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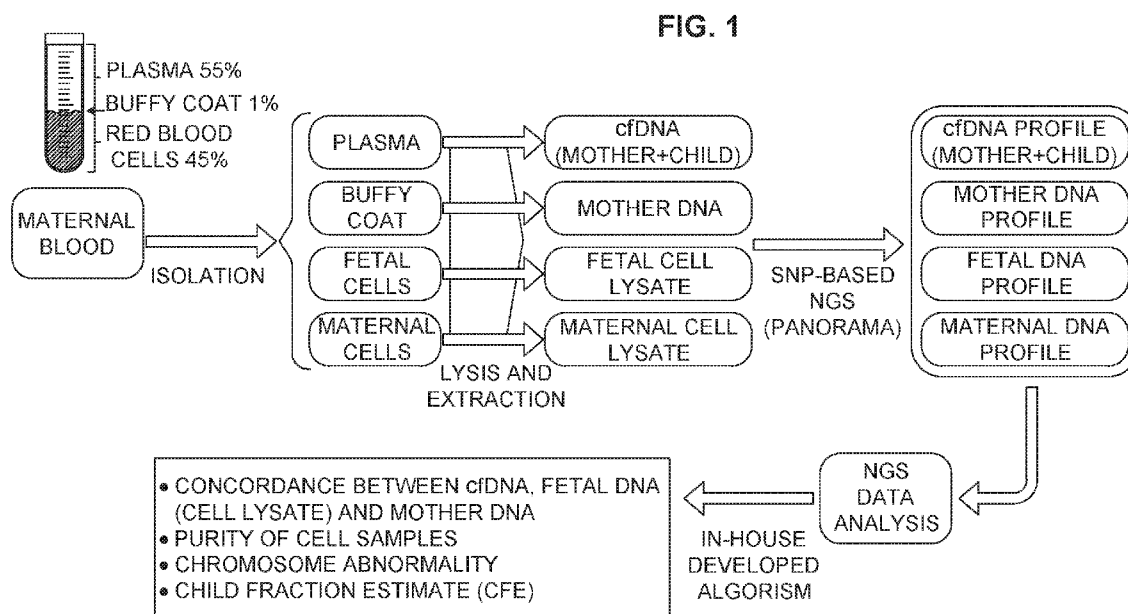
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(54) Title: METHODS FOR ANALYSIS OF CIRCULATING CELLS



(57) **Abstract:** The invention provides methods for characterizing and analyzing circulating cells. In particular, the invention provides methods for confirming the identity of an individual cell and that the obtained sample was derived from a single cell of a defined identity. Additional methods are provided for analyzing single cell samples to determine copy number variation and aneuploidy in the context of circulating fetal cells, microdeletions, single nucleic acid variations associated with cancer, or early relapse of cancer and metastasis.



TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW,
KM, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

— *of inventorship (Rule 4.17(iv))*

Published:

— *with international search report (Art. 21(3))*
— *before the expiration of the time limit for amending the
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amendments (Rule 48.2(h))*

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

30 July 2020 (30.07.2020)

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2019/066544

A. CLASSIFICATION OF SUBJECT MATTER
INV. C12Q1/6806 C12Q1/6886
ADD.

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 practicable, search terms used)

EPO-Internal, BIOSIS, EMBASE, FSTA, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2010/075459 A1 (CELULA INC [US]; OLIPHANT ARNOLD R [US] ET AL.) 1 July 2010 (2010-07-01) paragraphs [0009] - [0011], [0014], [0020] paragraphs [0033] - [0034], [0074] -----	1-15
X	US 2016/186253 A1 (TALASAZ AMIRALI HAJHOSSEIN [US] ET AL) 30 June 2016 (2016-06-30) paragraphs [0006] - [0009], [0014], [0086]; figure 8 paragraphs [0114] - [0118], [0208] - [0213] -----	1-15



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

24 March 2020

Date of mailing of the international search report

25/06/2020

Name and mailing address of the ISA/

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2019/066544

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. 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 additional sheet

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 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.:

1-15

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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-15

Method of determining the origin of circulating cell
suspected to be of fetal origin.

2. claims: 16-29, 31-40

Method for monitoring and detection of early relapse.

3. claim: 30

Method of determining the origin of circulating cells
suspected to be donor cells.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2019/066544

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