relation to the referral of Medicare beneficiaries to a durable medical equipment company, in violation of the Medicare antikickback law (42 U.S.C. 1320a–7b), and in violation of 18 U.S.C. 371. The court sentenced Dr. Caro to 2 years probation for the offense (*United States* v. *Eduardo Caro*, Docket No. 00CR020–05 (SEC) (D.P.R. July 13, 2001)).

At the time of Dr. Caro's criminal actions, he was a physician authorized to practice medicine in Puerto Rico as a Medicare provider and was authorized to prescribe, among other things, durable medical equipment to Medicare beneficiaries. The owner of a durable medical equipment company, authorized to sell to Medicare beneficiaries, offered and paid money to Dr. Caro to unlawfully induce him to refer patients to the medical equipment company. Dr. Caro received money in return for referring patients to the company for the furnishing of durable medical equipment and services payable under the Medicare program, the specific amount depending on the value of the service or equipment referred to the company. The unlawful kickback payments made to Dr. Caro allowed the company to improperly invoice Medicare for approximately $11,940.

In addition, Dr. Caro demonstrated a pattern of conduct sufficient to find reason to believe that he may violate requirements under the act relating to drug products. In July 2002, FDA issued Dr. Caro a Notice of Disqualification to Receive Investigational New Drugs. This action was based upon repeated and deliberate submissions of false information to drug sponsors in required reports for studies of investigational new drugs that are subject to section 505 of the act. In addition, Dr. Caro repeatedly and deliberately failed to comply with regulations governing the conduct of clinical investigators and the use of investigational new drugs in conducting two protocols sponsored by Daiichi Pharmaceutical Corp. Among other things, he submitted false information in required reports, deviated from protocols, maintained inaccurate and inadequate study records, failed to report adverse events, failed to properly account for the disposition of study medications, failed to obtain adequate institutional review board approval, and failed to obtain proper consent from study subjects or their legally authorized representatives. As a result, he is no longer entitled to receive investigational new drugs (Notice of Disqualification to Receive Investigational New Drugs, July 30, 2002).

As a result of Dr. Caro's conviction and pattern of conduct, FDA served him by certified mail on February 18, 2004, a notice proposing to debar him for 5 years from providing services in any capacity to a person that has an approved or pending drug product application. The proposal also offered Dr. Caro an opportunity for a hearing on the proposal. The proposal was based on a finding, under section 306(b)(2)(B)(ii) of the act (21 U.S.C. 335a(b)(2)(B)(ii)), that Dr. Caro was convicted of a felony under Federal law for engaging in a conspiracy to defraud the United States and has demonstrated a pattern of conduct sufficient to find that there is reason to believe that he may violate requirements under the act relating to drug products. Dr. Caro was provided 30 days to file objections and request a hearing. Dr. Caro did not request a hearing. His failure to request a hearing constitutes a waiver of his opportunity for a hearing and a waiver of any contentions concerning his debarment.

II. Findings and Order

Therefore, the Director, Center for Drug Evaluation and Research, under section 306(b)(2)(B)(ii) of the act and under authority delegated to him (Staff Manual Guide 1410.035), finds that Dr. Eduardo Caro Acevedo has been convicted of a felony under Federal law for engaging in a conspiracy to defraud the United States and has demonstrated a pattern of conduct sufficient to find that there is reason to believe that he may violate requirements under the act relating to drug products.

As a result of the foregoing findings, Dr. Caro is debarred for 5 years from providing services in any capacity to a person with an approved or pending drug product application under sections 505, 512, or 802 of the act (21 U.S.C. 355, 360b, or 382), or under section 351 of the Public Health Service Act (42 U.S.C. 262), effective March 24, 2005 (see sections 306(c)(1)(B) and (c)(2)(A)(iii) and 201(dd) of the act (21 U.S.C. 321(dd))). Any person with an approved or pending drug product application who knowingly uses the services of Dr. Caro, in any capacity, during his period of debarment, will be subject to civil money penalties (section 307(a)(6) of the act (21 U.S.C. 355b(a)(6))). If Dr. Caro, during his period of debarment, provides services in any capacity to a person with an approved or pending drug product application, he will be subject to civil money penalties (section 307(a)(7) of the act). In addition, FDA will not accept or review any abbreviated new drug applications submitted by or with the assistance of Dr. Caro during his period of debarment.

Any application by Dr. Caro for termination of debarment under section 306(d)(4) of the act should be identified with Docket No. 2001N–0541 and sent to the Division of Dockets Management (see **ADDRESSES**). All such submissions are to be filed in four copies. The public availability of information in these submissions is governed by 21 CFR 10.20(j). Publicly available submissions may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

Dated: March 5, 2005.

Steven K. Galson,

Acting Director, Center for Drug Evaluation and Research.

[FR Doc. 05–5781 Filed 3–23–05; 8:45 am]

BILLING CODE 160–01–S

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Government-Owned Inventions; Availability for Licensing

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

ACTION: Notice.

SUMMARY: The inventions listed below are owned by 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.

