binds to the cleaved mPrAg and is linked to a moiety that is detected by an imaging procedure, thereby forming a ligand-mPrAg complex that is translocated into the cell. The detectable moiety linked to the ligand in the ligand-mPrAg complex can be imaged before, during, or after translocation. Specific disease examples might include, but are not necessarily limited to, cancer, inflammation, and tumor progression or regression.

Inventors:

Thomas H. Bugge et al. (NIDCR)

Patent Status:

DHHS Reference No. E-295-2001/0 --
U.S. Provisional Application No. 60/317,550 filed 05 Sep 2001
PCT Application No. PCT/US02/28397 filed 05 Sep 2002
U.S. Patent Application No. 10/488,806 filed 04 Mar 2004

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PRAC & PRAC-Y: Small Nuclear Proteins Found in Prostate and Colon Cancer, and Uses Thereof

Description of Invention:

Prostate cancer is the most commonly diagnosed cancer and the second leading cause of cancer death in males in the United States. Currently, there are no curative therapies available for this cancer and therefore, novel approaches are needed to treat this disease. The present invention claims a small, nuclear protein, PRAC (Prostate/Rectum And Colon Protein) that could be used to diagnose and/or treat prostate or colon cancers. In conjunction with the composition of matter claims, defined methods of use might include: 1) immunogenic fragments to elicit T cell responses against cells that express PRAC; 2) gene therapy applications through the use of appropriate expression vectors containing the nucleic acid sequences of PRAC; 3) detection and potential staging of cancers expressing PRAC. These disclosed technologies could provide new and exciting methodologies to treat prostate and/or colon cancer.

Inventors:

Ira Pastan et al. (NCI)

Patent Status:

DHHS Reference No. E-053-2001/0 --
U.S. Provisional Application No. 60/282,704 filed 09 Apr 2001

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RASS1: A Novel Tumor Suppressor Gene Activated by Ras to Promote Apoptosis

Description of Invention:

Mutant ras oncogenes are frequently associated with human cancers, and activated Ras proteins have been found to mediate a broad array of biological effects. These effects are generated due to the ability of activated Ras to interact with numerous effector proteins, and the disclosed invention directly relates to such a novel effector, namely, RASS1. While many of Ras' activities are linked to cell growth and cell transformation, this putative tumor suppressor gene and its protein product seem to be effectors which mediate apoptotic cell death. The patent application contains composition of matter claims as well as method claims, all of which are directed to the detection, diagnosis, and treatment of cancer as well as providing data for cancer susceptibility or prognosis following diagnosis of a cancer. The application also provides claims directed toward gene therapy applications for this technology.

Inventors:

Geoffrey J. Clark and Michelle Vos (NCI)

Patent Status:

DHHS Reference No. E-237-2000/0 --
U.S. Provisional Application No. 60/251,971 filed 07 Dec 2000
PCT Application No. PCT/US01/48514 filed 07 Dec 2001, which published as WO 02/46223 on 13 Jun 2002
U.S. Patent Application No. 10/433,836 filed on 09 Oct 2003

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Protein Kinase A and the Carney Complex

Description of Invention:

The present invention provides compositions and methods useful in the diagnosis and prognosis of Carney complex (CNC), as well as methods and compositions for the identification of compounds useful in the treatment and/or prevention of CNC. CNC is a multiple endocrine neoplasia syndrome that affects the adrenal cortex, pituitary gland, thyroid gland and gonads. Additionally, compositions and methods are provided for the diagnosis and treatment of conditions associated with skin pigmentation defects, including but not limited to, freckling, as well as endocrine tumors including, but not limited to, adrenal and pituitary tumors. Finally, compositions and methods are provided for the diagnosis and treatment of various types of cancers associated with abnormal protein kinase A activity, and cancers and tumors in which protein kinase A regulatory subunit 1A acts as a tumor-suppressor gene. These actions are possible due to the identification of specific genetic sequences, and the use of this information in assay systems to detect, diagnose and treat the aforementioned conditions.

Inventors:

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Lawrence S. Kirschner (NICHD)

Patent Status:

DHHS Reference No. E-259-00/0 filed 25 Aug 2000

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NAG-1: A Non-Steroidal Anti-Inflammatory Drug Related Gene Which Has Anti-Tumorigenic Properties

Description of Invention:

Non-steroidal anti-inflammatory drugs (NSAIDs) are widely used in the treatment of inflammatory disease, and their anti-inflammatory effects are believed to result from their ability to inhibit the formation of prostaglandins by prostaglandin H synthase (COX). Two forms of prostaglandin H have been identified, COX-1 and COX-2. The former seems to be constitutively expressed in a variety of tissues while the high expression of the latter has been reported in colorectal tumors. NSAIDs have been shown to be effective in reducing human colorectal cancers and possibly breast and lung cancers. While the exact mechanism(s) by which NSAIDs function has not been elucidated, they could potentially play a critical role in detecting, diagnosing and treating inflammatory diseases as well as cancer. The present invention relates to screening methods for the identification of agonistic and/or antagonistic agents for the activation of the promoter region of NAG-1. Additional claims are directed to 1) the DNA sequence of NAG-1, 2) compositions containing the NAG-1 sequence and 3) methods for treating cancer patients using NAG-1.

Inventors:

Thomas E. Eling, Seung Joon Baek (NIEHS)

Patent Status:

DHHS Reference No. E-170-2000/0 --
U.S. Provisional Application No. 60/231,246 filed 08 Sep 2000
PCT Application No. PCT/US01/27544 filed 06 Sep 2001, which published as WO 02/20759 on 14 Mar 2002
U.S. Patent Application No. 10/363,514 filed 15 Aug 2003

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Assay for the Detection of a Variety of Tumors in Biological Specimens

Description of Invention:
The inventors have developed methods and reagents for the detection of bone sialoprotein (BSP) in biological samples. The technology relates to the disruption of a serum complex that masks the majority of BSP from established detection systems. Furthermore, there is evidence that there may be a more acidic form of BSP secreted not by normal bone, but only by tumors. Detection of BSP in serum may be a good marker of various bone diseases and a variety of cancers including breast, prostate, lung, and thyroid.

Inventors:
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Neal S. Fedarko (NICHD)
Marian F Young (NICHD)

Patent Status:
DHHS Reference No. E-173-1998/0 --
U.S. Patent No. 6,995,018 issued 07 Feb 2006
U.S. Patent Application No. 11/185,924 filed 19 Jul 2005

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Monoclonal Antibody Specific to Prostate Cells

Description of Invention:

Prostate Cancer is a disease affecting approximately 1 million men in the U.S.A., with an annual incidence of around 179,000 and approximately 30,000 deaths per year. It is estimated that one-third of men over 50 will develop prostate cancer at some time in their lives. Control of primary tumor by surgical resection and/or radiation has proven effective in a number of cases, however, metastatic spread, primarily to the bone, especially at late hormone independent stages of the disease, has been more difficult to control and monitor. With the aging of the U.S. population, it has been estimated that the number of prostate cancer cases will increase dramatically.

