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(30) Priority: **02.12.2009 US 283393 P**

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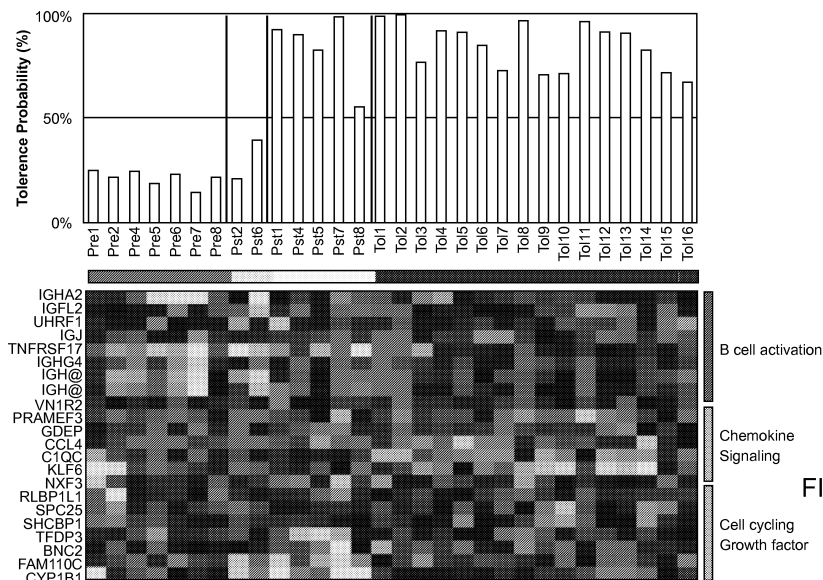
(62) Document number(s) of the earlier application(s) in accordance with Art. 76 EPC:  
**10835023.2 / 2 507 630**

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(54) **BIOMARKERS FOR DETERMINING AN ALLOGRAFT TOLERANT PHENOTYPE**

(57) Methods are provided for determining whether a subject has a graft tolerant phenotype. In practicing the subject methods, the expression level of one or more gene in a sample from the subject, e.g., a blood sample, is assayed to obtain a gene expression result, where the gene expression result includes a result for a biomarker of graft tolerance. The obtained gene expression result

is then employed to determine whether the subject has a graft tolerant phenotype. Also provided are compositions, systems and kits that find use in practicing the subject methods. The methods and compositions find use in a variety of applications, including the determination of an immunosuppressive therapy regimen.



**FIG. 3**



EUROPEAN SEARCH REPORT

Application Number  
EP 17 15 1969

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DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
X	DATABASE GEO-NCBI [Online] NCBI; 11 February 2008 (2008-02-11), "Agilent whole human genome microarray 4x44K", XP002594592, retrieved from NCBI Database accession no. GPL6480 * the whole document *	9-13	INV. G01N33/53 C12Q1/68
A	EP 1 731 620 A1 (INST NAT SANTE RECH MED [FR]) 13 December 2006 (2006-12-13) * paragraph [0011] - paragraph [0012] * * paragraph [0019]; table 1 * * examples 1-2 * * claims 1-23 *	1-8,14	TECHNICAL FIELDS SEARCHED (IPC)  C12Q
A	CHRISTOPHE BRAUD ET AL: "Immunosuppressive drug-free operational immune tolerance in human kidney transplant recipients: Part I. blood gene expression statistical analysis", JOURNAL OF CELLULAR BIOCHEMISTRY, vol. 103, no. 6, 15 April 2008 (2008-04-15), pages 1681-1692, XP055063802, ISSN: 0730-2312, DOI: 10.1002/jcb.21574 * the whole document *	1-8,14	
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<del>The present search report has been drawn up for all claims</del>			
Place of search <b>The Hague</b>		Date of completion of the search <b>10 May 2017</b>	Examiner <b>Aguilera, Miguel</b>
CATEGORY OF CITED DOCUMENTS X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document		T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons ..... & : member of the same patent family, corresponding document	

