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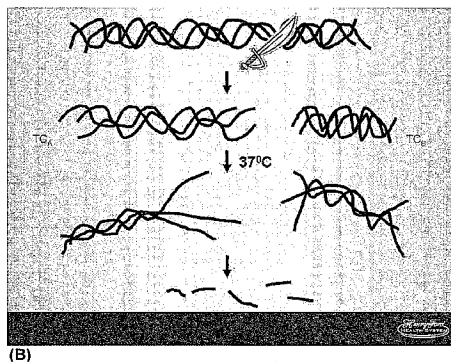
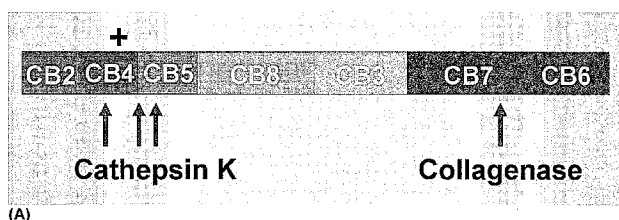
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- with international search report (Art. 21(3))
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))

[Continued on next page]

(54) Title: COLLAGEN-DERIVED PEPTIDE AS BIOMARKER, THERAPEUTIC AGENT AND TARGET



FIGURES 1(A)-(B)

(57) Abstract: Some embodiments comprise a novel peptide derived from Type 1 collagen which is a potent activator of ECM synthesis and remodeling and which may facilitate the detection and/or assessment of the presence of tumor cells, or other cells of interest, by detecting or assessing the presence of the peptide and/or its subfragments, and which may stimulate the production of proteases in a subject.



— *with sequence listing part of description (Rule 5.2(a))*

(88) Date of publication of the international search report:
30 December 2009

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 09/35876

A. CLASSIFICATION OF SUBJECT MATTER IPC(8) - G01N 33/53; A61K 38/00 (2009.01) USPC - 435/7.1; 530/325 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- 435/7.1; 530/325 Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched USPC- 435/7.92; 530/324 (text search) 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: type I collagen, HCOL1A1, cancer, tumor, neoplastic, 24-amino acid, deradation, MMP-1, MMP-3, marker, biomarker, hydroxyproline, hyp. GenCore6.3: SEQ ID NO: 1		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	HENKEL et al. Characterisation of a type-I collagen trimeric cross-linked peptide from calf aorta and its cross-linked structure. Detection of pyridinoline by time-of-flight secondary ion-mass spectroscopy and evidence for a new cross-link. Eur. J. Biochem. 1987, 165(2):427-436; pg 428, para 2; pg 430, para 2; Fig 3	1 ----- 2-4
X	US 2007/0299015 A1 (HARRIS et al.) 27 December 2007 (27.12.2007) para [0008], [0021], [0024]	5-6
Y	HONMA et al. Type I collagen gene suppresses tumor growth and invasion of malignant human glioma cells. Cancer Cell In. 2007, 7(12):1-9; abstract; pg 2, para 1; pg 3, para 6	2-4
Y	KYPRIOU et al. alpha 1 type I collagen preproprotein [Homo sapiens]. GenBank Accession No. NP_000079. 18 December 2007 [Retrieved from the Internet 02 November 2009: <http://www.ncbi.nlm.nih.gov/sviewer/viewer.fcgi?110349772:NCBI:19928605>]; amino acid residues 251-274	2-4
X	Kuboki, et al. Location of an intermolecular crosslink in bovine bone collagen. Connect Tissue Res. 1981;9(2):107-14; pg 112, Fig 4	1
A	SABEH et al. Tumor cell traffic through the extracellular matrix is controlled by the membrane-anchored collagenase MT1-MMP. J. Cell Biol. November 2004, 167(4):769-781	1-6
☒ 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 27 October 2009 (27.10.2009)		Date of mailing of the international search report 06 NOV 2009
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 09/35676

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:

- Group I: claims 1-6, drawn to a peptide of SEQ ID NO:1, and a method of using said peptide.
Group II: claims 7-12, drawn to a peptide of SEQ ID NO:2, and a method of using said peptide.
Group III: claims 13-18, drawn to a peptide of SEQ ID NO:3, and a method of using said peptide.
Group IV: claims 19-24, drawn to a peptide of SEQ ID NO:4, and a method of using said peptide.

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 special technical features for the following reasons:

The special technical feature of the inventions listed as Groups I-IV is the specific peptide recited therein. Although peptides of Groups I-IV share significant structural similarities, said similarities are not an improvement over prior art. Specifically, WO 2003/060145 A2 to Sun, et al. discloses a peptide comprising the claimed peptide of Group IV (Claim 12; SEQ ID NO 519, 251GARGLPGTAGLPGMKGHRGFSGLD 274). As the peptides of Groups I-IV do not share a novel significant structural element, the inventions of Groups I-IV do not share a special technical feature. Without a shared special technical feature, the inventions lack unity with one another.

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.:
Group I: claims 1-6

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 09/35876

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2003/0166033 A1 (EYRE) 4 September 2003 (04.09.2003)	1-6
A	US 6,107,047 A (FLEDELIUS et al.) 22 August 2000 (22.08.2000)	1-6
A	US 6,117,646 A (QVIST et al.) 12 September 2000 (12.09.2000)	1-6
A	WO 2003/060145 A2 (SUN et al.) 23 July 2003 (23.07.2003)	1-6
A	ARMSTRONG et al. Type I collagen promotes the malignant phenotype of pancreatic ductal adenocarcinoma. <i>Clin. Cancer Res.</i> November 2004, 10(21):7427-7437	1-6
A	MURAWAKI et al. Serum matrix metalloproteinase-3 (stromelysin-1) concentration in patients with chronic liver disease. <i>J. Hepatol.</i> September 1999, 31(3):474-481	1-6