The technology disclosed in the 5,489,525 patent relates to a monoclonal antibody which is capable of binding to a cell surface differentiation antigen specific for prostate adenocarcinomas and other prostate cancer cells. Accordingly, methods of therapy can be employed with this monoclonal antibody to destroy prostate cancer cells, and hence, this monoclonal antibody may be useful in therapy and/or the diagnosis of prostate cancer. This monoclonal antibody can be produced by recombinant DNA techniques, the host cell being a eucaryotic or procaryotic cell, preferably a eucaryotic cell and more preferably mammalian. Hence, a monoclonal antibody, a recombinant monoclonal antibody, single polypeptide binding molecules, and binding fragments thereof coupled to molecules which are cytotoxic to prostate cancer cells (e.g., chemotherapeutic agents, prodrugs, cytotoxic or inhibitory peptides, cytokines, enzymes, diphtheria toxin, Pseudomonas Exotoxin, etc.) could be used to develop a prostate cancer therapeutic or diagnostic test system.

Inventors:

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Patent Status:

DHHS Reference No. E-201-1992
U.S. Patent No. 5,489,525 issued 06 Feb 1996

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Calcium Channel Compositions and Methods of Use Thereof

Description of Invention:
This invention described in this patent application relates to the identification, isolation and cloning of a three cDNAs identified during a search of the short arm of chromosome 3 for a tumor suppressor gene (TSG) associated with lung cancer. The cDNA's are alternative isoforms which encode a protein which functions as a subunit of L-type voltage-dependent calcium channel. Type L voltage-dependent calcium channels represent one of five families of calcium channels, L, R, P, N, Q, which have been identified. Type L voltage-dependent calcium channels are found in a wide variety of tissues including the brain, muscle and the endocrine system.

The gene has been mapped to the short arm of chromosome 3 at 3p21.3. The gene, which corresponds to this cDNA is an alpha2delta-2 subunit, and has been shown to be deleted in lung and breast cancer. The scientists have demonstrated that the expression of this calcium channel has been shut off in lung cancer cells and hypothesize that this may lead to a malignant phenotype. Other cancers which may be associated with this 2-2 subunit include cervical cancer and head and neck carcinoma. Other non-malignant diseases which may also be associated with this 2-2 subunit include CNS diseases and cardiovascular diseases.

Possible applications of this technology include its use in drug screening assays; its use as an early diagnostic marker and/or as a prognostic or treatment indicator; its use in gene therapy where defective cells would be reconstituted with the gene and as a therapeutic agent for clearing autoantibodies which develop toward the alpha2delta-2 subunit in the disease Lambert-Eton myasthenia syndrome.

Inventors:
MI Lerman (NCI) et al.

Patent Status:
DHHS Reference No. E-194-1998/0 --
U.S. Provisional Application No. 60/114,359 filed 30 Dec 1998
U.S. Patent Application No. 09/470,443 filed 22 Dec 1999, which issued as U.S. Patent No. 6,441,156 on 27 Aug 2002
U.S. Patent Application No. 10/116,949 filed 05 Apr 2002

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Method For Detecting Radiation Exposure

Description of Invention:

Ionizing radiation has many medical, industrial and military uses. Ionizing radiation is often used in the therapy of diseases such as cancer, however, exposure to biologically significant levels of such radiation can also cause genotoxic stress. In addition, many individuals are potentially exposed to radiation through occupational or accidental exposure. Such radiation can elicit a variety of cellular responses, ranging from cell-cycle arrest to mutation, malignant transformation, or cell death. The present invention describes a method for detecting exposure of organisms to biologically significant or hazardous amounts of ionizing radiation.

This invention describes the identification of a large set of genes that are induced by ionizing radiation. Different patterns of gene induction are produced depending upon dose of radiation and time after treatment. Many of these genes are induced by physiological doses of radiation routinely used for cancer therapy. These gene sets may be useful as markers of exposure to hazardous radiation, or as markers to predict the likely response of a particular tumor to radiation therapy, and subsequently to track and access the response of patients to radiotherapy. In addition, these gene sets may also be useful in toxicological and epidemiological research and studies.

Inventors:

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Jeffrey Trent (NHGRI)

Patent Status:

DHHS Reference No. E-112-1999/0 --
U.S. Patent No. 7,008,768 issued 07 Mar 2006
U.S. Patent Application No. 11/370,079 filed 06 Mar 2006

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Mammalian Selenoprotein Differentially Expressed in Tumor Cells

Description of Invention:

This application describes the identification, cloning, and sequencing of a human protein which contains selenium. A murine homolog has also been identified. The gene encoding the protein has been localized to the short arm of chromosome 1 at 1p31. Early work indicates that levels of the protein and/or mRNA are decreased in prostate, liver, ovarian and fallopian tube cancers and in lymphoma. Thus, levels of the protein or mRNA may be useful clinically as diagnostic or prognostic tools. The fact that other selenium proteins are known to be involved in the immunological response and the fact that this protein was originally detected in T cells leads to a hypothesis that the protein may play a role in the immunological response. Antibodies and tools for expressing the protein recombinantly may be useful in conducting further research on the functionality of this protein. This selenoprotein may potentially mediate a chemopreventative effect of selenium in prostate cancer.

Inventors:

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JC Wooten (NLM)
K Jeang (NIAID)

Patent Status:

DHHS Reference No. E-011-1998/0 --
U.S Patent No. 6,849,417 issued 21 Feb 2005
U.S. Patent Application No. 10/919,554 filed 16 Aug 2004

Relevant Publication:

This research has been published, in part, in J. Biol. Chem. 1998 Apr 10; 272(15): 8910-15.

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Monoclonal Antibodies Specific And Inhibitory To Human Cytochrome P450 2C8, 2C9, 2C18 And 2C19 - New Avenues For Drug Discovery

Description of Invention:
The cytochrome P450 family of enzymes has primary responsibility for the metabolism of xenobiotic drugs and non-drug carcinogens and environmental chemicals, as well as some endobiotics. This laboratory has isolated monoclonal antibodies (MAbs) that are specific to and inhibit the ten major human cytochrome P450s (CYPs) that are responsible for the metabolism of most drugs. The MAb based analytic system identifies the P450s responsible for metabolism of a drug and is thus an entirely new system for Drug Discovery. Drug-drug toxicity can be due to drug partners competing for an individual P450 and be a cause of drug toxicity. Certain drugs given to genetically polymorphic individuals that are defective in a specific P450 can cause serious toxicity to the defective individual. In one case 6-10% of the world population are missing an important P450 (2D6).

The 2C family of cytochrome P450s metabolizes a very large and extensive number of drugs which include tolbutamide, S-Warfarin, mephenytoin, diazepam and taxol. The invention reports the production of inhibitory MAbs to the P450 2C family. The invention describes MAb 5-1-5 and 281-1-1 that specifically inhibit CYP 2C8, MAb 292-2-3 that specifically inhibits CYP 2C9, and MAb 592-2-5 that specifically inhibits both CYP 2C9 and 2C18. MAb 5-7-5 specifically inhibits CYP 2C9, 2C18, and 2C19. In addition MAb 1-68-11 previously reported specifically inhibits all four members of the 2C family, 2C8, 2C9, 2C18 and 2C19. The MAbs may be used as diagnostic probes identifying the single or several P450s responsible for a drugs metabolism and also yield important information on inter-individual differences. The MAb system identifies and characterizes the P450 based metabolism of drugs currently in use and drugs in the screening and development stages of Drug Discovery.

