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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))

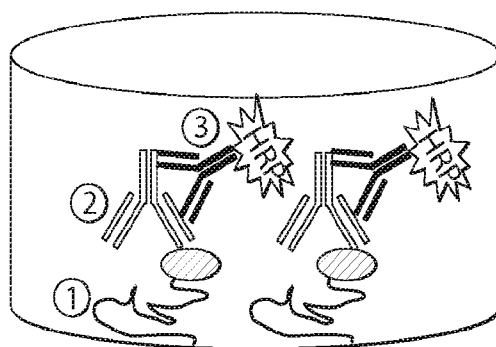
Published:

- 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:

17 December 2015

(54) Title: METHODS AND COMPOSITIONS FOR DETECTING ANTI-DRUG ANTIBODIES



- 1) GalNAc-siRNA conjugates
- 2) Anti-drug antibody
- 3) Anti-IgG/M HRP

Fig. 1

(57) Abstract: Assays, methods, reagents and kits for evaluating the level of an antibody against a nucleic acid molecule, e.g., a double-stranded oligonucleotide or RNA molecule (e.g., dsRNA), are disclosed herein.

INTERNATIONAL SEARCH REPORT

International application No

PCT/US2015/027341

A. CLASSIFICATION OF SUBJECT MATTER

INV. G01N33/53 C12Q1/68 C07K16/00
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)

G01N C12Q C07K

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, 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	JP 2012 228209 A (UNIV MIYAZAKI; KEIO GIJUKU) 22 November 2012 (2012-11-22) the whole document -----	1-64
X	BUHL ALEXANDER ET AL: "Novel biosensor-based analytic device for the detection of anti-double-stranded DNA antibodies", CLINICAL CHEMISTRY,, vol. 53, no. 2, 1 February 2007 (2007-02-01), pages 334-341, XP002519232, DOI: 10.1373/CLINCHEM.2006.077339 abstract, p. 335, col. 1, 3rd par., col. 2, line, p. 336, fig. 1 and col. 2, lines 1 - 20, p. 339, col. 1, 3rd par - p. 340, col. 1, 2nd par. ----- -/-	1,2, 27-30, 34,38,39

☒ 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 July 2015

Date of mailing of the international search report

21/10/2015

Name and mailing address of the ISA/

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2015/027341

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 filed:

☐ in the form of an Annex C/ST.25 text file.

☐ on paper or in the form of an image file.

b. ☐ furnished together with the international application under PCT Rule 13~~ter~~.1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.

c. ☒ furnished subsequent to the international filing date for the purposes of international search only:

☒ in the form of an Annex C/ST.25 text file (Rule 13~~ter~~.1(a)).

☒ on paper or in the form of an image file (Rule 13~~ter~~.1(b) and Administrative Instructions, Section 713).

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 forming part of the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2015/027341

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.:

1-64

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: 1-64

method for detecting antibodies specific for a nucleic acid, characterized by the use of a covalently immobilized nucleic acid as capture member, kit specifically designed to this method

2. claims: 65-71

method for the immobilization of a nucleic acid, characterized by modification of the 5' end of one or both strands, and immobilization via the modified 5' terminus

3. claim: 72(partially)

anti-nucleic-acid-antibody characterized by binding to a fluoro group of the nucleic acid

4. claim: 72(partially)

anti-nucleic-acid-antibody characterized by binding to nucleic acid ligand comprising one or more N-acetylgalactosamine groups

5. claims: 73-77

method for detecting antibodies specific for a nucleic acid, characterized by (i) providing a predetermined amount of an antibody that is fluorescently or radioactively labelled

INTERNATIONAL SEARCH REPORT

International application No

PCT/US2015/027341

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	FIEGEL F ET AL: "Autoantibodies to double-stranded DNA-Intermethod comparison between four commercial immunoassays and a research biosensor-based device", LUPUS, BASINGSTOKE, GB, vol. 19, no. 8, 1 July 2010 (2010-07-01), pages 957-964, XP009185499, ISSN: 0961-2033, DOI: 10.1177/0961203310369681 abstract, p. 958,959, "Assays", "Biosensor measurements" -----	1,2, 27-30, 34,38,39
A	E. JUNG ET AL: "RNA recognition by a human antibody against brain cytoplasmic 200 RNA", RNA, vol. 20, no. 6, 23 April 2014 (2014-04-23), pages 805-814, XP055204310, ISSN: 1355-8382, DOI: 10.1261/rna.040899.113 the whole document -----	1-64
A	US 2011/189300 A1 (MACLACHLAN IAN [CA] ET AL) 4 August 2011 (2011-08-04) paragraph [0118] - paragraph [0121] -----	1-64
A	ADAM JUDGE ET AL: "Overcoming the Innate Immune Response to Small Interfering RNA", HUMAN GENE THERAPY, vol. 19, no. 2, 1 February 2008 (2008-02-01), pages 111-124, XP055046609, ISSN: 1043-0342, DOI: 10.1089/hum.2007.179 abstract, p. 17, col. 2, line 11 - p. 118, col. 1, line 40, p. 121, col. 1, lines 50 - 54 -----	1-64

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2015/027341

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
JP 2012228209	A	22-11-2012	NONE

US 2011189300	A1	04-08-2011	AU 2005306533 A1 26-05-2006
			CA 2587411 A1 26-05-2006
			EP 1828219 A1 05-09-2007
			EP 2199298 A1 23-06-2010
			US 2006134189 A1 22-06-2006
			US 2011189300 A1 04-08-2011
			WO 2006053430 A1 26-05-2006
