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(54) Title: ANTIBODIES THAT IMMUNOSPECIFICALLY BIND TO TRAIL RECEPTORS

(57) Abstract: The present invention relates to antibodies and related molecules that immunospecifically bind to TRAIL receptor, TR7. Such antibodies have uses, for example, in the prevention and treatment of cancers and other proliferative disorders. The invention also relates to nucleic acid molecules encoding anti-TR7 antibodies, vectors and host cells containing these nucleic acids, and methods for producing the same. The present invention relates to methods and compositions for preventing, detecting, diagnosing, treating or ameliorating a disease or disorder, especially cancer and other hyperproliferative disorders, comprising administering to an animal, preferably a human, an effective amount of one or more antibodies or fragments or variants thereof, or related molecules, that immunospecifically bind to TRAIL receptor TR7.



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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US04/13900

A. CLASSIFICATION OF SUBJECT MATTER

IPC: C07K 16/00(2006.01);C12N 5/24(2006.01);A61K 39/395(2006.01)
C07K 14/00(2006.01)

USPC: 530/350,388.22;435/334;424/138.1

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. : 530/350, 388.22; 435/334; 424/138.1

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.
Y,T	VERMOT-DESROCHES C, et al. Characterization of monoclonal antibodies directed against trail or trail receptors. Cell Immunol. 2005 Jul-Aug; Vol. 236 (1-2): 86-9; see entire document (e.g., the abstract).	1-66 and 72-78
Y	GRIFFITH TS, et al. Functional analysis of TRAIL receptors using monoclonal antibodies. J Immunol. 1999 Mar 1; Vol. 162 (5): 2597-605; see entire document (e.g., the abstract).	1-66 and 72-78

☐ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

* Special categories of cited documents:	"T"
"A" document defining the general state of the art which is not considered to be of particular relevance	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

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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.: 1-66 and 72-78 (Species A)

- 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. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I. Claims 1-66 and 72-78, drawn to an antibody that binds TR7, a cell producing said antibody, and a kit comprising said antibody, and a method for treating, preventing, or ameliorating a cancer, said method comprising administering to an animal an antibody or fragment thereof.

Group II. Claims 67 and 68, insofar as the claims are drawn to a method for treating, preventing or ameliorating graft vs. host disease, said method comprising administering to an animal an antibody or fragment thereof.

Group III. Claims 67 and 68, insofar as the claims are drawn to a method for treating, preventing or ameliorating AIDS, said method comprising administering to an animal an antibody or fragment thereof.

Group IV. Claims 67 and 68, insofar as the claims are drawn to a method for treating, preventing or ameliorating a neurodegenerative disease, said method comprising administering to an animal an antibody or fragment thereof.

Group V. Claim 69, drawn to a method for inhibiting the growth of, or killing TR7-expressing cells, said method said method comprising administering to an animal an antibody or fragment thereof.

Group VI. Claim 70, drawn to a method for detecting expression of TR7, said method involving an immunoassay.

Group VII. Claim 71, insofar as the claim is drawn to a method for detecting or diagnosing cancer, said method involving an immunoassay.

Group VIII. Claim 71, insofar as the claim is drawn to a method for detecting or diagnosing a hyperproliferative disease other than cancer, said method involving an immunoassay.

Group IX. Claim 71, insofar as the claim is drawn to a method for prognosing cancer, said method involving an immunoassay.

Group X. Claim 71, insofar as the claim is drawn to a method for prognosing a hyperproliferative disease other than cancer, said method involving an immunoassay.

Group XI. Claim 71, insofar as the claim is drawn to a method for monitoring cancer, said method involving an immunoassay.

Group XII. Claim 71, insofar as the claim is drawn to a method for monitoring a hyperproliferative disease other than cancer, said method involving an immunoassay.

