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— with sequence listing part of description published separately in electronic form and available upon request from the International Bureau
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4 December 2008

(54) Title: HUMAN ANTIBODIES THAT BIND CD70 AND USES THEREOF

(57) Abstract: The present disclosure provides isolated monoclonal antibodies that specifically bind to CD70 with high affinity, particularly human monoclonal antibodies. Preferably, the antibodies bind human CD70. In certain embodiments, the antibodies are capable of being internalized into CD70-expressing cells or are capable of mediating antigen dependent cellular cytotoxicity. Nucleic acid molecules encoding the antibodies of this disclosure, expression vectors, host cells and methods for expressing the antibodies of this disclosure are also provided. Antibody-partner molecule conjugates, bispecific molecules and pharmaceutical compositions comprising the antibodies of this disclosure are also provided. This disclosure also provides methods for detecting CD70, as well as methods for treating cancers, such as renal cancer and lymphomas, using an anti-CD70 antibody of this disclosure.

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**A. CLASSIFICATION OF SUBJECT MATTER**

IPC: C12P 21/08(2006.01)

USPC: 530/387.3

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)  
U.S. : 530/387.3

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)  
Please See Continuation Sheet

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X, P	WO 2007/038637 A2 (Terrett et al) 5 April 2007 (5.04.2007) see SEQ ID NO:1 and 6	1-11, 18-21, 28, 29, 36-41 and 51-56
X	US 20060083736 A1 (Law et al) 20 April 2006 (20.042006) see entire document, e.g., pages 1-2, 4 and 8	1-10, 18-20, 36-41, 51-56

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	"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
"E"	earlier application or patent published on or after the international filing date	"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
"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)	"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
"O"	document referring to an oral disclosure, use, exhibition or other means	"&"	document member of the same patent family
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search  
17 August 2008 (17.08.2008)

Date of mailing of the international search report

07 OCT 2008

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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:  
Please See Continuation 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 additional fees, this Authority did not invite payment of any 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.: 1-11,18-21,28,29,36-41 and 51-56
- 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.

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### BOX III. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

Group I, claims 1-11, 18-21, 28, 29, 36-41 and 51-56, insofar as the claims are drawn to an antibody-partner molecule conjugate comprising an isolated human monoclonal antibody, or an antigen-binding portion thereof, wherein the antibody binds human CD70 and comprises (a) a heavy chain variable region CDR1 comprising SEQ ID NO: 13; (b) a heavy chain variable region CDR2 comprising SEQ ID NO: 19; (c) a heavy chain variable region CDR3 comprising SEQ ID NO:25; (d) a light chain variable region CDR1 comprising SEQ ID NO:31; (e) a light chain variable region CDR2 comprising SEQ ID NO:37; (f) a light chain variable region CDR3 comprising SEQ ID NO:43, and a partner molecule, wherein the partner molecule is a therapeutic agent, or compositions thereof.

Group II, claims 1-10, 12, 18-20, 22, 28, 30, 36-41 and 51-56, insofar as the claims are drawn to an antibody-partner molecule conjugate comprising an isolated human monoclonal antibody, or an antigen-binding portion thereof, wherein the antibody binds human CD70 and comprises (a) a heavy chain variable region CDR1 comprising SEQ ID NO: 14; (b) a heavy chain variable region CDR2 comprising SEQ ID NO: 20; (c) a heavy chain variable region CDR3 comprising SEQ ID NO:26; (d) a light chain variable region CDR1 comprising SEQ ID NO:32; (e) a light chain variable region CDR2 comprising SEQ ID NO:38; (f) a light chain variable region CDR3 comprising SEQ ID NO:44, and a partner molecule, wherein the partner molecule is a therapeutic agent, or compositions thereof.

