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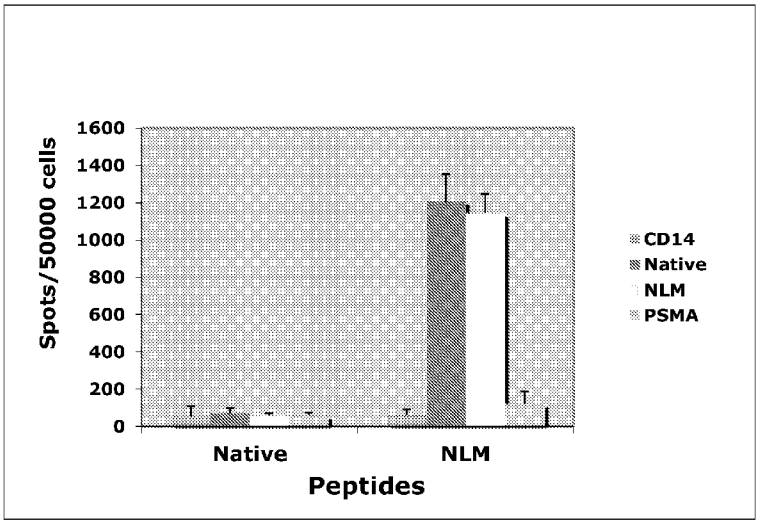
— *with international search report (Art. 21(3))*

— *with sequence listing part of description (Rule 5.2(a))*

(88) Date of publication of the international search report:
22 October 2015

(54) Title: IMMUNOGENIC WT-1 PEPTIDES AND METHODS OF USE THEREOF

Figure 2B



(57) Abstract: This invention provides peptides, immunogenic compositions and vaccines, and methods of treating, reducing the incidence of, and inducing immune responses to a WT1-expressing cancer, comprising heteroclitic peptides derived from the WT-1 protein.

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US14/11711

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A61K 39/00, 39/38 (2014.01)
USPC - 424/185.1, 184.1; 514/19.3, 19.6, 19.2, 19.4, 1.1, 1; 530/300
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): A61K 39/00, 39/38 (2014.01)
USPC: 424/185.1, 184.1; 514/19.3, 19.6, 19.2, 19.4, 1.1, 1; 530/300

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 Scholar; Pubmed; ScienceDirect; 'WT-1,' isolate, peptide, 'HLA,' 'class I,' 'class II'

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2012/0301492 A1 (GAIGER, A et al.) November 29, 2012; paragraphs [0008], [0047], [0070]	1, 3, 5/1, 5/3, 6
A	US 2006/0084609 A1 (SCHEINBERG, DA et al.) April 20, 2006; paragraph [0054]	1, 3, 5/1, 5/3, 6
A	US 2007/0082860 A1 (SUGIYAMA, H et al.) April 12, 2007; SEQ ID NO: 64	1, 3, 5/1, 5/3, 6

☐ Further documents are listed in the continuation of Box C. ☐

* 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	Date of mailing of the international search report
10 July 2014 (10.07.2014)	05 AUG 2014

Name and mailing address of the ISA/US	Authorized officer:
Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Shane Thomas PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

Form PCT/ISA/210 (second sheet) (July 2009)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US14/11711

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 filed or furnished:

   a. (means)

   ☒ on paper

   ☒ in electronic form

   b. (time)

   ☐ in the international application as filed

   ☐ together with the international application in electronic form

   ☒ subsequently to this Authority for the purposes of search

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 in 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/US14/11711

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.: 9-17
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.:

Group I: Claims 1, 3, 5 (in-part), 6, SEQ ID NO: 6

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/US14/11711

-Continued from 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, 3, 5 (in-part) and 6 are directed toward an isolated peptide comprising or consisting of the amino acid sequence of SEQ ID NO: 6 which binds to an HLA Class I molecule.

Groups II+: Claims 2 (in-part), 4 (in-part), 5 (in-part), 7 and 8 (in-part) are directed toward an isolated peptide comprising or consisting of the amino acid sequence selected from among SEQ ID NOs: 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 30, 31, 32, 33, 35, 36, 37, 38, 39, 41, 42, 43, 44, 46, 47, 48, 49, 50 and 55, wherein the peptide binds to an HLA class I or class II molecule.

