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report:

14 July 2016

- (15) Information about Correction:
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(54) Title: A MEDICAMENT FOR USE IN A METHOD OF INDUCING OR EXTENDING A CELLULAR CYTOTOXIC IMMUNE RESPONSE

(57) Abstract: The present invention relates to a medicament for use in a method of inducing a cellular cytotoxic immune response, the method comprising the steps of: i) administering to a patient a delivery system comprising (a) a molecule binding to a receptor on the surface of a dendritic cell, (b) an antigen-comprising protein bound to molecule of (a) and (c) a first adjuvant, wherein upon binding of the molecule of (a) to the receptor, the protein of (b) is internalized and processed in the dendritic cell and the antigen comprised in the protein is presented on the surface of the dendritic cell, thereby activating a T cell in the patient; and ii) administering to the patient a re-activator selected from the group consisting of (d) complexed interleukin 2 (IL-2cx), (e) a peptide-loaded major histocompatibility complex class I (MHC-I) presenting cell and a second adjuvant, and (f) a combination of (d) and (e), wherein the peptide is derived from the antigen-comprising protein as defined in step i), thereby reactivating the T cell activated in step i), wherein the re-activator of step ii) is administered in a time frame of from 0 h to 14 days after the administration of the delivery system of step i).



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INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2015/055574

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K39/00
ADD.
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 practicable, search terms used)
EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	A. BACHEM ET AL: "Superior antigen cross-presentation and XCR1 expression define human CD11c+CD141+ cells as homologues of mouse CD8+ dendritic cells", TRENDS IN IMMUNOLOGY, vol. 28, no. 2, 17 May 2010 (2010-05-17), pages 45-1281, XP055128162, ISSN: 1471-4906, DOI: 10.1016/j.it.2006.12.008 abstract ----- -/--	1-10,15

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 application or patent 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
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Authorized officer
Noë, Veerle

INTERNATIONAL SEARCH REPORT

International application No.

PCT/EP2015/055574

Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.c of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of a sequence listing:
- a. forming part of the international application as filed:
- in the form of an Annex C/ST.25 text file.
- on paper or in the form of an image file.
- b. furnished together with the international application under PCT Rule 13ter.1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.
- c. furnished subsequent to the international filing date for the purposes of international search only:
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- on paper or in the form of an image file (Rule 13ter.1(b) and Administrative Instructions, Section 713).
2. In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that forming part of the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments:

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2015/055574

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 all searchable 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 report covers 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.

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2015/055574

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>ANNABELL BACHEM ET AL: "Expression of XCR1 Characterizes the Batf3-Dependent Lineage of Dendritic Cells Capable of Antigen Cross-Presentation", FRONTIERS IN IMMUNOLOGY 2012, FRONTIERS RESEARCH FOUNDATION, SWITZERLAND</p> <p>, vol. 214, no. 1 1 July 2012 (2012-07-01), pages 1-12, XP002686944, ISSN: 1664-3224, DOI: 10.3389/FIMMU.2012.00214 Retrieved from the Internet: URL:http://www.frontiersin.org/Antigen_Presenting_Cell_Biology/10.3389/fimmu.2012.00214/abstract [retrieved on 2012-07-18] abstract</p>	1-10,15
X	<p>-----</p> <p>NESTLE F O ET AL: "Vaccination of melanoma patients with peptide- or tumor lysate-pulsed dendritic cells", NATURE MEDICINE, NATURE PUBLISHING GROUP, NEW YORK, NY, US, vol. 4, no. 3, 1 March 1998 (1998-03-01), pages 328-332, XP002122868, ISSN: 1078-8956, DOI: 10.1038/NM0398-328</p>	11-14
A	<p>abstract page 331, column 2, last paragraph - page 332, column 1, paragraph 4</p>	1-10,15
X	<p>-----</p> <p>WO 02/053176 A2 (HADASIT MED RES SERVICE [IL]; LOTEM MICHAL [IL]; PERETZ TAMAR [IL]; SH) 11 July 2002 (2002-07-11)</p>	11-14
A	<p>abstract page 3, paragraph 2 - page 5, paragraph 3 page 7, paragraph 2 page 12, last paragraph - page 13, paragraph 4 page 14, paragraph 3 page 16, paragraph 3-4 page 17, paragraph 2 page 27, last paragraph page 28, last paragraph - page 29, paragraph 1</p> <p>-----</p> <p style="text-align: center;">-/--</p>	1-10,15

