

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, CXCR4 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; kiser@m.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; pipia@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 lactams. 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; kiser@m.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 ¹³¹I, ⁹⁰Y, ¹⁷⁷Lu, and ¹⁵³Sm, have been employed for labeling mAbs for RIT applications. The pure B⁻ emitting radionuclide ⁹⁰Y 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