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(54) **Title:** PURIFICATION PROCESSES FOR ISOLATING PURIFIED VESICULAR STOMATITIS VIRUS FROM CELL CULTURE

(57) **Abstract:** Novel purification processes for obtaining vesicular stomatitis virus (VSV) of improved purity from mammalian cell culture are described herein. More particularly, in certain embodiments, a process is described for purifying VSV from cell culture fluid of a mammalian cell culture infected with VSV, the process comprising: clarifying the cell culture fluid by low-speed centrifugation and recovering the VSV in the supernatant; filtering the supernatant through a 0.2 to 0.45 μm filter and recovering the VSV in the filtered solution; loading the VSV filtered solution onto an anion exchange membrane adsorber equilibrated with a first pH buffered salt solution, eluting the VSV from the anion exchange membrane adsorber with a second pH buffered salt solution and recovering the eluted VSV fractions; purifying the recovered VSV by tangential flow filtration (TFF) using a TFF membrane having a molecular weight cutoff between 300 kDa and 1,000 kDa and recovering the VSV in the retentate, and filtering the VSV retentate through a 0.2 to 0.22 μm filter and recovering the VSV in the filtered solution.

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A. CLASSIFICATION OF SUBJECT MATTER INV. C12N7/02 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) 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, BIOSIS, EMBASE, WPI Data		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	BURKHART CHRISTOPH ET AL: "Characterization of T-helper epitopes of the glycoprotein of vesicular stomatitis virus" JOURNAL OF VIROLOGY, vol. 68, no. 3, 1994, pages 1573-1580, XP002462510 ISSN: 0022-538X	15-18
Y	the whole document ----- -/--	1-14
<input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C. <input checked="" type="checkbox"/> See patent family 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. *G* document member of the same patent family		
Date of the actual completion of the international search		Date of mailing of the international search report
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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 Morawetz, Renate

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International application No
PCT/US2007/009510

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	HECHT T T ET AL: "LIMITATION OF VESICULAR STOMATITIS VIRUS INFECTION BY THE HOST RESPONSE TO VESICULAR STOMATITIS VIRUS ASSOCIATED CELLULAR ANTIGENS" JOURNAL OF IMMUNOLOGY, vol. 129, no. 4, 1982, pages 1736-1741, XP002462511 ISSN: 0022-1767	15-18
Y	the whole document	1-14
X	WO 2005/098009 A (WYETH CORP [US]; CLARKE DAVID KIRKWOOD [US]; HENDRY ROGER MICHAEL [US]) 20 October 2005 (2005-10-20)	15-18
Y	the whole document	1-14
X	US 6 168 943 B1 (ROSE JOHN K [US]) 2 January 2001 (2001-01-02)	15-18
Y	the whole document	1-14
Y	SCHERR M ET AL: "Efficient gene transfer into the CNS by lentiviral vectors purified by anion exchange chromatography." GENE THERAPY, vol. 9, no. 24, December 2002 (2002-12), pages 1708-1714, XP002462512 ISSN: 0969-7128	1-14
Y	the whole document	1-14
Y	YAMADA KAORU ET AL: "LENTIVIRUS VECTOR PURIFICATION USING ANION EXCHANGE HPLC LEADS TO IMPROVED GENE TRANSFER" BIOTECHNIQUES, INFORMA LIFE SCIENCES PUBLISHING, WESTBOROUGH, MA, US, vol. 34, no. 5, May 2003 (2003-05), pages 1074-1080, XP001537620 ISSN: 0736-6205	1-14
Y	the whole document	1-14
Y	MORENWEISER R: "Downstream processing of viral vectors and vaccines" GENE THERAPY, vol. 12, no. Suppl. 1, October 2005 (2005-10), pages S103-S110, XP002462513 ISSN: 0969-7128	1-14
	the whole document	
	----- -/--	

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2007/009510

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>DE LAS MERCEDES SEGURA ET AL: "Downstream processing of oncoretroviral and lentiviral gene therapy vectors" BIOTECHNOLOGY ADVANCES, ELSEVIER PUBLISHING, BARKING, GB, vol. 24, no. 3, 30 January 2006 (2006-01-30), pages 321-337, XP005362294 ISSN: 0734-9750 the whole document</p> <p style="text-align: center;">-----</p>	1-14
A	<p>WO 03/093463 A (ONCOLYTICS BIOTECH INC [CA]; COFFEY MATTHEW C [CA]) 13 November 2003 (2003-11-13) the whole document</p> <p style="text-align: center;">-----</p>	

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2007/009510

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 2005098009	A	20-10-2005	AR 048596 A1	10-05-2006
			AU 2005230687 A1	20-10-2005
			BR PI0509683 A	30-10-2007
			CA 2561245 A1	20-10-2005
			EP 1756287 A2	28-02-2007
			KR 20070004822 A	09-01-2007

US 6168943	B1	02-01-2001	AU 714616 B2	06-01-2000
			AU 5634596 A	21-11-1996
			CA 2220133 A1	07-11-1996
			EP 0871482 A1	21-10-1998
			WO 9634625 A1	07-11-1996
			US 7153510 B1	26-12-2006
			US 2005238656 A1	27-10-2005

WO 03093463	A	13-11-2003	AU 2003229159 A1	17-11-2003
			BR 0309659 A	22-02-2005
			CA 2482512 A1	13-11-2003
			EP 1501921 A1	02-02-2005
			JP 2005523722 T	11-08-2005
			MX PA04010603 A	13-12-2004
			NZ 535944 A	30-11-2007
