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(88) Date of publication of the international search report:

16 April 2015

(54) Title: AMINO ACID AND PEPTIDE CONJUGATES AND CONJUGATION PROCESS

(57) Abstract: The present invention relates to amino acid and peptide conjugates, methods for making amino acid and peptide conjugates, conjugates produced by the methods, pharmaceutical compositions comprising the conjugates, methods of eliciting immune responses in a subject and methods of vaccinating a subject, uses of the conjugates for the same, and uses of the conjugates in the manufacture of medicaments for the same.



WO 2014/207708 A3

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/IB2014/062648

## A. CLASSIFICATION OF SUBJECT MATTER

**C07C 227/16 (2006.01) C07C 229/02 (2006.01) C07C 321/12 (2006.01) C07K 14/00 (2006.01) C07K 14/435 (2006.01)  
C07K 1/02 (2006.01)**

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)

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)

WPIDS, MEDLINE, HCA, BIOSIS, EPODOC, WPI: Keyword search (lipid, protein, peptide, epitope, antigen, linker, reacting, conjugate, fusion, self\_adjuvanting, lipidation, thiol, double bond, carbon and like terms).

REGISTRY, CAPLUS: Sub-structure search based on present formula (A) of claim 30 coupled with keywords (terms as above).

GENOMEQUEST: Sequence search based on sequences of present claim 88.

ESPACENET: Inventor + applicant search

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Documents are listed in the continuation of Box C		

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	"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
"E" earlier application or patent but published on or after the international filing date	"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
"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)	"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
"O" document referring to an oral disclosure, use, exhibition or other means	"&"	document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search 13 January 2015	Date of mailing of the international search report 13 January 2015
<b>Name and mailing address of the ISA/AU</b>  AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA Email address: pct@ipaustalia.gov.au	<b>Authorised officer</b>  Marc Kloth AUSTRALIAN PATENT OFFICE (ISO 9001 Quality Certified Service) Telephone No. +61 3 9935 9609

**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:  
the subject matter listed in Rule 39 on which, under Article 17(2)(a)(i), an international search is not required to be carried out, including
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 Supplemental Box for Details**

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 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.
C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		<b>PCT/IB2014/062648</b>
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X A	BOECKLER C. et al, "Design and Synthesis of Thiol-Reactive Lipopeptides", Bioorganic & Medicinal Chemistry Letters, 1998, 8, 2055-2058 abstract & page 2057, scheme 3	70 1-69, 71-93
X A	DONDONI A. et al, "A New Ligation Strategy for Peptide and Protein Glycosylation: Photoinduced Thiol-Ene Coupling", Chem. Eur. J., 2009, 15, 11444-11449 abstract & page 11446, table 2	70 1-69, 71-93
X A	LAU Y.F. et al, "Lipid-containing mimetics of natural triggers of innate immunity as CTL-inducing influenza vaccines", International Immunology, 2006, 18(12), 1801-1813 abstract & page 1803, figure 1, compounds Pam1Cys and Pam2Cys, and peptide constructs associated with these compounds	70-93 1-69
X A	WO 2013/036543 A2 (H. LEE MOFFITT CANCER CENTER AND RESEARCH INSTITUTE INC. et al) 14 March 2013 abstract & page 21, lines 20-22 and page 84, scheme 1	70-93 1-69
X A L	WO 1999/018206 A2 (THE GOVERNMENT OF THE UNITED STATES OF AMERICA, represented by THE SECRETARY, DEPARTMENT OF HEALTH AND HUMAN SERVICES) 15 April 1999 abstract & page 13, lines 10-14 and Fig. 3B, SEQ ID NO 55  Lack of Unity	70, 88-93 1-69, 71-87
P,X	WRIGHT T.H. <i>et al</i> , "Direct Peptide Lipidation through Thiol-Ene Coupling Enables Rapid Synthesis and Evaluation of Self-Adjuvanting Vaccine Candidates", Angew. Chem. Int. Ed., 12 August 2013, 52, 10616-10619 abstract & page 10617, schemes 1-3	1-93
P,X	WO 2014/088432 A1 (CALLAGHAN INNOVATION RESEARCH LIMITED) 12 June 2014 abstract & SEQ ID NO 89	70, 88-93

**Supplemental Box****Continuation of: Box III**

This International Application does not comply with the requirements of unity of invention because it does not relate to one invention or to a group of inventions so linked as to form a single general inventive concept.

