(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
27 February 2014 (27.02.2014)

WIPO | PCT

(10) International Publication Number
WO 2014/031648 A3

(51) International Patent Classification:
G01N 33/53 (2006.01) *C12P 21/08* (2006.01)
C07K 16/00 (2006.01)

(21) International Application Number:
PCT/US2013/055803

(22) International Filing Date:
20 August 2013 (20.08.2013)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
61/691,675 21 August 2012 (21.08.2012) US
61/790,880 15 March 2013 (15.03.2013) US

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(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

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

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))*

— *with sequence listing part of description (Rule 5.2(a))*

(88) Date of publication of the international search report:
1 May 2014

WO 2014/031648 A3

(54) Title: ANTIBODIES TO RISPERIDONE AND USE THEREOF

(57) Abstract: Disclosed is an antibody which binds to risperidone, which can be used to detect risperidone in a sample such as in a competitive immunoassay method. The antibody can be used in a lateral flow assay device for point-of-care detection of risperidone, including multiplex detection of aripiprazole, quetiapine, olanzapine, and risperidone in a single lateral flow assay device.

INTERNATIONAL SEARCH REPORT

~~4013/055803 10.03.2014~~

International application No.
PCT/US13/55803

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - G01N 33/53; C07K 16/00; C12P 21/08 (2014.01)

USPC - 435/7.1, 4; 530/388.9, 389.9, 388.1, 387.1, 386, 380, 350

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): G01N 33/53; C07K 16/00; C12P 21/08 (2013.01)
USPC: 435/7.1, 4; 530/388.9

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)

MicroPatent (US-G, US-A, EP-A, EP-B, WO, JP-bib, DE-C,B, DE-A, DE-T, DE-U, GB-A, FR-A); Google Scholar; Google Patents; Google; PubMed; risperidone, immunoassay, minibody, 'lateral flow test,' marker

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 7901949 B2 (RAJ, B) March 8, 2011; figure 1; column 9, lines 16-31; Claim 10	1-4, 11, 18-30
A	US 2010/0266502 A1 (KIMURA, N) October 21, 2010; SEQ ID NO: 48	1-4, 11, 18-30
A	US 2005/0163708 A1 (ROBINSON, R et al.), July 28, 2005; SEQ ID NO: 44	1-4, 11, 18-30

☐ 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
18 February 2014 (18.02.2014)	10 MAR 2014

Name and mailing address of the ISA/US	Authorized officer:
Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Shane Thomas PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US13/55803

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:

-***-Please See Supplemental Page-***-

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.:

Groups I+: 1-4, 11 and 18-30 (in-part), SEQ ID NOs 3, 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.