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2015/055574

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>WO 2009/065561 A2 (BUNDESREPUBLIK DEUTSCHLAND LET [DE]; KROCZEK RICHARD [DE]) 28 May 2009 (2009-05-28) abstract page 1, paragraph 1 page 3, lines 24-29 page 11, line 28 - page 12, line 24 page 13, lines 6-13 page 23, lines 2-4 page 24, lines 15-16 page 30, lines 14-16 page 33, line 20 - page 34, line 8</p>	1-10,15
A	<p>HARTUNG E ET AL: "Targeting of antigen via XCR1, the lineage marker for cross-presenting dendritic cells, elicits potent CD8 cytotoxicity in vivo", IMMUNOLOGY, BLACKWELL PUBLISHING, OXFORD, GB, vol. 137, no. Supplement 1, 5 September 2012 (2012-09-05), page 22, XP008170463, ISSN: 0019-2805, DOI: 10.1111/IMM.12001 [retrieved on 2012-09-12] abstract</p>	1-10,15
A	<p>BOYMAN ONUR ET AL: "Selective stimulation of T cell subsets with antibody-cytokine immune complexes", SCIENCE, AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE, US, vol. 311, no. 5769, 1 March 2006 (2006-03-01), pages 1924-1927, XP002457765, ISSN: 0036-8075, DOI: 10.1126/SCIENCE.1122927 abstract</p>	1-10,15

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2015/055574

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 02053176	A2	11-07-2002	AU 2002219485 A1
			WO 02053176 A2

WO 2009065561	A2	28-05-2009	AU 2008328183 A1
			BR PI0819295 A2
			CA 2705588 A1
			CN 101896191 A
			EP 2062592 A1
			EP 2200633 A2
			JP 2011503219 A
			JP 2015007052 A
			US 2010310562 A1
			WO 2009065561 A2

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. claims: 1-10, 15

A medicament for use in a method of inducing a cellular cytotoxic immune response, the method comprising the steps of

1.5 i) administering to a patient a delivery system comprising (a) a molecule binding to a receptor on the surface of a dendritic cell, (b) an antigen-comprising protein bound to molecule of (a) and (c) a first adjuvant, wherein upon binding of the molecule of (a) to the receptor, the protein of (b) is internalized and processed in the dendritic cell and the antigen comprised in the protein is presented on the surface of the dendritic cell, thereby activating a T cell in the patient; and
ii) administering to the patient a re-activator selected from the group consisting of (d) complexed interleukin 2 (IL-2cx), (e) a peptide-loaded major histocompatibility complex class I (MHC-I) presenting cell and a second adjuvant, and (f) a combination of (d) and (e), wherein the peptide is derived from the antigen-comprising protein as defined in step i), thereby re-activating the T cell activated in step i), wherein the re-activator of step ii) is administered in a time frame of from 0 h to 14 days after the administration of the delivery system of step i).

2. claims: 11-14

A medicament for use in a method of extending a cellular cytotoxic immune response against an antigen-comprising protein, the method comprising the step of

i) administering to a patient having T cells activated against an antigen a peptide-loaded major histocompatibility complex class I (MHC-I) presenting cell and a second adjuvant, wherein the peptide is derived from the antigen-comprising protein, thereby re-activating the activated T cell, and optionally further administering complexed interleukin 2 (IL-2cx), wherein the re-activator of step i) is administered in a time frame of from 0 h to 14 days after the T cells were activated against an antigen, preferably wherein the re-activator of step i) is administered only once in a time frame of from 0 h to 14 days after the T cells were activated against an antigen.
