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(54) Title: ASSAY TO DETECT REPLICATION COMPETENT VIRUSES

(57) Abstract: A biological assay for detecting a non-selective replication competent virus (RCV) in a preparation of selectively-replicating virus. The method comprises -passaging the virus preparation at least once on cells that differentially amplify the selectively-replicating virus versus a replication competent virus and further analyzing the virus preparation, thereby detecting the presence of a replication competent virus. The further analysis of the virus preparation includes one or more of the following: detecting increased cytopathic effect; detecting increased virus production; detecting increased potency to kill normal cells; detecting an altered restriction digest pattern; detecting an altered viral genome sequence; detecting anticipated recombinants with PCR amplification; and detecting acute hepatotoxicity in an animal administered the virus preparation. In one embodiment, the assay detects replication competent adenoviruses in a preparation of an oncolytic adenovirus.



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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/18243

A. CLASSIFICATION OF SUBJECT MATTER														
IPC(7) : C12Q 1/68, 1/70, 1/04, 1/02, 1/06; C12N 15/861, 15/63, 5/10, 15/64, 7/01, 7/02														
US CL : 435/320.1, 5, 6, 325, 366, 235.1, 236, 239, 371														
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) U.S. : 435/320.1, 5, 6, 325, 366, 235.1, 236, 239, 371														
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 practicable, search terms used) Please See Continuation Sheet														
C. DOCUMENTS CONSIDERED TO BE RELEVANT														
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.												
A	US 6,248,514 B1 (HUTCHINS et al.) 19 June 2001 (19.06.2001), columns 2-3, column 15.	1-29												
A	US 6,265,212 B1 (FALLAUX et al.) 24 July 2001 (24.07.2001), column 18, lines 7-37.	1-29												
A	LOCHMULLER et al. Emergence of Early Region 1-Containing Replication-Competent Adenovirus in Stocks of Replication-Defective Adenovirus Recombinants (deltaE1 + deltaE3) During Multiple Passages in 293 Cells. December 1994, Vol. 5, pages 1485-1491, especially 1487-1488.	1-29												
A	DION et al. Supernatant Rescue Assay vs. Polymerase Chain Reaction for Detection of Wild Type Adenovirus-Contaminating Recombinant Adenovirus Stocks. 1996, Vol. 56, pages 99-107, especially pages 105-106.	1-29												
☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.														
<table border="0"> <tr> <td>* Special categories of cited documents:</td> <td>"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</td> </tr> <tr> <td>"A" document defining the general state of the art which is not considered to be of particular relevance</td> <td>"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</td> </tr> <tr> <td>"E" earlier application or patent published on or after the international filing date</td> <td>"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</td> </tr> <tr> <td>"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)</td> <td>"&" document member of the same patent family</td> </tr> <tr> <td>"O" document referring to an oral disclosure, use, exhibition or other means</td> <td></td> </tr> <tr> <td>"P" document published prior to the international filing date but later than the priority date claimed</td> <td></td> </tr> </table>			* Special categories of cited documents:	"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	"A" document defining the general state of the art which is not considered to be of particular relevance	"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	"E" earlier application or patent published on or after the international filing date	"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	"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)	"&" document member of the same patent family	"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	
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Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703)305-3230		Authorized officer - <i>David Guzo</i> Telephone No. (703) 308-0196												

INTERNATIONAL SEARCH REPORT

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Continuation of B. FIELDS SEARCHED Item 3:

WEST, Dialog, Medline, Biotech, Biosci, Biosis

Search terms: replication competent, screen, adenovirus, selectively replicating, RCV, RCA, MRC5, tissue specific, E1, E2, E4