-***- 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 1-30 and SEQ ID NOs: 3 (antibody light chain variable region amino acid sequence), 4 (antibody heavy chain variable region amino acid sequence) are directed toward an isolated antibody or a binding fragment thereof, which binds to risperidone and which: (i) is an antibody selected from the group consisting of: a) an isolated antibody or a fragment thereof comprising a light chain variable region comprising the amino acid sequence of SEQ ID NO:3, SEQ ID NO:7, SEQ ID NO:68, SEQ ID NO:70, SEQ ID NO:72, SEQ ID NO: 76, SEQ ID NO:78, SEQ ID NO:86, SEQ ID NO:88, SEQ ID NO:90, SEQ ID NO:94, or SEQ ID NO:100; b) an isolated antibody or a fragment thereof comprising a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:4, SEQ ID NO:8, SEQ ID NO:58, SEQ ID NO:60, SEQ ID NO:62, SEQ ID NO:64, SEQ ID NO:66, SEQ ID NO:74, SEQ ID NO:80, SEQ ID NO:82, SEQ ID NO:84, SEQ ID NO:92, SEQ ID NO:96, or SEQ ID NO:98; c) an isolated antibody or a fragment thereof comprising a light chain variable region having the amino acid sequence of SEQ ID NO:3 and a heavy chain variable region having the amino acid sequence of SEQ ID NO:4; or d) an isolated antibody or a fragment thereof comprising a light chain variable region having the amino acid sequence of SEQ ID NO:7 and a heavy chain variable region having the amino acid sequence of SEQ ID NO:8; e) an isolated antibody or a fragment thereof comprising a light chain variable region having an amino acid sequence selected from the group consisting of: SEQ ID NO:68, SEQ ID NO:70, and SEQ ID NO:72 and a heavy chain variable region having an amino acid sequence selected from the group consisting of: SEQ ID NO:58, SEQ ID NO:60, SEQ ID NO:62, SEQ ID NO:64, and SEQ ID NO:66; f) an isolated antibody or a fragment thereof comprising a light chain variable region having an amino acid sequence selected from the group consisting of: SEQ ID NO:76 and SEQ ID NO:78 and a heavy chain variable region having the amino acid sequence of SEQ ID NO:74; g) an isolated antibody or a fragment thereof comprising a light chain variable region having an amino acid sequence selected from the group consisting of: SEQ ID NO:86, SEQ ID NO:88, and SEQ ID NO:90 and a heavy chain variable region having an amino acid sequence selected from the group consisting of: SEQ ID NO:80, SEQ ID NO:82, and SEQ ID NO:84; h) an isolated antibody or a fragment thereof comprising a light chain variable region having the amino acid sequence of SEQ ID NO:94 and a heavy chain variable region having the amino acid sequence of SEQ ID NO:92; or an isolated antibody or a fragment thereof comprising a light chain variable region having the amino acid sequence of SEQ ID NO:100 and a heavy chain variable region having an amino acid sequence selected from the group consisting of: SEQ ID NO:96 and SEQ ID NO:98; or (ii) competes for an epitope which is the same as an epitope bound by the antibody of (i); and an assay kit comprising the antibody; an assay device comprising the antibody; a method of detecting risperidone in a sample, the method comprising: (i) contacting a sample with an antibody labeled with a detectable marker, wherein the labeled antibody and risperidone present in the sample form a labeled complex; and (ii) detecting the labeled complex so as to detect risperidone in the sample; and a competitive immunoassay method for detecting risperidone in a sample, the method comprising: (i) contacting a sample with the antibody, and with risperidone or a competitive binding partner of risperidone, wherein one of the antibody and the risperidone or competitive binding partner thereof is labeled with a detectable marker, and wherein sample risperidone competes with the risperidone or competitive binding partner thereof for binding to the antibody; and (ii) detecting the label so as to detect sample risperidone.

The isolated antibody or a binding fragment thereof, which binds to risperidone and which: (i) is an antibody selected from the group consisting of: a) an isolated antibody or a fragment thereof comprising a light chain variable region comprising an amino acid sequence; b) an isolated antibody or a fragment thereof comprising a heavy chain variable region comprising an amino acid sequence; or (ii) competes for an epitope which is the same as an epitope bound by the antibody of (i) will be searched to the extent that they encompass SEQ ID NOs: 3 (antibody light chain variable region amino acid sequence), 4 (antibody heavy chain variable region amino acid sequence). It is believed that Claims 1-4, 11 and 18-30 (in-part) encompass this first named invention and thus these claims will be searched to the extent that they encompass SEQ ID NOs: 3 (antibody light chain variable region amino acid sequence), 4 (antibody heavy chain variable region amino acid sequence. Applicants must 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. Additional SEQ ID NOs can be searched upon the payment of additional fees. An Exemplary Election would be: SEQ ID NOs: 7 (antibody light chain variable region amino acid sequence), 8 (antibody heavy chain variable region amino acid sequence).

Groups I+ share the technical elements including (i) an isolated antibody or a binding fragment thereof, which binds to risperidone and comprising a light chain variable region comprising an amino acid sequence, and a heavy chain variable region comprising an amino acid sequence, or an antibody which competes for an epitope which is the same as an epitope bound by the antibody of (i); and an assay kit comprising the antibody; an assay device comprising the antibody; a method of detecting risperidone in a sample, the method comprising: (i) contacting a sample with an antibody labeled with a detectable marker, wherein the labeled antibody and risperidone present in the sample form a labeled complex; and (ii) detecting the labeled complex so as to detect risperidone in the sample; and a competitive immunoassay method for detecting risperidone in a sample, the method comprising: (i) contacting a sample with the antibody, and with risperidone or a competitive binding partner of risperidone, wherein one of the antibody and the risperidone or competitive binding partner thereof is labeled with a detectable marker, and wherein sample risperidone competes with the risperidone or competitive binding partner thereof for binding to the antibody; and (ii) detecting the label so as to detect sample risperidone.

