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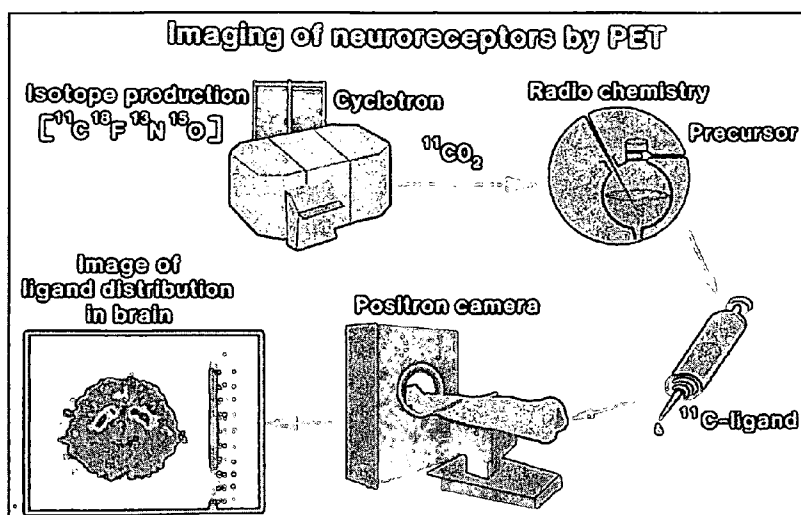
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— with international search report

[Continued on next page]

(54) Title: METHODS FOR DIAGNOSING DISEASES AND EVALUATING TREATMENTS THEREFOR USING PET

FIG. 1



(57) Abstract: The present invention relates to methods for determining whether a mammal has a disease, such as diabetes, using PET data analysis techniques. These methods include administering to a mammal a PET-compatible tracer, such as a radioligand specific for a vesicular monoamine transporter 2 (VMAT2) receptor, and measuring total functional  $\beta$ -cell capacity (volume) of the mammal's pancreas using PET data analysis techniques. Methods for tracking the efficacy of a treatment for diabetes, for evaluating the regeneration of  $\beta$ -cells in a pancreas, and for monitoring a patient with a transplanted pancreas are also provided.

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## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 08/05994

<b>A. CLASSIFICATION OF SUBJECT MATTER</b> IPC(8) - A61K 49/00 (2008.04) USPC - 514/866; 424/9.1 According to International Patent Classification (IPC) or to both national classification and IPC		
<b>B. FIELDS SEARCHED</b> Minimum documentation searched (classification system followed by classification symbols) USPC - 514/866; 424/9.1 Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched USPC - 514/866; 424/9.1 Search Terms Below Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) PUBWest (USPT, PGPB, EPAB, JPAB); google.com Search Terms Used: langerhans, islets, regeneration, detection, significant, binding, capacity, tetrabenazine, imaging, dihydrotetrabenazine, VMAT2, test, testing, detection, detecting, tracers, vesicular, monoamine, transporter, disease, diabetes, alzheimer's		
<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2006/0117397 A1 (Rutkowski et al.) 01 June 2006 (01.06.2006) entire document, especially Abstract; paras [0012]; [0024]; [0033]; [0046]; [0049]; [0056]; [0066]; [0068]	1-33
Y	US 2005/0260697 A1 (Wang et al.) 24 November 2005 (24.11.2005) entire document, especially Abstract; paras [0073]; [0099]; [0104]; [0125]; [0159]; [0212]; [0232]; [0239]	1-33
Y	US 5,278,308 A (Kung) 11 January 1994 (11.01.1994) entire document, especially Abstract	8-10, 13-15, 20-24
Y	US 5,762,937 A (Atkinson et al.) 09 June 1998 (09.06.1998) entire document, especially Abstract; col. 2, ln. 13-25; col. 5, ln. 34-45	32, 33
<input type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/>		
* 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 09 October 2008 (09.10.2008)		Date of mailing of the international search report <b>30 OCT 2008</b>
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. 571-273-3201		Authorized officer: Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

**INTERNATIONAL SEARCH REPORT**

International application No.

PCT/US 08/05994

**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:  
please see supplemental box

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 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.:

**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.

**INTERNATIONAL SEARCH REPORT**  
Information on patent family members

International application No.

PCT/US 08/05994

continuation of Box III:

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: claims 1-16 and 29-30: directed to a method of diagnosing diabetes comprising carrying out a PET Scan and applying a PANC MAP.

Group II: claims 17-28: directed to a method using PET imaging data and BP positive voxels

Group III: claims 31-33: directed to a method for evaluating whether a treatment for diabetes in a patient comprising calculating a significant binding capacity for a vesicular monamine transporter 2 (VMAT2) PET scan.

The inventions listed as Groups I - III do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Group I does not include the inventive concept of a method using BP positive voxels as required by Group II or calculating a significant binding capacity for a vesicular monamine transporter 2 (VMAT2) PET scan as required by Group III.

Group II does not include the inventive concept of diagnosing diabetes comprising applying a PANC MAP as required by Group I or calculating a significant binding capacity for a vesicular monamine transporter 2 (VMAT2) PET scan as required by Group III.

Group III does not include the inventive concept of diagnosing diabetes comprising applying a PANC MAP as required by Group I or calculating a significant binding capacity for a vesicular monamine transporter 2 (VMAT2) PET scan as required by Group III.

Groups I-III share the technical feature of a PET Scan in diagnosing diabetes. However, this shared technical feature does not represent a contribution over the prior art of US 2006/0062756 A1 to Woodward (23 March 2006), which teaches using PET Scans in diagnosing diabetes (Title and Abstract). As the above connector position assurance device was known at the time, as evidenced by the teaching of Woodward, this cannot be considered a special technical feature that would otherwise unify the groups.

Groups I-III therefore lack unity under PCT Rule 13 because they do not share a same or corresponding special technical feature.