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#### 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))
- (88) Date of publication of the international search report: 1 September 2016

### (54) Title: METHODS AND COMPOSITIONS FOR PROGNOSIS AND TREATMENT OF CANCERS

(57) Abstract: The invention provides methods of using expression levels of one or more immune cell gene signatures and/or combinations of immune cell gene signatures as selection criteria for selecting a patient having cancer for treatment with an immunotherapy. The invention further provides methods for selecting a patient having cancer who may benefit from a particular immunotherapy, such as an activating immunotherapy or a suppressing immunotherapy and administering to the patient the activating immunotherapy or suppressing immunotherapy to treat the cancer.

### INTERNATIONAL SEARCH REPORT

International application No PCT/US2015/067878

a. classification of subject matter INV. C12Q1/68

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) C12Q

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT				
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.		
X	EP 2 484 762 A1 (UNIV KURUME [JP]) 8 August 2012 (2012-08-08) table 4	1-8,27, 44-51		
Α	EP 2 615 181 A1 (UNIV GRENOBLE 1 [FR]; CT HOSPITALIER UNIVERSITAIRE GRENOBLE [FR]; CENT) 17 July 2013 (2013-07-17) paragraph [0008] - paragraph [0020]	1		
X	US 2011/070268 A1 (BRICHARD VINCENT [BE] ET AL) 24 March 2011 (2011-03-24) claim 1; table 1	1-7,27		
X	WO 2014/078468 A2 (SQUIBB BRISTOL MYERS CO [US]) 22 May 2014 (2014-05-22)  paragraph [0077]; claims 1,2	1-8,27, 44-59, 61-67		
	-/			

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 April 2016	11/07/2016	
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  Cornelis, Karen	

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# **INTERNATIONAL SEARCH REPORT**

International application No PCT/US2015/067878

	ation). DOCUMENTS CONSIDERED TO BE RELEVANT	T
ategory*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2011/094483 A2 (H LEE MOFFITT CANCER CT & RES [US]; MULE JAMES J [US]; COPPOLA DOMENIC) 4 August 2011 (2011-08-04) page 3 - page 4	1-7,27, 44-59, 61-67
X	DOMENIC) 4 August 2011 (2011-08-04) page 3 - page 4  W0 2014/023706 A1 (INST NAT SANTE RECH MED [FR]; UNIV PARIS DESCARTES [FR]; ASSIST PUBL H) 13 February 2014 (2014-02-13) page 5 - page 8	1-7,27

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International application No. PCT/US2015/067878

# **INTERNATIONAL SEARCH REPORT**

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
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.:
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, 27, 44-59, 61-67(all partially)
<b>Remark on Protest</b> 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, 27, 44-59, 61-67(all partially)

A method to select a patient having cancer for a treatment with immunotherapy by determining the expression level of an immune cell gene signature whereby such a signature is characterised by comprising at least one of the following: CD8a, GZMA, GZMB, IFNgamma, EOMES or PRF1.

2. claims: 1-67(partially)

A method to select a patient having cancer for a treatment with immunotherapy by determining the expression level of an immune cell gene signature whereby such a signature is characterised by comprising at least one of the following: FOXP3

3. claims: 1-67(partially)

A method to select a patient having cancer for a treatment with immunotherapy by determining the expression level of an immune cell gene signature whereby such a signature is characterised by comprising at least one of the following: MS4A1 or CD48

4-23. claims: 1-67(partially)

A method to select a patient having cancer for a treatment with immunotherapy by determining the expression level of an immune cell gene signature whereby such a signature is characterised by comprising at least one of the following gene sets as defined in each group of claim 1

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### **INTERNATIONAL SEARCH REPORT**

Information on patent family members

International application No PCT/US2015/067878

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