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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,
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FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL,
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2 October 2008

(54) **Title:** **ANTIBODIES TO SARS CORONAVIRUS**

(57) **Abstract:** The present invention relates to antibodies including human antibodies and antigen-binding portions thereof that specifically bind to human severe acute respiratory syndrome coronavirus (SARS-CoV S) protein, and that function to neutralize SARS-CoV. The invention also relates to antibodies that are bispecific, derivatized, single chain antibodies or portions of fusion proteins. The invention also relates to isolated heavy and light chain immunoglobulins derived from human anti- SARS-CoV S protein antibodies and nucleic acid molecules encoding such immunoglobulins. The present invention also relates to methods of using the antibodies and compositions for diagnosis and treatment. The invention also, provides gene therapy methods using nucleic acid molecules encoding the heavy and/or light immunoglobulin molecules that comprise the human anti-SARS-CoV S protein antibodies. The invention also relates to transgenic animals or plants comprising nucleic acid molecules of. the present invention.



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INTERNATIONAL SEARCH REPORT

International application No

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A. CLASSIFICATION OF SUBJECT MATTER

INV. C07K16/10

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, WPI Data, BIOSIS, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2006/051091 A (CRUCCELL HOLLAND BV [NL]; TER MEULEN JAN HENRIK [NL]; VAN DEN BRINK EDW) 18 May 2006 (2006-05-18) page 17 - page 87	1, 2, 10-16, 19-29
Y	page 24, line 27 - page 25, line 26	3-9, 17, 18
X	WO 2005/060520 A (DANA FARBER CANCER INST INC [US]; MARASCO WAYNE [US]; SUI JIANHUA [US]) 7 July 2005 (2005-07-07) the whole document	1, 10, 14-16, 26, 27
Y		3-9, 17, 18

☒ 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 document but published on or after the international filing date

¹L¹ 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

¹P" document published prior to the international filing date but later than the priority date claimed

"T¹" 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

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International application No

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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 2005/054469 A (CANADA NATURAL RESOURCES [CA]; BERRY JODY [CA] ; JONES STEVEN [CA] ; YUA) 16 June 2005 (2005-06-16) page 3 - page 31; figure 13	1, 10, 26, 27
Y	page 8 - page 12; figures 7-10	3-9, 17, 18
X	TER MEULEN J ET AL: "Human monoclonal antibody as prophylaxis for SARS coronavirus infection in ferrets" LANCET THE, LANCET LIMITED. LONDON, GB, vol. 363, no. 9427, 26 June 2004 (2004-06-26), pages 2139-2141, XP004778367 ISSN: 0140-6736 the whole document	1, 2, 10, 20-27
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X	wo 2005/056585 A (AGENCY SCIENCE TECH & RES [SG] ; SHEN SHUO [SG] ; HONG WANJIN [SG] ; LIM) 23 June 2005 (2005-06-23) page 2 - page 41; tables 3,4	1, 2, 10, 26, 27
X	BRINK VAN DEN EN ET AL: "Molecular and Biological Characterization of Human Monoclonal Antibodies to the Spike and Nucleocapsid Proteins of Severe Acute Respiratory Syndrome Coronavirus" JOURNAL OF VIROLOGY, THE AMERICAN SOCIETY FOR MICROBIOLOGY, US, vol. 79, no. 3, 1 February 2005 (2005-02-01), pages 1635-1644, XP009049268 ISSN: 0022-538X the whole document	1
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INTERNATIONAL SEARCH REPORT

International application No

PCT/US2007/012136

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>TRIPP, R A ET AL: "Monoclonal antibodies to SARS-associated coronavirus (SARS-CoV): Identification of neutralizing and antibodies reactive to S, N, M and E viral proteins"</p> <p>JOURNAL OF VIROLOGICAL METHODS, AMSTERDAM, NL, vol . 128, no. 1-2, 1 September 2005 (2005-09-01) , pages 21-28, XP004978384 ISSN: 0166-0934 page 24 - page 26; tables 1,2</p>	1
X	<p>SZU-CHIA LAI ET AL: "Characterization of neutralizing monoclonal antibodies recognizing a 15-residues epitope on the spike protein HR2 region of severe acute respiratory syndrome coronavirus (SARS-CoV)"</p> <p>JOURNAL OF BIOMEDICAL SCIENCE, KLUWER ACADEMIC PUBLISHERS, DO, vol . 12, no. 5, 1 October 2005 (2005-10-01) , pages 711-727, XP019272217 ISSN: 1423-0127 the whole document</p>	1
Y	<p>SOLA I ET AL: "Transgenic Mice Secreting Coronavirus Neutralizing Antibodies into the Milk"</p> <p>JOURNAL OF VIROLOGY, THE AMERICAN SOCIETY FOR MICROBIOLOGY, US, vol . 72, no. 5, 1 May 1998 (1998-05-01) , pages 3762-3772, XP002937185 ISSN: 0022-538X the whole document</p>	17, 18
Y	<p>US 5 849 992 A (MEADE HARRY [US] ET AL) 15 December 1998 (1998-12-15) the whole document</p>	17, 18
Y	<p>US 5 959 177 A (HEIN MICH B [US] ET AL) 28 September 1999 (1999-09-28) cited in the application column 3 - column 60</p>	17, 18
Y	<p>KO K ET AL: "Plant biopharming of monoclonal antibodies"</p> <p>VIRUS RESEARCH, AMSTERDAM, NL, vol . III , no. , 1, 1 July 2005 (2005-07-01) , pages 93-100, XP004894068 ISSN: 0168-1702 the whole document</p>	17, 18

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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A.	<p>ZHANG MEI-YUN ET AL: "Human monoclonal antibodies to the S glycoprotein and related proteins as potential therapeutics for SARS."</p> <p>CURRENT OPINION IN MOLECULAR THERAPEUTICS</p> <p>APR 2005,</p> <p>vol. 7, no. 2, April 2005 (2005-04), pages 151-156, XP002485797</p> <p>ISSN: 1464-8431</p> <p>the whole document</p> <p>-----</p>	

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2007/012136

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:

Although claims 20-29 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged, effects of the compound/composition.
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:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers allsearchable 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 the required additional search fees were paid.
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

Information on patent family members

International application No

PCT/US20070121 36

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
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