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Previous Correction:
see Notice of 13 March 2008

(54) Title: CO-CULTURE LYMPHOID TISSUE EQUIVALENT (LTE) FOR AN ARTIFICIAL IMMUNE SYSTEM (AIS)

(57) Abstract: The present invention relates to methods for preparing an artificial immune system. The artificial immune system comprises a cell culture comprising T cells, B cells and antigen-primed dendritic cells. The artificial immune system of the present invention can be used for in vitro testing of vaccines, adjuvants, immunotherapy candidates, cosmetics, drugs, biologies and other chemicals.

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INTERNATIONAL SEARCH REPORT

International application No
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A. CLASSIFICATION OF SUBJECT MATTER
INV. C12N5/06 G01N33/50

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)
C12N G01N

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	NEVES A R ET AL: "DENDRITIC CELLS DERIVED FROM METASTATIC CANCER VACCINATED WITH ALLOGENEIC DENDRITIC CELL-AUTOLOGOUS TUMOR CELL HYBRIDS EXPRESS MORE CD86 AND INDUCE HIGHER LEVELS OF INTERFERON-GAMMA IN MIXED LYMPHOCYTE REACTIONS" CANCER IMMUNOLOGY AND IMMUNOTHERAPY, BERLIN, DE, vol. 54, no. 1, January 2005 (2005-01), pages 61-66, XP009053938 ISSN: 0340-7004 page 62, right-hand column page 63 ----- -/--	1,2

[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
25 February 2008	03/03/2008

Name and mailing address of the ISA/	Authorized officer
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	Herrmann, Klaus

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Form PCT/ISA/210 (second sheet) (April 2005)

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	BÜCHELE S ET AL: "Presentation of tetanus toxoid to autologous T cells by dendritic cells generated from human blood. Improved specificity with dendritic cells generated without fetal calf serum." ADVANCES IN EXPERIMENTAL MEDICINE AND BIOLOGY 1997, vol. 417, 1997, pages 233-237, XP009095838 ISSN: 0065-2598 the whole document	14-20
X	BAI L ET AL: "Generation of dendritic cells from human bone marrow mononuclear cells: Advantages for clinical application in comparison to peripheral blood monocyte derived cells" INTERNATIONAL JOURNAL OF ONCOLOGY, vol. 20, no. 2, February 2002 (2002-02), pages 247-253, XP009095837 ISSN: 1019-6439 the whole document	14-20
A	US 2005/282148 A1 (WARREN WILLIAM L [US] ET AL) 22 December 2005 (2005-12-22) the whole document	1,2, 14-20
A	SUEMATSU S ET AL: "Generation of a synthetic lymphoid tissue-like organoid in mice" NATURE BIOTECHNOLOGY, NATURE PUBLISHING GROUP, NEW YORK, NY, US, vol. 22, no. 12, 2004, pages 1539-1545, XP003013991 ISSN: 1087-0156 the whole document	1,2, 14-20
A	BROMELOW K V ET AL: "Whole blood assay for assessment of the mixed lymphocyte reaction" JOURNAL OF IMMUNOLOGICAL METHODS, ELSEVIER SCIENCE PUBLISHERS B.V.,AMSTERDAM, NL, vol. 247, no. 1-2, 1 January 2001 (2001-01-01), pages 1-8, XP004228393 ISSN: 0022-1759 the whole document	1,2, 14-20

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2007/013871

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. [X] 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.:

1, 2, 14-20

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.

[X] 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, 2

A cell culture comprising T cells, B cells and antigen-primed dendritic cells.

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2. claims: 3-5

A cell culture comprising T cells, B cells, antigen-primed dendritic cells and serum-free cell culture media.

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3. claims: 6-13

A cell culture comprising T cells, B cells and serum-free cell culture media.

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4. claims: 14-20

A method for testing an immune response to an antigen comprising: preparing a cell culture comprising T cells, B cells and serum-free cell culture media; priming dendritic cells with an antigen; adding to the cell culture the antigen-primed dendritic cells and analyzing the effect the antigen has on the T cells and/or B cells in the cell culture.

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5. claims: 21, 22

A method for testing an immune response to an antigen comprising: preparing a cell culture comprising T cells, B cells, serum-free cell culture media and antigen-prepulsed dendritic cells and analyzing the effect the antigen has on the T cells and/or B cells in the cell culture.

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6. claims: 23, 24

A method for testing an immune response to an antigen comprising: preparing a cell culture comprising T cells, B cells, serum-free cell culture media and dendritic cells; adding soluble antigen to the cell culture and analyzing the effect the antigen has on the T cells and/or B cells in the cell culture.

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7. claims: 25, 26

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

A method for testing an immune response to an antigen comprising: preparing a cell culture comprising T cells, B cells, serum-free cell culture media and antigen-prepulsed dendritic cells; adding further soluble antigen to the cell culture and analyzing the effect the antigen has on the T cells and/or B cells in the cell culture.

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8. claims: 27, 28

A method for testing an immune response to an antigen comprising: preparing a cell culture comprising T cells, B cells and antigen-prepulsed dendritic cells and analyzing the effect the antigen has on the T cells and/or B cells in the cell culture.

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9. claims: 29, 30

A method for testing an immune response to an antigen comprising: preparing a cell culture comprising T cells, B cells and dendritic cells; adding soluble antigen to the cell culture and analyzing the effect the antigen has on the T cells and/or B cells in the cell culture.

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10. claims: 31, 32

A method for testing an immune response to an antigen comprising: preparing a cell culture comprising T cells, B cells and antigen-prepulsed dendritic cells; adding soluble antigen to the cell culture and analyzing the effect the antigen has on the T cells and/or B cells in the cell culture.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2007/013871

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2005282148 A1	22-12-2005	US 2006270029 A1	30-11-2006
		US 2007026392 A1	01-02-2007
		US 2007154956 A1	05-07-2007