

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
15 June 2000 (15.06.2000)

PCT

(10) International Publication Number
WO 00/34442 A3

- (51) International Patent Classification⁷: C12N 5/08, 5/06, 15/63, 5/22, 5/16, 11/16, C12M 3/00, C12N 11/02
- (21) International Application Number: PCT/US99/29257
- (22) International Filing Date: 10 December 1999 (10.12.1999)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data: 60/111,760 11 December 1998 (11.12.1998) US
- (71) Applicant: ADVANCE TISSUE SCIENCES, INC.
[US/US]: 10933 North Torrey Pines Road, La Jolla, CA 92037-1005 (US).
- (72) Inventors: LEE, Ann, A.; 680 Serra Street, Stanford, CA 94305 (US). ZELTINGER, Joan; 4136 Camino Ticino, San Diego, CA 92122 (US). KLADAKIS, Stephanie, M.; 1518 Lake View Lane, Atlanta, GA 30339 (US).
- (74) Agents: CORUZZI, Laura, A. et al.; Pennie & Edmonds LLP, 1155 Avenue of the Americas, New York, NY 10036 (US).
- (81) Designated States (*national*): AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW.
- (84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent

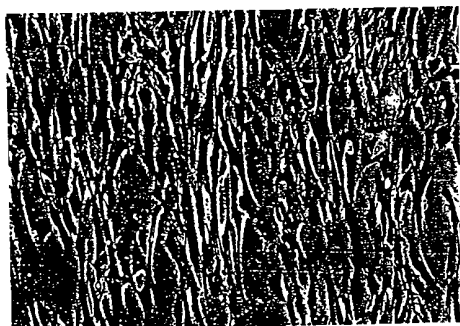
[Continued on next page]

(54) Title: APPLICATION OF SHEAR FLOW STRESS TO SMOOTH MUSCLE CELLS FOR THE PRODUCTION OF IMPLANTABLE STRUCTURES



A

(57) Abstract: The present invention relates to methods for the growth of smooth muscle cells in culture for the production of tissue-engineered grafts or other implantable replacement structures. More specifically, the invention relates to the application of shear flow stress to smooth muscle cells in culture, wherein the cells align perpendicular to the direction of flow, thus more closely approximating the orientation of the cells *in vivo*. The resulting cultures and methods are useful for the production of improved vascular grafts, vessels and other implantable structures for the correction of defects or abnormal tissues in the body.



B



WO 00/34442 A3



(AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

(88) Date of publication of the international search report:
1 November 2001

Published:

— with international search report

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.

INTERNATIONAL SEARCH REPORT

Int. Application No PCT/US 99/29257
--

A. CLASSIFICATION OF SUBJECT MATTER
 IPC 7 C12N5/08 C12N5/06 C12N15/63 C12N5/22 C12N5/16
 C12N11/16 C12M3/00 C12N11/02

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)
 IPC 7 C12N C12M

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	ZIEGLER, T. ET AL.: "Co-culture of endothelial cells and smooth muscle cells in a flow environment: an improved culture model of the vascular wall?" CELLS AND MATERIALS, vol. 5, no. 2, 1995, pages 115-124, XP000864797 cited in the application	1-3,25
Y	abstract page 117, column 1, line 16 -page 119, column 1, line 24 page 124, column 2, line 33 - line 35	21,29
Y	WO 95 25547 A (UNIVERSITY OF WASHINGTON) 28 September 1995 (1995-09-28) abstract page 3, line 27 -page 5, line 13 page 20; claim 1	21,29
	-/--	

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	"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
"E" earlier document but published on or after the international filing date	"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
"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)	"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.
"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search 27 July 2000	Date of mailing of the international search report 21/08/2000
---	--

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 Fuchs, U
--	------------------------------------

2

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 99/29257

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	LEE, A.A.: "Mechanisms of fluid shear stress-induced alignment in cultured vascular smooth muscle cells" FASEB JOURNAL, vol. 13, no. 5, 15 March 1999 (1999-03-15), page A1020 XP000929487 the whole document ---	1-3,8, 10,12,19
A	WO 97 49799 A (ADVANCED TISSUE SCIENCES) 31 December 1997 (1997-12-31) cited in the application the whole document ---	1-50
A	CUCINA, A. ET AL.: "Haemodynamic forces modulate simultaneously the release of growth factors and the organisation of cytoskeleton of aortic smooth muscle-cells" MINERVA CARDIOANGIOLOGICA, vol. 44, no. 12, December 1996 (1996-12), pages 637-643, XP000864786 the whole document ---	1-50
A	RESNICK, N. ET AL.: "Platelet-derived growth factor B chain promoter contains a cis-acting fluid shear-stress-responsive element" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, vol. 90, no. 10, 15 May 1993 (1993-05-15), pages 4591-4595, XP002075319 the whole document -----	21-24, 27-30, 33-36

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No PCT/US 99/29257
--

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9525547 A	28-09-1995	AU 2195095 A	09-10-1995
WO 9749799 A	31-12-1997	US 5792603 A AU 3581797 A CA 2261027 A EP 0927245 A	11-08-1998 14-01-1998 31-12-1997 07-07-1999