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- (81) **Designated States** (*unless otherwise indicated, for every kind of national protection available*): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP,

KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

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- (88) **Date of publication of the international search report:**
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(54) **Title:** BIOLOGICALLY ACTIVE GRAFT FOR SKIN REPLACEMENT THERAPY

(57) **Abstract:** The present invention relates to a biologically active graft (BAG) composition and methods for its preparation and use. More particularly, it details a method for preparing a non-immunogenic tissue graft composition comprising esophagus mucosa, basement membrane and tunica submucosa as intact natural sheet forms (Ad integrum), delaminated from the tunica muscularis and adventitia of an esophagus of a warm-blooded vertebrate. The composition is capable of serving as a substitute for skin autograft for skin replacement therapy and induces stromal cells regeneration when implanted in warm-blooded vertebrate including human subjects.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB2012/057150

A. CLASSIFICATION OF SUBJECT MATTER

C12N5/071 (2010.01)
A61K35/37 (2006.01)
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, A61K

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 practicable, search terms used)

EPODOC, WPI, TXTUS0, TXTUS1, TXTUS2, TXTUS3, TXTUS4, TXTUS5, TXTEP1, TXTGB1, TXTWO1, TXTAU1, TXTCA1, MEDLINE, BIOSIS, NPL, EMBASE, XPESP, XPESP2, Google.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	BHRANY AMIT D, <i>et al.</i> Development of an esophagus acellular matrix tissue scaffold. Tissue engineering. Feb 2006. VOL: 12 No: 2 Pags: 319 - 330 ISSN 1076-3279 (Print). see the whole document, especially Materials and Methods (first paragraph) and Discussion.	1-6
A	15/12/2006, OZEKI M <i>et al.</i> Evaluation of decellularized esophagus as a scaffold for cultured esophageal epithelial cells. Journal of Biomedical Materials Research - Part A 15/12/2006 VOL: 79 No: 4 Pags: 771 - 778 ISSN 0021-9304 (Print) ISSN 1552-4965 (Electronic) Doi: doi:10.1002/jbm.a.30885. see the whole document, especially Materials and Methods and Discussion	1-6

Further documents are listed in the continuation of Box C.

See patent family annex.

<p>* Special categories of cited documents:</p> <p>"A" document defining the general state of the art which is not considered to be of particular relevance.</p> <p>"E" earlier document but published on or after the international filing date</p> <p>"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)</p> <p>"O" document referring to an oral disclosure use, exhibition, or other means.</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p>	<p>"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</p> <p>"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</p> <p>"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 documents, such combination being obvious to a person skilled in the art</p> <p>"&" document member of the same patent family</p>
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Date of the actual completion of the international search
11/07/2013

Date of mailing of the international search report
(23/07/2013)

Name and mailing address of the ISA/

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/IB2012/057150

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.: **4, 5**
because they relate to subject matter not required to be searched by this Authority, namely:
Claims 4 and 5 concern subject matter which, in the opinion of this authority, falls under the provisions of PCT Rule 67.1(iv), relating to a method for treatment of the human or animal body by therapy. Nevertheless, a search was performed in respect of these claims, on the basis of the effects attributed to the claimed composition.
2. Claims Nos.: **6**
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:
Claim 6 is unclear (PCT Article 6) and does not contain technical features (PCT Rule 6.3). Nevertheless, a search was performed in respect of this claim, on the basis of the uses attributed to the composition.
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:

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.:

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/IB2012/057150

C (continuation).		DOCUMENTS CONSIDERED TO BE RELEVANT
Category *	Citation of documents, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 6893666 B2 (SPIEVACK ALAN R) 17/05/2005. See the whole document.	1-6
A	US 2010028396 A1 (WARD BRIAN RODERICK ET AL.) 04/02/2010. See the whole document, especially paragraphs [0004], [0005], [0065], [0093]; example 1; and claims 1 and 3.	1-6
A	BADYLAK S F <i>et al.</i> Extracellular matrix as a biological scaffold material: Structure and function. Acta Biomaterialia January 2009. VOL: 5, No: 1 Pags: 1 - 13 ISSN 1742-7061. Doi: doi:10.1016/j.actbio.2008.09.013. See the whole document.	1-6

INTERNATIONAL SEARCH REPORT

International application No.

Information on patent family members

PCT/IB2012/057150

Patent document cited in the search report	Publication date	Patent family member(s)	Publication date
US2003059405 A1	27.03.2003	US2012035276 A1	09.02.2012
		US2009053279 A1	26.02.2009
		AU2005200350 A1	24.02.2005
		AU2005200350B B2	15.03.2007
		JP2003252769 A	10.09.2003
		JP4942908B B2	30.05.2012
		US2003133916 A1	17.07.2003
		US2003064112 A1	03.04.2003
		US6890563 B2	10.05.2005
		US2003059411 A1	27.03.2003
		US6890562 B2	10.05.2005
		US2003064111 A1	03.04.2003
		US6849273 B2	01.02.2005
		US2003059410 A1	27.03.2003
		US6887495 B2	03.05.2005
		US2003059409 A1	27.03.2003
		US6852339 B2	08.02.2005
		US2003059407 A1	27.03.2003
		US6783776 B2	31.08.2004
		US2003059406 A1	27.03.2003
		US6869619 B2	22.03.2005
		US6893666 B2	17.05.2005
		US2003059404 A1	27.03.2003
		US6861074 B2	01.03.2005
		US2003054022 A1	20.03.2003
		US6890564 B2	10.05.2005
		WO0145765 A1	28.06.2001
		JP2003518078 A	03.06.2003
		JP3824537B B2	20.09.2006
		ES2322662T T3	24.06.2009
		ES2275147T T3	01.06.2007
		EP2055325 A2	06.05.2009
		EP1749543 A1	07.02.2007
		EP1749543 B1	18.02.2009
		EP1428540 A1	16.06.2004
		EP1428540 B1	18.10.2006
		EP1239897 A1	18.09.2002
		EP1239897 B1	24.03.2004
		DK1749543T T3	15.06.2009
		DK1428540T T3	19.02.2007
		DE60031461T T2	23.08.2007
		DE60009339T T2	19.08.2004
		CA2393468 A1	28.06.2001
CA2393468 C	20.03.2012		
AU2590601 A	03.07.2001		
AU777652B B2	28.10.2004		
AT422908T T	15.03.2009		
AT342742T T	15.11.2006		
AT262358T T	15.04.2004		
US6579538 B1	17.06.2003		

INTERNATIONAL SEARCH REPORT

International application No.

Information on patent family members

PCT/IB2012/057150

Patent document cited in the search report	Publication date	Patent family member(s)	Publication date
		US6576265 B1	10.06.2003
----- US5300306 A -----	----- 05.04.1994 -----	----- NONE -----	----- -----
US2010028396 A1	04.02.2010	US8415159 B2 WO2010014021 A1 JP2011529375 A EP2326336 A1 EP2326336 A4 CN102256609 A CA2731374 A1 AU2009277252 A1	09.04.2013 04.02.2010 08.12.2011 01.06.2011 22.08.2012 23.11.2011 04.02.2011 04.02.2010
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