Inventors:
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Patent Status:
DHHS Reference No. E-077-1999/0 --
U.S. Patent No. 6,623,960 issued 23 Sep 2003
U.S. Patent Application No. 10/616,760 filed 09 Jul 2003

Related Technologies:
See Monoclonal Antibodies (MAbs) Define Human Cytochrome P450 Drug Metabolism

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Monoclonal Antibodies Specific for Human Thymidylate Synthase

Description of Invention:
The antibodies described in this invention detect human thymidylate synthase (TS) in small samples of preserved tissues. TS has traditionally been quantitated with biochemical assays, which have limited sensitivity, require a fair amount of fresh or fresh frozen tissue, and cannot distinguish enzyme activity in heterogeneous cell populations in human tissue. The novel TS-directed antibodies have little cross-reactivity and can be used with several different immunoassay techniques. Sensitive quantification of TS in human tissues can be used to diagnose a patient's stage of cancer, to detect certain metabolic diseases, or to monitor a patient's therapy.

Inventors:
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C-M Liang (NCI)

Patent Status:
Serial No. 07/690,841 filed 24 Apr 1991, which issued as US Patent 6,221,620 on 24 Apr 2001

Related Technologies: * Serial No. 60/008,494 filed 11 Dec 1995 and Serial No. 08/762,264 filed 09 Dec 1996; Methods for Determining the Prognosis of Breast Cancer Using Antibodies Specific for Thymidylate Synthase; PG Johnston, C Allegra (NCI) * Serial No. 60/007,825 filed 01 Dec 1995 and Serial No. 08/758,034 filed 27 Nov 1996; Method for Predicting the Efficacy of a Chemotherapeutic Regimen for Gastric and Gastrointestinal Cancer Using Antibodies Specific for Thymidylate Synthase; PG Johnston, ER Fisher, CJ Allegra (NCI)

Relevant Publication: * PG Johnston, R Mick, W Recant, KA Behan, ME Dolan, MJ Ratain, E Beckmann, RR Weichselbaum, CJ Allegra, EE Vokes; Thymidylate synthase expression and response to neoadjuvant chemotherapy in patients with advanced head and neck cancer; J Natl Cancer Inst 89(4), 308-313 (1997) * BC Pestalozzi, HF Peterson, RD Gelber, A Goldhirsch, BA Gusterson, H Trihia, J Lindtner, H Cortes-Funes, E Simmoncini, MJ Byrne, R Golouh, CM Rudenstam, M Castiglione-Gertsch, CJ Allegra, PG Johnston; Prognostic importance of thymidylate synthase expression in early breast cancer; J Clin Oncol 15(5), 1923-1931 (1997) * BC Pestalozzi, CJ McGinn, TJ Kinsella, JC Drake, MC Glennon, CJ Allegra, PG Johnston; Increased thymidylate synthase protein levels are principally associated with proliferation but not cell cycle phase in asynchronous human cancer cells; Br J Cancer 71(6), 1151-1157 (1995) * PG Johnston, HJ Lenz, CG Leichman, KD Danenberg, CJ Allegra, PV Danenberg, L Leichman; Thymidylate synthase gene and protein expression correlate and are associated with response to 5-fluorouracil in human colorectal and gastric tumors; Cancer Res 55(7), 1407-1412 (1995) * PG Johnston, ER Fisher, HE Rockette, B Fisher, N Wolmark, JC Drake, BA Chabner, CJ Allegra; The role of thymidylate synthase expression in

prognosis and outcome of adjuvant chemotherapy in patients with rectal cancer; J Clin Oncol 12(12), 2640-2647 (1994) * PG Johnston, JC Drake, SM Steinberg, CJ Allegra; Quantitation of thymidylate synthase in human tumors using an ultrasensitive enzyme-linked immunoassay; Biochem Pharmacol 45(12), 2483-2486 (1993)

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Method and Composition for Detecting Dihydropyrimidine Dehydrogenase Splicing Mutations

Description of Invention:

Dihydropyrimidine dehydrogenase (DPD) is the first and rate limiting enzyme in the three step metabolic pathway of the catabolism of thymidine and uracil. In mammals, this pathway is the route for synthesis of beta-alanine. DPD can be considered an enzyme that is expressed in most cells, but has been studied extensively in liver, lymphocytes, and the CNS. DPD is responsible for the metabolism of fluoropyrimidine drugs, such as the much used chemotherapeutic agent 5-fluorouracil. The invention covers isolated nucleic acids that code for DP. It also includes nucleic acids that code for a DPD polypeptide that specifically binds to an antibody generated against an immunogen consisting of DPD polypeptide and its amino acid sequence. Also claimed are methods for determining whether a cancer patient is at risk of a toxic reaction to 5-fluorouracil. The methods involve analyzing DPD DNA or mRNA a sample from the patient to determine the amount of intact DPD nucleic acid.

Inventors:

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Pedro Fernandez-Salguero (NCI)

Patent Status:

DHHS Reference No. E-157-94/1 filed 20 Mar 1996

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PB39, A Novel Isolated Complete cDNA Whose Function is Dysregulated in Prostate Cancer

Description of Invention:

This technology describes the identification and cloning of two cDNAs derived from a human prostate cancer. In addition, the technology describes the cDNA for the murine homolog as well as the murine genomic sequence has been determined. The human gene is located on chromosome 11 and the gene product appears to exist in two forms, PB-39A (adult) and PB-39B (fetal). The products of the gene, which correspond to these cDNAs, are over-expressed in prostate cancer and PB-39 is over-expressed in prostate intraepthielial neoplasia (PIN). PIN is an early precursor of cancer; therefore, the PB-39B gene product may serve as an early marker for prostate cancer. The over-expression of PB-39A or PB-39B in prostate cancer when compared to normal tissue indicates that either may be used in the diagnosis of prostate cancer. Early results indicated that PB-39B may be a more reliable indicator (3/4 samples were positive for PB-39B while 5/11 samples were positive for PB-39A).

Inventors:

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Patent Status:

Serial No. 60/094,137 filed 24 Jul 1998 PCT/US99/16831 filed 23 Jul 1999

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A Basal Cell Carcinoma Tumor Suppressor Gene

Description of Invention:
Novel human nucleic acid sequences and polypeptides derived from the tumor suppressor, PTC or patched gene which have been mapped to human chromosome 9q22.3-q31, have been discovered for use in cancer diagnosis and therapy. Mutations of this gene are associated with Nevoid Basal Cell Carcinoma Syndrome (NBCCS) a disease associated with skin cancer and human developmental defects such as Gorlin Syndrome comprising skeletal defects, craniofacial and brain abnormalities. Methods of detection of PTC in a tissue sample have been found as well as recombinant cells, antibodies, and pharmacological compositions useful in treatment of the disease. Methods of diagnosis of and therapy for NBCCS have also been found. The PTC gene is thought to encode a protein which selectively switches off growth factor production in certain cells by interaction with members of the family of proteins encoded by the "hedgehog" gene, which instructs cells during development and growth. NBCCS is the result of abnormal PTC gene products that encode non-functional or functionally reduced NBCCS polypeptides. This lack of function may be caused by insertions, deletions, point mutations, splicing errors, premature termination codons, missing initiators, etc. The tumors caused by NBCCS are slow growing tumors that rarely metastasize, but which can cause significant morbidity and occasional mortality from local invasion. The PTC gene is also associated with medulloblastomas and trichoepitheliomas. Newly discovered germline and sporadic mutations associated with NBCCS have been disclosed and claimed in the International (PCT) application.

