

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
29 December 2005 (29.12.2005)

PCT

(10) International Publication Number  
WO 2005/123772 A3

(51) International Patent Classification:

A61K 38/17 (2006.01) A61P 35/00 (2006.01)  
A61P 29/00 (2006.01)

(21) International Application Number:

PCT/IL2005/000638

(22) International Filing Date: 16 June 2005 (16.06.2005)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

60/580,106 17 June 2004 (17.06.2004) US

(71) Applicants (for all designated States except US): **YIS-SUM RESEARCH DEVELOPMENT COMPANY** [IL/IL]; Hi Tech Park, Edmond Safra Campus, Givat Ram, 39135 Jerusalem (IL). **HADASIT MEDICAL RESEARCH SERVICES** [IL/IL]; P.O.Box 12000, Kiryat Hadassah, 91120 Jerusalem (IL).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **BEN NERIAH, Yionon** [IL/IL]; 5 Mevo Duvdevan Street, 90805 Mevasseret Zion (IL). **PIKARSKY, Eli** [IL/IL]; 29/4 Yaakov Zur Street, 96411 Jerusalem (IL).

(74) Agent: **REINHOLD COHN AND PARTNERS**; P.O.Box 4060, 61040 Tel Aviv (IL).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

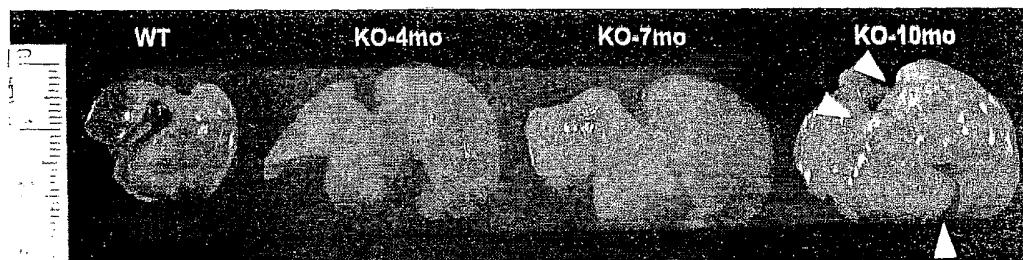
- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

(88) Date of publication of the international search report:

2 February 2006

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.

(54) Title: ANTI-CANCER THERAPY



(57) Abstract: A method of prevention progression from chronic inflammatory condition to cancer, by administration an NF- B inhibitor, anti TNF agent or an NSAID. The method can also be used to prevent cancer in an individual having a high probability (genetic) of developing the types of cancer usually associated with inflammation.

WO 2005/123772 A3

**INTERNATIONAL SEARCH REPORT**

International Application No  
PCT/IL2005/000638

<b>A. CLASSIFICATION OF SUBJECT MATTER</b>		
A61K38/17      A61P29/00      A61P35/00		
According to International Patent Classification (IPC) or to both national classification and IPC		
<b>B. FIELDS SEARCHED</b>		
Minimum documentation searched (classification system followed by classification symbols) A61K C07K 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		
<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>MAYO M W ET AL: "The transcription factor NF-kappaB: control of oncogenesis and cancer therapy resistance" BBA - REVIEWS ON CANCER, ELSEVIER SCIENCE BV, AMSTERDAM, NL, vol. 1470, no. 2, 27 March 2000 (2000-03-27), pages M55-M62, XP004281881 ISSN: 0304-419X cited in the application page M59, column 1, line 36 - column 2, line 10</p> <p align="center">----- -/--</p>	1-17
<input checked="" type="checkbox"/> Further documents are listed in the continuation of box C. <input type="checkbox"/> Patent family members are listed in annex.		
° Special categories of cited documents :		
<p>*A* document defining the general state of the art which is not considered to be of particular relevance</p> <p>*E* earlier document but published on or after the international filing date</p> <p>*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)</p> <p>*O* document referring to an oral disclosure, use, exhibition or other means</p> <p>*P* document published prior to the international filing date but later than the priority date claimed</p>	<p>*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</p> <p>*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</p> <p>*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.</p> <p>* &amp; * document member of the same patent family</p>	
Date of the actual completion of the international search	Date of mailing of the international search report	
29 November 2005	20/12/2005	
Name and mailing address of the ISA	Authorized officer	
<p>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</p>	Favre, N	

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/IL2005/000638

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	LIN ANNING ET AL: "NF-kappaB in cancer: A marked target." SEMINARS IN CANCER BIOLOGY, vol. 13, no. 2, April 2003 (2003-04), pages 107-114, XP002356257 ISSN: 1044-579X page 112, column 1, line 16 - line 23 -----	1-17
X	PERKINS N D: "The Rel/NF-kappaB family: friend and foe" TRENDS IN BIOCHEMICAL SCIENCES, ELSEVIER, HAYWARDS, GB, vol. 25, no. 9, 1 September 2000 (2000-09-01), pages 434-440, XP004210315 ISSN: 0968-0004 abstract -----	1-17
X	COUSSENS LISA M ET AL: "Inflammation and cancer." NATURE (LONDON), vol. 420, no. 6917, 2002, pages 860-867, XP002356258 ISSN: 0028-0836 cited in the application abstract -----	1-17
X	TOMITA T ET AL: "TRANSCRIPTION FACTOR DECOY FOR NFKB INHIBITS CYTOKINE AND ADHESION MOLECULE EXPRESSIONS IN SYNOVIAL CELLS DERIVED FROM RHEUMATOID ARTHRITIS" RHEUMATOLOGY, OXFORD UNIVERSITY PRESS, LONDON, GB, vol. 39, 2000, pages 749-757, XP002951052 ISSN: 1462-0324 abstract -----	1-17
A	LAVON I ET AL: "HIGH SUSCEPTIBILITY TO BACTERIAL INFECTION, BUT NO LIVER DYSFUNCTION, IN MICE COMPROMISED FOR HEPATOCYTE NF-KAPPAB ACTIVATION" NATURE MEDICINE, NATURE PUBLISHING GROUP, NEW YORK, NY, US, vol. 6, no. 5, May 2000 (2000-05), pages 573-577, XP000962406 ISSN: 1078-8956 cited in the application the whole document -----	1-17
	-/--	

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/IL2005/000638

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	PIKARSKY ELI ET AL: "NF-kappaB functions as a tumour promoter in inflammation-associated cancer" NATURE (LONDON), vol. 431, no. 7007, 23 September 2004 (2004-09-23), pages 461-466, XP002356259 ISSN: 0028-0836 the whole document	1-17
P,X	----- NICKOLOFF BRIAN J ET AL: "Inflammation and cancer: Is the link as simple as we think?" JOURNAL OF INVESTIGATIVE DERMATOLOGY, vol. 124, no. 6, June 2005 (2005-06), pages X-xiv, XP002356260 ISSN: 0022-202X the whole document	1-17
P,X	----- BEACHY PHILIP A ET AL: "Mending and malignancy." NATURE. 23 SEP 2004, vol. 431, no. 7007, 23 September 2004 (2004-09-23), page 402, XP002356261 ISSN: 1476-4687 the whole document	1-15