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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))*

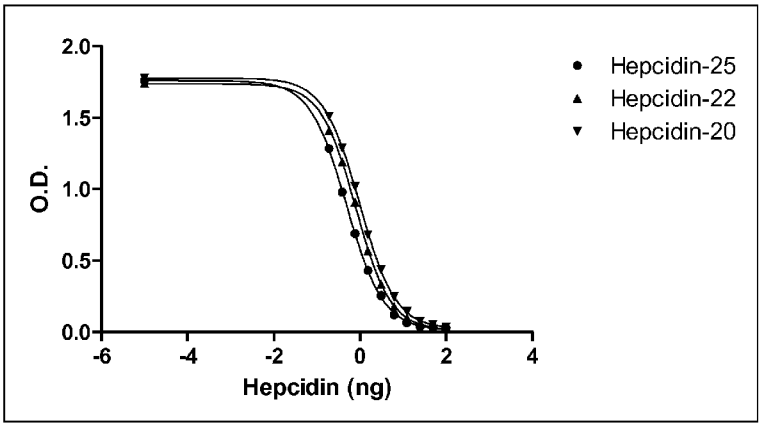
Published:

— *with international search report (Art. 21(3))*

[Continued on next page]

(54) Title: ANTI-HEPCIDIN ANTIBODIES AND USES THEREOF

FIGURE 16



(57) Abstract: The present application relates to antibodies that specifically bind to hepcidin and methods of using the antibodies. Another aspect relates to antibodies which bind hepcidin and regulate iron homeostasis. Another aspect relates to the use of humanized antibodies which bind hepcidin for the treatment of a disease or condition associated with hepcidin.

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— *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:
18 December 2014

INTERNATIONAL SEARCH REPORT

PCT/US14/26804 03.10.2014

International application No.
PCT/US 14/26804

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A61K 39/00, A61K 39/395, C07K 16/00 (2014.01)
CPC - A61K 38/00, A61K 2039/505
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 39/00, A61K 39/395, C07K 16/00 (2014.01)
CPC - A61K 38/00, A61K 2039/505

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
USPC - 424/139.1, 424/158.1, 530/389.2

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
WEST; PatBase; Google Scholar
search terms - Hepcidin, cdr, cdr1, cdr2, cdr3, anti, antibod$, immunog$, residues, termin$, N, ggctacacattcactgattatgct, igg1, igg4, injec$, mouse, murine, rodent, mice

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2011/0150888 A1 (FOLTZ et al.) 23 June 2011 (23.06.2011) para [0010]; [0067]; [0076].	4-6
X	US 2012/0003696 A1 (KULAKSIZ et al.) 05 January 2012 (05.01.2012) abstract; para [0101].	3
A	US 2010/0285027 A1 (VAULONT et al.) 11 November 2010 (11.11.2010) para [0001]; [0016]-[0025]; [0064]; SEQ ID NOs: 7, 8.	1, 2, 16-18
A	US 2012/0177639 A1 (BAURIN et al.) 12 July 2012 (12.07.2012) para [0022], SEQ ID NO: 9.	1, 2, 16
A	US 2010/0146650 A1 (GOETSCH et al.) 10 June 2010 (10.06.2010) para [0199], Table 5, SEQ ID NO: 53.	1, 2, 17
A	US 2004/0005643 A1 (DE SANTIS et al.) 08 January 2004 (08.01.2004) para [0022], [0067], SEQ ID NO: 10.	1, 2, 16
A	US 2011/0293630 A1 (STITT et al.) 01 December 2011 (01.12.2011) para [0019], SEQ ID NO: 125.	1, 2, 16
A	US 2012/0114672 A1 (ROHLFF et al.) 10 May 2012 (10.05.2012) para [0059], SEQ ID NO: 121.	1, 2, 16
A	US 2006/0134116 A1 (RANCOURT et al.) 22 June 2006 (22.06.2006) para [0012], SEQ ID NO: 1.	1, 2, 16

☒ 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
10 September 2014 (10.09.2014)	03 OCT 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: Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	GenBank Accession No BF583451, CGAP_Co24 Mus musculus cDNA clone, January 2011, [found online 9/10/14] at <http://www.ncbi.nlm.nih.gov/nucest/BF583451. sequence.	1, 2, 17
A	GenBank Accession No MMU55552, Mus musculus anti-DNA immunoglobulin heavy chain IgG mRNA, antibody 452p.153, partial cds, September 2001, [found online 9/10/14] at <http://www.ncbi.nlm.nih.gov/nuccore/1872424. sequence.	1, 2, 18
A	US 2009/032449 A1 (ABURATANI et al.) 31 December 2009 (31.12.2009) para [0771], SEQ ID NO: 116.	16
A	US 2006/0233794 A1 (LAW et al.) 19 October 2006 (19.10.2006) para [0121], SEQ ID NO: 5.	17
A	US 2010/0111852 A1 (YOSHIDA K.) 06 May 2010 (06.05.2010) para [0046], SEQ ID NO: 45.	17
A	US 2004/0197325 A1 (LAW et al.) 07 October 2004 (07.10.2004) para [0018], SEQ ID NO: 3.	18
A	GenBank Accession No JN573653, Mus musculus monoclonal antibody 4B12 heavy chain variable region, January 2012, [found online 9/10/14] at <http://www.ncbi.nlm.nih.gov/nuccore/JN573653. sequence.	18
A	US 2011/0135663 A1 (ZHANG M.) 09 June 2011 (09.06.2011) para [0025], SEQ ID NO: 14.	18
A	US 2004/0241651 A1 (OLEK et al.) 02 December 2004 (02.12.2004) para [0015], SEQ ID NO: 289464.	18
A	US 6,210,670 B1 (BERG E.) 03 April 2001 (03.04.2001) Fig 7, SEQ ID NO: 1.	18

