

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
28 March 2002 (28.03.2002)

PCT

(10) International Publication Number
WO 02/024929 A3

- (51) International Patent Classification⁷: **C12N 15/62**, 15/63, 5/10, C07K 14/705, A61K 38/17
- (74) Agents: **NEIMARK, Sheridan** et al.; 624 Ninth Street N.W., Suite 300, Washington, DC 20001-5303 (US).
- (21) International Application Number: PCT/US01/29873
- (22) International Filing Date:
24 September 2001 (24.09.2001)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:
60/234,843 22 September 2000 (22.09.2000) US
- (71) Applicant (for all designated States except US): **RAMOT UNIVERSITY AUTHORITY FOR APPLIED RESEARCH & INDUSTRIAL DEVELOPMENT LTD.** [IL/IL]; P.O. Box 39296, 61392 Tel Aviv (IL).
- (71) Applicant (for SD only): **MCINNIS, Patricia** [US/US]; 2325 42nd Street, N.W., Apt. 203, Washington, DC 20007 (US).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): **EHRlich, Rachel** [IL/IL]; 32nd Smadar Street, Herzelia (IL). **ROTEM-YEHUDAR, Rinat** [IL/IL]; 1st Yaakov Meridor Street, Tel Aviv (IL). **LAHAM, Nihay** [AU/IL]; P.O. Box 327, 37 Tawfik Zaid Street, 20200 Shefa-ram (IL).
- (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, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.
- (84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, 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, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).
- Published:
— with international search report
- (88) Date of publication of the international search report:
8 May 2003
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: A SOLUBLE BETA 2 MICROGLOBULIN (β 2M)/HFE MONOCHAIN FOR BIOTECHNOLOGICAL AND THERAPEUTIC APPLICATIONS

(57) Abstract: A soluble beta2m/HFE monochain which is a polypeptide comprising human beta2m, or an analog or active fragment thereof, linked to the alpha1-alpha3 domains of human HFE, or an analog or active fragment thereof, by means of a flexible linker peptide, or a functional derivative or salt of said polypeptide. This invention also relates to therapeutic interventions for iron overload disorders and chronic infections.



WO 02/024929 A3

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 01/29873

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/62 C12N15/63 C12N5/10 C07K14/705 A61K38/17

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 7 C12N C07K A61K

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)

EMBL, SEQUENCE SEARCH, EPO-Internal, WPI Data, PAJ, BIOSIS, MEDLINE, CHEM ABS Dat

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>IKUTA K ET AL: "Overexpression of hemochromatosis protein, HFE, alters transferrin recycling process in human hepatoma cells"</p> <p>BIOCHIMICA ET BIOPHYSICA ACTA. MOLECULAR CELL RESEARCH, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 1496, no. 2-3, 17 April 2000 (2000-04-17), pages 221-231, XP004278134</p> <p>ISSN: 0167-4889</p> <p>cited in the application</p> <p>the whole document</p> <p style="text-align: center;">---</p> <p style="text-align: center;">-/--</p>	<p>1-7, 10-17,19</p>



Further documents are listed in the continuation of box C.



Patent family members are listed in 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

23 September 2002

Date of mailing of the international search report

15. 01. 2003

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

Devijver, K

INTERNATIONAL SEARCH REPORT

Inter national Application No

PCT/US 01/29873

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 00 37482 A (PROGENITOR INC ;CALIFORNIA INST OF TECHN (US)) 29 June 2000 (2000-06-29) page 20, line 30 -page 21, line 26; claims 1-13 ---	1-7, 10-17,19
X	US 6 011 146 A (MOTTEZ ESTELLE ET AL) 4 January 2000 (2000-01-04) abstract; claims 1-4; figures 1,3; tables 1,2 column 2, line 63 -column 3, line 4 column 7, line 57 -column 8, line 37 ---	1-6, 12-15,19
A	GUSSOW D ET AL: "THE HUMAN BETA-2 MICROGLOBULIN GENE PRIMARY STRUCTURE AND DEFINITION OF THE TRANSCRIPTIONAL UNIT" JOURNAL OF IMMUNOLOGY, vol. 139, no. 9, 1987, pages 3132-3138, XP002214372 ISSN: 0022-1767 ---	
A	FEDER ET AL: "A NOVEL MHC CLASS I-LIKE GENE IS MUTATED IN PATIENTS WITH HEREDITARY HAEMOCHROMATOSIS" NATURE GENETICS, NEW YORK, NY, US, vol. 13, August 1996 (1996-08), pages 399-408, XP002113585 ISSN: 1061-4036 cited in the application ---	
A	US 5 739 281 A (HOLTET THOR LNS ET AL) 14 April 1998 (1998-04-14) -----	

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 01/29873

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:

Although claims 7, 10, 11, 16 and 17 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.:

1-7, 10-17, 19

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: 1-7,10-17,19

Soluble beta2m/HFE monochain. Such a monochain further including a therapeutic bound thereto. DNA molecule encoding said monochain, vector containing said DNA, cell transformed with said vector and method of producing said monochain. Method for reducing intracellular iron absorption comprising administering said monochain. Method for delivering a therapeutic. Method for treatment of a brain tumor. Pharmaceutical composition comprising said monochain.

2. Claim : 8

Method for reducing intracellular iron absorption comprising administering beta2m or an analog, active fragment, functional derivative or salt thereof.

3. Claims: 9,18

Method for reducing intracellular iron absorption comprising administering HFE or an analog, active fragment, functional derivative or salt thereof.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 01/29873

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 0037482	A	29-06-2000	US 6284732 B1	04-09-2001
			AU 3117200 A	12-07-2000
			EP 1140131 A2	10-10-2001
			WO 0037482 A2	29-06-2000
			US 2002165162 A1	07-11-2002

US 6011146	A	04-01-2000	US 6153408 A	28-11-2000
			US 5976551 A	02-11-1999

US 5739281	A	14-04-1998	AU 674568 B2	02-01-1997
			AU 6038094 A	29-08-1994
			CA 2155335 A1	18-08-1994
			WO 9418227 A2	18-08-1994
			EP 0686162 A1	13-12-1995
			FI 953705 A	03-08-1995
			JP 8506243 T	09-07-1996
			NO 952989 A	03-10-1995
			NZ 261571 A	24-03-1997
			US 5917018 A	29-06-1999
