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(54) Title: METHODS AND COMPOSITIONS FOR IDENTIFYING AND TREATING SUBJECTS AT RISK OF POOR CANCER SURVIVAL

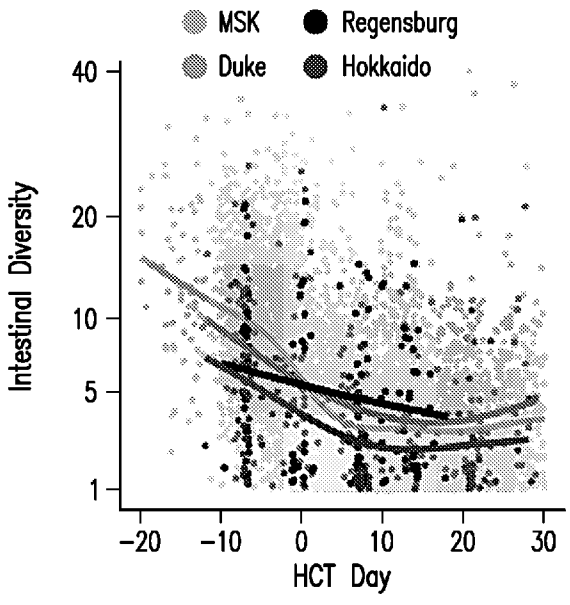

FIG. 1A

(57) Abstract: The present disclosure relates to compositions and methods for predicting cancer survival in a subject after receiving a treatment (*e.g*, allogeneic hematopoietic-cell transplantation). The present disclosure further discloses compositions and methods for treating said subject.

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 21/18582

A. CLASSIFICATION OF SUBJECT MATTER

IPC - A61K 35/74, C12N 1/21 (2021.01)

CPC - A61K 35/741, A61K 35/74, A61K 45/06, A61P 35/00, C12Q 1/04, A61K 2035/115

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	WO 2018/064165 A2 (BOARD OF REGENTS, THE UNIVERSITY OF TEXAS SYSTEM) 05 April 2018 (05.04.2018) para [0007], [0030], [00129], [00130], [00165]	1, 3, 6/(1,3), 33, (35-37)/33, 43 ---- 5/(1,3)
Y	US 2016/0143961 A1 (EPIVA BIOSCIENCE, INC.) 26 May 2016 (26.05.2016) Claim 1, Claim 15	5/(1,3)

☐ 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
"D" document cited by the applicant in the international application
"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
26 July 2021	SEP 09 2021
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-8300	Authorized officer Lee Young Telephone No. PCT Helpdesk: 571-272-4300

INTERNATIONAL SEARCH REPORT

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Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.c of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of a sequence listing:

   a. ☐ forming part of the international application as filed:

      ☐ in the form of an Annex C/ST.25 text file.

      ☐ on paper or in the form of an image file.

   b. ☐ furnished together with the international application under PCT Rule 13*ter*.1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.

   c. ☒ furnished subsequent to the international filing date for the purposes of international search only:

      ☒ in the form of an Annex C/ST.25 text file (Rule 13*ter*.1(a)).

      ☐ on paper or in the form of an image file (Rule 13*ter*.1(b) and Administrative Instructions, Section 713).

2. ☒ In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that forming part of the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

INTERNATIONAL SEARCH REPORT

International application No.
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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.: 7-24, 28-32, 38-42, 45-46
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:

- see extra sheet for Box No. III Observations where unity of invention is lacking -

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, 3, (5-6)(in part), 33, (35-37)(in part), 43

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 21/18582

Continuation of:
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 searched, the appropriate additional search fees must be paid.

Group I: claims 1, 3, (5-6)(in part), 33, (35-37)(in part), 43, drawn to a method for treating a subject having a cancer, comprising: identifying a subject that is not likely to exhibit cancer survival if the level of the diagnostic bacterium or spore thereof is lower than the reference diagnostic bacterium or spore thereof.

Group II: claims 2, 4, (5-6)(in part), 34, (35-37)(in part), 44, drawn to a method for treating a subject having a cancer, comprising: identifying a subject that is not likely to exhibit cancer survival if the level of the diagnostic bacterium or spore thereof is higher than the reference diagnostic bacterium or spore thereof.

Group III: claims 25-27, drawn to a pharmaceutical composition comprising a therapeutic bacterium or a spore thereof.