Inventors:
M Dean et al. (NCI)

Patent Status:
Serial No. 60/017,906 filed 17 May 1996

Serial No. 08/857,636 filed 16 May 1997
PCT/US97/08433

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Methods for Determining the Prognosis of Breast Cancer Using Antibodies Specific for Thymidylate Synthase

Description of Invention:

Thymidylate synthase provides the sole de novo source of thymidylate for DNA synthesis. It is also a critical therapeutic target for the fluoropyrimidine cytotoxic drugs, such as fluorouracil ("5-FU") and flurodeoxyureidine ("FudR"). In pre-clinical and clinical studies increased expression of thymidylate synthase protein has been associated with resistance to 5-FU. The quantitation of thymidylate synthase has traditionally been performed using enzymatic biochemical assays; however, these assays have major limitations when applied to human tumor tissue samples. Recently, monoclonal antibodies have been developed to human thymidylate synthase that have the required sensitivity and specificity to detect and quantitate thymidylate synthase enzyme in formalin-fixed tissue sections. Hence, this invention provides a method for determining the prognosis of a patient afflicted with breast cancer, by obtaining a solid breast tumor tissue sample, measuring the level of thymidylate synthase expression in the tissue sample using antibody specific for thymidylate synthase. This invention further provides a method for predicting the benefit of chemotherapy for a patient afflicted with breast cancer. The above mentioned invention is derived from the discovery that high thymidylate synthase expression is associated with a poor prognosis in node-positive, but not in node-negative, breast cancer patients. Further, with some 2,504 patients, thymidylate synthase expression was not found to be correlated with other prognostic factors including tumor size, ER status, PR Status, tumor grade, vessel invasion, and histology. The above mentioned invention is available for licensing on an exclusive or non-exclusive basis.

Inventors:

Drs. Patrick G. Johnston (NCI) and Carmen J. Allegra (NCI)

Patent Status:

Serial No. 09/152,647 filed 14 Sep 1998

Serial No. 09/310,459 filed 12 May 1999

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Novel FUSE-Binding Protein And cDNA

Description of Invention:

This invention includes the gene sequence for a novel proto-oncogene binding protein that is valuable for studying the regulation of genes responsible for transforming normal cells to cancer cells. The c-myc proto-oncogene plays a central role in normal cell proliferation and programmed cell death; factors that inhibit its expression thus contribute to the formation of a variety of tumors. This newly isolated gene sequence encodes a protein that binds to the far-upstream element (FUSE) of the c-myc gene, which has been shown to be required for its maximal transcription. The FUSE-binding protein gene sequence may be used to analyze mutations, translocations, and other genetic derangements that are associated with abnormalities of the FUSE protein or c-myc expression. Such DNA probes also may be useful for diagnosing a variety of physiologic and pathologic conditions, such as the transformation of normal cells to tumor cells. The FUSE-binding protein also may be used for developing mAbs that can be used to detect and quantitate the protein in biologic samples.

Inventors:

DL Levens
RC Duncan
MI Avigan (NCI)

Patent Status:

U.S. Patent 5,580,760 issued 03 Dec 1996 U.S. Patent 5,734,016 issued 31 Mar 1998
PCT/US97/21679 filed 21 Nov 1997

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AIB-1, A Steroid Receptor Co-Activator Amplified In Breast And Ovarian Cancer

Description of Invention:

Breast cancer is the number one cancer in U.S. women, with over 185,000 cases in 1996 and an estimated 44,560 deaths in the past year. Breast cancer arises from estrogen-responsive breast epithelial cells. Estrogen activity is thought to promote the development of breast cancer, and many breast cancers are initially dependent on estrogen at the time of diagnosis. Anti-estrogen compositions have therefore been used to treat breast cancer. AIB-1 (Amplified in Breast Cancer-1) is a novel gene that is pivotal to a crucial metabolic pathway linked to the growth and progression of human breast cancer. In many cancers, especially breast cancer, tumor cells have amplified copies of genes that can give the cancer a growth advantage. AIB-1, located on the long arm of chromosome 20, is one such amplified gene. High-level AIB-1 amplification and overexpression have been observed in several estrogen receptor (ER) positive breast and ovarian cancer cell lines, as well as in uncultured breast cancer specimens. AIB-1 has also been found to be expressed in prostate epithelial cells. AIB-1 is the most recently identified member of a gene family known as SRC-1 (steroid receptor coactivator), all of which interact with genes for steroid hormone receptors, ultimately enhancing tumor cell growth. This invention provides the gene for AIB-1, a novel steroid receptor co-activator which is overexpressed in breast cancer cells. It also encompasses diagnostic assays for steroid hormone-responsive cancers and screening assays to identify compounds which could inhibit interactions of the co-activator with steroid hormone receptors and other proteins in this pathway.

Inventors:

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JM Trent (NHGRI)

Patent Status:

Serial No. 60/049,728 filed 17 Jun 1997 PCT/US98/12689 filed 17 Jun 1998

Serial No. 09/125,632 filed 21 Aug 1998

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Recombinant DNA Clone Encoding Laminin Receptor

Description of Invention:

A recombinant DNA clone that encodes high-affinity cell surface receptors for laminin, a glycoprotein component of basement membranes, offers an important tool for studying a variety of normal and abnormal cell processes including tumor metastases. These laminin receptors have been shown to inhibit metastases. These recombinant receptors can be used in diagnostic methods, to assess the content of laminin receptor mRNA, and to determine the pattern of laminin receptor genes in different tissue and tumor cell populations.

Inventors:

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UM Wewer
MC Jaye
WN Drohan (NCI)

Patent Status:

Serial No. 06/911,863 filed 26 Sep 1986, which issued as U.S. Patent No. 4,861,710 on 29 Aug 1989

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Process For Producing Monoclonal Antibodies Reactive With Human Breast Cancer

Description of Invention:

Breast cancer is the second leading cause of cancer death among women, having only recently been surpassed by lung cancer. The incidence rate has remained somewhat steady, and is currently about 108 per 100,000. This invention describes a process to produce antibodies from hybridoma cultures for the detection, prognosis, and treatment of human breast cancer. These eleven antibodies are activated only by tumor cells from human mammary cells and not by apparently normal human tissues. The isotypes of ten of the antibodies are IgG of various subclasses, and one is IgM. The antibodies may be useful in five major areas in the management of human breast cancer: (1) the diagnosis of primary and metastatic breast tumor lesions by assay of human body fluids; (2) the in-situ detection, via gamma scanning, of primary or metastatic breast tumor lesions; (3) the treatment of primary or metastatic breast cancer using one or a combination of the antibodies either alone or coupled with toxic drugs, compounds, or radioactive isotopes; (4) use of the antibodies in the staining of populations of human cells in tissue sections from tumor lesions to indicate the degree of malignancy of the cell populations; and (5) the detection of micro-lesions containing only a few tumor cells that could not be detected by conventional staining techniques. A patent for this invention has been issued by the U.S. Patent and Trademark Office.

