

REVISED VERSION

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
14 December 2006 (14.12.2006)

PCT

(10) International Publication Number
WO 2006/131928 A3

(51) International Patent Classification:

C12N 15/55 (2006.01) *C12Q 1/68* (2006.01)
C12N 9/64 (2006.01)

(21) International Application Number:

PCT/IL2006/000676

(22) International Filing Date: 8 June 2006 (08.06.2006)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

60/688,320	8 June 2005 (08.06.2005)	US
60/699,427	15 July 2005 (15.07.2005)	US
60/704,414	2 August 2005 (02.08.2005)	US

(71) Applicant (for all designated States except US): **COMPUT-GEN LTD.** [IL/IL]; 72 Pinchas Rosen Street, 69512 Tel Aviv (IL).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **SELLA-TAVOR, Osnat** [IL/IL]; 18 Kfar Kish, 19330 Kfar Kish (IL). **POL-LOCK, Sarah** [IL/IL]; 16/2 Hoshea Street, 63506 Tel-aviv (IL). **COJOCARU, Gad, S.** [IL/IL]; 41/7 Hasayfan Street, 47248 Ramat-hasharon (IL). **NOVIK, Amit** [IL/IL]; 31 Hasayfan Street, 40600 Tel-mond (IL). **BAZAK, Lily** [IL/IL]; 46 Raynes Street, 53461 Givatayim (IL). **TSYP-KIN, Elena** [IL/IL]; 105/7 Even Gvirol Street, 64046 Tel-aviv (IL). **WALLACH, Shira** [IL/IL]; 40 Bnei Brit Street, 45265 Hod-hasharon (IL). **SAMEAH-GREEN-WALD, Shirley** [IL/IL]; 33/7 Arlozorov Street, 44453 Kfar-saba (IL).

(74) Agents: **WEBB, Cynthia** et al.; Webb & Associates, P.O. Box 2189, 76121 Rehovot (IL).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, 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, 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
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments
- 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:

7 June 2007

Date of publication of the revised international search report:
19 July 2007

(15) Information about Correction:

see PCT Gazette No. 29/2007 of 19 July 2007

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: NOVEL NUCLEOTIDE AND AMINO ACID SEQUENCES, AND ASSAYS AND METHODS OF USE THEREOF FOR DIAGNOSIS

(57) Abstract: Novel splice variants, amino acid sequences and nucleotide sequences thereof, and methods of using same.

WO 2006/131928 A3

INTERNATIONAL SEARCH REPORT

CORRECTED VERSION

International application No

PCT/IL2006/000676

A. CLASSIFICATION OF SUBJECT MATTER

INV. C12N15/55 C12N9/64 C12Q1/68

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

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, WPI Data, BIOSIS, EMBASE, Sequence Search

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE EMBL [Online] 30 January 2005 (2005-01-30), "Homo sapiens matrix metalloproteinase 11 (stromelysin 3) (MMP11) gene, complete cds." XP002409211 retrieved from EBI accession no. EM_PRO:AY899208 Database accession no. AY899208 sequence comprises SEQ ID NO:346, 347, 349-352, 355, 358-360, 362 abstract	2
X	----- US 5 484 726 A (BASSET PAUL [FR] ET AL) 16 January 1996 (1996-01-16) example 12 ----- -/--	68



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

27 November 2006

Date of mailing of the international search report

09.05.2007

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

Kania, Thomas

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IL2006/000676**Box 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:

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 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:

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.:

1-3, 65-94 partially; 4-14 completely

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: 1-3, 65-94 partially; 4-14 completely

Subject-matter as claimed corresponding to HSSTROL3 PEA-1-P4 and HSSTROL3 PEA-1-T5 according to SEQ ID NO:339, 346, 347, 349-352, 355-360, 362, 364, 370-375, 652

2. claims: 1-3, 65-94 partially; 15-25 completely

Subject-matter as claimed corresponding to HSSTROL3 PEA-1-P5 and HSSTROL3 PEA-1-T6 according to SEQ ID NO:340, 346, 347, 349-360, 362, 365, 373-375, 382-387, 653

