

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
30 July 2009 (30.07.2009)

(10) International Publication Number
WO 2009/093242 A3

PCT

(51) International Patent Classification:
C12N 15/62 (2006.01) A61K 31/4745 (2006.01)

(21) International Application Number:
PCT/IL2009/000089

(22) International Filing Date:
22 January 2009 (22.01.2009)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
61/006,634 24 January 2008 (24.01.2008) US
61/136,356 29 August 2008 (29.08.2008) US

(71) Applicant (for all designated States except US): YEDA RESEARCH AND DEVELOPMENT CO. LTD. [IL/IL]; at the Weizmann Institute of Science, P.O. Box 95, 76100 Rehovot (IL).

(72) Inventors; and

(75) Inventors/Applicants (for US only): ALON, Uri [IL/IL]; 12/22 Neve Metz Street, The Weizmann Institute of Science, 76100 Rehovot (IL). SIGAL, Alex [IL/US]; 1200 East California Blvd., M/C 147-75, Pasadena, CA 91125 (US). MILO, Ron [IL/IL]; 19 Rothschild Street, 44449 Kfar-Saba (IL). DANON, Tamar [IL/IL]; Kfar Uriah, House 211, 99735 Doar-Na Shimshon (IL). COHEN, Ariel [IL/IL]; 20 HaDekel Street, 73130 Moshav Gimzo (IL). GEVA-ZATORSKY, Naama [IL/IL]; Meshek 42, P.O. Box 191, 79205 Moshav Benaya (IL). FRENKEL-MORGENSTERN, Milana [IL/IL]; 57 Derech Yavne, 76344 Rehovot (IL). COHEN, Lydia [IL/IL]; 22/19 Maapiley Egoz Street, 67297 Tel-Aviv (IL). PERZOV, Natalie [IL/IL]; 47/1 Ahad HaAm Street, 46385 Herzlia (IL). EDEN, Eran [IL/IL]; 52 Golda Meir Street, 34982 Haifa (IL).

(74) Agents: G.E EHRlich (1995) LTD. et al.; 11 Menachem Begin Street, 52521 Ramat Gan (IL).

(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, 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, 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, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

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))
- with sequence listing part of description (Rule 5.2(a))

(88) Date of publication of the international search report:
19 November 2009

(54) Title: CELL POPULATIONS FOR POLYPEPTIDE ANALYSIS AND USES OF SAME

(57) Abstract: Nucleic acid construct systems are disclosed. The constructs comprise: (i) a first nucleic acid construct comprising a first nucleic acid sequence encoding a first reporter polypeptide linked to an additional nucleic acid sequence capable of inserting the first nucleic acid construct into a genome of a host cell such that an endogenous polypeptide covalently attached to the first reporter polypeptide is expressed in the cell; and (ii) a second nucleic acid construct comprising a second nucleic acid sequence encoding a second reporter polypeptide, linked to an additional nucleic acid sequence capable of inserting in a non-directed manner the second nucleic acid construct into a genome of a host cell such that an endogenous polypeptide covalently attached to the second reporter polypeptide is expressed in the cell, wherein the first reporter polypeptide and the second reporter polypeptide are distinguishable. Cells and cell populations comprising same as well as methods of generating same are also disclosed. In addition, use of the novel construct systems are disclosed for identifying target agents are also disclosed.



WO 2009/093242 A3

INTERNATIONAL SEARCH REPORT

International application No

PCT/IL2009/000089

A. CLASSIFICATION OF SUBJECT MATTER
 INV. C12N15/62 A61K31/4745

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 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)

EPO-Internal, BIOSIS, EMBASE, 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	SIGAL ALEX ET AL: "Variability and memory of protein levels in human cells" NATURE (LONDON), vol. 444, no. 7119, November 2006 (2006-11), pages 643-646, XP002535091 ISSN: 0028-0836 page 644, right-hand column, line 33 - page 645, left-hand column, line 9; figure 4 page 645, right-hand column, line 67 - page 646, left-hand column, line 11	1-25, 27-38, 40
A	EP 1 464 960 A (CELLZOME AG [DE]) 6 October 2004 (2004-10-06)	
A	WO 98/20031 A (JARVIK JONATHAN W [US]) 14 May 1998 (1998-05-14)	
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☒ 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

28 September 2009

Date of mailing of the international search report

05/10/2009

Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2
 NL - 2280 HV Rijswijk
 Tel. (+31-70) 340-2040,
 Fax: (+31-70) 340-3016

