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PCT

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- (51) International Patent Classification:
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- (22) International Filing Date: 5 October 2007 (05.10.2007)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:
60/850,136 6 October 2006 (06.10.2006) US
- (71) Applicant (for all designated States except US): THE
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Fruit Street, Boston, MA 02114 (US).

AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

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- (74) Agents: RESNICK, David, S. et al.; Nixon Peabody LLP, 100 Summer Street, Boston, MA 02110-2131 (US).
- (81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM,

Declaration under Rule 4.17:

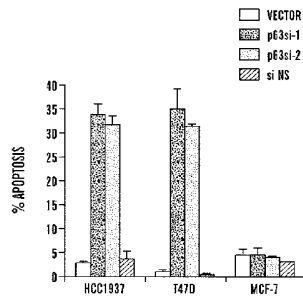
— of inventorship (Rule 4.17(iv))

Published:

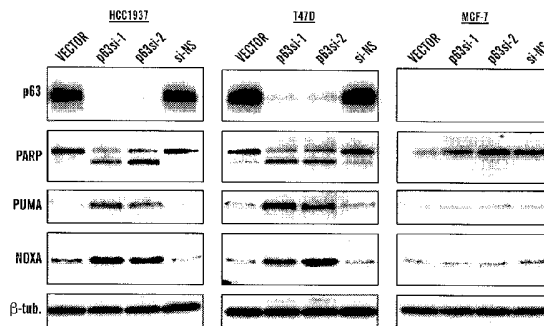
— without international search report and to be republished upon receipt of that report

— with sequence listing part of description published separately in electronic form and available upon request from the International Bureau

(54) Title: METHODS TO DETERMINE RESPONSIVENESS TO CISPLATIN TREATMENT



B



A

(57) Abstract: The present invention relates, generally, to methods to identify subjects responsive to p73/p63 targeting agents such as platinum-based chemotherapy agents such as, but not limited to, cisplatin and cisplatin derivatives and analogues thereof. More particularly, the present invention relates to methods to identify a cancer responsive to a p73/p63 targeting treatment, such as chemotherapeutic agents such as cisplatin, by determining if the cancer expresses and/or has the activity of p63 isoforms such as DNp63 isoforms, and expresses and/or has the activity of p73 isoforms such as TAp73 or DNp73 isoforms. The present invention also relates to methods to identify a cancer unresponsive to a p73/p63 targeting treatment, such as chemotherapeutic agents such as cisplatin by determining if the cancer lacks the expression and/or activity of p63 isoforms such as DNp63 isoforms. The invention further provides kits to determine the expression and/or activity of p63 isoforms such as DNp63 isoforms, and/or the expression and/or activity of p73 isoforms such as TAp73 and/or DNp73 isoforms in a biological sample.

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25 September 2003 (25.09.2003)

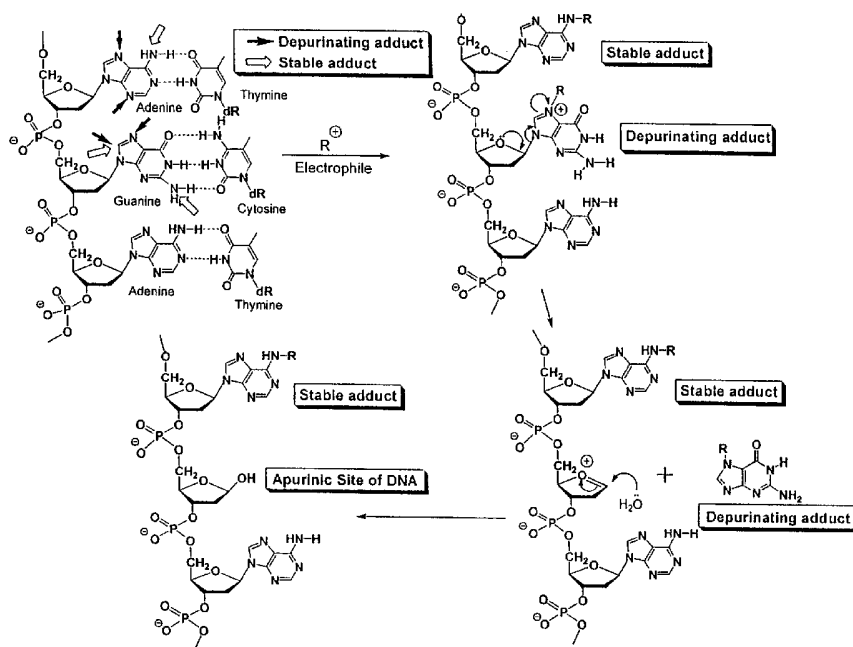
PCT

(10) International Publication Number
WO 03/077900 A1

- (51) International Patent Classification⁷: A61K 31/195, 31/40
- (74) Agents: STEFFEY, Charles, E. et al.; P.O. Box 2938, Minneapolis, MN 55402 (US).
- (21) International Application Number: PCT/US03/07686
- (81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (22) International Filing Date: 12 March 2003 (12.03.2003)
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- (26) Publication Language: English
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- (84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).
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- Published: — with international search report

