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— *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))*

(88) Date of publication of the international search report:
30 November 2017 (30.11.2017)

WO 2017/182783 A3

(54) Title: INACTIVATION OF DNA REPAIR AS AN ANTICANCER THERAPY

(57) Abstract: This invention relates to the modulation of DNA repair and nucleic acid editing mechanisms for use in the treatment of cancer. This invention relates to the inactivation of DNA repair and mechanisms for use in the treatment of cancer. This invention also relates to screening for new anti-cancer agents.

INTERNATIONAL SEARCH REPORT

International application No
PCT/GB2017/051062

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K31/00 C12N9/22 C12Q1/00 G01N33/68 A61P35/00
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 C12Q 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, BIOSIS, EMBASE, FSTA, 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	WO 2009/027641 A2 (CANCER RES INST ROYAL [GB]; BREAKTHROUGH BREAST CANCER [GB]; MARTIN SA) 5 March 2009 (2009-03-05) claims 1-60 ----- -/--	1-4, 7-10, 12-24, 26-30

[X] Further documents are listed in the continuation of Box C.

[X] 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	Date of mailing of the international search report
18 October 2017	26/10/2017

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Habedanck, Robert

INTERNATIONAL SEARCH REPORT

International application No.
PCT/GB2017/051062

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.:

29, 30(completely); 1-4, 7-10, 12-24, 26-28(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.

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	AMIT KUMAR SRIVASTAVA ET AL: "Enhanced expression of DNA polymerase eta contributes to cisplatin resistance of ovarian cancer stem cells", PROCEEDINGS NATIONAL ACADEMY OF SCIENCES PNAS, vol. 112, no. 14, 23 March 2015 (2015-03-23), pages 4411-4416, XP55391406, US ISSN: 0027-8424, DOI: 10.1073/pnas.1421365112 abstract ----- P. CEPPI ET AL: "Polymerase mRNA Expression Predicts Survival of Non-Small Cell Lung Cancer Patients Treated with Platinum-Based Chemotherapy", CLINICAL CANCER RESEARCH, vol. 15, no. 3, 1 February 2009 (2009-02-01), pages 1039-1045, XP55391707, US ISSN: 1078-0432, DOI: 10.1158/1078-0432.CCR-08-1227 abstract ----- GRACE E. COGGINS ET AL: "N -Aroyl Indole Thiobarbituric Acids as Inhibitors of DNA Repair and Replication Stress Response Polymerases", ACS CHEMICAL BIOLOGY, vol. 8, no. 8, 16 May 2013 (2013-05-16), pages 1722-1729, XP55304767, US ISSN: 1554-8929, DOI: 10.1021/cb400305r abstract ----- WO 2014/195331 A1 (INVECTYS [FR]) 11 December 2014 (2014-12-11) claim 1 ----- K S RAO ET AL: "MutagenicityTesting Applied for Regulation of Developing Products", CURRENT SEPARATIONS, vol. 20, no. 4, 1 January 2004 (2004-01-01), pages 141-144, XP55391851, the whole document page 142, right column, paragraph 1, 2 page 143, left column, paragraph 2 page 144, left column, paragraph 3 ----- -/--	1-4, 12-23, 26-28 1-4, 12-23, 26-28 1-4, 12-23, 26-28 1-4, 12-23, 26-28 22,23, 27,28

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	SLEBOS R J C ET AL: "Mutations in Tetranucleotide repeats following DNA damage depend on repeat sequence and Carcinogenic agent", CANCER RESEARCH, & 103RD ANNUAL MEETING OF THE AMERICAN-ASSOCIATION-FOR-CANCER-RESEARCH; CHICAGO, IL, USA; MARCH 31 -APRIL 04, 2012, vol. 62, 1 November 2002 (2002-11-01), pages 6052-6060, XP003010917, ISSN: 0008-5472 abstract	27-29
X	WO 2014/204578 A1 (GEN HOSPITAL CORP [US]) 24 December 2014 (2014-12-24) example 2d	30
X,P	EP 3 133 165 A1 (F HOFFMANN-LA ROCHE AG [CH]) 22 February 2017 (2017-02-22) claims 1-6	26
X	WO 2014/190311 A2 (NSABP FOUNDATION INC [US]; POGUE-GEILE KATHERINE LEA [US]; PAIK SOONMY) 27 November 2014 (2014-11-27) claims 1-26	26
X	US 2002/198264 A1 (GERSON STANTON L [US] ET AL) 26 December 2002 (2002-12-26) paragraphs [0005], [0009]; example 7	1,2, 7-10, 12-21
X	US 2008/108061 A1 (INAZAWA JOHJI [JP] ET AL) 8 May 2008 (2008-05-08) paragraph [0024]; claims 5-29,33-34	1-27
X	MOHD A B ET AL: "Truncation of the C-terminus of human MLH1 blocks intracellular stabilization of PMS2 and disrupts DNA mismatch repair", DNA REPAIR, ELSEVIER, AMSTERDAM, NL, vol. 5, no. 3, 7 March 2006 (2006-03-07), pages 347-361, XP024977208, ISSN: 1568-7864, DOI: 10.1016/J.DNAREP.2005.11.001 [retrieved on 2006-03-07] page 350, right column, paragraph 2 page 351, right column, paragraph 2; figure 2; table 1; compounds MLH1-L749X	22-24

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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.
X	A FEDIER ET AL: "Increased sensitivity of p53-deficient cells to anticancer agents due to loss of Pms2", BRITISH JOURNAL OF CANCER, vol. 87, no. 9, 21 October 2002 (2002-10-21), pages 1027-1033, XP055415923, GB ISSN: 0007-0920, DOI: 10.1038/sj.bjc.6600599 abstract -----	1,2, 7-10, 12-24, 26-29
A	MARK R KELLEY ET AL: "Targeting DNA repair pathways for cancer treatment: what's new?", FUTURE ONCOLOGY, vol. 10, no. 7, 1 May 2014 (2014-05-01), pages 1215-1237, XP055415986, GB ISSN: 1479-6694, DOI: 10.2217/fon.14.60 abstract -----	1-4, 7-10, 12-24, 26-30

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/GB2017/051062

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2009027641 A2	05-03-2009	US 2011212101 A1	01-09-2011
		WO 2009027641 A2	05-03-2009
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WO 2014190311 A2	27-11-2014	US 2014348821 A1	27-11-2014
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US 2002198264 A1	26-12-2002	AU 2003213144 A1	09-09-2003
		US 2002198264 A1	26-12-2002
		US 2006241186 A1	26-10-2006
		US 2012065145 A1	15-03-2012
		WO 03070234 A1	28-08-2003
US 2008108061 A1	08-05-2008	NONE	

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. claims: 1-4, 12-23, 26-28(all partially)

A method for treating cancer comprising administering a modifier of a DNA repair or nucleic acid editing gene, screening and diagnostic methods, wherein the gene includes DNA polymerase ?

2-28. claims: 30(completely); 1-29(partially)

same as invention 1, but wherein the gene is DNA pol-?, DNA pol-?, MLH1, MutLa, MutLp, MutLy, PMS1, PMS2, MLH3, ADAR1, ADAR2, ADAR3, ADARB2-AS1, AICDA, APOBEC3D, APOBEC3B, APOBEC3C, APOBEC3G, APOBEC3F, APOBEC3A, APOBEC3H, APOBEC1, A1CF, APOBEC2, APOBEC4, APOBEC3AP1 or APOBEC3B-AS1, respectively

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