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[Continued on next page]

(54) Title: ULTRALONG COMPLEMENTARITY DETERMINING REGIONS AND USES THEREOF



(57) Abstract: Disclosed herein are immunoglobulin constructs comprising at least one immunoglobulin domain or fragment thereof; and a therapeutic polypeptide or derivative or variant thereof attached to or inserted into said immunoglobulin domain. Also provided are immunoglobulin constructs comprising a mammalian immunoglobulin heavy chain comprising at least a portion of a knob domain in the complementarity- determining region 3 (CDR3H) or fragment thereof; and a therapeutic polypeptide attached to or inserted into said knob domain of the CDR3H. Also provided are immunoglobulin constructs comprising a mammalian immunoglobulin heavy chain comprising at least a portion of a stalk domain in the complementarity-determining region 3 (CDR3H) or fragment thereof; and a therapeutic polypeptide attached to or inserted into said stalk domain of the CDR3H. Also described herein are methods and compositions comprising the immunoglobulin constructs described herein for treatment and prevention of a disease or condition in a subject.

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(88) **Date of publication of the international search report**:
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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2013/020903

A. CLASSIFICATION OF SUBJECT MATTER

C07K 16/18(2006.01)i, C40B 40/10(2006.01)i, C40B 40/08(2006.01)i, C12N 15/13(2006.01)i, C12N 15/63(2006.01)i, A61K 39/395(2006.01)i, A61P 35/00(2006.01)i

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 16/18; C07H 21/04; C40B 50/00; C40B 40/08; C07K 16/00; A61K 48/00

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
Korean utility models and applications for utility models
Japanese utility models and applications for utility models

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
eKOMPASS(KIPO internal) & Keywords: ultralong CDR3, antibody, cysteine motif, multiple cysteine residues

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	SAINI, SURINDER S. et al., `Exceptionally long CDR3H region with multiple cysteine residues in functional bovine IgM antibodies`, European Journal of Immunology, 05 August 1999, Vol. 29, No. 8, pp. 2420-2426. See figure 1; page 2421, 2423 and 2424; table 1; abstract.	1-6,9-11,38-40,48,50-53,70,71,73-76,84,86-89,109,110,114,115,117,118,120-122,159,161,163-165,172-174
A		7,8,12-15,19-37,49,54-69,72,77-83,85,90-108,111-113,116,119,123-134,136-158,187,188
A	US 2003-0170646 A1 (KAUSHIK, AZAD et al.) 11 September 2003 See figure 1; paragraph [0006]; abstract.	1-15,19-40,48-134,136-159,161,163-165,172-174,187,188
A	US 2011-0172125 A1 (LADNER, ROBERT C.) 14 July 2011 See paragraph [0004]; abstract.	1-15,19-40,48-134,136-159,161,163-165,172-174,187,188

☒ 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 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
24 June 2013 (24.06.2013)	**25 June 2013 (25.06.2013)**

Name and mailing address of the ISA/KR
Korean Intellectual Property Office
189 Cheongsa-ro, Seo-gu, Daejeon Metropolitan City, 302-701, Republic of Korea
Facsimile No. 82-42-472-7140

Authorized officer
HEO, Joo Hyung
Telephone No. 82-42-481-8150

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2013/020903

Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item1.c of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of:

   a. a sequence listing filed or furnished

   - ☐ on paper
   - ☒ in electronic form

   b. time of filing or furnishing

   - ☐ contained in the international application as filed
   - ☐ filed together with the international application in electronic form
   - ☒ furnished subsequently to this Authority for the purposes of search

2. ☐ In addition, in the case that more than one version or copy of a sequence listing 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.
PCT/US2013/020903

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.: 175-186
because they relate to subject matter not required to be searched by this Authority, namely:
Claims 175-186 pertain to methods for treatment of the human body, and thus relate to a subject matter which this International Searching Authority is not required, under Article 17(2)(a)(i) of the PCT and Rule 39.1(iv) of the Regulations under the PCT, to search.

2. ☒ Claims Nos.: 17, 18, 42-47, 169, 170, 176-186
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:
Claims 17, 18, 42-47, 169, 170 and 176-186 are unclear since they are referring to the multiple dependent claims which do not comply with PCT Rule 6.4(a).

3. ☒ Claims Nos.: 16, 41, 135, 160, 162, 166-168, 171, 175
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:

1. ☐ As all required addtional 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 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/US2013/020903

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 2010-028791 A1 (PHILOCHEM AG) 18 March 2010 See claims 1 and 8.	1-15,19-40,48-134,136-159,161,163-165,172-174,187,188
A	US 2003-0088074 A1 (HAMERS, RAYMOND et al.) 08 May 2003 See claim 11.	1-15,19-40,48-134,136-159,161,163-165,172-174,187,188

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.
PCT/US2013/020903

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2003-0170646 A1	11.09.2003	US 2003-0224433 A1	04.12.2003
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