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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))

(88) Date of publication of the international search report:
9 September 2011

(54) Title: IMPROVED METHODS AND COMPOSITIONS FOR VEIN HARVEST AND AUTOGRAFTING

(57) Abstract: The leading cause of graft failure is the subsequent development of intimal hyperplasia, which represents a response to injury that is thought to involve smooth muscle proliferation, migration, phenotypic modulation, and extracellular matrix (ECM) deposition. Surgical techniques typically employed for vein harvest - stretching the vein, placing the vein in low pH, solutions, and the use of toxic surgical skin markers - are shown here to cause injury. The invention therefore provides for non-toxic surgical markers than also protect against stretch-induced loss of functional viability, along with other additives. Devices and compositions for reducing physical stress or protecting from the effects flowing therefrom, also are provided.



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INTERNATIONAL SEARCH REPORT

International application No

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A. CLASSIFICATION OF SUBJECT MATTER
 INV. A61K35/44 A61K31/185 A61M39/06
 ADD.

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)

A61K A61M

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, COMPENDEX, EMBASE, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	FULTON G J ET AL: "Preservation of the endothelium in venous bypass grafts: Relevance for graft patency gregory", THE ASIA PACIFIC HEART JOURNAL, ELSEVIER, vol. 6, no. 2, 1 September 1997 (1997-09-01), pages 98-106, XP004886201, ISSN: 1328-0163, DOI: DOI:10.1016/S1328-0163(97)90003-8	35-40
A	page 102 ----- -/--	1-34, 41-57



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

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Name and mailing address of the ISA/

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INTERNATIONAL SEARCH REPORT

International application No

PCT/US2010/059459

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	DRIES D ET AL: "The influence of harvesting technique on endothelial preservation in saphenous veins", JOURNAL OF SURGICAL RESEARCH, ACADEMIC PRESS INC., SAN DIEGO, CA, US, vol. 52, no. 3, 1 March 1992 (1992-03-01), pages 219-225, XP023022281, ISSN: 0022-4804 [retrieved on 1992-03-01] -----	1-34, 41-57
A	WO 2007/002139 A2 (UNIV PENNSYLVANIA [US]; LATIES ALAN [US]; MITCHELL CLAIRE [US]) 4 January 2007 (2007-01-04) -----	1-34, 41-54
A	CARIO-TOUMANIANTZ CHRYSTELLE ET AL: "P2X7 receptor activation-induced contraction and lysis in human saphenous vein smooth muscle", CIRCULATION RESEARCH, vol. 83, no. 2, 27 July 1998 (1998-07-27), pages 196-203, XP002635435, ISSN: 0009-7330 -----	1-34, 41-57
X	EP 1 281 357 A2 (UNIV DUKE [US]; MEDTRONIC INC [US]) 5 February 2003 (2003-02-05) paragraphs [0014], [0047]; figure 1 -----	35-40
X	WO 2007/070301 A2 (REGENERATION TECH INC [US]; SQUILLACE DONNA [US]; ALEXANDER ANTHONY [U]) 21 June 2007 (2007-06-21) paragraph [0230] -----	35,40
Y		36-39
Y	KARABULUT O ET AL: "The effects of various preparation techniques by means of cleaning solutions and applied pressures on the surface morphology of saphenous vein endothelial cells during coronary bypass surgery: A light and scanning electron microscopical study", SCANNING, vol. 21, no. 2, March 1999 (1999-03), pages 149-150, XP009150017, & PROCEEDINGS OF SCANNING 99; CHICAGO, ILLINOIS, USA; MARCH-APRIL 1999 ISSN: 0161-0457 page 150 -----	35-40

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2010/059459

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2007002139 A2	04-01-2007	US 2009220516 A1	03-09-2009
EP 1281357 A2	05-02-2003	NONE	
WO 2007070301 A2	21-06-2007	US 2007260109 A1	08-11-2007

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. claims: 1-34, 41-57

method of treating a vein explant by stabilizing the vein explant in a buffered solution comprising a P2X7 receptor antagonist, vein transplant kit comprising a tissue marking pen comprising a P2X7 receptor antagonist and a physiologic buffered solution and buffered solution comprising heparin and a P2X7 receptor antagonist

2. claims: 35-40

device for flushing the lumen of a vein explant designed to prevent flushing pressures greater than 200 mm Hg

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2010/059459

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:

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 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.:

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.