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Published:

- with international search report (Art. 21(3))
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12 September 2014

(54) Title: OLIGOOXOPIPERAZINES FOR P53 REACTIVATION

(57) Abstract: The present invention relates to oligoxxopiperazines for reactivating p53. Methods of using the oligoxxopiperazines are also disclosed.



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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.:
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 attached 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.:
1-18

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.

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A61K 31/497 (2014.01)

USPC - 514/252.11

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 31/497 (2014.01)

USPC - 514/252.11

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
USPC - 514/253.12; 544/357

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

Patbase (pgpb, uspt, usoc, epab, jpab, dwpi, tdbd), Dialog Proquest (npl), Google Patents (pl, npl), Google scholar (pl, npl); Search Terms: Oligoxxopiperazine, oxopiperazine, creb, p300, p53, mimics, hif, hypoxia, c-terminal, cancer, hpv, treat, inhibit, anticancer, anti-cancer, mimetic, Arora, oligo, oligomer, cisplatin

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2012/0040992 A1 (ARORA, et al.) 16 February 2012 (16.02.2012) entire document, especially para [0060], [0110]-[0114], [0122]-[0123], [0128]-[0134], [0198]; Table 3	1-18
Y	Grossman, et al. "p300/MDM2 complexes participate in MDM2-mediated p53 degradation." Molecular cell, 1998, Vol 2.4, pp 405-415. pg 406, col 2; pg 407, col 2	1-18
Y	US 2010/0062051 A1 (SHIN, et al.) 11 March 2010 (11.03.2010) entire document, especially para [0006], [0086], [0090]	16-18
A	Tosovska., et al. "Oligoxxopiperazines as nonpeptidic alpha-helix mimetics." Organic letters, 2010, Vol. 12.7, pp 1588-1591. Entire document	1-18

☐ 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

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Date of mailing of the international search report

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Attachment to Box.No.III:

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 1-18 directed to a method of treating or preventing in a subject a disorder mediated by interaction of E6 with CREB-binding protein and/or p300, said method comprising administering to the subject an oligooxopiperazine that substantially mimics helix aB of the C-terminal transactivation domain of Hypoxia-Inducible Factor 1a under conditions effective to treat or prevent the disorder.

Group II - Claims 19-45 directed to a method of inducing apoptosis and decreasing survival and/or proliferation of a cell, said method comprising contacting the cell with an oligooxopiperazine that substantially mimics helix aB of the C-terminal transactivation domain of HIF 1a under conditions effective to induce apoptosis of the cell.

Group III - Claims 46-58 directed to a method of preventing or reversing inactivation of p53 in a cell, said method comprising contacting the cell with an oligooxopiperazine that substantially mimics helix aB of the C-terminal transactivation domain of HIF 1a under conditions effective to prevent or reverse inactivation of p53 in a cell.

Group IV - Claims 59-72 directed to a method of inhibiting p300-mediated acetylation of a transcription factor in a cell, said method comprising contacting the cell with an oligooxopiperazine that substantially mimics helix aB of the C-terminal transactivation domain of HIF 1a under conditions effective to inhibit p300-mediated acetylation of the transcription factor in the cell.

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:

Special Technical Features

Groups II-IV do not include a method of treating or preventing in a subject a disorder mediated by interaction of E6 with CREB-binding protein and/or p300, as required by Group I.

Groups I and III-IV do not include a method of inducing apoptosis and decreasing survival and/or proliferation of a cell, as required by Group II.

Groups I-II and IV do not include a method of preventing or reversing inactivation of p53 in a cell, as required by Group III.

Groups I-III do not include a method of inhibiting p300-mediated acetylation of a transcription factor in a cell, as required by Group IV.

Common Technical Features

Groups I-IV share the technical feature of a method comprising administering to a subject or contacting a cell an effective amount of a oligooxopiperazine that substantially mimics helix aB of the C-terminal transactivation domain of Hypoxia-Inducible Factor 1a.

This shared technical feature, however, does not constitute a contribution over the prior art as being anticipated by US 2012/0040992 A1 to Arora et al. (hereinafter 'Arora') which discloses a method comprising administering to a subject (para [0132]) or contacting a cell (para [0099]) an effective amount of a oligooxopiperazine (para [0132]-[0133]) of formula I or formula I-A (para [0060]-[0084]; para [0102]-[0103]) which substantially mimics an alpha-helix involved in protein-protein interactions (para [0112]-[0113]) and which according to the Applicant's instant specification substantially mimics helix aB of the C-terminal transactivation domain of Hypoxia-Inducible Factor 1a [para [0035]-[0036], Formula I; para [0124], BB2-162).

As said method was known in the art at the time of the invention this cannot be considered a special technical feature that would otherwise unify the groups.

Groups I-IV therefore lack unity under PCT Rule 13.2, because they do not share a same or corresponding special technical feature providing a contribution over the prior art.