

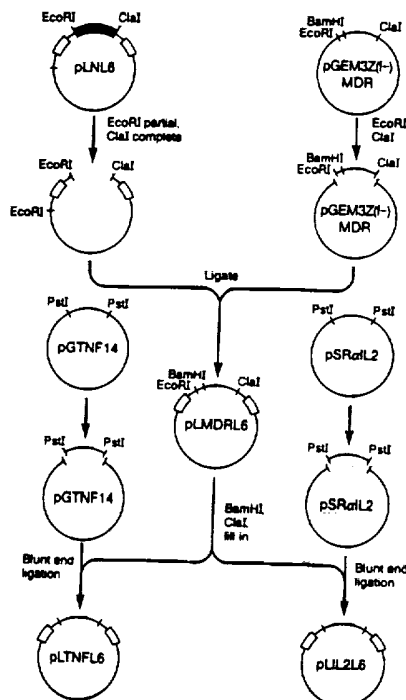


INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁵ : C12N 15/86, 15/48, A61K 37/02 C12N 15/62, 15/28, C07K 13/00 A61K 47/00, C12N 5/10	A3	(11) International Publication Number: WO 91/06658 (43) International Publication Date: 16 May 1991 (16.05.91)
(21) International Application Number: PCT/US90/06141 (22) International Filing Date: 23 October 1990 (23.10.90) (30) Priority data: 426,986 24 October 1989 (24.10.89) US 474,169 2 February 1990 (02.02.90) US 488,706 2 March 1990 (02.03.90) US (71) Applicant: CETUS CORPORATION [US/US]; 1400 Fifty-Third Street, Emeryville, CA 94608 (US). (72) Inventors: KRIEGLER, Michael ; 1424 Lake Street, San Francisco, CA 94118 (US). PEREZ, Carl, F. ; 2421 Val- ley Street, Berkeley, CA 94702 (US).		(74) Agent: GIOTTA, Gregory, J.; Cetus Corporation, 1400 Fifty-Third Street, Emeryville, CA 94608 (US). (81) Designated States: AT (European patent), AU, BE (Euro- pean patent), CA, CH (European patent), DE (Euro- pean patent), DK (European patent), ES (European pa- tent), FR (European patent), GB (European patent), GR (European patent), IT (European patent), JP, LU (Euro- pean patent), NL (European patent), SE (European pa- tent). Published <i>With international search report.</i> <i>Before the expiration of the time limit for amending the</i> <i>claims and to be republished in the event of the receipt of</i> <i>amendments.</i> (88) Date of publication of the international search report: 17 October 1991 (17.10.91)

(54) Title: INFECTIVE PROTEIN DELIVERY SYSTEM**(57) Abstract**

A virion expression system for a desired protein packaged in an envelope derived from a retrovirus useful in administering proteins which cross cell membranes in order to serve their function. Preferred virions are those that carry an RNA sequence that encodes cytokines or lymphokines, and includes IL-2, multiple drug resistance protein, and TNF.



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INTERNATIONAL SEARCH REPORT

International Application No PCT/US 90/06141

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all) *		
According to International Patent Classification (IPC) or to both National Classification and IPC		
IPC ⁵ : C 12 N 15/86, 15/48, A 61 K 37/02, C 12 N 15/62, 15/28, C 07 K 13/00, A 61 K 47/00, C 12 N 5/10		
II. FIELDS SEARCHED		
Minimum Documentation Searched *		
Classification System	Classification Symbols	
IPC ⁵	C 12 N, C 07 K	
Documentation Searched other than Minimum Documentation to the extent that such Documents are included in the Fields Searched *		
III. DOCUMENTS CONSIDERED TO BE RELEVANT³		
Category *	Citation of Document, ¹¹ with indication, where appropriate, of the relevant passages ¹²	Relevant to Claim No. ¹³
Y	Cell, vol. 53, 8 April 1988, Cell Press, Plc., M. Kriegler et al.: "A novel form of TNF/cachectin is a cell surface cytotoxic transmembrane protein: Ramifications for the complex physiology of TNF", pages 45-53 see page 51, column 2, lines 10-40	1-18,23-27
X	Journal of Virology, vol. 61, no. 5, May 1987, American Society for Microbiology, Plc., M.A. Bender et al.: "Evidence that the packaging signal of moloney murine leukemia virus extends into the gag region", pages 1639-1646 see the whole document, specially page 16040; figure 1 and construction cited in the application	1,3,6,8,9, 10,11,12
Y		1-18,28,30, 31
-./.		
<div style="display: flex; justify-content: space-between;"> <div style="width: 45%;"> <p>* Special categories of cited documents: ¹⁰</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> </div> <div style="width: 50%;"> <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</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 such documents, such combination being obvious to a person skilled in the art.</p> <p>"&" document member of the same patent family</p> </div> </div>		
IV. CERTIFICATION		
Date of the Actual Completion of the International Search	Date of Mailing of this International Search Report	
2nd August 1991	11 SEP 1991	
International Searching Authority	Signature of Authorized Officer	
EUROPEAN PATENT OFFICE	MISS T. TAZELAAR	

