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(54) Title: TARGETING CD24-SIGLEC INTERACTIONS FOR TREATING SUBJECTS WITH PREDIABETES OR DIABETES

FIG. 1A

MGRAMVARLGLGLLLLALLLPTQIYS**SETTTGTSSNSSQSTSNSGLAP**
NPTNATTKPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRT
PEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVS
VLTVLHQDWLNGKEYKCKVSNKALPAPIEKTIISKAKGQPREPQVYTL
PPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLD
SDGSFFLYSKLTVDKSRWQOGNVFSCSVMHEALHNHYTQKSLSLSPGK

FIG. 1B

MGRAMVARLGLGLLLLALLLPTQIYS**SETTTGTSSNSSQSTSNSGLAP**
NPTNATTKVPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISR
TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVV
SVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTIISKAKGQPREPQVYTL
PPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLD
SDGSFFLYSKLTVDKSRWQOGNVFSCSVMHEALHNHYTQKSLSLSPGK

FIG. 1C

MGRAMVARLGLGLLLLALLLPTQIYS**SETTTGTSSNSSQSTSNSGLAP**
NPTNATTKAPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISR
TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVV
SVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTIISKAKGQPREPQVYTL
PPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLD
SDGSFFLYSKLTVDKSRWQOGNVFSCSVMHEALHNHYTQKSLSLSPGK

(57) Abstract: Provided herein are methods and compositions for lowering low-density lipoprotein cholesterol or glucose levels, and for treating subjects with prediabetes or diabetes by targeting CD24-Siglec interactions.



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))*

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INTERNATIONAL SEARCH REPORT

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PCT/US 20/16874

A. CLASSIFICATION OF SUBJECT MATTER IPC - C07K 14/705; A61K 39/00; A61K 38/00; G01N 33/53; G01N 33/00 (2020.01) CPC - C07K 14/705; C07K 14/70596; C07K 2319/30; C07K 14/4713; C07K 14/47; A61K 38/177; G01N 33/92; G01N 33/543 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) See Search History document Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched See Search History document Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) See Search History document		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	US 2018/0110828 A1 (ONCOIMMUNE, INC.) 26 April 2018 (26.04.2018), Abstract, para [0002], [0004], [0005], [0006], [0031], [0033], [0034], [0044], [0045], [0053], SEQ ID NO: 1, SEQ ID NO: 2, and SEQ ID NO: 6	1-2, 4, 8, 10-14, 16-24, 25/(1-2,4,8,10-14,16-24) ----- 3, 5-7, 9, 25/(3,5-7,9)
Y	US 2018/0237516 A1 (PROTHENA BIOSCIENCES LIMITED) 23 August 2018 (23.08.2018), Abstract, para [0005], [0118], [0119], [0120], [0181], and [0183]	3, 5-7, 9, 25/(3,5-7,9)
A	US 2013/0296249 A1 (LIU et al.) 07 November 2013 (07.11.2013), Abstract, para [0006], [0027], [0030], and [0031]	1-14, 16-25
A	~ HANEFELD et al., The use of lipid-lowering therapy and effects of antihyperglycaemic therapy on lipids in subjects with type 2 diabetes with or without cardiovascular disease: a pooled analysis of data from eleven randomized trials with insulin glargine 100 U/mL. Cardiovasc Diabetol. 2017, Vol. 16(1):66. PDF File: pg 1-9. Entire Documentation especially Abstract; pg 3, col 2, last para; and pg 4, Table 2	1-14, 16-25
A	~ VAZQUEZ-BENITEZ et al., Preventable Major Cardiovascular Events Associated With Uncontrolled Glucose, Blood Pressure, and Lipids and Active Smoking in Adults With Diabetes With and Without Cardiovascular Disease: A Contemporary Analysis. Diabetes Care. 2015, Vol. 38(5), p. 905-12. Entire Documentation especially Abstract; pg 908, Table 1; and pg 909, Table 2	1-14, 16-25
A	~ CHEN et al., Siglec-G/10 in self-nonsel self discrimination of innate and adaptive immunity. Glycobiology. 2014, Vol. 24(9), p. 800-6. Entire Documentation especially Abstract	1-14, 16-25
<input type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> 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 "D" document cited by the applicant in the international application "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 11 May 2020		Date of mailing of the international search report 04 AUG 2020
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. 571-273-8300		Authorized officer Lee Young Telephone No. PCT Helpdesk: 571-272-4300

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 20/16874

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.: 26
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 searched, the appropriate additional search fees must be paid.

