(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
7 March 2013 (07.03.2013)

WIPO | PCT

(10) International Publication Number
WO 2013/033609 A3

(51) **International Patent Classification:**
G01N 33/574 (2006.01) ***C07K 16/00*** (2006.01)

(21) **International Application Number:**
PCT/US20 12/053472

(22) **International Filing Date:**
31 August 2012 (31.08.2012)

(25) **Filing Language:** English

(26) **Publication Language:** English

(30) **Priority Data:**

61/529,500	31 August 2011 (31.08.2011)	US
61/542,403	3 October 2011 (03.10.2011)	US

(71) **Applicant** *(for all designated States except US):* **ONCO¬ CYTE CORPORATION** [US/US]; 1301 Harbor Bay Parkway, Alameda, CA 94502 (US).

(72) **Inventors; and**

(75) **Inventors/Applicants** *(for US only):* **CHAPMAN, Karen** [US/US]; 1301 Harbor Bay Parkway, Alameda, CA 94502 (US). **WAGNER, Joseph** [US/US]; 1301 Harbor Bay Parkway, Alameda, CA 94502 (US). **WEST, Michael** [US/US]; 1301 Harbor Bay Parkway, Alameda, CA 94502 (US). **KIDD, Jennifer, Lorrie** [US/US]; 1301 Harbor Bay Parkway, Alameda, CA 94502 (US). **PRENDES, Maria** [US/US]; 1301 Harbor Bay Parkway, Alameda, CA 94502 (US). **LACHER, Marcus** [CH/US]; 1301 Harbor Bay Parkway, Alameda, CA 94502 (US).

(74) **Agent: MITTLER, E., Stewart;** 1301 Harbor Bay Parkway, Alameda, CA 94502 (US).

(81) **Designated States** *(unless otherwise indicated, for every kind of national protection available):* AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, 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, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) **Designated States** *(unless otherwise indicated, for every kind of regional protection available):* ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— *with international search report (Art. 21(3))*

(88) **Date of publication of the international search report:**
27 June 2013

WO 2013/033609 A3

(54) **Title:** METHODS AND COMPOSITIONS FOR THE TREATMENT AND DIAGNOSIS OF CANCER

(57) **Abstract:** The invention relates to methods of detecting cancer in a sample obtained from subject. The invention also provides kits and reagents for detecting cancer as well therapeutics and methods of treating cancer.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 12/53472

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. Ill 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:
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 l+: claims 1-13 and 20, drawn to a method of detecting cancer in a sample comprising a) contacting the sample with one or more agents that detect expression of at least one of the specified markers, c) contacting a non-cancerous cell, with the one or more agents from b); and d) comparing the expression level of one or more of the markers in the sample with the expression level of one or more of the markers in the non-cancerous cell, wherein a higher level of expression in the sample compared to the non-cancerous cell indicates that the sample has cancer cells. The first invention (claims 1-7 and 11-13) is restricted to the SLC35D gene and an anti-SLC35D antibody. Should an additional fee(s) be paid, Applicant is invited to elect an additional gene(s)/marker(s) to be searched.

Group II: claims 14-19, drawn to a kit for detecting cancer in a sample comprising a plurality of agents that specifically bind to a molecule encoded for by the specified gene.
« *.*.*:« ::.*****:.*:« *:*« « .:.*:« « See supplemental Sheet to continue **********"

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 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.:
1-7 and 11-13, restricted to the SLC35D gene and an anti-SLC35D antibody

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/US 12/53472

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - G01N 33/574, C07K 16/00 (2013.01)
USPC - 435/7.23, 530/389.7

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)
USPC- 435/7.23, 530/389.7

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
USPC- 424/174.1 ; 435/7.1 , 436/501 , 530/387.1 , 530/387.3, 530/391 .3

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
PubWEST(PGPB,USPT,USOC,EPAB,JPAB),Google,Google Scholar: SLC35D, solute carrier family 35, UGTrel7, UGTREL7, UDP-glucuronic acid/UDP-N-acetylgalactosamine dual transporter, UDP-glucuronic acid/UDP-N-acetylgalactosamine transporter, UDP-GlcA/UDP-GalNAc transporter

