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(54) Title: METHODS FOR PROGNOSING, DIAGNOSING, AND TREATING GASTRIC CANCER

(57) Abstract: The current disclosure provides an miRNA signature for detecting gastric cancer. Aspects of the disclosure relate to a method for treating, evaluating, prognosing, and/or diagnosing a patient for treating a patient with gastric cancer, the method comprising treating the patient for gastric cancer after the expression level of miR-30a-5p, miR-134-5p, miR-337-3p, miR-659-3p, and miR-3917 has been determined in a sample from the patient.

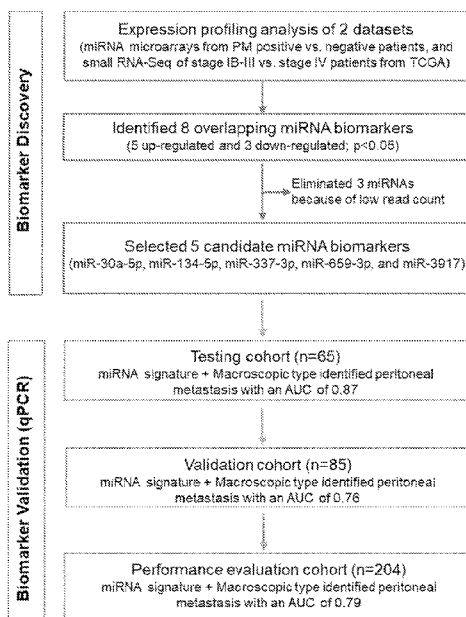


FIG. 1A



**Declarations under Rule 4.17:**

- *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*
- *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))*

**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))*

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

23 July 2020 (23.07.2020)

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US19/67942

## A. CLASSIFICATION OF SUBJECT MATTER

IPC - C12Q 1/6886; G01N 33/50; A61B 5/145; A61P 35/00 (2020.01)

CPC - C12Q 1/6886; G01N 33/5091; A61B 5/145; A61P 35/00

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	US 2017/0233822 A1 (AGENCY FOR SCIENCE, TECHNOLOGY AND RESEARCH, et al.) 17 August 2017; paragraphs [0005], [0007], [0047], [0053], [0129], [0174]; Claims 1 and 11	1, 4, 46, 75, 121-122
A	WO 2018/165532 A1 (BAYLOR RESEARCH INSTITUTE) 13 September 2018; paragraphs [0005]-[0008]	1, 4, 46, 75, 121-122
A	US 2012/0214690 A1 (THE OHIO STATE UNIVERSITY) 23 August 2012; entire document	1, 4, 46, 75, 121-122

 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

"&amp;" document member of the same patent family

Date of the actual completion of the international search

31 March 2020 (31.03.2020)

Date of mailing of the international search report

10 JUN 2020

Name and mailing address of the ISA/US

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# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US19/67942

**Box No. I** Nucleotide and/or amino acid sequence(s) (Continuation of item I.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 13ter.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 13ter.1(a)).
    - on paper or in the form of an image file (Rule 13ter.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.

PCT/US19/67942

**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.: 9-45, 49-74, 78-120  
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.:  
1-8, 46-48, 75-77, 121-122; miR-30a-5p (biomarker)

**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/US19/67942

\*\*\*-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+, 1-8, 46-48, 75-77, 121-122 and miR-30a-5p (biomarker) are directed toward methods for treating, evaluating, prognosing, and/or diagnosing a patient for treating a patient with gastric cancer.

The methods will be searched to the extent that they encompass miR-30a-5p (first exemplary biomarker). Applicant is invited to elect additional biomarker(s), and available as an option within at least one searchable claim, to be searched. Additional biomarker(s) will be searched upon the payment of additional fees. It is believed that claims 1 (in-part), 4 (in-part), 46 (in-part), 75 (in-part), and 121-122 (each in-part) encompass this first named invention and thus these claims will be searched without fee to the extent that they encompass miR-30a-5p (biomarker). Applicants must specify the searchable claims that encompass any additionally elected biomarker(s). Applicants must further indicate, if applicable, the searchable claims which encompass the first named invention, if different than what was indicated above for this group. Failure to clearly identify how any paid additional invention fees are to be applied to the "+" group(s) will result in only the first claimed invention to be searched/examined. An exemplary election would be miR-134-Sp (biomarker).

No technical features are shared between the biomarkers of Groups I+ and, accordingly, these groups lack unity a priori.

Additionally, even if Groups I+ were considered to share the technical features including: a method for treating a patient with gastric cancer, the method comprising treating the patient for gastric cancer after the expression level of one or more biomarkers has been determined in a sample from the patient; a method for evaluating a gastric cancer patient comprising measuring the level of expression of one or more biomarkers in a sample from the patient; a method of prognosing and/or diagnosing a patient with gastric cancer comprising a) measuring the level of expression of one or more biomarkers in a sample from the patient; b) comparing the level(s) of expression to a control sample(s) or control level(s) of expression; and, c) prognosing and/or diagnosing the patient based on the levels of measured expression; a kit comprising 1, 2, 3, 4, or 5 detection agents for determining expression levels of biomarkers for gastric cancer; these shared technical features are previously disclosed by WO 2018/165532 A1 (BAYLOR RESEARCH INSTITUTE) (hereinafter 'Baylor').

Baylor discloses a method for treating a patient with gastric cancer (gastric cancer treatment; abstract; claim 1), the method comprising treating the patient for gastric cancer after the expression level of one or more biomarkers has been determined in a sample from the patient (method comprising treating the patient for gastric cancer after the expression level of one or more biomarkers has been determined in a sample from the patient; claim 1); a method for evaluating a gastric cancer patient comprising measuring the level of expression of one or more biomarkers in a sample from the patient (a method for evaluating a gastric cancer patient comprising measuring the level of expression of one or more biomarkers in a sample from the patient; claim 1); a method of prognosing and/or diagnosing a patient with gastric cancer (a method of prognosing and/or diagnosing a patient with gastric cancer; abstract; paragraph [0003]) comprising a) measuring the level of expression of one or more biomarkers in a sample from the patient (measuring the level of expression of one or more biomarkers in a sample from the patient; claim 1); b) comparing the level(s) of expression to a control sample (s) or control level(s) of expression (b) comparing the level(s) of expression to a control sample(s) or control level(s) of expression; claim 1); and, c) prognosing and/or diagnosing the patient based on the levels of measured expression (prognosing and/or diagnosing the patient based on the levels of measured expression; abstract; paragraph [0003]); a kit comprising 1, 2, 3, 4, or 5 detection agents for determining expression levels of biomarkers for gastric cancer (a kit comprising detection agents for determining expression levels of biomarkers for gastric cancer; claims 1, 55).

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