Inventors:

J Schlom
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M Nuti
PM Hand
FC Austin (NCI)

Patent Status:

Serial No. 06/330,959 filed 15 Dec 1981
U.S. Patent 4,522,918 issued 11 Jun 1985

Serial No. 06/707,400 filed 01 Mar 1985
U.S. Patent 4,612,282 issued 16 Sep 1986

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Colon Mucosa Gene Having Down-Regulated Expression In Colon Adenomas And Adenocarcinomas

Description of Invention:

Tumor suppressor genes that are down-regulated in colon adenomas and adenocarcinomas have been identified and isolated that may be valuable for the study and treatment of these disorders as well as for detecting and identifying other tumor suppressor genes. Colorectal cancer is a significant problem in the U.S., with 130,000 new cases per year and more than 65,000 deaths per year. Colorectal cancer is a multistep process involving the loss of function of so-called tumor suppressor genes as well as the activation of oncogenes. Studies in cell cultures have shown that the transfer of wild-type tumor suppressor genes to colon cancer cells lacking this gene suppresses tumorigenicity. cDNAs encoding an mRNA that is down-regulated in adenocarcinomas and adenomas of the colon have been isolated and cloned. The mRNA encodes a polypeptide of about 84,500 daltons. This down-regulated in adenoma (DRA) gene maps to chromosome 7, in which abnormalities have previously been linked to colorectal carcinomas. The polypeptide product of the cDNA may be used for studying the process of tumorigenesis and suppression. In addition, the DRA gene and/or polypeptide may be valuable as therapy for colon cancer or for staging colon tumors. Finally, this invention includes nucleotide probes for detecting and isolating other tumor suppressor genes.

Inventors:

CW Schweinfest
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Patent Status:

Serial No. 08/424,567 filed 17 Apr 1995
U.S. Patent 5,569,755 issued 29 Oct 1996

Serial No. 08/711,928 filed 11 Sep 1996
U.S. Patent 5,831,015 issued 03 Nov 1998

Serial No. 09/184,937 filed 02 Nov 1998

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Cell Matrix Receptor System And Use In Cancer Diagnosis And Management

Description of Invention:

A method of diagnosis and management of cancer, particularly breast cancer, is provided. The method involves interfering with the mechanism by which tumor cells adhere to the various membranes and tissues of the body, enabling replication, using cell receptors specific for the laminin molecule. The laminin molecule normally adheres to collagen IV of the membranes and tissues. The novel laminin molecule disclosed binds the cell receptor of the tumor cell because it has an affinity for the receptor but it does not have an affinity for collagen IV which is part of the membranes and tissues of the body. Other applications include possible burn therapy through the promotion of adhesion and growth of epithelial cells, which form the covering of most internal organs and outer surface layers of skin. Secondly, this invention provides a method for evaluating the effectiveness of chemotherapeutic agents designed to affect the receptor in cancer cells. The invention discloses a kit for detecting the presence of metastasizing cancer cells having this cell receptor. A method of separation of metastatic cancer cells expressing the cell receptor from a mixed population of cells is also provided. Also provided is a method of detecting breast cancer using radiolabelled antibodies specific to the cell receptor.

Inventors:

LA Liotta
NC Rao
V Terranova (NCI)

Patent Status:

Serial No. 06/481,934 filed 04 Apr 1983
U.S. Patent No. 4,565,789 issued 21 Jan 1986

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Soluble Interleukin-2 Receptor As A Disease Indicator And A Method Of Assaying The Same

Description of Invention:

Soluble IL-2 receptor is produced in response to immune activation and by some malignant cells. For instance, elevated levels of IL-2 have been detected in patients with adult T-cell leukemia, Sezary syndrome, Hodgkin's disease, chronic lymphocytic leukemia, multiple myeloma, and solid tumors. The systemic level of IL-2 receptor is also relevant in the diagnosis and treatment of such diseases as rheumatoid arthritis and systemic lupus erythematosis and may be used to titrate immunosuppressive therapy in such applications as graft rejection. The invention disclosed in the patent is a sandwich immunoassay useful for determining the amount of IL-2 receptor in a sample. The invention also discloses a method of detecting such disturbed or abnormal conditions in humans which release soluble IL-2 receptor in bodily fluids.

Inventors:

D Nelson
W Biddison
L Rubin
W Greene
W Leonard
R Yarchoan (NCI)

Patent Status:

Serial No. 06/724,897 filed 19 Apr 1985
U.S. Patent No. 4,707,443 issued 17 Nov 1987

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Novel Epidermal Growth Factor Receptor (ErbB-3) And Antibodies

Description of Invention:

ErbB-3 is a member of the type I family of growth factor receptors. ErbB-3 is a 148 kd transmembrane polypeptide which has between 64-67% homology to contiguous regions within the tyrosine kinase domains of the EGFR and erbB-2 proteins, respectively. ErbB-3 has been mapped to human chromosome 12 ql 11-13 and has been shown to be expressed as a 6.2 kb transcript in a variety of normal tissues of epithelial origin. Markedly elevated erbB-3 mRNA levels have been demonstrated in certain human mammary tumor cell lines. These findings suggest that increased erbB-3 expression may play a role in oncogenesis. U.S. Patent 5,183,884 includes claims to the cDNA encoding erbB-3, vectors containing the cDNA and cells transformed with the vector containing the cDNA encoding erbB-3. The DNA can be used in diagnostic applications or for production of the protein.

U.S. Patent 5,480,968 includes claims to the erbB-3 protein and antibodies to erbB-3. Such antibodies include both monoclonal and polyclonal antibodies. The antibodies may be labeled allowing for detection of erbB-3, or conjugated with a cytotoxic agent for use as a therapeutic. The divisional applications, U.S. Patent No. 5,820,859 and U.S. Patent No. 5,916,755, include claims to DNA and antibody based diagnostic methods, drug screening assays, therapeutic applications utilizing antibody conjugates or ligands which block the binding of an activating ligand to erbB-3; activating or blocking ligands which bind to erbB-3.

Inventors:

M Kraus (NCI)
SA Aaronson (NCI)

Patent Status:

DHHS Reference No. E-221-1989/0 --
U.S. Patent No. 5,183,884 issued 02 Feb 1993

DHHS Reference No. E-221-1989/1 --
U.S. Patent No. 5,480,968 issued 02 Jan 1996
U.S. Patent No. 5,820,859 issued 13 Oct 1998
U.S. Patent No. 5,916,755 issued 29 Jun 1999
U.S. Patent No. 6,639,060 issued 28 Oct 2003
U.S. Patent Application No. 10/693,030 filed 24 Oct 2003

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Truncated Hepatocyte Growth Factor Variants

Description of Invention:

HGF/NK2, a truncated form of a hepatocyte growth factor (HGF), may offer an improved method of diagnosing and treating proliferative disorders such as cancers. Elevated levels of HGF are associated with both cancerous and noncancerous conditions. This truncated form of HGF is an antagonist of HGF and can be used to effectively counteract its effects on cells. Its cDNA can also be used as a probe to detect increased levels of HGF mRNA in cells.

