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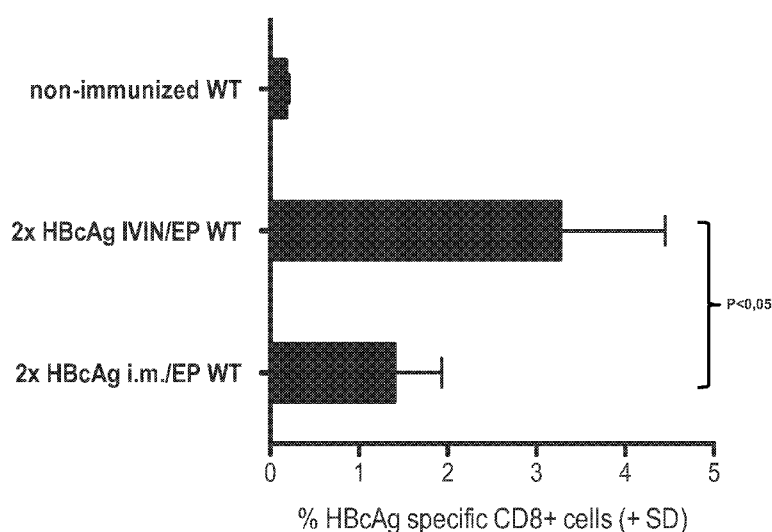
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6 November 2014

(54) Title: INJECTION NEEDLE, DEVICE, IMMUNOGENIC COMPOSITIONS AND METHOD OF USE

Figure 69 HBcAg-CTL precursor frequency



(57) Abstract: Several needle assemblies and intracellular delivery devices that are used for the delivery of prophylactic and/or therapeutic material (i.e., delivered agents) into a tissue of a subject are disclosed. Preferably, the needle assemblies and/or the intracellular delivery devices comprise needles and/or needle electrodes, which are disposed in an array (e.g., a Y-type array having three outer needles and a center needle), wherein each needle in the array has a closed end and a plurality of apertures along each needle barrel, and the apertures on the needle barrels of the outer needles of the array are positioned to deliver the delivered agent toward the apertures of the center needle and/or an adjacent needle, but not outside of the active zone defined by the area within the needle array and the apertures on the needle barrel of the center needle are positioned to deliver the delivered agent toward the outer needles. The devices may be used to deliver immunogenic compositions such as those that illicit an immune response to the hepatitis c virus in naive or in chronically HCV infected individuals.

INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2013/003034

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61M5/158 A61K39/29
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)
A61M 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, 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	WO 2011/073796 A2 (CHRONTECH PHARMA AB [SE]; SALLBERG MATTI [SE]; FRELIN LARS [SE]) 23 June 2011 (2011-06-23) figure 5 page 6, lines 4-16 page 51, last paragraph ----- -/-	1-20



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

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Name and mailing address of the ISA/

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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	FRELIN L ET AL: "Low dose and gene gun immunization with a hepatitis C virus nonstructural (NS) 3 DNA-based vaccine containing NS4A inhibit NS3/4A-expressing tumors in vivo", GENE THERAPY, NATURE PUBLISHING GROUP, GB, vol. 10, 1 January 2003 (2003-01-01), pages 686-699, XP002285892, ISSN: 0969-7128, DOI: 10.1038/SJ.GT.3301933 abstract page 695, right-hand column -----	1-20
Y	GARCIA-NAVARRO R ET AL: "Protection against woodchuck hepatitis virus (WHV) infection by gene gun coimmunization with WHV core and interleukin-12", JOURNAL OF VIROLOGY, vol. 75, no. 19, October 2001 (2001-10), pages 9068-9076, XP002723966, ISSN: 0022-538X the whole document -----	1-20
A	US 2003/206919 A1 (SALLBERG MATTI [SE]) 6 November 2003 (2003-11-06) the whole document -----	1-20

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/IB2013/003034

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2011073796	A2	23-06-2011	
		AU 2010332400 A1	19-07-2012
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		WO 2004048402 A2	10-06-2004

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB2013/003034

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.:

1-20

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: 1-20

A product combination for use in improving an immune response comprising a) an electroporation device that comprises a plurality of needles each having a closed end and a plurality of apertures along the barrel of said needles, wherein the apertures on separate needles oppose one other but said apertures do not face away from each other, so as to create a zone of injection existing in a region of tissue between the opposing apertures of said plurality of needles, wherein at least two of said plurality of needles are capable of passing current so as to enhance delivery of a nucleic acid within said zone of injection; and b) a nucleic acid encoding an antigen; and wherein said product combination improves an immune response in a subject as compared to an immune response resulting from delivery of said nucleic acid using a conventional injection device in combination with electroporation, and subject-matter relating thereto.

2. claims: 21-122, 131-138, 155

An immunogenic composition comprising (a) a polynucleotide encoding a hepatitis C virus NS3/4A polypeptide and (b) an IL-12 polypeptide or a polynucleotide encoding an IL-12 polypeptide, and subject-matter relating thereto.

3. claims: 123-130

A method of generating an immune response to an antigen in a subject comprising: administering to a subject by the "apparatus disclosed herein", a nucleic acid encoding an antigen, wherein the amount of nucleic acid encoding the antigen that is administered to said subject by said apparatus is lower than the amount of nucleic acid encoding the antigen that is required to obtain an equivalent immune response in a subject when said nucleic acid encoding said antigen is administered by injection with a needle having a single aperture, such as a conventional hypodermic needle, and electroporation.

4. claims: 139-154

An improved method of delivering an immunogenic composition comprising a nucleic acid encoding an antigen, wherein the improvement comprises elicitation of an immune response by delivering an amount of a nucleic acid encoding an antigen that is lower than the amount of nucleic acid encoding the antigen that is required to obtain an

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

equivalent/insufficient to generate an immune response in a subject when said nucleic acid encoding said antigen is administered by injection with a needle having a single aperture, such as a conventional hypodermic needle, and electroporation.

5. claims: 156-164

A method of reducing an amount of an immunogenic composition necessary to elicit an immune response in a mammalian subject comprising the steps of: injecting an immunogenic composition into said subject at an injection site, wherein said immunogenic composition is injected in an amount insufficient to elicit an immune response in the absence of further treatment; and electroporating said subject at said injection site; thereby eliciting an immunogenic response.
