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(54) Title: COMBINATION TREATMENTS DIRECTED TOWARD PROGRAMMED DEATH LIGAND-1 (PD-L1) POSITIVE CANCERS

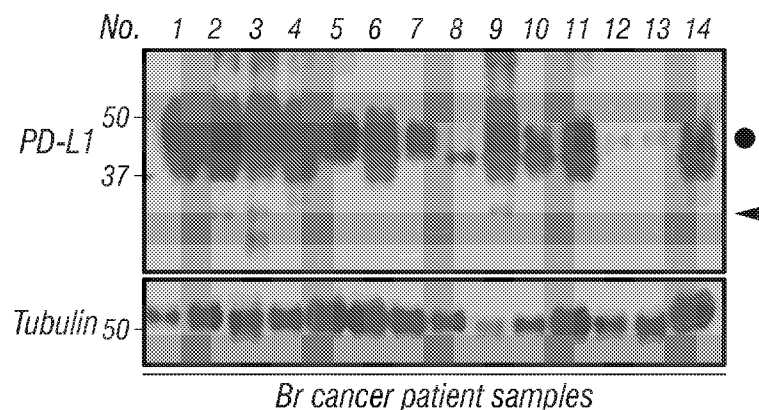


FIG. 1A

(57) Abstract: Provided are methods of treating cancers using a sugar analog, including methods of sensitizing cancers to EGF inhibitor-, PD-1 inhibitor-, and/or PD-L1 inhibitor-based therapies by administering a sugar analog, such as, for example, 2-Deoxy-D-glucose (2-DG), F-Fucose, and 2-F-peracetyl-Fucose.



Published:

- *with international search report (Art. 21(3))*
- *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US17/25539

A. CLASSIFICATION OF SUBJECT MATTER

IPC - A61K 9/00, 9/20, 9/48, 31/70, 31/7004 45/06 (2017.01)

CPC - A61K 9/00, 9/20, 9/48, 9/0095, 9/4858, 9/2059, 9/4866, 31/70, 31/7004, 45/06

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)

See Search History document

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

See Search History document

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

See Search History document

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X ----- Y	US 2005/0245462 A1 (TIDMARSH) November 3, 2005; abstract; paragraphs [0025], [0029], [0068], [0071]	1, 3/1, 5/3/1, 6/5/3/1 --- 2, 3/2, 5/3/2, 6/5/3/2, 17-18, 19/17-18, 20/19/17-18, 35-36, 37/35-36, 38/35-36, 39/38/35-36, 41-42, 43/41-42, 47-48, 49/47-48, 50/49/47-48
Y	US 2016/0067337 A1 (BRISTOL-MYERS SQUIBB COMPANY) March 10, 2016; abstract; paragraph [0014]	2, 3/2, 5/3/2, 6/5/3/2, 35-36, 37/35-36, 38/35-36, 39/38/35-36, 47-48, 49/47-48, 50/49/47-48
Y	US 2015/0359883 A1 (GERON CORPORATION) December 17, 2015; abstract	17-18, 19/17-18, 20/19/17-18
Y	WO 2016/007513 A1 (DANA-FARBER CANCER INSTITUTE, INC.) January 14, 2016; abstract; paragraph [00044]; claims 1-2	41-42, 43/41-42
Y	US 2015/0376216 A1 (CENTRE NATIONAL DE LA RECHERCHE SCIENTIFIQUE, et al.) December 31, 2015; paragraph [0015]	37/35-36, 43/41-42

☐ 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 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

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11 SEP 2017

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US17/25539

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.: 4, 7-16, 21-34, 40, 44-46, 51-52
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 Supplemental Page-

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.:
1-2, 3/1-2, 5/3/1-2, 6/5/3/1-2, 17-18, 19/17-18, 20/19/17-18, 35-36, 37/35-36, 38/35-36, 39/38/35-36, 41-42, 43/41-42, 47-48, 49/47-48, 50/49/47-48

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/US17/25539

.-***-Continued from Box No. 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 1-3, 5-6, 17-20, 35-39, 41-43, and 47-50 are directed toward methods of treating cancers using a sugar analog, including methods of sensitizing cancers to EGF inhibitor-, PD-1 inhibitor-, and/or PD-L1 inhibitor-based therapies.

Group II, Claims 53-55 are directed toward a method of characterizing a sample comprising measuring the level of PD-L1 glycosylation in the sample.

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 special technical features of Group I include methods of treating cancers using a sugar analog, including methods of sensitizing cancers to EGF inhibitor-, PD-1 inhibitor-, and/or PD-L1 inhibitor-based therapies, not present in Group II; the special technical features of Group II include measuring the level of PD-L1 glycosylation in a sample, not present in Group I.

Groups I and II share the technical features including: PD-L1 and glycosyl or sugar moieties.

However, these shared technical features are previously disclosed by the article 'PD-L1 protein expression in breast cancer is rare, enriched in basal-like tumors and associated with infiltrating lymphocytes' by Ali et al. (hereinafter 'Ali').

Ali discloses glycosylated PD-L1 (glycosylated PD-L1; page 1489, second column, second paragraph).

Since none of the special technical features of the Groups I and II inventions are found in more than one of the inventions, and since all of the shared technical features are previously disclosed by the Ali reference, unity of invention is lacking.