III. DOCUMENTS CONSIDERED TO BE RELEVANT (CONTINUED FROM THE SECOND SHEET)		
Category *	Citation of Document, " with indication, where appropriate, of the relevant passages	Relevant to Claim No.
Y	EP, A, 0243204 (CETUS CORP.) 28 October 1987 see the whole document --	1-18, 28, 30, 31
Y	EP, A, 0334301 (VIAGENE) 27 September 1989 see the whole document --	1, 6, 8, 9, 10, 11, 12, 14, 18, 28
Y	EP, A, 0317649 (TEIJIN LTD) 31 May 1989 see the whole document --	23-27
P,X	UCLA Symp. Mol. Cell. Biol., New Ser., vol. 103, 1989, Alan R. Liss, Inc., (New York, US), M. Kriegler et al.: "Two forms of tumor necrosis factor/cachectin and their roles in local and systemic inflammatory responses", pages 203-222 see the whole article --	1-34
P,X	Cell, vol. 63, no. 2, 19 October 1990, (Cambridge, MA, US), C. Perez et al.: "A nonsecretable cell surface mutant of tumor necrosis factor (TNF) kills by cell-to-cell contact", pages 251-258 see the whole article --	1-34, 42-47, 51-56
Y	Science, vol. 243, 3 March 1989, L.L. Randall et al.: "Unity in function in the absence of consensus in sequence: Role of leader peptides in export", pages 1156-1159 see the whole article --	23-27, 42-47, 51-56
Y	Nucleic Acids Research, vol. 14, no. 11, 1986, IRL Press Ltd, (Oxford, GB), G. Von Heijne: "A new method for predicting signal sequence cleavage sites", pages 4683-4691 see the whole article --	23-27, 42-47, 51-56
Y	Nucleic Acids Research, vol. 12, no. 13, July 1984, IRL Press Ltd, (Oxford, GB), M.E.E. Watson: "Compilation of published signal sequences", pages 5145-5164 see the whole article --	23-27
Y	EP, A, 0196864 (CETUS COPP.) 8 October 1986 see the whole document -----	23-27

FURTHER INFORMATION CONTINUED FROM THE SECOND SHEET

V. ☒ OBSERVATION WHERE CERTAIN CLAIMS WERE FOUND UNSEARCHABLE ¹

This International search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claim numbers * because they relate to subject matter not required to be searched by this Authority, namely:

* Claims searched incompletely: 12,13,54-56

Claims not searched 35-41 and 48,50

See PCT-Rule 39.1 (iv): methods for treatment of the human or animal body by surgery or therapy as well as diagnostic methods

2. ☐ Claim numbers 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. ☐ Claim numbers because they are dependent claims and are not drafted in accordance with the second and third sentences of PCT Rule 6.4(a)

VI. ☒ OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING ²

This International Searching Authority found multiple inventions in this International application as follows:

Please see form PCT/ISA/206 sent to you on 9th April 1991

1. ☒ As all required additional search fees were timely paid by the applicant, this International search report covers all searchable claims of the International application
2. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims of the International application for which fees were paid, specifically claims:
3. ☐ 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 claim numbers:
4. ☐ As all searchable claims could be searched without effort justifying an additional fee, the International Searching Authority did not invite payment of any additional fee

Remark on Protest

- ☐ The additional search fees were accompanied by applicant's protest.
- ☒ No protest accompanied the payment of additional search fees

ANNEX TO THE INTERNATIONAL SEARCH REPORT ON INTERNATIONAL PATENT APPLICATION NO.

US 9006141
SA 42502

This annex lists the patent family members relating to the patent documents cited in the above-mentioned international search report. The members are as contained in the European Patent Office EDP file on 03/09/91
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP-A- 0243204	28-10-87	JP-A- 63157985	30-06-88
EP-A- 0334301	27-09-89	AU-A- 3364089	16-10-89
		GB-A- 2236753	17-04-91
		WO-A- 8909271	05-10-89
EP-A- 0317649	31-05-89	JP-A- 63258583	26-10-88
		WO-A- 8810302	29-12-88
EP-A- 0196864	08-10-86	JP-A- 62055087	10-03-87