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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 February 2013

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(54) Title: NON-HUMAN ANIMALS EXPRESSING ANTIBODIES HAVING A COMMON LIGHT CHAIN

(57) Abstract: A genetically modified mouse is provided, wherein the mouse expresses an immunoglobulin light chain repertoire characterized by a limited number of light chain variable domains. Mice are provided that express just one or a few immunoglobulin light chain variable domains from a limited repertoire in their germline. Methods for making light chain variable regions in mice, including human light chain variable regions, are provided. Methods for making human variable regions suitable for use in multispecific binding proteins, e.g., bispecific antibodies, are provided.

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2012/034737

A. CLASSIFICATION OF SUBJECT MATTER
INV. A01K67/027
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)
A01K

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, BIOSIS, Sequence Search, EMBASE, 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	US 2006/015957 A1 (LONBERG NILS [US] ET AL) 19 January 2006 (2006-01-19)	1,2,5-7
Y	figure 52; examples 25-27	3,4
Y	WO 2004/009618 A2 (CRUCELL HOLLAND BV [NL]; VAN BERKEL PATRICK HENDRIKUS C [NL]; BRUS RON) 29 January 2004 (2004-01-29) claims 1-54	1-7
X,P	WO 2011/097603 A1 (REGENERON PHARMA [US]; MCWHIRTER JOHN [US]; MACDONALD LYNN [US]; STEVE) 11 August 2011 (2011-08-11) the whole document	1-20

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[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 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	Date of mailing of the international search report
14 November 2012	06/12/2012

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, Fax: (+31-70) 340-3016	Vollbach, Silke

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2012/034737

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)

   [X] on paper

   [X] in electronic form

   b. (time)

   [X] in the international application as filed

   [X] 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:

INTERNATIONAL SEARCH REPORT

International application No.
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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.:

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/US2012/034737

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	JAKOBOVITS AYA ET AL: "From XenoMouse technology to panitumumab, the first fully human antibody product from transgenic mice", NATURE BIOTECHNOLOGY, NATURE PUBLISHING GROUP, NEW YORK, NY, US, vol. 25, no. 10, 1 October 2007 (2007-10-01), pages 1134-1143, XP002556637, ISSN: 1087-0156, DOI: 10.1038/NBT1337 [retrieved on 2007-10-05] page 1135 - page 1136; figure 1	8-20
Y	MARVIN JONATHAN S ET AL: "Recombinant approaches to IgG-like bispecific antibodies", ACTA PHARMACOLOGICA SINICA, NATURE PUBLISHING GROUP, US, CN, vol. 26, no. 6, 1 June 2005 (2005-06-01), pages 649-658, XP002412036, ISSN: 1671-4083, DOI: 10.1111/J.1745-7254.2005.00119.X figures 2,3	8-20
Y	NICHOLSON I C ET AL: "Antibody repertoires of four- and five-feature translocus mice carrying human immunoglobulin heavy chain and kappa and lambda light chain yeast artificial chromosomes", THE JOURNAL OF IMMUNOLOGY, THE AMERICAN ASSOCIATION OF IMMUNOLOGISTS, US, vol. 163, 1 January 1999 (1999-01-01), pages 6898-6906, XP002974255, ISSN: 0022-1767 the whole document	1-20

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
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Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2006015957 A1	19-01-2006	US 7041871 B1	09-05-2006
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		WO 2011097603 A1	11-08-2011

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. claims: 1-7

   Genetically modified mice that express a limited number of human light chain variable (VL) domains and having deleted the germline Ig V kappa, J kappa gene segment or a combination thereof, wherein the kappa : lamda light chain ratio is about the same as the wildtype ratio.

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2. claims: 8-12

   Genetically modified mice that express a limited number of human light chain variable (VL) domains and having deleted the germline Ig V kappa, J kappa gene segment or a combination thereof, wherein the kappa light chain usage is 100 to 1000 fold.

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3. claims: 13-16

   Genetically modified mice that express a limited number of human light chain variable (VL) domains and having deleted the germline Ig V kappa, J kappa gene segment or a combination thereof, wherein the huma Vl domain is associated with a human heavy chaim variable domain.
