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(71) Applicants: **THE J. DAVID GLADSTONE INSTITUTES** [US/US]; 1650 Owens Street, San Francisco, California 94158 (US). **THE REGENTS OF THE UNIVERSITY OF CALIFORNIA** [US/US]; 1111 Franklin Street, Twelfth Floor, Oakland, California 94607-5200 (US).

(72) Inventors: **OTT, Melanie**; 141 Tamalpais Avenue, Mill Valley, California 94941 (US). **KONDRATOWICZ, Andrew S.**; 1650 Owens Street, San Francisco, California 94158 (US). **KROGAN, Nevan John**; 509 Ellsworth Street, San Francisco, California 94110 (US). **SHAH, Priya Shirish**; 927 Lake Street, San Francisco, California 94118 (US). **FONTAINE, Krystal Ann**; 49 Ramona Avenue, #3, San Francisco, California 94103 (US).

(74) Agent: **BORDEN, Paula A.**; 1900 University Avenue, Suite 200, East Palo Alto, California 94303 (US).

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Declarations under Rule 4.17:

— of inventorship (Rule 4.17(iv))

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:

1 September 2016

(54) Title: COMPOSITIONS AND METHODS FOR TREATING DENGUE VIRUS INFECTION

(57) Abstract: The present disclosure provides methods of treating a flavivirus infection, and compositions for use in the methods.



WO 2016/007540 A3

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 15/39424

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A61K 39/42 (2015.01)

CPC - A61K 2039/505; C07K 2317/21; A61K 38/00

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 39/42 (2015.01)

CPC: A61K 2039/505; C07K 2317/21; A61K 38/00

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
USPC: 424/147.1, 514/44.00A, 514/3.7, 424/159Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
PatBase; Keyword limited: treating Dengue virus infection administering leucine-rich repeat kinase 2 (LRRK2) inhibitor

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 2012/0040961 A1 (GRAY, et al.) 16 February 2012 (16.02.2012), entire document, especially: para [0021]; PARA [0068]; para [0070]; para [0071]; para [0244]; para [0245]; para [0252]; Table 4, pg 50, Compound IV-38.	1-3,10-12 ----- 8-9
Y	XIONG, Y et al. "ArfGAP1 Is a GTPase Activating Protein for LRRK2: Reciprocal Regulation of ArfGAP1 by LRRK2", The Journal of Neuroscience. 2012. Vol. 32 (11), pp 3877-3886, entire document, especially: abstract; pg 3877, col 1, para 1; pg 3877, col 2, para 2.	8-9
A	GARDET, A et al. "LRRK2 Is Involved in the IFN-gamma Response and Host Response to Pathogens", Journal of Immunology. 2010. Vol. 185, pp 5577-5585, entire document.	1-3,8-12
A	HAKIMI, M et al. "Parkinson's disease-linked LRRK2 is expressed in circulating and tissue immune cells and upregulated following recognition of microbial structures", J. Neural Transm. 2011. Vol. 118 (5), pp 795-808, entire document.	1-3,8-12

☐ 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

27 October 2015 (27.10.2015)

Date of mailing of the international search report

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Mail Stop PCT, Attn: ISA/US, Commissioner for Patents
P.O. Box 1450, Alexandria, Virginia 22313-1450

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Authorized officer:

Lee W. Young

PCT Helpdesk: 571-272-4300
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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 15/39424

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.: claims 13-19
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 box---

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.:
1-3,8-12

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 15/39424

BOX III: lack of unity

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 1-12, drawn to a method of treating a Dengue virus infection in an individual, the method comprising administering to the individual an effective amount of a leucine-rich repeat kinase 2 (LRRK2) inhibitor. Claim 1 will be searched to the extent that the LRRK2 inhibitor is a compound of Formula I listed in instant claim 3. It is believed that claims 1-3, 8-12 (in part) encompass this first named invention, and thus these claims will be searched without fee. Applicant is invited to elect additional compounds of Formula I, wherein each additional compound elected will require one additional invention fee. Applicants must specify the claims that encompass any additionally elected compound. 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 LRRK2 inhibitor is a compound of Formula II listed in instant claim 4 (i.e., claims 1-2, 4 and 8-12 (in part)).

Group 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 features:

The special technical feature of each invention of Group I+ is a unique pyrazolopyridine compound, which is not required in any other invention of the group.

Shared Technical Features:

The inventions of Group I+ share the technical feature of a method of treating a Dengue virus infection in an individual, the method comprising administering to the individual an effective amount of a leucine-rich repeat kinase 2 (LRRK2) inhibitor. However, these shared technical feature does not provide a contribution over the prior art as being obvious over US 2012/0040961 A1 to Gray et al. (hereinafter 'Gray'). Gray teaches a method of treating (para [0071]) a virus infection (para [0021]) in an individual (para [0070]), the method comprising administering to the individual an effective amount of a leucine-rich repeat kinase 2 (LRRK2) inhibitor (Table 4, pg 50, Compound IV-38; see instant specification in para [0086] LRRK2 inhibitor), but does not specifically teach treating a Dengue virus infection specifically. However, it would have been obvious to a person having ordinary skill in the art that if LRRK2 inhibitor can be used to treat virus infections in general, then it may be used to treat Dengue virus infections, and routine experimentation would show which infections are susceptible to treatment.

As the shared 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, Groups I+ lack unity under PCT Rule 13.

Note: claims 13-19 are determined unsearchable because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).