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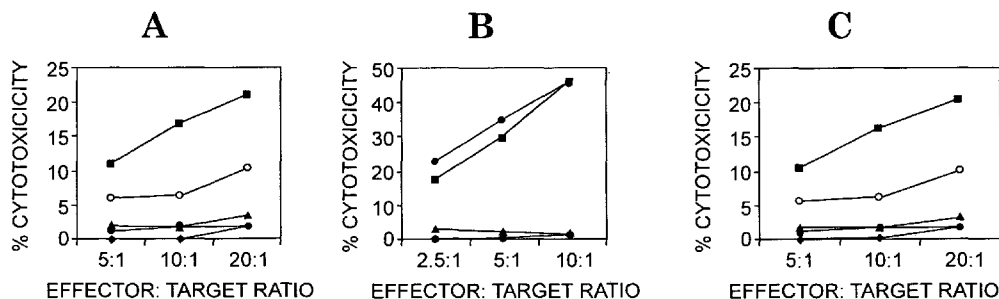
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- with sequence listing part of description published separately in electronic form and available upon request from the International Bureau

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21 August 2008

(54) Title: MULTI-EPI TOPE PEPTIDE-LOADED DENDRITIC CELL IMMUNOTHERAPY FOR CANCER



(57) Abstract: The invention involves peptides of from about 7 to about 50 amino acid residues in length that have epitopes that bind to more than one HLA class II protein and stimulate CD4+ T cells for treatment of cancer from one of three serine proteases overexpressed in ovarian cancer and other cancers - stratum corneum chymotryptic enzyme, matriptase, and hepsin. Since the peptides bind to more than one HLA class II protein variant, they can be used to treat cancer in most patients of a population having a variety of HLA class II alleles. The peptides can be loaded onto autologous dendritic cells of a cancer patient and infused into the patient to activate a CD4+ and CD8+ T cell response that recognizes tumor cells expressing the peptide antigen.

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2007/024300**A. CLASSIFICATION OF SUBJECT MATTER****C07K 14/00(2006.01)i**

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 C07K 14/00, A61K 39/395, C12N 15/11

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

N.A.

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

eKIPASS, WPI, USPTO, PAJ, NCBI, INSPECT "Serine protease 14, Matriptase, MT-SP1, Prostamin, TADG-15, cancer, Tumor, Serine protease, immunogenic, immunotherapy, peptide, ovarian, ovary, hepsin, SCCE, etc."

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 6649741 A2 (O'Brien, T.J., et al., US) 18 Nov 2003 - see abstract; col.3, ll.31-51; col.19, l.55 ~ col.21, l.26; and Table 1	1-11
X	US 7030231 B1 (Craik, C.S., et al., US) 18 Apr 2006 - see col.2, ll.38-42; col.3, ll.50-67; Figures 3 & 4 - see SEQ ID NO:51(col.125) for SEQ ID NO:6 of the present invention	1-11
X	US 2006/0104979 A1 (Craik, C.S., et al., US) 18 May 2006 - see [0348]; SEQ ID NO:34; page 59; [0356]; Figures 3 & 4 - see SEQ ID NO:51(page 67) for SEQ ID NO:6 of the present invention	1-11
A	J. Biol. Chem. Vol.274(26):18231-18236 (Lin, C.Y., US) 25 Jun 1999 "Molecular cloning of cDNA for matriptase, a matrix-degrading serine protease with trypsin-like activity" - see abstract; and Figure 4 - see Swissprot accession no. Q9Y5Y6, which is defined as Suppressor of tumorigenicity protein 14(Serine protease 14); Matriptase; Membrane-type serine protease 1(MT-SP1); Prostamin; Tumor-associated differentially-expressed gene 15 protein(Serine protease TADG-15). - see GenBank accession no. AAH30532 from the DB accession BC030532	1-11

 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 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

30 JUNE 2008 (30.06.2008)

Date of mailing of the international search report

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2007/024300

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	Proc. Natl. Acad. Sci. U.S.A. Vol.96(20):11054-11061 (Takeuchi, T., et al., US) 28 Sep 1999 "Reverse biochemistry: use of macromolecular protease inhibitors to dissect complex biological processes and identify a membrane-type serine protease in epithelial cancer and normal tissue" - see the whole document	1-11
A	US 5972616 A2 (O'Brien, T.J., et al., US) 26 Oct 1999 "TADG-15: an extracellular serine protease overexpressed in breast and ovarian carcinomas" - see abstract; and Figures 10 & 11	1-11
A	Clin Cancer Res. Vol.10(1 Pt 1):202-211. (Parr, C., et al., UK) 1 Jan 2004 "The hepatocyte growth factor regulatory factors in human breast cancer." - see the whole document	1-11

X	US 6875609 B2 (O'Brien, T.J., et al., US) 5 Apr 2005 - see abstract; col.3, ll.18-29; col.24, l.17 ~ col.30, l.12; Table 8; and claims	12-22

X	US 2004/0224891 A1 (O'Brien, T.J., et al., US) 11 Nov 2004 - see abstract; [0011]-[0016]; [0050]-[0051]; [0131]-[0132]; [0165]-[0185]; claims - see SEQ ID NO:33,35,36,38,43,46,86 for SEQ ID NO:15 of the present invention - see SEQ ID NO:49,89,93,100 for SEQ ID NO:16 of the present invention	23-33

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2007/024300

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 the extra sheet for the detail

- 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 fee, this Authority did not invite payment of any additional fee.
- 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.

Lack of Unity of Invention

This ISA found multiple inventions in this application as follows:

Group 1 : claims 1-11 are drawn to an invention featuring an antigenic matriptase.

Group 2 : claims 12-22 are drawn to an invention featuring an antigenic hepsin.

Group 3 : claims 23-33 are drawn to an invention featuring an antigenic stratum corneum chymotryptic enzyme (SCCE).

Inventions belonging to Groups 1-3 do not share a single general inventive concept linking the four Groups together under PCT Rule 13.1.

The single general concept linking the three Groups together is merely "an immunogenic peptide of 7-50 amino acid residues derived from a serine protease involved in ovarian cancer".

This common concept is, however, described in US 2004/0224891 A1 (O'Brien, T.J., et al., US) 11 Nov 2004 and does not represent any contribution over the prior art.

Hence the inventions listed as Groups 1-3 do not relate to a single general inventive concept under PCT Rule 13.1 because the above mentioned common concept fails to make a contribution over the prior art within the meaning of PCT Rule 13.2.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

PCT/US2007/024300

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 6649741 B1	18.11.2003	AT 258060 E	15.02.2004
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		WO 2004/075723 A2	10.09.2004