

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
16 February 2006 (16.02.2006)

PCT

(10) International Publication Number
WO 2006/017531 A3

(51) International Patent Classification:
C12Q 1/68 (2006.01)

(21) International Application Number:
PCT/US2005/027480

(22) International Filing Date: 3 August 2005 (03.08.2005)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/599,425 6 August 2004 (06.08.2004) US

(71) Applicant (for all designated States except US): **GENENTECH, INC.** [US/US]; 1 DNA Way, South San Francisco, California 94080-4990 (US).

(72) Inventor; and

(75) Inventor/Applicant (for US only): **WAGNER, Klaus W.** [DE/US]; 509 Burlingame Avenue, Burlingame, California 94010 (US).

(74) Agent: **MARSCHANG, Diane L.**; Genentech, Inc., MS 49, 1 DNA Way, South San Francisco, California 94080 (US).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM,

AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

(88) Date of publication of the international search report:
27 April 2006

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: ASSAYS AND METHODS USING BIOMARKERS

(57) Abstract: Methods and assays examining expression of one or more biomarkers in a mammalian tissue or cell sample are provided. According to the disclosed methods and assays, detection of the expression of one or more such biomarkers is predictive or indicative that the tissue or cell sample will be sensitive to apoptosis-inducing agents such as Apo2L/TRAIL and anti-DR5 agonist antibodies. Certain biomarkers which may be examined include fucosyltransferases, in particular fucosyltransferase 3 (FUT3) and/or fucosyltransferase 6 (FUT6), as well as sialyl Lewis A and/or X antigens. Kits and articles of manufacture are also provided.



WO 2006/017531 A3

INTERNATIONAL SEARCH REPORT

International application No
PC/US2005/027480

A. CLASSIFICATION OF SUBJECT MATTER

C12Q1/68

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)
C12Q

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, PAJ, BIOSIS, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 97/25428 A (GENENTECH, INC) 17 July 1997 (1997-07-17) claims 11-6,21-23	1-38
A	WO 99/36535 A (GENENTECH, INC; ASHKENAZI, AVI, J; KELLEY, ROBERT, F; O'CONNEL, MARK,) 22 July 1999 (1999-07-22) claims 1-30 ----- -/--	1-38

☒ 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

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)

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.

Z document member of the same patent family

Date of the actual completion of the international search

17 February 2006

Date of mailing of the international search report

09/03/2006

Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Schmitt, A

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2005/027480

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	ASHKENAZI A ET AL: "SAFETY AND ANTITUMOR ACTIVITY OF RECOMBINANT SOLUBLE APO2 LIGAND" JOURNAL OF CLINICAL INVESTIGATION, NEW YORK, NY, US, vol. 104, no. 2, July 1999 (1999-07), pages 155-162, XP000973369 ISSN: 0021-9738 cited in the application the whole document	1-38
A	----- WALCZAK HENNING ET AL: "Tumoricidal activity of tumor necrosis factor-related apoptosis-inducing ligand in vivo" NATURE MEDICINE, NATURE PUBLISHING GROUP, NEW YORK, NY, US, vol. 5, no. 2, February 1999 (1999-02), pages 157-163, XP002176064 ISSN: 1078-8956 cited in the application the whole document	1-38
A	----- MATSUMOTO S ET AL: "Cimetidine increases survival of colorectal cancer patients with high levels of sialyl Lewis-X and sialyl Lewis-A epitope expression on tumour cells." BRITISH JOURNAL OF CANCER. 21 JAN 2002, vol. 86, no. 2, 21 January 2002 (2002-01-21), pages 161-167, XP002368202 ISSN: 0007-0920 the whole document	1-38
A	----- UGORSKI MACIEJ ET AL: "Sialyl Lewis(a): a tumor-associated carbohydrate antigen involved in adhesion and metastatic potential of cancer cells." ACTA BIOCHIMICA POLONICA. 2002, vol. 49, no. 2, 2002, pages 303-311, XP002368203 ISSN: 0001-527X cited in the application the whole document	1-38
A	----- AZUMA YUTARO ET AL: "Expression of cell surface Lewis X and Y antigens and FUT4 mRNA is increased in Jurkat cells undergoing apoptosis." BIOCHIMICA ET BIOPHYSICA ACTA. 11 JUN 2004, vol. 1672, no. 3, 11 June 2004 (2004-06-11), pages 157-163, XP002368228 ISSN: 0006-3002 the whole document -----	1-38

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2005/027480

Box 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 1 - 38 are directed to methods of treatment of or surgical methods performed on the human or animal body, the search has been carried out and based on the alleged effects of the compound.
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 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 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.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2005/027480

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9725428	A	17-07-1997	AU 729279 B2	01-02-2001
			AU 1824897 A	01-08-1997
			CA 2241572 A1	17-07-1997
			EP 0873407 A1	28-10-1998
			JP 2001510321 T	31-07-2001
			JP 2005237370 A	08-09-2005
			US 6030945 A	29-02-2000
WO 9936535	A	22-07-1999	AU 2325199 A	02-08-1999
			CA 2318029 A1	22-07-1999
			EP 1045906 A1	25-10-2000
			JP 2002508962 T	26-03-2002
			US 6740739 B1	25-05-2004