These amounts include approximately $16 million by which suppliers in North Carolina and Tennessee will benefit due to implementation of the BIPA ambulance mileage provision for the period of July 1, 2001 through March 31, 2002.

Executive Order 12866 directs agencies to assess all costs and benefits of available regulatory alternatives and, if regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety effects, distributive impacts, and equity). A regulatory impact analysis (RIA) must be prepared for major rules with economically significant effects ($100 million or more in any 1 year). The aggregate amount of program spending to comply with the court's order will be approximately $81 million. Therefore this notice is not a major notice as defined in Title 5, United States Code, section 804(2) and is not an economically significant notice under Executive Order 12866.

The RFA requires agencies to analyze options for regulatory relief of small entities. For purposes of the RFA, small entities include small businesses, nonprofit organizations, and government agencies. Most hospitals and most other providers and suppliers are small entities, either by nonprofit status or by having revenues of $6 million to $29 million in any 1 year. Individuals and States are not considered to be small entities. We have determined that this notice will not have a significant economic impact on a substantial number of small entities. Therefore, we are not preparing an analysis for the RFA.

In addition, section 1102(b) of the Act requires us to prepare a regulatory impact analysis if a rule may have a significant impact on the operations of a substantial number of small rural hospitals. This analysis must conform to the provisions of section 604 of the RFA. For purposes of section 1102(b) of the Act, we define a small rural hospital as a hospital that is located outside of a Metropolitan Statistical Area and has fewer than 100 beds. We have determined that this notice will not have a significant effect on the operations of a substantial number of small rural hospitals. Therefore, we are not preparing an analysis for section 1102(b) of the Act.

Section 202 of the Unfunded Mandates Reform Act of 1995 also requires that agencies assess anticipated costs and benefits before issuing any rule that may result in expenditures in any 1 year by State, local, or tribal governments, in the aggregate, or by the private sector, of $110 million. This notice has no consequential effect on State, local, or tribal governments or on the private sector.

Executive Order 13132 establishes certain requirements that an agency must meet when it promulgates a rule that imposes substantial direct requirement costs on State and local governments, preempts State law, or otherwise has Federalism implications. This notice will not have a substantial effect on State or local governments.

In accordance with the provisions of Executive Order 12866, this regulation was reviewed by the Office of Management and Budget.

Authority: Sections 1102 and 1871 of the Social Security Act (42 U.S.C. 1302 and 1395hh).

(Catalog of Federal Domestic Assistance Program No. 93.774, Medicare—Supplementary Medical Insurance Program)

Dated: April 1, 2003.

Thomas A. Scully,

Administrator, Centers for Medicare & Medicaid Services.

Dated: April 11, 2003.

Tommy G. Thompson,

Secretary.

[FR Doc. 03–9503 Filed 4–15–03; 8:45 am]

BILLING CODE 4120–01–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.

Method and Materials for Promoting Migration of T Cells to the Vasculature of a Tumor

Patrick Hwu and Mary Tschoi (NCI). Serial No. 60/447,497 filed 14 Feb 2003. *Licensing Contact:* Jonathan Dixon; (301) 435–5559; *dixonj@od.nih.gov*.

Adoptive immunotherapy with T cells is a promising therapeutic modality for cancer. However, the effectiveness of this method of treatment appears to be limited by the inefficient migration of T cells to the tumor site. The present invention provides materials and methods that promote the migration of T cells to the vasculature of a tumor.

This invention discloses a novel method of administering modified autologous T cells, which bind to cell-surface molecules on endothelial cells of the vasculature of a tumor. Using the disclosed method and modified T cells, investigators were able to promote the migration of T cells to molecules expressed on the vasculature of tumors. It is anticipated that this method and these modified autologous T cells will improve the effectiveness of adoptive immunotherapy for a variety of tumors, including melanoma and many carcinomas and sarcomas.

This research has been described, in part, in Dudley *et al.*, Science 298:850–854 (25 October 2002).

Amplification and Overexpression of Septin9 MLL Septin-Like Fusion (MSF) and Methods Related Thereto

Cristina Montagna *et al.* (NCI). DHHS Reference No. E–003–2003. *Licensing Contact:* Matthew Kiser; (301) 435–5236; *kiserm@od.nih.gov*.

This invention pertains to methods of detecting cancer, a method of inhibiting a protein, oligonucleotides for use therein, a method of inducing apoptosis, methods of testing a candidate drug for efficacy as an anti-cancer drug and methods for evaluating the progression of cancer.

The inventors have demonstrated that the Septin9 gene in mice (MSF gene in humans) is amplified in cancer models for breast cancer. Furthermore, it has been shown that the product encoded by this gene is overexpressed in cancer. In this regard, the present invention provides methods of detecting cancer in a mammal. One method comprises determining whether or not the mammal has an amplification of the Septin9 (MSF) locus or an ortholog of the gene. In this method, overexpression of the protein or of the nucleic acid molecule is indicative of cancer. Another method

comprises determining whether or not the mammal has an overexpression of a protein or of a nucleic acid molecule, wherein the protein or the nucleic acid molecule is encoded by a MSF gene, a Septin9 gene, or an ortholog. In this method, overexpression of the protein or the nucleic acid molecule is indicative of cancer.

Additionally, the present invention also provides a method of inhibiting a protein encoded by the Septin9 gene (MSF gene) or an ortholog in a cell. The method comprises administering to the cell an interference RNA in an amount sufficient to reduce mRNA stability and inhibit protein synthesis. Isolated or purified oligonucleotides, which are suitable for use in the above method, are also disclosed.