[Continued on next page]

(54) Title: A UNIFYING MECHANISM AND METHODS TO PREVENT CANCER AND NEURODEGENERATIVE DISEASES



(57) Abstract: The present invention relates to methods for preventing the development of cancer or neurodegenerative diseases by administering N-Acetylcysteine (NAC), melatonin, or a combination thereof. The present invention also relates to methods for diagnosing cancer and/or neurodegenerative disease by detecting or determining the amount of dopamine metabolites, 4-CE, 2-CE, methylation of CE or CE-Q conjugates.

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PCT

WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<p>(51) International Patent Classification ⁶ : A61K 31/71 // (A61K 31/71, 31:195)</p>	<p>A1</p>	<p>(11) International Publication Number: WO 97/29759 (43) International Publication Date: 21 August 1997 (21.08.97)</p>
<p>(21) International Application Number: PCT/EP97/00627 (22) International Filing Date: 12 February 1997 (12.02.97) (30) Priority Data: MI96A000277 14 February 1996 (14.02.96) IT (71) Applicant (for all designated States except US): ZAMBON GROUP S.P.A. [IT/IT]; Via della Chimica, 9, I-36100 Vicenza (IT). (72) Inventors; and (75) Inventors/Applicants (for US only): DE FLORA, Silvio [IT/IT]; Via Ghirardelli Pescetto, 15, I-16167 Genova Nervi (IT). ALBINI, Adriana [IT/IT]; Salita della Provvidenza, 14/1b, I-16134 Genova (IT).</p>		<p>(81) Designated States: BR, CA, JP, US, Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE). Published <i>With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i></p>
<p>(54) Title: PHARMACEUTICAL COMPOSITION ENABLING TO INHIBIT CANCER METASTASIS FORMATION CONTAINING N-ACETYL-CYSTEINE AND DOXORUBICIN</p>		
<p>(57) Abstract The therapeutic association of N-acetyl-cysteine with Doxorubicin shows a remarkable synergic effect in inhibiting cancer metastasis formation. Pharmaceutical compositions containing the association and kit suitable for the administration of the two drugs are described.</p>		

United States Patent [19]

Myers, Jr. et al.

[11] **4,331,648**

[45] **May 25, 1982**

[54] **N-ACETYL-CYSTEINE PROTECTS AGAINST CARDIAC DAMAGE FROM SUBSEQUENTLY-ADMINISTERED CARDIO-TOXIC ANTHRA-CYCLINE IN CANCER THERAPY**

[75] Inventors: **Charles E. Myers, Jr.**, Rockville, Md.; **James H. Doroshov**, Upland, Calif.; **Gershon Y. Locker**, Chicago, Ill.

[73] Assignee: **The United States of America as represented by the Secretary of the Department of Health and Human Services**, Washington, D.C.

[21] Appl. No.: **190,064**

[22] Filed: **Sep. 23, 1980**

Related U.S. Application Data

[63] Continuation-in-part of Ser. No. 100,496, Dec. 5, 1979, abandoned, which is a continuation of Ser. No. 24,246, Mar. 27, 1979, abandoned.

[51] Int. Cl.³ **A61K 31/70; A61K 31/71**

[52] U.S. Cl. **424/10; 424/180; 424/181**

[58] Field of Search **424/10**

[56] References Cited

U.S. PATENT DOCUMENTS

4,267,163 5/1981 DeFelice 424/180

OTHER PUBLICATIONS

Chemical Abstracts, 79: 142981a, (1973).

Chemical Abstracts, 92: 52213r, (1980).

Primary Examiner—Jerome D. Goldberg
Attorney, Agent, or Firm—Holman & Stern

[57] ABSTRACT

The cardiac damage, occurring after treatment with an anthracycline, such as adriamycin, is prevented when N-acetyl-cysteine is orally administered about one hour prior to the treatment with the anthracycline.

