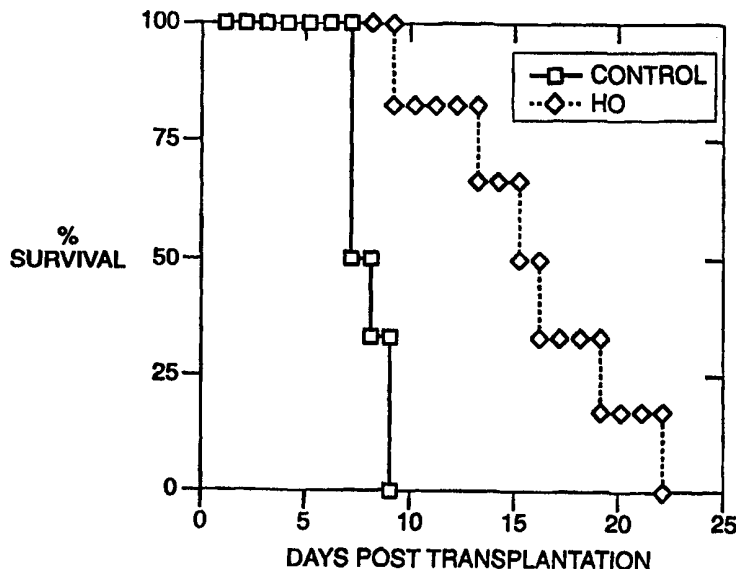




INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<p>(51) International Patent Classification ⁷ : C12N 15/53, 15/63, 15/85, 15/861, 15/87, 15/88, 9/02, A61K 48/00</p>	<p>A3</p>	<p>(11) International Publication Number: WO 00/36113 (43) International Publication Date: 22 June 2000 (22.06.00)</p>
<p>(21) International Application Number: PCT/US99/30089 (22) International Filing Date: 17 December 1999 (17.12.99) (30) Priority Data: 09/216,005 17 December 1998 (17.12.98) US (71) Applicant (for all designated States except US): SANGSTAT MEDICAL CORPORATION [US/US]; 6300 Dumbarton Circle, Fremont, CA 94555 (US). (72) Inventors; and (75) Inventors/Applicants (for US only): BUELOW, Roland [DE/US]; 2747 Ross Road, Palo Alto, CA 94303 (US). WOO, Jacky [GB/US]; Apartment 22, 620 Iris Avenue, Sunnyvale, CA 94303 (US). IYER, Suhasini [IN/US]; 1 Elmwood Drive, San Ramon, CA 94583 (US). (74) Agents: TRECARTIN, Richard, F. et al.; Flehr Hohbach Test Albritton & Herbert LLP, 4 Embarcadero Center, Suite 3400, San Francisco, CA 94111-4187 (US).</p>	<p>(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, 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, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, 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), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).</p> <p>Published <i>With international search report.</i></p> <p>(88) Date of publication of the international search report: 31 August 2000 (31.08.00)</p>	

(54) Title: EXTENDING GRAFT SURVIVAL BY HEME OXYGENASE-I EXPRESSION INDUCED IMMUNOMODULATION



(57) Abstract

Methods are provided wherein the survival of an organ transplant is enhanced by introducing into cells of the transplant a nucleic acid molecule that modulates heme oxygenase-I activity therein. Nucleic acid molecules that modulate heme oxygenase-I activity and therefore find use in the described methods include, for example, molecules that encode a polypeptide that itself exhibits heme oxygenase-I activity or antisense oligonucleotides that act to inhibit heme oxygenase-I activity in a cell.

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece			TR	Turkey
BG	Bulgaria	HU	Hungary	ML	Mali	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MN	Mongolia	UA	Ukraine
BR	Brazil	IL	Israel	MR	Mauritania	UG	Uganda
BY	Belarus	IS	Iceland	MW	Malawi	US	United States of America
CA	Canada	IT	Italy	MX	Mexico	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NE	Niger	VN	Viet Nam
CG	Congo	KE	Kenya	NL	Netherlands	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NO	Norway	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	NZ	New Zealand		
CM	Cameroon			PL	Poland		
CN	China	KR	Republic of Korea	PT	Portugal		
CU	Cuba	KZ	Kazakistan	RO	Romania		
CZ	Czech Republic	LC	Saint Lucia	RU	Russian Federation		
DE	Germany	LI	Liechtenstein	SD	Sudan		
DK	Denmark	LK	Sri Lanka	SE	Sweden		
EE	Estonia	LR	Liberia	SG	Singapore		

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 99/30089

A. CLASSIFICATION OF SUBJECT MATTER
 IPC 7 C12N15/53 C12N15/63 C12N15/85 C12N15/861 C12N15/87
 C12N15/88 C12N9/02 A61K48/00