-***-Continued on Next Supplemental Page-***-

-***-Continued from Box No. III: Observations Where Unity Of Invention Is Lacking:

-Continued from Previous Page:

However, these shared technical elements are previously disclosed by US 2012/0071636 A1 to Salamone, et al. (hereinafter 'Salamone') in view of US 2009/0325193 A1 to Grenier, et al. (hereinafter 'Grenier'). Salamone discloses an islolated antibody or a binding fragment thereof, which binds to an antipsychotic medication (an isolated antibody or a binding fragment thereof which binds to risperidone and paliperidone (an isolated antibody or a binding fragment thereof which binds to an antipsychotic medication); paragraph [0019]), and its use for immunoassays on a human fluid sample (immunoassays on a human fluid sample; paragraph [0019]) to monitor patients treated with an antipsychotic (to monitor patients treated with risperidone or paliperidone (an antipsychotic); paragraph [0025]).

Salamone does not disclose comprising a light chain variable region comprising an amino acid sequence, and a heavy chain variable region comprising an amino acid sequence, or an antibody which competes for an epitope which is the same as an epitope bound by the antibody; and and an assay kit comprising the antibody; an assay device comprising the antibody; a method of detection in a sample, the method comprising: (i) contacting a sample with an antibody labeled with a detectable marker, wherein the labeled antibody present in the sample form a labeled complex; and (ii) detecting the labeled complex so as to detect a component in a sample; and a competitive immunoassay method for detecting a component in a sample, the method comprising: (i) contacting a sample with the antibody, with a competitive binding partner thereof is labeled with a detectable marker, and wherien the sample competes with a competitive binding partner thereof for binding to the antibody; and (ii) detecting the label so as to detect sample.

Grenier discloses antibodies capable of binding to a drug (antibodies capable of binding to an immunosuppressant drug (a drug); paragraph [0012]), wherein the antibody comprises light chains (light chains; paragraph [0023]), and heavy chains (heavy chains; paragraph [0023]), each of which comprises amino acid sequences (immunoglobulin sequences (amino acid sequences); paragraph [0023]); and an assay kit comprising the antibody (abstract; paragraphs [0012], [0023]); an assay device comprising the antibody (abstract; paragraphs [0012], [0023]); a method of detection in a sample (paragraph [0108]), the method comprising: (i) contacting a sample with an antibody labeled with a detectable marker (paragraphs [0096], [0097], [0108]), wherein the labeled anibody present in the sample form a labeled complex (paragraphs [0096], [0097], [0108]); and (ii) detecting the labeled complex so as to detect a component in a sample (paragraphs [0096], [0097], [0108]); and a competitive immunoassay method for detecting a component in a sample (paragraphs [0096], [0097], [0108]; Claims 15-17), the method comprising: (i) contacting a sample with the antibody, with a competitive binding partner thereof is labeled with a detectable marker (paragraphs [0096], [0097], [0108]; Claims 15-17), and wherein the sample competes with a competitive binding partner thereof for binding to the antibody (paragraphs [0096], [0097], [0108]; Claims 15-17); and (ii) detecting the label so as to detect sample (paragraphs [0096], [0097], [0108]).

It would have been obvious to a person of ordinary skill in the art, at the time of the invention, to have modified the previous disclosure of Salamone regarding antibodies that bind to antipsychotic drugs with the antibodies that bind to drugs, the antibodies comprising light and heavy chain amino acid sequences, as previously disclosed by Grenier, for providing antibodies having a desired type of chains or framework, for providing antibodies effective for use to monitor patients being treated with antipsychotics, as disclosed by Salamone, for providing both a moiety which would have allowed surface attachment of an antibody, and which would have provided a desirable framework for interaction with an available tagged or catalytically active second antibody for use in a standard immunoassay, for enabling the detection of the drug in a sample from a patient using the antibodies, without undue experimentation or testing.

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 Salamone and Grenier references, unity of invention is lacking.