WORLD INTELLECTUAL PROPERTY ORGANIZATION International Bureau



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁶ :		(11) International Publication Numbe	r: WO 97/44065
A61K 48/00	A3	(43) International Publication Date:	27 November 1997 (27.11.97)

PCT/US97/08463 (21) International Application Number:

(22) International Filing Date: 20 May 1997 (20.05.97)

(30) Priority Data: 08/650.726 20 May 1996 (20.05.96)

US

(71) Applicant: CYTOTHERAPEUTICS, INC. [US/US]; Two Richmond Square, Providence, RI 02906 (US).

(72) Inventors: HAMMANG, Joseph, P.; 3 Prospect Street, Barrington, RI 02806 (US). AEBISCHER, Patrick; Chemin de Plantaz 65, CH-1095 Lutry (CH).

(74) Agents: BALDWIN, Geraldine, F. et al.; Pennie & Edmonds LLP, 1155 Avenue of the Americas, New York, NY 10036 (US).

(81) Designated States: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GH, HU, IL, IS, JP, KG, KP, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, UZ, VN, YU, ARIPO patent (GH, KE, LS, MW, SD, SZ, UG), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).

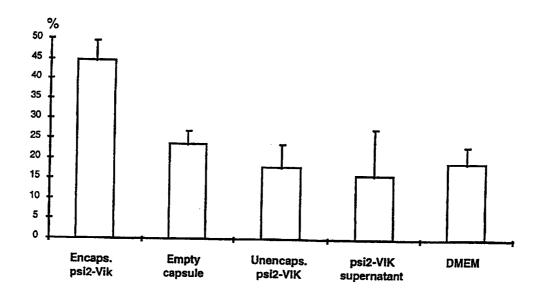
Published

With international search report.

Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(88) Date of publication of the international search report: 24 December 1997 (24.12.97)

(54) Title: DEVICE AND METHOD FOR ENCAPSULATED GENE THERAPY



(57) Abstract

Methods and devices are provided for gene therapy using encapsulated packaging cell lines to deliver viral particles carrying at least one heterologous gene encoding at least one biologically active molecule.

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
ΑZ	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	TM	Turkmenistan
BF	Burkina Faso	GR	Greece		Republic of Macedonia	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	NZ	New Zealand		
CM	Cameroon		Republic of Korea	PL	Poland		
CN	China	KR	Republic of Korea	PT	Portugal		
CU	Cuba	ΚZ	Kazakstan	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		

Interr nal Application No PCT/US 97/08463

A. CLASS	IFICATION OF SUBJECT MATTER A61K48/00		
According t	to International Patent Classification (IPC) or to both national clas	ssification and IPC	
B. FIELDS	SEARCHED		
Minimum d	ocumentation searched (classification system followed by classi A61K	fication symbols)	
11700	AOIK		
Documenta	ation searched other than minimum documentation to the extent t	hat such documents are included in the fields se	arched
Electronic	data base consulted during the international search (name of da	ta base and, where practical, search terms used)
0.000186	ENTS CONSIDERED TO BE RELEVANT		
Category °		e relevant passages	Relevant to claim No.
Category	Citation of document, was indication, where appropriate, or the		
х	WO 92 19195 A (UNIV BROWN RES	FOUND) 12	1-21
	November 1992 cited in the application		
	see page 4, line 5 - page 11,	line 24	
x	WO 95 05452 A (CYTOTHERAPEUTIC	רכ זאר	1-21
^	BAETGE E EDWARD (US); HAMMANG		
	(US);) 23 February 1995	1: 24	
	see page 12, line 2 - page 39	, line 34	
Α	WO 95 26411 A (UAB RESEARCH FO	OUNDATION) 5	
	October 1995		
	cited in the application see page 4, line 19 - page 5,	line 18	
		-/	
į		-/	
[V] E.	ther documents are listed in the continuation of box C.	Patent family members are listed	in annex.
		<u> </u>	
i '	ategories of cited documents :	"T" later document published after the inte or priority date and not in conflict with	the application but
consi	nent defining the general state of the art which is not idered to be of particular relevance	cited to understand the principle or the invention	
filing		"X" document of particular relevance; the cannot be considered novel or canno	t be considered to
which	ent which may throw doubts on priority claim(s) or his cited to establish the publication date of another	involve an inventive step when the do "Y" document of particular relevance; the	plaimed invention
"O" dooun	on or other special reason (as specified) nent referring to an oral disclosure, use, exhibition or	cannot be considered to involve an in document is combined with one or m ments, such combination being obvio	ore other such docu-
'P' docum	means nent published prior to the international filing date but than the priority date claimed	in the art. *&* document member of the same patent	
	a actual completion of the international search	Date of mailing of the international sea	
	15 October 1997	1 0 11 97	
		1 0, 11, 97	
Name and	mailing address of the ISA European Patent Office, P.B. 5818 Patentiaan 2	Administra attact	
	NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Sitch, W	