Authorized officer

Marinoni J-C

INTERNATIONAL SEARCH REPORT

International application No

PCT/IL2009/000089

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 94/16092 A (JARVIK JONATHAN WALLACE [US]) 21 July 1994 (1994-07-21). -----	
A	SIGAL ALEX ET AL: "Generation of a fluorescently labeled endogenous protein library in living human cells." NATURE PROTOCOLS 2007, vol. 2, no. 6, 2007, pages 1515-1527, XP002535092 ISSN: 1750-2799 -----	
A	JARVIK J W ET AL: "CD-TAGGING: A NEW APPROACH TO GENE AND PROTEIN DISCOVERY AND ANALYSIS" BIOTECHNIQUES, INFORMA LIFE SCIENCES PUBLISHING, WESTBOROUGH, MA, US, vol. 20, no. 5, 1 May 1996 (1996-05-01), pages 896-904, XP002022832 ISSN: 0736-6205 -----	
A	MILO RON: "Dynamic proteomics in mammalian cells: capabilities and challenges" MOLECULAR BIOSYSTEMS, vol. 3, no. 8, 2007, pages 542-546, XP002535093 ISSN: 1742-206X(print) 1742-2051(ele -----	
A	SIGAL ALEX ET AL: "Dynamic proteomics in individual human cells uncovers widespread cell-cycle dependence of nuclear proteins" NATURE METHODS, vol. 3, no. 7, July 2006 (2006-07), pages 525-531, XP002535094 ISSN: 1548-7091 -----	
A	FUTAMI K ET AL: "Increased chemotherapeutic activity of camptothecin in cancer cells by siRNA-induced silencing of WRN helicase" BIOLOGICAL AND PHARMACEUTICAL BULLETIN 200710 JP, vol. 30, no. 10, October 2007 (2007-10), pages 1958-1961, XP002547022 ISSN: 0918-6158 1347-5215 -----	
A	GUO J ET AL: "Enhanced chemosensitivity to irinotecan by RNA interference-mediated down-regulation of the nuclear factor-[kappa]B p65 subunit" CLINICAL CANCER RESEARCH 20040515 US, vol. 10, no. 10, 15 May 2004 (2004-05-15), pages 3333-3341, XP002547023 ISSN: 1078-0432 -----	
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INTERNATIONAL SEARCH REPORT

International application No

PCT/IL2009/000089

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,A, L	LAZZARINI R ET AL: "Enhanced antitumor therapy by inhibition of p21<waf1> in human malignant mesothelioma" CLINICAL CANCER RESEARCH 20080815 US, vol. 14, no. 16, 15 August 2008 (2008-08-15), pages 5099-5107, XP002547024 ISSN: 1078-0432	
P,A, L	DATABASE BIOSIS [Online] BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; April 2008 (2008-04), MARTIN SCOTT E ET AL: "RNAi screening identifies TAK1 as a potential target for the enhanced efficacy of traditional cytotoxic agents in breast cancer cells" XP002547025 Database accession no. PREV200800490092 abstract & PROCEEDINGS OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH ANNUAL MEETING, vol. 49, April 2008 (2008-04), page 1390, 99TH ANNUAL MEETING OF THE AMERICAN-ASSOCIATION-FOR-CANCER-RESEARCH; SAN DIEGO, CA, USA; APRIL 12 -16, 2008 ISSN: 0197-016X	
P,X	COHEN A A ET AL: "Dynamic Proteomics of Individual Cancer Cells in Response to a Drug" SCIENCE (WASHINGTON D C), vol. 322, no. 5907, December 2008 (2008-12), pages 1511-1516, XP002535095 ISSN: 0036-8075 the whole document	1-23,25, 27-38,40

INTERNATIONAL SEARCH REPORT

International application No.

PCT/IL2009/000089

Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.b of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:
- a. type of material
- ☒ a sequence listing
- ☐ table(s) related to the sequence listing
- b. format of material
- ☒ on paper
- ☒ in electronic form
- c. time of filing/furnishing
- ☒ contained in the international application as filed
- ☒ filed together with the international application in electronic form
- ☐ furnished subsequently to this Authority for the purpose of search
2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments:

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IL2009/000089

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:
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:

see additional sheet

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.:
1-23,25,27-38,40 completely; 24, 41-44 partially
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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

Invention 1: 1-23,25,27-38,40 completely; claim 24 partially

Cells expressing 2 proteins linked to reporter polypeptides, and related nucleic acid systems.

Invention 166: claim 39

A method for isolating a polypeptide from a cell population by using an antibody

Inventions 2-165: claim 26 completely; claim 24 partially

The polypeptides of SEQ ID No. 1-164, each individually.

Invention 167: claims 41-44 partially

Pharmaceutical composition comprising camptothecin and an agent capable of downregulating DNA helicase DDX5 of SEQ ID No. 165 and method for treating cancer using the same

Invention 168: claims 41-44 partially

Pharmaceutical composition comprising camptothecin and an agent capable of downregulating replication factor C activator 1 (RFC1) of SEQ ID No. 166 and method for treating cancer using the same

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/IL2009/000089

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
EP 1464960	A	06-10-2004	NONE	
WO 9820031	A	14-05-1998	AU 5168598 A CA 2271228 A1	29-05-1998 14-05-1998
WO 9416092	A	21-07-1994	DE 69431285 D1 DE 69431285 T2 EP 0656954 A1 ES 2181714 T3 US 5652128 A US 6096717 A US 5916810 A US 6080541 A	10-10-2002 31-07-2003 14-06-1995 01-03-2003 29-07-1997 01-08-2000 29-06-1999 27-06-2000