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Declarations under Rule 4.17:

— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*

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:
5 October 2017

(54) Title: IMMUNOASSAY CONTROLS AND THE USE THEREOF

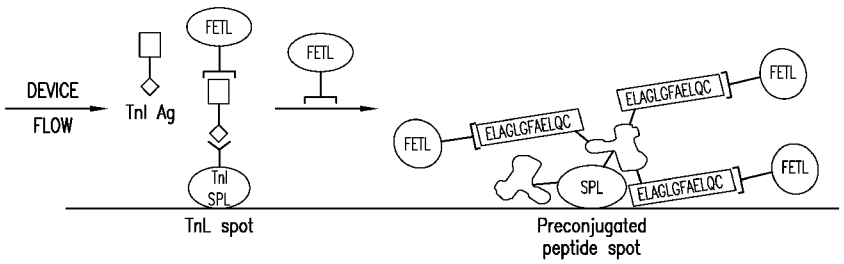

FIG. 1

(57) Abstract: The present invention relates to compositions and methods use in designing immunoassay controls. In various aspects, the invention provides synthetic peptides comprising the sequence CPRRPYIL or an analog thereof; ELAGLGFAELQC or an analog thereof; and CDWRKNIDAL or an analog thereof; specific binding reagents that bind to a CPRRPYIL, ELAGLGFAELQC or CDWRKNIDAL peptide; methods of producing such reagents; and assays utilizing such reagents to provide assay controls signals that are unrelated to the measurement of the analyte or analytes of interest in that no reagents used in the analyte assay(s) contribute to the control signal.

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US17/21211

A. CLASSIFICATION OF SUBJECT MATTER

IPC - G01N 33/53, 33/563, 33/68; C07K 7/06, 16/18 (2017.01)

CPC - G01N 33/53, 33/563, 33/68; C07K 7/06, 16/18

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.
A	US 2014/0377879 A1 (ALERE SWITZERLAND GMBH) December 25, 2014; paragraphs [0018]-[0020], [0027], [0045], [0056], [0064], [0069], [0083]-[0084], [0087], [0091], [0105], [0120], [0172]	1, 2, 3/1-2, 4/1-2, 5/4/1-2, 25-27, 28/25-27
A	US 2001/0008774 A1 (MAY, et al.) July 19, 2001; paragraphs [0001], [0006]-[0007], [0016], [0019]	1, 2, 3/1-2, 4/1-2, 5/4/1-2, 25-27, 28/25-27
A	US 2006/0036072 A1 (LICHA, et al.) February 16, 2006; paragraph [0161]; SEQ ID NO: 194	1, 2, 3/1-2, 4/1-2, 5/4/1-2, 25-27, 28/25-27
A	US 2003/0105299 A1 (ACHILEFU, et al.) June 5, 2003; paragraph [0049]; SEQ ID NO: 8	1, 2, 3/1-2, 4/1-2, 5/4/1-2, 25-27, 28/25-27

☐ 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	Date of mailing of the international search report
02 August 2017 (02.08.2017)	25 AUG 2017
Name and mailing address of the ISA/ Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-8300	Authorized officer Shane Thomas PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

Form PCT/ISA/210 (second sheet) (January 2015)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US17/21211

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.: 6-24, 29, 30, 35, 36, 41, 42
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:
-***-Continued Within the Next Supplemental Box-***-

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 (in-part), 2 (in-part), 3 (in-part), 4 (in-part), 5 (in-part), 25-28

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/US17/21211

-***-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.

Groups I+, Claims 1-5, 25-28, 31-34, 37-40 and SEQ ID NO: 1 are directed toward an assay device and method.

The device and method will be searched to the extent they encompass a peptide encompassing SEQ ID NO: 1 (first exemplary peptide) and an antibody that binds thereto. Applicant is invited to elect additional peptide(s), with specified SEQ ID NO: for each, and corresponding antibody(ies) thereto, to be searched. Additional peptide sequence(s) and corresponding antibody(ies) thereto will be searched upon the payment of additional fees. It is believed that claims 1 (in-part), 2 (in-part), 3 (in-part), 4 (in-part), 5 (in-part) and 25-28 encompass this first named invention and thus these claims will be searched without fee to the extent that they encompass SEQ ID NO: 1 (peptide) and antibody(ies) thereto. Applicants must specify the claims that encompass any additionally elected peptide sequence(s) and corresponding antibody(ies) thereto. Applicants must further indicate, if applicable, the 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 a peptide encompassing SEQ ID NO: 4 (first exemplary elected peptide) and antibodies thereto.

No technical features are shared between the peptide sequences and/or antibodies of Groups I+ and, accordingly, these groups lack unity a priori.

