



- (51) **International Patent Classification:**
A61K 47/00 (2006.01) A61K 39/385 (2006.01)
- (21) **International Application Number:**
PCT/US2013/047079
- (22) **International Filing Date:**
21 June 2013 (21.06.2013)
- (25) **Filing Language:** English
- (26) **Publication Language:** English
- (30) **Priority Data:**
61/662,687 21 June 2012 (21.06.2012) US
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- (81) **Designated States** (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY,

BZ, CA, CH, CL, 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, 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, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

- (84) **Designated States** (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

- as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))

Published:

- with international search report (Art. 21(3))
- with sequence listing part of description (Rule 5.2(a))

- (88) **Date of publication of the international search report:**
2 April 2015

(54) **Title:** PEPTIDE CONJUGATED PARTICLES

Figure 1

C.

Particle	Z-average size by intensity (nm)	ζ-potential (mV)
PLG (Phosphoryl)	624.5	-32.7 ± 4.71
PLG-PHEMA	429.9	-67.4 ± 10.9
Polystyrene	503.6	-63.4 ± 6.97

(57) **Abstract:** The present invention provides compositions comprising peptide-coupled biodegradable poly(lactide-co-glycolide) (PLG) particles. In particular, PLG particles are surface-functionalized to allow for coupling of peptide molecules to the surface of the particles (e.g., for use in eliciting induction of immunological tolerance).



INTERNATIONAL SEARCH REPORT

4013/04/073/17.01.2014
International application No.

PCT/US13/47079

A. CLASSIFICATION OF SUBJECT MATTER IPC(8) - A61K 47/00, 39/385 (2014.01) USPC - 424/193.1, 812; 530/806 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) IPC(8): A01N 25/00; A61K 47/00, 39/385 (2014.01) USPC: 424/193.1, 450, 812; 514/785, 772, 1.1; 435/177; 436/823; 530/806 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) MicroPatent (US-G, US-A, EP-A, EP-B, WO, JP-bib, DE-C,B, DE-A, DE-T, DE-U, GB-A, FR-A); Google; Google Scholar; Google Patent; Science Direct; ProQuest; antigen, coupled, 'carrier particle', 'negative zeta potential', 'zeta potential', copolymer, 'molar ratio', 'surface functionalized', 'carboxylate', 'antigen-specific tolerance', transplantation, rejection, 'poly(lactic-co-glycolic acid)', anaphylaxis, polystyrene		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X — Y	WO 2011/133617 A1 (HONG, S et al.) October 27, 2011; abstract; paragraphs [0005], [0006], [00023], [00027], [00032], [00041], [00043], [00049], [00050], [00052], [00068], [00070]; table 1; Claim 1	1-3, 5-18, 21/1-3, 21/5-18 — 4, 19, 20, 21/4, 21/19, 21/20, 22-33
Y	BATTAGLIA, M et al. Rapamycin and Interleukin-10 Treatment Induces T Regulatory Type 1 Cells That Mediate Antigen-Specific Transplantation Tolerance. Diabetes. January 2006, Vol. 55, pp 40-49; abstract	22-29
Y	CHAUHAN, A et al. Unexpected In Vivo Anti-Inflammatory Activity Observed for Simple, Surface Functionalized Poly(amidoamine) Dendrimers. Biomacromolecules. 6 April 2009, Vol. 10, pp 1195-1202. page 1199, right column, first paragraph; page 1201, left column, seventh paragraph. DOI: 10.1021/bm9000298	19, 20, 21/19, 21/20
Y	US 7829113 B2 (OKADA, K et al.) November 9, 2010; column 42, lines 25-29; column 74, lines 51-54	30-33
Y	WO 2011/150573 A1 (LI, X et al.) December 8, 2011; Claim 3	4, 21/4
Y	NYGAARD, U et al. The Allergy Adjuvant Effect Of Particles – Genetic Factors Influence Antibody And Cytokine Responses. BMC Immunology. 21 June 2005, Vol. 6, pp 1-10; page 4, left column, first paragraph. DOI:10.1186/1471-2172-6-11	28
<input type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/>		
* 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 10 January 2014 (10.01.2014)		Date of mailing of the international search report 17 JAN 2014
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201		Authorized officer: Shane Thomas PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

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:

-Please See Supplemental Page-

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.:
1-33

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.

****-Continuation of Box No. III - Observations where unity of invention is lacking:

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I: Claims 1-33 are directed toward a composition comprising: an antigen coupled to a carrier particle with a negative zeta potential; a method of inducing antigen-specific tolerance in a subject comprising: administering to said subject, an effective amount of a composition comprising an antigen-coupled particle to said subject, wherein said particle has a negative zeta potential; and a process for the preparation of an immune modified particle with a negative zeta potential, said process comprising: contacting an immune modified particle precursor with a buffer solution under conditions effective to form the immune modified particle with a negative zeta potential.

Group II: Claims 34-36 are directed toward a composition comprising an antigen encapsulated within the core of a surface-functionalized liposome.

The inventions listed as Groups I-II do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: the special technical features of Group I include an antigen coupled to a carrier particle with a negative zeta potential; a method of inducing antigen-specific tolerance in a subject comprising: administering to said subject, an effective amount of a composition comprising an antigen-coupled particle to said subject, wherein said particle has a negative zeta potential; and a process for the preparation of an immune modified particle with a negative zeta potential, said process comprising: contacting an immune modified particle precursor with a buffer solution under conditions effective to form the immune modified particle with a negative zeta potential, which is not present in Group II; the special technical features of Group II including an antigen encapsulated within the core of a surface-functionalized liposome.

Groups I and II share the technical features including a composition comprising an antigen associated with a particle.

However, these shared technical features are previously disclosed by US 4,565,696 A to Heath, et al. (hereinafter 'Heath'). Heath discloses a composition (composition; column 2, lines 4-6) comprising an antigen (immunogen (antigen); abstract, column 1, lines 64-67) associated with a particle (covalently-linked to (associated with) a liposome (particle); abstract; column 1, lines 64-67).

Since none of the special technical features of the Groups I-II inventions is found in more than one of the inventions, and since all of the shared technical features are previously disclosed by the Heath reference, unity of invention is lacking.