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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))

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(54) Title: METHODS OF TREATING INFLAMMATION

(57) Abstract: The present invention relates to methods of decreasing inflammation by inhibiting polo-like kinase (Plk)

**INTERNATIONAL SEARCH REPORT**

International application No.

PCT/US 11/55437

**A. CLASSIFICATION OF SUBJECT MATTER**

IPC(8) - A61K 31/497; 31/517; 31/519 (2012.01)

USPC - 514/252.11, 514/258.1, 514/262.1

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)

USPC: 514/252.11, 258.1, 262.1

IPC(8): A61K 31/497; 31/517; 31/519 (2012.01)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

USPC: 514/183, 247, 248, 252.1, 256, 277, 579, 646, 660, 675, 678, 690

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

PubWEST (DB=PGPB,USPT,USOC,EPAB,JPAB; PLUR=NO; OP=ADJ), Google Scholar, Google Patents

Search Terms Used: polo-like linase, PLK, endome, dendritic, RIG-1, pan-specific, BI2536, poloxipan, GW843682X, binds, inhibits, pathogen, virus

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X ---	US 2006/0035909 A1 (Fuksova et al.) 16 February 2006 916.02.2006) esp: abstract; paras [0206], [0207], [0048], [0006], [0052], [0180], [0208], [0220], [0238].	1, 2, 9 -----
Y		3, 10, 12
Y	Lund et al. Toll-like Receptor 9-mediated Recognition of Herpes Simplex Virus-2 by Plasmacytoid Dendritic Cells. J. Exp. Med.; August 4, 2003; Volume 198; No. 3; 513-520. esp: abstract; pg 514 first column last paragraph.	3
Y	Strebhardt. Multifaceted polo-like kinases: drug targets and antitargets for cancer therapy. Nature Reviews; August 2010; Vol. 9; pg 643-660.	10, 12
Y	Reindl et al. A Pan-Specific Inhibitor of the Polo-Box Domains of Polo-like Kinases Arrests Cancer Cells in Mitosis. ChemBioChem; April 6, 2009; Vol. 10; pg 1145-1148. abstract only [online]; downloaded from <a href="http://onlinelibrary.wiley.com/doi/10.1002/cbic.200900059/abstract">http://onlinelibrary.wiley.com/doi/10.1002/cbic.200900059/abstract</a> on 01.04.2012	10, 12

Further documents are listed in the continuation of Box C.

* Special categories of cited documents:	"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
"A" document defining the general state of the art which is not considered to be of particular relevance	"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
"E" earlier application or patent but published on or after the international filing date	"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
"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)	"&" document member of the same patent family
"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	

Date of the actual completion of the international search 1 April 2012 (01.04.2012)	Date of mailing of the international search report <b>25 APR 2012</b>
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

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 11/55437

**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.: 11  
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 1-3, 9, 10 and 12, directed to a method of decreasing inflammation associated with an innate immune response to a pathogen or pathogen derived molecule, comprising administering to a subject in need thereof a polo-like kinase (PLK) inhibitor.

Group II: claims 4, 5, 9, 10 and 12, directed to a method of treating inflammation comprising administering to a subject in need thereof a polo-like kinase (PLK) inhibitor.

- Please see extra sheet for continuation -

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, 9, 10 and 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.

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Continuation of Box III: Lack of Unity of Invention

Group III: claims 6, 7, 8-10 and 12, directed to a method of decreasing anti-viral cytokine expression in a subject, comprising administering to a subject in need thereof a PLK inhibitor.

Group IV: claims 13-16, directed to a method for identifying genes or genetic elements associated with a pathogen specific response, comprising: a) contacting a dendritic cell with a toll-like receptor agonist; and b) identify a gene or genetic element whose expression is modulated by step a).

The inventions listed as Groups I - IV 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 feature of the claims of Groups I-IV are disclosed in the Group descriptions, above. There is no common technical element shared by all of the above groups. Groups I-III are related to inhibition of Polo-Like Kinase (PLK), Groups I and II are further related to reduction of inflammation by inhibition of PLK. Groups I and IV are further related to pathogen infection. These common technical elements do not represent an improvement over the prior art of US 2006/0035909 A1 to Fuksova et al., which teaches the use of 8-azapurine derivatives (para [0005]) for the inhibition of PLK enzymes (para [0200]), including PLK-1 (para [0206], [0207]), and treating inflammation (para [0048]) by reducing the expression of cytokines (para [0233]), further wherein the conditions treated may be viral (para [0052]), or due to another pathogen (para [0225]). Therefore, the inventions of Groups I - IV lack unity of invention under PCT Rule 13 because they do not share a same or corresponding special technical feature.