Groups I+ share the technical features including: a device comprising; a substrate defining at least one diagnostic lane; a sample application zone; a dried reagent zone; and a detection zone comprising at least one control zone and at least one assay zone; wherein: (a) the at least one control zone comprises an antibody that specifically binds a peptide, and wherein the dried reagent zone comprises the peptide; or (b) the at least one control zone comprises a peptide and wherein the dried reagent zone comprises an antibody that specifically binds the peptide; and a method of normalising an assay result for an analyte of interest, comprising; providing an immunoassay device comprising a sample application zone, a reagent zone, and a diagnostic lane comprising at least one control binding zone and at least one assay binding zone, wherein the assay binding zone is a region of the device which generates a detectable signal indicative of the amount of the analyte of interest present in a sample, wherein: (a) the at least one control binding zone comprises an antibody that specifically binds a peptide and the reagent zone comprises the peptide; or (b) the at least one control binding zone comprises a peptide and the reagent zone comprises an antibody that specifically binds the peptide; applying the sample to the sample application zone; forming a mixture within the reagent zone between the sample and a reagent incorporated in the reagent zone; flowing the sample reagent mixture along the diagnostic lane: detecting a signal resulting from binding of the antibody that specifically binds a peptide at the control zone; detecting a signal indicative of the amount of the analyte of interest present in the sample at the assay zone; and modulating the response at the assay zone based on the response obtained at the control zone.

However these shared technical features are previously disclosed by US 2014/0377879 A1 to Alere Switzerland GmbH (hereinafter 'Alere') in view of US 2001/0008774 A1 to May et al. (hereinafter 'May').

Alere discloses a device (a device; abstract) comprising; a substrate (a porous carrier (a substrate); paragraph [0018]) defining at least one diagnostic (diagnostic; paragraph [0064]) lane (microchannel (lane); paragraph [0069]); a sample application zone (a sample receiving portion of a test strip (a sample application zone); paragraph [0091]); a dried reagent zone (a dried reagent zone; paragraphs [0019], [0032], [0105]); and a detection zone (a detection zone; paragraph [0019]) comprising at least one control zone (comprising at least one control zone; paragraphs [0045], [0056]) and at least one assay zone (and at least one test (assay) zone; paragraphs [0019], [0083]); wherein the dried reagent zone comprises an antibody that specifically binds a peptide (wherein the reagent zone comprises a specific binding reagent (an antibody) labelled with a detectable particle; paragraphs [0019], [0027], [0105]); and a method of normalising an assay result for an analyte of interest (a method of normalising an assay result for an analyte of interest; paragraphs [0087], [0172]), comprising; providing an immunoassay device (providing a device comprising a specific binding agent (an immunoassay device); abstract, paragraphs [0019], [0066]) comprising a sample application zone (comprising a sample receiving portion of a test strip (a sample application zone); paragraph [0091]), a reagent zone (a reagent zone; paragraphs [0019], [0027], [0032]), and a diagnostic (diagnostic; paragraph [0064]) lane (microchannel (lane); paragraph [0069]) comprising at least one control binding zone comprising at least one control zone; paragraphs [0045], [0056]) and at least one assay zone (and at least one test (assay) zone; paragraphs [0019], [0083]), wherein the assay binding zone is a region of the device which generates a detectable signal indicative of the amount of the analyte of interest present in a sample (wherein the assay binding zone is a region of the device which generates a detectable signal indicative of the amount of the analyte of interest present in a sample; paragraphs [0019], [0020], [0028]), wherein: the at least one reagent zone comprises an antibody that specifically binds a peptide (wherein the reagent zone comprises a specific binding reagent (an antibody) labelled with a detectable particle; paragraphs [0019], [0027], [0105]); applying the sample to the sample application zone (applying the sample to the sample receiving (application) zone; paragraph [0091]); forming a mixture within the reagent zone between the sample and a reagent incorporated in the reagent zone (forming a mixture within the reagent zone between the sample and a reagent incorporated in the reagent zone; paragraphs [0019], [0091]); flowing the sample reagent mixture along the diagnostic lane (flowing the sample reagent mixture along the diagnostic lane; paragraphs [0019], [0064], [0091]): detecting a signal indicative of the amount of the analyte of interest present in the sample at the assay zone (detecting a signal indicative of the amount of the analyte of interest present in the sample at the assay zone; paragraphs [0087], [0091], [0172]); and modulating the response at the assay zone based on the response obtained at the control zone (normalizing (modulating) the response at the assay zone based on the response obtained at the control zone; paragraphs [0087], [0091], [0172]).

Alere does not disclose wherein: (a) the at least one control zone comprises an antibody that specifically binds a peptide, or (b) the at least one control zone comprises a peptide; and detecting a signal resulting from binding of the antibody that specifically binds a peptide at the control zone

May discloses an analytical device (an analytical device; abstract) for a liquid sample (for a liquid sample; abstract) applied to a porous carrier (applied to a porous carrier; abstract), including a control zone comprising an immobilized analyte that binds to excess labelled specific binding reagent (a control zone comprising an immobilized analyte that binds to excess labelled specific binding reagent; paragraphs [0008], [0016], [0019]).

-***-Continued Within the Next Supplemental Box-***-

-***-Continued from Previous Supplemental Box-***-

It would have been obvious to a person of ordinary skill in the art at the time of the invention was made to have modified the disclosure of Alere to have provided a control zone comprising an analyte, such as a peptide hormone capable of being bound by a specific binding reagent, such as a mobile antibody, as disclosed by May, in the control zone disclosed by Alere, in order to enable the accurate normalization and calibration of the amount of the same analyte detected in the assay zone, as disclosed by Alere.

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 a combination of the Alere and May references, unity of invention is lacking.