hewesj@mail.nih.gov for more information.

Monoclonal Antibodies Specific for the E2 Glycoprotein of Hepatitis C Virus and Their Use in the Diagnosis, Treatment and Prevention of Hepatitis C

Description of Technology: Hepatitis C virus is an enveloped, single-stranded RNA virus, approximately 50 nm in diameter, that has been classified as a separate genus in the Flaviviridae family. Most persons infected with hepatitis C virus develop chronic infection. These chronically infected individuals have a relatively high risk of developing chronic hepatitis, liver cirrhosis and hepatocellular carcinoma. There is currently no vaccine to prevent the hepatitis C virus infection. The present invention relates to human monoclonal antibodies which exhibit immunological binding affinity for the hepatitis C virus E2 glycoprotein and are cross-reactive against different hepatitis C virus strains. These antibodies may be used in passive immunoprophylaxis for the prevention of hepatitis C virus infection and/or in passive immunotherapy for the treatment of hepatitis C.

Applications: In vitro diagnostic assay for identifying patients infected with hepatitis C virus and contaminated blood samples; method of preventing infection using monoclonal antibodies that neutralize E2 glycoproteins from different genotypes of hepatitis C virus.

Market: Over 4 million people in the U.S. are infected with hepatitis C virus. An estimated 150 to 200 million people are infected with hepatitis C virus worldwide.

Inventors: Suzanne U. Emerson (NIAID), Robert H. Purcell (NIAID), Harvey J. Alter (NIAID), *et al.*

Related Publication: DJ Schofield *et al.* Human monoclonal antibodies that react with the E2 glycoprotein of hepatitis C virus and possess neutralizing activity. Hepatology. 2005 Nov;42(5):1055–1062.

Patent Status: U.S. Provisional Application No. 60/250,561, filed 01 Dec 2000 (HHS Reference No. E–017–2001/0–US–01); PCT Application No. PCT/US01/45221, filed 30 Nov 2001, published as WO 02/055560 on 18 Jul 2002 (HHS Reference No. E–017–2001/0–PCT–02); U.S. Patent Application No. 10/432,006 filed 16 May 2003, issued as U.S. Patent No. 6,924,362 on 02 Aug 2005 (HHS Reference No. E–017–2001/0–US–03)

Licensing Contact: Chekesha S. Clingman, Ph.D.; 301/435–5018; *clingmac@mail.nih.gov*.

Collaborative Research Opportunity: The NIAID Laboratory of Infectious Diseases is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize these monoclonal antibodies. For more information, please contact Robert H. Purcell, M.D., Co-chief, Laboratory of Infectious Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, 50 South Drive, Bldg. 50, Rm. 6523, Bethesda, MD 20892–8009; Phone (301) 496–5090; Fax (301) 402–0524.

Major Neutralization Site of Hepatitis E Virus and Use of This Neutralization Site in Methods of Vaccination

Description of Technology: Hepatitis E is endemic in many countries throughout the developing world, in particular on the continents of Africa and Asia. The disease generally affects young adults and has a very high mortality rate, up to 20%, in pregnant women. This invention relates to the identification of a neutralization site of hepatitis E virus (HEV) and neutralizing antibodies that react with it. The neutralization site is located on a polypeptide from the ORF2 gene (capsid gene) of HEV. This neutralization site was identified using a panel of chimpanzee monoclonal antibodies that are virtually identical to human antibodies. Since this neutralization site is conserved among genetically divergent strains of HEV, the neutralizing monoclonal antibodies may be useful in the diagnosis, treatment and/or prevention of hepatitis E. Furthermore, immunogens that encompass this neutralization site may be used in vaccination to effectively prevent, and/or reduce the incidence of HEV infection. Polypeptides containing this neutralization site may be useful in evaluating vaccine candidates for the production of neutralizing antibodies to HEV.

Inventors: Suzanne U. Emerson (NIAID), Robert H. Purcell (NIAID), *et al.*

Related Publications:

1. YH Zhou *et al.* A truncated ORF2 protein contains the most immunogenic site on ORF2: antibody responses to non-vaccine sequences following challenge of vaccinated and non-vaccinated macaques with HEV. Vaccine 2005 May 2;23(24):3157–3165.

2. DJ Schofield *et al.* Monoclonal antibodies that neutralize HEV recognize an antigenic site at the carboxyterminus of an ORF2 protein vaccine. Vaccine 2003 Dec 12;22(2):257–267.

3. YH Zhou *et al.* An ELISA for putative neutralizing antibodies to hepatitis E virus detects antibodies to genotypes 1, 2, 3, and 4. Vaccine 2004 Jun 30;22(20):2578–2585.

