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(54) Title: ANTIBODIES AGAINST CASPASE-8, THEIR PREPARATION AND USE

(57) Abstract: The invention relates to antibodies to a specific region in caspase-8, and to their use.

INTERNATIONAL SEARCH REPORT

International Application No.
PCT/IL02/00734

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07K16/40 C07K14/47 C12N9/64 G01N33/53

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 C07K G01N

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)

BIOSIS, EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	MEDEMA JAN PAUL ET AL: "Bcl-xL acts downstream of caspase-8 activation by the CD95 death-inducing signaling complex." JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 273, no. 6, 6 February 1998 (1998-02-06), pages 3388-3393, XP002229994 ISSN: 0021-9258	1-16, 25
Y	page 3389, left-hand column, paragraph 2 page 3390, right-hand column, paragraph 3 -page 3391, left-hand column, paragraph 1; figure 4 --- -/--	17-21

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in 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)
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- *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

5 February 2003

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INTERNATIONAL SEARCH REPORT

 Internati Application No
 PCT/IL 02/00734

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	"Anti-caspase 8 (GD-13); Product number C2976" SIGMA PRODUCT INFORMATION, 'Online! September 1999 (1999-09), XP002229995 Retrieved from the Internet: <URL:http://www.sigmaaldrich.com/ProductLo okup.html?ProdNo=C2976&Brand=SIGMA> 'retrieved on 2003-01-24!	1-16,25
Y	the whole document	17-21
X	"Caspase-8 (1C12) Monoclonal Antibody" CELL SIGNALING PRODUCT SPECIFICATION, 'Online! 1999, XP002229996 Retrieved from the Internet: <URL:http://www.cellsignal.com/product.asp ?catalog%5Fname=CellSignal&category%5Fname =Apoptosis+%2F+Caspase&product%5Fid=9746> 'retrieved on 2003-01-24!	1-16,25
Y	the whole document	17-21
Y	WO 00 77201 A (ASTRAZENECA UK LTD ;ASTRAZENECA AB (SE)) 21 December 2000 (2000-12-21) example VI	17-21
Y	RODIER F ET AL: "Polyomavirus large T-antigen protects mouse cells from Fas-, TNF-alpha- and taxol-induced apoptosis." ONCOGENE, vol. 19, no. 54, 2000, pages 6261-6270, XP008012999 ISSN: 0950-9232 figure 5	17-21
A	BOLDIN M P ET AL: "INVOLVEMENT OF MACH, A NOVEL MORT1/FADD-INTERACTING PROTEASE, IN FAS/APO-1- AND TNF RECEPTOR-INDUCED CELL DEATH" CELL, CELL PRESS, CAMBRIDGE, NA, US, vol. 85, no. 6, 14 June 1996 (1996-06-14), pages 803-815, XP002037501 ISSN: 0092-8674 figure 1	17-21
P,X	NIIKURA YUICHI ET AL: "Monitoring of caspase-8/FLICE processing and activation upon Fas stimulation with novel antibodies directed against a cleavage site for caspase-8 and its substrate, FLICE-like inhibitory protein (FLIP)." JOURNAL OF BIOCHEMISTRY (TOKYO), vol. 132, no. 1, July 2002 (2002-07), pages 53-62, XP001109528 ISSN: 0021-924X the whole document	1-21,25

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IL 02/00734

Box I Observations where certain claims were found unsearchable (Continuation of item 1 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 12-16 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 II Observations where unity of invention is lacking (Continuation of item 2 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

International Application No
PCT/IL 02/00734

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 0077201 A	21-12-2000	AU 5544500 A WO 0077201 A1	02-01-2001 21-12-2000