



(51) International Patent Classification:

C07K 16/18 (2006.01) C07K 16/44 (2006.01)
C07K 16/36 (2006.01)

(21) International Application Number:

PCT/EP2014/002023

(22) International Filing Date:

24 July 2014 (24.07.2014)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

1300501-2 24 July 2013 (24.07.2013) SE

(71) Applicant: KLARESKOG, Lars [SE/SE]; Vanadisvägen 22B, S-113 46 Stockholm (SE).

(72) Inventors; and

(71) Applicants: MALMSTRÖM, Vivianne [SE/SE]; Vinter-
tullstorget 16, S-116 43 Stockholm (SE). ÅKERBLÖM
STEEN, Johanna Maria [SE/SE]; Grondalsvagan 48, 2tr,
S-117 68 Stockholm (SE). LIGHTWOOD, Daniel John
[GB/GB]; 208 Bath Road, Berkshire, SL13WE Slough
(GB). RAPECKI, Stephen Edward [GB/GB]; 208 Bath
Road Berkshire, SL13WE Slough (GB).

(74) Agent: HOLMBERG, Martin; BERGENSTRÄHLE & LINDVALL AB, P.O. Box 17704, S-118 93 Stockholm (SE).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM,

AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY,
BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM,
DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT,
HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR,
KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME,
MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ,
OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA,
SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM,
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM,
ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Published:

- with international search report (Art. 21(3))
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))
- with sequence listing part of description (Rule 5.2(a))

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

7 May 2015

(54) Title: NOVEL ANTIBODIES FOR THE DIAGNOSIS AND TREATMENT OF RHEUMATOID ARTHRITIS

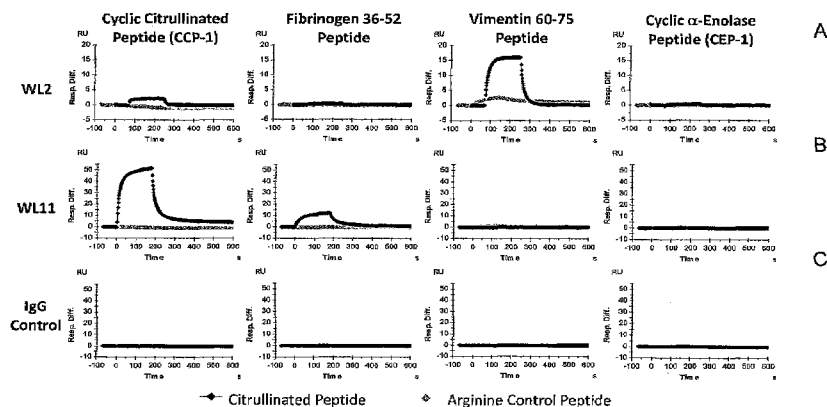


Fig. 1

(57) Abstract: Novel antibodies or binding fragments thereof, which exhibit specific binding to citrullinated epitopes are disclosed, as well as pharmaceutical compositions comprising said antibodies, use of the antibodies and compositions comprising the same, in diagnosis, in prognostics, treatment and/or alleviation of rheumatoid arthritis, as well as processes for generating and preparing said antibodies.

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2014/002023

A. CLASSIFICATION OF SUBJECT MATTER

INV. C07K16/18 C07K16/36 C07K16/44
ADD.

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)
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 practicable, search terms used)

EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	K. AMARA ET AL: "Monoclonal IgG antibodies generated from joint-derived B cells of RA patients have a strong bias toward citrullinated autoantigen recognition", SCIENCE, vol. 297, no. 5589, 25 February 2013 (2013-02-25), pages 2066-455, XP055149378, ISSN: 0036-8075, DOI: 10.1126/science.1073924 the whole document, in particular table 1 and online supplemental material S2 and S3 ----- -/--	1-4,8-22



Further documents are listed in the continuation of Box C.



