detectable by MRI or CT, which functions as a surrogate for the motion of the therapeutic agent through the solid tissue. In other particular embodiments, the tracer is the therapeutic agent conjugated to an imaging moiety. The method of this invention uses non-toxic macromolecular MRI contrast agents comprised of chelated Gd(III). In particular, the surrogate tracer used in this invention is a serum albumin conjugated with either a gadolinium chelate of 2-(p-isothiocyanotobenzyl)-6-methyldiethylenetriamine pentaacetic acid or with iopanoic acid. These macromolecular imaging agents have clearance properties that mimic the pharmacokinetic properties of co-administrated drugs, so as to be useful in quantifying the range and dosage level of therapeutic drugs using MR imaging.

Refinement of Isointensity Surfaces

Peter Yim (CC)
DHHS Reference No. E–078–2002/0 filed Feb 22, 2002
Licensing Contact: Dale Berkley; 301/435–5019; *berkleyd@od.nih.gov*

The invention is a method for reconstructing arterial geometry from magnetic resonance angiography (MRA) using isosurfaces deformed to conform to the boundaries of objects in the image with minimal a priori assumptions of object shape. The method determines the degree of stenosis in digital phantoms with an accuracy of at least 10%. This method, unlike previous techniques, does not require the imposition of a pre-defined surface mesh onto the image or user interaction for definition of the vessel axes. Here, the deformable model surface mesh is generated by the isosurface algorithm. Accordingly, the new method requires minimal user interaction and provides highly accurate results when applied to the evaluation of vascular stenoses. The methodology may also be applicable for reconstruction of the geometry of vascular aneurysms from MRA. Other potential applications include precision surface reconstruction of vascular surfaces from computed tomographic angiography (CTA) and precision reconstruction of the surface of the colon from computed tomography (CT).

Automated Centerline Detection Algorithm for Colon-Like 3D Surfaces

Gheorghe Iordanescu (CC), Ronald Summers (CC), Juan Cebral
DHHS Reference No. E–311–2001 filed Dec. 27, 2001
Licensing Contact: Dale Berkley; 301/435–5019; *berkleyd@od.nih.gov*

The invention is a method for obtaining the centerline of a colon-like surface, which is an important tool for virtual colonoscopy. The invention uses only three steps: (1) Computing a shrunken version of the colon surface (2) modeling the shrunken colon by an ordered group of 3D points and (3) selecting equally distanced planes to define equal length segments along the centerline. The centerline is a vital parameter for any virtual colonoscopy technique as it defines a navigation path along which the imaging proceeds and it provides a natural coordinate system for describing polyp detections. A virtual colonoscopy method is described and claimed in NIH-owned U.S. Patent No. 6,246,784. However, detecting the centerline of the colon is a challenging problem for which a number of approaches have been developed. Most of these approaches are not fully automatic, are slow and require the original CT images. The method of this invention is fully automatic, relatively quick and uses only the 3D surface rather than the original CT images.

Discovery of Novel Inhibitors of HIV–1 Integrase That Can Be Used for the Treatment of Retroviral Infection Including AIDS

Terrence R. Burke, Jr., Xuechen Zhang, Godwin C. G. Pais, Christophe Marchand, Evguenia Svarovskaia, Vinay K. Pathak, and Yves Pommier (NCI)
DHHS Reference No. E–317–2001/0 filed Dec. 07, 2001
Licensing Contact: Sally Hu; 301/435–5606; *hus@od.nih.gov*

This invention provides azido group-containing diketo acids that can inhibit HIV–1 integrase in vitro efficiently while being highly selective for the strand transfer step of the integration reaction. Human Immunodeficiency Virus (HIV) and other retroviruses require three viral enzymes for replication: Reverse transcriptase, protease and integrase. The prognosis of AIDS has been improved recently by the discovery and application of reverse transcriptase and protease inhibitors. However, a significant fraction of patients fail to respond to such treatments and viral resistance remains a major problem. Furthermore, anti-AIDS combinations are often not well tolerated. Thus, HIV integrase is a rational target for AIDS therapy because genetic studies demonstrated that the enzyme is essential for viral replication while being without a cellular equivalent. Therefore, specific integrase inhibitors should be effective and devoid of toxicity. Since this invention involves the discovery of novel HIV–1 integrase inhibitors that are derived from diketo acids with a different anti-HIV mechanism from that of reverse transcriptase and protease inhibitors, these azide group-containing compounds may represent potential new therapeutics for treatment of retroviral infections, including AIDS.

