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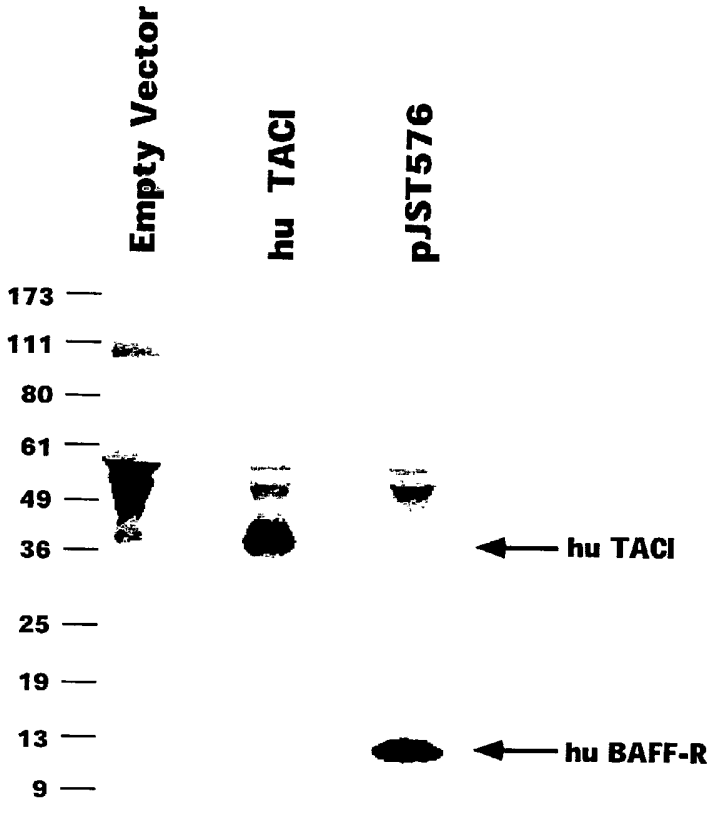
[Continued on next page]

(54) Title: RECEPTOR NUCLEIC ACIDS AND POLYPEPTIDES

(57) Abstract: Disclosed are nucleic acids encoding BAFF-R polypeptides, as well as antibodies to BAFF-R polypeptides and pharmaceutical compositions including same. Methods of treating tumorigenic and autoimmune conditions using the nucleic acids, polypeptides, antibodies and pharmaceutical compositions of this invention are also provided.



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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.

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— *of inventorship (Rule 4.17(iv)) for US only*

Published:
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see PCT Gazette No. 14/2003 of 3 April 2003, Section II

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 01/28006

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12N15/12 C12N15/62 C12N15/10 C12N5/10 C12P21/02
C07K14/715 C07K16/28 C07H21/04 C12Q1/68 A61K38/17
A61K48/00 G01N33/53 G01N33/68

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 C12P C07K C07H C12Q A61K 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)
EMBL, EPO-Internal, WPI Data, PAJ, BIOSIS, MEDLINE, 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 00 43032 A (MACKAY FABIENNE ;APOTECH SA (CH); TSCHOPP JURG (CH); SCHNEIDER PAS) 27 July 2000 (2000-07-27) page 15, line 17-20 page 26, line 27 -page 27, line 12 ---	1-38, 47-49, 53-55
X	SCHNEIDER P ET AL.: "BAFF, a novel ligand of the tumor necrosis factor family, stimulates B cell growth" JOURNAL OF EXPERIMENTAL MEDICINE, vol. 189, no. 11, 7 June 1999 (1999-06-07), pages 1747-1756, XP000915409 ISSN: 0022-1007 cited in the application page 1751, right-hand column, line 12 -page 1752, left-hand column, line 6 --- -/--	1-38, 47-49, 53-55

[X] Further documents are listed in the continuation of box C.

[X] 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	Date of mailing of the international search report
18 March 2003	28. 03. 2003

Name and mailing address of the ISA	Authorized officer
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	van de Kamp, M

Form PCT/ISA/210 (second sheet) (July 1992)

