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(71) Applicant (for all designated States except US): **UNIVERSITY OF UTAH RESEARCH FOUNDATION** [US/US]; 615 Arapen Drive, Suite 310, Salt Lake City, UT 84108 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **RUTTER, Jared** [US/US]; 1743 E. Browning Avenue, Salt Lake City, UT 84108 (US). **HAO, Huai-xiang** [CN/US]; 1114 Medical Plaza, University Of Utah, Salt Lake City, UT 84112 (US). **SWATEK, Wojtek** [US/US]; 173s 1200e, Salt Lake City, UT 84102 (US).

(74) Agents: **CLEVELAND, Janell, T.** et al.; Needle & Rosenberg, P.c., Suite 1000, 999 Peachtree Street, Atlanta, GA 30309-3915 (US).

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(88) Date of publication of the international search report:
5 June 2008

(54) Title: PAS KINASE REGULATES ENERGY HOMEOSTASIS

(57) Abstract: Disclosed are compositions and methods related to PAS Kinase and various diseases and disorders associated therewith. Included are methods for treating insulin resistance, cancer, and diabetes comprising administering a composition that inhibits PAS Kinase and methods, including high throughput screening methods, for identifying test compounds that modulate PAS Kinase.



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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 07/70634

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A61K 31/53; C12N 9/12 (2008.01)

USPC - 514/243, 435/194

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)

USPC: 514/243, 435/194

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
USPC: 435/194; 435/320.1; 435/325; 435/69.1; 435/254.11; 435/15; 530/300; 530/350; 536/23.2; 536/23.5; 536/23.1

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

PubWEST(PGPB,USPT,USOC,EPAB,JPAB); Google; Pubmed

Search terms: PASK, Pas kinase, per-arnt-sim, insulin resistance, type 2 diabetes, metabolic syndrome, mitochondrial metabolism

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	US 2005/0107386 A1 (NARLA et al.) 19 May 2005 (19.05.2005); para [0039], [0050], [0051], [0055], [0085], [0121], [0227]	1-4, 14 and 15 ----- 5
Y	RITZ et al. Mitochondrial function, energy expenditure, aging and insulin resistance. Diabetes Metab. Dec 2005 (12.2005), 31(2): 5S67-5S73; pg 5S71, para 5	5
A	XAVIER et al. Involvement of Per-Arnt-Sim (PAS) kinase in the stimulation of preproinsulin and pancreatic duodenum homeobox 1 gene expression by glucose. PNAS Jun 2004, 101(22):8319-8324	1-5, 14 and 15

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Further documents are listed in the continuation of Box C.

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* 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

21 January 2008 (21.01.2008)

Date of mailing of the international search report

25 MAR 2008

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Mail Stop PCT, Attn: ISA/US, Commissioner for Patents
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Authorized officer:

Lee W. Young

PCT Helpdesk: 571-272-4300
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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 07/70634

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:

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 1-5, 14, 15 directed to a method of treating insulin resistance in a subject comprising administering to the subject a composition that inhibits PASK (claims 1-4 and 15); a method of increasing mitochondrial metabolism a cell, comprising inhibiting PASK (claim 5); a method of treating diabetes type I in a subject, comprising administering to the subject a composition that inhibits PASK (claim 14).
- Group II: claims 6-9, 11, directed to a method of screening for a test compound that modulates PASK.
- Group III: claims 10 and 12 directed to a compound identified by the method of claim 6.
- Group IV: claims 13, directed to a method of treating cancer in a subject administering to the subject an effective amount of a composition that inhibits PASK.

*****SEE SUPPLEMENTAL BOX TO CONTINUE*****

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.:
1-5 and 14-15

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.

SUPPLEMENTAL BOX

Continuation of Box III:

This International Searching Authority found multiple inventions in this international application, as follows:

The inventions listed as Groups I-IV 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 technical features for the following reasons:

As to Groups I, II and IV, the inventions of said groups do not relate to a single general inventive concept under PCT Rule 13.1 because under PCT Rule 13.2, unity of invention exists only when there is a shared same or corresponding special technical feature is a contribution over the prior art.

The common technical feature of said Groups I, II and IV is modulating PASK activity. However, this is not an improvement over the article entitled "Involvement of Per-Arnt-Sim (PAS) kinase in the stimulation of preproinsulin and pancreatic duodenum homeobox 1 gene expression by glucose" by Xavier et al. (PNAS 01 Jun 2004, 101(22):8319-8324), disclosing that PASK is regulated by glucose, both posttranscriptionally and at the level of the gene expression, and that PASK activity is required for glucose-stimulated insulin expression in Min-6 cells. Thus, the shared technical feature cannot function as a novel (special) technical feature to maintain unity of invention among Groups I, II, and IV.

As to Groups II and III, the technical feature of said groups resides in the step of observing the effect of the candidate compounds on PASK activity in a screening assay. As the nature of the candidate compounds is not disclosed, there is no teaching whether the same or a corresponding special technical feature is present in any of said candidate compounds. In addition, no manufacturing relationship exists between the screening method and the claimed compounds. Thus, unity of invention among groups II and III is lacking.

Finally, the screening methods of Group II are not methods of using claimed compounds. In the absence of any teaching as to the structure required for a compound to act as a modulator of PASK, there is no single general concept that links the method to the claimed compounds. Thus, Groups I-IV do not relate to a single general inventive concept because they do not share a same or corresponding special technical feature, and unity of invention is lacking.