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Declarations under Rule 4.17:

- as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))
- of inventorship (Rule 4.17(iv))

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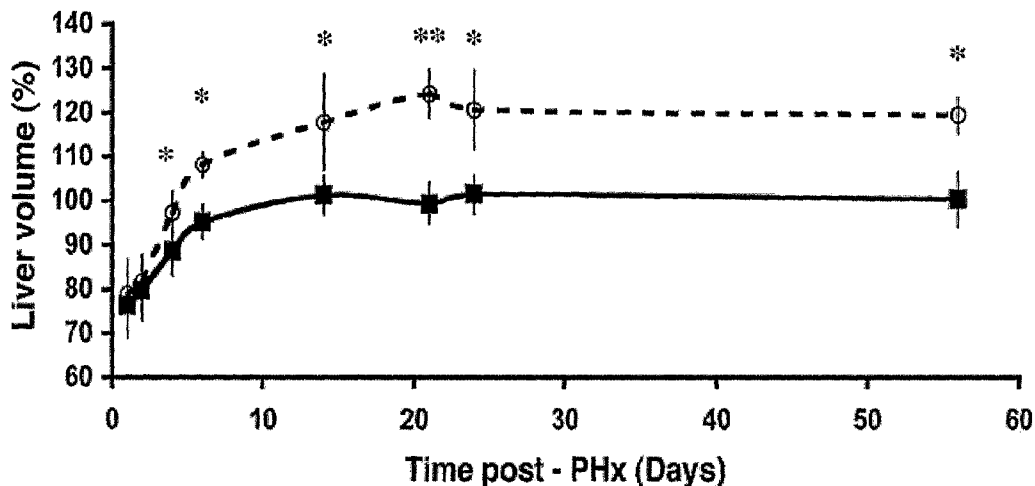


Fig. 3D

(57) Abstract: The present invention relates to the regulatory role of caspase-8 in infection by intracellular pathogen, inflammation and wound healing.

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INTERNATIONAL SEARCH REPORT

International application No
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A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K38/48 A61P1/16

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)
A61K A61P

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	WO 03/020759 A (YEDA RES & DEV [IL]; WALLACH DAVID [IL]; GONCHAROV TANYA [IL]; KOLUMAM) 13 March 2003 (2003-03-13) claims; examples	1-16, 40-54
Y	GUICCIARDI M E ET AL: "Apoptosis: a mechanism of acute and chronic liver injury" GUT, vol. 54, no. 7, July 2005 (2005-07), pages 1024-1033, XP009098109 ISSN: 0017-5749 page 1025, column 1, paragraph 3 - page 1026, column 2, paragraph 2; figures; table 1 page 1028, column 1, paragraph 2 - column 2, paragraph 1	1-16, 40-54

Further documents are listed in the continuation of Box C.

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
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- *&* document member of the same patent family

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INTERNATIONAL SEARCH REPORT

International application No

PCT/IL2007/000786

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>PROSSER COLETTE C ET AL: "Molecular therapy for hepatic injury and fibrosis: where are we?" WORLD JOURNAL OF GASTROENTEROLOGY : WJG 28 JAN 2006; vol. 12, no. 4, 28 January 2006 (2006-01-28), pages 509-515, XP009098119 ISSN: 1007-9327 page 509, column 2, paragraph 2 - page 511, column 1, paragraph 1; figures -----</p>	1-64
Y	<p>KANG TAE-BONG ET AL: "Caspase-8 serves both apoptotic and nonapoptotic roles" JOURNAL OF IMMUNOLOGY, THE WILLIAMS AND WILKINS CO. BALTIMORE, US, vol. 173, no. 5, 1 September 2004 (2004-09-01), pages 2976-2984, XP002417111 ISSN: 0022-1767 cited in the application page 2982, column 2, paragraph 3; figures -----</p>	1-16, 40-54
E	<p>WO 2007/105199 A (YEDA RES & DEV [IL]; WALLACH DAVID [IL]; APPEL ELENA [IL]; KOVALENKO A) 20 September 2007 (2007-09-20) claims; examples -----</p>	1-16, 40-54
T	<p>BEN MOSHE TEHILA ET AL: "Role of caspase-8 in hepatocyte response to infection and injury in mice" HEPATOLOGY, vol. 45, no. 4, April 2007 (2007-04), pages 1014-1024, XP002476162 ISSN: 0270-9139 the whole document -----</p>	
X	<p>SELZNER MARKUS ET AL: "Mechanisms of ischemic injury are different in the steatotic and normal rat liver" HEPATOLOGY, vol. 32, no. 6, December 2000 (2000-12), pages 1280-1288, XP002491474 ISSN: 0270-9139 page 1283, column 2, paragraph 1 - page 1284, column 1, paragraph 2 ----- -/--</p>	17-39, 56-64

INTERNATIONAL SEARCH REPORT

International application No

PCT/IL2007/000786

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>OH H -Y ET AL: "Dexamethasone protects primary cultured hepatocytes from death receptor-mediated apoptosis by upregulation of cFLIP" CELL DEATH AND DIFFERENTIATION, vol. 13, no. 3, March 2006 (2006-03), pages 512-523, XP002491475 ISSN: 1350-9047 page 521, column 1, paragraph 2 - paragraph 3; figures</p>	1-64
X	<p>HAINSWORTH A H ET AL: "Up - regulation of cellular FLICE - like inhibitory protein (CFLIP) in brain after traumatic brain injury (TBI) in mice and humans." SOCIETY FOR NEUROSCIENCE ABSTRACT VIEWER AND ITINERARY PLANNER, vol. 2003, 2003, pages Abstract No. 743.3 URL-http://sf, XP009104188 & 33RD ANNUAL MEETING OF THE SOCIETY OF NEUROSCIENCE; NEW ORLEANS, LA, USA; NOVEMBER 08-12, 2003 the whole document</p>	17-39, 56-64
A	<p>FAUSTO NELSON ET AL: "Liver regeneration" HEPATOLOGY, vol. 43, no. 2, Suppl. 1, February 2006 (2006-02), pages S45-S53, XP009104187 ISSN: 0270-9139 cited in the application the whole document</p>	
A	<p>MCDONALD III E R ET AL: "Suppression of caspase-8- and -10-associated RING proteins results in sensitization to death ligands and inhibition of tumor cell growth" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE, WASHINGTON, DC, vol. 101, no. 16, 20 April 2004 (2004-04-20), pages 6170-6175, XP002432883 ISSN: 0027-8424 cited in the application the whole document</p>	

INTERNATIONAL SEARCH REPORT

International application No.
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Box No. 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:

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 No. 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:

see additional sheet

1. As all required additional search fees were timely paid by the applicant, this international search report covers allsearchable claims.
2. As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.
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 and, where applicable, the payment of a protest fee.
- The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-16, 40-54

Caspase-8 or compounds increasing its activity for preventing and/or treating inflammation

2. claims: 17-39, 55-64

Caspase-8 inhibitors for facilitating or accelerating healing of a wounded or injured tissue or organ

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/IL2007/000786

Patent document cited in search report	Publication date	Patent family member(s)	Publication date	
WO 03020759	A	13-03-2003	BR 0212287 A	14-09-2004
			CA 2459136 A1	13-03-2003
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			EP 1423422 A2	02-06-2004
			JP 2005501545 T	20-01-2005
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			US 2005048639 A1	03-03-2005
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WO 2007105199	A	20-09-2007	NONE	
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