EPO FORM 1503 03.02 (P04C01)



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EP 17 15 1969

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DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
A	<p>BROUARD S ET AL: "Identification of a peripheral blood transcriptional biomarker panel associated with operational renal allograft tolerance", PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES, NATIONAL ACADEMY OF SCIENCES, US, vol. 104, no. 39, 25 September 2007 (2007-09-25), pages 15448-15453, XP002594926, ISSN: 0027-8424, DOI: 10.1073/PNAS.0705834104 [retrieved on 2007-09-14] * abstract *</p> <p style="text-align: center;">-----</p>	1-8,14	
A	<p>FLECHNER S M ET AL: "Kidney transplant rejection and tissue injury by gene profiling of biopsies and peripheral blood lymphocytes", AMERICAN JOURNAL OF TRANSPLANTATION, BLACKWELL MUNKSGAARD, DK, vol. 4, no. 9, 1 September 2004 (2004-09-01), pages 1475-1489, XP008103279, ISSN: 1600-6135, DOI: 10.1111/J.1600-6143.2004.00526.X [retrieved on 2004-06-07] * the whole document *</p> <p style="text-align: center;">-----</p> <p style="text-align: right;">-/--</p>	1-8,14	
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<del>The present search report has been drawn up for all claims</del>			
Place of search		Date of completion of the search	Examiner
The Hague		10 May 2017	Aguilera, Miguel
CATEGORY OF CITED DOCUMENTS		T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons ..... & : member of the same patent family, corresponding document	
X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document			

EPO FORM 1503 03.02 (P04C01)



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DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
A	SARWAL M ET AL: "MOLECULAR HETEROGENEITY IN ACUTE RENAL ALLOGRAFT REJECTION IDENTIFIED BY DNA MICROARRAY PROFILING", NEW ENGLAND JOURNAL OF MEDICINE, MASSACHUSETTS MEDICAL SOCIETY, BOSTON, MA, US, vol. 349, no. 2, 10 July 2003 (2003-07-10), pages 125-138, XP009045203, ISSN: 1533-4406, DOI: 10.1056/NEJMOA035588 * the whole document *	1-8,14	
A	PIERRE SAINT-MEZARD ET AL: "Analysis of independent microarray datasets of renal biopsies identifies a robust transcript signature of acute allograft rejection", TRANSPLANT INTERNATIONAL, vol. 22, no. 3, 1 March 2009 (2009-03-01), pages 293-302, XP055063955, ISSN: 0934-0874, DOI: 10.1111/j.1432-2277.2008.00790.x * abstract *	1-8,14	
<del>The present search report has been drawn up for all claims</del>			TECHNICAL FIELDS SEARCHED (IPC)
Place of search <b>The Hague</b>		Date of completion of the search <b>10 May 2017</b>	Examiner <b>Aguilera, Miguel</b>
<b>CATEGORY OF CITED DOCUMENTS</b> X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document		T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons ..... & : member of the same patent family, corresponding document	

1 EPO FORM 1503 03.02 (P04C01)



Application Number

EP 17 15 1969

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**CLAIMS INCURRING FEES**

The present European patent application comprised at the time of filing claims for which payment was due.

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Only part of the claims have been paid within the prescribed time limit. The present European search report has been drawn up for those claims for which no payment was due and for those claims for which claims fees have been paid, namely claim(s):

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No claims fees have been paid within the prescribed time limit. The present European search report has been drawn up for those claims for which no payment was due.

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**LACK OF UNITY OF INVENTION**

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

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see sheet B

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All further search fees have been paid within the fixed time limit. The present European search report has been drawn up for all claims.

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As all searchable claims could be searched without effort justifying an additional fee, the Search Division did not invite payment of any additional fee.

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Only part of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the inventions in respect of which search fees have been paid, namely claims:

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None of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the invention first mentioned in the claims, namely claims:

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1-14 (partially)

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The present supplementary European search report has been drawn up for those parts of the European patent application which relate to the invention first mentioned in the claims (Rule 164 (1) EPC).