Patent Status: U.S. Patent No. 6,930,176, issued 16 Aug 2005 (HHS Reference No. E–043–2000/0–US–04); EP Application 00982311.3, filed on 30 Nov 2000, published as 1235862 on 04 Sept 2002 (HHS Reference No. E–043–2000/0–EP–03); U.S. Patent No. 7,148,323, issued 12 Dec 2006 (HHS Reference No. E–043–2000/0–US–05)

Licensing Contact: Chekesha S. Clingman, Ph.D.; 301/435–5018; *clingmac@mail.nih.gov*.

Collaborative Research Opportunity: The NIAID Laboratory of Infectious Diseases is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize these antibodies or structures they interact with. For more information, please contact Robert H. Purcell, M.D., Co-chief, Laboratory of Infectious Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, 50 South Drive, Bldg. 50, Rm. 6523, Bethesda, MD 20892–8009; Phone (301) 496–5090; Fax (301) 402–0524.

Dated: April 17, 2007.

Steven M. Ferguson,

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

[FR Doc. E7–7930 Filed 4–25–07; 8:45 am]

BILLING CODE 4140–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Government-Owned Inventions; Availability for Licensing

AGENCY: National Institutes of Health, Public Health Service, HHS.

ACTION: Notice.

SUMMARY: The inventions listed below are owned by an agency of the U.S. Government and are available for licensing in the U.S. in accordance with 35 U.S.C. 207 to achieve expeditious commercialization of results of federally-funded research and development. Foreign patent applications are filed on selected inventions to extend market coverage for companies and may also be available for licensing.

ADDRESSES: Licensing information and copies of the U.S. patent applications listed below may be obtained by writing

to the indicated licensing contact at the Office of Technology Transfer, National Institutes of Health, 6011 Executive Boulevard, Suite 325, Rockville, Maryland 20852–3804; telephone: 301/496–7057; fax: 301/402–0220. A signed Confidential Disclosure Agreement will be required to receive copies of the patent applications.

GDF15, a Marker and Cause of Morbidity in Thalassemia

Description of Technology: 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 GDF15 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:

1. Diagnostic test to detect increased risk for thalassemia-related complications.
2. Treatment of thalassemia by administration of a GDF15 antagonist.
3. Treatment of iron-dysregulated diseases.
4. Treatment of ineffective erythropoiesis.
5. 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).

Publications: In Review.

Patent Status: U.S. Provisional Application No. 60/864,705 filed 07 Nov. 2006 (HHS Reference No. E–022–2007/0-US–01).

Licensing Status: Available for exclusive or nonexclusive licensing.

Licensing Contact: Tara L. Kirby, PhD; 301/435–4426; *tarak@mail.nih.gov.*

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 GDF15 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.

Methods for Treating Autoimmune Inflammatory Disease by Blocking DR3–TL1A Interactions

Description of Technology: As a group, autoimmune inflammatory diseases occur in greater than five percent of the United States population, and represent the fourth-largest cause of disability among women. This disease group includes asthma, multiple sclerosis, rheumatoid arthritis, and lupus, among others. Treatments generally include immunosuppressants or anti-inflammatory drugs; recently, more specific immunomodulatory therapies such as TNF-alpha antagonists have been developed.

The invention discloses methods for treatment of autoimmune inflammatory disease by blocking the interaction between one particular TNF family ligand, TL1A (or TNFSF15), and its receptor, DR3 (or TNFRSF25). The inventors have shown that the DR3–TL1A interaction is critical for development of disease in mouse models of asthma and multiple sclerosis. Additionally, mice lacking the DR3 receptor have normal immune system development and response to immune challenge. Thus, a treatment for autoimmune disease that blocks the DR3–TL1A interaction may provide a potent therapy without inducing global immunosuppression.

Applications: Development of therapeutics for autoimmune inflammatory disease.

Market: More than five percent of the United States population has an autoimmune disease; The market size for rheumatoid arthritis is predicted to be $10 billion by 2008.

Development Status: Early stage.

Inventors: Richard M. Siegel and Francoise Meylan (NIAMS).

Patent Status: U.S. Provisional Application No. 60/879,668 filed 10 Jan 2007 (HHS Reference No. E–011–2007/0–US–01).

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

Licensing Contact: Tara Kirby, PhD; 301/435–4426; *tarak@mail.nih.gov.*

Genetic Markers for Body Size in Dogs

Description of Technology: 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).

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.

Patent Status: U.S. Provisional Application No. 60/856,411 filed 02 Nov 2006 (HHS Reference No. E–009–2007/0–US–01).