This research is described, in part, in Montagna *et al.*, The septin 9 (MSF) gene is amplified and overexpressed in mouse mammary gland adenocarcinomas and human breast cancer cell lines, Cancer Research, in press.

Methods of Inhibiting Metastasis or Growth of a Tumor Cell

Sam Hwang (NCI).
Serial No. 60/425,472 filed 12 Nov 2002.
Licensing Contact: Jonathan Dixon; (301) 435–5559; e-mail: *dixonj@od.nih.gov*.

Cancer metastasis is the primary mechanism of clinical morbidity and mortality in patients from cancer. Recently, chemokine receptors have been shown to potentially play a role in tumor metastasis. One such receptor, CXC Chemokine Receptor-4 (CXCR-4), is expressed in many cancer-derived cell lines, from breast carcinoma and melanoma.

The present invention discloses the use of polypeptides to block CXCR-4-mediated metastasis. One such polypeptide, an 18 amino acid peptide named T22, has been shown to block CXCR-4 in CXCR-4-expressing melanoma cells. This invention shows that CXCR-4 can be blocked through the use of the T22 peptide to prevent the spreading of melanoma tumor cells in the lungs in a murine model of melanoma metastasis. By not allowing cells to metastasize, this invention could potentially reduce the morbidity and mortality that are normally associated with metastatic melanoma.

Method of Distinguishing Epithelioid Melanoma from Fibroblastoid Melanoma

Denise Simmons (NCI).
DHHS Reference No. E–233–2002 filed 31 Oct 2002.
Licensing Contact: Matthew Kiser; (301) 435–5236; *kiserm@od.nih.gov*.

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.

This research is described, in part, in Simmons *et al.*, Carcinogenesis, Vol. 23 No. 11, pp 1821–1830, November 2002.

Chondropsin-Class Antitumor V-ATPase Inhibitor Compounds, Compositions and Methods of Use Thereof

Michael Boyd and Kirk Gustafson (NCI).
DHHS Reference No. E–191–2002 filed 24 Jul 2002.
Licensing Contact: George Pipia; (301) 435–5560; *pipiag@od.nih.gov*.

Vacuolar type (H+) ATPase (V-ATPase) has been described as ''a universal proton pump of eukaryotes''. V-ATPase is responsible for maintaining internal acidity and is important in myriad of physiological functions, such as sorting of membrane proteins, proinsulin conversion, neurotransmitter uptake, and cellular degradation process. This new chondropsin, Poecillastrin-A, is a cytotoxic, 33-member ring, macrolide lactam, isolated from the sponge Poecillastra sp. It is structurally related to the chondropsin class of macrolide lactams. However, it possesses unique patterns of methylation and oxygenation, and it is the first member of this family of polyketide derivatives with a 33-membered macrocyclic ring. Its in vitro antitumor activity is comparable to that of the chondropsins, however the new structural features found in Poecillastrin-A broaden the known structural diversity of this family of potent antiproliferative and cytotoxic macrolide lantams. The chondropsins and poecillastrin A produce a distinctive pattern of differential cytotoxicity in the NCI's 60 cell antitumor screen that directly correlates with selective V-ATPase inhibitors. This compound and its derivatives could be directed to any cancer types and may have applicability as highly selective anticancer small molecule inhibitors.

This research is described, in part, in M. A. Rashid *et al.*, Organic Letters 2002, 4, 3293–3296. Also, for a reference on selective V-ATPase inhibitors see: M. R. Boyd *et al.*, J. Pharmacol. Exp. Ther. 2001, 297, 114–120.

Scorpionate-Like Pendant Macrocyclic Ligands, Complexes and Compositions Thereof, and Methods of Using Same

Martin Brechbiel and Hyun-soon Chong (NCI).
DHHS Reference No. E–063–2002/0 filed 03 Jun 2002.
Licensing Contact: Matthew Kiser; (301) 435–5236; kiserm@od.nih.gov.

Monoclonal antibodies (mAbs) have been employed as targeting biomolecules for the delivery of radionuclides into tumor cells in radioimmunotherapy (RIT). Numerous clinical trials have been performed to validate this modality of cancer therapy. Several useful B^- emitting radionuclides, including ^{131}I, ^{90}Y, ^{177}Lu, and ^{153}Sm, have been employed for labeling mAbs for RIT applications. The pure B^- emitting radionuclide ^{90}Y has been extensively studied in RIT due to its physical properties. The macrocyclic chelating agent 1,4,7,10-tetraazacyclododecane-N,N′,N″,N‴-tetraacetic acid (''DOTA'') is well-known to be an effective chelator of Y(III) and lanthanides. In general, DOTA conjugated to mAbs displays relatively slow and inefficient radiolabeling with Y(III) isotopes under mild conditions. This is contrary to the rapid and high-yield radiolabeling (> 90%) of mAbs conjugated with bifunctional derivatives of the acyclic chelating agent diethylenetriaminepentaacetic acid (DTPA). Thus, there is still a need for a compound that possesses complex stability comparable to that of DOTA, the excellent practical complexation kinetics of DTPA, and increased stability in vitro and in vivo. The subject invention provides such a compound.

The invention provides substituted 1,4,7-triazacyclononane-N,N′,N″-triacetic acid compounds with a pendant donor amino group, metal

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*.

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*.

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 menopausal 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.

[FR Doc. 03–9284 Filed 4–15–03; 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.

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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; *hus@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