Group III, claims 1-10, 13, 18-20, 23, 28, 31, 36-41 and 51-56, insofar as the claims are drawn to an antibody-partner molecule conjugate comprising an isolated human monoclonal antibody, or an antigen-binding portion thereof, wherein the antibody binds human CD70 and comprises (a) a heavy chain variable region CDR1 comprising SEQ ID NO: 15; (b) a heavy chain variable region CDR2 comprising SEQ ID NO: 21; (c) a heavy chain variable region CDR3 comprising SEQ ID NO:27; (d) a light chain variable region CDR1 comprising SEQ ID NO:33; (e) a light chain variable region CDR2 comprising SEQ ID NO:39; (f) a light chain variable region CDR3 comprising SEQ ID NO:45, and a partner molecule, wherein the partner molecule is a therapeutic agent, or compositions thereof.

Group IV, claims 1-10, 14, 18-20, 24, 28, 32, 36-41 and 51-56, insofar as the claims are drawn to an antibody-partner molecule conjugate comprising an isolated human monoclonal antibody, or an antigen-binding portion thereof, wherein the antibody binds human CD70 and comprises (a) a heavy chain variable region CDR1 comprising SEQ ID NO: 16; (b) a heavy chain variable region CDR2 comprising SEQ ID NO: 22; (c) a heavy chain variable region CDR3 comprising SEQ ID NO:28; (d) a light chain variable region CDR1 comprising SEQ ID NO:34; (e) a light chain variable region CDR2 comprising SEQ ID NO:40; (f) a light chain variable region CDR3 comprising SEQ ID NO:46, and a partner molecule, wherein the partner molecule is a therapeutic agent, or compositions thereof.

Group V, claims 1-10, 15, 18-20, 25, 28, 33, 36-41 and 51-56, insofar as the claims are drawn to an antibody-partner molecule conjugate comprising an isolated human monoclonal antibody, or an antigen-binding portion thereof, wherein the antibody binds human CD70 and comprises (a) a heavy chain variable region CDR1 comprising SEQ ID NO: 17; (b) a heavy chain variable region CDR2 comprising SEQ ID NO: 23; (c) a heavy chain variable region CDR3 comprising SEQ ID NO:29; (d) a light chain variable region CDR1 comprising SEQ ID NO:35; (e) a light chain

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variable region CDR2 comprising SEQ ID NO:41; (f) a light chain variable region CDR3 comprising SEQ ID NO:47, and a partner molecule, wherein the partner molecule is a therapeutic agent, or compositions thereof.

Group VI, claims 1-10, 16, 18-20, 26, 28, 34, 36-41 and 51-56, insofar as the claims are drawn to an antibody-partner molecule conjugate comprising an isolated human monoclonal antibody, or an antigen-binding portion thereof, wherein the antibody binds human CD70 and comprises (a) a heavy chain variable region CDR1 comprising SEQ ID NO: 17; (b) a heavy chain variable region CDR2 comprising SEQ ID NO: 23; (c) a heavy chain variable region CDR3 comprising SEQ ID NO:75; (d) a light chain variable region CDR1 comprising SEQ ID NO:35; (e) a light chain variable region CDR2 comprising SEQ ID NO:41; (f) a light chain variable region CDR3 comprising SEQ ID NO:47, and a partner molecule, wherein the partner molecule is a therapeutic agent, or compositions thereof.

Group VII, claims 1-10, 17, 18-20, 27, 28, 35-41 and 51-60, insofar as the claims are drawn to an antibody-partner molecule conjugate comprising an isolated human monoclonal antibody, or an antigen-binding portion thereof, wherein the antibody binds human CD70 and comprises (a) a heavy chain variable region CDR1 comprising SEQ ID NO: 18; (b) a heavy chain variable region CDR2 comprising SEQ ID NO: 24; (c) a heavy chain variable region CDR3 comprising SEQ ID NO:30; (d) a light chain variable region CDR1 comprising SEQ ID NO:36; (e) a light chain variable region CDR2 comprising SEQ ID NO:42; (f) a light chain variable region CDR3 comprising SEQ ID NO:48, and a partner molecule, wherein the partner molecule is a therapeutic agent, or compositions thereof and an isolated human monoclonal antibody that comprises (a) a heavy chain variable region CDR1 comprising SEQ ID NO: 18; (b) a heavy chain variable region CDR2 comprising SEQ ID NO: 24; (c) a heavy chain variable region CDR3 comprising SEQ ID NO:30; (d) a light chain variable region CDR1 comprising SEQ ID NO:36; (e) a light chain variable region CDR2 comprising SEQ ID NO:42; (f) a light chain variable region CDR3 comprising SEQ ID NO:48.