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 EMBL 'Online! embl; 9 November 1998 (1998-11-09) NCI-CGAP: "qx03d08.x1 NCI_CGAP_Lym12 Homo sapiens cDNA clone IMAGE:2000271 3', mRNA sequence" Database accession no. AI250289 XP002206618 the whole document ---	7
X	DATABASE EMBL 'Online! EMBL; 2 October 1997 (1997-10-02) CLARK G: "Human DNA sequence from clone CTA-250D10 on chromosome 22 Contains the genes for SREBF2 (sterol regulatory element binding transcription factor 2), NAGA (alpha-N-acetylgalactosaminidase), a gene similar to neuronal-specific septin 3, a pseudogene similar to ANT2 .. etc." Database accession no. Z99716 XP002206619 nucleotides 69341-70018 ---	7
X	GROSS J A ET AL.: "TACI and BCMA are receptors for a TNF homologue implicated in B-cell autoimmune disease" NATURE, vol. 404, 27 April 2000 (2000-04-27), pages 995-999, XP002140939 ISSN: 0028-0836 cited in the application the whole document ---	20-25, 28,32-38
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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	YU G ET AL.: "APRIL and TALL-I and receptors BCMA and TACI: system for regulating humoral immunity" NATURE IMMUNOLOGY, vol. 1, no. 3, September 2000 (2000-09), pages 252-256, XP000982268 ISSN: 1529-2908 the whole document	20-25, 28,32-38
X	DOMINGUES H M: "Rational design strategies to improve cytokine foldability and minimization of a functional motif: The IL-4 case" THESIS UNIVERSITY OF UTRECHT, 26 May 1999 (1999-05-26), XP002159805	39-42
Y	page 48, line 25 -page 51, line 6 page 94; table III	43
Y	WOOD S J ET AL: "Prolines and amyloidogenicity in fragments of the Alzheimer's peptide beta/A4" BIOCHEMISTRY, vol. 34, no. 3, 24 January 1995 (1995-01-24), pages 724-730, XP002050228 ISSN: 0006-2960 abstract page 724, right-hand column, line 24 -page 725, left-hand column, line 18 table 1 page 729, left-hand column, line 38 -right-hand column, line 8	43
A	SCHEIN C H: "Production of soluble recombinant proteins in bacteria" BIO/TECHNOLOGY, vol. 7, no. 11, 1 November 1989 (1989-11-01), pages 1141-1149, XP000068927 ISSN: 0733-222X abstract	39
A	KWON K-S ET AL.: "Single amino acid substitutions of alpha-1-antitrypsin that confer enhancement in thermal stability." JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 269, no. 13, 1994, pages 9627-9631, XP002206613 ISSN: 0021-9258 abstract	39
P,X	WO 01 12812 A (MACKAY FABIENNE ;APOTECH R & D S A (CH); TSCHOPP JURG (CH); SCHNEI) 22 February 2001 (2001-02-22) the whole document	20-25, 28,32-38

-/--

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
T	THOMPSON J S ET AL.: "BAFF-R, a newly identified TNF receptor that specifically interacts with BAFF." SCIENCE (WASHINGTON D C), vol. 293, no. 5537, 14 September 2001 (2001-09-14), pages 2108-2111, XP002206614 ISSN: 0036-8075 the whole document	1-9,13, 14, 32-34, 37,38, 47,53
T	YAN M ET AL.: "Identification of a novel receptor for B lymphocyte stimulator that is mutated in a mouse strain with severe B cell deficiency." CURRENT BIOLOGY, vol. 11, no. 19, 2001, pages 1547-1552, XP002206615 ISSN: 0960-9822 the whole document	47,53
T	SCHIEMANN B ET AL.: "An essential role for BAFF in the normal development of B cells through a BCMA-independent pathway." SCIENCE (WASHINGTON D C), vol. 293, no. 5537, 14 September 2001 (2001-09-14), pages 2111-2114, XP002206616 ISSN: 0036-8075 the whole document	
T	WALDSCHMIDT T J ET AL.: "Long live the mature B cell: A BAFFling mystery resolved." SCIENCE (WASHINGTON D C), vol. 293, no. 5537, 14 September 2001 (2001-09-14), pages 2012-2013, XP002206617 ISSN: 0036-8075 the whole document	

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 01/28006

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. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 20-31 are directed to a diagnostic method practised on the human/animal body and/or 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. [X] 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:

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:

see additional sheet

1. [X] 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.

[X] No protest accompanied the payment of additional search fees.

Continuation of Box I.2

Present claims 34, 36 and 38 relate to compounds defined by reference to a desirable characteristic or property, namely binding BAFF-R, binding a BAFF-R-encoding nucleic acid, or modulating BAFF-R activity. The claims cover all compounds 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. 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 compounds 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 been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to compounds which are antibody or antisense molecules.

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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. Claims: 1-38,44-55

An isolated nucleic acid comprising a sequence encoding a polypeptide at least 50% or 90% identical to a polypeptide comprising the amino acid sequence of SEQ ID NO:5, e.g., complementary to at least a portion of SEQ ID NOs 1-4 or 6. Said nucleic acid, said polypeptide binding BAFF. A vector, a host cell and a pharmaceutical composition comprising said nucleic acid. A substantially purified polypeptide encoded by said nucleic acid, and a pharmaceutical composition comprising said polypeptide. An antibody binding to said polypeptide, and compositions containing said antibody. A method of producing said polypeptide. Methods of using said polypeptide (BAFF-R), nucleic acid (BAFF-R nucleic acid) or antibody in diagnosis, treatment, prevention or delaying conditions. Methods of using BAFF-R protein or nucleic acid in identifying compounds. An isolated nucleic acid molecule encoding at least a portion of a BAFF-R protein comprising an amino acid sequence selected from the group consisting of SEQ ID NOs 13 and 15-32 (e.g., as a portion of a chimeric protein), an isolated nucleic acid molecule encoding a BAFF-R protein comprising an amino acid sequence of SEQ ID NO:14 (e.g., as a portion of a chimieric protein), and the corresponding isolated polypeptides.

2. Claims: 39-43

A method of decreasing aggregation of a recombinantly expressed protein comprising, a) identifying regions of conserved amino acids between homologs of a target protein that aggregates as a recombinantly expressed protein, b) substituting at least one non-conserved amino acid in said target protein to form a mutated target protein; wherein said mutated target protein displays reduced aggregation when recombinantly expressed. Said method wherein a non-conserved nonpolar amino acid is changed to an uncharged polar amino acid (e.g., Pro, Ser or Ala).

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US 01/28006

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