HGF/NK1, another truncated form of HGF, has partial agonist/antagonist properties. Thus, it may be useful either as an antagonist of an HGF or as an agonist to reinforce the action of endogenous growth factor, depending on the circumstances. A technique has been developed to produce large quantities of biologically active HGF/NK1 and HGF/NK2 using a prokaryotic expression system.

Potential Area of Application:

- cancer therapeutic
- cancer diagnostic
- wound healing

Main Advantage of Invention:

- behaves like HGF/SF
- method of producing large quantities

Inventors:

Jeffrey S. Rubin (NCI) et al.

Patent Status:

DHHS Reference No. E-044-1991/2 --
U.S. Patent 6,566,098 issued 20 May 2003
U.S. Patent Application No. 10/283,769 filed 23 Oct 2002

Relevant Publication:

V Cioce, KG Csaky, AML Chan, DP Bottaro, WG Taylor, R Jensen, SA Aaronson, JS Rubin. Hepatocyte growth factor (HGF)/NK1 is a naturally occurring HGF/scatter factor variant with partial agonist/antagonist activity. J Biol Chem. 1996 May 31;271(22):13110-13115. [PubMed abs]

Licensing Status:

- Therapeutics available for exclusive or non-exclusive licensing.
- Diagnostics available for non-exclusive licensing.

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Hepatocellular Carcinoma Oncogene

Description of Invention:
Hepatocellular carcinoma is a liver cancer which has high levels of incidence in Asian populations, e.g., China, Korea. Incidence of hepatocellular carcinoma is greater among chronic carriers of hepatitis. A transforming sequence or oncoprotein, hhcM has been identified which is the amplified gene expression product of hepatoma. Antibodies to the hhcM product or the cDNA itself can be used for diagnostic, therapeutic, and screening tests. They may also be used as research tools in studying hepatocellular carcinoma.

Inventors:
SS Yang (NCI)

Patent Status:
Serial No. 08/471,540 filed 06 Jun 1995
U.S. Patent 5,702,907 issued 30 Dec 1997
DIV of

Serial No. 08/324,445 filed 18 Oct 1994
U.S. Patent 5,811,262 issued 22 Sep 1998
which is FWC of

Serial No. 07/575,524 filed 31 Aug 1990 (Aban)
which is CIP of

Serial No. 07/451,953 filed 19 Dec 1989
which was Aban in favor of FWC

Serial No. 07/774,156 filed 15 Oct 1991
U.S. Patent 5,403,926 issued 04 Apr 1995

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ERBB2 Promoter Binding Protein In Neoplastic Disease

Description of Invention:

Isolation of a novel ERBB2 promotor binding protein offers to improve the diagnosis and, specifically, the detection and monitoring of neoplastic diseases. This invention has particular application for the early detection of breast cancer. The HER-2/neu (ERBB2/c-erbB-2), or ERBB2, gene sequence appears to be one of the primary genes responsible for the transition of normal epithelial cells toward carcinoma and the subsequent development of invasive and metastatic cancer. For women, early detection of breast cancer is crucial for survival; however, by the time the gene product of ERBB2 is measurable by current methods, the prognosis of patients is not good. This invention improves on earlier methods for detecting and treating breast cancer by providing a purified and isolated DNA binding protein that specifically binds to the promoter region of the c-ERBB2 (HER-2/neu) gene sequence (hence the term HER-2 promoter binding protein, HPBF). Antibodies specific for this DNA binding protein, called HPBF, can be used to assay for the presence of HPBF in a biological sample and, thus, detect the presence of cancer. The purified HPBF also can be used to test the ability of substances to inhibit the activity of HPBF and thus potentially halt or reverse growth of the cancer. This invention includes antisense nucleotides that effectively prevent HPBF from binding to the promoter.

Inventors:

Raziuddin and F Sarkar (NCI)

Patent Status:

DHHS Reference No. E-184-1993/0 --
U.S. Patent 5,518,885 issued 21 May 1996
U.S. Patent 5,654,406 issued 05 Aug 1997

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Self-Assembling Recombinant Papillomavirus Capsid Proteins

Description of Invention:
This invention is an enzyme-linked immunosorbent assay (ELISA) to detect humoral immunity response to papillomavirus infection in humans and other vertebrates. Assays have thus far been produced based upon serum immunoglobulin recognition of conformational epitopes of papillomavirus virion proteins on purified virus-like particles for HPV16, which is the HPV type most frequently found in cervical cancer. Assays for other high-risk cervical cancer HPV types (HPV18, HPV31, and HPV45) and for low-risk genital HPV types (HPV6 and HPV11) are under development using the same technology. The ELISA test for the genital HPV types may be useful as an adjunct to the Papanicolaou (PAP) test for identifying women with an increased risk of developing cervical cancer.

Inventors:
Douglas R. Lowy (NCI)
John T. Schiller (NCI)
Reinhard Kirnbauer (NCI)

Patent Status:
U.S. Patent 5,437,951 issued 01 Aug 1995 (DHHS Reference No. E-253-1993/0-US-01)
U.S. Patent 5,756,284 issued 26 May 1998 (DHHS Reference No. E-253-1993/0-US-02)
U.S. Patent 5,709,996 issued 20 Jan 1998 (DHHS Reference No. E-253-1993/0-US-03)
U.S. Patent 5,871,998 issued 16 Feb 1999 (DHHS Reference No. E-253-1993/0-US-04)
U.S. Patent 5,744,142 issued 28 Apr 1998 (DHHS Reference No. E-253-1993/0-US-05)
U.S. Patent 5,716,620 issued 10 Feb 1998 (DHHS Reference No. E-253-1993/0-US-06)
U.S. Patent 5,985,610 issued 16 Nov 1999 (DHHS Reference No. E-253-1993/0-US-07)
U.S. Patent Application No. 09/316,487 filed 21 May 1999 (DHHS Reference No. E-253-1993/0-US-08)
U.S. Patent Application No. 10/371,846 filed 21 Feb 2003 (DHHS Reference No. E-253-1993/0-US-10)

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Methods of Determining the Prognosis of an Adenocarcinoma

Description of Invention:
Available for licensing and commercial development is a novel method for determining the prognosis of a subject with adenocarcinoma in an organ, such as the lung, and to aid in the selection of a specific therapeutic regimen. Lung adenocarcinoma (AC) is the predominant histological subtype of lung cancer, which is the leading cause of cancer deaths worldwide. The risk of metastasis remains substantial in AC patients, even when a curative resection of early-stage AC is performed. The prognosis includes the determination of the likelihood of survival, the likelihood of metastasis, or both. The method includes quantization of the expression of a plurality of Th1 and Th2 cytokines of interest in the adenocarcinoma and in non-cancerous tissue in the organ. Altered expression of one or more of the Th1 and Th2 cytokines in the adenocarcinoma as compared to the non-cancerous tissue determines the prognosis for the subject. The method is capable of distinguishing patients with lymph node metastasis versus those with short term survival. Furthermore, methods are provided for evaluating the effectiveness of anti-cancer agents.