**LACK OF UNITY OF INVENTION  
SHEET B**Application Number  
EP 17 15 1969

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The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

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## 1. claims: 1-14(partially)

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Methods for determining an allograft tolerant phenotype comprising evaluating the level of expression of the BNC2 gene. Methods of managing immunosuppressive therapy based on evaluating the level of expression of said gene. Systems, kits and computer programs for carrying out said methods.

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## 2-33. claims: 1-14(partially)

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Methods for determining an allograft tolerant phenotype comprising evaluating the level of expression of the C1QC gene. Methods of managing immunosuppressive therapy based on evaluating the level of expression of said gene. Systems, kits and computer programs for carrying out said methods.

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[idem for each one of the genes listed in Tables 1A and 1B]

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**ANNEX TO THE EUROPEAN SEARCH REPORT  
ON EUROPEAN PATENT APPLICATION NO.**

EP 17 15 1969

5 This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report.  
The members are as contained in the European Patent Office EDP file on  
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

10-05-2017

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Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 1731620 A1	13-12-2006	EP 1731620 A1	13-12-2006
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EPO FORM P0459

For more details about this annex : see Official Journal of the European Patent Office, No. 12/82

专利名称(译)	用于确定同种异体耐受性表型的生物标记物		
公开(公告)号	<a href="#">EP3185013A3</a>	公开(公告)日	2017-10-11
申请号	EP2017151969	申请日	2010-12-01
[标]申请(专利权)人(译)	斯坦福大学		
申请(专利权)人(译)	THE利兰·斯坦福，齐齐哈尔大学董事会		
当前申请(专利权)人(译)	THE利兰·斯坦福，齐齐哈尔大学董事会		
[标]发明人	SARWAL MINNIE M LI LI		
发明人	SARWAL, MINNIE M. LI, LI		
IPC分类号	G01N33/53 C12Q1/68		
CPC分类号	C12Q1/6883 C12Q1/6888 C12Q2600/158 C12Q2600/106 G01N33/6893 G01N2800/245 G01N2800/52		
审查员(译)	AGUILERA, MIGUEL		
优先权	61/283393 2009-12-02 US PCT/US2010/058496 2010-12-01 WO		
其他公开文献	EP3185013A2 EP3185013B1		
外部链接	<a href="#">Espacenet</a>		

摘要(译)

提供了用于确定受试者是否具有移植耐受表型的方法。在实施主题方法时，测定来自受试者的样品（例如血液样品）中的一种或多种基因的表达水平以获得基因表达结果，其中基因表达结果包括移植耐受性生物标志物的结果。然后使用获得的基因表达结果确定受试者是否具有移植耐受表型。还提供了可用于实践主题方法的组合物，系统和试剂盒。该方法和组合物可用于多种应用，包括免疫抑制治疗方案的确定。

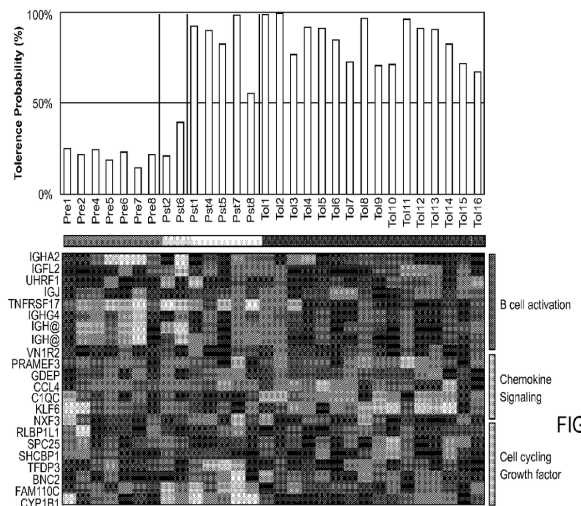


FIG. 3