Licensing Status: Available for non-exclusive licensing.

Licensing Contact: Tara L. Kirby, PhD.; 301/435–4426; *tarak@mail.nih.gov.*

A Neuronal Avalanche Size (NAS) Assay to Screen for Cognitive Enhancers and Anti-Epileptics

Description of Technology: Currently available methods of detecting and measuring EEG activity only crudely classify normal and abnormal activity or distinguish epileptic activity early in the onset of its deviation from normal activity. Available for licensing are methods for recognizing a new pattern of EEG activity called neuronal avalanche size (NAS) that has been correlated with cognitive function and epilepsy. The NAS uses extracellular field potentials to measure the distribution of synchronized neurons in the cortex (neuronal avalanches) and thus the state of the cortical network. When the avalanche size reaches a power law with a slope of $-3/2$, the system is in the critical state and the cortical network is functioning optimally to spread information throughout the network. If the system slope deviates from $-3/2$, the system is outside the critical state and is either epileptic or sub-critical. In animal studies measurement of NAS quantified a drug's potential to increase cognitive functioning and induce or reduce epilepsy.

The NAS assay may thus enable high-throughput *in vitro* screens to select anti-epileptics and cognitive enhancing drugs for continued drug development. Because avalanches represent scale-invariant dynamics they can also be recorded using surface (EEG) electrodes. This technology may thus be useful in assessing cognitive function, epileptic pathology and in selecting and monitoring drug therapy for epileptic patients.

Applications:

1. *In vitro* screen to assess drugs for potential use as anti-epileptics for drugs with the propensity to cause epilepsy.

2. *In vitro* screen to assess drugs with the ability to enhance cognitive function, and ultimately, relieve cognitive defects associated with psychiatric illnesses and neurological disorders.

3. EEG monitoring of patients for diagnosis and drug selection and monitoring.

Market:

1. Epilepsy affects approximately 2.7 million people in the United States, and over 50 million people worldwide.

2. The cost of epilepsy in the United States is $12.8 billion per year, where eighty percent of this cost is due to patients with intractable seizures.

3. The cost for developing and commercializing new drugs is approximately $1 billion.

4. Schizophrenia affects about 1 out of 100 people in the United States, resulting in a public health burden of $40 billion per year in the U.S. alone.

5. Atypical neuroleptics alleviate cognitive deficits in schizophrenia and are now prescribed to more than 70 percent of all schizophrenic patients, totaling annual sales of $8.7 billion in 2003.

6. Atypical neuroleptics have variable efficacy in alleviating symptoms, and act on multiple, poorly understood pathways simultaneously resulting in many side effects.

7. The proposed *in vitro* screen could tremendously facilitate the development of more efficient and selective psychotropic drugs to alleviate cognitive deficits in schizophrenia.

Development Status: In vivo and *in vitro* data are available.

Inventors: Dietmar Plenz (NIMH).

Publications:

1. JM Beggs, D Plenz. Neuronal avalanches in neocortical circuits. J Neurosci. 2003 Dec 3;23(35):11167–77.

2. CV Stewart, D Plenz. Inverted-U profile of dopamine-NMDA-mediated spontaneous avalanche recurrence in superficial layers of rat prefrontal cortex. J Neurosci. 2006 Aug 2;26(31):8148–59.

Patent Status: U.S. Provisional Application No. 60/707,651 filed 12 Aug 2005 (HHS Reference No. E–294–2005/0–US–01); PCT Application No. PCT/US2006/031884 filed 14 Aug 2006 (HHS Reference No. E–294–2005/1–PCT–01).

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

Licensing Contact: Norbert Pontzer, J.D., Ph.D.; 301/435–5502; *pontzern@mail.nih.gov.*

Collaborative Research Opportunity: The NIMH/Section of Neural Network physiology is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize the NAS assay. Please contact Dietmar Plenz at *plenzd@mail.nih.gov* for more information.

Method for Promoting Stem Cell Proliferation and Survival

Description of Technology: 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:

1. Clinical treatment for stroke and other neurodegenerative diseases by administration of agents that promote stem cell survival and proliferation.

2. Increased generation of stem cells *in vitro.*

3. Screening assays for agents that promote proliferation of stem cells or inhibit proliferation of cancer cells.

4. Diagnostic assay for cancer to determine the phosphorylation state of the protein in tumors.

Market:

1. Prognostic marker to help determine response of individuals with cancer.

2. Commercial suppliers or large-scale users of stem cells.

Development Status:

1. 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.

2. 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).

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.