See patent family 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 application or patent 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

9 March 2015

Date of mailing of the international search report

13/03/2015

Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040,
Fax: (+31-70) 340-3016

Authorized officer

Bayer, Annette

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2014/002023

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2009/147201 A2 (MODIQUEST B V [NL]; RAATS JOZEF MARIA HENDRIK [NL]; CHIRIVI RENATO GER) 10 December 2009 (2009-12-10) page 3, line 31 - page 4, line 5 page 12, line 15 - line 25 page 13, line 9 - line 15 page 22, line 18 - page 26, line 29 claims 1,3-29; figures 4,6,8-10; examples 1,10-12; sequence 38 -----	1-4,8-22
A	ZOLTÁN SZEKANECZ ET AL: "Anti-Citrullinated Protein Antibodies in Rheumatoid Arthritis: As Good as it Gets?", CLINICAL REVIEWS IN ALLERGY & IMMUNOLOGY, vol. 34, no. 1, 1 February 2008 (2008-02-01), pages 26-31, XP055149426, ISSN: 1080-0549, DOI: 10.1007/s12016-007-8022-5 the whole document, in particular page 28, right-hand column, last full paragraph - page 29, right-hand column, second paragraph -----	1-4,8-22
A	MCKAY BROWN ET AL: "Tolerance to single, but not multiple, amino acid replacements in antibody V-H CDR2: A means of minimizing B cell wastage from somatic hypermutation?", THE JOURNAL OF IMMUNOLOGY, THE AMERICAN ASSOCIATION OF IMMUNOLOGISTS, US, vol. 156, no. 9, 1 January 1996 (1996-01-01), pages 3285-3291, XP002649029, ISSN: 0022-1767 the whole document -----	1-4,8-14

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2014/002023

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 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.:
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 No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

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 fees, this Authority did not invite payment of additional fees.
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.:

4(completely); 1-3, 8-22(partially)

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/EP2014/002023

Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.c of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:
- a. (means)
- ☒ on paper
- ☒ in electronic form
- b. (time)
- ☒ in the international application as filed
- ☒ together with the international application in electronic form
- ☐ subsequently to this Authority for the purpose of search
2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments:

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. claims: 4(completely); 1-3, 8-22(partially)

An antibody that binds at least one citrullinated epitope, said antibody comprising a HCDR1 of SEQ ID NO: 19, a HCDR2 of SEQ ID NO: 20 and a HCDR3 of SEQ ID NO: 21 and related subject-matter.

2. claims: 5(completely); 1-3, 8-22(partially)

An antibody that binds at least one citrullinated epitope, said antibody comprising a HCDR1 of SEQ ID NO: 25, a HCDR2 of SEQ ID NO: 26 and a HCDR3 of SEQ ID NO: 27 and related subject-matter.

3. claims: 6(completely); 1-3, 8-22(partially)

An antibody that binds at least one citrullinated epitope, said antibody comprising a HCDR1 of SEQ ID NO: 31, a HCDR2 of SEQ ID NO: 32 and a HCDR3 of SEQ ID NO: 33 and related subject-matter.

4. claims: 7(completely); 1-3, 8-22(partially)

An antibody that binds at least one citrullinated epitope, said antibody comprising a HCDR1 of SEQ ID NO: 69, a HCDR2 of SEQ ID NO: 79 and a HCDR3 of SEQ ID NO: 88 and related subject-matter.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2014/002023

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2009147201 A2	10-12-2009	AU 2009253923 A1	10-12-2009
		CA 2726511 A1	10-12-2009
		CN 102056944 A	11-05-2011
		EA 201001865 A1	30-06-2011
		EP 2294086 A2	16-03-2011
		JP 5528436 B2	25-06-2014
		JP 2011523555 A	18-08-2011
		KR 20110015035 A	14-02-2011
		US 2011243945 A1	06-10-2011
		WO 2009147201 A2	10-12-2009