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 14/26804

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.: 7-15, 19-45
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:
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.

--continued on next extra page attached hereto--

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.:

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.

continuation of Box No III:

Group I+, claims 1, 2 and 16-18, directed to an antibody, or antigen-binding fragment thereof, that specifically binds to hepcidin. The first invention of Group I+ is restricted to the first named amino acid sequences for heavy chain variable region CDR1, CDR2 and CDR3 (sequences SEQ ID NOs: 55, 58 and 61 respectively), and the first named amino acid sequences for light chain variable region CDR1, CDR2 and CDR3 (sequences SEQ ID NOs: 64, 67 and 70 respectively). Group I+ will be searched to the extent that it reads on sequences SEQ ID NOs: 55, 58, 61, 64, 67 and 70, without fee. It is believed that claims 1, 2 and 16, read on this first named invention. Applicants must 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. An exemplary election would be the second amino acid sequences for heavy chain variable region CDR1, CDR2 and CDR3 (sequences SEQ ID NOs: 56, 59 and 62 respectively), and the second named amino acid sequences for light chain variable region CDR1, CDR2 and CDR3 (sequences SEQ ID NOs: 65, 68 and 71 respectively) (claims 1 (in part), 2 and 17).

Group II, claims 3-6, directed to an antibody, or antigen-binding fragment thereof, that specifically binds to an epitope comprising amino acid residues 1-9 of hepcidin

The inventions listed as Groups I+ and II do not relate to a single special technical feature 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 II includes the special technical feature of an antibody, or antigen-binding fragment thereof, that specifically binds to an epitope comprising amino acid residues 1-9 of hepcidin, prepared by injecting a rodent with a peptide having an amino acid sequence of hepcidin or a hepcidin peptide described herein, which is not required by Group I+.

The special technical feature of each invention listed as Groups I+ is the specific sequences for heavy chain CDR1-3 and light chain CDR1-3 recited therein, not required in any other invention in Group I+ or Group II.

Common Technical Features
The inventions of Groups I+ and II share the common technical feature of an antibody, or antigen-binding fragment thereof, that specifically binds to hepcidin.

The inventions of Groups I+ share the common technical feature of a heavy chain variable region and a light chain variable region, wherein said heavy and light chain variable regions comprise a CDR1, CDR2 and CDR3, respectively, each having an amino acid sequence. However, these shared technical features do not represent a contribution over prior art, because the shared technical features are anticipated by reference US 2010/0285027 A1 to Vaulont et al. (hereinafter Vaulont).

Vaulont teaches an antibody, or antigen-binding fragment thereof, that specifically binds to hepcidin (para [0001]), comprising a heavy chain variable region and a light chain variable region, wherein said heavy and light chain variable regions comprise a CDR1, CDR2 and CDR3, respectively, each having an amino acid sequence (para [0016]-[0019]).

As the technical features were known in the art at the time of the invention, they cannot be considered special technical features that would otherwise unify the groups.

Therefore, Group I+ and II inventions lack unity under PCT Rule 13 because they do not share the same or corresponding special technical feature.

Note: Claims 7-15 and 19-45 are found unsearchable because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Note: Claim 2 is improperly self dependent. For the purposes of this invitation, claim 2 is treated as dependent from claim 1.

Note: It is believed (based in part on the client's election in response to the LoU) that claim 17 improperly claims ?said heavy chain CDR3 encoded by SEQ ID NO: 61?, and for the purposes of this search and opinion claim 17 is treated as the following:

17. An antibody, or antigen-binding fragment thereof, that specifically binds to hepcidin, wherein said antibody, or antigen-binding fragment thereof, comprises a heavy chain CDR1 encoded by SEQ ID NO: 56, a heavy CDR2 encoded by SEQ ID NO: 59, a heavy chain CDR3 encoded by SEQ ID NO: 62, a light chain CDR1 encoded by SEQ ID NO: 65, a light CDR2 encoded by SEQ ID NO: 68, and a light chain CDR3 encoded by SEQ ID NO: 71.