Patent Status:

1. U.S. Provisional Application No. 60/715,935 filed 08 Sep 2005 (HHS Reference No. E–239–2005/0–US–01).

2. PCT Application No. PCT/US2006/034988 filed 07 Sep 2006 (HHS Reference No. E–239–2005/0–PCT–02).

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

Licensing Contact: Fatima Sayyid, M.H.P.M.; 301/435–4521; *sayyidf@mail.nih.gov.*

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.*

Preparation and Use of Androgenic Compounds: Nandrolone 17beta-carbonates

Description of Invention: Hypogonadism is defined as deficient or absent male gonadal function that results in insufficient testosterone secretion. Hypogonadism can be caused by surgery; radiation; genetic and developmental disorders; liver and kidney disease; infection; and certain auto-immune disorders. The most common genetic disorders are Klinefelter syndrome found in men and Turner syndrome in women.

Hypogonadism affects an estimated 4 to 5 million men in the United States, and although it may occur in men at any age, low testosterone levels are especially common in older males. More than 60% of men over age 65 have free testosterone levels below the normal values of men aged 30 to 35. Studies suggest that hypogonadism in adult men is often underdiagnosed and under treated. This may be because the symptoms are easily attributed to aging or other medical causes, or ignored by patients and physicians. In fact, only about 5% of hypogonadal men receive testosterone replacement. Some experts also believe that we need to reevaluate normal testosterone levels and lower the diagnostic cutoff for hypogonadism. By doing so, many patients who we now consider to be ''low-normal'' would probably be considered candidates for androgen replacement.

The inventors have discovered androgenic compounds, the lead compound being 17beta-carbonates of nandrolone derivatives. These compounds can be used to treat hypogonadism, as hormonal therapy and as a male contraceptive. The disclosed carbonates have potent activity when administered as an oral composition. In addition, long-lasting activity has also been observed with subcutaneous administration in laboratory animals. It is foreseen that these androgens can be utilized in hormonal replacement therapy for both men and women, which constitute a huge market both in the United States and abroad.

Inventors: Richard P. Blye and Hyun K. Kim (NICHD).

Patent Status: U.S. Provisional Application No. 60/650,376 filed 04 Feb 2005 (HHS Reference No. E–181–2004/0–US–01); PCT Application No. PCT/US2006/02436 filed 24 Jan 2006 (HHS Reference No. E–181–2004/0–PCT–02).

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

Licensing Contact: Tara L. Kirby, PhD; 301/435–4426; tarak@mail.nih.gov.

Collaborative Research Opportunity: The NICHD Contraception & Reproductive Health Branch 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.

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

Description of Technology: 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 J. Pavan and Stacie K. Loftus (NHGRI).

Patent Status: HHS Reference No. E–014–2002/0—Research Tool.

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

Licensing Contact: Tara L. Kirby, PhD; 301/435–4426; *tarak@mail.nih.gov.*

RAB38, a Target for Treatment of Melanoma and Pigmentation Disorders

Description of Technology: 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:

1. Marker protein and target for antigen-specific immunotherapy in patients with malignant melanoma.

2. Therapeutics and diagnostics for melanin-related disorders.

Development Status: Early stage.

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

Publications: 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.

Patent Status:

1. U.S. National Stage Application No. 10/501,611 filed 20 Nov 2005, claiming priority to 18 Jan 2002 (HHS Reference No. E–315–2001/0–US–07).

2. Foreign counterparts pending in Australia, Canada, Europe, and Japan.

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

Licensing Contact: Tara L. Kirby, Ph.D; 301/435–4426; *tarak@mail.nih.gov.*

Novel Dmt-Tic Analogues Specific for Delta- and Mu-Opioid Receptors

Description of Technology: Opioid receptor modulators, used historically for pain control, have more recently been shown to possess broader therapeutic potential in areas such as opiate and alcohol abuse, neurological disease or injury, neuropeptide or neurotransmitter imbalance, and immune system dysfunction. Furthermore, their interaction with key reward pathways presents interesting avenues for exploration in the treatment of food as an addictive substance, due to the fact that obesity is a major health problem in the U.S. Also, evidence of modulatory interactions between delta- and mu-opioid receptors has spurred interest in new opioid ligands possessing mixed and dual specificity for these receptors. These bifunctional compounds are particularly promising for treatment of addiction and treatment of pain with the elimination of drug tolerance.

The inventors have developed a wide variety of highly selective Dmt-Tic analogues with potential therapeutic applications. These analogues include specific agonists and antagonists of the delta- and mu-opioid receptors and combinations thereof.

