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(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

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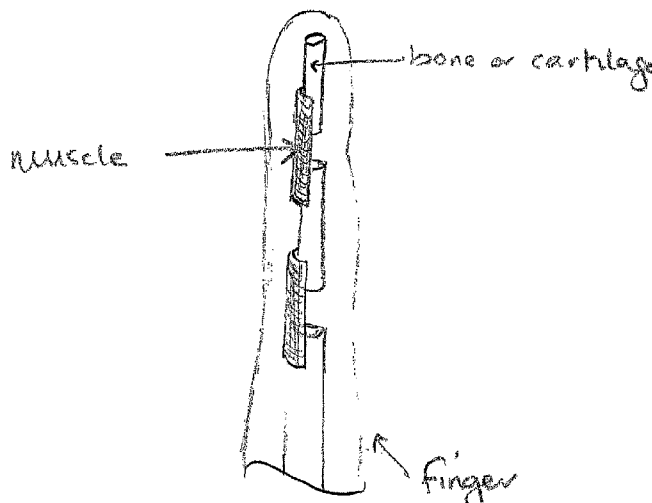
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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: PRODUCTION OF TISSUE ENGINEERED DIGITS AND LIMBS



(57) Abstract: The invention pertains to methods of producing artificial composite tissue constructs that permit coordinated motion. Biocompatible structural matrices having sufficient rigidity to provide structural support for cartilage-forming cells and bone-forming cells are used. Biocompatible flexible matrices seeded with muscle cells are joined to the structural matrices to produce artificial composite tissue constructs that are capable of coordinated motion.

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**INTERNATIONAL SEARCH REPORT**

International application No  
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<b>A. CLASSIFICATION OF SUBJECT MATTER</b>		
INV. A61L27/38	A61L27/36	A61L27/48
A61L27/56		
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) 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, WPI Data, PAJ, BIOSIS, EMBASE		
<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	WO 99/48541 A (UNIV PITTSBURGH [US]; UNIV CARNEGIE MELLON [US]) 30 September 1999 (1999-09-30) page 7, lines 4-37 page 9 - page 11 figure 8	1-15
A	US 2004/005297 A1 (CONNELLY PATRICK R [US] ET AL) 8 January 2004 (2004-01-08) page 2 - page 4 figure 1	
A	US 6 530 956 B1 (MANSMANN KEVIN A [US]) 11 March 2003 (2003-03-11) column 4 - column 5	
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<input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C. <span style="margin-left: 200px;"><input checked="" type="checkbox"/> See patent family annex.</span>		
* 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. *&* document member of the same patent family		
Date of the actual completion of the international search  14 February 2007		Date of mailing of the international search report  20/02/2007
Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016		Authorized officer  Quincy, Marie-France

INTERNATIONAL SEARCH REPORT

International application No  
PCT/US2006/008962

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>KLEBE R J: "CYTOSCRIBING: A METHOD FOR MICROPOSITIONING CELLS AND THE CONSTRUCTION OF TWO- AND THREE-DIMENSIONAL SYNTHETIC TISSUES" EXPERIMENTAL CELL RESEARCH, SAN DIEGO, CA, US, vol. 179, no. 2, 1988, pages 362-373, XP009007735 ISSN: 0014-4827 abstract</p>	
X	<p>EP 1 405 649 A (ETHICON INC [US]) 7 April 2004 (2004-04-07) page 2, paragraphs 1,8 page 3, line 26, paragraph 18 page 4, paragraphs 21-24,35 page 6, paragraph 44 page 8, paragraph 62</p>	16-31
X	<p>WO 2005/020849 A2 (MAYO FOUNDATION [US]; JABBARI ESMAIEL [US]; YASZEMSKI MICHAEL J [US];) 10 March 2005 (2005-03-10) page 1, paragraph 4 pages 3-4, paragraphs 10,11</p>	16
X	<p>WO 03/007790 A2 (DEPUY PRODUCTS INC [US]; MALAVIYA PRASANNA [US]; MELICAN MORA C [US];) 30 January 2003 (2003-01-30) page 8, line 15 - line 22 page 15, line 7 - line 10</p>	16-18

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US2006/008962

## 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 13-15 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: 1-15

Method of producing an artificial composite tissue construct comprising providing a first structural matrix with an isolated population of cells such as cartilage- or bone-forming cells; providing a second flexible matrix which is seeded with muscle progenitor cells; and joining both matrices together.

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2. claims: 16-31

Product and its method of production which is a composite scaffold for regenerated bone tissue fabricated by mixing a synthetic polymer with submucosa and whereby the porosity of the composite material is controlled via porogens.

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# INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2006/008962

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9948541	A	US 6143293 A	07-11-2000
US 2004005297	A1	NONE	
US 6530956	B1	NONE	
EP 1405649	A	AU 2003248414 A1 CA 2443070 A1 JP 2004267754 A US 2004062753 A1	22-04-2004 27-03-2004 30-09-2004 01-04-2004
WO 2005020849	A2	AU 2004268013 A1 CA 2535857 A1 EP 1664168 A2	10-03-2005 10-03-2005 07-06-2006
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