

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
28 March 2002 (28.03.2002)

PCT

(10) International Publication Number
WO 02/024940 A3

- (51) International Patent Classification⁷: **G01N 33/50**
- (21) International Application Number: PCT/EP01/11492
- (22) International Filing Date:
20 September 2001 (20.09.2001)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:
60/234,161 20 September 2000 (20.09.2000) US
- (71) Applicant (*for all designated States except US*): **INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (I.N.S.E.R.M.)** [FR/FR]; 101, rue de Tolbiac, F-75654 Paris Cedex 13 (FR).
- (72) Inventors; and
- (75) Inventors/Applicants (*for US only*): **VIVIER, Eric** [FR/FR]; 20bis, Chemin du Boudard, F-13260 Cassis (FR). **VELY, Frédéric** [FR/FR]; Résidence du Vallat, La Farandole, F-13260 Cassis (FR). **TOMASELLO, Elena** [FR/FR]; 38, Allée des Pins, F-13009 Marseille (FR).
- (74) Agents: **PEAUCELLE, Chantal** et al.; Cabinet Armengaud Aine, 3, Avenue Bugeaud, F-75116 Paris (FR).
- (81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.
- (84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).
- Published:**
— *with international search report*
- (88) Date of publication of the international search report:
9 October 2003
- 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.*



WO 02/024940 A3

(54) Title: MEANS FOR THE IDENTIFICATION OF COMPOUNDS CAPABLE OF INHIBITING KARAP-TRANSDUCED SIGNALS

(57) Abstract: The present application relates to transgenic animals over-expressing KARAP, knock-in animals bearing non functional KARAP, and to method and kits for the identification of compounds capable of inhibiting a KARAP-transduced immune signal.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 01/11492

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 G01N33/50

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 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)

EPO-Internal, WPI Data, PAJ, BIOSIS

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 06557 A (SCHERING CORP) 11 February 1999 (1999-02-11) page 60, line 25 -page 61, line 20	3
Y	page 59, line 32 -page 62, line 6; claims 19,20	1-3
Y	----- PALONEVA J ET AL: "LOSS-OF-FUNCTION MUTATIONS IN TYROBP (DAP12) RESULT IN A PRESENILE DEMENTIA WITH BONE CYSTS" NATURE GENETICS, NATURE AMERICA, NEW YORK, US, vol. 25, no. 3, July 2000 (2000-07), pages 357-361, XP002955803 ISSN: 1061-4036 cited in the application page 359, left-hand column, paragraph 2 abstract ----- -/--	1-3

 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)
- *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

26 February 2003

Date of mailing of the international search report

13/03/2003

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

Cuendet, P

INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 01/11492

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	BAKKER A B H ET AL: "DAP12 deficient mice reveal a critical role for DAP12 receptor complexes in T cell priming in vivo." FASEB JOURNAL, vol. 14, no. 6, 20 April 2000 (2000-04-20), page A1019 XP009004196 Joint Annual Meeting of the American Association of Immunologists and the Clinical Immunology Society; Seattle, Washington, USA; May 12-16, 2000 ISSN: 0892-6638 abstract ----	1-3
A	WO 98 49292 A (INST NAT SANTE RECH MED ;VELY FREDERIC (FR); VIVIER ERIC (FR); TOM) 5 November 1998 (1998-11-05) cited in the application page 21, line 15-24; claims 30,31 ----	3
P,Y	BAKKER ALEXANDER B H ET AL: "DAP12-deficient mice fail to develop autoimmunity due to impaired antigen priming." IMMUNITY, vol. 13, no. 3, September 2000 (2000-09), pages 345-353, XP002232702 ISSN: 1074-7613 the whole document ----	1-3
P,Y	TOMASELLO E ET AL: "Combined natural killer cell and dendritic cell functional deficiency in KARAP/DAP12 loss-of-function mutant mice" IMMUNITY, CELL PRESS, US, vol. 13, no. 3, September 2000 (2000-09), pages 355-364, XP002222816 ISSN: 1074-7613 the whole document -----	1-3

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP 01/11492

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:

2. Claims Nos.: 4-12, 13-14
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:
see FURTHER INFORMATION sheet PCT/ISA/210

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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 4-12, 13-14

Present claims 4-12 relate to a compound/method defined by reference to a desirable characteristic or property, namely compounds being "KARAP-inhibiting". The claims cover all compounds/methods having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds/methods. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compound/method by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has not been carried for claims 4-12.

Present claims 13-14 relate to an extremely large number of possible kits. In fact, the claims contain so many options, variables, possible permutations that a lack of clarity (and/or conciseness) within the meaning of Article 6 PCT arises to such an extent as to render a meaningful search of the claims impossible. Consequently, no search has been carried out for claims 13-14.

Comment regarding searched claims 1-3 (and claims not searched): non-patentability according to Rule 39.1(ii) PCT - Essentially biological process for the production of animals, i.e. missing restriction to "non human mammals", cf. p.8, line 24.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 01/11492

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9906557	A	11-02-1999	AU 8661498	A 22-02-1999
			EP 1003861	A2 31-05-2000
			JP 2001512017	T 21-08-2001
			WO 9906557	A2 11-02-1999
			US 6416973	B1 09-07-2002
WO 9849292	A	05-11-1998	FR 2762844	A1 06-11-1998
			EP 0977855	A2 09-02-2000
			WO 9849292	A2 05-11-1998
			JP 2002503094	T 29-01-2002