10 Claims, No Drawings



(51) International Patent Classification:
A61K 31/32 (2006.01) A61P 35/00 (2006.01)
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RM2008A000426 4 August 2008 (04.08.2008) IT

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(75) Inventors/Applicants (for US only): PELLERITO, Claudia [IT/IT]; c/o Dipartimento Chimica Inorganica, e Analitica "S. Cannizzaro", Viale delle Scienze - Ed 17, I-90128 Palermo (IT). PRINZIVALLI, Cristina [IT/IT]; c/o Dipartimento Chimica Inorganica, e Analitica "S. Cannizzaro", Viale delle Scienze - Ed 17, I-90128 Palermo (IT). PELLERITO, Ornella [IT/IT]; c/o Dipartimento Scienze Biochimiche, "Paolo Giaccone", Viale del

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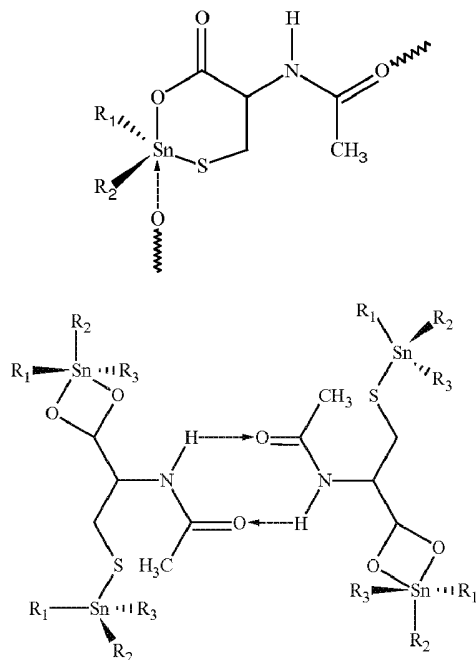
(74) Agents: GERVASI, Gemma et al.; Notarbartolo & Gervasi S.p.a., Corso di Porta Vittoria 9, I-20122 Milan (IT).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

[Continued on next page]

(54) Title: ORGANOTIN(IV) COMPLEXES WITH N-ACETYLCYSTEINE POSSESSING ANTITUMORAL ACTIVITY, PROCESS FOR THEIR PRODUCTION AND THEIR USE



(57) Abstract: Organotin(IV) compounds with N-acetylcysteine having the general formula (1) or (2); wherein: R₁, R₂ and R₃ are each independently selected from the group consisting of: H, an alkyl, alkoxy, alkenyl or alkynyl group with up to 12 carbon atoms, an isocyclic or heterocyclic aromatic or aralkyl group with up to 12 carbon atoms, and they are preferably chosen from methyl, ethyl, butyl or phenyl, are synthesized by simple procedures from commercial products, and are active as anti-cancer agents. In particular, the Bu₂Sn-N-acetylcysteinate derivative was found to have a potent and selective anti-cancer activity in vitro against several cancer cell lines.

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(30) Priority Data:
61/101,443 30 September 2008 (30.09.2008) US

(71) Applicant (for all designated States except US): **THE HOSPITAL FOR SICK CHILDREN** [CA/CA]; 555 University Avenue, Toronto, Ontario, M5G 1X8 (CA).

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(74) Agent: **BELLIVEAU, Michael, J.**; Clark & Elbing LLP, 101 Federal Street, Boston, MA 02110 (US).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM,

AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

— as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))

Published:

— with international search report (Art. 21(3))

— before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))

(54) Title: COMPOSITIONS FOR PROLIFERATION OF CELLS AND RELATED METHODS

(57) Abstract: We have discovered that p63 inhibition results in increased cellular proliferation. We have also performed a screen for agents capable of increasing cellular proliferation, (e.g., of stem cells such as skin-derived precursors (SKPs)). The invention therefore provides compositions, methods, and kits for increasing proliferation of cells, using compounds that decrease p63 expression or activity or using the compounds described herein. The invention also features methods of using these compounds for increasing hair growth, improving skin health, or promoting skin repair in a subject.



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C12N 15/113 (2010.01) A61K 31/7088 (2006.01)
A61K 48/00 (2006.01) A61P 17/00 (2006.01)

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(71) Applicant (for all designated States except US): **OPKO
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(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

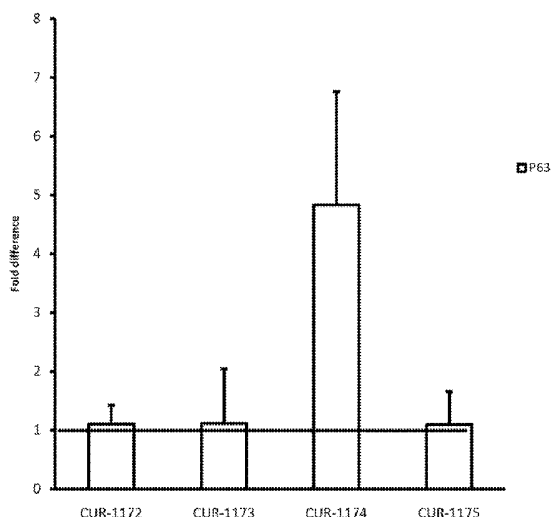
— of inventorship (Rule 4.17(iv))

