

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
7 May 2009 (07.05.2009)

(10) International Publication Number
WO 2009/059143 A3

PCT

(51) International Patent Classification:
A61K 38/00 (2006.01)

(21) International Application Number:
PCT/US2008/082002

(22) International Filing Date:
31 October 2008 (31.10.2008)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/984,044 31 October 2007 (31.10.2007) US

(71) Applicant (for all designated States except US): **CENTOCOR, INC.** [US/US]; 200 Great Valley Parkway, Malvern, Pennsylvania 19355 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **BLAKE, Simon** [GB/US]; 145 King of Prussia Road, Radnor, Pennsylvania 19087 (US). **STOJANOVIC-SUSULIC, Vedrana** [US/US]; 145 King of Prussia Road, Radnor, Pennsylvania 19087 (US). **WARE, Mark** [GB/US]; 3210 Merryfield Row, San Diego, California 92121 (US). **WU, Linda** [US/US]; 145 King of Prussia Road, Radnor, Pennsylvania 19087 (US).

(74) Agent: **BAUMEISTER, Kirk**; Johnson & Johnson, One Johnson & Johnson Plaza, New Brunswick, New Jersey 08933 (US).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

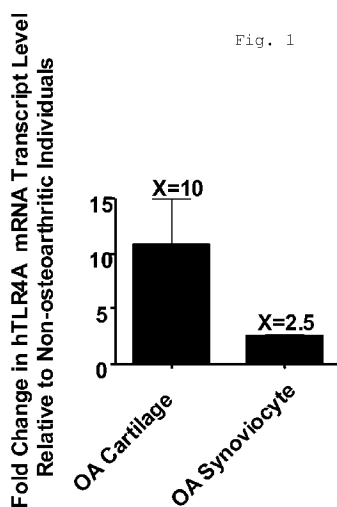
(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

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:
30 December 2009

(54) Title: USE OF TOLL-LIKE RECEPTOR 4 ANTAGONISTS FOR THE TREATMENT OR PREVENTION OF OSTEOARTHRITIC CONDITIONS



(57) Abstract: Methods for treating or preventing osteoarthritic conditions using Toll-Like Receptor 4 (TLR4) antagonists are disclosed.

WO 2009/059143 A3

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 08/82002

A. CLASSIFICATION OF SUBJECT MATTER IPC(8) - A61K 38/00 (2009.01) USPC - 514/2 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- 514/2 Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched USPC- 514/2 (text search-see search terms below) Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) PubWEST (USPT, PGPB, EPAB, JPAB), Google Patent/Scholar Search terms: toll like receptor, TLR4, osteoarthritis, MTS510, antibody, antagonist		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2007/0244066 A1 (DeLeo et al.) 18 October 2007 (18.10.2007) para [0022], [0024]	1-3, 7-9
A	US 2006/0211752 A1 (KOHN et al.) 21 September 2006 (21.09.2006)	1-3, 7-9
A	US 2006/0165686 A1 (Elson et al.) 27 July 2006 (27.07.2006)	1-3, 7-9
<input type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/>		
* 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 01 April 2009 (01.04.2009)		Date of mailing of the international search report 16 APR 2009
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 08/82002

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:

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, and 7-9, directed to a method of treating or preventing an osteoarthritic condition comprising administering an antibody effective as an antagonist for Toll Like Receptor 4 (TLR4).

Group II: claims 1, 4, 5, 7 and 10, directed to a method of treating or preventing an osteoarthritic condition comprising administering a peptide effective as an antagonist for Toll Like Receptor 4 (TLR4), wherein the peptide has SEQ ID NO: 4.

- 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 and 7-9

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.

Continuation of Box III: Lack of Unity of Invention

Group III: claims 1, 4, 6, 7, 11 and 12, directed to a method of treating or preventing an osteoarthritic condition comprising administering a peptide effective as an antagonist for Toll Like Receptor 4 (TLR4), wherein the peptide has SEQ ID NO: 10.

The inventions listed as Groups I - III 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 Group I claims is a method of treating or preventing an osteoarthritic condition comprising administering an antibody effective as an antagonist for Toll Like Receptor 4 (TLR4). - not required by the claims of Groups II or III. The special technical feature of the Group II claims is a method of treating or preventing an osteoarthritic condition comprising administering a peptide effective as an antagonist for Toll Like Receptor 4 (TLR4), wherein the peptide has SEQ ID NO: 4 - not required by the claims of Groups I or III. The special technical feature of the Group III claims is a method of treating or preventing an osteoarthritic condition comprising administering a peptide effective as an antagonist for Toll Like Receptor 4 (TLR4), wherein the peptide has SEQ ID NO: 10 - not required by the claims of Groups I or II.

The common technical element shared by the above groups is that they are related to osteoarthritis in relation to Toll Like Receptor 4, and inhibition thereof. The use of antibodies against TLR4 to treat osteoarthritis does not represent an improvement over the prior art of US 2006/0165686 A1 to Elson et al. (see abstract, para [0007], [0009]). Further, treatment of a condition associated with arthritis using a peptide having SEQ ID NO: 4 is also taught in the prior art of US 2005/0089957 A1 to Goddard et al. (see SEQ ID NO: 14, as well as para [0006]). Therefore, the inventions of Groups I-III lack unity of invention under PCT Rule 13 because they do not share a same or corresponding special technical feature.