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 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 practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	ABRAHAM, N.G. ET AL.: "Retinal pigment epithelial cell-based gene therapy against hemoglobin toxicity" INTERNATIONAL JOURNAL OF MOLECULAR MEDICINE, vol. 1, no. 4, April 1998 (1998-04), pages 657-663, XP000864607 abstract page 657, column 2, line 37 - line 42 page 658, column 1, line 6 - line 33 page 662, column 1, line 27 - line 34 --- -/--	23-25

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.
- *Z* document member of the same patent family

Date of the actual completion of the international search

26 May 2000

Date of mailing of the international search report

13/06/2000

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

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 99/30089

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	SOARES, M.P. ET AL.: "Expression of heme oxygenase-1 can determine cardiac xenograft survival" NATURE MEDICINE, vol. 4, no. 9, September 1998 (1998-09), pages 1073-1077, XP002131423	1-22
A	abstract page 1073, column 2, line 9 -page 1074, column 1, line 10 page 1073; table 1 page 1074, column 2, line 15 -page 1075, column 2, line 2 page 1075, column 2, line 39 -page 1076, column 1, line 4 page 1076, column 1, line 22 - line 30	23-25
Y	HANCOCK, W.W. ET AL.: "Antibody-induced transplant arteriosclerosis is prevented by graft expression of anti-oxidant and anti-apoptotic genes" NATURE MEDICINE, vol. 4, no. 12, 1 December 1998 (1998-12-01), pages 1392-1396, XP000907202	1-22
A	abstract page 1394, column 1, line 12 -column 2, line 2 page 1395; figures 4A,4B page 1395, column 2, line 3 -page 1396, column 1, line 24	23-25
Y	SQUIERS, E.C. ET AL.: "Prolongation of porcine islet xenograft survival in mice after therapy with immunosuppressive peptides" TRANSPLANTATION, vol. 66, no. 11, 15 December 1998 (1998-12-15), pages 1558-1565, XP000864600	1,5-12
	abstract page 1558, column 2, line 4 - line 19 page 1559, column 2, line 41 - line 49 page 1559; figure 1 page 1560; table 1 page 1560, column 2, line 26 -page 1561, column 1, line 12	
P,X	WO 99 23215 A (UNIVERSITY OF FLORIDA) 14 May 1999 (1999-05-14) abstract page 5, line 21 -page 6, line 1 page 9, line 10 - line 20 page 22; figure 4B claims 1-4,6,7,9,13	1-25

-/--

INTERNATIONAL SEARCH REPORT

Inter. Application No

PCT/US 99/30089

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	<p>AMERSI, F. ET AL.: "Upregulation of oxygenase-1 protects genetically fat Zucker rat livers from ischemia/perfusion injury" JOURNAL OF CLINICAL INVESTIGATION, vol. 104, no. 11, 1 December 1999 (1999-12-01), pages 1631-1639, XP002138430 abstract page 1632, column 1, line 26 - line 58 page 1635, column 2, line 4 -page 1636, column 1, line 5 page 1635; figures 5,6 page 1636, column 2, line 24 - line 34 page 1637, column 2, line 37 - line 43 page 1638, column 2, line 52 -page 1639, column 1, line 3</p>	1,2,6,7, 10,12, 13,17, 18,21, 24,25
P,X	<p>--- MAGEE, J.C. ETAL.: "Gene Transfer of Immunosuppressive Peptides B2702 and RDP1257 Prolongs Allograft Survival: Evidence Suggesting a Role for Heme Oxygenase-I" TRANSPLANTATION PROCEEDINGS, vol. 31, no. 1-2, February 1999 (1999-02), page 1194 XP000864594 the whole document</p>	1,5,7,8, 11,12
E	<p>--- WO 00 12118 A (PRESIDENT AND FELLOWS OF HARVARD COLLEGE) 9 March 2000 (2000-03-09) abstract page 22, line 20 -page 23, line 2 page 26, line 4 - line 29 SEQ ID NO: 1 page 45 -page 46 claims 6,7,10,11,13</p>	1-5,9, 10, 12-16, 20,21, 23-25
A	<p>--- WO 98 09618 A (SANGSTAT MEDICAL CORPORATION) 12 March 1998 (1998-03-12) the whole document</p>	1-25
A	<p>--- YOSHIDA, T. ET AL.: "Human heme oxygenase cDNA and induction of its mRNA by hemin" EUROPEAN JOURNAL OF BIOCHEMISTRY, vol. 171, no. 3, February 1988 (1988-02), pages 457-461, XP002100377 the whole document</p>	1-25

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 99/ 30089

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:

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.

INTERNATIONAL SEARCH REPORT

information on patent family members

International Application No

PCT/US 99/30089

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9923215 A	14-05-1999	AU 1374599 A	24-05-1999
WO 0012118 A	09-03-2000	NONE	
WO 9809618 A	12-03-1998	US 5756492 A	26-05-1998
		AU 4734497 A	26-03-1998
		CA 2234886 A	12-03-1998
		EP 0865275 A	23-09-1998
		JP 11507083 T	22-06-1999
		US 6060467 A	09-05-2000