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Published:

- with international search report (Art. 21(3))
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))

(88) Date of publication of the international search report:
27 January 2011

(54) Title: COMPOUNDS AND METHODS FOR TREATING BONE DISORDERS AND CONTROLLING WEIGHT

(57) Abstract: The present invention provides peptides and methods of their use in treating bone disorders and bone-related conditions and in treating obesity.



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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 10/37390

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - C07K 7/00; A61F 2/28 (2010.01)

USPC - 530/300; 623/16.11

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- 530/300; 623/16.11

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)

PubWEST, Google Scholar

Search Terms: IGFBP, carrier, diluent, bulking agent, broken, defective, transplant, graft, cancer, joint replacement, fusion, facet repair, degeneration, dental implant, tooth, bone marrow deficit, intervertebral, fracture, chin, mouth, jaw, implant, resorption inhibition, bone format

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2004/0005579 A1 (Birse et al), 08 Jan. 2004 (08.01.2004), para [0030], [0303], [0206], [0311], SEQ ID NO 3356	1, 4-6, 8-11, 13-18, 20-26, 31 and 32
Y	WO 2009/019254 A1 (Tonshoff et al.), 12 Feb. 2009 (12.02.2009), pg 3, ln 11, 17,19-23, pg 4, ln 23; pg 14, ln 16-17; pg 16, ln 14-27, SEQ ID NO 3, claim 1, 18	1, 4-6, 8-11, 13-18, 20-26, 31 and 32,
Y	WO 2008/019491 A1 (Moreno et al), 21 Feb. 2008 (21.02.2008), pg 2, para 4	8
Y	Hoeflich et al., 'Growth Inhibition in Giant Growth Hormone Transgenic Mice by Overexpression of Insulin-Like Growth Factor-Binding Protein-2', Endocrinology, 2001, Vol. 142, No. 5, pages 1889-1898, abstract, Fig. 4	20-26
Y	Huynh et al, 'Insulin-Like Growth Facotr-Binding Protein 2 Secreted by a Tumorigenic Cell Line Supports Ex Vivo Expansion of Mouse Hematopoietic Stem Cells' Stem Cells, 2008 , Vol. 26, No. 6, pages 1628-1635 (pages 1-18)	31-32

☐ 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

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Date of mailing of the international search report

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INTERNATIONAL SEARCH REPORT

International application No.

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Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.c of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of a sequence listing filed or furnished:

a. (means)



on paper



in electronic form

b. (time)



in the international application as filed



together with the international application in electronic form



subsequently to this Authority for the purposes of search

2. ☐ In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

INTERNATIONAL SEARCH REPORT

International application No.

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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.: 7, 12, 19, 27-30, 33-35
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, 4-6, 8-11, 13-18, 20-26, 31 and 32, directed to a compound comprising a peptide having the amino acid sequence HLGLEEPKKLR or KHHLGLEEPKKLR, or an analog, prodrug or pharmaceutically acceptable salt thereof.

- 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.:
Claims 1, 4-6, 8-11, 13-18, 20-26, 31 and 32, directed to a compound comprising a peptide having the amino acid sequence HLGLEEPKKLR or KHHLGLEEPKKLR, or an analog, prodrug or pharmaceutically acceptable salt thereof.

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.

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Continuation of Box III: Lack of Unity of Invention

Group II: claims 2, 4-6, 8-11, 13-18, 20-26, 31 and 32, directed to a compound of Formula I:

X-Y-R1-R2-R3-R4-R5-R6-R7-R8-R9-R10-R11-R12-Y'-X';

wherein X is either present or absent, and when present is a capping group; a polyalkylene oxide, or a peptide consisting of from 2-10 amino acids of any type, optionally also comprising an n-terminal capping group or polyalkylene oxide;

Y is present or absent, and when present comprises a linking group;

R1, R2, R10, R11 and R13 are positively charged (at pH 6.0) amino acids;

R3-R9 and R12 are any amino acid;

Y' is present or absent, and when present is a linking group; and

X' is present or absent, and when present is a capping group; a polyalkylene oxide, or a peptide of from 2-10 amino acids optionally also comprising a c-terminal capping group or polyalkylene oxide;

limited to wherein, based on the first option (alphabetically) for each multi-option position in the sequence, the peptide comprises the following sequence:

Arg-Arg-Ala-Ala-Ala-Ala-Ala-Ala-Arg-Arg-Ala-Arg.

Group III: claims 2-6, 8-11, 13-18, 20-26, 31 and 32, directed to a peptide comprising Formula I as in Group II; limited to wherein, based on the first listed option (or, if no list is provided, alphabetically) for each multi-option position in claim 3, the peptide comprises the following sequence:

Lys-Lys-Arg-Ala-Gly-Ala-Glu-Glu-Pro-Lys-Lys-Ala-Lys. (Applicant may elect for additional sequences to be searched under Groups II or III by providing a SEQ ID NO: that corresponds to a fully defined sequence (no variable or optional amino acids in the sequence) and paying an additional invention fee for each SEQ ID NO.)

The inventions listed as Groups I - III 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 special technical feature of the Group I claims is a compound comprising a peptide having the amino acid sequence HLGLEPKKLR or KHHLGLEPKKLR, or an analog, prodrug or pharmaceutically acceptable salt thereof. The special technical feature of the claims of Groups II and III is a compound of Formula I, wherein each Group is directed to a different particular sequence.

The only common technical element shared by the above groups is that they are related to compounds comprising peptides, modified peptides or analogs that have a pattern of amino acids that corresponds to human IFGBP2 amino acids 171-183 (see Binkert et al.; Fig. 1). This common technical element is obvious over the prior art of US 2008/0286287 A1 to Russo et al. (see abstract, para [0019], [0024], [0028], [0033], [0062], [0063]), wherein the specific residues cited by Russo (179-184) comprise the c-terminus of SEQ ID NO: 1, or SEQ ID NO: 3, and wherein a person skilled in the art would have understood para [0062] as teaching peptides or analogs comprising at least said portion, and further comprising about 10 or more residues either n-terminal or c-terminal to said residues ("peptides, for example, of at least about 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40...contiguous amino acids which comprise an activity of a parent molecule"), thus encompassing the full sequence as in claim 1, as well as a peptide which comprises Formula I, wherein the n-terminal and c-terminal linking and capping groups were absent. Therefore, the inventions of Groups I-III lack unity of invention under PCT Rule 13 because they do not share a same or corresponding special technical feature.