

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference DUVAL15533MC	FOR FURTHER ACTION see Form PCT/ISA/220 as well as, where applicable, item 5 below.	
International application No. PCT/EP2016/082745	International filing date (<i>day/month/year</i>) 28 December 2016 (28-12-2016)	(Earliest) Priority Date (<i>day/month/year</i>) 29 December 2015 (29-12-2015)
Applicant INSERM (INSTITUT NATIONAL DE LA SANTE ET DE LA...		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 7 sheets.

It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

a. With regard to the **language**, the international search was carried out on the basis of:

- the international application in the language in which it was filed
- a translation of the international application into _____, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b))

b. This international search report has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43.6**bis**(a)).

c. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. **Certain claims were found unsearchable** (See Box No. II)

3. **Unity of invention is lacking** (see Box No III)

4. With regard to the **title**,

- the text is approved as submitted by the applicant
- the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

- the text is approved as submitted by the applicant
- the text has been established, according to Rule 38.2, by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority

6. With regard to the **drawings**,

- a. the figure of the **drawings** to be published with the abstract is Figure No. _____
 - as suggested by the applicant
 - as selected by this Authority, because the applicant failed to suggest a figure
 - as selected by this Authority, because this figure better characterizes the invention
- b. none of the figures is to be published with the abstract

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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.:

1-15(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.

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A. CLASSIFICATION OF SUBJECT MATTER
INV. G01N33/574
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)
G01N

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, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	NICOLAS JOSE LLOSA ET AL: "Immune checkpoints expression in MSI versus MSS colorectal cancers and their potential therapeutic implications", J CLIN ONCOL, vol. 32, 1 May 2014 (2014-05-01), page 5s, XP055273851, abstract ----- -/--	1-15

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 February 2017	Date of mailing of the international search report 09/05/2017
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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 Wiesner, Martina
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INTERNATIONAL SEARCH REPORT

International application No

PCT/EP2016/082745

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>Y. XIAO ET AL: "The Microsatellite Instable Subset of Colorectal Cancer Is a Particularly Good Candidate for Checkpoint Blockade Immunotherapy", CANCER DISCOVERY, vol. 5, no. 1, 1 January 2015 (2015-01-01) , pages 16-18, XP055271983, US ISSN: 2159-8274, DOI: 10.1158/2159-8290.CD-14-1397 the whole document</p>	1-6,14, 15
Y	<p>N. J. LLOSA ET AL: "The Vigorous Immune Microenvironment of Microsatellite Instable Colon Cancer Is Balanced by Multiple Counter-Inhibitory Checkpoints", CANCER DISCOVERY, vol. 5, no. 1, 1 January 2015 (2015-01-01) , pages 43-51, XP055349318, US ISSN: 2159-8274, DOI: 10.1158/2159-8290.CD-14-0863 page 49, right-hand column, paragraph 2; figure 2</p>	1-15
Y	<p>NICOLAS LLOSA ET AL: "The vigorous immune microenvironment of microsatellite instable colon cancer is balanced by multiple counter-inhibitory checkpoints", JOURNAL FOR IMMUNOTHERAPY OF CANCER, BIOMED CENTRAL LTD, LONDON, UK, vol. 3, no. 2, 4 November 2015 (2015-11-04), page 1, XP021235584, DOI: 10.1186/2051-1426-3-S2-P410 figure 2</p>	1-15
Y	<p>G. BRANDACHER: "Prognostic Value of Indoleamine 2,3-Dioxygenase Expression in Colorectal Cancer: Effect on Tumor-Infiltrating T Cells", CLINICAL CANCER RESEARCH, vol. 12, no. 4, 15 February 2006 (2006-02-15), pages 1144-1151, XP055273302, US ISSN: 1078-0432, DOI: 10.1158/1078-0432.CCR-05-1966 the whole document</p>	1-6
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INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2016/082745

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	ZORAN GATALICA ET AL: "Programmed death 1 (PD-1) lymphocytes and ligand (PD-L1) in colorectal cancer and their relationship to microsatellite instability status.", J CLIN ONCOL, vol. 32, no. 5s, 30 May 2014 (2014-05-30), XP055199884, abstract	7-15
A	----- PIN WU ET AL: "PD-L1 and Survival in Solid Tumors: A Meta-Analysis", PLOS ONE, vol. 10, no. 6, 26 June 2015 (2015-06-26), page e0131403, XP055273298, DOI: 10.1371/journal.pone.0131403 abstract	1-15
A	----- NICOLÁS J LLOSA ET AL: "Immune checkpoints in MSI and CSI colorectal cancers and their translational implications", JOURNAL FOR IMMUNOTHERAPY OF CANCER, BIOMED CENTRAL LTD, LONDON, UK, vol. 1, no. Suppl 1, 7 November 2013 (2013-11-07), page P161, XP021167111, ISSN: 2051-1426, DOI: 10.1186/2051-1426-1-S1-P161 the whole document	1-15
A	----- JUNG HO KIM: "Molecular and prognostic heterogeneity of microsatellite-unstable colorectal cancer", WORLD JOURNAL OF GASTROENTEROLOGY, vol. 20, no. 15, 1 January 2014 (2014-01-01), page 4230, XP055271940, CN ISSN: 1007-9327, DOI: 10.3748/wjg.v20.i15.4230 the whole document	1-15
A	----- US 2015/210769 A1 (FREEMAN GORDON JAMES [US] ET AL) 30 July 2015 (2015-07-30) paragraph [0464] - paragraph [0465] -----	1-15

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Information on patent family members

International application No

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Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2015210769	A1	30-07-2015	
		AU 2015209145 A1	07-07-2016
		CA 2935423 A1	30-07-2015
		EA 201691488 A1	28-02-2017
		EP 3097121 A1	30-11-2016
		JP 2017506067 A	02-03-2017
		KR 20160110995 A	23-09-2016
		PH 12016501456 A1	22-08-2016
		SG 11201604939S A	30-08-2016
		TW 201536808 A	01-10-2015
		US 2015210769 A1	30-07-2015
		UY 35967 A	31-08-2015
		WO 2015112900 A1	30-07-2015

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. claims: 1-15(partially)

Method for predicting the survival time of a patient suffering from a microsatellite unstable colorectal cancer and a method for determining whether a patient suffering from a microsatellite unstable colorectal cancer will achieve a response with an immune checkpoint inhibitor comprising i) determining the expression level of the gene encoding for IDO-1 in a tumor tissue sample obtained from the patient, and ii) comparing the expression level determined at step i) with a predetermined reference value; and a method of treating the thus identified patients.

2-15. claims: 1-15(partially)

Method for predicting the survival time of a patient suffering from a microsatellite unstable colorectal cancer and a method for determining whether a patient suffering from a microsatellite unstable colorectal cancer will achieve a response with an immune checkpoint inhibitor comprising i) determining the expression level of at least one gene selected from the group consisting of CD40, CD274, ICOS, TNFRSF9, TNFRSF18, LAG3, IL2RB, HAVCR2, TNFRSF4, CD276, CTLA4, PDCD1LG2, VTCN 1 and PDCD 1 in a tumor tissue sample obtained from the patient, and ii) comparing the expression level determined at step i) with a predetermined reference value; and a method of treating the thus identified patients.