Group IV: claims 47-50, drawn to a kit for identifying a subject having a cancer as not likely to exhibit cancer survival, wherein the kit comprising means for detecting the level of a diagnostic bacterium or a spore thereof.

The inventions listed as Groups I through IV 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:

Special Technical Features

Groups I and II include the special technical feature of a method which differs from the special technical feature of a composition, as disclosed by Groups III and IV.

Group I includes the special technical feature of identifying a subject that is not likely to exhibit cancer survival if the level of the diagnostic bacterium or spore thereof is lower than the reference diagnostic bacterium or spore thereof, not required by Group II.

Group II includes the special technical feature of identifying a subject that is not likely to exhibit cancer survival if the level of the diagnostic bacterium or spore thereof is higher than the reference diagnostic bacterium or spore thereof, not required by Group I.

Group III includes the special technical feature of a pharmaceutical composition, not required by Group IV.

Group IV includes the special technical feature of a kit comprising means for detecting the level of a diagnostic bacterium or a spore thereof, not required by Group III.

Common Technical Features

The inventions of Groups I-IV share the technical feature of a bacterium or a spore.
The inventions of Groups I, II and IV share the technical feature of detecting the level of a diagnostic bacterium or a spore thereof.
The inventions of Groups I and II share the technical feature of determining a level of a diagnostic bacterium or a spore thereof in a sample of the subject; and comparing the level of the diagnostic bacterium or spores thereof to a reference diagnostic bacterium or a spore thereof level.

However, these shared technical features do not represent a contribution over prior art in view of WO 2018/064165 A2 Board of Regents, The University of Texas System (hereinafter "Univ Texas").

Univ Texas teaches (instant claim 1) a method for treating a subject having a cancer (para [0030], a method of predicting a response (e.g., patient survival) to an immune checkpoint inhibitor in a patient having a cancer comprising detecting a microbial profile in a sample obtained from said patient.), comprising:
(a) determining a level of a diagnostic bacterium or a spore thereof in a sample of the subject (para [00129], methods of obtaining a microbiome profile, comprising the steps of: i) obtaining a sample obtained from a subject (e.g., a human subject).);
(b) comparing the level of the diagnostic bacterium or spores thereof to a reference diagnostic bacterium or a spore thereof level (para [00129], ii) isolating one or more bacterial species from the sample, iii) isolating one or more nucleic acids from at least one bacterial species, iv) sequencing the isolated nucleic acids, and v) comparing the sequenced nucleic acids to a reference nucleic acid sequence.);
(c) identifying the subject as not likely to exhibit cancer survival if the level of the diagnostic bacterium or spore thereof is lower than the reference diagnostic bacterium or spore thereof (para [00130], the microbiome profile is identified to be favorable for immune checkpoint therapy. A favorable microbial profile would have a high relative abundance of one or more bacterial species from the phylum Firmicutes, class Clostridia, order Clostridiales, family Ruminococcaceae, genus Ruminococcus, genus Hydrogenoanaerobacterium, genus Faecalibacterium, phylum Actinobacteria, class Coriobacteriia, order Coriaobacteriales, family Coriobacteriaceae, domain Archaea, phylum Cyanobacteria, phylum Euryarchaeota or family Christensenellaceae., Note, Univ Texas teaches "the subject is likely to exhibit cancer survival, if the level of the bacterium is higher than the reference" is the same as the claimed "the subject as not likely to exhibit cancer survival if the level of the diagnostic bacterium is lower than the reference".); and

----continued on next sheet----

Continuation of:
Box No. III. Observations where unity of invention is lacking

(d) treating the subject identified as not likely to exhibit cancer survival with a cancer treatment (para [0030], a patient is administered an immune checkpoint inhibitor if the patient is predicted to have a favorable response to the immune checkpoint inhibitor.),
wherein the diagnostic bacterium is a bacterium of the taxonomic group selected from the group consisting of: Clostridia, Actinobacteria, Ruminococcus, Ruminococcaceae, Cyanobacteria and any combinations thereof (para [00130]).

As said technical features were known in the art at the time of the invention, these cannot be considered special technical features that would otherwise unify the groups.

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

Item 4 (continued):
Claims 7-24, 28-32, 38-42, 45-46 are held unsearchable because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).