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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:

24 December 2014

(54) Title: METHODS AND COMPOSITIONS FOR THE GENERATION AND USE OF CONFORMATION-SPECIFIC ANTI-BODIES

(57) Abstract: The present invention features methods and compositions for the generation and use of conformation-specific anti-bodies or fragments thereof.



INTERNATIONAL SEARCH REPORT

International application No.

PCT/US14/27017

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A61K 38/10 (2014.01)

USPC - A61K 38/10

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): A61K 31/473, 38/10, 38/17; C12N 9/90 (2014.01)

USPC: 435/7.1, 7.6, 7.72, 7.93, 7.94, 7.95; CPC: C12N 9/90; A61K 31/473, 38/10, 38/17

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-Granted, US-Applications, EP-A, EP-B, WO, JP, DE-G, DE-A, DE-T, DE-U, GB-A, FR-A); ProQuest; IP.com; Google; Google Scholar; PatSeer; isolated, 'conformation specific,' binding moiety,' trans, 'pT231-tau'

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y --- A	US 2013/0028900 A1 (LU, KP et al.) January 31, 2013; abstract; paragraphs [0016], [0034], [0037]	1-3, 5-7, 9/1-9/3, 9/5-9/7, 10/1-10/3, 10/5-10/7, 11/10/1-11/10/3, 11/10/5-11/10/7, 13/1-13/3, 13/5-13/7, 14/13/1-14/13/3, 14/13/5-14/13/7, 15/13/3-15/13/3, 15/13/5,-15/13/7, 16/15/13/1-16/15/13/3, 16/15/13/5-16/15/13/7, 17/16/15/13/1-17/16/15/1 3/3, 17/16/15/13/5-17/16/15/1 3/7, 18/16/15/13/1-18/16/15/1 3/3, 18/16/15/13/5-18/16/15/1 3/7, 19/13/1-19/13/3, 19/13/15-19/13/7, 20/1-20/3, 20/5-20/7, 21/20/1-21/20/3, 21/20/5-21/20/7, 22/1-22/3, 22/5-22/7 ----- ... Next Page ...

☒ 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

23 October 2014 (23.10.2014)

Date of mailing of the international search report

28 OCT 2014

Name and mailing address of the ISA/US

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C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	... Continued from Previous Page ...	4, 8, 9/4, 9/8, 10/4, 10/8, 11/10/4, 11/10/8, 13/4, 13/8, 14/13/4, 14/13/8, 15/13/4, 15/13/8, 16/15/13/4, 16/15/13/8, 17/16/15/13/4, 17/16/15/13/8, 18/16/15/13/4, 18/16/15/13/8, 19/13/4, 19/13/8, 20/4, 20/8, 21/20/4, 21/20/8, 22/4, 22/8
Y --- A	US 2012/0183560 A1 (AKASSOGLU, K) July 19, 2012; abstract; paragraphs [0009]-[0014]; Claims 9, 10, 14, 15; SEQ ID NOs: 5-8	1-3, 9/1-9/3, 10/1-10/3, 11/10/1-11/10/3, 13/1-13/3, 14/13/1-14/13/3, 15/13/3-15/13/3, 16/15/13/1-16/15/13/3, 17/16/15/13/1-17/16/15/13/3, 18/16/15/13/1-18/16/15/13/3, 19/13/1-19/13/3, 20/1-20/3, 21/20/1-21/20/3, 22/1-22/3 ----- 4, 9/4, 10/4, 11/10/4, 13/4, 14/13/4, 15/13/4, 16/15/13/4, 17/16/15/13/4, 18/16/15/13/4, 19/13/4, 20/4, 21/20/4, 22/4
Y --- A	US 2008/0118505 A1 (TEDDER, TF) May 22, 2008; abstract; figure 17, HB22-33; paragraph [0111]	1-3, 9/1-9/3, 10/1-10/3, 11/10/1-11/10/3, 13/1-13/3, 14/13/1-14/13/3, 15/13/3-15/13/3, 16/15/13/1-16/15/13/3, 17/16/15/13/1-17/16/15/13/3, 18/16/15/13/1-18/16/15/13/3, 19/13/1-19/13/3, 20/1-20/3, 21/20/1-21/20/3, 22/1-22/3 ----- 4, 9/4, 10/4, 11/10/4, 13/4, 14/13/4, 15/13/4, 16/15/13/4, 17/16/15/13/4, 18/16/15/13/4, 19/13/4, 20/4, 21/20/4, 22/4
Y --- A	US 2010/0278832 A1 (KAMOGAWA, Y et al.) November 4, 2010; abstract; paragraph [0075]; Claim 9; SEQ ID NOs: 4, 5, 26	5-7, 9/5-9/7, 10/5-10/7, 11/10/5-11/10/7, 13/5-13/7, 14/13/5-14/13/7, 15/13/5-15/13/7, 16/15/5-16/15/13/7, 17/16/15/13/5-17/16/15/13/7, 18/16/15/13/5-18/16/15/13/7, 19/13/5-19/13/7, 20/5-20/7, 21/20/5-21/20/7, 22/5-22/7 ----- 8, 9/8, 10/8, 11/10/8, ... Next Page ...

