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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))*
— *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))*
— *of inventorship (Rule 4.17(iv))*

Published:
— *with international search report (Art. 21(3))*
— *with sequence listing part of description (Rule 5.2(a))*

(88) Date of publication of the international search report:
03 April 2025 (03.04.2025)

(54) Title: UNIVERSAL LAMP FOR CAPTURING NON-COGNATE NUCLEIC ACIDS IN LAMP CONCATEMERS

(57) Abstract: Universal LAMP can be used to capture target nucleic acid sequences within LAMP concatemers without having to design new LAMP primers for each target. These universal LAMP primers can be used in a variety of amplification techniques and can be included in a kit.

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 24/34311

A. CLASSIFICATION OF SUBJECT MATTER

IPC - INV. C12Q 1/68, C12Q 1/6806, C12Q 1/6853 (2024.01)
ADD. C12Q 1/6897, C12Q 1/6844 (2024.01)

CPC - INV. C12Q 1/686, C12Q 1/6806, C12Q 1/6848, C12Q 1/6853
ADD. C12Q 1/689, C12Q 1/6895, C12Q 2525/301, C12Q 2531/119

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 2015/0126382 A1 (WARTHOE) 07 May 2015 (07.05.2015) abstract, para [0072], [0131], [0133], [0134], [0138], [0147]	1-4
A	US 2021/0403979 A1 (BOARD OF REGENTS, THE UNIVERSITY OF TEXAS SYSTEM) 30 December 2021 (30.12.2021) whole doc.	1

☐ 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
07 October 2024	NOV 07 2024
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 Kari Rodriquez 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 fi led.

   b. ☐ furnished subsequent to the international fi ling date for the purposes of international search (Rule 13ter.1(a)),

      ☐ accompanied by a statement to the effect that the sequence listing does not go beyond the disclosure in the international application as filed.

2. ☐ With regard to any nucleotide and/or amino acid sequence disclosed in the international application, this report has been established to the extent that a meaningful search could be carried out without a WIPO Standard ST.26 compliant sequence listing.

3. Additional comments:

INTERNATIONAL SEARCH REPORT

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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.: 5-34, 38
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.:
1-4

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 24/34311

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 1-4, directed to a method of amplifying a target nucleic acid sequence using a universal loop-mediated isothermal amplification (LAMP) target sequence.

Group II: Claims 35-37, directed to a kit comprising: a forward universal LAMP handle and a reverse universal LAMP handle.

The groups of inventions listed above 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

Group I has the special technical feature of a method, not required by Group II.

Group II has the special technical feature of a composition, not required by Group I.

Common Technical Features

The inventions of Groups I and II share the technical feature of a universal LAMP handle.

However, these shared technical features do not represent a contribution over prior art in view of US 2015/0126382 A1 (Warthoe).

Warthoe teaches a method of amplifying a target nucleic acid sequence using a loop-mediated isothermal amplification (LAMP) target sequence (abstract, the method comprising a sequence of steps for pre-amplifying the sample by means of a polymerase chain reaction, followed by a sequence of steps comprising an isothermal amplification of the pre-amplified sample.), the method comprising:
a) providing a target nucleic acid sequence, wherein said target nucleic acid sequence comprises a target-specific hybridization region (para [0131], The objective of Example 1 was to investigate if PCR-pre-amplification of a target sequence from the organism Candida glabrata may be performed using some of the primers conventionally used for LAMP amplification of the same target sequence.; [0133], A pair of primers conventionally used for LAMP amplification of the target Candida glabrata sequence were designed and produced.....The primers FIP and BIP were then used both in the PCR step an in the LAMP-like step according to the invention.);
b) carrying out a nucleic acid amplification step using a forward primer and a reverse primer (para [0134], A PCR reaction using FIP and BIP as primers was performed.);
c) carrying out amplification using LAMP with universal priming sequences which recognize the universal support region, thereby producing concatameric amplicons comprising amplified copies of the target nucleic acid sequence (para [0138], Surprisingly, a reaction product rapidly occurred in the PCR/LAMP assay.....These results demonstrated that a pre-amplification product from a PCR using FIP and BIP primers may be used as templates in LAMP-like reactions in which the F3 and B3 (displacement primers) conventionally and essentially used in normal LAMP are left out.).

Warthoe does not specifically teach carrying out a nucleic acid amplification step using a forward primer and a reverse primer, wherein both primers comprise a universal LAMP handle, wherein said universal LAMP handles comprise a universal amplification support region comprising one or more regions for hybridization of universal priming sequences, thereby producing a universal LAMP target sequence, wherein said universal LAMP target sequence comprises a target sequence flanked by universal handles on both a 3' and 5' terminus of the target sequence. However, Warthoe does not teach applying target sequence pre-amplification with PCR primers followed by LAMP amplification (para [0147], PCR outer (0.4 uM POF; 0.4 uM POB) followed by LAMP (1.6 uM FIP; 1.6 uM BIP;0.8 uM LF; 0.8 uM LB; 0.2 uM F3; 0.2 uM B3).; [0056], FIG. 2 shows the primer design of the primers used in Example 2. Arrows show the direction of primer extension DNA synthesis. The first L-primer FIP (primer (c) according to the invention) comprises the two parts FIP 3' (part c1) and FIP 5' (part c2). The second L-primer BIP (primer (d) according to the invention) comprises the two parts BIP 3' (part d1) and BIP 5' (part d2). The primers LF and LB are the optional primers (e) and (f) according to the invention. Primers F3 and B3 are the displacement primers essential to conventional isothermal loop-mediated amplification. Primers POF and POB are outer primers used in Example 2 for PCR.). It would have been obvious to one of ordinary skill in the art to have recognized that PCR pre-amplification resulted in a double strand DNA comprising 5'-POF-F3-FIP3'-LB at one terminal and 5'-POB-B3-BIP3'-LF at the other terminal (see Fig. 2 in Warthoe). The pre-amplification PCR product essentially comprises a universal LAMP handle comprising a universal amplification support region comprising one or more regions for hybridization of universal priming sequences, thereby producing a universal LAMP target sequence, wherein said universal LAMP target sequence comprises a target sequence flanked by universal handles on both a 3' and 5' terminus of the target sequence, given that the pre-amplification PCR product can be amplified with LAMP primer set (para [0147], PCR outer (0.4 uM POF; 0.4 uM POB) followed by LAMP (1.6 uM FIP; 1.6 uM BIP; 0.8 uM LF; 0.8 uM LB; 0.2 uM F3; 0.2 uM B3.)). Accordingly, it would have been obvious to one of ordinary skill in the art to have used the pre-amplification PCR product of Warthoe, as an universal LAMP handle, in the process of routine practice.

Accordingly, the inventions listed as Groups I and II above lack unity of invention under PCT Rule 13 because they do not share a same or corresponding special technical feature providing contribution over prior art.

Note: Claims 5-34 and 38 have been held unsearchable because they are not drafted in accordance with the second and third sentences of Rule 6.4(a).