In assessing whether there is more than one invention claimed, I have given consideration to those features which can be considered to potentially distinguish the claimed combination of features from the prior art. Where different claims have different distinguishing features they define different inventions.

The present invention *prima facie* resides in a method for making an amino acid- or peptide conjugate, the method involving the hydrothiolation of a carbon-carbon double bond with a thiol of a lipid-containing conjugation partner with an amino acid-comprising conjugation partner as set out in present claim 1.

The International Searching Authority (ISA) has found that there are at least three different inventions based on the following features that separate the claims into distinct groups:

**Invention 1:** Claims 1-70 (in full) are directed towards a method for making an amino acid- or peptide conjugate, the method of which involving the hydrothiolation of a carbon-carbon double bond with a thiol of a lipid-containing conjugation partner with an amino acid-comprising conjugation partner.

**Invention 2:** Claims 71-87 (in full) & 90-93 (in part) are directed towards amino acid- or peptide conjugates *per se* according to present formula (V) and pharmaceutical compositions comprising the same.

**Invention 3:** Claims 88-89 (in full) & 90-93 (in part) are directed towards isolated peptides *per se* comprising an amino acid sequence selected from the group consisting of SEQ ID Nos 1-5, 8-12 or 14-18 and pharmaceutical compositions comprising the same.

PCT Rule 13.2, first sentence, states that unity of invention is only fulfilled when there is a technical relationship among the claimed inventions involving one or more of the same or corresponding special technical features. PCT Rule 13.2, second sentence, defines a special technical feature as a feature which makes a contribution over the prior art.

When there is no special technical feature common to all the claimed inventions there is no unity of invention.

In the above groups of claims, the identified features may have the potential to make a contribution over the prior art but are not common to all the claimed inventions and therefore cannot provide the required technical relationship. Therefore there is no special technical feature common to all the claimed inventions and the requirements for unity of invention are consequently not satisfied *a priori*.

In addition, Invention 3 can be divided into three further inventions based on the following features that separate the claims into distinct groups:

**Invention 3A:** Claims 88-93 (in part) are directed towards isolated peptides *per se* comprising an amino acid sequence selected from the group consisting of SEQ ID Nos 1-5 and pharmaceutical compositions comprising the same.

**Invention 3B:** Claims 88-93 (in part) are directed towards isolated peptides *per se* comprising an amino acid sequence selected from the group consisting of SEQ ID 8-12 and pharmaceutical compositions comprising the same.

**Invention 3C:** Claims 88-93 (in part) are directed towards isolated peptides *per se* comprising an amino acid sequence selected from the group consisting of SEQ ID Nos 14-18 and pharmaceutical compositions comprising the same.

In the above groups of claims, the identified features may have the potential to make a contribution over the prior art but are not common to all the claimed inventions and therefore cannot provide the required technical relationship. The only feature common to all of the claimed inventions and which provides a technical relationship among them is that the sequences of each group of invention contain specific amino acid motifs which are derived from the NY-ESO-1 gene. However this feature does not make a contribution over the prior art because it is disclosed in:

D5: WO 1999/018206 A2 THE GOVERNMENT OF THE UNITED STATES OF AMERICA 15 April 1999 (see abstract)

**Supplemental Box**

Therefore in light of this document this common feature cannot be a special technical feature. Therefore there is no special technical feature common to all the claimed inventions and the requirements for unity of invention are consequently not satisfied *a posteriori*.

**INTERNATIONAL SEARCH REPORT**

Information on patent family members

International application No.

**PCT/IB2014/062648**

This Annex lists known patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

<b>Patent Document/s Cited in Search Report</b>		<b>Patent Family Member/s</b>	
<b>Publication Number</b>	<b>Publication Date</b>	<b>Publication Number</b>	<b>Publication Date</b>
WO 2013/036543 A2	14 March 2013	US 2014161725 A1	12 Jun 2014
WO 1999/018206 A2	15 April 1999	AU 9572098 A	27 Apr 1999
		EP 1021535 A2	26 Jul 2000
		EP 1021535 B1	07 Mar 2007
		EP 1806403 A2	11 Jul 2007
		US 7084239 B1	01 Aug 2006
WO 2014/088432 A1	12 June 2014		

**End of Annex**