Minimally Immunogenic Germline Sequence Variants of COL–1 Antibody and Their Use

Syed Kashmiri (NCI), Eduardo Padlan (NIDDK), and Jeffrey Schlom (NCI)

U.S. Provisional Application No. 60/562,781 filed 15 Apr 2004 (DHHS Reference No. E–105–2004/0–US–01) and U.S. Provisional Application No.

60/580,839 filed 16 Jun 2004 (DHHS Reference No. E–105–2004/1–US–01)

Licensing Contact: Jeffrey Walenta; 301/435–4633; *walentaj@mail.nih.gov.*

This invention relates to humanized monoclonal antibodies that bind to the tumor antigen carcinoembryonic antigen (CEA). More specifically, the present technology relates to humanized COL–1 antibodies that have minimal immunogenicity and retain antigen-binding affinity for CEA. CEA is over expressed in 95% of gastrointestinal and pancreatic tumors. Because CEA is over expressed consistently, it is anticipated that CEA would be an excellent target for an antibody-based therapeutics.

The invention also discloses a novel method for humanizing monoclonal antibodies. This humanization method encompasses grafting xenogenic Specificity Determining Regions (SDRs) onto Complementarity Determining Regions (CDR) templates derived from several different human germline sequences. The use of several different human germline sequences greatly reduces the potential for immunogenicity and greatly minimizes the number of SDRs required for equivalent or better antigen binding of the antibody.

This humanization method is applicable to development of antibodies to any immunogenic epitopes.

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

Modulating p38 Kinase Activity

Jonathan D. Ashwell et al. (NCI)

PCT Application filed 04 Feb 2005 (DHHS Reference No. E–010–2004/2–PCT–01)

Licensing Contact: Marlene Shinn-Astor; 301/435–4426; *shinnm@mail.nih.gov.*

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.

References: JM Salvador *et al.*, ''The autoimmune suppressor Gadd45alpha inhibits the T cell alternative p38 activation pathway,'' Nat. Immunol. advance online publication, 27 Feb 2005 (doi:10.1038/ni1176); JM Salvador *et al.*, ''Alternative p38 activation pathway medicated by T cell receptor-proximal tyrosine kinases,'' Nat. Immunol. advance online publication, 27 Feb 2005 (doi:10.1038/ni1177).

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

Mu Opiate Receptor Knockout Mouse

George R. Uhl (NIDA)

DHHS Reference No. E–034–2003/0—Research Material

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

The researchers produced heterozygous and homozygous mu opiate receptor knockout mice that displayed 54% and 0% of wild-type levels of mu opiate receptor expression, respectively. These knockout mice were generated by injecting 15–20 homologous, recombinant ES cells into blastocysts harvested from C57BL/6J mice and by implanting the blastocysts into the uteri of pseudopregnant CD–1 mice.

Morphine acts on opiate receptors found on spinal and supraspinal neurons in the central nervous system. There are three main subtypes of these receptors, mu, kappa, delta. Morphine produces an analgesic effect by acting through these receptors, especially the mu receptor. However, the roles played by each of these receptors in pain processing in either drug-free or morphine-treated states are not clear. A mu opiate receptor knockout mouse model can be used to elucidate mechanistic and behavioral roles of this receptor subtype.

Reference: I. Sora et al., ''Opiate receptor knockout mice define mu receptor roles in endogenous mociceptive responses and morphine-induced analgesia,'' Proc. Natl. Acad. Sci. USA 18 Feb 1997 94(4):1544–1549.

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

Tryptophan as a Functional Replacement for ADP-ribose-arginine in Recombinant Proteins

Joel Moss et al. (NHLBI)

U.S. Patent Application No. 10/517,565 filed 07 Dec 2004 (DHHS Ref. No. E–160–2002/0–US–03), claiming priority to 28 Jun 2002; Foreign rights available

Licensing Contact: Marlene Shinn-Astor; 301/435–4426; *shinnm@mail.nih.gov.*

Bacterial toxins such as cholera toxin and diphtheria toxin catalyze the ADP-ribosylation of important cellular target proteins in their human hosts, thereby, as in the case of cholera toxin, irreversibly activating adenylyl cyclase. In this reaction, the toxin transfers the ADP-ribose moiety of Nicotinamide Adenine Dinucleotide (NAD) to an acceptor amino acid in a protein or peptide. ADP-ribosylation leads to a peptide/protein with altered biochemical or pharmacological properties. Mammalians proteins catalyze reactions similar to the bacterial toxins. The ADP-ribosylated proteins represent useful pharmacological agents, however, their use is limited by the inherent instability of the ADP-ribose-protein linkage.

The NIH announces a new technology wherein recombinant proteins are created that substitute tryptophan for an arginine, thereby making the protein more stable, and better suited as agents for therapeutic purposes. The modification creates an effect similar to ADP-ribosylation of the arginine. An example of a protein that can be modified is the defensin molecule, which is a broad-spectrum antimicrobial that acts against infectious agents and plays an important role in the innate immune defense in vertebrates.

In addition to licensing, the technology is available for further development through collaborative

research opportunities with the inventors.