INTERNATIONAL SEARCH REPORT

International application No.

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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.: 12, 23, 35
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.:

Group I: Claims 1-11, 13-22

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/US14/27017

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	... Continued from Previous Page ...	... Continued from Previous Page ... 13/8, 14/13/8, 15/13/8, 16/15/13/8, 17/16/15/13/8, 18/16/15/13/8, 19/13/8, 20/8, 21/20/8, 22/8
Y --- A	US 2011/0104756 A1 (RODRIGUEZ, M et al.) May 5, 2011; abstract; Figure 11A; paragraph [0139]	5-7, 9/5-9/7, 10/5-10/7, 11/10/5-11/10/7, 13/5-13/7, 14/13/5-14/13/7, 15/13/5-15/13/7, 16/15/5-16/15/13/7, 17/16/15/13/5-17/16/15/1 3/7, 18/16/15/13/5-18/16/15/1 3/7, 19/13/5-19/13/7, 20/5-20/7, 21/20/5-21/20/7, 22/5-22/7 ----- 8, 9/8, 10/8, 11/10/8, 13/8, 14/13/8, 15/13/8, 16/15/13/8, 17/16/15/13/8, 18/16/15/13/8, 19/13/8, 20/8, 21/20/8, 22/8
A	US 2008/0248043 A1 (BABCOOK, JS et al.) October 9, 2008; paragraphs [0016], [0026], [0031], [0041], [0047], [0056], [0069], [0240]	1-11, 13-22
A	NAKAMURA, K et al. Proline Isomer-Specific Antibodies Reveal The Early Pathogenic Tau Conformation In Alzheimer's Disease. Cell. 30 March 2012, Vol. 149; pages 232-244; Summary; page 233, column 1, paragraph 2, column 2, paragraph 3. DOI 10.1016/j.cell.2012.02.016.	1-11, 13-22
A	US 7161060 B1 (DUFF, K et al.) January 9, 2007; abstract	1-11, 13-22

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International application No.

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***-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.

Group I: Claims 1-11 and 13-22 are directed toward an isolated conformation-specific binding moiety, optionally an antibody or monoclonal antibody, wherein said moiety comprises one or more heavy chain variable regions and one or more light chain variable regions; and methods of treating, monitoring or diagnosing tauopathy comprising said conformation-specific binding moiety.

Groups II+: Claims 24-27, 32 (in-part), 33 (in-part), 34 (in-part) and 36 (in-part) are directed toward an isolated conformation-specific binding moiety, optionally an antibody or a monoclonal antibody, wherein said binding moiety comprises one or more light chain variable regions having SEQ ID NOs: 16-18, or variants thereof and one or more heavy chain variable regions with SEQ ID NOs: 13-15 or variants thereof; and a pharmaceutical composition comprising the binding moiety and a pharmaceutically acceptable carrier.

The isolated conformation-specific binding moiety wherein said binding moiety comprises one or more light chain variable regions and one or more heavy chain variable regions will be searched to the extent that the one or more light chain variable regions encompasses SEQ ID NO: 16 (Mus musculus amino acid sequence), and the one or more heavy chain variable regions encompasses SEQ ID NO: 13 (Mus musculus amino acid sequence). It is believed that claims 24 (in-part), 32 (in-part), 33 (in-part) and 34 (in-part) encompass this first named invention and thus these claims can be searched, upon the payment of additional fees, to the extent that they encompass SEQ ID NOs: 13 (Mus musculus amino acid sequence) and 16 (Mus musculus amino acid sequence). Applicants must specify the claims that encompass any additionally elected sequences. Applicants must further 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. An exemplary election would be: a binding moiety comprising a heavy chain variable region of SEQ ID NO: 14 (Mus musculus amino acid sequence); and a light chain variable region of SEQ ID NO: 17 (Mus musculus amino acid sequence).

