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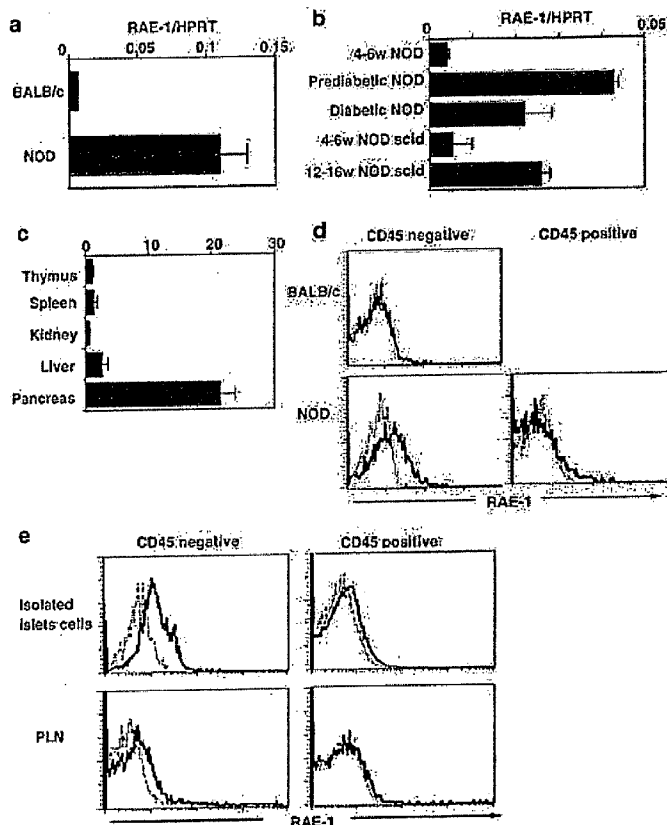
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[Continued on next page]

(54) Title: MODULATION OF NKG2D AND METHOD FOR TREATING OR PREVENTING SOLID ORGAN ALLOGRAFT REJECTION



(57) Abstract: The present invention relates to methods and compositions for treating and/or preventing autoimmune and/or inflammatory disease. In particular, the present invention provides therapeutics for impairing the expansion and function of autoreactive T cells, NK cells and/or NKT cells, by modulating NKG2D. The present application also relates to method for treating or preventing solid organ allograft rejection, the method comprising administering an agent that reduces ligand-induced NKG2D activation of cells (such as an antibody that binds NKG2D) and an inhibitor of lymphocyte co-stimulation to a subject in need thereof (such as CTLA4-Ig or LEA29Y)



FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL,
PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM,
GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

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INTERNATIONAL SEARCH REPORT

International application No
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A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K39/395

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)
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, BIOSIS, EMBASE, Sequence Search, FSTA

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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Y	LARSEN C P ET AL: "Rational development of LEA29Y (belatacept), a high-affinity variant of CTLA4-Ig with potent immunosuppressive properties" AMERICAN JOURNAL OF TRANSPLANTATION, BLACKWELL MUNKSGAARD,, DK, vol. 5, no. 3, March 2005 (2005-03), pages 443-453, XP002393471 ISSN: 1600-6135 the whole document	1-24
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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

Date of the actual completion of the international search

5 February 2008

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18/02/2008

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INTERNATIONAL SEARCH REPORT

International application No

PCT/US2007/068348

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	VINCENTI F ET AL: "COSTIMULATION BLOCKADE WITH BELATACEPT IN RENAL TRANSPLANTATION" NEW ENGLAND JOURNAL OF MEDICINE, MASSACHUSETTS MEDICAL SOCIETY, BOSTON, MA, US, vol. 353, no. 8, 25 August 2005 (2005-08-25), pages 770-781, XP009070530 ISSN: 1533-4406 the whole document	1-24
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INTERNATIONAL SEARCH REPORT

International application No

PCT/US2007/068348

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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X	MAIER STEFAN ET AL: "Inhibition of natural killer cells results in acceptance of cardiac allografts in CD28-/- mice" NATURE MEDICINE, vol. 7, no. 5, May 2001 (2001-05), pages 557-562, XP002467594 ISSN: 1078-8956 the whole document	1-24
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INTERNATIONAL SEARCH REPORT

International application No

PCT/US2007/068348

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,Y	<p>LI ET AL: "CTLA4-Ig-Based Conditioning Regimen to Induce Tolerance to Cardiac Allografts" JOURNAL OF SURGICAL RESEARCH, ACADEMIC PRESS INC., SAN DIEGO, CA, US, vol. 136, no. 2, 15 November 2006 (2006-11-15), pages 238-246, XP005741054 ISSN: 0022-4804 the whole document</p> <p>-----</p>	1-24

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2007/068348

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:
see FURTHER INFORMATION sheet PCT/ISA/210
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:

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.:

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

Continuation of Box II.1

Although claims 1-24 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.

Continuation of Box II.1

Claims Nos.: -

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2007/068348

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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