Group VIII, claims 43-44, insofar as the claims are drawn to a method of inhibiting growth of a renal tumor cell expressing CD70 comprising contacting said renal tumor cell with the antibody-partner molecule conjugate comprising an isolated human monoclonal antibody, or an antigen-binding portion thereof, wherein the antibody binds human CD70, and a partner molecule, wherein the partner molecule is a therapeutic agent such that growth of said renal tumor cell is inhibited.

Group IX, claims 42-44, insofar as the claims are drawn to a method of inhibiting growth of a lymphoma tumor cell expressing CD70 comprising contacting said lymphoma tumor cell with the antibody-partner molecule conjugate comprising an isolated human monoclonal antibody, or an antigen-binding portion thereof, wherein the antibody binds human CD70, and a partner molecule, wherein the partner molecule is a therapeutic agent such that growth of said lymphoma tumor cell is inhibited.

Group X, claims 45-47, insofar as the claims are drawn to a method of treating renal cell carcinoma in a subject comprising administering to the subject an antibody-partner molecule conjugate comprising an isolated human monoclonal antibody, or an antigen-binding portion thereof, wherein the antibody binds human CD70, and a partner molecule, wherein the partner molecule is a therapeutic agent such that said renal cell carcinoma is treated in the subject.

Group XI, claims 45-47, insofar as the claims are drawn to a method of treating lymphoma in a subject comprising administering to the subject an antibody-partner molecule conjugate comprising an isolated human monoclonal antibody, or an antigen-binding portion thereof, wherein the antibody binds human CD70, and a partner molecule, wherein the partner molecule is a therapeutic agent such that said lymphoma is treated in the subject.

Group XII, claim 48, insofar as the claim is drawn to a method of treating an autoimmune disease in a subject comprising administering to the subject an antibody-partner molecule conjugate comprising an isolated human monoclonal antibody, or an antigen-binding portion thereof, wherein the antibody binds human CD70, and a partner molecule, wherein the partner molecule is a therapeutic agent such that said autoimmune disease is treated in the subject.

Group XIII, claim 48, insofar as the claim is drawn to a method of preventing an autoimmune disease in a subject comprising administering to the subject an antibody-partner molecule conjugate comprising an isolated human monoclonal antibody, or an antigen-binding portion thereof, wherein the antibody binds human CD70, and a partner molecule, wherein the partner molecule is a therapeutic agent such that said autoimmune disease is prevented in the subject.

Group XIV, claim 49, insofar as the claim is drawn to a method of treating inflammation in a subject comprising administering to the subject an antibody-partner molecule conjugate comprising an isolated human monoclonal antibody, or an antigen-binding portion thereof, wherein the antibody binds human CD70, and a partner molecule, wherein the partner molecule is a therapeutic agent such that the inflammation is treated in the subject.

Group XV, claim 49, insofar as the claim is drawn to a method of preventing inflammation in a subject comprising administering to the subject an antibody-partner molecule conjugate comprising an isolated human monoclonal antibody, or an antigen-binding portion thereof, wherein the antibody binds human CD70, and a partner molecule, wherein the partner molecule is a therapeutic agent such that the inflammation is prevented in the subject.

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Group XVI, claim 50, insofar as the claim is drawn to a method of treating a viral infection in a subject comprising administering to the subject an antibody-partner molecule conjugate comprising an isolated human monoclonal antibody, or an antigen-binding portion thereof, wherein the antibody binds human CD70, and a partner molecule, wherein the partner molecule is a therapeutic agent such that the viral infection is treated in the subject.

Group XVII, claims 61-63, insofar as the claims drawn to isolated nucleic acid molecule encoding a monoclonal antibody, or an antigen-binding portion thereof, comprising: a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 6 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 12, or expression vectors or host cells comprising said nucleic acid.

