

complexes thereof, compositions thereof and methods of using same. The compounds of the present invention possess the same octadentate coordinating groups as DOTA and DTPA; however, these compounds have a combined macrocyclic and acyclic character. The macrocyclic component chosen is based upon 1,4,7-triazacyclononane-N,N',N''-triacetic acid ("NOTA"), while the acyclic component is a pendant bis(carboxymethyl)amino donor group that is connected by an alkylene bridge that is optionally substituted with an aralkyl group. The cooperative binding of the pendant donor groups coupled with the pre-organization and macrocyclic effect of the NOTA sub-structure accelerates complexation with metal ions and isotopes (e.g., Y(III), Gd(III); etc.) while maintaining a high level of stability of the complexes.

#### Compositions and Methods for Inhibiting Vascular Channels and Methods of Inhibiting Proliferation

Myung Hee Park, Paul M.J. Clement, Hartmut M. Hanauske-Abel, Edith C. Wolff, Hynda K. Kleinman, Bernadette M. Cracchiolo (NIDCR). DHHS Reference No. E-320-2001/0 filed 23 Aug 2001 and PCT/US02/26909 filed 23 Aug 2002.

*Licensing Contact:* Matthew Kiser; (301) 435-5236; [kiserm@od.nih.gov](mailto:kiserm@od.nih.gov).

Angiogenesis, the recruitment of new blood vessels, is recognized as an important factor in tumor proliferation in many types of cancer. It is generally accepted that therapeutic approaches that inhibit angiogenesis effectively limit, or even prevent, the formation of solid tumors. It has also been shown that anti-angiogenic therapeutics allow conventional radiation therapy and chemotherapy to be more effective.

This invention pertains to certain compounds that inhibit angiogenesis in a previously unrecognized way. These compounds also inhibit the proliferation of cells within intraepithelial neoplasias (clusters of abnormally proliferating epithelial cells that are the origin of cancers). The subject compounds specifically block the formation of the amino acids hypusine and hydroxyproline. The former is the critical residue of eukaryotic translation initiation factor 5A (eIF5A), which is important in cell cycle progression, and hydroxyproline constitutes the critical residue of the collagens. The targeted enzymes are deoxyhypusine hydroxylase and prolyl 4-hydroxylase, respectively.

This invention provides evidence for an important role of eIF-5A in angiogenesis, and discloses a family of

compounds with useful clinical properties. Specifically, these compounds include the core structures and potential derivatives of ciclopirox olamine, deferiprone, deferoxamine, and 2,2'-dipyridyl.

Ciclopirox olamine has potential for treatment of oral-pharyngeal cancer, and chemoprevention and treatment of cervical and vulvar cancer. Notably, this drug is FDA-approved in the USA as a topical medication against fungal infections while, in Europe, it is also approved for the treatment of yeast infections of the genital tract. The compound has a known clinical profile and lacks teratogenicity, potentially expediting clinical trials for new cancer treatment indications.

#### sFRP and Peptide Motifs That Interact With sFRP and Methods of Their Use

Jeffrey Rubin, Aykut Uren (both of NCI), Matthew Gillespie, Nicole Horwood, (both of St. Vincent's Institute of Medical Research), Brian Kay and Bernard Weisblum  
Serial No. PCT/US02/00869 filed 10 Jan 2002; Serial No. 60/260,908 filed 10 Jan 2001.

*Licensing Contact:* Susan S. Rucker; (301) 435-4478; email: [ruckers@od.nih.gov](mailto:ruckers@od.nih.gov).

These patent applications describe and claim inventions related to the protein sFRP-1 and methods of regulating signal transduction pathways using sFRP-1. sFRP-1 is a member of a family of secreted proteins (secreted Frizzled Related Proteins) that were originally identified as being able to bind to Wnt proteins. When bound to Wnts, sFRP-1 alters the ability of Wnt protein to bind its receptor (Frizzled), typically acting as an antagonist of Wnt signaling.

More particularly, the patent applications and inventions claimed therein relate to methods for influencing bone remodeling using sFRP-1. In particular, the patent application and claimed inventions relate to methods of inhibiting osteoclastogenesis with the sFRP-1 protein. The ability to inhibit osteoclast formation may be of value in developing treatments for diseases such as post menopaual osteoporosis, Paget's disease, lytic bone metastases, multiple myeloma, hyperparathyroidism, rheumatoid arthritis, periodontitis and hypercalcemia of malignancy.

In addition to describing the method of inhibiting osteoclast formation, the patent applications disclose various peptides containing a conserved motif that allows the peptide containing the motif to bind to sFRP-1.

This work has been published as WO 02/055547 (July 10, 2002).

Dated: April 8, 2003.

**Steven M. Ferguson,**

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

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## 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.

#### Scytovirins and Related Conjugates, Antibodies, Compositions, Nucleic Acids, Vectors, Host Cells, Methods of Production and Methods of Using Scytovirin

Michael R. Boyd (NCI), Barry R. O'Keefe (NCI), Tawnya C. McKee (NCI), Heidi R. Bokesch (SAIC).

Serial No. 60/381,322 filed 16 May 2002,

*Licensing Contact:* Sally Hu; (301) 435-5606; [huss@od.nih.gov](mailto:huss@od.nih.gov).