Groups I+, Claims 1-25, directed to a method of treating a subject in need thereof with diabetes, prediabetes or at risk of developing diabetes, comprising administering a CD24 protein to the subject, for reducing serum LDL-C levels, and further wherein the subject has been previously treated with another LDL-C-lowering drug. The other LDL-C-lowering drug will be searched to the extent that the LDL-C-lowering drug encompasses wherein the other LDL-C-lowering drug is a statin. It is believed that claims 1-14, 16-25 encompass this first named invention, and thus these claims will be searched without fee to the extent that they encompass wherein the other LDL-C-lowering drug is a statin. Additional other LDL-C-lowering drug will be searched upon the payment of additional fees.
*****Continued in the 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.:
1-14, 16-25, limited to wherein the other LDL-C-lowering drug is a statin

- 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.

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Continuation of:
Box No III (unity of invention is lacking)

(Continuation of Groups I+) Applicants must specify the claims that encompass any additionally elected other LDL-C-lowering drug. 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. An exemplary election would be wherein the other LDL-C-lowering drug is an antagonist of PCSK9 [claims (1-13), 15, (16-25)].

The inventions listed as Groups I+ 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 Feature

Among Groups I+, each of the other LDL-C-lowering drug, a statin, or an antagonist of PCSK9, is structurally and functionally different from one another.

Common Technical Features

The inventions of Groups I+ share the technical features of a method of treating a subject in need thereof with diabetes, prediabetes or at risk of developing diabetes, comprising administering a CD24 protein to the subject (claim 1);
-- for reducing serum LDL-C levels (claim 2); and
-- wherein the subject has been previously treated with another LDL-C-lowering drug, wherein the other LDL-C-lowering drug is not a CD24 protein (claim 13).

However, these shared technical features do not represent a contribution over prior art as being anticipated by US 20180110828 A1 to ONCOIMMUNE, INC. (hereinafter 'Oncolmmune') as follows:

Oncolmmune discloses a method of treating a subject in need thereof with diabetes, prediabetes or at risk of developing diabetes (para [0004] - 'method for reducing LDL-C levels in a subject by administering a CD24 protein to a subject in need thereof'; para [0002] - 'low-density lipoprotein (LDL) cholesterol (LDL-C)'; para [0044] - 'subject may also be diabetic'), comprising
--administering a CD24 protein to the subject (para [0004] - 'reducing LDL-C levels in a subject by administering a CD24 protein to a subject in need thereof'; para [0002] - 'low-density lipoprotein (LDL) cholesterol (LDL-C)'; para [0044] - 'subject may also be diabetic');
-- for reducing serum LDL-C levels (para [0004] - 'reducing LDL-C levels in a subject by administering a CD24 protein to a subject in need thereof'; para [0053] - 'the amount of LDL-C in the sample...a blood sample such as serum'); and
-- wherein the subject has been previously treated with another LDL-C-lowering drug, wherein the other LDL-C-lowering drug is not a CD24 protein (para [0004] - 'reducing LDL-C levels in a subject by administering a CD24 protein to a subject in need thereof'; para [0045] - 'subject may have been previously treated with a LDL-C-lowering drug, such as a statin').

Without a shared special technical feature, the inventions lack unity with one another.

Groups I+ therefore lack unity under PCT Rule 13 because they do not share a same or corresponding special technical feature.

Continuation of item 4: Claim 26 is not drafted in accordance with the second and third sentences of Rule 6.4 (a). This claim is improper multiple dependent claims.

Note:

- I) Claim 2 contains the first appeared abbreviation "LDL-C" with no full name introduced.
- II) Claim 15 contains the first appeared abbreviation "PCSK9" with no full name introduced.