Dated: November 4, 2002.

Jack Spiegel,

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

[FR Doc. 02–28537 Filed 11–7–02; 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, DHHS.

ACTION: Notice.

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

ADDRESSES: Licensing information and copies of the U.S. patent applications listed below may be obtained by writing to the indicated licensing contact at the Office of Technology Transfer, National Institutes of Health, 6011 Executive Boulevard, Suite 325, Rockville, Maryland 20852–3804; telephone: 301/496–7057; fax: 301/402–0220. A signed Confidential Disclosure Agreement will be required to receive copies of the patent applications.

Regulation of INS (3456) P4 Signalling by a Reversible Kinase/Phosphatase and Methods and Compositions Related Thereto

Dr. Stephen Shears (NIEHS)
DHHS Reference No. E–105–2002/0 filed Mar 18, 2002
Licensing Contact: Marlene Shinn; 301/435–4426; *shinnm@od.nih.gov*.

Signaling entities are frequently controlled by quite delicate shifts in the dynamic balance of regulatory signals with competing impacts. Ion channels provide particularly impressive

examples of the degree of signal amplification that can result; switching the conductance state of a single channel can influence the transmembrane movement of millions of ions per second. Both stimulatory (Ca^{2t} and CaMKII) and inhibitory ($Ins(3,4,5,6)P_4$ signals converge on the family of so-called ''Ca^{2t}-activated'' Cl^- channels. Thus receptor-dependent changes in $Ins(3,4,5,6)P_4$ levels is a topic of general biological significance, in that it impacts upon regulation of salt and fluid secretion from epithelial cells, cell volume homeostasis, and electrical excitability in neurons and smooth muscle. Unfortunately, understanding of the cellular control on $Ins(3,4,5,6)P_4$-signaling has been rudimentary, because the pathway of $Ins(3,4,5,6)P_4$ synthesis has not previously been characterized.

The NIH announces new treatment methods for asthma, bronchitis and cystic fibrosis. The treatments consist of either increasing or decreasing the activity of inositol 1,3,4,5,6 pentakisphosphate 1-phosphatase in a patient, thereby controlling $Ins(3,4,5,6)P_4$-signaling which in turn affects the choride channels and mucus secretion produced. This modulation of inositol 1,3,4,5,6 pentakisphosphate 1-phosphatase is accomplished with the help of an inositol phosphate kinase, which can also act as an inositol pentakisphosphate 1-phosphatase.

Mutated Constitutively Active Nuclear Orphan Receptor

Masahiko Negishi, Akiko Ueda, Lars C. Pedersen, Satoru Kakizaki, Tatsuya Sueyoshi (NIEHS)
DHHS Reference No. E–034–2002/0 filed Feb. 19, 2002
Licensing Contact: Marlene Shinn; 301/435–4426; *shinnm@od.nih.gov*.

The constitutively active nuclear orphan receptor (CAR) activates transcription of genes encoding various drug-metabolizing enzymes such as cytochromes P450 in response to drug exposures. Induction of these enzymes confers on organisms a higher metabolic capability to defend themselves against xenochemical toxicity and/or carcinogenicity. Direct drug responses, however, have not been demonstrated with CAR in a cell-mediated transfectin assay, due to its *in vitro* constitutive activity.

The NIH announces the creation of an altered CAR molecule, with decreased constitutive activity *in vitro* using site-directed mutagenesis to the receptor. This alteration allows the CAR molecule to be directly activated by drugs and can be used for *in vitro* drug screening that will make the screenings more efficient and cost effective.

