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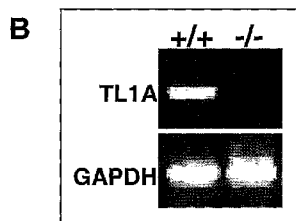
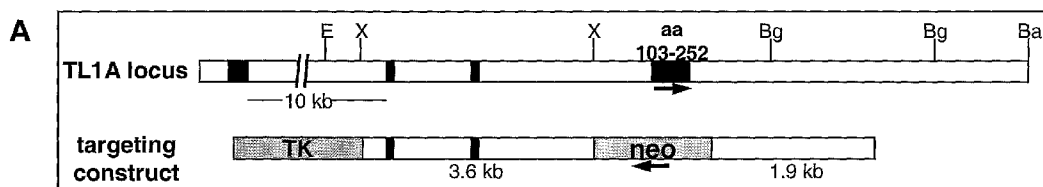
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(54) Title: TL1A IN THE TREATMENT OF DISEASE



(57) Abstract: Methods of modulating TL1A for the treatment of disease are disclosed.

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INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER		
INV. A61K39/395 A61P29/00	A61K38/17 A61P37/02	A61P25/00 A61P1/04
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, BIOSIS, EMBASE, WPI Data, Sequence Search		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2003/129189 A1 (YU GUO-LIANG [US] ET AL) 10 July 2003 (2003-07-10) page 4, paragraph [0023] pages 39 and 40 , paragraphs [0296] and [0297] page 50, paragraph [0375] page 60, paragraph [0470] page 64, paragraphs [0516] and [0519] page 110, paragraph [1039] page 11, left-hand column, paragraph 2; claim 26; examples 34-38; sequences 20,21 page 62, left-hand column, last paragraph - page 63, right-hand column, last paragraph page 65, right-hand column, paragraph 4 - last paragraph ----- -/--	1-76
<input checked="" type="checkbox"/>	Further documents are listed in the continuation of Box C.	<input checked="" type="checkbox"/>
<input checked="" type="checkbox"/>	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	
Date of the actual completion of the international search 19 March 2007	Date of mailing of the international search report 05/04/2007	
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 Loubradou, Gabriel	

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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>US 2003/198640 A1 (YU GUO-LIANG [US] ET AL) 23 October 2003 (2003-10-23) page 4, paragraphs [0027] to [0029] page 50, paragraphs [0327] to [0328] pages 67 and 68, paragraph [0470] page 71, paragraph [0507] claims 1-17; examples 12-14, 21-23, 35-38; sequences 1, 2</p>	19-76
A	<p>-----</p> <p>WEINSTOCK-GUTTMAN B ET AL: "COMBINATION THERAPY FOR MULTIPLE SCLEROSIS THE TREATMENT STRATEGY OF THE FUTURE?" CNS DRUGS, ADIS INTERNATIONAL, AUCKLAND, NZ, vol. 18, no. 12, 2004, pages 777-792, XP009056907 ISSN: 1172-7047 the whole document</p>	16
A	<p>-----</p> <p>PAPADAKIS KONSTANTINOS A ET AL: "Dominant role for TL1A/DR3 pathway in IL-12 plus IL-18-induced IFN-gamma production by peripheral blood and mucosal CCR9(+) T lymphocytes" JOURNAL OF IMMUNOLOGY, vol. 174, no. 8, April 2005 (2005-04), pages 4985-4990, XP002407269 ISSN: 0022-1767 abstract page 4988, right-hand column, last paragraph - page 4989, right-hand column, paragraph 2</p>	19-76
A	<p>-----</p> <p>MIGONE THI-SAU ET AL: "TL1A is a TNF-like ligand for DR3 and TR6/DcR3 and functions as a T cell costimulator" IMMUNITY, CELL PRESS, US, vol. 16, no. 3, March 2002 (2002-03), pages 479-492, XP002397922 ISSN: 1074-7613 abstract page 489, right-hand column, paragraph 2 page 489, right-hand column, last paragraph - page 490, left-hand column, paragraph 1</p> <p>-----</p> <p style="text-align: center;">-/--</p>	37-76

