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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: PRESERVED VIABLE CARTILAGE, METHOD FOR ITS PRESERVATION, AND SYSTEM AND DEVICES USED THEREFOR

(57) Abstract: The present invention provides methods for providing cartilage-containing tissue for grafting, comprising providing excised cartilage-containing tissue; and treating said excised cartilage-containing and cryogenically preserving the treated cartilage-containing tissue under appropriate cryogenic preservation conditions so as to yield cryogenically preserved cartilage-containing tissue having at least 10% viable chondrocytes throughout the cartilage portion of the cartilage-containing tissue after preservation, as tested in a live/dead ratio assay. Treatment may comprise providing one or a plurality of incisions in said cartilage portion to a predetermined depth therein and/or introducing a cryoprotectant agent at least into said cartilage portion. The invention also provides viable cartilage obtainable by the methods of the invention, methods of grafting such preserved, viable cartilage containing tissue in a recipient, as well as apparatuses, vessels and systems for preparing a cartilage-containing tissue for cryogenic preservation and subsequent grafting in a recipient.

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INTERNATIONAL SEARCH REPORT

International application No
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A. CLASSIFICATION OF SUBJECT MATTER
INV. A01N1/02

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)
A01N

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X,Y	K.MULDREW ET AL: "Cryobiology of Articular Cartilage: Ice Morphology and ecovery of Chondrocytes" CRYOBIOLOGY, vol. 40, 2000, pages 102-109, XP002411853 cited in the application page 103, left-hand column, paragraph 2 - page 107, left-hand column, paragraph 2 -----	1-24, 34-37
X,Y	K.MULDREW ET AL.: "136. Chondrocyte sensitivity to Lethal Injury Correlates with Proximity to the Cartilage Surface" CRYOBIOLOGY, vol. 32, 1995, page 589, XP002411854 abstract ----- -/--	1-24, 34-37

Further documents are listed in the continuation of Box C.

See patent family 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.
- "&" document member of the same patent family

Date of the actual completion of the international search

15 December 2006

Date of mailing of the international search report

08. 03. 2007

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INTERNATIONAL SEARCH REPORT

International application No

PCT/IL2006/000231

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X,Y	K.MULDREW: "6. Cryopreservation of Articular Cartilage" CRYOBIOLOGY, vol. 33, 1996, pages 616-617, XP002411855 abstract -----	1-24, 34-37
Y	MULDREW K ET AL: "Localization of freezing injury in articular cartilage" CRYOBIOLOGY, ACADEMIC PRESS INC, US, vol. 31, 1994, pages 31-38, XP002313331 ISSN: 0011-2240 cited in the application page 32, right-hand column, paragraph 2 page 37, left-hand column, paragraph 1 page 37, right-hand column, paragraph 1 -----	1-24, 34-37
X	MULDREW K ET AL: "Transplantation of articular cartilage following a step-cooling cryopreservation protocol" CRYOBIOLOGY, ACADEMIC PRESS INC, US, vol. 1,2,1143, 2001, pages 260-267, XP002313330 ISSN: 0011-2240 cited in the application the whole document -----	1,3,11, 14,17
X	WO 91/06213 A (CRYOLIFE INC [US]) 16 May 1991 (1991-05-16) page 1, line 5 - line 13 page 2, line 5 - line 19 page 4, line 3 - line 32 page 7, line 5 page 7, line 19 - line 24 page 15 - page 19; example 2 page 18; table 2 -----	1,3,11, 14,15
X	CSÖNGE L ET AL: "Banking of osteochondral allografts, part II. Preservation of chondrocyte viability during long-term storage" CELL AND TISSUE BANKING, vol. 3, 2002, pages 161-168, XP002313332 ISSN: 1389-9333 abstract page 162, right-hand column, paragraph 3 page 163, left-hand column, paragraph 7 - right-hand column, paragraph 2 page 165, right-hand column, paragraph 3 -----	1,3,11, 14-16
X	N.M. JOMHA ET AL.: "Cryopreservation of intact human articular cartilage" JOURNAL OF ORTHOPADIC RESEARCH, vol. 20, 2002, pages 1253-1255, XP002411856 page 1254 -----	1,3,11, 14-16
4	----- -/--	

INTERNATIONAL SEARCH REPORT

International application No

PCT/IL2006/000231

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 6 740 484 B1 (KHIRABADI BIJAN S [US] ET AL) 25 May 2004 (2004-05-25) cited in the application figure 8 column 4, line 43 - line 63 column 5, line 40 page 16 - page 17; example 2 -----	1,3,11, 14
X	EP 0 664 080 A (SEITAI KAGAKU KENKYUSHO KK [JP]) 26 July 1995 (1995-07-26) page 3, line 27 - line 28 page 3, line 32 - line 33 page 5, line 1 - line 9 -----	18,19, 21,22
P,X	WO 2005/032251 A (I M T INTERFACE MULTIGRAD TECH [IL]; DAMARI UDI [IL]; LEVI HOLTZMAN RI) 14 April 2005 (2005-04-14) cited in the application page 5, line 18 - line 21 page 7, line 21 - page 13, line 4 page 25 - page 26 -----	1,3,11, 12,14-17

INTERNATIONAL SEARCH REPORT

International application No.
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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 claim 17 is 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 tissue.
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.:

1-24, 34-37

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: 1-24, 34-37

A method for providing viable cartilage-containing tissue, comprising: (a) providing excised cartilage-containing tissue; and (b) treating said excised cartilage-containing tissue as described in claims 1-10 and (c) cryogenically preserving the treated cartilage-containing tissue as described in claims 1-3;

- a method further comprising (d) thawing as described in claim 11,
- a method further comprising the provision and connection of a pulling member as described in claim 12;
- a method further comprising the introduction as described in claim 13;
- cartilage-containing tissue as described in claims 14-16;
- a method of grafting as described in claim 17;
- apparatus as described in claims 18-24;
- system as described in claims 34-37.

2. claims: 25-33

Vessel for containing a cartilage-containing tissue, comprising a substantially impermeable body having a first open end and a second open end at longitudinally opposite ends thereof and defining a containing volume; a first end plug and a second end plug for reversibly sealing said first open end and said second open end, respectively, as described in claims 25-33.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/IL2006/000231

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9106213	A	16-05-1991	AU 7740091 A 31-05-1991
			CA 2067203 A1 04-05-1991
			EP 0500788 A1 02-09-1992
			US 5131850 A 21-07-1992

US 6740484	B1	25-05-2004	AU 4230200 A 14-11-2000
			CA 2368884 A1 19-10-2000
			DE 60007304 D1 29-01-2004
			DE 60007304 T2 16-09-2004
			EP 1182926 A1 06-03-2002
			JP 2002541160 T 03-12-2002
			WO 0060935 A1 19-10-2000
			US 6194137 B1 27-02-2001

EP 0664080	A	26-07-1995	CA 2141012 A1 26-07-1995

WO 2005032251	A	14-04-2005	EP 1677594 A1 12-07-2006