Bone-Forming Composition, Methods for Making and Methods of Use

Mahesh H. Mankani, Sergei Kuznetsov, Pamela G. Robey (NIDCR)
DHHS Reference No. E–263–2001/0 filed Jan. 25, 2002
Licensing Contact: Marlene Shinn; 301/435–4426; *shinnm@od.nih.gov*.

Transplantation of bone marrow stromal cells (BMSCs) offers a method for repairing and/or closing large bone defects. Although most bone defects occur as a result of trauma, bone loss can also arise from congenital disorders, neoplasms, and/or infections. To make BMSC transplantation most useful as a method for engineering new bone, it would be helpful to optimize the growth rate, extent, and strength of newly formed bone. Current methods of transplantation produce bone that is nonuniform in size, shape and form, making it difficult to compare bone samples directly.

The NIH announces a new method of forming bone tissue based on using a combination of bone marrow stromal cells and hydroxyapatite/tricalcium phosphate particles. The newly created bone has desired dimensions, which are similar, consistent, and/or identical to the shapes of the preformed compositions. When the composition is made with human BMSCs derived from pathological tissue, and transplanted into immunodeficient mice, the new bone reproduces features of the original disease, allowing for the testing of agents that inhibit, stimulate, or modify bone formation.

Methods of Making, Using and Pharmaceutical Formulations Comprising 7-Alpha,11-Beta-Dimethyl-17-Beta-Hydroxyestra-4,14-Dien-3-One and 17 Esters Thereof and 7-Alpha,11-Beta-Dimethyl-17-Beta-Hydroxyestra-4-en-3-One 17-Undecanoate

Drs. Richard Blye and H.K. Kim (NICHD)
DHHS Reference No. E–069–2000/3 filed Mar. 29, 2002 (PCT–CIP Patent Application)
Licensing Contact: Marlene Shinn; 301/435–4426; *shinnm@od.nih.gov*.

The NIH announces a new technology that relates to compounds that possess potent androgenic activity. These compounds offer a potential therapeutic benefit in the treatment of hypogonadism, regardless of cause, as an adjuvant in hormone replacement therapy for both men and women and for androgen stimulation of anabolism in a broad spectrum of disease entities involving debilitation.

These compounds exhibit both oral and parenteral androgenic activity. Oral activity appears greater than that of methyltestosterone. Parenteral activity as an aqueous suspension is substantially longer than that produced by testosterone enanthate or testosterone cypionate. Since these compounds lack a 17-alkyl moiety, they are expected to show less hepatotoxicity upon oral administration. Claims in this patent application are drawn to the new androgenic compounds themselves, their method of preparation, pharmaceutical formulations containing the new androgens and their utility and use in a wide spectrum of therapeutic applications.

Dated: November 4, 2002.

Jack Spiegel,

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

[FR Doc. 02–28538 Filed 11–7–02; 8:45 am]

BILLING CODE 4140–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Notice of Meeting; Interagency Autism Coordinating Committee

The National Institutes of Health (NIH) hereby announces a meeting of the Interagency Autism Coordinating Committee (IACC) to be held on November 22, 2002, on the NIH campus in Bethesda, Maryland.

The Children's Health Act of 2000 (Pub. L. 106–310), Title I, section 104, mandated the establishment of an Interagency Autism Coordinating Committee (IACC) to coordinate autism research and other efforts within the Department of Health and Human Services (DHHS). In April 2001, Secretary Tommy Thompson delegated the authority to establish the IACC to the National Institutes of Health (NIH). The National Institute of Mental Health (NIMH) at the NIH has been designated the lead for this activity.

The IACC meeting will be open to the public, with attendance limited to space available. Individuals who plan to attend and need special assistance, such as sign language interpretation or other reasonable accommodations, should notify the contact person listed below in advance of the meeting.

Name of Committee: Interagency Autism Coordinating Committee.

Date: November 22, 2002.

Time: 8:30 a.m.–5:15 p.m.

Agenda: Discussion of autism activities across Federal agencies.

Place: National Institutes of Health, 9000 Rockville Pike, Building 31,