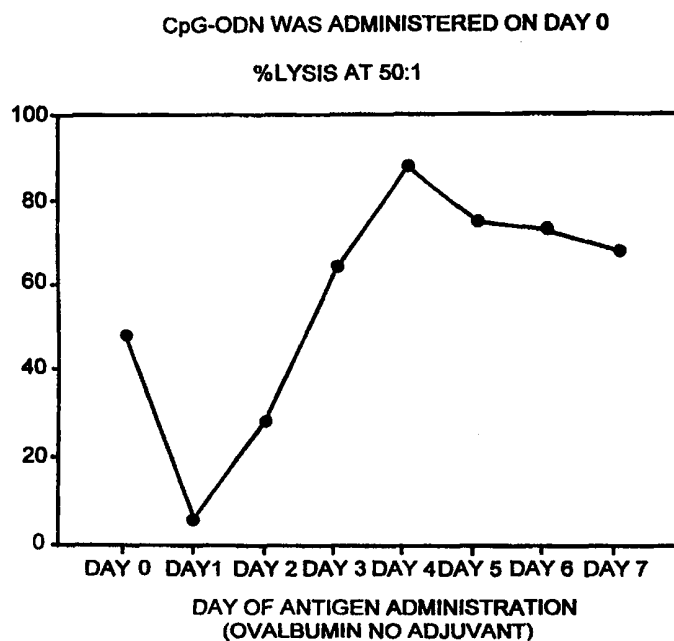




INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<p>(51) International Patent Classification⁶ : C12N 15/11, A61K 39/39, 31/70, C07H 21/04 // A61K 45/00</p>	A3	<p>(11) International Publication Number: WO 99/58118</p> <p>(43) International Publication Date: 18 November 1999 (18.11.99)</p>
<p>(21) International Application Number: PCT/IB99/01285</p> <p>(22) International Filing Date: 14 May 1999 (14.05.99)</p> <p>(30) Priority Data: 60/085,516 14 May 1998 (14.05.98) US 09/241,653 2 February 1999 (02.02.99) US</p> <p>(71) Applicants: CPG IMMUNOPHARMACEUTICALS GMBH [DE/DE]; Max-Volmer-Strasse 4, D-40724 Hilden (DE). CPG IMMUNOPHARMACEUTICALS, INC. [US/US]; Suite 120, 55 William Street, Wellesley, MA 02481 (US).</p> <p>(72) Inventors: WAGNER, Hermann; Institute of Medical Microbiology Immunology and Hygiene, Trogerstrasse 9, D-81675 Munich (DE). LIPFORD, Grayson; Institute of Medical Microbiology Immunology and Hygiene, Trogerstrasse 9, D-81675 Munich (DE).</p> <p>(74) Agent: LOCKHART, Helen, C.; Wolf, Greenfield & Sacks, P.C., 600 Atlantic Avenue, Boston, MA 02210 (US).</p>	<p>(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, 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, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).</p> <p>Published <i>With international search report.</i> <i>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>(88) Date of publication of the international search report: 13 January 2000 (13.01.00)</p>	

(54) Title: METHODS FOR REGULATING HEMATOPOIESIS USING CpG-OLIGONUCLEOTIDES



(57) Abstract

The invention relates to methods for regulating hematopoiesis using CpG containing oligonucleotides. In particular, the invention relates to methods of treating thrombopoiesis and anemia by regulating hematopoiesis. The invention also relates to method of regulating immune system remodelling by administering CpG oligonucleotides to control hematopoiesis.

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/IB 99/01285

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C12N15/11 A61K39/39 A61K31/70 C07H21/04 //A61K45/00

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)
IPC 6 A61K C12N

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)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 18810 A (UNIV IOWA RES FOUND ;KLINE JOEL N (US); KRIEG ARTHUR M (US)) 7 May 1998 (1998-05-07) cited in the application page 9 -page 10 page 15, line 11 -page 21, line 24 page 25, line 5 -page 34, line 20 page 42 -page 52	1-12, 14-26
Y	page 63 -page 67, line 9 claims 1-35	1-5
Y	WO 96 02555 A (UNIV IOWA RES FOUND) 1 February 1996 (1996-02-01) page 7, line 5 -page 8, line 6 claims 1-21 page 12 -page 17 page 21, line 10 - line 26	1-5
	-/--	

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

* Special categories of cited documents :

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- "E" earlier document but published on or after the international filing date
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- "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
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- "&" document member of the same patent family

Date of the actual completion of the international search 17 November 1999	Date of mailing of the international search report 03/12/1999
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Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer Andres, S
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INTERNATIONAL SEARCH REPORT

International Application No

PCT/IB 99/01285

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>WO 97 28259 A (UNIV CALIFORNIA) 7 August 1997 (1997-08-07) page 4, line 19 -page 8, line 4 page 11 -page 15 page 17, line 27 -page 18 page 24, line 12 -page 27, line 18</p>	1-6, 10, 13-21, 26
A	<p>AGRAWAL S. ET AL.: "Toxicologic effects of an oligodeoxynucleotide phosphorothioate and its analogs following intravenous administration in rats." ANTISENSE NUCLEIC ACID DRUG DEV 1997 DEC;7(6):575-84, XP002122934 cited in the application the whole document</p>	27-65
A	<p>WO 98 11211 A (HYBRIDON INC) 19 March 1998 (1998-03-19) abstract</p>	27-65
A	<p>G. B. LIPFORD ET AL: "Immunostimulatory DNA: sequence-dependent production of potentially harmful or useful cytokines" EUROPEAN JOURNAL OF IMMUNOLOGY, vol. 12, no. 27, page 3420-3426 XP002077483 ISSN: 0014-2980 cited in the application</p>	
P, X	<p>KRIEG AM. ET AL.: "CpG DNA induces sustained IL-12 expression in vivo and resistance to Listeria monocytogenes challenge." J IMMUNOL 1998 SEP 1;161(5):2428-34, XP002122935 figure 2</p>	1-4, 6-9, 13, 14, 16, 17, 26
T	<p>JAKOB T. ET AL.: "Bacterial DNA and CpG-containing oligodeoxynucleotides activate cutaneous dendritic cells and induce IL-12 production: implications for the augmentation of Th1 responses." INT ARCH ALLERGY IMMUNOL 1999 FEB-APR;118(2-4):457-61, XP002122936</p>	1-5

INTERNATIONAL SEARCH REPORT

International application No.

PCT/IB 99/01285

Box I Observations where certain claims were found unsearchable (Continuation of item 1 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:
Remark: Although claims 1-65
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 II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

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

See additional sheet

1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all
searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment
of any additional fee.
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.
- No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-26

A method for inducing an antigen-specific immune response.

2. Claims: 27-50

A method for treating or preventing thrombocytopenia.

3. Claims: 51-65

A method for treating anemia.

INTERNATIONAL SEARCH REPORT

information on patent family members

International Application No

PCT/IB 99/01285

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9818810 A	07-05-1998	AU 5242498 A EP 0948510 A	22-05-1998 13-10-1999
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WO 9811211 A	19-03-1998	US 5856462 A AU 4339997 A EP 0928335 A	05-01-1999 02-04-1998 14-07-1999