INTERNATIONAL SEARCH REPORT

International application No

PCT/US2006/020234

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>KANG Y J ET AL: "Involvement of TL1A and DR3 in induction of pro-inflammatory cytokines and matrix metalloproteinase-9 in atherogenesis" CYTOKINE, ACADEMIC PRESS LTD, PHILADELPHIA, PA, US, vol. 29, no. 5, 7 March 2005 (2005-03-07), pages 229-235, XP004772023 ISSN: 1043-4666 the whole document</p> <p style="text-align: center;">-----</p>	
A	<p>YANG CHIA-RON ET AL: "Soluble decoy receptor 3 induces angiogenesis by neutralization of TL1A, a cytokine belonging to tumor necrosis factor superfamily and exhibiting angiostatic action." CANCER RESEARCH, vol. 64, no. 3, 1 February 2004 (2004-02-01), pages 1122-1129, XP002407270 ISSN: 0008-5472 the whole document</p> <p style="text-align: center;">-----</p>	
A	<p>ZHANG J ET AL: "Modulation of T-cell responses to alloantigens by TR6/DcR3." THE JOURNAL OF CLINICAL INVESTIGATION. JUN 2001, vol. 107, no. 11, June 2001 (2001-06), pages 1459-1468, XP002407271 ISSN: 0021-9738 the whole document</p> <p style="text-align: center;">-----</p>	
A	<p>HSU TSUI-LING ET AL: "Attenuation of Th1 Response in Decoy Receptor 3 (DcR3) Transgenic Mice" FASEB JOURNAL, vol. 18, no. 4-5, 2004, pages Abst. 774.25 URL-http://ww, XP009080504 & FASEB MEETING ON EXPERIMENTAL BIOLOGY: TRANSLATING THE GENOME; WASHINGTON, DISTRICT OF COLUMBIA, USA; APRIL 17-21, 2004 ISSN: 0892-6638 the whole document</p> <p style="text-align: center;">-----</p>	37-76
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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.
A	<p>CHANG YUNG-CHI ET AL: "Modulation of macrophage differentiation and activation by decoy receptor 3." JOURNAL OF LEUKOCYTE BIOLOGY, vol. 75, no. 3, March 2004 (2004-03), pages 486-494, XP002425307 ISSN: 0741-5400 abstract page 486, right-hand column, paragraph 2 - last paragraph page 492, left-hand column, paragraph 2 - page 493, paragraph 3</p>	37-76
A	<p>PAPADAKIS KONSTANTINOS A ET AL: "TL1A synergizes with IL-12 and IL-18 to enhance IFN-gamma production in human T cells and NK cells" JOURNAL OF IMMUNOLOGY, vol. 172, no. 11, 1 June 2004 (2004-06-01), pages 7002-7007, XP002425334 ISSN: 0022-1767 the whole document</p>	
A	<p>PREHN JOHN L ET AL: "Potential role for TL1A, the new TNF-family member and potent costimulator of IFN-gamma, in mucosal inflammation." CLINICAL IMMUNOLOGY (ORLANDO, FLA.) JUL 2004, vol. 112, no. 1, July 2004 (2004-07), pages 66-77, XP002425309 ISSN: 1521-6616 abstract</p>	19-54
A	<p>BAMIAS GIORGOS ET AL: "Expression, localization, and functional activity of TL1A, a novel Th1-polarizing cytokine in inflammatory bowel disease." JOURNAL OF IMMUNOLOGY (BALTIMORE, MD. : 1950) 1 NOV 2003, vol. 171, no. 9, 1 November 2003 (2003-11-01), pages 4868-4874, XP002425310 ISSN: 0022-1767 the whole document</p>	19-54

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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:

1. Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 1-76 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/composition.
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.:

1-36 (partially), 37-76 (completely)
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.:

Remark on Protest

- The additional search fees were accompanied by the applicant's protest.
- 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:

1. claims: 1, 5-8, 15-18 (all partially) and 2

A method of treating multiple sclerosis in a subject comprising administrating an anti-TL1A blocking antibody or antigen binding fragment thereof

2. claims: 1,5-8, 15-18 (all partially) and 3

A method of treating multiple sclerosis in a subject comprising administrating an anti-DR3 blocking antibody or antigen binding fragment thereof

3. claims: 1, 15-18 (all partially) and 4, 9-14

A method of treating multiple sclerosis in a subject comprising administrating a soluble decoy DR3 polypeptide

4. claims: 1, 15-18 (all partially)

A method of treating multiple sclerosis in a subject comprising administrating an anti-TL1A or anti-DR3 aptamer

5. claims: 1, 15-18 (all partially)

A method of treating multiple sclerosis in a subject comprising administrating an RNAi inhibitor of TL1A or DR3

6. claims: 19, 23-26, 33-36 (all partially) and 20

A method of treating ulcerative colitis in a subject comprising administrating an anti-TL1A blocking antibody or antigen binding fragment thereof

7. claims: 19, 23-26, 33-36 (all partially) and 21

A method of treating ulcerative colitis in a subject comprising administrating an anti-DR3 blocking antibody or antigen binding fragment thereof

8. claims: 19, 33-36 (all partially) and 22, 27-32

A method of treating ulcerative colitis in a subject comprising administrating a soluble decoy DR3 polypeptide

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

9. claims: 19, 33-36 (all partially)

A method of treating mutiple sclerosis in a subject
comprising administrating an anti-TL1A or anti-DR3 aptamer

10. claims: 19, 33-36 (all partially)

A method of treating mutiple sclerosis in a subject
comprising administrating an RNAi inhibitor of TL1A or DR3

11. claims: 37-76

A method of modulating (reducing or enhancing) an innate
immunity response comprising administrating an agent that
block TL1A signaling

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2006/020234

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2003129189	A1	10-07-2003	NONE
US 2003198640	A1	23-10-2003	NONE
WO 0046247	A	10-08-2000	NONE
WO 2005018571	A	03-03-2005	CA 2536086 A1 03-03-2005 EP 1667730 A2 14-06-2006