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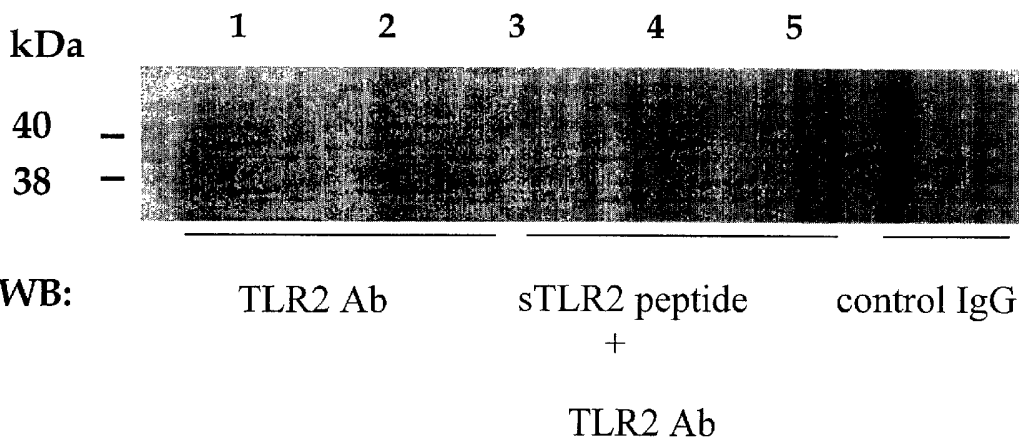
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Declarations under Rule 4.17:

— as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for the following designations 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, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB,

[Continued on next page]

(54) Title: A SOLUBLE TOLL-LIKE RECEPTOR



(57) Abstract: A novel, soluble protein similar to the known Toll-like receptor (TLR) family is disclosed. The present invention relates to these new soluble polypeptides, to nucleotide sequences encoding the polypeptides, to antibodies selectively binding to the polypeptide and to expression systems suitable for producing the polypeptide. The polypeptide is useful for modulating inflammatory reactions in mammals that include the actions of TLR.

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- GR, IE, IT, LU, MC, NL, PT, SE, SK, TR*), OAPI patent (*BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG*)
- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for the following designations *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, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW*, ARIPO patent (*GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW*), Eurasian patent (*AM, AZ, BY, KG, KZ, MD, RU, TJ, TM*), European patent (*AT, BE, BG, CH, CY, CZ, DE, DK, EE,*

- ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR*), OAPI patent (*BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG*)
- of inventorship (Rule 4.17(iv)) for US only

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 02/10410

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/12 C07K14/705 C07K16/28 C12N5/10 A61K38/17
//A61P1/00,A61P11/00,A61P17/00

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

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, BIOSIS, MEDLINE, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	FLO T H ET AL: "Detection of soluble TLR2 in human serum samples by ELISA." JOURNAL OF ENDOTOXIN RESEARCH, vol. 6, no. 2, 2000, page 106 XP001052916 6th Conference of the International Endotoxin Society;Paris, France; August 24-27, 2000 ISSN: 0968-0519 the whole document --- -/--	1-7,10

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.
- *Z* document member of the same patent family

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20/03/2003

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 02/10410

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	FILIPP DOMINIK ET AL: "Soluble CD14 enriched in colostrum and milk induces B cell growth and differentiation." PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES, vol. 98, no. 2, 16 January 2001 (2001-01-16), pages 603-608, XP002187481 January 16, 2001 ISSN: 0027-8424 the whole document ---	1-6, 8-27
X	LABETA MARIO O ET AL: "Innate recognition of bacteria in human milk is mediated by a milk-derived highly expressed pattern recognition receptor, soluble CD14." JOURNAL OF EXPERIMENTAL MEDICINE, vol. 191, no. 10, 15 May 2000 (2000-05-15), pages 1807-1812, XP002187480 ISSN: 0022-1007 the whole document ---	1-6, 8-12, 14-19, 21-25, 27
X	DU ET AL.: "Analysis of Tlr4-mediated LPS signal transduction in macrophages by mutational modification of the receptor" BLOOD CELLS, MOLECULES AND DISEASES, vol. 25, no. 6, 15 November 1999 (1999-11-15), pages 328-338, XP002183507 the whole document ---	1-6, 10-27
X	WO 99 37772 A (BORN TERESA L ;SIMS JOHN E (US); IMMUNEX CORP (US)) 29 July 1999 (1999-07-29) the whole document ---	1, 2, 8, 10-27
X	EP 0 864 585 A ((HAYB) HAYASHIBARA SEIBUTSU KAGAKU) 16 September 1998 (1998-09-16) the whole document ---	1, 2, 8, 10-27
X	XU YINGWU ET AL: "Structural basis for signal transduction by the Toll/interleukin-1 receptor domains." NATURE (LONDON), vol. 408, no. 6808, 2000, pages 111-115, XP002183508 ISSN: 0028-0836 the whole document ---	1, 2, 7, 8, 11-13
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INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 02/10410

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>PRUITT JEFFREY H ET AL: "Increased soluble interleukin-1 type II receptor concentrations in postoperative patients and in patients with sepsis syndrome." BLOOD, vol. 87, no. 8, 1996, pages 3282-3288, XP001041460 ISSN: 0006-4971 the whole document</p>	1,2,8,10
A	<p>O'NEILL L A J ET AL: "The IL-1 receptor/toll-like receptor superfamily: crucial receptors for inflammation and host defense" IMMUNOLOGY TODAY, ELSEVIER PUBLICATIONS, CAMBRIDGE, GB, vol. 21, no. 5, May 2000 (2000-05), pages 206-209, XP004198146 ISSN: 0167-5699 page 209, column 1, paragraph 2</p>	14-27
A	<p>MANTOVANI A ET AL: "Decoy receptors: a strategy to regulate inflammatory cytokines and chemokines" TRENDS IN IMMUNOLOGY, ELSEVIER, CAMBRIDGE, GB, vol. 22, no. 6, 1 June 2001 (2001-06-01), pages 328-336, XP004249049 ISSN: 1471-4906 the whole document</p>	
A	<p>KOLB A F: "The prospects of modifying the antimicrobial properties of milk" BIOTECHNOLOGY ADVANCES, ELSEVIER PUBLISHING, BARKING, GB, vol. 19, no. 4, July 2001 (2001-07), pages 299-316, XP004274975 ISSN: 0734-9750 the whole document</p>	

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP 02/10410

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 claim 27 is 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
PCT/EP 02/10410

Patent document cited in search report	A	Publication date	Patent family member(s)	Publication date
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