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Declarations under Rule 4.17:

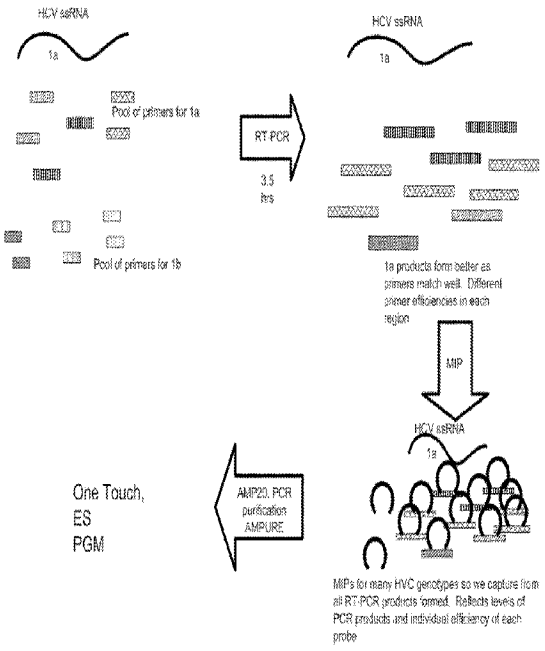
— *as to the identity of the inventor (Rule 4.17(i))*

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

[Continued on next page]

(54) Title: MOLECULAR INVERSION PROBES

(57) Abstract: Provided herein can be a method comprising forming a molecular inversion probe (MIP; a single stranded linear molecule containing two target binding arms where the arms may be separated by a backbone sequence) to selectively target nucleotide template from any source (viral, prokaryotic, and eukaryotic) to obtain information including amount of transcript and sequence data.



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— *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:
13 March 2014

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2013/041675

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - C12Q 1/70 (2014.01)
USPC - 435/6.11
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)
IPC(8) - C07H 21/04; C12N 7/00; C12Q 1/68, 1/70; G01N 33/48, 33/50 (2014.01)
USPC - 424/189.1; 435/5, 6.11, 6.12; 536/23.1, 24.32, 24.33

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
CPC - A61K 38/00; C07K 14/005; C12Q 1/6827, 1/6883, 1/689 (2013.01)

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Orbit, Google Patents, Google Scholar, NCBI BLAST

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 2011/156795 A2 (DIAMOND et al) 15 December 2011 (15.12.2011) entire document	1, 2, 4-33
Y	US 2010/0184205 A1 (BENTWICH et al) 22 July 2010 (22.07.2010) entire document	1, 2, 4-33
Y	US 2011/0150922 A1 (SALLBERG et al) 23 June 2011 (23.06.2011) entire document	1, 2, 4-33
Y	US 2003/0053987 A1 (DONNELLY et al) 20 March 2003 (20.03.2003) entire document	14
Y	US 2003/0211467 A1 (SCHLAUDER et al) 13 November 2003 (13.11.2003) entire document	16
Y	US 2011/0059513 A1 (SCHEEL et al) 10 March 2011 (10.03.2011) entire document	18, 33

☐ Further documents are listed in the continuation of Box C. ☐

* 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
24 December 2013	14 JAN 2014
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. 571-273-3201	Authorized officer: Blaine R. Copenheaver PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

Form PCT/ISA/210 (second sheet) (July 2009)

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 need to be paid.

Group I+: claims 1-33 are drawn to a single-stranded or predominately single-stranded nucleic acid probe for identifying one or more hepatitis viruses, or variants, mutations, subtypes, or strains thereof in a sample, the probe comprising a first probe sequence; a second probe sequence; wherein the first probe sequence can be an odd numbered SEQ ID NO selected from SEQ ID NO:1 to SEQ ID NO: 873; and the second probe sequence has a SEQ ID NO that is one number greater than the SEQ ID NO of the first probe sequence.

The first invention of Group I+ is restricted to a single-stranded nucleic acid probe for identifying one or more hepatitis viruses, or variants, mutations, subtypes, or strains thereof in a sample, the probe comprising a first probe sequence and a second probe sequence, wherein the first probe sequence is selected to be SEQ ID NO:1, and the second probe sequence is selected to be SEQ ID NO:2. It is believed that claims 1-33 read on this first named invention and thus these claims will be searched without fee to the extent that they read on SEQ ID NOs:1 and 2.