Cannula for Pressure Mediated Drug Delivery

Stephen Wiener, Robert Hoyt, John Deleonardis, Randal Clevenger, Robert Lutz, Brian Safer (NHLBI)

PCT Application No. PCT/US99/11277 filed 21 May 1999, which published as WO 99/59666 on 25 Nov 1999 (DHHS Reference No. E–196–1998/2–PCT–01); U.S., Australian, Japanese, and European rights pending

Licensing Contact: Michael Shmilovich; 301/435–5019; *shmilovm@mail.nih.gov*.

Available for licensing are methods and devices for selective delivery of therapeutic substances to specific histologic or microanatomic areas of organs (introduction of the therapeutic substance into a hollow organ space (such as an hepatobiliary duct or the gallbladder lumen) at a controlled pressure, volume or rate allows the substance to reach a predetermined cellular layer (such as the epithelium or sub-epithelial space). The volume or flow rate of the substance can be controlled so that the intralumenal pressure reaches a predetermined threshold level beyond which subsequent subepithehal delivery of the substance occurs. Alternatively, a lower pressure is selected that does not exceed the threshold level, so that delivery occurs substantially only to the epithelial layer. Such site-specific delivery of therapeutic agents permits localized delivery of substances (for example to the interstitial tissue of an organ) in concentrations that may otherwise produce systemic toxicity. Occlusion of venous or lymphatic drainage from the organ can also help prevent systemic administration of therapeutic substances, and increases selective delivery to superficial epithelial cellular layers. Delivery of genetic vectors can also be better targeted to cells where gene expression is desired. The access device comprises a cannula with a wall piercing tracar within the lumen. Two axially spaced inflatable balloons engage the wall securing the cannula and sealing the puncture site. A catheter equipped with an occlusion balloon is guided through the cannula to the location where the therapeutic substance is to be delivered.

Dated: March 17, 2005.

Steven M. Ferguson,

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

[FR Doc. 05–5875 Filed 3–23–05; 8:45 am]

BILLING CODE 4140–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Clinical Center; Amended Notice of Meeting

Notice is hereby given of a change in the meeting of the NIH Advisory Board for Clinical Research, March 28, 2005, 10 a.m. to March 28, 2005, 2 p.m., National Institutes of Health, Building 10, 10 Center Drive, Medical Board Room 4–2551, Bethesda, MD, 20892 which was published in the **Federal Register** on March 11, 2005, FR 70 12223.

The open session will occur from 10 a.m.–1 p.m. The closed session will begin approximately at 1 p.m. and run until 2 p.m. The meeting will be held in the Clinical Center, Bldg. 10, Rm. 4–2551, CRC Medical Board Room. The meeting is partially closed to the public.

Dated: March 17, 2005.

LaVerne Y. Stringfield,

Director, Office of Federal Advisory Committee Policy.

[FR Doc. 05–5872 Filed 3–23–05; 8:45 am]

BILLING CODE 4140–01–M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Heart, Lung, and Blood Institute; Notice of Closed Meeting

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

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

Name of Committee: National Heart, Lung, and Blood Institute Special Emphasis Panel, Review of Research Projects (Cooperative Agreements) (U01s).

Date: April 18, 2005.

Time: 2 p.m. to 3:30 p.m.

Agenda: To review and evaluate cooperative agreement applications.

Place: National Institutes of Health, 6701 Rockledge Drive, Bethesda, MD 20892, (Telephone Conference Call).

Contact Person: Keith A. Mintzer, PhD, Scientific Review Administrator, Review Branch, Division of Extramural Affairs, National Heart, Lung, and Blood Institute, National Institutes of Health, 6701 Rockledge Drive, Room 7186, MSC 7924, Bethesda, MD 20892, 301–435–0280.

(Catalogue of Federal Domestic Assistance Program Nos. 93.233, National Center for Sleep Disorders Research; 93.837, Heart and Vascular Diseases Research; 93.838, Lung Diseases Research; 93.839, Blood Diseases and Resources Research, National Institutes of Health, HHS)

Dated: March 17, 2005.

LaVerne Y. Stringfield,

Director, Office of Federal Advisory Committee Policy.

[FR Doc. 05–5870 Filed 3–23–05; 8:45 am]

BILLING CODE 4140–01–M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Institute of Diabetes and Digestive and Kidney Diseases; Notice of Closed Meetings

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

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

Name of Committee: National Institute of Diabetes and Digestive and Kidney Diseases Special Emphasis Panel, Antidepressant Therapy for Functional Dyspepsia.

Date: April 4, 2005.

Time: 3 p.m. to 4:30 p.m.

Agenda: To review and evaluate grant applications.

Place: National Institutes of Health, Two Democracy Plaza, 6707 Democracy Boulevard, Bethesda, MD 20892. (Telephone Conference Call).

Contact Person: Lakshmanan Sankaran, PhD, Scientific Review Adminstrator, Review Branch, DEA, NIDDk, National Institutes of Health, Room 777, 6707 Democracy Boulevard, Bethesda, MD 20892–5452, (301) 594–7799, *Is38oz@nih.gov*.

This notice is being published less than 15 days prior to the meeting due to the timing