1. This International Searching Authority considers that the international application does not comply with the requirements of unity of invention (Rules 13.1, 13.2 and 13.3) for the reasons indicated below:

The inventions listed as Groups I-XVII do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

In this case, the special technical feature presented in claim I is an antibody-partner molecule conjugate comprising an isolated human monoclonal antibody, or an antigen-binding portion thereof, wherein the antibody binds human CD70, and a partner molecule, wherein the partner molecule is a therapeutic agent. However, US 2006/0083736 A1 (Law et al., April 2006) teach such human antibodies which specifically bind to human CD70 conjugated to therapeutic agents; see entire document (e.g., paragraphs [0002]-[0018]). Accordingly, the technical feature recited in claim 1, does not constitute a special technical feature as defined by PCT Rule 13.1, as it does not define a contribution over the prior art.

Therefore, the special technical feature of the invention of Group I is making an isolated human monoclonal antibody, or an antigen-binding portion thereof, wherein the antibody binds human CD70 and comprises (a) a heavy chain variable region CDR1 comprising SEQ ID NO: 13; (b) a heavy chain variable region CDR2 comprising SEQ ID NO: 19; (c) a heavy chain variable region CDR3 comprising SEQ ID NO:25; (d) a light chain variable region CDR1 comprising SEQ ID NO:31; (e) a light chain variable region CDR2 comprising SEQ ID NO:37; (f) a light chain variable region CDR3 comprising SEQ ID NO:43, and a partner molecule, wherein the partner molecule is a therapeutic agent, or compositions thereof.

Therefore, the special technical feature of the invention of Group II is making an isolated human monoclonal antibody, or an antigen-binding portion thereof, wherein the antibody binds human CD70 and comprises (a) a heavy chain variable region CDR1 comprising SEQ ID NO: 14; (b) a heavy chain variable region CDR2 comprising SEQ ID NO: 20; (c) a heavy chain variable region CDR3 comprising SEQ ID NO:26; (d) a light chain variable region CDR1 comprising SEQ ID NO:32; (e) a light chain variable region CDR2 comprising SEQ ID NO:38; (f) a light chain variable region CDR3 comprising SEQ ID NO:44, and a partner molecule, wherein the partner molecule is a therapeutic agent, or compositions thereof.

Therefore, the special technical feature of the invention of Group III, is making an isolated human monoclonal antibody, or an antigen-binding portion thereof, wherein the antibody binds human CD70 and comprises (a) a heavy chain variable region CDR1 comprising SEQ ID NO: 15; (b) a heavy chain variable region CDR2 comprising SEQ ID NO: 21; (c) a heavy chain variable region CDR3 comprising SEQ ID NO:27; (d) a light chain variable region CDR1 comprising SEQ ID NO:33; (e) a light chain variable region CDR2 comprising SEQ ID NO:39; (f) a light chain variable region CDR3 comprising SEQ ID NO:45, and a partner molecule, wherein the partner molecule is a therapeutic agent, or compositions thereof.

Therefore, the special technical feature of the invention of Group IV, is making an isolated human monoclonal antibody, or an antigen-binding portion thereof, wherein the antibody binds human CD70 and comprises (a) a heavy chain variable region CDR1 comprising SEQ ID NO: 16; (b) a heavy chain variable region CDR2 comprising SEQ ID NO: 22; (c) a heavy chain variable region CDR3 comprising SEQ ID NO:28; (d) a light chain variable region CDR1 comprising SEQ ID NO:34; (e) a light chain variable region CDR2 comprising SEQ ID NO:40; (f) a light chain variable region CDR3 comprising SEQ ID NO:46, and a partner molecule, wherein the partner molecule is a therapeutic agent, or compositions thereof.

