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(54) Title: PEPTIDOMIMETIC MACROCYCLES

(57) Abstract: The present invention provides novel peptidomimetic macrocycles and methods of using such macrocycles for the treatment of disease.



INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 12/41181

A. CLASSIFICATION OF SUBJECT MATTER IPC(8) - A61K 38/12; C07K 5/00; A61K 38/00; C12P 21/04 USPC - 530/317 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 - 530/317 Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched USPC - 530/323; 435/71.1 (text search, terms below) Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) PatBase; PubWEST(PGPB,USPT,EPAB,JPAB); Google Scholar (text search, terms below) Search Terms: Macrocycl*, peptide, peptide-mimetic, peptidomimetic, chromosomal passenger complex, borealin, CDCA8, DasraB, treat*, cancer*, tumor*, neoplasm*, malignan*, survivin, INCENP, Aurora B, helic* or helix, a-heli*, alpha-heli*, crosslink*, link*, disubst		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2008/0262200 A1 (NASH) 23 October 2008 (23.10.2008); Abstract, Table 3, paras [0023], [0062], [0071], [0137], [0169]	1-9
Y	US 2010/0184047 A1 (NAKAMURA et al.) 22 July 2010 (22.07.2010); Abstract, paras [0279]-[0282]	1-9
Y	Jeyaprakash et al. Structure of a survivin-borealin-INCENP core complex reveals how chromosomal passengers travel together. Cell, 2007, vol 131, pp 271-285; Figures 3A and 3B, (page 274, col 1, para 4), (page 277, col 1, para 1 - col 2, para 2)	1-9
☐ 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 05 December 2012 (05.12.2012)		Date of mailing of the international search report 23 JAN 2013
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 12/41181

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.: 37-40
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 extra sheet for continuation -

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.:
1-9 restricted to SEQ ID NO: 1

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 12/41181

Continuation of:

Box NO 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.

Group I+: claims 1-9, drawn to a peptidomimetic macrocycle comprising an amino acid sequence which is at least about 60% identical to an amino acid sequence chosen from the group consisting of the amino acid sequences in Table 1, 2, 3, or 7a. The first invention is restricted to the first amino acid sequence in Table 1 Ac-LXSFLXDFDREVEIRIKQIES-NH₂. Should an additional fee(s) be paid, Applicant is invited to elect an additional amino acid sequence(e) to be searched. The exact claims searched will depend on Applicant's election.

[NOTE: Claim 36 is dependent on any of the preceding claims. However, there is no antecedent v+w in claims 1-9. Accordingly, claim 36 is revised to depend on any of the claims 10-35.]

Group II: claims 10-36, drawn to the peptidomimetic macrocycle, wherein the peptidomimetic macrocycle has the formula I.

The inventions listed as Groups I+ and II 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 of Group I+ do not include the inventive concept of the peptidomimetic macrocycle having formula I, as required by Group II.

The inventions of Groups I+ and II share the technical feature of a peptidomimetic macrocycle. However, this shared technical feature does not represent a contribution over prior art as being anticipated by US 2009/0047711 A1 (Nash). Nash discloses the peptidomimetic macrocycle, wherein the peptidomimetic macrocycle has the formula I, wherein each A, C, D, and E is independently a natural or non-natural amino acid; Bis a natural amino acid; R1 and R2 are independently -H; L is a macrocycle-forming linker of the formula -L1-L2-; L1 and L2 are independently [-R4-K-R4-]_n; each R4 is alkylene; each K is S; R7 is -H; R8 is -H; v and w are independently integers from 1-1000; u, x, y and z are independently integers from 0-10; and n is an integer from 1-5 (para [0093], Table 6, first example). As said composition was known in the art at the time of the invention, this cannot be considered a special technical feature that would otherwise unify the groups.

Another special technical feature of the inventions listed as Groups I+ is the specific amino acid sequences recited therein. The inventions do not share a special technical feature. This is because first, no significant structural similarities can readily be ascertained among different groups of amino acid sequences represented by, for example in Table 1 of instant specification, Ac-LXSFLXDFDREVEIRIKQIES-NH₂, Ac-VXIRIXQIESDRQNLLKEVDNL-NH₂, and Ac-VDXLYNXEILRLPKALREMNWL-NH₂. Second, the different cross-linked residues in the amino acid sequences within a group that share structural similarities, may confer different structural stability, affinity for a target, resistance to proteolytic degradation and cell penetrance and consequently, these amino acid sequences do not share a special technical feature. Without a shared special technical feature, the inventions lack unity with one another.

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