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	Bret, et al. Expression of genes encoding for proteins involved in heparan sulphate and chondroitin sulphate chain synthesis and modification in normal and malignant plasma cells. Br J Haematol. 2009, 145(3):350-68; Abstract, pg 3, pg 4, 3rd para; pg 5, 6th para; pg 6, last para; pg 7, 2nd para; Table IV	1-7, 11, 13 ---------- 12
Y	Jafar-Nejad, et al. Role of glycans and glycosyltransferases in the regulation of Notch signaling. Glycobiology. 2010, 20(8):931-49; Abstract, pg 942, col 1, last para; pg 944, 1st col, last para	12
Y	Ranganathan, et al. Notch signalling in solid tumours: a little bit of everything but not all the time. Nat Rev Cancer May 201 1, 11(5):338-51	12
A	Nishimura, et al. Tissue-specific mRNA expression profiles of human solute carrier 35 transporters. Drug Metab Pharmacokinet. 2009, 24(1):91-9.	1-7 and 11-13
A	US 201 1/0053792 A1 (Kemmner) 03 March 201 1 (03.03.201 1) Abstract, para [0054], [0060], Table 1, item 6912667	1-7 and 11-13
A	US 2010/0003255 A1 (Croner, et al.) 07 January 201 0 (07.01 .2010) Abstract, para [0064], Table 1, item 80922; Table 2, item N80922	1-7 and 11-13
A	US 2010/0131432 A1 (Kennedy, et al.) 27 May 2010 (27.05.2010) Abstract, para [0222], [0223], [0229]-[0231], [0236], [0237], [0277], [0361], Table 4, item 3216276; claims 1, 8-10, 12	1-7 and 11-13
A	Kumamoto, et al. Increased expression of UDP-galactose transporter messenger RNA in human colon cancer tissues and its implication in synthesis of Thomsen-Friedenreich antigen and sialyl Lewis A/X determinants. Cancer Res. 2001 , 61(11):4620-7.	1-7 and 11-13

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

* 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 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

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
05 February 2013 (05.02.2013)	04 MAR 2013

Name and mailing address of the ISA/US	Authorized officer:
Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 12/53472

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	Vastermark, et al. Functional specialization in nucleotide sugar transporters occurred through differentiation of the gene cluster EamA (DUF6) before the radiation of Viridiplantae. BMC Evolutionary Biology ePub May 201 1, 11:123	1-7 and 11-13

In Continuation of Box III. Observations where unity of invention is lacking:

The inventions listed as Groups I+ and II 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 inventions of Group I+ do not include the inventive concept of a kit for detecting cancer in a sample, said kit comprising a plurality of agents that specifically bind to specified molecules, as required by Group II.

The inventions of Group II do not include the inventive concept of a method of detecting cancer in a sample comprising a) contacting the sample with one or more agents that detect expression of at least one of the specified markers, c) contacting a non-cancerous cell, with the one or more agents from b); and d) comparing the expression level of one or more of the markers in the sample with the expression level of one or more of the markers in the non-cancerous cell, wherein a higher level of expression in the sample compared to the non¬cancerous cell indicates that the sample has cancer cells, as required by Group I+.

The inventions of Group I+ share the technical feature of a method of detecting cancer in a sample comprising a) contacting the sample with one or more agents that detect expression of at least one of the specified marker, c) contacting a non-cancerous cell, with the one or more agents from b); and d) comparing the expression level of one or more of the markers in the sample with the expression level of one or more of the markers in the non-cancerous cell, wherein a higher level of expression in the sample compared to the non¬cancerous cell indicates that the sample has cancer cells. However, this shared technical feature does not represent a contribution over prior art as being anticipated by US 201 1/0206702 A1 to Polakis, et al. (25 August 201 1) (hereinafter "Polakis") that discloses said method (para [0028], "... a method of diagnosing the presence of a tumor in a mammal, wherein the method comprises detecting the level of expression of a gene encoding a TAT polypeptide (a) in a test sample of tissue cells obtained from said mammal, and (b) in a control sample of known normal non-cancerous cells of the same tissue origin or type, wherein a higher level of expression of the TAT polypeptide in the test sample, as compared to the control sample, is indicative of the presence of tumor in the mammal from which the test sample was obtained"). As said method was known in the art at the time of the invention, this cannot be considered a special technical feature that would otherwise unify the groups.

Another special technical feature of the inventions listed as Group I+ is the specific expression detecting agent recited therein. The inventions do not share a special technical feature, because antibody and nucleic acid do not share a special technical feature as they are distinct expression detecting agents, and further because Polakis discloses both of them (para [0028], nucleic acids; para [0029], antibody). As no significant structural similarities can readily be ascertained among the ligands. Without a shared special technical feature, the inventions lack unity with one another.

Another special technical feature of the inventions listed as Group I+ is the specific marker recited therein. As no significant structural similarities can readily be ascertained among the markers, the inventions do not share a special technical feature. Without a shared special technical feature, the inventions lack unity with one another.

Groups I+ and II therefore lack unity under PCT Rule 13 because they do not share a same or corresponding special technical feature.