3. claims: 1-3, 65-94 partially; 26-36 completely

Subject-matter as claimed corresponding to HSSTROL3 PEA-1-P7 and HSSTROL3 PEA-1-T10 according to SEQ ID NO:343, 346, 347, 349-352, 357-360, 362, 366, 373-378, 654

4. claims: 1-3, 65-94 partially; 37-47 completely

Subject-matter as claimed corresponding to HSSTROL3 PEA-1-P8 and HSSTROL3 PEA-1-T11 according to SEQ ID NO:344, 346, 347, 349-352, 355-362, 367, 370-375, 379-381, 655, 670, 698, 699

5. claims: 1-3, 65-94 partially; 48-63 completely

Subject-matter as claimed corresponding to HSSTROL3 PEA-1-P9 and HSSTROL3 PEA-1-T12 according to SEQ ID NO:345-347, 349-352, 357, 359, 362, 368, 373-378, 654

6. claims: 1-3, 65-94 partially; 64 completely

Subject-matter as claimed corresponding to HSSTROL3 PEA-1-P11 and HSSTROL3 PEA-1-T2 according to SEQ ID NO:338, 346-352, 355, 357-359, 362, 369, 370-375

7. claims: 1,65-67,71-94 partially

Subject-matter as claimed corresponding to HSSTROL3 PEA-1-T8 according to SEQ ID NO:341, 346, 347, 349-355, 357-360, 362, 373-375, 382-387

8. claims: 1,65-67,71-94 partially

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Subject-matter as claimed corresponding to HSSTROL3 PEA-1-T9
according to SEQ ID NO:342, 346, 347, 349-353, 355-360, 362,
373-375, 382-384

INTERNATIONAL SEARCH REPORT

Information on patent family members

CORRECTED VERSION

International application No

PCT/IL2006/000676

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
US 5484726	A	16-01-1996	NONE	
WO 2004052301	A2	24-06-2004	AU 2003300851 A1 US 2004110152 A1	30-06-2004 10-06-2004
US 5952200	A	14-09-1999	NONE	
WO 03048734	A2	12-06-2003	AU 2002362055 A1	17-06-2003
WO 2005072050	A	11-08-2005	AU 2005207882 A1 CA 2554440 A1	11-08-2005 11-08-2005
WO 2005072053	A	11-08-2005	NONE	

INTERNATIONAL SEARCH REPORT

International application No

PCT/IL2006/000676

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 2004/052301 A2 (ISIS PHARMACEUTICALS INC [US]; BAKER BRENDA F [US]; COWSERT LEX M [US]) 24 June 2004 (2004-06-24)	
A	----- LUO DAOCHUN ET AL: "Alternative splicing and promoter usage generates an intracellular stromelysin 3 isoform directly translated as an active matrix metalloproteinase" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 277, no. 28, 12 July 2002 (2002-07-12), pages 25527-25536, XP002409130 ISSN: 0021-9258 -----	
A	US 5 952 200 A (JOHNSON LEWIS D [US] ET AL) 14 September 1999 (1999-09-14)	
A	----- WO 03/048734 A2 (ONCOMEDX INC [US]; KOPRESKI MICHAEL [US]) 12 June 2003 (2003-06-12) -----	
A	----- GURURAJAN R ET AL: "Isolation and Characterization of Two Novel Metalloproteinase Genes Linked to theCdc2LLocus on Human Chromosome 1p36.3" GENOMICS, ACADEMIC PRESS, SAN DIEGO, US, vol. 52, no. 1, 15 August 1998 (1998-08-15), pages 101-106, XP004449078 ISSN: 0888-7543 -----	
A	----- GELFAND M S ET AL: "ASDB: Database of alternatively spliced genes" NUCLEIC ACIDS RESEARCH, OXFORD UNIVERSITY PRESS, SURREY, GB, vol. 27, no. 1, 1 January 1999 (1999-01-01), pages 301-302, XP002165716 ISSN: 0305-1048 -----	
P,X	----- WO 2005/072050 A (COMPUGEN USA INC [US]) 11 August 2005 (2005-08-11) page 480 - page 524 -----	1-14, 65-94
P,X	----- WO 2005/072053 A (COMPUGEN LTD [IL]) 11 August 2005 (2005-08-11) page 1026 - page 1068 -----	1-14, 65-94