Applications:
Prognosis of adenocarcinoma, aid in the selection of specific therapeutic regimens and evaluation of the effectiveness of anti-cancer agents.

Development Status:
The technology is in early stage of development.

Inventors:
Curtis C. Harris (NCI)
Masahiro Seike (NCI)
Xin Wei Wang (NCI)

Patent Status:
DHHS Reference No. E-263-2006/0 --
U.S. Provisional Application No. 60/830,936 filed 14 Jul 2006

DHHS Reference No. E-085-2007/0 --
U.S. Provisional Application No. 60/885,101 filed 17 Jan 2007

Licensing Status:
Available for non-exclusive or exclusive licensing.

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Novel Monoclonal Antibody Microarray

Description of Invention:

Gene expression profiling at the mRNA level has proven to be a powerful and useful tool, however this approach suffers from inherent limitations: 1) the mRNA abundance does not typically correlate well with protein abundance and 2) protein structure, activity, and function can be altered and regulated by post-translational modifications. Thus, there is growing recognition that these approaches should be complemented by profiles of the gene products or proteins themselves. The present invention provides methods for constructing and using a novel Monoclonal Antibody Microarray which allows high-throughput determination of protein expression profiles from serum, tissue, and cultured cells.

The Monoclonal Antibody Microarray consists of more than 1000 different antibodies immobilized on a glass slide, which recognize antigens from several groups of proteins, including cytokines, kinases, apoptotic proteins, growth factor receptors, tumor suppressors, and oncoproteins. Protein samples to be identified and quantified are labeled with fluorescence and hybridized to the antibodies immobilized on the arrays. By differentially labeling two protein samples (dual-color labeling) and co-hybridizing to the same microarray, a direct comparative analysis of protein expression can be performed using as little as 100 ìg of total protein. This method allows a large number of samples to be screened in parallel on identical arrays.

Applications:

- High-throughput analysis of protein expression
- Direct measurement of protein expression at the gene product or post-translational levels

Development Status:

- The microarrays' performance was tested by proteomic profiling of two NCI-60 cancer cell lines (Renal UO-31 and Leukemia HL-60), demonstrating a high level of reproducibility.
- The microarrays' performance was further evaluated by analysis of the protein expression profiles of 12 Borderline ovarian and 9 Adenocarcinoma ovarian tumors using normal ovarian surface epithelial cells as a reference cell line. It was possible to detect 77 proteins that showed statistically significant ($p<0.05$) differences distinguishing Borderline tumors and Adenocarcinoma tumors, demonstrating that the novel microarrays described are useful tools for proteomics.

Inventors:

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Lionel Best (NCI)
David J. Munroe (NCI)

Patent Status:
DHHS Reference No. E-207-2006/0 --
U.S. Provisional Application No. 60/797,301 filed 02 May 2006

Licensing Status:
Available for non-exclusive or exclusive licensing.

Collaborative Research Opportunity:
The NCI-Laboratory of Molecular Technology is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize this novel monoclonal antibody microarray. Please contact Betty Tong, Ph.D. at 301-594-4263 or tongb@mail.nih.gov for more information.

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Method for Determining Redox Status of a Tissue

Description of Invention:

This invention describes methods for diagnosis and therapy of cancer and other pathologies associated with oxidative stress by administering a nitroxyl contrast agent and employing magnetic resonance imaging (MRI). Tumor tissues exhibit viable but hypoxic regions that allow them to reduce nitroxide compounds more efficiently than normal tissue. The paramagnetic relaxivity of nitroxide compounds makes it possible to use standard MRI scanners to determine the redox status of tissue in vivo. By determining the redox status of a tumor it is possible to not only diagnose a tumor due to its enhanced reduction of intracellular nitroxide contrast agent, but also to determine appropriate radiation treatment fields spatially to deliver therapeutic doses of radiation, and to determine appropriate timing sequences after the administration of a nitroxide contrast agent such that the maximum difference between normal and tumor tissue with respect to the radioprotective form of the nitroxide is present in the normal tissue, thereby limiting collateral damage to the normal tissue.

Inventors:

James B. Mitchell et al. (NCI)

Patent Status:

DHHS Reference No. E-258-2005/0 --
U.S. Provisional Application No. 60/707,518 filed 11 Aug 2005

Licensing Status:

In addition to licensing, the technology is available for further development through collaborative research opportunities with the inventors.

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Selections of Genes and Methods of Using the Same for Diagnosis and for Targeting the Therapy of Select Cancers

Description of Invention:
Available for licensing and commercial development are selections of expressed genes that function to characterize neuroblastoma in patients, and methods of using the same for targeting the therapy of neuroblastoma and for predicting the outcome of the therapy. The invention also relates to the use of supervised pattern recognition methods, such as artificial neural networks using high dimensional data, such as gene expression profiling data, for the prognosis of patients with neuroblastoma to predict their outcome.

Currently, patients with neuroblastoma are classified into risk groups (e.g., according to the Children's Oncology Group risk-stratification) to guide physicians in the choice of the most appropriate therapy. Despite this careful stratification, the survival rate for patients with high-risk neuroblastoma remains <30%, and it is not possible to predict which of these high-risk patients will survive or succumb to the disease. The inventors performed gene expression profiling using cDNA microarrays containing 42,578 clones and used artificial neural networks to develop an accurate predictor of survival for each individual patient with neuroblastoma. Using principal component analysis we found that neuroblastoma tumors exhibited inherent prognostic specific gene expression profiles, achieving 88% accuracy. They identified 19 genes, including 2 prognostic markers reported previously, MYCN and CD44, which correctly predicted outcome for 98% of these patients.

Inventors:
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Jun S. Wei (NCI)
Braden T. Greer (NCI)

Patent Status:
DHHS Reference No. E-324-2001/2-US-01 -- U.S. Provisional Application No. 60/598,728 filed 03 Aug 2004

Relevant Publication: Jun S. Wei, Braden T. Greer, Frank Westermann, Seth M. Steinberg, Chang-Gue Son, Qing-Rong Chen, Craig C. Whiteford, Sven Bilke, Alexei L. Krasnoselsky, Nicola Cenacchi, Daniel Catchpoole, Frank Berthold, Manfred Schwab, and Javed Khan, "Prediction of Clinical Outcome Using Gene Expression Profiling and Artificial Neural Networks for Patients with Neuroblastoma", Cancer Research 64, 6883-6891, October 1, 2004.

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Selections of Genes

Description of Invention:
The invention provides selections of genes expressed in a cancer cell that function to characterize such cancer, and methods of using the same for diagnosis and for targeting the therapy of selected cancers. In particular, methods are provided to classify cancers belonging to distinct diagnostic categories, which often present diagnostic dilemmas in clinical practice, such as the small round blue cell tumors (SRBCTs) of childhood, including neuroblastoma (NB), rhabdomyosarcoma RMS), Burkitt's lymphoma (BL), and the Ewing family of tumors (EWS). More specifically, the invention is an application of Artificial Neural Networks (ANNs) for the diagnostic classification of cancers based on gene expression profiling data derived from cDNA microarrays. The ANNs were trained using as models. The ANNs then correctly classified all samples tested and identified the genes most relevant to the classification. Their study demonstrated the potential applications of these methods for tumor diagnosis and for the identification of candidate targets for therapy. The uniqueness of this method is taking gene expression data generated by microarrays, minimizing the genes from the original 1000s to less than 100, identifying which genes are the most relevant to a classification, which gives an immediate clue to the actual biological processes involved, not just surrogate markers which have no bearing on the biology.

