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HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR,  
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MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ,  
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[Continued on next page]

(54) Title: REGULATION OF GLUCOSE METABOLISM USING ANTI-CGRP ANTIBODIES

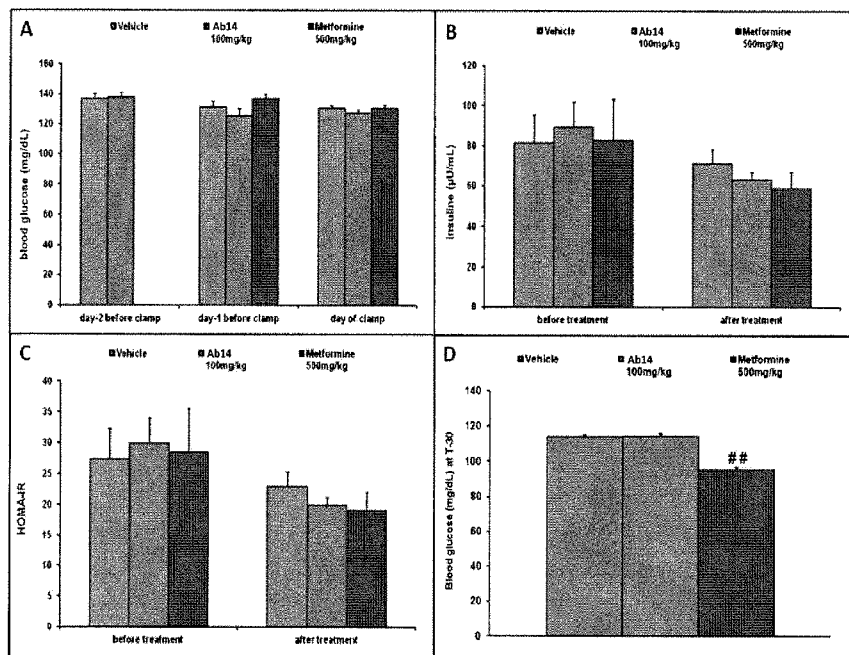


Figure 1: Blood glucose and plasma insulin levels before and after treatment.

(57) Abstract: The present disclosure provides methods for the prevention or treatment of metabolic disorders. In exemplary embodiments, methods of administering an anti-CGRP antibody are provided, optionally in combination with a second agent, wherein peripheral and/or hepatic glucose utilization is increased, thereby preventing or treating diseases and disorders associated with insulin resistance. Compositions comprising an anti-CGRP antibody are also provided, optionally in combination with a second agent, which are suitable for administration to increase peripheral and/or hepatic glucose utilization and thereby prevent or treat diseases and disorders associated with insulin resistance.

WO 2015/003122 A3



**Declarations under Rule 4.17:**

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

— *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))*

**Published:**

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

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

**(88) Date of publication of the international search report:**

19 March 2015

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 14/45389

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A61K 39/395, A61P 3/08, C07K 16/26 (2014.01)

CPC - A61K 2039/505, C07K 2316/96

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 39/395, A61P 3/08, C07K 16/26 (2014.01)

CPC - A61K 2039/505, C07K 2316/96

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched  
CPC: C07K 16/18, C07K 16/26Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
PatBase, Google Patents, Google Scholar, Google Web, search terms: CGRP, calcitonin gene-related peptide human antibody, glucose utilization, hepatic hepatocyte, insulin resistance, normoglycemia, lean tissue, body fat, diabetes, type II diabetes, delay onset, pancreatic beta cells, obesity, high-fat diet, diabetic fatty (ZDF) rat, antibody fragmen

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 5,364,841 A (COOPER et al.) 15 November 1994 (15.11.1994) col 3, ln 59-61, col 4, ln 43-50, ln 62-68, col 5, ln 1-16, col 6, ln 38-44, col 8, ln 17-32, ln 32-35, col 9, ln 6-8, ln 19-36, col 10, ln 5-14, Figs 1, 2A, 3	1-7, 42-45
Y	US 2012/0294797 A1 (KOVACEVICH et al.) 22 November 2012 (22.11.2012) para [0016], [0099], [0100], [0303], [0494]	1-7, 42-45
Y	US 5,942,227 A (COOPER et al.) 24 August 1999 (24.08.1999) col 4 ln 15-50, col 7, ln 1-41	7

 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

"&amp;" document member of the same patent family

Date of the actual completion of the international search

07 January 2015 (07.01.2015)

Date of mailing of the international search report

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## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 14/45389

**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.: 8-41 and 46-47  
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.

Group I: Claims 1, 4, 6-7 (in part), and 42-45, drawn to methods involving increasing peripheral and/or hepatic glucose utilization and achieve sustained normoglycemia in a subject

Group II: Claims 2 and 6-7 (in part), drawn to a method of decreasing insulin resistance in a subject

Group III: Claims 3, 5 and 6-7 (in part), drawn to a method of treating, preventing or controlling obesity, and increasing the ratio of lean tissue to body fat in a subject

---please see continuation on 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.:

**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/US 14/45389

Continuation of: Box No. III Observations where unity of invention is lacking

The inventions listed as Groups I, II, and 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:

Special Technical Features

Group I requires increasing peripheral and/or hepatic glucose utilization and achieve sustained normoglycemia in a subject, not required by Groups II and III.

Group II requires decreasing insulin resistance in a subject, not required by Groups I and III.

Group III requires treating, preventing or controlling obesity and increasing the ratio of lean tissue to body fat in a subject, not required by Groups I and II.

Common Technical Features

The feature shared by Groups I, II, and III is the administration of an anti-human CGRP antibody or antibody fragment to a subject. However, this shared technical feature does not represent a contribution over prior art, because the shared technical feature is taught by US 2009/0220489 A1 to Zeller et al. (hereinafter 'Zeller'). Zeller discloses anti-human CGRP antibody (abstract; para [0025]) and methods for treating CGRP associated disorders by administering said anti-CGRP antagonist antibody (abstract; para [0015]). As the technical feature was known in the art at the time of the invention, it cannot be considered a special technical feature that would otherwise unify the groups.

Groups I, II, and III therefore lack unity of invention under PCT Rule 13 because they do not share a same or corresponding special technical feature.