[Continued on next page]

(54) Title: TREATMENT OF TUMOR PROTEIN 63 (p63) RELATED DISEASES BY INHIBITION OF NATURAL ANTI-SENSE TRANSCRIPT TO p63

FIGURE 1

Fold difference in mRNA copy # compared to control



(57) Abstract: The present invention relates to antisense oligonucleotides that modulate the expression of and/or function of Tumor Protein 63 (p63), in particular, by targeting natural antisense polynucleotides of Tumor Protein 63 (p63). The invention also relates to the identification of these antisense oligonucleotides and their use in treating diseases and disorders associated with the expression of p63.

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C 0 7 C 323/58		7419-4H		

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(22) 出願日 平成6年(1994)7月28日

(71) 出願人 000000066

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岐阜県可児市阜ヶ丘9-128

(74) 代理人 弁理士 川口 義雄 (外2名)

(54) 【発明の名称】 ミエローマ系腫瘍抗癌剤

(57) 【要約】

【目的】 ミエローマ系腫瘍抗癌剤を開発し、提供すること。

【構成】 有効成分としてN-アセチル-L-システインを含有することを特徴とするミアローマ系腫瘍抗癌剤

Document is not available for XP022344808

Document is not available for XP002665835

Document is not available for XP002665836

Document is not available for XP002665837

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(21) International Application Number:

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(22) International Filing Date: 8 February 2006 (08.02.2006)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

60/651,101 8 February 2005 (08.02.2005) US

(71) Applicant (for all designated States except US): **THE UNIVERSITY OF NORTH CAROLINA AT CHAPEL HILL** [US/US]; OFFICE OF TECHNOLOGY DEVELOPMENT, Cb4105, 308 Bynum Hill, Chapel Hill, North Carolina 27599-4105 (US).

(72) Inventors; and

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(54) Title: METHOD FOR TREATING PROSTATE CONDITIONS

(57) Abstract: The invention provides a method for inhibiting the aberrant growth of cells in a prostate tissue in an individual comprising administering to the individual an amount of an inhibitor of the Breast Cancer Resistance Protein (BCRP/ABCG2), where the amount of the BCRP inhibitor is effective to inhibit the growth of the aberrantly growing cells. The method is also useful for treating prostate tumors or benign prostatic hyperplasia/hypertrophy (BPH). Also disclosed is the phenotype for prostate stem cells as determined by immunohistochemical localization methods. The prostate stem cells are positive for BCRP protein, negative for androgen receptor protein, negative for p63 protein, and negative for synaptophysin.



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United States Patent [19][11] **Patent Number:** **5,978,740****Armistead et al.**[45] **Date of Patent:** **Nov. 2, 1999**

[54] **MOLECULES COMPRISING A CALCINEURIN-LIKE BINDING POCKET AND ENCODED DATA STORAGE MEDIUM CAPABLE OF GRAPHICALLY DISPLAYING THEM**

[75] Inventors: **David M. Armistead**, Maynard; **Matthew James Fitzgibbon**, Millis; **Mark Andrew Fleming**, Cambridge; **James P. Griffith**, Weston; **Eunice E. Kim**, Framingham; **Joseph L. Kim**, Natick; **Michael D. Sintchak**, Winchester; **John Allan Thomson**, Belmont; **Keith P. Wilson**, Hopkinton, all of Mass.

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[52] **U.S. Cl.** **702/19; 702/27**

[58] **Field of Search** 364/496-499, 364/578; 702/19, 27

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[57] **ABSTRACT**

The present invention relates to crystallized molecules and molecular complexes which comprise the active site binding pocket or the FKBP12/FK506 binding pocket of calcineurin or close structural homologues to either binding pocket. This invention also relates to a data storage material encoded with the corresponding structure coordinates of those crystallized molecules or molecular complexes. Such data storage material is capable of displaying such molecules and molecular complexes as a graphical three-dimensional representation on a computer screen. In addition, this invention relates to methods of using the structure coordinates of those molecules or molecular complexes to solve the structure of homologous proteins. This invention also relates to methods of using the structure coordinates to screen and design compounds that bind to calcineurin or homologues thereof.

6 Claims, 109 Drawing Sheets