Inventors:
Javed Khan and Paul S. Meltzer (NHGRI)
et al.

Patent Status:
DHHS Reference No. E-324-2001/1-US-01 -- U.S. Patent Application No. 10/159,563 filed 31 May 2002

Relevant Publication: The technology is further described in J. Khan et al., "Classification and diagnostic prediction of cancers using gene expression profiling and artificial neural networks," Nature Medicine 7(6): 673-679, June 2001.

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Novel Methods and Compositions for Diagnosing AIDS and Other Diseases Involving Immune System Activation

Description of Invention:

Available for licensing and commercial development are methods and compositions suitable for monitoring the progression of AIDS and other diseases whose progression involves immune system activation in mammals, such as cancer, atherosclerosis, Alzheimer's disease, inflammation, autoimmune disorder, allergic asthma, Crohn's disease, Grave's disease, lupus, multiple sclerosis, Parkinson's disease, allograft transplant rejection, and graft vs. host disease.

In particular, the invention relates to the use of the TRAIL (TNF-related apoptosis-inducing ligand) and TRAIL compounds to monitor the progression of AIDS, and such other diseases. This is accomplished by assessing the presence or concentration of TRAIL, especially mTRAIL, sTRAIL, the TRAIL DR5 receptor molecule, and biological molecules that activate TRAIL or its receptor. These biological molecules include p53, alpha- and beta-interferon, as well as additional compounds such as CD69 and HLA-DR. Also claimed are kits for immunoassays to determine the presence or concentration of a TRAIL compound in a biological fluid, suitable for determining whether the mammal suffers from any of the above diseases.

TRAIL can be used as a new surrogate biomarker to monitor the progression of HIV infection and other conditions and diseases associated with immune system activation. In the case of HIV infection, measuring levels of this biomarker can distinguish among infected individuals with high viral load, infected individuals with low viral load, and uninfected individuals. Only two surrogate markers are currently recognized by the Food and Drug Administration as clinically relevant to HIV progression, HIV viral load and the absolute number of peripheral CD4+ T cells. Tests for assessing HIV viral load employ PCR, the use of which has drawbacks, including cross-contamination. TRAIL has mechanistic implications for HIV-1 pathogenesis and directly correlates to viral load but not necessarily inversely with CD4+ T cell count. Other surrogate markers have been proposed but do not consistently reflect AIDS progression in all individuals or may result in overlooking possible treatments that may affect disease progression but do not affect the chosen marker. Therefore, use of this new biomarker to assess disease progression in infected individuals and to evaluate the effectiveness of various treatment regimens has several advantages over currently used methods, since TRAIL is a death molecule involved in CD4+ T cell depletion in HIV/AIDS. TRAIL, its receptor, and activating molecules can all be used as sensitive markers for CD4 T cell activation and apoptosis.

Inventors:

Gene M. Shearer and Jean-Philippe Herbeuval (NCI)

Patent Status:

DHHS Reference No. E-045-2004/0 --
U.S. Provisional Application No. 60/564,588 filed 23 Apr 2004

DHHS Reference No. E-045-2004/1 --
U.S. Provisional Application No. 60/634,255 filed 12 Dec 2004

DHHS Reference No. E-045-2004/2 --
PCT Application No. PCT/US2005/13554 filed 21 Apr 2005

Relevant Publication:

7. Herbeuval JP, Hardy AW, Boasso A, Anderson SA, Dolan MJ, Dy M, Shearer GM. Regulation of TNF-related apoptosis-inducing ligand on primary CD4+ T cells by HIV-1: role of type I IFN-producing plasmacytoid dendritic cells. Proc Natl Acad Sci U S A. 2005 Sep 27;102(39):13974-9.
8. Herbeuval JP, Grivel JC, Boasso A, Hardy AW, Chougnet C, Dolan MJ, Yagita H, Lifson JD, Shearer GM "CD4+ T-cell death induced by infectious and noninfectious HIV-1: role of type 1 interferon-dependent, TRAIL/DR5-mediated apoptosis" Blood. 2005 Nov 15;106(10):3524-31.
9. Herbeuval JP, Boasso A, Grivel JC, Hardy AW, Anderson SA, Dolan MJ, Chougnet C, Lifson JD, Shearer GM "TNF-related apoptosis-inducing ligand (TRAIL) in HIV-1-infected patients and its in vitro production by antigen-presenting cells" Blood. 2005 Mar 15;105(6):2458-64.

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Tissue Microarray For Rapid Molecular Profiling

Description of Invention:

Recent advances in molecular medicine have provided new opportunities to understand cellular and molecular mechanisms of disease and to select appropriate treatment regimens with the greatest likelihood of success. The clinical application of novel molecular, genetic and genomic discoveries has been impeded by the slow and tedious process of evaluating biomarkers in large numbers of clinical specimens. The present invention provides a method of high-throughput molecular profiling of very large numbers of tissue specimens, such as tumors, with minimal tissue requirements. This procedure provides a target for rapid parallel analysis of biological and molecular characteristics (such as gene dosage and expression) from hundreds of morphologically controlled tumor specimens. Multiple sections can be obtained from such tissue microarrays ("tissue chips") so that each section contains hundreds or thousands of different tissue specimens that maintain their assigned locations. Different in situ analyses, such as histological, immunological, or molecular, are performed on each section to determine the frequency and significance of multiple molecular markers in a given set of tissues. This method can also be combined with other technologies such as high-throughput genomics surveys using DNA microarrays. DNA microarrays enable analysis of thousands of genes from one tissue specimen in a single experiment, whereas the tissue microarrays make it possible to analyze hundreds or thousands of tissue specimens in a single experiment using a single gene or protein probe. Together the DNA and tissue microarray technologies will be very powerful for the rapid analysis of markers associated with disease prognosis or therapy outcome.

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DENTAL TECHNOLOGIES

Genetic Polymorphisms Of Interleukin-1 Alpha And Beta Associated With Early Onset Periodontitis

Description of Invention:
Periodontal disease occurs in 10-20% of adults, and constitutes a major cause of tooth loss. About 0.5% of U.S. adolescents between the ages of 14 to 17 years old (about 70,000) have localized early onset periodontitis and 0.1% (17,000) have the more destructive form known as generalized early onset periodontitis. Both types of early onset periodontitis often lead to tooth loss before the age of 20. Extrapolation of these figures up to age 35 leads to estimates of early onset periodontitis having a major impact on the dental health of 400,000 individuals in the U.S. population. Discovery of genetic polymorphisms at the interleukin 1 alpha and 1 beta genes significantly associated with disease risk allows genetic testing to be used to predict disease prior to onset. This can be used to target clinical efforts for disease prevention to those individuals at greatest risk. The genetic test can also justify more aggressive therapeutic treatments for individuals already affected by the early onset periodontitis who, based on their genetic profile, are predicted to exhibit very rapid disease progression.

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