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- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: METHOD FOR THE IN VITRO PRODUCTION OF CARTILAGE-LIKE TISSUE

(57) Abstract: A method for the in vitro production of cartilage-like tissue is disclosed. Said method comprises the cultivation of chondrogenic cells in presence of bivalent cation dependent constituents of the extracellular matrix (BCDM) and/or human serum wherein an inhibitory activity of cartilage maturation has been selectively removed from said human serum. The resulting cartilage-like tissue can be used for the repair of chondral and/or osteochondral defects in subjects or animals.



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INTERNATIONAL SEARCH REPORT

International Application No
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A. CLASSIFICATION OF SUBJECT MATTER
INV. C12N5/08 C12N5/06 A61L27/38

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)
C12N A61L

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 practical, search terms used)

EPO-Internal, BIOSIS, WPI Data, PAJ, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2001/012965 A1 (THOMAS EUGENE J-M A ET AL) 9 August 2001 (2001-08-09)	1,5-7, 11,13, 18-22, 26-28
Y	paragraphs [0001], [0023] - [0026], [0032] - [0036], [0041] - [0045], [0047] - [0053], [0062], [0096]; claims 1,19	1-12, 15-17
X	US 2001/014473 A1 (MULLER WERNER ET AL) 16 August 2001 (2001-08-16)	18-22, 26-28
Y	abstract paragraphs [0001], [0018], [0026], [0037], [0041], [0059], [0060], [0070] ----- -/-	12

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in 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 document 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

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Date of the actual completion of the international search

17 November 2004

Date of mailing of the international search report

26. 11. 2004

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/CH2004/000312

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	HAUSELMANN H J ET AL: "From chondrocyte culture to joint cartilage replacement: De novo cartilage synthesis in vitro" SCHWEIZERISCHE MEDIZINISCHE WOCHENSCHRIFT, vol. 128, no. 21, 23 May 1998 (1998-05-23), pages 824-832, XP008035307 ISSN: 0036-7672	18-22, 26-28
Y	abstract page 829, paragraph 1 - paragraph 2	15-17
X	HEDBOM E ET AL: "Culture of articular chondrocytes in alginate gel--a means to generate cartilage-like implantable tissue." OSTEOARTHRITIS AND CARTILAGE / OARS, OSTEOARTHRITIS RESEARCH SOCIETY, 2001, vol. 9 Suppl A, 2001, pages S123-S130, XP008035306 ISSN: 1063-4584	18-22, 26-28
Y	abstract page S125, column 2, last paragraph - page S126, column 1, paragraph 2 page S127, column 2, last paragraph - page S128	8
X	US 6 235 316 B1 (ADKISSON HUSTON D) 22 May 2001 (2001-05-22) column 1, line 8 - line 27 column 4, line 19 - line 22 column 12, line 65 - column 13, line 32	18-22, 26-28
Y	CAJU DU M V L ET AL: "ISOLATION OF SEVERAL FRACTIONS FROM HUMAN SERUM, INHIBITING RABBIT CARTILAGE METABOLISM IN VITRO" ACTA ENDOCRINOLOGICA, SCANDINAVIAN UNIVERSITY PRESS, OSLO, NO, vol. 122, no. 2, 1990, pages 277-282, XP008035362 ISSN: 0001-5598 page 277, column 1, paragraphs 1,2 page 279, column 1, last paragraph - page 280, column 2, paragraph 2 page 280, column 1, lines 5-18 page 281, column 2, paragraphs 4,5	1-12, 15-17
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INTERNATIONAL SEARCH REPORT

International Application No
PCT/CH2004/000312

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	TAMPONNET C ET AL: "RABBIT ARTICULAR CHONDROCYTES IN ALGINATE GEL CHARACTERISATION OF IMMOBILIZED PREPARATIONS AND POTENTIAL APPLICATIONS" APPLIED MICROBIOLOGY AND BIOTECHNOLOGY, vol. 37, no. 3, 1992, pages 311-315, XP008035359 ISSN: 0175-7598 abstract page 314, column 2, paragraph 4 - page 315, column 1 -----	
A	HAEUSELMANN H J ET AL: "ADULT HUMAN CHONDROCYTES CULTURED IN ALGINATE FORM A MATRIX SIMILAR TO NATIVE HUMAN ARTICULAR CARTILAGE" AMERICAN JOURNAL OF PHYSIOLOGY. CELL PHYSIOLOGY, AMERICAN PHYSIOLOGICAL SOCIETY, US, vol. 271, no. 3, September 1996 (1996-09), pages C742-C752, XP000882049 ISSN: 0363-6143 abstract page C743, column 1, last paragraph page C751, column 1, line 3 - line 9 -----	
A	VAN SUSANTE J L ET AL: "Responsiveness of bovine chondrocytes to growth factors in medium with different serum concentrations." JOURNAL OF ORTHOPAEDIC RESEARCH : OFFICIAL PUBLICATION OF THE ORTHOPAEDIC RESEARCH SOCIETY. JAN 2000, vol. 18, no. 1, January 2000 (2000-01), pages 68-77, XP008035352 ISSN: 0736-0266 abstract -----	5

INTERNATIONAL SEARCH REPORT

International application No.
PCT/CH2004/000312

Box 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:
Although claims 20-22 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
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 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:

see additional 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 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.
- ☒ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1,5-12,15-29(partially); 13-14 (completely)

Method for the production of a cartilage-like tissue in vitro comprising the step of cultivation of chondrogenic cells in the presence of at least bivalent cation dependent constituents of the extracellular matrix; Cartilage-like tissue obtained by this method; implant comprising said cartilage-like tissue; method of treatment using said cartilage-like tissue;method of joining siad cartilage-like tissue patches together.

2. claims: 1,5-12,15-29 (partially); 2-4 (completely)

Method for the production of a cartilage-like tissue in vitro comprising the step of cultivation of chondrogenic cells in the presence of at least human serum wherein an inhibitory activity of cartilage maturation has been selectively removed; Cartilage-like tissue obtained by this method; implant comprising said cartilage-like tissue; method of treatment using said cartilage-like tissue;method of joining siad cartilage-like tissue patches together.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/CH2004/000312

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
US 2001012965	A1	09-08-2001	AU 771467 B2	25-03-2004
			AU 3383900 A	21-09-2000
			CA 2362658 A1	08-09-2000
			EP 1158938 A1	05-12-2001
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			WO 0051527 A1	08-09-2000
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