

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
12 June 2008 (12.06.2008)

PCT

(10) International Publication Number
WO 2008/068638 A3

(51) International Patent Classification:

C12N 15/11 (2006.01) A61K 31/7125 (2006.01)
C07H 21/00 (2006.01) A61P 37/04 (2006.01)

(21) International Application Number:

PCT/IB2007/004389

(22) International Filing Date:

25 September 2007 (25.09.2007)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

60/847,811 27 September 2006 (27.09.2006) US

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

AE, AG, AL, AM, 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).

Published:

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

(88) Date of publication of the international search report:

13 November 2008

(54) Title: CPG OLIGONUCLEOTIDE ANALOGS CONTAINING HYDROPHOBIC T ANALOGS WITH ENHANCED IMMUNOSTIMULATORY ACTIVITY

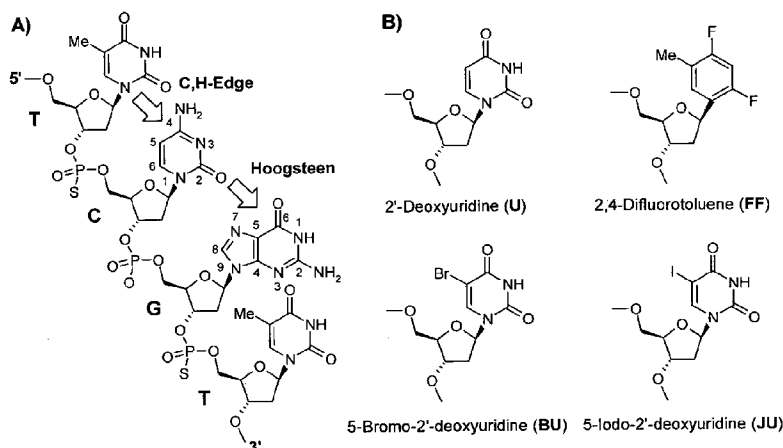


Figure 1

(57) Abstract: The invention relates to oligonucleotides including at least one lipophilic substituted nucleotide analog and a pyrimidine-purine dinucleotide. The invention also relates to pharmaceutical compositions and methods of use thereof.

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INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2007/004389

A. CLASSIFICATION OF SUBJECT MATTER
INV. C12N15/11 C07H21/00 A61K31/7125 A61P37/04

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
C12N C07H

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, CHEM ABS Data, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>WO 2005/030259 A (COLEY PHARM GROUP INC [US]; COLEY PHARM GMBH [DE]; VOLLMER JOERG [DE];) 7 April 2005 (2005-04-07)</p> <p style="text-align: center; margin-top: 20px;">table 1</p>	<p>1-14, 20-25, 28, 32-34, 37, 39-42, 46, 48, 49, 52, 59-62, 64, 66, 67, 69, 70, 75-94</p>

Further documents are listed in the continuation of Box C.

See patent family annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *&* document member of the same patent family

Date of the actual completion of the international search

24 July 2008

Date of mailing of the international search report

31/07/2008

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INTERNATIONAL SEARCH REPORT

International application No

PCT/IB2007/004389

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>TSAO ET AL: "Optically detected magnetic resonance study of the interaction of an arsenic(III) derivative of cacodylic acid with EcoRI methyltransferase. Optically detected magnetic resonance study of the interaction of an arsenic(III) derivative of cacodylic acid with EcoRI methyltransferase"</p> <p>BIOCHEMISTRY, AMERICAN CHEMICAL SOCIETY. EASTON, PA, US, vol. 30, no. 18, 1 January 1991 (1991-01-01), pages 4565-4572, XP002357069 ISSN: 0006-2960 abstract</p>	<p>1-4, 10-13, 17, 22-25, 27,28, 32-34, 40,41, 44,46, 49,61, 66,67</p>
Y	<p>WO 01/83503 A (HYBRIDON INC [US]) 8 November 2001 (2001-11-08) pages 9,10; claims 1,3,4; figures 1B-3,1B-4</p>	<p>1-94</p>
X	<p>figure 1B-3</p>	<p>1-5,7, 10,11, 22-25, 27,28, 32-34, 40-42, 66,67, 76-94</p>
Y	<p>AGRAWAL SUDHIR ET AL: "Medicinal chemistry and therapeutic potential of CpG DNA"</p> <p>TRENDS IN MOLECULAR MEDICINE, ELSEVIER CURRENT TRENDS, vol. 8, no. 3, 1 March 2002 (2002-03-01), pages 114-121, XP009073678 ISSN: 1471-4914 page 117</p>	<p>1-94</p>
Y	<p>EUGEN ULMANN ET AL: "Recent advances in the development of immunostimulatory oligonucleotides"</p> <p>CURRENT OPINION IN DRUG DISCOVERY AND DEVELOPMENT, CURRENT DRUGS, LONDON, GB, vol. 6, no. 2, 1 January 2003 (2003-01-01), pages 204-217, XP009103505 ISSN: 1367-6733 page 208</p>	<p>1-94</p>
	<p style="text-align: center;">----- -/--</p>	

INTERNATIONAL SEARCH REPORT

International application No

PCT/IB2007/004389

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	R. P. IYER, ET AL.: "Modified Oligonucleotides - Synthesis, Properties and Applications" CURRENT OPINION IN MOLECULAR THERAPEUTICS, vol. 1, no. 3, 1999, pages 344-358, XP009103623 page 352 - page 354	1-94

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB2007/004389

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 76-94 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. As all required additional search fees were timely paid by the applicant, this international search report covers allsearchable claims.
2. As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.
3. As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/IB2007/004389

Patent document cited in search report	A	Publication date	Patent family member(s)	Publication date
WO 2005030259	A	07-04-2005	AU 2004275876 A1	07-04-2005
			CA 2536139 A1	07-04-2005
			EP 1663316 A2	07-06-2006
			JP 2007506790 T	22-03-2007
			US 2005130911 A1	16-06-2005
WO 0183503	A	08-11-2001	AT 292638 T	15-04-2005
			AU 5736601 A	12-11-2001
			AU 2001257366 B2	16-03-2006
			CA 2407942 A1	08-11-2001
			DE 60109916 D1	12-05-2005
			DE 60109916 T2	19-01-2006
			EP 1278761 A2	29-01-2003
			ES 2238044 T3	16-08-2005
			JP 2003531915 T	28-10-2003
			PT 1278761 T	31-08-2005