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(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, 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, IS, JP, KE, KG, KM, 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, PE, PG, PH, PL, PT, RO, RS, RU, 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.

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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))*

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:
5 January 2012

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(54) Title: ANTIBODIES WITH MODIFIED AFFINITY TO FCRN THAT PROMOTE ANTIGEN CLEARANCE

(57) Abstract: An objective of the present invention is to provide methods for facilitating antigen-binding molecule-mediated antigen uptake into cells, methods for facilitating the reduction of antigen concentration in plasma, methods for increasing the number of antigens to which a single antigen-binding molecule can bind, methods for improving pharmacokinetics of antigen-binding molecules, antigen-binding molecules improved for facilitated antigen uptake into cells, antigen-binding molecules capable of facilitating the reduction of antigen concentration in plasma, antigen-binding molecules capable of repeatedly binding to antigens, antigen-binding molecules with improved pharmacokinetics, pharmaceutical compositions comprising such an antigen-binding molecule, and methods for producing those described above. The present inventors discovered that antigen uptake into cells is facilitated by an antibody having human FcRn-binding activity at the plasma pH and a lower antigen-binding activity at the early endosomal pH than at the plasma pH; such antibodies can increase the number of antigens to which a single antibody molecule can bind; the reduction of antigen in plasma can be facilitated by administering such an antibody; and antibody pharmacokinetics can be improved by using such antibodies.

INTERNATIONAL SEARCH REPORT

International application No
PCT/JP2011/001888

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07K16/00
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 practical, search terms used)
EPO-Internal, EMBASE, BIOSIS, Sequence Search, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	YEUNG YIK ANDY ET AL: "Engineering Human IgG1 Affinity to Human Neonatal Fc Receptor: Impact of Affinity Improvement on Pharmacokinetics in Primates", JOURNAL OF IMMUNOLOGY, AMERICAN ASSOCIATION OF IMMUNOLOGISTS, US, vol. 182, no. 12, 1 June 2009 (2009-06-01) , pages 7663-7671, XP002566420, ISSN: 0022-1767, DOI: DOI:10.4049/JIMMUNOL.0804182 figure 5 ----- -/--	1,5, 12-29, 48-57

X Further documents are listed in the continuation of Box C.

X 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 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
19 October 2011	02/11/2011

Name and mailing address of the ISA/	Authorized officer
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INTERNATIONAL SEARCH REPORT

International application No
PCT/JP2011/001888

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DALL'ACQUA W F ET AL: "Increasing the affinity of a human IgG1 for the neonatal Fc receptor: biological consequences", JOURNAL OF IMMUNOLOGY, AMERICAN ASSOCIATION OF IMMUNOLOGISTS, US, vol. 169, no. 9, 1 November 2002 (2002-11-01), pages 5171-5180, XP002384463, ISSN: 0022-1767 cited in the application the whole document	1-29, 48-57
A	WO 00/42072 A2 (GENENTECH INC [US]) 20 July 2000 (2000-07-20) claims 31, 32, 34	1-29, 48-57
A	SHIELDS R L ET AL: "High resolution mapping of the binding site on human IgG1 for FcgammaRI, FcgammaRII, FcgammaRIII, and FcRn and design of IgG1 variants with improved binding to the FcgammaR", JOURNAL OF BIOLOGICAL CHEMISTRY, THE AMERICAN SOCIETY OF BIOLOGICAL CHEMISTS, INC., BALTIMORE, MD, US, vol. 276, no. 9, 2 March 2001 (2001-03-02) , pages 6591-6604, XP002271092, ISSN: 0021-9258, DOI: DOI:10.1074/JBC.M009483200 the whole document	1-29, 48-57
X	US 2007/148164 A1 (FARRINGTON GRAHAM K [US] ET AL) 28 June 2007 (2007-06-28) paragraph [0307]; claims 1-3,5,11,13,20	6-11, 13-29

INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP2011/001888

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.:

1-29, 48-54(completely); 55-57(partially)

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 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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. claims: 1-5, 12, 48-54(completely); 13-29, 55-57(partially)

   Claims relating to antigen-binding molecules comprising an antigen-binding domain and a human FcRn binding domain with increased affinity to the human FcRn in the neutral pH range; methods for producing such molecules or methods of screening for such molecules

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2. claims: 6-11(completely); 13-29(partially)

   Claims relating to antigen-binding molecules comprising an antigen-binding domain and a human FcRn-binding domain which lead to enhanced antigen clearance

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3. claims: 30-47(completely); 55-57(partially)

   Claims relating to methods of increasing antigen clearance by increasing the human FcRn binding activity in the neutral pH range of an antigen-binding molecule wherein the antigen-binding molecule comprises an antigen-binding domain and a human FcRn binding domain

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/JP2011/001888

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 0042072 A2	20-07-2000	AU 778683 B2	16-12-2004
		AU 2008229968 A1	06-11-2008
		BR 0008758 A	04-12-2001
		CA 2359067 A1	20-07-2000
		CN 1343221 A	03-04-2002
		CN 1763097 A	26-04-2006
		EP 1141024 A2	10-10-2001
		EP 2364997 A2	14-09-2011
		EP 2366713 A2	21-09-2011
		HU 0104865 A2	29-04-2002
		JP 2003512019 A	02-04-2003
		JP 2010227116 A	14-10-2010
		KR 20060067983 A	20-06-2006
		KR 20080090572 A	08-10-2008
		KR 20090078369 A	17-07-2009
		KR 20100045527 A	03-05-2010
		MX PA01007170 A	30-07-2002
		NZ 539776 A	22-12-2006
		PL 349770 A1	09-09-2002
		US 2006194290 A1	31-08-2006
		US 2006194291 A1	31-08-2006
		ZA 200105484 A	29-07-2002
US 2007148164 A1	28-06-2007	NONE	