The isolated peptide can be searched to the extent that it encompasses a peptide that binds to HLA class II molecules and has SEQ ID NO: 8 (Human peptide amino acid sequence). It is believed that Claims 2 (in-part), 4 (in-part), 5 (in-part) and 8 (in-part) encompass this first named invention and thus these claims can be searched without fee to the extent that they encompass SEQ ID NO: 8 (Human peptide amino acid sequence). Applicants must further indicate, if applicable, the claims which encompass the first named invention, if different than what was indicated above for this group. Failure to clearly identify how any paid additional invention fees are to be applied to the "+" group(s) will result in only the first claimed invention to be searched/examined. An exemplary election would be: SEQ ID NO: 9 (Human peptide amino acid sequence).

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 a peptide having SEQ ID NO: 6, which is not present in Groups II+; the special technical features of Groups II+ including peptides having any of SEQ ID NOs: 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 30, 31, 32, 33, 35, 36, 37, 38, 39, 41, 42, 43, 44, 46, 47, 48, 49, 50 and 55.

Groups I-II+ share the technical features including isolated peptides which bind to HLA class I molecules. Groups II+ share the technical features including: an isolated peptide consisting of the amino acid sequence selected from among SEQ ID NO: 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 30, 31, 32, 33, 35, 36, 37, 38, 39, 41, 42, 43, 44, 46, 47, 48, 49, 50 and 55; wherein said isolated peptide binds to an HLA class I molecule, an HLA class II molecule, or the combination thereof; an isolated class I binding peptide selected from SEQ ID NOs: 30, 31, 32, 33, 34, 35, 36, 37, 38, 41, 42, 47 and 48; and an isolated class II binding peptide selected from SEQ ID NOs: 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 39, 43, 44, 46, 49, 50 and 55.

However, these shared technical features are previously disclosed by the combination of US 2012/0301492 A1 to Gaiger, et al. (hereinafter 'Gaiger') in view of US 2006/0084609 A1 to Scheinberg, et al. (hereinafter 'Scheinberg'). Gaiger discloses isolated peptides (WT1 peptides; paragraph [0047]) which bind to MHC class I and II molecules (which bind to MHC class I and II molecules; paragraph [0008]); including peptides which are subsequences of SEQ ID NOs: 8 (SEQ ID NO: 258; paragraph [0048]; Table XLII, 100% identical to residues 1-9 of SEQ ID NO: 8 of the instant PCT application), and 42 (residues 2-9 of SEQ ID NO: 36 are 100% identical to residues 1-8 of SEQ ID NO: 42 of the instant PCT application; Table XIX of the Gaiger reference); and wherein said peptides may include lengths of 23, 18, 15, or 8-10 residues (said peptides may include lengths of 23, 18, 15, or 8-10 residues; paragraph [0047]), as well as full-length WT1 sequences including the peptide sequences (full-length WT1 sequences including the peptide sequences; SEQ ID NO: 319, residues 170-179 and 235-243; full-length WT1 protein (full-length WT1 sequnce); paragraphs [0047], [0055], [0057]), including SEQ ID NO: 8 (SEQ ID NO: 8; paragraph [0055], residues 170-192 of SEQ ID NO: 319) and SEQ ID NO: 42 (SEQ ID NO: 42; paragraph [0055], residues 235-249 of SEQ ID NO: 319). Gaiger does not disclose wherein isolated peptides binding to an HLA class I molecule, an HLA class II molecule, or the combination thereof; an isolated class I binding peptide selected from SEQ ID NOs: 30, 31, 32, 33, 34, 35, 36, 37, 38, 41, 42, 47 and 48; and an isolated class II binding peptide selected from SEQ ID NOs: 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 39, 43, 44, 46, 49, 50 and 55. Scheinberg discloses isolated peptides binding to an HLA class I or class II molecule (isolated peptides binding to an HLA class I or class II molecule; paragraph [0054]), wherein said peptides are derived from WT1 (wherein the peptides are derived from WT1; paragraph [0015]). It would have been obvious to a person of ordinary skill in the art, at the time of the invention, to have modified the previous disclosure of Gaiger, in order to have extended said peptides to lengths of 15 or 18 amino acids, based on the known full-length sequence provided by Gaiger, in order to have produced peptides consisting of or comprising SEQ ID NOs: 8 and 42, for providing peptides capable of binding to HLA class I or Class II, based on the disclosure of Scheinberg. Additionally, it would have been obvious to a person of ordinary skill in the art would have accurately assessed the potential for the additional amino acids in the peptide, for increasing the binding affinity and effectiveness of the extended peptide.

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 a combination of the Gaiger and Scheinberg references, unity of invention is lacking.