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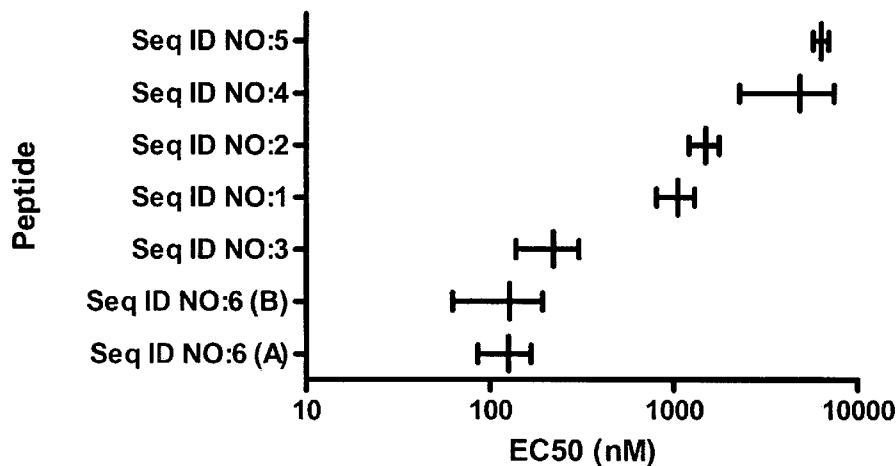
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(54) Title: METHODS AND COMPOSITIONS FOR THE TREATMENT OF HEART FAILURE AND OTHER DISORDERS

Figure 1. EC<sub>50</sub> of peptides in *in vitro* cGMP assay





(57) Abstract: Peptides that act as GC-C receptor agonists and contain at least one D-cys and are useful for the treatment of diuresis and heart disease as well as other disorders are described.

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## INTERNATIONAL SEARCH REPORT

International application No.  
**PCT/US2008/054972**

<b>A. CLASSIFICATION OF SUBJECT MATTER</b>		
<i>C07K 14/00(2006.01)i</i>		
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) IPC 8 C07K 14/00, C07K 7/08, A61K 39/395		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched N.A.		
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) eKIPASS, WPI, USPTO, PAJ, NCBI, CAPLUS(STN), INSPECT "heat-stable enterotoxin, Guanylyl Cyclase C receptor, GC-C receptor, CCELCCNPACTGC, non-natural analogue, isomer, D-enantiomer, atriuretic peptide, agonist, etc."		
<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X Y	WO 2005087797 A1 (MICROBIA INC., US) 22 Sep 2005 METHODS AND COMPOSITIONS FOR THE TREATMENT OF GASTROINTESTINAL DISORDERS - see abstract; p.1, lines 16~17; p.3, line 20 ~ p.9, line 10; p.9, lines 11 ~ 25; p.41, line 11; and p.56, lines 11 ~ 12	1 2-5, 23 & 24
X	J Med Chem. Vol.45(8):1731-1734. (Wolfe H.R., et al., US) 11 Apr 2002 "A comparative molecular field analysis (COMFA) of the structural determinants of heat-stable enterotoxins mediating activation of guanylyl cyclase C." - see the abstract; Figs. 1 ~ 3; and p.1732, the left col. the 2nd paragraph ~ p.1733, the left col. the 2nd paragraph	1-5, 23 & 24
Y	WO 2004071436 A2 (Thomas Jefferson Univ., US) 10 Feb 2004 "THE USE OF GCC LIGANDS" - see p.5, lines 11 ~ 16; p.13, line 26 ~p.14, line 8; and SEQ ID NO:29	1-5, 23 & 24
A	US 20040266989 A (Currie, M.G., et al., US) 30 Dec 2004 - see abstract; [0002]; [0012] ~ [0013]; and [0029]	1-5, 23 & 24
<input type="checkbox"/> Further documents are listed in the continuation of Box C. <input checked="" type="checkbox"/> 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 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 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 14 AUGUST 2008 (14.08.2008)		Date of mailing of the international search report <b>14 AUGUST 2008 (14.08.2008)</b>
Name and mailing address of the ISA/KR  Korean Intellectual Property Office Government Complex-Daejeon, 139 Seonsa-ro, Seo-gu, Daejeon 302-701, Republic of Korea Facsimile No. 82-42-472-7140		Authorized officer SHIN, Weon Hye Telephone No. 82-42-481-5591 

**INTERNATIONAL SEARCH REPORT**

International application No.

**PCT/US2008/054972****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.: 45-77  
because they relate to subject matter not required to be searched by this Authority, namely:  
Claims 45-77 are considered a therapeutic method to treat human body, which falls into the category of methods for treatment of the human body or animal body by surgery or therapy as well as diagnostic methods. [Article 17(2)(a)(i), Rule 39.1(iv) PCT]
2.  Claims Nos.: 19-21,42,79,80,82,83 & 30-40  
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:  
- see the extra sheet
3.  Claims Nos.: 6-18,22,25-29,41,43,44,78,81,84  
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 an additional fee, this Authority did not invite payment of any additional fee.
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/US2008/054972**

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2005087797 A1	22.09.2005	AU 2005-222387 A1	22.09.2005
		BR 200508558 A	07.08.2007
		CA 2558050 A1	22.09.2005
		EP 1730172 A1	13.12.2006
		JP 2008-501310	24.01.2008
		KR 2007007332 A	15.01.2007
		NO 20064121 A	22.11.2006
		US 2006-258593 AA	16.11.2006
WO 2004-071436 A2	26.08.2004	EP 1599165 A2	30.11.2005
		US 2004-258687 A1	23.12.2004
US 2004-0266989 A1	30.12.2004	US 2005-020811 AA	27.01.2005
		US 2006-258593 AA	16.11.2006
		US 2006-281682 A1	14.12.2006

Regarding Box No.II.2 :

1. Claims 19-21,42,79,80,82,83 are in reference to claims that are multiple dependent claims, which are not subjected to the meaningful search in accordance with the second and the third sentence of Rule 6.4(a). Meaningful search for the subject matter of claims 19-21,42,79,80,82,83 therefore requires undue burden: no meaningful search would be made. [Article 17(2)(a)(ii), Article 6 PCT]

2. Claim 30 is directed to the peptide of Figure 3a and 3b and is thus not considered clear and concise.

The subject matter of claims 31-40 is referred to SEQ ID NOs:1~5, respectively. Amino acid sequences corresponding to SEQ ID NOs:1~5, however, are not described anywhere in the application.

Claims 30-40 are thus considered so unclear and unsupported by the description that no meaningful search could be made [Article 17(2)(a)(ii), Article 6 PCT]

3. There is no segment in Box NO.II of the International Search Report to mark claims with regard to sequences. No meaningful search could be made for claims 30-40 for the following reason:

Present claims 30-40 are directed to subject matters related to amino acid sequences. The applicant however failed to furnish either sequence listing or sequence table but listed the sequences in Figures at the time of filing.

The applicant, within the prescribed time limit, did not furnish sequence listing in electronic form with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.

Because it is undue burden to the ISA to search for an invention relating to various numbers of peptides comprising amino acid sequence without the sequence listing in an electronic form with the standard. No meaningful search could be made for the present invention without the sequence listing.

\*\*\* Nonetheless, this ISA searched for an invention of one aa sequence (SEQ ID NO:7) only, in accordance with Rule 13<sup>ter</sup>.1(d).