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(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, 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, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

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Declaration under Rule 4.17:
— *of inventorship (Rule 4.17(iv))*

Published:
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(88) Date of publication of the international search report:
18 December 2008

(54) Title: COMPOSITIONS AND METHODS FOR THE TREATMENT OF INFECTIONS AND TUMORS

(57) Abstract: PD-1 antagonists are disclosed that can be used to reduce the expression or activity of PD-1 in a subject. An immune response specific to an infectious agent or to tumor cells can be enhanced using these PD- 1 antagonists in conjunction with an antigen from the infectious agent or tumor. Thus, subjects with infections, such as persistent infections can be treated using PD-1 antagonists. In addition, subjects with tumors can be treated using the PD-1 antagonists. In several examples, subjects can be treated by transplanting a therapeutically effective amount of activated T cells that recognize an antigen of interest and by administering a therapeutically effective amount of a PD-1 antagonist.

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INTERNATIONAL SEARCH REPORT

International application No
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A. CLASSIFICATION OF SUBJECT MATTER
INV. C07K16/28 A61K39/395 A61K39/12 A61P31/14 A61P31/18
A61P31/20

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 A61P

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, 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	STROME SCOTT E ET AL: "B7-H1 blockade augments adoptive T-cell immunotherapy for squamous cell carcinoma." CANCER RESEARCH, vol. 63, no. 19, 1 October 2003 (2003-10-01), pages 6501-6505, XP002487684 ISSN: 0008-5472 the whole document	1,15, 17-20
Y	WO 2006/133396 A (DANA FARBER CANCER INST INC [US]; BRIGHAM & WOMENS HOSPITAL [US]; UNIV) 14 December 2006 (2006-12-14) examples 1-14	1-11,15, 17-36, 38-44

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[X] Further documents are listed in the continuation of Box C.

[X] 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	Date of mailing of the international search report
14 July 2008	24/09/2008

Name and mailing address of the ISA/	Authorized officer
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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.
Y	BARBER DANIEL L ET AL: "Restoring function in exhausted CD8 T cells during chronic viral infection" NATURE, NATURE PUBLISHING GROUP, LONDON, vol. 439, no. 7077, 9 February 2006 (2006-02-09), pages 682-687, XP002419629 ISSN: 0028-0836 the whole document	1-11,15, 17-36, 38-44
Y	RIDDELL S R ET AL: "Principles for adoptive T cell therapy of human viral diseases." ANNUAL REVIEW OF IMMUNOLOGY 1995, vol. 13, 1995, pages 545-586, XP002487685 ISSN: 0732-0582 the whole document	1-11,15, 17-36, 38-44
Y	RILEY ET AL: "The road to recovery: translating PD-1 biology into clinical benefit" TRENDS IN IMMUNOLOGY, ELSEVIER, RAHWAY, NJ, US, vol. 28, no. 2, 22 December 2006 (2006-12-22), pages 48-50, XP005867493 ISSN: 1471-4906 the whole document	1-11,15, 17-36, 38-44
Y	DAY CHERYL L ET AL: "PD-1 expression on HIV-specific T cells is associated with T-cell exhaustion and disease progression." NATURE 21 SEP 2006, vol. 443, no. 7109, 21 September 2006 (2006-09-21), pages 350-354, XP002487713 ISSN: 1476-4687 the whole document	1-11,15, 17,36, 38-44
Y	PETROVAS CONSTANTINOS ET AL: "PD-1 is a regulator of virus-specific CD8+ T cell survival in HIV infection." THE JOURNAL OF EXPERIMENTAL MEDICINE 2 OCT 2006, vol. 203, no. 10, 2 October 2006 (2006-10-02), pages 2281-2292, XP002487714 ISSN: 0022-1007 the whole document	1-11,15, 17-36, 38-44

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2007/088851

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

Although claims 1-11, 15, 17-36 and 38-44 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 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. [X] 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:

1. claims: 2-8, 11, 22-28, 32, 36 (all completely) and 1, 9-10, 15, 17-21, 29-31, 33-35, 38-44 (all partially)

   A method for inducing an immune response to an antigen of interest in a mammalian subject, wherein the subject has a viral infection and/or the antigen of interest is a viral antigen, comprising administering to the subject a therapeutically effective amount of activated T cells, wherein the T cells specifically recognize the antigen of interest, and a therapeutically effective amount of a PD-1 antagonist, thereby inducing the immune response to the antigen of interest.

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2. claims: 12-14 (all completely) and 1, 9-10, 15, 17-21, 29, 33-35 (all partially)

   A method for inducing an immune response to an antigen of interest in a mammalian subject, wherein the recipient has a tumor, comprising administering to the subject a therapeutically effective amount of activated T cells, wherein the T cells specifically recognize the antigen of interest, and a therapeutically effective amount of a PD-1 antagonist, thereby inducing the immune response to the antigen of interest.

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3. claims: 16, 37 (all completely) and 1, 9-10, 15, 17-21, 29 (all partially)

   A method for inducing an immune response to an antigen of interest in a mammalian subject, wherein the antigen of interest is a fungal antigen, comprising administering to the subject a therapeutically effective amount of activated T cells, wherein the T cells specifically recognize the antigen of interest, and a therapeutically effective amount of a PD-1 antagonist, thereby inducing the immune response to the antigen of interest.

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4. claims: 45-55

   A method of treating a subject with a persistent infection of a pathogen, comprising administering to the subject a therapeutically effective amount of a Programmed Death (PD-1) antagonist and a therapeutically effective amount of an antigenic molecule from the pathogen, thereby treating the persistent infection in the subject.

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5. claims: 56-63

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

A method of treating a subject with a tumor, comprising administering to the subject a therapeutically effective amount of a Programmed Death (PD-1) antagonist and a therapeutically effective amount of a tumor antigen, thereby treating the subject.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2007/088851

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2006133396 A	14-12-2006	AU 2006254902 A1	14-12-2006
		CA 2611861 A1	14-12-2006
		EP 1907000 A2	09-04-2008