Applicant is invited to elect additional first and second probes sequences with specified SEQ ID NOs for each probe to be searched in a specific combination by paying additional fees for each set of election. An exemplary election would be a single-stranded nucleic acid probe for identifying one or more hepatitis viruses, or variants, mutations, subtypes, or strains thereof in a sample, the probe comprising a first probe sequence and a second probe sequence, wherein the first probe sequence is selected to be SEQ ID NO:3, and the second probe sequence is selected to be SEQ ID NO:4. Additional probe sequences will be searched upon the payment of additional fees. Applicants must specify the claims that read on any additional elected inventions. Applicants must further indicate, if applicable, the claims which read on 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.

The inventions listed in Groups I+ 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:

The Groups I+ formulas do not share a significant structural element responsible for identifying one or more hepatitis viruses, requiring the selection of alternatives for the first and second probe sequences "the first probe sequence can be an odd numbered SEQ ID NO selected from SEQ ID NO:1 to SEQ ID NO: 873; and the second probe sequence has a SEQ ID NO that is one number greater than the SEQ ID NO of the first probe sequence".

The Groups I+ share the technical features of a single-stranded or predominately single-stranded nucleic acid probe for identifying one or more hepatitis viruses, or variants, mutations, subtypes, or strains thereof in a sample, the probe comprising a first probe sequence that hybridizes to a 5' end of a target sequence in a genomic region of one or more hepatitis viruses, or variants, mutations, subtypes, or strains thereof; a second probe sequence that hybridizes to a 3' end of the target sequence of the one or more hepatitis viruses, or variants, mutations, subtypes, or strains thereof, and a backbone sequence between the first and second probe sequences. However, these shared technical features do not represent a contribution over the prior art. Specifically, WO 2011/156795 A2 to Diamond et al. discloses a single-stranded or predominately single-stranded nucleic acid probe for identifying one or more hepatitis viruses, or variants, mutations, subtypes, or strains thereof in a sample (a short single stranded DNA containing the complementary sequence, Para. [0165]; one or more probes to each of HIV, Hepatitis B, Hepatitis C, and Trypanosoma cruzi, Para. [0103]; a single probe can be used both to detect an organism of interest within a sample, Para. [088]; sequences present in the probe that identify the sample, Para. [0166]), the probe comprising a first probe sequence that hybridizes to a 5' end of a target sequence in a genomic region of one or more hepatitis viruses, or variants, mutations, subtypes, or strains thereof; a second probe sequence that hybridizes to a 3' end of the target sequence of the one or more hepatitis viruses, or variants, mutations, subtypes, or strains thereof (two homologous probe sequences separated by a backbone sequence, where the first homologous probe sequence is at a first terminus of the nucleic acid and the second homologous probe sequence is at the second terminus to the nucleic acid, Para. [048]; a probe provided by the invention that specifically hybridizes to a target sequence present in the genome of an organism of interest, Para. [052]; a first terminus a first homologous probe sequence that specifically hybridizes to a first target sequence present in the genome of the at least one target organism; and at a second terminus a second homologous probe sequence that specifically hybridizes to a second target sequence present in the genome of the at least one target organism; and a backbone sequence in between the first and second terminus, claim 1; genomic DNA sequences against which probes may be designed and the sets of particular strains of target organisms, Para. [0116]; one or more probes to each of HIV, Hepatitis B, Hepatitis C, and Trypanosoma cruzi, Para. [0103]), and a backbone sequence between the first and second probe sequences (two homologous probe sequences separated by a backbone sequence, Para. [048]; left probe arm, the extension region, the right probe arm, and the 21-nucleotides of backbone sequence between, Para. [0265]).

The inventions listed in Groups I+ therefore lack unity under Rule 13 because they do not share a same or corresponding special technical features.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2013/041675

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 filed or furnished:

   a. (means)

   ☐ on paper

   ☒ in electronic form

   b. (time)

   ☒ in the international application as filed

   ☐ together with the international application in electronic form

   ☒ subsequently to this Authority for the purposes of search

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 in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

Specifically, SEQ ID NO: 1 was searched.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2013/041675

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.: 34-92
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

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, 2, 4-33, limited to the first probe sequence is selected to be SEQ ID NO:1, and the second probe sequence is selected to be SEQ ID NO:2.

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.