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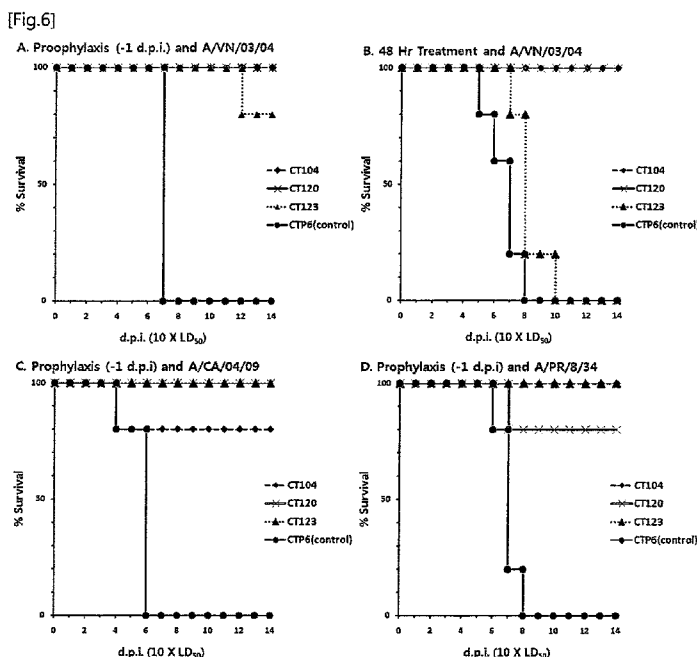
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[Continued on next page]

(54) Title: HUMAN MONOCLONAL ANTIBODIES DERIVED FROM HUMAN B CELLS AND HAVING NEUTRALIZING ACTIVITY AGAINST INFLUENZA A VIRUSES



(57) Abstract: The present invention relates to human monoclonal antibodies derived from human B cells present in the blood of patients who had recovered from infection with influenza A viruses, wherein the monoclonal antibodies have neutralizing activity against influenza A viruses. The anti-influenza A virus monoclonal antibody of the present invention has binding and neutralizing activities against at least one influenza A virus selected from the group consisting of influenza A virus H1, H2 and H5 subtypes, and thus it is useful for the prevention and treatment of a disease caused by the influenza A virus and is also useful for diagnosis of influenza A virus infection.

WO 2011/111966 A3



— *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))*

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— *with sequence listing part of description (Rule 5.2(a))*

INTERNATIONAL SEARCH REPORT

International application No.
PCT/KR2011/001563**A. CLASSIFICATION OF SUBJECT MATTER***C07K 16/10(2006.01)i, C12N 15/44(2006.01)i, C12N 15/63(2006.01)i, G01N 33/53(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 16/10

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: monoclonal antibody, H1N1, B cell

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	FRIESEN, R. H. E. et al, 'New class of monoclonal antibodies against severe influenza: prophylactic and therapeutic efficacy in ferrets.' PLoS One, 08 February 2010, Vol. 5, Issue 2, e9106. See the abstract, figure 2 and materials and methods.	1-28,35-36
X	THROSBY, M. et al, 'Heterosubtypic neutralizing monoclonal antibodies cross-protective against H5N1 and H1N1 recovered from human IgM+ memory B cells.' PLoS One, 16 December 2008, Vol. 3, Issue 12, e3942. See the abstract, figures 5, 10, table 3 and materials and methods.	1-28,35-36
X	US 2010-0040635 A1 (HOROWITZ LAWRENCE et al.) 18 February 2010 See the abstract, example 1 and claims 1-35, 59.	1-28,35-36
A	HANSON, B. et al, 'Passive immunoprophylaxis and therapy with humanized monoclonal antibody specific for influenza A H5 hemagglutinin in mice.' Respiratory Research, 14 October 2006, Vol. 7, issue 126. See the whole document.	1-28,35-36

 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

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Name and mailing address of the ISA/KR

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/KR2011/001563**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.: 29-34
because they relate to subject matter not required to be searched by this Authority, namely:
Claims 29-34 pertain to methods for treating of the human body by therapy, as well as diagnostic methods, 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.:
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.: 34,37
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:

(Continued on Supplemental Box)

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 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/KR2011/001563

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	HIFUMI, E. et al, 'Characteristic features of InfA-15 monoclonal antibody recognizing H1, H3 and H5 subtypes of hemagglutinin of influenza virus A type.' Journal of Bioscience and Bioengineering, 02 March 2010, Vol. 109, No. 6, Pages 598-608. See the whole document.	1-28,35-36
A	LIM, A. P. C. et al, 'Neutralizing human monoclonal antibody against H5N1 influenza HA selected from a Fab-phage display library,' Virology Journal. 28 October 2008, Vol. 5, Issue 130. See the abstract, figure 4 and methods.	1-28,35-36

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

PCT/KR2011/001563

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2010-0040635 A1	18.02.2010	AU 2009-228058 A1	01.10.2009
		CA 2719201 A1	01.10.2009
		CN 102046656 A	04.05.2011
		EP 2274334 A2	19.01.2011
		IL208313D0	30.12.2010
		JP 2011-516423 A	26.05.2011
		WO 2009-121004 A2	01.10.2009
		WO 2009-121004 A3	25.03.2010
		WO 2009-121004 A3	01.10.2009

Continuation of: Box III

Group I: Claims 1-3, (20-23, 25-28, 35-37 (all partial)) are directed to an anti-influenza A virus monoclonal antibody having neutralizing activity against influenza A virus H1, H2 or H5 subtype.

Group II: Claims 6, 7, 14, 15, (4, 5, 12, 13, 20-23, 25-28, 35-27(all partial)) are directed to an antibody comprising SEQ ID: NO 1-6 as each CDRs.

Group III: Claims 8, 9, 16, 17, (4, 5, 12, 13, 20-23, 25-28, 35-27(all partial)) are directed to an antibody comprising SEQ ID: NO 7, 2, 8-11 as each CDRs.

Group IV: Claims 10, 11, 18, 19, (4, 5, 12, 13, 20-23, 25-28, 35-27(all partial)) are directed to an antibody comprising SEQ ID: NO 12, 2, 13-16 as each CDRs.

Group V: Claim 25 is directed to a method of screening an antibody having a neutralizing activity against influenza virus A.

The only common technical feature between Groups I-V is an anti-influenza virus A monoclonal antibody. However, this feature is known in the art. For instant, PLoS One, Vol. 5, Issue 2, e9106 (2010.02.08) discloses a neutralizing human monoclonal antibody against influenza virus A, see the whole document. In the light of PLoS One, Vol. 5, Issue 2, e9106, this feature lacks novelty and/or inventive step.

Therefore, there is no technical relationship left over the prior art among the claimed inventions leaving the claims without a single general inventive concept. Hence there is lack of unity "a posteriori" (PCT Rules 13.1 and 13.2).