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Published:
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— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: MODULATION OF GLUCOSE-6-PHOSPHATASE TRANSLOCASE EXPRESSION

(57) Abstract: Compositions and methods are provided for decreasing blood glucose levels in an animal, comprising administering to said animal an antisense inhibitor of glucose-6-phosphatase translocase expression alone or in combination with at least one glucose-lowering drug. Also provided are compositions and methods for treating diabetes and other metabolic disorders.

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US05/14116

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) : A61K 31/70; C07H 21/04

US CL : 514/44; 536/24.5

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)

U.S. :

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)

Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	Kurukulasuriya R. et al. (2003) Curr Med Chem. Jan;10(2):123-53. (pages 123, 134-136, and 144)	1 and 6-20
Y	Gustafson et al. (2001) Biochem J. 358:665-671	1 and 6-20
Y	Simon et al. (2000) Archives of Biochemistry and Biophysics 373(2):418-428 (see entire document)	1 and 6-20
Y	Herling et al. (1999) European J. Pharmacology 386:75-82	1 and 6-20
Y	Bernard-Helary et al. (2002) GLIA 37:379-382	1-4 and 6-20
Y	Liang et al. (Feb. 2004) Diabetes 53:410-417	1-4 and 6-20
Y	Vickers et al. (2003) J. Biol. Chem. 278:7108-7118 (pages 7108-9, 7115-6, 7117)	1-4 and 6-20
Y	Chen (US Patent No. 6,623,947)	1-4 and 6-20
X, P	Palma (US 20050272080 A1) (Sequence 428370 matches SEQ ID NO: 27 of the instant application)	5

☐ 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 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
30 December 2005 (30.12.2005)	22 FEB 2006
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 Louis V. Wollenberger Telephone No. 571-272-1600

Form PCT/ISA/210 (second sheet) (April 2005)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US05/14116

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 Continuation 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 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.: 1-20 and SEQ ID NO:27

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

International application No.
PCT/US05/14116

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.

Groups 1-84, claim(s) 1-20, drawn to an oligomeric compound that inhibits the expression of glucose-6-phosphatase translocase, and to the use said compound in medicaments, wherein said oligomeric compound is selected from SEQ ID Nos: 27-61, 145-154, 157-161, 163-169, 171-173, 175-181, 183-190, 192-196, or 198-201.

The inventions listed as Groups 1-84 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: The inventions listed as Groups 1-84 specifically claim oligomeric compounds having sequences selected from one of SEQ ID NO: 27-201, specifically enumerated above.

This international searching authority considers that the international application does not comply with the requirements of unity of invention (Rules 13.1, 13.2 and 13.3) for the reasons indicated below.

According to the guidelines in Section (f) of Annex B of the PCT Administrative Instructions, the requirement of a technical interrelationship and the same or corresponding special technical features as defined in Rule 13.2, shall be considered to be met when the alternatives are of a similar nature.

Sections (f)(i), (ii), and (iii) of Annex B of the PCT Administrative Instructions state:

(i) When the Markush grouping is for alternatives of chemical compounds, they shall be regarded as being of a similar nature where the following criteria are fulfilled:
(A) all alternatives have a common property or activity, and
(B) (1) a common structure is present, i.e., a significant structural element is shared by all of the alternatives, or (B) (2) in cases where the common structure cannot be the unifying criteria, all alternatives belong to a recognized class of chemical compounds in the art to which the invention pertains.
(ii) In paragraph (f)(i)(B)(1), above, the words "significant structural element is shared by all of the alternatives" refer to cases where the compounds share a common chemical structure which occupies a large portion of their structures, or in case the compounds have in common only a small portion of their structures, the commonly shared structure constitutes a structurally distinctive portion in view of existing prior art, and the common structure is essential to the common property or activity. The structural element may be a single component or a combination of individual components linked together.
(iii) In paragraph (f)(i)(B)(2), above, the words "recognized class of chemical compounds" mean that there is an expectation from the knowledge in the art that members of the class will behave in the same way in the context of the claimed invention. In other words, each member could be substituted one for the other, with the expectation that the same intended result would be achieved.

In the instant case, 84 alternative polynucleotide sequence SEQ ID NOs are recited in claim 5. The alternative polynucleotides do not appear to share a common property or activity or a common structure or significant structural element or belong to a recognized class of chemical compounds, according to the criteria in B(f)(iii), above, wherein each member could be substituted for the other with the expectation that the same result would be achieved.

Although the antisense sequences of the instant application all target the same gene, each antisense sequence behaves in a different way in the context of the claimed invention. Each sequence targets a different and specific region of the target gene, and, absent evidence to the contrary, each sequence modifies (either increases or decreases) the expression of the gene to varying degrees. Each member of the class cannot be substituted, one for the other, with the expectation that the same intended result would be achieved. In fact, the instant description at pages 62, 64-6, and 78, Tables 4, 5, 11 indicates that the claimed polynucleotides inhibit gene expression to variable degrees; thus, the oligos do not behave in the same way or perform the same function with the same efficiency.

Further, although the instant antisense sequences target the same gene, the sequences do not meet the criteria of (B)(1), as they do not share, one with another, a common core structure. Accordingly, unity of invention between the antisense sequences of the instant application is lacking and each antisense sequence claimed is considered to constitute a special technical feature.

Applicants will obtain a search of the first sequence listed in the claim of the elected invention. For every other sequence applicants wish to have searched, applicants need to elect the sequence and pay an additional fee.

Continuation of B. FIELDS SEARCHED Item 3:
STN (Embase, Medline, Biosis, CaPlus); PubMed; EAST (foreing and domestic patents and patent application publications); STIC-Biotech sequence search of commercial and non-commercial databases for sequences matching SEQ ID NO:27