

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
13 June 2002 (13.06.2002)

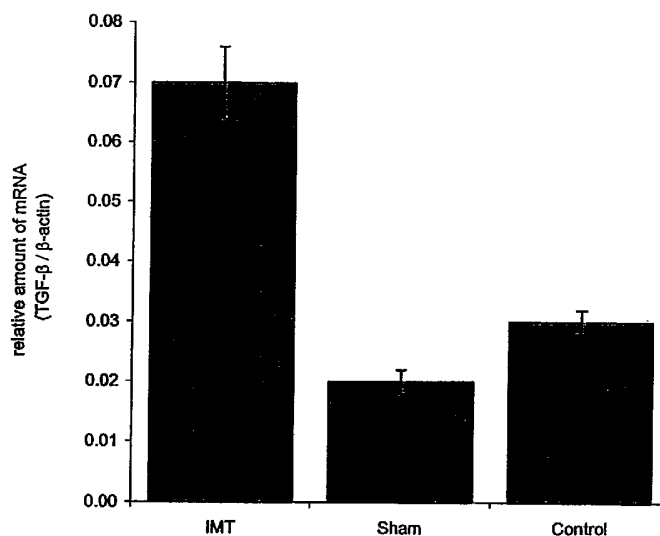
PCT

(10) International Publication Number
WO 02/045724 A3

- (51) International Patent Classification⁷: A61K 35/14, 41/00, C12N 5/06
- (74) Agent: HIRONS, Robert, G.; Ridout & Maybee LLP, 150 Metcalfe Street, 19th Floor, Ottawa, Ontario K2P 1P1 (CA).
- (21) International Application Number: PCT/CA01/01746
- (22) International Filing Date: 5 December 2001 (05.12.2001)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data: 2,327,630 5 December 2000 (05.12.2000) CA
- (71) Applicant (for all designated States except US): VASO-GEN IRELAND LIMITED [IE/IE]; Shannon Airport House, Shannon, County Clare (IE).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): BOLTON, Anthony, Ernest [GB/GB]; Ivy Cottage, Sherwood Road, Tideswell, Derbyshire SK17 8HS (GB). MANDEL, Arkady [CA/CA]; 277 Hidden Trail, North York, Ontario M2R 3S7 (CA). SAUDER, Daniel, Nathan [CA/US]; 212 Lambeth Road, Baltimore, MD 21210 (US).
- (81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, 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, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW.
- (84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (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, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).
- Published:
— with international search report
— before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

[Continued on next page]

(54) Title: USE OF MODIFIED MAMMALIAN BLOOD FOR TREATING TRANSFORMING GROWTH FACTOR RELATED DISEASES



(57) Abstract: A process of increasing the expression of TGF-β1 from cells in a mammalian patient, comprises administering to the patient an effective amount of stressed mammalian blood cells, said stressed cells having been extracorporeally subjected to at least one stressor selected from oxidative stress and ultraviolet radiation, to obtain a pharmaceutically useful composition. The composition shows potential in the treatment of ulcers in mammalian patients, to accelerate the healing thereof.



WO 02/045724 A3



(88) Date of publication of the international search report:
16 January 2003

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

International Application No

PCT/CA 01/01746

A. CLASSIFICATION OF SUBJECT MATTER
 IPC 7 A61K35/14 A61K41/00 C12N5/06

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 A61K C12N

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, CHEM ABS Data, EMBASE, MEDLINE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 00 67764 A (VASOGEN INC.) 16 November 2000 (2000-11-16) claims 1-19 page 14, line 27 -page 17, line 29	1-10
Y	A GÖRLACH ET AL: "Oxidative stress and expression of p22phox are involved in the up-regulation of tissue factor in vascular smooth muscle cells in response to activated platelets" THE FASEB JOURNAL, vol. 14, August 2000 (2000-08), pages 1518-1528, XP002218115 abstract	1-10

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
- *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

24 October 2002

Date of mailing of the international search report

15/11/2002

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

Siatou, E

INTERNATIONAL SEARCH REPORT

 International Application No
 PCT/CA 01/01746

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 00 41705 A (DESROSIER CHRISTINE ;CHENG HUIFANG (CA); HAMET PAVEL (CA); TREMBLA) 20 July 2000 (2000-07-20) claims 1-18 -----	1-10
Y	C. J. O'CALLAGHAN ET AL: "Mechanical Strain-Induced Matrix Production by Human Vascular Smooth Muscle Cells. Role of TGF-beta1" HYPERTENSION, vol. 36, September 2000 (2000-09), pages 319-324, XP002218116 abstract -----	1-10
A	US 5 980 954 A (A. E. BOLTON ET AL) 9 November 1999 (1999-11-09) claims 1-12 -----	1-10
A	US 5 834 030 A (BOLTON ANTHONY E) 10 November 1998 (1998-11-10) the whole document -----	1-10

INTERNATIONAL SEARCH REPORT

International application No.
PCT/CA 01/01746

Box I Observations where certain claims were found unsearchable (Continuation of item 1 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:
see FURTHER INFORMATION sheet PCT/ISA/210

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 II Observations where unity of invention is lacking (Continuation of item 2 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 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

Continuation of Box I.2

Present claims 1 and 8-10 (in part) relate to a use of stressed blood cells for a therapeutic application defined by reference to a desirable characteristic or property, namely inadequate expression of TGF-beta1. The claims cover all use having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such uses. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the use by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the use of stressed mammalian blood cells for the treatment of ulcers.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

In International Application No
PCT/CA 01/01746

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 0067764	A	16-11-2000	AU 4738500 A	21-11-2000
			WO 0067764 A2	16-11-2000
			EP 1181026 A2	27-02-2002
WO 0041705	A	20-07-2000	AU 3028000 A	01-08-2000
			WO 0041705 A1	20-07-2000
			EP 1146885 A1	24-10-2001
US 5980954	A	09-11-1999	US 5591457 A	07-01-1997
			AU 724265 B2	14-09-2000
			AU 3844297 A	06-03-1998
			WO 9807436 A1	26-02-1998
			EP 0920322 A1	09-06-1999
			JP 2000517302 T	26-12-2000
			NZ 334635 A	25-08-2000
			US 2002086064 A1	04-07-2002
			US 6204058 B1	20-03-2001
			AT 219953 T	15-07-2002
			AU 3506293 A	03-09-1993
			AU 681999 B2	18-09-1997
			AU 3506393 A	03-09-1993
			CA 2129630 A1	08-08-1993
			DE 69332087 D1	08-08-2002
			DE 69332087 T2	24-10-2002
			EP 1243278 A2	25-09-2002
			EP 0680346 A1	08-11-1995
			WO 9315778 A1	19-08-1993
			WO 9315779 A1	19-08-1993
JP 7503722 T	20-04-1995			
NZ 249176 A	26-11-1996			
US 5834030 A	10-11-1998			
US 5834030	A	10-11-1998	AT 219953 T-	15-07-2002
			AU 681999 B2	18-09-1997
			AU 3506393 A	03-09-1993
			CA 2129630 A1	08-08-1993
			DE 69332087 D1	08-08-2002
			DE 69332087 T2	24-10-2002
			EP 1243278 A2	25-09-2002
			EP 0680346 A1	08-11-1995
			WO 9315779 A1	19-08-1993
			JP 7503722 T	20-04-1995
			NZ 249176 A	26-11-1996
			AU 3506293 A	03-09-1993
			WO 9315778 A1	19-08-1993
			US 5591457 A	07-01-1997
			US 2002086064 A1	04-07-2002
			US 6204058 B1	20-03-2001
			US 5980954 A	09-11-1999