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

~~In order for more than one species to be examined, the appropriate additional examination fees must be paid. The species are as follows:~~

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Species A. The claims of any of Groups I-XII to the extent that those claims are directed to an antibody, fragment or derivative of the antibody produced by the cell line deposited under ATCC Deposit No. PTA-4178.

Species B. The claims of any of Groups I-XII to the extent that those claims are directed to an antibody, fragment or derivative of the antibody produced by the cell line deposited under ATCC Deposit No. PTA-4539.

Species C. The claims of any of Groups I-XII to the extent that those claims are directed to an antibody, fragment or derivative of the antibody produced by the cell line deposited under ATCC Deposit No. PTA-4376.

Species D. The claims of any of Groups I-XII to the extent that those claims are directed to an antibody, fragment or derivative of the antibody produced by the cell line deposited under ATCC Deposit No. PTA-4547.

The inventions listed as Groups I-XII 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:

The special technical feature of Group I is making and using an antibody that binds TR7.

The special technical feature of Group II is treating, preventing or ameliorating graft vs. host disease, said method comprising administering to an animal an antibody or fragment thereof.

The special technical feature of Group III is treating, preventing or ameliorating AIDS, said method comprising administering to an animal an antibody or fragment thereof.

The special technical feature of Group IV is treating, preventing or ameliorating a neurodegenerative disease, said method comprising administering to an animal an antibody or fragment thereof.

The special technical feature of Group V is inhibiting the growth of, or killing TR7-expressing cells, said method comprising administering to an animal an antibody or fragment thereof.

The special technical feature of Group VI is detecting expression of TR7; said method involving an immunoassay.

The special technical feature of Group VII is detecting or diagnosing cancer, said method involving an immunoassay.

The special technical feature of Group VIII is detecting or diagnosing a hyperproliferative disease other than cancer, said method involving an immunoassay.

The special technical feature of Group IX is prognosing cancer, said method involving an immunoassay.

The special technical feature of Group X is prognosing a hyperproliferative disease other than cancer, said method involving an immunoassay.

The special technical feature of Group XI is monitoring cancer, said method involving an immunoassay.

The special technical feature of Group XII is monitoring a hyperproliferative disease other than cancer, said method involving an immunoassay.

Accordingly, the inventions of Groups I-XII 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. In addition, PCT Rules 13.1 and 13.2 do not provide for a single general inventive concept to comprise more than the first mentioned product, the first mentioned method for making said product, and the first mentioned method for using said product.

The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons:

It is recognized that the claims are directed to different species of antibodies, which are fragments or derivatives of an antibody produced by a hybridoma cell line deposited under an ATCC accession number selected from the group consisting of PTA-4178, PTA-4539, PTA-4376, and PTA-4547. Each antibody produced by one of these different hybridoma cell lines is unique, as each comprises a unique amino acid sequence. Moreover, each fragment or derivative of each of these antibodies is unique, as each comprises unique light and heavy chain variable regions, which comprise unique sets of complementarity-determining regions (CDRs).

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Accordingly, the special technical feature of Species A of the inventions of Groups I-XII is making the antibody produced by the cell line deposited under ATCC Deposit No. PTA-4178, a derivative thereof, or a fragment thereof.

The special technical feature of Species B of the inventions of Groups I-XII is making the antibody produced by the cell line deposited under ATCC Deposit No. PTA-4539, a derivative thereof, or a fragment thereof.

The special technical feature of Species C of the inventions of Groups I-XII is making the antibody produced by the cell line deposited under ATCC Deposit No. PTA-4376, a derivative thereof, or a fragment thereof.

The special technical feature of Species D of the inventions of Groups I-XII is making the antibody produced by the cell line deposited under ATCC Deposit No. PTA-4547, a derivative thereof, or a fragment thereof.

Therefore, Species A-D of the inventions of Groups I-XII 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:

MEDLINE: ATCC PTA-4178; cell line; hybridoma; antibody; TR7; cancer; treatment; immunoconjugate; immuntoxin; cell line; kit; derivative; recombinant