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(71) Applicant: YISSUM RESEARCH DEVELOPMENT
COMPANY OF THE HEBREW UNIVERSITY OF
JERUSALEM LTD. [IL/IL]; Hi Tech Park, Edmond J.
Safra Campus, Givat Ram, 91390 Jerusalem (IL).

(72) Inventors: KOTLER, Moshe; 57 Hador Street, 90805
Mevasseret Zion (IL). NOWARSKI, Roni; Dep. of Patho-
logy and Immunology, The Hebrew University Hadassah
Medical School, 91120 Jerusalem (IL). BRIT-
AN-ROSICH, Elena; Dep. of Pathology and Immunology,
The Hebrew University Hadassah Medical School, 91120
Jerusalem (IL). BARAZ, Lea; 1/37 Givat Beit Hakerem,
96268 Jerusalem (IL).

(74) Agent: REINHOLD COHN AND PARTNERS;
P.O.B.13239, 61131 Tel Aviv (IL).

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KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD,
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12 December 2013

(54) Title: CELLULAR APOBEC3 PROTEINS AND MODULATORS THEREOF FOR REGULATING DNA REPAIR PRO-
CESSES AND TREATING PROLIFERATIVE DISEASES

(57) Abstract: The present invention provides methods, compositions and kits for modulating DSB repair processes in a subject in
need thereof. More specifically, the invention provides the use of compounds that modulate the expression or activity of at least one
APOBEC family member for modulating DSB repair processes.



INTERNATIONAL SEARCH REPORT

International application No
PCT/IL2013/050130

A. CLASSIFICATION OF SUBJECT MATTER INV. A61K38/16 A61K38/50 C12N9/78 A61P35/00 G01N33/00 ADD.		
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) A61K C12N G01N A61P		
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 practicable, search terms used) EPO-Internal, WPI Data, BIOSIS		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2010/039223 A2 (UNIV CALIFORNIA [US]; NIXON DOUGLAS F [US]; CHAMPIAT STEPHANE [FR]; GA) 8 April 2010 (2010-04-08) see Seq.14, cl.1-7, [002], [0054], [214]-[241], [273]-[299]	1-6, 11-15, 23-28, 30-34
X	WO 2007/137591 A2 (STATENS SERUMINSTITUT [DK]; FOMSGAARD ANDERS [DK]) 6 December 2007 (2007-12-06) see Cl.1-4, cl.32	15-24
A	WO 2005/117947 A1 (DEUTSCHES KREBSFORSCH [DE]; LOECHELT MARTIN [DE]; MUENK CARSTEN [DE]) 15 December 2005 (2005-12-15) see pages 1-2 and cl.1-4 ----- -/-	1-34
☒ 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 application or patent 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 June 2013		Date of mailing of the international search report 21/10/2013
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 Merckling-Ruiz, V

INTERNATIONAL SEARCH REPORT

International application No
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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2010/081621 A1 (HOLDEN LAUREN [US] ET AL) 1 April 2010 (2010-04-01) see [005], [02]-[022], [080], [117] -----	1-34
X	MARIN M ET AL: "HIV-1 Vif protein binds the editing enzyme APOBEC3G and induces its degradation", NATURE MEDICINE, NATURE PUBLISHING GROUP, NEW YORK, NY, US, vol. 9, no. 11, 1 November 2003 (2003-11-01), pages 1398-1403, XP002328599, ISSN: 1078-8956, DOI: 10.1038/NM946 abstract -----	15-22
X	FRIEDLER ASSAF ET AL: "Peptides derived from HIV-1 Vif: A non-substrate based novel type of HIV-1 protease inhibitors", JOURNAL OF MOLECULAR BIOLOGY, vol. 287, no. 1, 19 March 1999 (1999-03-19), pages 93-101, XP002699351, ISSN: 0022-2836 see abstract and Fig.1 -----	15-22

INTERNATIONAL SEARCH REPORT

International application No.

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Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.c 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. (means)
- ☒ on paper
- ☒ in electronic form
- b. (time)
- ☐ in the international application as filed
- ☐ together with the international application in electronic form
- ☒ 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/IL2013/050130

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 all searchable 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.:

1-8, 11-34(all partially)

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:

1. claims: 1-8, 11-34(all partially)

peptide comprising VKHH (seq.66), use alone or in combination with a genotoxic agent, for treating a proliferative disease, use for determining the efficacy of the treatment with a genotoxic agent in a patient having a proliferative disorder

2. claims: 1-8, 11-34(all partially)

peptide comprising KGWF (seq.68), use alone or in combination with a genotoxic agent, for treating a proliferative disease, use for determining the efficacy of the treatment with a genotoxic agent in a patient having a proliferative disorder

3. claims: 1-8, 11-34(all partially)

peptide comprising HLYYF or RLYYF (seq.67), use alone or in combination with a genotoxic agent, for treating a proliferative disease, use for determining the efficacy of the treatment with a genotoxic agent in a patient having a proliferative disorder

4. claims: 1-8, 11-34(all partially)

peptide derived from residues 211-240 of APOBEC3G (seq.86), use alone or in combination with a genotoxic agent, for treating a proliferative disease, use for determining the efficacy of the treatment with a genotoxic agent in a patient having a proliferative disorder

5. claims: 9(completely); 1-4, 11-14, 23-26, 28, 31-34(partially)

a nucleic acid inhibitor specific for APOBEC, use alone or in combination with a genotoxic agent, for treating a proliferative disease, use for determining the efficacy of the treatment with a genotoxic agent in a patient having a proliferative disorder

6. claims: 10(completely); 1-4, 11-14, 23-26, 28, 31-34(partially)

a mutated APOBEC3G peptide devoid of cytidine deaminase activity and comprising at least one of substitutions W285A and E259Q, use alone or in combination with a genotoxic agent, for treating a proliferative disease, use for determining the efficacy of the treatment with a genotoxic

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

agent in a patient having a proliferative disorder

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/IL2013/050130

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2010039223 A2	08-04-2010	US 2011274709 A1 WO 2010039223 A2	10-11-2011 08-04-2010
WO 2007137591 A2	06-12-2007	AT 486088 T EP 2021356 A2 WO 2007137591 A2	15-11-2010 11-02-2009 06-12-2007
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US 2010081621 A1	01-04-2010	NONE	