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[Continued on next page]

(54) Title: COMPOUNDS AND METHODS FOR THE TREATMENT OF RENAL DISEASE

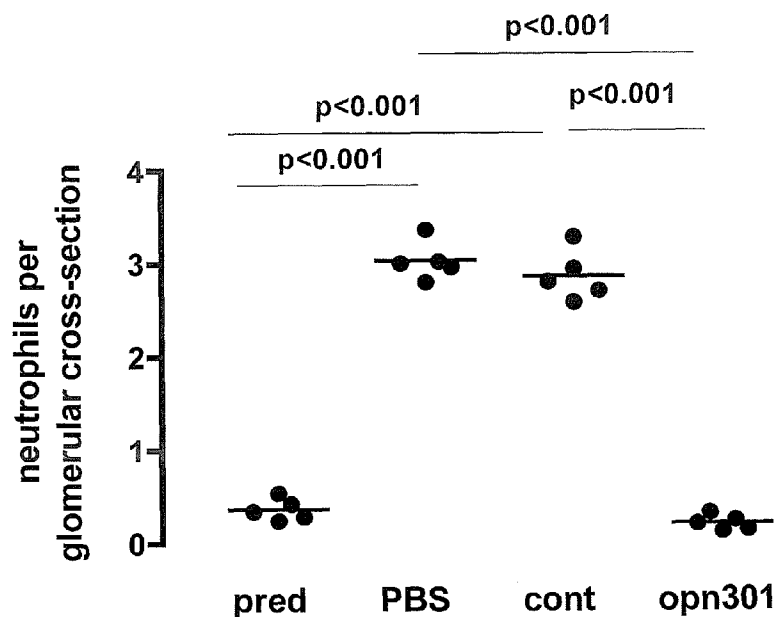


Figure 1

(57) Abstract: The present invention provides compounds and methods for the treatment and prophylaxis of renal disease and inflammation. In particular the invention provides methods for the treatment of kidney disease and failure through the administration of compounds which function as inhibitors of TLR2 function and expression.



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INTERNATIONAL SEARCH REPORT

International application No
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A. CLASSIFICATION OF SUBJECT MATTER

INV. A61K39/395 A61K38/17 C07K14/705 A61P37/06

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)

C07K A61K

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, WPI Data, PAJ, BIOSIS, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	LEEMANS JAKLIEN C ET AL: "Renal-associated TLR2 mediates ischemia/reperfusion injury in the kidney" JOURNAL OF CLINICAL INVESTIGATION, vol. 115, no. 10, October 2005 (2005-10), pages 2894-2903, XP002502398 ISSN: 0021-9738 the whole document, especially discussion -----	1-8
Y	EP 1 293 566 A (NESTLE SA [CH]) 19 March 2003 (2003-03-19) paragraphs [0010] - [0012], [0018] - [0024], [0056], [0057], [0077]; claims 1-27 ----- -/--	1-8

☒ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

* 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 document 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

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INTERNATIONAL SEARCH REPORT

International application No

PCT/EP2008/058732

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 2005/079419 A (UNIV CALIFORNIA [US]; RAZ EYAL [US]; REDECKE VANESSA DOREEN [US]; HORN) 1 September 2005 (2005-09-01) paragraphs [0003], [0030], [0031], [0036], [0048] - [0051], [0088], [0096], [0097], [0103]; claims 1-23 -----	1-8, 13-15
A	ANDERS H-J ET AL: "Signaling danger: toll-like receptors and their potential roles in kidney disease" JOURNAL OF THE AMERICAN SOCIETY OF NEPHROLOGY, WILLIAMS AND WILKINS, BALTIMORE, MD, US, vol. 15, no. 4, 1 January 2004 (2004-01-01), pages 854-867, XP003004580 ISSN: 1046-6673 the whole document, especially table 4 -----	
P,X	PALSSON-MCDERMOTT E M ET AL: "The potential of targeting Toll-like receptor 2 in autoimmune and inflammatory diseases" IRISH JOURNAL OF MEDICAL SCIENCE, CAHILL, DUBLIN, IE, vol. 176, no. 4, 1 December 2007 (2007-12-01), pages 253-260, XP009106439 ISSN: 0021-1265 the whole document, especially page 256, right-hand column, first paragraph, page 258, left-hand column, second paragraph - right-hand column, last paragraph -----	1-8, 13-15

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2008/058732

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:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers allsearchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an 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 reportcovers 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.:

see annex

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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

Invention 1: claims 1-8, 13-15 (all partially)

A method of reducing one or more biological activities of TLR2 in a TLR2 expressing cell or tissue implicated in renal disease or inflammation comprising contacting the cell or tissue with an antagonist of TLR2 activity or expression in an amount sufficient to reduce one or more biological activities of TLR2 in the cell or tissue, wherein the antagonist is a protein.

Inventions 2-7: claims 1-8, 13-15 (all partially)

A method as recited for invention 1 wherein each of the following TLR2 antagonists belongs to a separate invention: a peptide, a peptidomimetic, a nucleic acid, a carbohydrate, a lipid and a small molecule compound.

Invention 8: claims 1-8, 13-15 (all partially), 9-12 (complete)

A method of reducing one or more biological activities of TLR2 in a TLR2 expressing cell or tissue implicated in the onset or progression of autoimmune arthritis comprising contacting the cell or tissue with an antagonist of TLR2 activity in an amount sufficient to reduce one or more biological activities of TLR2 in the cell or tissue, wherein the antagonist is an antibody which has binding specificity to human TLR2.

Invention 9: claims 1-8, 14-17 (all partially)

A method of reducing one or more biological activities of TLR2 in a TLR2 expressing cell or tissue implicated in the onset or progression of autoimmune arthritis comprising contacting the cell or tissue with an antagonist of TLR2 expression in an amount sufficient to reduce one or more biological activities of TLR2 in the cell or tissue, wherein the antagonist inhibits the expression of nucleic acid encoding the TLR2 protein and wherein said antagonist is an anti-sense oligonucleotide

Inventions 10-17: claims 1-8, 14-17 (all partially)

A method as recited for invention 9 wherein each of the following TLR2 antagonists belongs to a separate invention: triple helix molecules, anti-sense DNA, anti-sense RNA, ribozyme, iRNA, miRNA, siRNA and shRNA molecule.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Invention 18: claims 18-43

A method for the treatment and/or prophylaxis of a renal disorder as recited in present claim 18 and related subject-matter.

Invention 19: claims 44-49

A pharmaceutical composition as recited in present claim 44.

Invention 20: claims 50-77

An agent which modulates the function or expression of TLR2 for the preparation of a medicament for the treatment of renal inflammation and disease and related subject-matter

Invention 21: claim 78

A screening method for the identification of compounds which suppress TLR2 mediated inflammation and associated cell, tissue or organ damage occurring during a renal disorder as recited in present claim 78.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2008/058732

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
EP 1293566	A	19-03-2003	AT 360694 T	15-05-2007
			DE 60219808 T2	17-01-2008
			DK 1430133 T3	17-09-2007
			WO 03025015 A2	27-03-2003
			ES 2286292 T3	01-12-2007
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WO 2005079419	A	01-09-2005	NONE	