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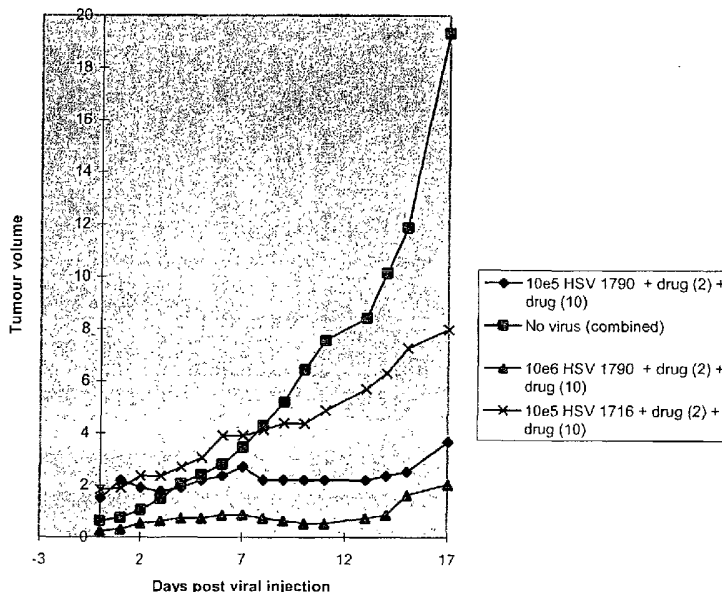
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[Continued on next page]

(54) Title: ONCOLYTIC HERPES SIMPLEX VIRUS ENCODING A HETEROLOGOUS NITROREDUCTASE



(57) Abstract: An herpes simplex virus wherein the herpes simplex virus genome comprises nucleic acid encoding a nitroreductase (NTR) is disclosed. Disclosed herpes simplex viruses are indicated to be useful in the treatment of cancer which may involve gene directed enzyme produg therapy.

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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

INTERNATIONAL SEARCH REPORT

PCT/GB2004/004851

A. CLASSIFICATION OF SUBJECT MATTER IPC 7 C12N15/869 A61K35/76 C12N7/01 C12N9/02 A61K38/44 A61K31/395				
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) EPO-Internal, BIOSIS, EMBASE, WPI Data, Sequence Search				
C. DOCUMENTS CONSIDERED TO BE RELEVANT				
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.		
Y	WO 99/55345 A (GEN HOSPITAL CORP) 4 November 1999 (1999-11-04) page 28, lines 19-22; claims 1-51 -----	1-57		
Y	VARGHESE SUSAN ET AL: "Oncolytic herpes simplex virus vectors for cancer virotherapy." CANCER GENE THERAPY, vol. 9, no. 12, December 2002 (2002-12), pages 967-978, XP002313119 ISSN: 0929-1903 page 970, right-hand column, paragraph 1 ----- -/--	1-57		
<input checked="" type="checkbox"/> Further documents are listed in the continuation of box C. <input checked="" type="checkbox"/> Patent family members are listed in annex.				
* Special categories of cited documents :				
<table style="width: 100%; border: none;"> <tr> <td style="width: 50%; border: none; vertical-align: top;"> *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 </td> <td style="width: 50%; border: none; vertical-align: top;"> *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. *&* document member of the same patent family </td> </tr> </table>			*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. *&* document member of the same patent family
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. *&* document member of the same patent family			
Date of the actual completion of the international search <p style="text-align: center;">18 July 2005</p>	Date of mailing of the international search report <p style="text-align: center;">03/08/2005</p>			
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 <p style="text-align: center;">Huber, A</p>			

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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>WO 03/018788 A (GROVE JANE ISABEL ; LOVERING ANDREW LEE (GB); ML LAB PLC (GB); SEARLE) 6 March 2003 (2003-03-06) page 15, lines 12-18; claims 8,39,45 page 5, lines 21,22 page 13, lines 18,19</p> <p>-----</p>	1-57
Y	<p>WEEDON S J ET AL: "SENSITISATION OF HUMAN CARCINOMA CELLS TO THE PRODRUG CB1954 BY ADENOVIRUS VECTOR-MEDIATED EXPRESSION OF E. COLI NITROREDUCTASE" INTERNATIONAL JOURNAL OF CANCER, NEW YORK, NY, US, vol. 86, no. 6, 15 June 2000 (2000-06-15), pages 848-854, XP001015211 ISSN: 0020-7136 the whole document</p> <p>-----</p>	1-57
Y	<p>MCNEISH I A ET AL: "VIRUS DIRECTED ENZYME PRODRUG THERAPY FOR OVARIAN AND PANCREATIC CANCER USING RETROVIRALLY DELIVERED E. COLI NITROREDUCTASE AND CB1954" GENE THERAPY, MACMILLAN PRESS LTD., BASINGSTOKE, GB, vol. 5, no. 8, August 1998 (1998-08), pages 1061-1069, XP000901446 ISSN: 0969-7128 abstract</p> <p>-----</p>	1-57
Y	<p>LIU B L ET AL: "ICP34.5 deleted herpes simplex virus with enhanced oncolytic, immune stimulating, and anti-tumour properties." GENE THERAPY, vol. 10, no. 4, February 2003 (2003-02), pages 292-303, XP002313120 ISSN: 0969-7128 cited in the application the whole document</p> <p>-----</p>	1-57

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Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.b of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:

a. type of material

a sequence listing

table(s) related to the sequence listing

b. format of material

in written format

in computer readable form

c. time of filing/furnishing

contained in the international application as filed

filed together with the international application in computer readable form

furnished subsequently to this Authority for the purpose of search

2. In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

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Box II Observations where certain claims were found unsearchable (Continuation of item 2 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:

Although claims 31 and 51-54 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.
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 III Observations where unity of invention is lacking (Continuation of item 3 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

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Patent document cited in search report		Publication date		Patent family member(s)	Publication date
WO 9955345	A	04-11-1999	CA	2327506 A1	04-11-1999
			EP	1073442 A1	07-02-2001
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