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(54) Title: METHODS AND KITS FOR DETECTION OF 11-DEHYDRO-THROMBOXANE B2

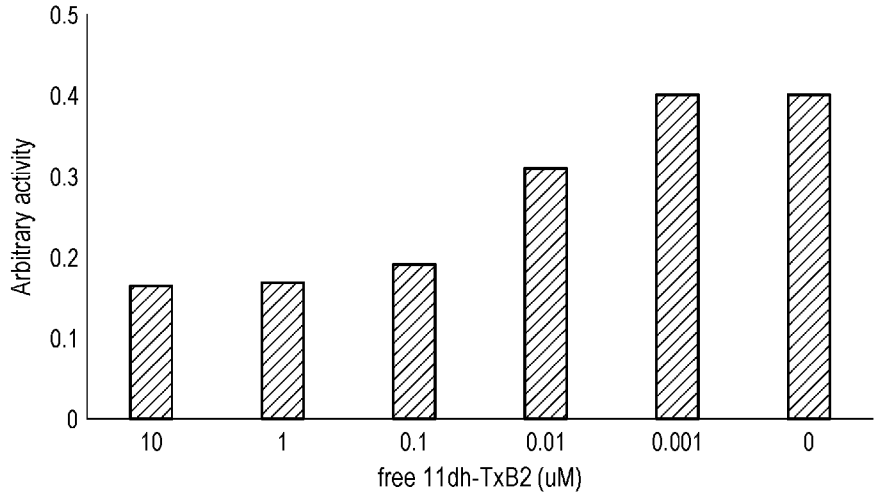

FIG. 1

(57) Abstract: Methods, compositions and kits for quantitatively determining specified amounts of 11dhTxB2 in microliter to milliliter quantities of a given sample, wherein, the sample is a biological fluid. Specifically, the biological fluid is a quantity of 1 ml or less of urine from a human subject. The methods may be in the form of consolidated assays that can be run in a high throughput, automation format, such as an enzyme-linked immunosorbent assay (ELISA). Further, the ELISA may be modified into a chemiluminescence assay in order to increase sensitivity and linear range and to reduce the reaction time.

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[Continued on next page]

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— *with international search report (Art. 21(3))*

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 19/38994

A. CLASSIFICATION OF SUBJECT MATTER

IPC - G01N 33/558, G01N 33/70, G01N 33/9486 (2020.01)

CPC - G01N 33/558, G01N 33/70, G01N 33/9486

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 2004/0126826 A1 (YUSUF et al.) 01 July 2004 (01.07.2004) Abstract; para [0014]; para [0023]; para [0035]; para [0057]; para [0061]; para [0063-[0064]; para [0067]; para [0073]-[0074]; para [0077]; para [0079];-para [0080]; para [0082]; para [0091]; para [0103]; claim 11	15-19 --- 1-14, 20-23
Y	US 2014/0273269 A1 (EPINEX DIAGNOSTICS INC) 18 September 2014 (18.09.2014) para [0008]; para [0056]; para [0070]; claim 1; claim 5-6; claim 20	1-12, 20-21
Y	MORELLO et al. "A chemiluminescent immunoassay for urinary thromboxane B2" Prostaglandins. July 1991, Vol. 42 No. 1 pp 55-70 especially, Abstract; page 60, para 2; page 60, Fig. 1; page 68, para 2	13-14
Y	US 2006/0275860 A1 (KJAER et al.) 07 December 2006 (07.12.2006) Abstract; para [0005]-[0006]; para [0068]	22
Y	CN 1912594 A (FUJIAN HONG CHENG BIOLOG MEDICI) 14 February 2007 (14.02.2007) Abstract; page 4, para 3; claim 1 translation at page 2, para 5	23
Y	US 5,798,273 A (SHULER et al.) 25 August 1998 (15.08.1998) Abstract; col. 1, ln 14-21; claim 1-2	1-5

☐ 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
6 April 2020	15 MAY 2020
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

International application No.
PCT/US 19/38994

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:
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 1-14, directed to an assay or method of testing at least one biological sample for the presence and amount of thromboxane A2 metabolite (11dhTxB2).

Group II, claims 15-23, directed to a kit.

The inventions listed as Groups I-II do not relate to a single special technical feature under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

----------continued on supplemental 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 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.:

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/US 19/38994

Continuation of Box III: observations where unity of invention is lacking:

Special technical features:

Group I has the special technical feature of providing an assay, providing a sample, and measuring/detecting a signal, that is not required by Group II.

Group II has the special technical feature of a kit, that is not required by Group I.

Common technical features:

Groups I-II share the common technical feature of an assay selected from the group consisting of enzyme linked immunosorbent assay, chemiluminescence assay and quantitative lateral flow assay for quantitatively determining specified amounts of a metabolite present in a sample, wherein the sample is a biological fluid, wherein the assay comprises at least one control run in parallel with the sample as tested.

However, this shared technical feature does not represent a contribution over prior art, because this shared technical feature is previously disclosed by US 2004/0126826 A1 to Yusuf et al. (hereinafter 'Yusuf').

Yusuf discloses a quantitative lateral flow assay or chemiluminescence assay for the identification and quantification of metabolites indicating aspirin sensitivity in a sample (Abstract- "detecting the concentration of a metabolite in a fluid sample is provided. Devices..."; para [0014]- "object of one aspect of the present invention to provide a rapid, non-invasive, reproducible method for determining aspirin resistance... Determination of the degree of resistance to aspirin is used to predict the risk of a cardiovascular event or other condition that would benefit from lowering thromboxane A2 levels"; [0064] "chemiluminescent labels"; para [0082]- "measurement of analyte or simultaneous measurement of two or more analytes (such as 11-dehydro thromboxane B 2 and creatinine) can also be performed using...lateral flow"), wherein the sample is a biological fluid (para [0057] "Various methods can be used to measure the level of thromboxane-A2 metabolites in a sample of biological fluid"), wherein the assay comprises at least one control run in parallel with the sample as tested (para [0030]-[0034] "an immunoassay device is provided comprising a first strip having an antibody moiety which specifically binds the analyte to be determined and a second strip containing at least one standardized concentration of the analyte to be determined, wherein upon addition of a test sample, analyte in the test sample competes with analyte on the second strip for binding by the antibody moiety...The device comprises a first strip of absorbent material having a recognition molecule dispersed therein and a second non-absorbent strip have predetermined amounts of an analyte standard immobilized thereon, wherein upon immersion of the device in a sample fluid the recognition molecules are mobilized to competitively bind to the analyte on the second strip or the analyte in the sample fluid whereby the amount of recognition molecule bound to the second strip is inversely proportional to the concentration of analyte in the sample fluid"; [0082]).

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

Therefore, Group I-II inventions lack unity under PCT Rule 13 because they do not share the same or corresponding special technical feature.