Some disclosed analogues are di- and tri-peptidic derivatives of the Dmt-Tic pharmacophore; in addition to opioid receptor specificity, two of these derivatives have been shown to inhibit the activity of human multidrug resistance glycoprotein 1 (hMDR1) and may represent a novel chemosensitizing agent for treating cancer, and may also be used for reducing tolerance to morphine, the drug of choice in most hospitals around the world, thereby increasing its effectiveness. Also disclosed are compounds produced through derivatization of Dmt-Tic reference compounds with lysine, resulting in an unexpected and broad range of delta-and/or mu-opioid receptor modulation. The inventors have also prepared symmetric and asymmetric Dmt-Tic di-peptides that are potent dual delta- and mu-opioid receptor antagonists and that can pass through the gastrointestinal and blood-brain barriers. Finally, the inventors have prepared various fluorescent Dmt-Tic analogs that are useful for study of delta- and mu-opioid receptor structure and function.

Applications:

1. Potential opiate, food, and alcohol addiction therapeutics.

2. Potential therapeutics for pain treatment.

3. Potential therapeutics for cancer.

4. Tools for screening ligand binding activity and differentiating between delta- and mu-opioid receptors.

Market:

1. In 2004, approximately 22 million Americans over the age of 12 required treatment for alcohol or illicit drug abuse and addiction; 13 million of these were classified as alcoholics.

2. Approximately 50 million Americans suffer from pain, and an estimated 1.5 billion people suffer from moderate to severe pain worldwide.

3. Two-thirds of the U.S. population is overweight, with a quarter designated as obese (9 million of whom are children); the number of overweight Americans doubled between 1980–1999 and is predicted to increase 20% by 2013 to 140 million.

Development Status: In vitro data are available.

Inventors: Lawrence H. Lazarus (NIEHS) et al.

Publications:

1. G. Balboni et al. Effect of lysine at C-terminus of the Dmt-Tic opioid pharmacophore. J Med Chem. 2006 Sep 7;49(18):5610–5617.

2. T Lovekamp et al. Inhibition of human multidrug resistance P-glycoprotein 1 by analogues of a potent delta-opioid antagonist. Brain Res. 2001 May 25;902(1):131–134.

3. T Li et al. Potent Dmt-Tic pharmacophoric delta- and mu-opioid receptor antagonists. J Med Chem. 2005 Dec 15;48(25):8035–8044.

4. T Li et al. Transformation of a mu-opioid agonist into biologically potent mu-opioid antagonists. Bioorg Med Chem. 2007 Feb 1;15(3):1237–1251.

5. G. Balboni et al. Highly selective fluorescent analogue of the potent *elta-opioid receptor antagonist Dmt-Tic. J Med Chem. 2004 Dec 16:47(26):6541–6546.

Patent Status:

1. U.S. Patent No. 6,753,317 issued 22 Jun 2004 (HHS Reference No. E–103–2000/0–US–02).

2. U.S. Patent No. 6,916,905 issued 12 Jul 2005 (HHS Reference No. E–103–2000/1–US–01).

3. U.S. Patent Application No. 10/280,752 filed 16 Nov 2005 (HHS Reference No. E–103–2000/2–US–02).

4. U.S. Provisional Application No. 60/834,438 filed 31 Jul 2006 (HHS Reference No. E–103–2000/3–US–01).

5. PCT Application No. PCT/US06/33560 filed 30 Aug 2006 (HHS Reference No. E–305–2005/0–PCT–02).

Licensing Status: Available for exclusive or nonexclusive licensing.

Licensing Contact: Tara L. Kirby, PhD; 301/435–4426; *tarak@mail.nih.gov.*

Dated: April 17, 2007.

Steven M. Ferguson,

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

[FR Doc. E7–7933 Filed 4–25–07; 8:45 am]

BILLING CODE 4140–01–P

DEPARTMENT OF HOMELAND SECURITY

Coast Guard

[USCG–2007–27858]

National Boating Safety Advisory Council; Vacancies

AGENCY: Coast Guard, DHS.

ACTION: Request for applications.

SUMMARY: The Coast Guard seeks applications for membership on the National Boating Safety Advisory Council (NBSAC). NBSAC advises the Coast Guard on matters related to recreational boating safety.

DATES: Application forms should reach us on or before August 17, 2007.

ADDRESSES: You may request an application form by writing to Commandant, Office of Boating Safety (CG–3PCB–1), U.S. Coast Guard, 2100 Second Street, SW., Washington, DC 20593–0001; by calling 202–372–1062; or by faxing 202–372–1932. Send your application in written form to the above street address. This notice and the application form are also available on the Internet at: *http://www.uscgboating.org/nbsac/nbsac.htm.*

FOR FURTHER INFORMATION CONTACT: Mr. Jeff Ludwig, Executive Secretary of