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(54) Title: PROTEIN KINASE C ZETA AS A DRUG TARGET FOR ARTHRITIS AND OTHER INFLAMMATORY DISEASES

(57) Abstract: The present invention is based on the discovery that ζ PKC expression is increased in the tissues of arthritis patients as compared to normal individuals. Accordingly, the present invention provides methods of diagnosing, prognosing, and monitoring the course of arthritis in a patient based on increased ζ PKC gene expression in arthritic tissue. The present invention further provides compounds that inhibit the expression of ζ PKC for use as remedies in the treatment of arthritis, including, but not limited to, inhibitory polynucleotides and polypeptides, small molecules, and peptide inhibitors. In addition, the present invention provides pharmaceutical formulations and routes of administration for such remedies, as well as methods for assessing their efficacy.

WO 2004/104217 A3

INTERNATIONAL SEARCH REPORT

ational Application No
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A. CLASSIFICATION OF SUBJECT MATTER IPC 7 G01N33/68 C12Q1/48 A61K31/00 A61K38/00 C12N15/11 A61K31/7105		
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 7 G01N C12Q A61K C12N		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
Electronic data base consulted during the International search (name of data base and, where practical, search terms used) EPO-Internal, BIOSIS, EMBASE, WPI Data		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	HUSSAIN SHAISTA ET AL: "Activation of protein kinase Czeta is essential for cytokine-induced metalloproteinase-1, -3, and -9 secretion from rabbit smooth muscle cells and inhibits proliferation" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 277, no. 30, 28 July 2002 (2002-07-28), pages 27345-27352, XP002312855 ISSN: 0021-9258 the whole document	1-34, 37-40
<input checked="" type="checkbox"/> Further documents are listed in the continuation of box C.		
<input type="checkbox"/> Patent family members are listed in annex.		
° Special categories of cited documents :		
A document defining the general state of the art which is not considered to be of particular relevance	*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	
E earlier document but published on or after the international filing date	*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	
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)	*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.	
O document referring to an oral disclosure, use, exhibition or other means	*&* document member of the same patent family	
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 <p style="text-align: center; font-size: 1.2em;">31 January 2005</p>	Date of mailing of the international search report <p style="text-align: center; font-size: 1.2em;">25. 05. 2005</p>	
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer <p style="text-align: center; font-size: 1.2em;">Pellegrini, P</p>	

INTERNATIONAL SEARCH REPORT

International Application No
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>JORDAN N J ET AL: "DIFFERENTIAL EFFECTS OF PROTEIN KINASE C INHIBITORS ON CHEMOKINE PRODUCTION IN HUMAN SYNOVIAL FIBROBLASTS" BRITISH JOURNAL OF PHARMACOLOGY, BASINGSTOKE, HANTS, GB, vol. 117, no. 6, 1996, pages 1245-1253, XP008031180 ISSN: 0007-1188 the whole document</p> <p style="text-align: center;">-----</p>	<p>1-34, 37-40</p>

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2004/014759

Box 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:

- Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 31-42 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound.
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 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:

see additional 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 an additional fee, this Authority did not invite payment of any additional fee.
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.:
1-30 (completely), 31-32 (in part), 34, 37-38 (in part), 40

Remark on Protest

- The additional search fees were accompanied by the applicant's protest.
- No protest accompanied the payment of additional search fees.

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-30 (completely), 31-32 (in part), 34, 37-38 (in part),
40

Method of i.a. diagnosing and prognosing arthritis, and method of screening anti-arthritis compounds, based on detecting altered expression or activity of PKC-zeta. Method of treating arthritis based on administering a molecule which is Ro-31-8220, bisindolylmaleimide or the peptide 2089.

2. claims: 31-32 (in part), 33, 37-38 (in part),39

Method of treatment of arthritis based on administering an antisense polynucleotide against PKC-zeta.

3. claims: 31-32 (in part), 35, 36 (in part), 37-38 (in part), 41,
42 (in part), 43-44 (in part)

Method of treatment of arthritis based on administering a siRNA molecule against PKC- zeta, in particular the siRNA molecule of figure 1 corresponding to SEQ ID NO:21 and 33; such siRNA molecule per se.