1

Intern all Application No
PCT/US 97/08463

Clontwation) DOCUMENT'S CONSIGERED TO BE RELEVANT Catagory* Citation of document, with indication, where appropriate, of the relevant passages A TAKAMIYA ET AL: "AN EXPERIMENTAL MODEL OF RETROVIRUS GENE THERAPY FOR MALIGNANT BRAIN TUMORS* JOURNAL OF NEUROSURGERY, vol. 79, no. 1, July 1993, pages 104-110, XP002043680 cited in the application see page 104 see abstract A DATABASE MEDLINE FILE SERVER STN KARLSRUHE ABSTRACT 97104002, AEBISCHER ET AL: "GENE THERAPY FOR AMYOTROPHIC LATERAL SCLEROSIS (ALS) USING A POLYMER ENCAPSULATED XENOGENIC CELL LINE ENGINEERED TO SECRETE HCNTF" XP002043681 see abstract & HUMAN GENE THERAPY, vol. 7, no. 7, 1 May 1996, pages 851-860,
A TAKAMIYA ET AL: "AN EXPERIMENTAL MODEL OF RETROVIRUS GENE THERAPY FOR MALIGNANT BRAIN TUMORS" JOURNAL OF NEUROSURGERY, vol. 79, no. 1, July 1993, pages 104-110, XP002043680 cited in the application see page 104 see abstract A DATABASE MEDLINE FILE SERVER STN KARLSRUHE ABSTRACT 97104002, AEBISCHER ET AL: "GENE THERAPY FOR AMYOTROPHIC LATERAL SCLEROSIS (ALS) USING A POLYMER ENCAPSULATED XENOGENIC CELL LINE ENGINEERED TO SECRETE HCNTF" XP002043681 see abstract & HUMAN GENE THERAPY, vol. 7, no. 7, 1 May 1996,
RETROVIRUS GENE THERAPY FOR MALIGNANT BRAIN TUMORS" JOURNAL OF NEUROSURGERY, vol. 79, no. 1, July 1993, pages 104-110, XP002043680 cited in the application see page 104 see abstract A DATABASE MEDLINE FILE SERVER STN KARLSRUHE ABSTRACT 97104002, AEBISCHER ET AL: "GENE THERAPY FOR AMYOTROPHIC LATERAL SCLEROSIS (ALS) USING A POLYMER ENCAPSULATED XENOGENIC CELL LINE ENGINEERED TO SECRETE HCNTF" XP002043681 see abstract & HUMAN GENE THERAPY, vol. 7, no. 7, 1 May 1996,
FILE SERVER STN KARLSRUHE ABSTRACT 97104002, AEBISCHER ET AL: "GENE THERAPY FOR AMYOTROPHIC LATERAL SCLEROSIS (ALS) USING A POLYMER ENCAPSULATED XENOGENIC CELL LINE ENGINEERED TO SECRETE HCNTF" XP002043681 see abstract & HUMAN GENE THERAPY, vol. 7, no. 7, 1 May 1996,

1

Int. ational application No. PCT/US 97/08463

Box I	Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)
This Inte	ernational Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
1. X	Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely: see FURTHER INFORMATION sheet PCT/ISA/210
2.	Ctaims 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 Int	ernational 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.:
Remar	K 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

Remark: Although claims 9-20 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Intermation on patent family members

Interne al Application No
PCT/US 97/08463

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9219195 A	12-11-92	AT 156344 T AU 666118 B AU 2004192 A AU 3902095 A DE 69221484 D EP 0585368 A JP 6507412 T NO 933842 A	15-08-97 01-02-96 21-12-92 01-02-96 11-09-97 09-03-94 25-08-94 25-10-93
WO 9505452 A	23-02-95	AU 7568094 A CA 2169292 A FI 960611 A NO 960547 A US 5639275 A US 5656481 A US 5653975 A	14-03-95 23-02-95 09-04-96 12-04-96 17-06-97 12-08-97 05-08-97
WO 9526411 A	05-10-95	AU 2194895 A	17-10-95