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30 April 2009

(54) Title: SCREENING METHODS USING G-PROTEIN COUPLED RECEPTORS AND RELATED COMPOSITIONS

(57) Abstract: The present invention provides screening methods for GPCRs based on the discovery that the affinity of a receptor agonist for a GPCR (such as the parathyroid hormone receptor) when not bound to a G-protein is correlated with the length of time over which the agonist is effective, independently of its pharmacokinetic properties. The invention also provides PTH- and PTHrP-derived polypeptides.



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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 08/09288

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A61K 38/04, A61K 38/00 (2009.01)

USPC - 930/10, 514/2

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 -- 930/10, 514/2, 930/120, 514/12, 514/14, 514/15

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)

WEST -- PGPB,USPT,USOC,EPAB,JPAB; Dialog Classic Files ? 654, 652, 351, 349, 315, 6, 35, 65, 155; Google Scholar; USPTO Web Page; Entrez Pubmed; Search terms -- GPCR agonist, R0 state, Rg state, GTP gamma S, affinity determination, N-terminal binding domain, PTH, PTHR, PTHrP, cAMP assay, intracellular calcium, competition

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X -- Y -- A	HOARE, S.R.J., et al. Evaluating the signal transduction mechanism of the parathyroid hormone 1 receptor. Journal of Biological Chemistry, March 2001, Vol. 276, pages 7741-7753; pg 7741, abstract, col 1-2; pg 7742, col 2, para 2; pg 7743, Fig 1; pg 7744, col 1, para 1; pg 7745, col 1-2; pg 7747, col 2, para 1; pg 7750, col 2, para 1; pg 7752, col 1, para 3	33, 34, 37 ----- 1-32 ----- 40-50
Y . A	US 2006/0078559 A1 (MIGEOTTE et al.) 13 April 2006 (13.04.2006) para [0024], [0029], [0100], [0104], [0113], [0118], [0161], [0155], [0180], [0204], [0222], [0283], [0363]-[0365], [0460]	1-32
A	US 2004/0176285 A1 (JUPPNER et al.) 09 September 2004 (09.09.2004) para [0026], SEQ ID NO: 8.	40-50
A	US 2003/0171288 A1 (STEWART) 11 September 2003 (11.09.2003) SEQ ID NO: 4.	68-72

☐ Further documents are listed in the continuation of Box C.

* 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

25 February 2009 (25.02.2009)

Date of mailing of the international search report

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 08/09288

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.: 39
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:
Claim 39 directed to the polypeptide of claim 33 selected from the group consisting of any of those identified as RG selective in the table of Figure 26B is unsearchable because the data in Figure 26B does not provide sufficient information to determine the chemical identity of the listed species.

3. ☒ Claims Nos.: 51-67 and 73-86
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 1-32 are directed to a method for determining whether a candidate compound is a long acting agonist of a G protein coupled receptor (GPCR), and a method for determining whether a candidate compound is a short acting agonist of a G protein coupled receptor (GPCR).

Group II+ claims 33-50 are directed to a polypeptide having affinity for PTH RG and a low affinity for PTH R.sup.o. The first named invention within Group II is restricted to those claims specific to SEQ ID NO: 4. An additional search fee is required for each additional sequence desired.

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 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.:
Group 1 claims 1-32, Group 2 claims 33-50 restricted to those claims specific to SEQ ID NO: 4 (namely claims 33, 34, 37, 39-50), and Group 3 claims 68-72 restricted to those claims specific to SEQ ID NO: 10.
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

International application No.

PCT/US 08/09288

Continuation of Box III

Group III+ claims 68-72 are directed to a polypeptide. The first named invention within Group III is restricted to those claims specific to SEQ ID NO: 10. An additional search fee is required for each additional sequence desired.

There is no special technical feature shared by the Groups and based on the unique amino acid sequences of the claimed inventions. The amino acid sequences represented by the unique sequences designated Group II+ and Group III+ do not relate to a single general inventive concept because, under PCT Rule 13.2, the different polypeptides represented by the amino acid sequences are not common to one another but are different because they are composed of unique amino acid sequences.