This invention provides: (1) Isolated and purified antiviral peptides or antiviral proteins named Scytovirins isolated and purified from aqueous extracts containing the cyanobacteria, *Scytonema varium*; (2) an antibody which binds an epitope of Scytovirin isolated and purified from *Scytonema*

varium; (3) a purified nucleic acid molecule that comprises a sequence which encodes an amino acid sequence homologous to Scytovirin; (4) a vector comprising the isolated and purified nucleic acid molecule and a host cell or organism comprising the vector; (5) a conjugate comprising the peptide and an effector component; and (6) a method of inhibiting prophylactically and therapeutically a viral infection. Thus, this invention may represent potential new therapeutics for treatment of retroviral infections, including AIDS. This invention is further described in Bokesch *et al.*, "A Potent Anti-HIV Protein from the Cultured Cyanobacteria *Scytonema varium*," *Biochemistry*, 2003, 42, 2578–2584.

#### **Benzoylalkylindolepyridinium Compounds and Pharmaceutical Compositions Comprising Such Compounds**

William G. Rice, Mingjun Huang, Robert W. Buckheit, Jr., David G. Covell, Grzegorz Czerwinski, Christopher Michejda, and Vadim Makarov (NCI).

DHHS Reference No. E–278–98/1 filed 18 Dec 2000 (PCT/US01/48311).

*Licensing Contact:* Sally Hu; (301) 435–5606; e-mail: [hus@od.nih.gov](mailto:hus@od.nih.gov).

The present invention provides novel antiviral compounds active against HIV. These compounds, referred to as benzoylalkylindolepyridinium compounds (BAIPs) are effective against HIV isolates that have developed mutations rendering conventional drugs ineffective. BAIPs apparently do not require intracellular phosphorylation nor bind to the reverse transcriptase (RT) active site, which distinguishes their mechanism of action from the dideoxynucleoside (ddN) and acyclic nucleoside phosphonate (ANP) nucleoside analog drugs. ddN and ANP have proven clinically effective against limited human immunodeficiency virus (HIV) infection, but resistance rapidly emerges due to mutations in and around the RT active site. The BAIPs also may be distinguished from non-nucleoside reverse transcriptase inhibitors (NNRTIs), in part because the BAIPs bind to a different site on the RT enzyme. The usage of NNRTIs is limited by the rapid emergence of resistant strains also. Moreover, unlike the NNRTIs, BAIPs of the present invention have been shown to be effective against HIV-1, HIV-2 and simian immunodeficiency virus (SIV) proliferation. Thus, BAIPs are broadly antiviral, non-nucleoside reverse transcriptase inhibitors (BANNRTIs).

#### **Spontaneous Breathing Apparatus and Method**

Theodor Kolobow (NHLBI).  
Serial No. 08/933,003 filed 18 Sep 1997;  
PCT/US98/19714 filed 18 Sep 1998;  
Serial No. 09/555,229 filed 26 May 2000.

*Licensing Contact:* Michael Shmilovich; 301/435–5019; email: [mish@codon.nih.gov](mailto:mish@codon.nih.gov).

A novel assisted breathing system and method that greatly decreases/eliminates the work of breathing and is under the total control of the patient.

The system includes a minitracheostomy tube, a reverse thrust gas insufflation catheter introduced through a special minitracheostomy tube to deliver well humidified air/oxygen to near the carina, and a threshold valve to limit airway plateau pressure. Inspiration is effected through spontaneous closing of the glottic opening, while expiration follows opening of the glottis. The patient can control the rate of respiration and tidal volumes. Lung inflation is therefore passive and accounts for the nominal work of breathing. Speech, sound, and coughing ability remains unimpeded.

#### **Ultrasound-Hall Effect Imaging System And Method**

Han Wen (NHLBI).  
Serial No. 60/021,204 filed 03 Jul 1996;  
PCT/US97/11272 filed 02 Jul 1997;  
Serial No. 09/202,459 filed 14 Dec 1998; and related foreign patent applications.

*Licensing Contact:* Michael Shmilovich; (301) 435–5019; email: [mish@codon.nih.gov](mailto:mish@codon.nih.gov).

The invention provides for a novel ultrasound-based imaging modality that is based on the interaction of a static magnetic field and conductive moieties in the imaged sample under electrical excitation. The invention also provides a novel ultrasound-based imaging modality that provides a contrast mechanism which reflects the conductivity distribution of the medium being imaged. The disclosed methods and system have the following advantages over other ultrasonic imaging systems: (a) The method is not limited to contrast based solely on acoustic properties; (b) it dispenses with acoustic beam excitation and is suitable for fast 2D and 3D image formation with wide angle signal reception. A working prototype system has been constructed and demonstrated 3D imaging. Results are published in peer reviewed journals: H. Wen, *Ultrason. Imaging* 2000 Apr;22(2):123–136; H. Wen, *Ultrason. Imaging* 1999 Jul;21(3):186–200; H. Wen *et al.*, *Ultrason. Imaging* 1998

Jul;20(3):206–220; H. Wen *et al.*, *IEEE TransBiomed. Eng.* 1998 Jan;45(1):119–124.

Dated: April 8, 2003.

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#### **Mutant A. nidulans Strains Requiring Anticancer or Antifungal Compounds for Growth**

Katherine Jung *et al.* (NCI)  
DHHS Reference No. E–312–2002/0  
(Biological Materials)

*Licensing Contact:* Susan Ano; 301/435–5515; [anos@od.nih.gov](mailto:anos@od.nih.gov).

This technology describes four genetically modified strains of *Aspergillus nidulans* that bear mutations in the gene encoding  $\gamma$ -tubulin, a protein required for initiation of microtubule formation and mitosis. As a result of the mutations, these strains require the presence of an antimicrotubule agent as either an absolute or conditional requirement for growth, making the strains useful for