Groups III+: Claims 28-31, 32 (in-part), 33 (in-part), 34 (in-part) and 36 (in-part) are directed toward an isolated conformation-specific binding moiety, optionally an antibody or a monoclonal antibody, wherein said binding moiety comprises one or more light chain variable regions with SEQ ID NOs: 19-21, or variants thereof; and a pharmaceutical composition comprising the binding moiety and a pharmaceutically acceptable carrier.

The inventions listed as Groups I-III+ 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 special technical features of Group I include methods of treating, monitoring or diagnosing tauopathy, which are not present in Groups II+ or III+; the special technical features of Groups II+ including a binding moiety comprising one or more light chain variable regions having SEQ ID NOs: 16-18, which are not present in Groups I or III+; the special technical features of Groups III+ including a binding moiety comprising one or more light chain variable regions having SEQ ID NOs: 19-21.

Groups I-III+ share the technical features including an isolated conformation-specific binding moiety, optionally an antibody or monoclonal antibody, wherein said moiety comprises one or more light chain variable regions. Groups I-II+ share the technical features including one or more heavy chain variable regions. Groups II+-III+ share the technical features including a pharmaceutical composition comprising a binding moiety and a pharmaceutically acceptable carrier. Groups II+ share the technical features including an isolated conformation-specific binding moiety, optionally an antibody or a monoclonal antibody, wherein said binding moiety comprises one or more heavy chain variable regions with SEQ ID NOs: 13-15, or variants thereof and one or more light chain variable with SEQ ID NOs: 16-18, or variants thereof; and a pharmaceutical composition comprising the binding moiety and a pharmaceutically acceptable carrier. Groups III+ share the technical features including an isolated conformation-specific binding moiety, optionally an antibody or a monoclonal antibody, wherein said binding moiety comprises one or more light chain variable regions with SEQ ID NOs: 19-21, or variants thereof; and a pharmaceutical composition comprising the binding moiety and a pharmaceutically acceptable carrier.

However, these shared technical features are previously disclosed by US 2008/0248043 A1 to Babcook, et al. (hereinafter 'Babcook'). Babcook discloses an isolated (isolated; abstract) conformation-specific (conformation-specific; paragraphs [0069], [0240]) binding moiety (heavy and light chain immunoglobulins (binding moiety); abstract), optionally an antibody or monoclonal antibody (an antibody; abstract), wherein said moiety comprises one or more light chain variable regions (wherein said moiety comprises one or more light chain variable regions; paragraph [0016]); and one or more heavy chain variable regions (one or more heavy chain variable regions; paragraph [0016]); a pharmaceutical composition comprising a binding moiety and a pharmaceutically acceptable carrier (a pharmaceutical composition comprising a binding moiety and a pharmaceutically acceptable carrier; paragraph [0197]); an isolated (isolated; abstract) conformation-specific (conformation-specific; paragraphs [0069], [0240]) binding moiety (antibody immunoglobulin (binding moiety); abstract), wherein said binding moiety comprises one or more heavy chain variable regions (wherein said binding moiety comprises one or more heavy chain variable regions; paragraph [0016]) with SEQ ID NOs: 13-15, or variants thereof (with the sequence GYYMH (SEQ ID NO: 13, or a variant thereof); page 31, column 1, antibody 5E1.2, SEQ ID NO: 18 of the Babcook reference (note that the instant PCT application describes variants as having up to 5 or more substitutions in a complementarity determining region); instant PCT application; page 10, lines 9-14) and one or more light chain variable regions (and one or more light chain variable regions; paragraph [0016]) with SEQ ID NOs: 16-18, or variants thereof (with the sequence WASTRES (SEQ ID NO: 17); page 31, column 2, antibody 5E1.2, SEQ ID NO: 20 of the Babcook reference); and an isolated (isolated; abstract) conformation-specific (conformation-specific; paragraphs [0069], [0240]) binding moiety (antibody immunoglobulin (binding moiety); abstract), wherein said binding moiety comprises one or more light chain variable regions (wherein said binding moiety comprises one or more light chain variable regions; paragraph [0016]) with SEQ ID NOs: 19-21, or variants thereof (with the sequence WASTRES (SEQ ID NO: 20); page 31, column 2, antibody 5E1.2, SEQ ID NO: 20 of the Babcook reference).

Since none of the special technical features of the Groups I-III+ inventions is found in more than one of the inventions, and since all of the shared technical features are previously disclosed by the Babcook reference, unity of invention is lacking.