Title: METHODS AND COMPOSITIONS FOR DIAGNOSING AND MONITORING THE STATUS OF TRANSPLANT REJECTION AND IMMUNE DISORDERS

Abstract: The invention presents methods of using splice variants and reagents thereof for diagnosing and monitoring the status of transplants and immune disorders including diagnosing, monitoring and predicting transplant rejection or non-rejection, steroid responsiveness, and onset or flare of immune disorders.
INTERNATIONAL SEARCH REPORT

International application No
PCT/US07/18135

A CLASSIFICATION OF SUBJECT MATTER
IPC C12Q 1/68(2006 01)

USPC 435/6,7 1
According to International Patent Classification (IPC) or to both national classification and IPC

B DOCUMENTS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
US 435/6, 7 1

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)
Medline, USPAT, USPGPUB, Derwent, USOCR, EPO, IPO

C DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
<thead>
<tr>
<th>Category *</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No</th>
</tr>
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<tbody>
<tr>
<td>X</td>
<td>Keemblyethey et al., &quot;Mouse Glucose Transporter 9 Splice Variants Are Expressed in Adult Liver and Kidney and Are Up-regulated in Diabetes,&quot; Mol Endocrinol March 2006, Vol 20, No 3, pp 686-697</td>
<td>1-3, 7-9, 12, 26 and 33</td>
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<td>X</td>
<td>US 6,905,827 (WOHLGEMUTH et al) 14 June 2005 (14 06 2005), entire document</td>
<td>1-26</td>
</tr>
</tbody>
</table>

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
b earlier application or patent published on or after the international filing date
L document which may throw doubt on priority claims 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

Date of the actual completion of the international search
26 August 2008 (26 08 2008)

Name and mailing address of the ISA/US
Mail Stop PCT, Attn: ISA/US
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
Facsimile No (571) 272-3201

Date of mailing of the international search report
10 SEP. 2008

Authorized for this search report
Molly E. Baughman
Telephone No 571 272-0700

Form PCT/ISA/210 (second sheet) (April 2007)
## 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. 1-35 and 38
   - 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:

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 additional fees, this Authority did not invite payment of any 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. 1-35 and 38.

**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.

Form PCT/ISA/210 (continuation of first sheet(2)) (April 2007)
<table>
<thead>
<tr>
<th>Category</th>
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<td>P,Y</td>
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BOX III OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1 In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s) 1-35 and 38, drawn to a method for diagnosing or monitoring the status of a transplant or an immune disorder.

Group II, claim(s) 36, drawn to a method for making a probe that improves the diagnosis or monitoring of the status of a transplant or an immune disorder.

Group II, claim(s) 37, drawn to a method for improving the diagnosis or monitoring of the status of a patient with a transplant or a subject with an immune disorder.

The inventions listed as Groups I-III do not relate to a single general inventive concept under PCT Rule 13.2 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: the special technical feature, a method comprising the steps (a) selecting a splice variant of a gene, where the gene is known to have utility in diagnosing or monitoring the status of the transplant or immune disorder (b) detecting expression of the splice variant in a sample using a probe that specifically detects the expression of the splice variant, and (c) diagnosing or monitoring the status of the transplant or immune disorder based on the expression of the splice variant in the sample, does not provide contribution over the prior art (see Yu et al (US 2005/0186637 A1), specifically, paragraph [0585]).