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(71) Applicant and

(72) Inventor: **MULTHOFF, Gabriele** [DE/DE]; Kirchen-
strasse 17c, 81675 München (DE).

(74) Agent: **STEINECKE, Peter**; Müller Fottner Steinecke,
P.O. Box 31 01 40, 80102 München (DE).

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MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC,
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ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.

(54) Title: USE OF GRANZYME B AS AN HSP70/HSP70 PEPTIDE DEPENDENT INDUCER OF APOPTOSIS IN TUMOR
CELLS

(57) Abstract: The present invention relates to a method of inducing or enhancing the expression of granzyme B in natural killer (NK) cells. The present invention relates also to a use of said NK cells for the preparation of a pharmaceutical composition for the treatment of tumors, viral or bacterial infections or inflammatory diseases. Further, the present invention relates to the use of granzyme B for the treatment of tumors, viral or bacterial infections or inflammatory diseases, wherein the tumor cells or the cells affected by said infection or inflammation express Hsp70 in their cell surface.



WO 2004/018002 A3

INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N5/08 A61K38/48 A61K35/14

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

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)

WPI Data, PAJ, EPO-Internal, MEDLINE, BIOSIS, CHEM ABS 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 99 49881 A (MULTHOFF GABRIELE) 7 October 1999 (1999-10-07) cited in the application page 1, paragraph 1 page 3, paragraph 5 page 8, paragraph 2 -page 9, paragraph 1 page 11, paragraph 2 page 21 -page 26; examples 1-3 -----	12,13, 16,22-24
X	US 6 261 839 B1 (MULTHOFF GABRIELE ET AL) 17 July 2001 (2001-07-17) column 1, line 65 -column 2, line 53; claims 1,19,20 ----- -/--	12,13, 16,22-24

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

☒ Patent family members are listed in annex.

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Date of the actual completion of the international search

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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

Sitch, W

INTERNATIONAL SEARCH REPORT

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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.
A	DATABASE BIOSIS 'Online! BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; October 2001 (2001-10) MULTHOFF GABRIELE ET AL: "A 14-mer Hsp70 peptide stimulates natural killer (NK) cell activity" Database accession no. PREV200200042332 XP002276403 abstract & CELL STRESS AND CHAPERONES, vol. 6, no. 4, October 2001 (2001-10), pages 337-344, ISSN: 1355-8145 ---	
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X	WO 99 43840 A (BOEHRINGER INGELHEIM PHARMA) 2 September 1999 (1999-09-02) page 6, line 24 -page 7, line 7 page 17, line 20 -page 18, line 14 ---	14,15, 17-24
X	WO 01 80880 A (BARTH STEFAN ;ENGERT ANDREAS (DE); STOECKER MICHAEL (DE)) 1 November 2001 (2001-11-01) page 9, paragraph 4 -page 10, paragraph 1 claims 1,8,18 ---	14,15, 17-24
X	SHAFFER W M ET AL: "HUMAN LYSOSOMAL CATHEPSIN G AND GRANZYME B SHARE A FUNCTIONALLY CONSERVED BROAD SPECTRUM ANTIBACTERIAL PEPTIDE" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 266, no. 1, 1991, pages 112-116, XP002276402 ISSN: 0021-9258 page 112, left-hand column, paragraph 1 -right-hand column, paragraph 3 page 115, right-hand column, paragraph 3 --- -/--	14,15, 17-24

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International Application No

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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.
X	DATABASE BIOSIS 'Online! BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 1997 HOMMEL-BERREY GRACE A ET AL: "Granzyme B independently of perforin mediates noncytolytic intracellular inactivation of vesicular stomatitis virus" Database accession no. PREV199799800859 XP002276404 abstract & CELLULAR IMMUNOLOGY, vol. 180, no. 1, 1997, pages 1-9, ISSN: 0008-8749	14,15, 17-24
P,X	WO 03 007889 A (RES DEV FOUNDATION) 30 January 2003 (2003-01-30) paragraph '0015! - paragraph '0017! paragraph '0029! paragraph '0126! - paragraph '0127! paragraph '0231!	14,15, 17,21,24
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INTERNATIONAL SEARCH REPORT

International Application No

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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.
T	DATABASE BIOSIS 'Online! BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 17 October 2003 (2003-10-17) GROSS CATHARINA ET AL: "Cell surface-bound heat shock protein 70 (Hsp70) mediates perforin-independent apoptosis by specific binding and uptake of granzyme B." Database accession no. PREV200300583456 XP002276406 abstract & JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 278, no. 42, 17 October 2003 (2003-10-17), pages 41173-41181, ISSN: 0021-9258 -----	

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP 03/09341

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 1, 2, 9-11, 21-24 (all partially), and claims 3, 16-20 (all completely) 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

Information on patent family members

International Application No

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