Therefore, the special technical feature of the invention of Group V is making an isolated human monoclonal antibody, or an antigen-binding portion thereof, wherein the antibody binds human CD70 and comprises (a) a heavy chain variable region CDR1 comprising SEQ ID NO: 17; (b) a heavy chain variable region CDR2 comprising SEQ ID NO: 23; (c) a heavy chain variable region CDR3 comprising SEQ ID NO:29; (d) a light chain variable region CDR1 comprising SEQ ID NO:35; (e) a light chain variable region CDR2 comprising SEQ ID NO:41; (f) a light chain variable region CDR3 comprising SEQ ID NO:47, and a partner molecule, wherein the partner molecule is a therapeutic agent, or compositions thereof.

Therefore, the special technical feature of the invention of Group VI is making an isolated human monoclonal antibody, or an antigen-binding portion thereof, wherein the antibody binds human CD70 and comprises (a) a heavy chain variable region CDR1 comprising SEQ ID NO: 17; (b) a heavy chain variable region CDR2 comprising SEQ ID NO: 23; (c) a heavy chain variable region CDR3 comprising SEQ ID NO:75; (d) a light chain variable region CDR1 comprising SEQ ID NO:35; (e) a light chain variable region CDR2 comprising SEQ ID

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NO:41; (f) a light chain variable region CDR3 comprising SEQ ID NO:47, and a partner molecule, wherein the partner molecule is a therapeutic agent, or compositions thereof.

Therefore, the special technical feature of the invention of Group VII is making an isolated human monoclonal antibody, or an antigen-binding portion thereof, wherein the antibody binds human CD70 and comprises (a) a heavy chain variable region CDR1 comprising SEQ ID NO: 18; (b) a heavy chain variable region CDR2 comprising SEQ ID NO: 24; (c) a heavy chain variable region CDR3 comprising SEQ ID NO:30; (d) a light chain variable region CDR1 comprising SEQ ID NO:36; (e) a light chain variable region CDR2 comprising SEQ ID NO:42; (f) a light chain variable region CDR3 comprising SEQ ID NO:48, and a partner molecule, wherein the partner molecule is a therapeutic agent, or compositions thereof or making an isolated human monoclonal antibody that comprises (a) a heavy chain variable region CDR1 comprising SEQ ID NO: 18; (b) a heavy chain variable region CDR2 comprising SEQ ID NO: 24; (c) a heavy chain variable region CDR3 comprising SEQ ID NO:30; (d) a light chain variable region CDR1 comprising SEQ ID NO:36; (e) a light chain variable region CDR2 comprising SEQ ID NO:42; (f) a light chain variable region CDR3 comprising SEQ ID NO:48.

Therefore, the special technical feature of the invention of Group VIII is inhibiting the growth of a renal tumor cell expressing CD70.

Therefore, the special technical feature of the invention of Group IX is inhibiting the growth of a lymphoma tumor cell expressing CD70.

Therefore, the special technical feature of the invention of Group X is treating renal cell carcinoma in a subject.

Therefore, the special technical feature of the invention of Group XI is treating lymphoma in a subject.

Therefore, the special technical feature of the invention of Group XII is treating an autoimmune disease in a subject.

Therefore, the special technical feature of the invention of Group XIII is preventing an autoimmune disease in a subject.

Therefore, the special technical feature of the invention of Group XIV is treating inflammation in a subject.

Therefore, the special technical feature of the invention of Group XV is preventing inflammation in a subject.

Therefore, the special technical feature of the invention of Group XVI is treating a viral infection in a subject.

Therefore, the special technical feature of the invention of Group XVII is making an isolated nucleic acid molecule encoding a monoclonal antibody, or an antigen-binding portion thereof, comprising: a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 6 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 12, or expression vectors or host cells comprising said nucleic acid.

Accordingly, the inventions of Groups I- XVII do not share the same or corresponding special technical feature so as to form a single general inventive concept under PCT Rules 13.1 and 13.2.

Continuation of B. FIELDS SEARCHED Item 3:

WEST (PGPB, USPT, USOC, JPAB, EPAB, DWPI) and MEDLINE search terms CD70, humanized antibody

Sequence search of SEQ ID NO:13, 19, 25, 31, 37 and 43