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(54) Title: REPLIKIN PEPTIDES IN RAPID REPLICATION OF GLIOMA CELLS AND IN INFLUENZA EPIDEMICS

(57) Abstract: Peptides of influenza virus hemagglutinin protein and Plasmodium falciparum malaria antigen, antibodies specific for the peptides, influenza vaccines, malaria vaccines and methods of stimulating the immune response of a subject to produce antibodies to influenza virus or malaria are disclosed. Also disclosed are methods for formulating vaccines for influenza virus.

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/08990

According to international Pattern Classification (PC) or to both national classification and IPC B. FIELDS SEARCHED  Minimum documentation searched (classification system followed by classification symbols)  U.S.: 530/300, 387.1, 389.1, 424/204.1; 514/2  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)  Please See Continuation Sheet  C. DOCUMENTS CONSIDERED TO BE RELEVANT  Category*  X. Glation of document, with indication, where appropriate, of the relevant passages  Figure 1, first line, right hand side sequenc(ERR), 3008, column 1, Viruses and Other Ag and Immunization.  X. Spraid adaguates of old-documents are listed in the continuation of Box C.  SPIED STATE of the sta	A. CLASSIFICATION OF SUBJECT MATTER  IPC(7) : A61K 38/00; C07K 14/11  FOR CO. 2007 1 2009 1 404/2041 514/2					
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"E" earlier application or patent 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 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 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 of particular relevance; the claimed invention 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 taken alone  "Y" document of particular relevance; the claimed invention 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 novel or cansidered to involve an inventive step when the document is taken alone  "Y" document of particular relevance; the claimed invention cannot be considered novel or cansidered novel or an inventive step when the document is taken alone  "Y" document of particular relevance; the claimed invention cannot be considered novel or cansidered novel or cannot be considered novel or novel of particular relevance; the claimed invention cannot be considered novel or cannot be considered novel	"A" document defining the general state of the art which is not considered to be of and not in conflict with the application but cited to understand the principle or theory underlying the invention					
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"O" document referring to an oral disclosure, use, exhibition or other means to a person skilled in the art  "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  O9 June 2005 (09.06.2005)  Name and mailing address of the ISA/US  Mail Stop PCT, Attn: ISA/US  Commissioner of Patents  P.O. Box 1450  Alexandria, Virginia 22313-1450  Facsimile No. (703) 305-3230  to a person skilled in the art  document member of the same patent family  ##" document member of the same patent fami	"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				when the document is combined	
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Name and mailing address of the ISA/US  Mail Stop PCT, Attn: ISA/US  Commissioner of Patents  P.O. Box 1450  Alexandria, Virginia 22313-1450  Facsimile No. (703) 305-3230  Authorized officer  Myon C. Hill  Telephone No. 571-272-1600			Date of n	nailing of the international search	ch report	
Facsimile No. (703) 305-3230	Name and mailing address of the ISA/US  Mail Stop PCT, Attn: ISA/US  Commissioner of Patents  P.O. Box 1450  Myron S. Hill					

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/08990

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)			
This international report has not been	n established in respect of certain claims under Article 17(2)(a) for the following reasons:		
Claim Nos.:     because they relate to	subject matter not required to be searched by this Authority, namely:		
2. Claim Nos.: 10,12,17 because they relate to an extent that no mean Please See Continuati	parts of the international application that do not comply with the prescribed requirements to such ingful international search can be carried out, specifically:		
3. Claim Nos.: because they are depe	ndent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).		
Box II Observations where un	uity of invention is lacking (Continuation of Item 2 of first sheet)		
This International Searching Authori Please See Continuation Sheet	ty found multiple inventions in this international application, as follows:		
searchable claims.  2. As all searchable claim payment of any addition.  3. As only some of the results of the	onal search fees were timely paid by the applicant, this international search report covers all ms could be searched without effort justifying an additional fee, this Authority did not invite onal fee.  Equired additional search fees were timely paid by the applicant, this international search report ms for which fees were paid, specifically claims Nos.:		
restricted to the invent	I search fees were timely paid by the applicant. Consequently, this international search report is tion first mentioned in the claims; it is covered by claims Nos.:  additional search fees were accompanied by the applicant's protest.  protest accompanied the payment of additional search fees.		

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PCT/US03/08990		

#### Continuation of Box I Reason 2:

Claims 10, 12, and 17 contain the limitation "at least two consecutive years, including the current year" and this is not searchable because the current year changes. Claims 18-23 are drawn to algorithms and are not searchable as written. Claims 24-31 are a product and method of using depending on the method of claim 23 and cannot be searched because the product is not determined. Claims 44 and 45 are not searchable because it is not known the correlation between replikin and microorganism and it is also not known what is indicated by such a finding. Claims 46-48 are not searchable because it is not known what the result is or what the enzyme is.

## BOX II. 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 claim(s) 1,2, 9, 11, 15, and 16, drawn to an influenza peptide, and method of using.

Group II, claim(s) 3-8, drawn to an antibody or cocktail of antibodies against inflenza.

Group III, claim(s) 13, drawn to an antisense nucleic acid complementary to the sequence of an influenza HN mRNA.

Group IV, claim(s) 14, drawn to an antisense nucleic acid complementary to the sequence of an influenza HN genome.

Group V, claim(s) 32-37, drawn to a malerial vaccine comprising a P. falciparum replikin.

Group VI, claim(s) 38-40, drawn to an antibody that binds to a P. falciparum replikin.

Group VII, claim(s) 41-43, drawn to a method to stimulate the immune system of a subject.

The inventions listed as Groups I-VII 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: Group I is directed to an isolated influenza virus peptide (an isolated influenza peptide having about 7-50 residues comprising at least one lysine located 6 to 10 residues away from a second lysine[symbol=k], one histidine residue[h], and at least 6% lysine), which is the first product. However, because Gao et al. (Identification and characterization of T helper epitopes in the nucleoprotein of influenza A virus. Journal of Immunology 1989 Vol. 143, pages 3007-3014) disclose a peptide that meets the limitations of claim 1 (an isolated influenza peptide having about 7-50 residues comprising at least one lysine located 6 to 10 residues away from a second lysine[symbol=k], one histidine residue[h], and at least 6% lysine (a 20-mer peptide shown in Figure 1, top line, right side (ERRNKYLEEHPSAGKDPKKT)), no special technical feature exists for Group I as defined by PCT Rule 13.2, because it does not define a contribution over the prior art. The technical features of Groups II-XIV are drawn to products and methods having different goals, method steps and starting materials, which do not require each other for their practice and do not share the same or a corresponding technical feature. Groups II-IV relate to influenza antibodies and nucleic acid (different products), not an influenza peptide which is the first named product. Groups V-VII do not relate to the influenza peptide product of Group I. Groups V-VII are drawn to P. falciparum peptide and antibodies and a method of using. Shi et al. (Immunogenicity and in vitro protective efficacy of a recombinant multistage Plasmodium falciparum candidate vaccine. 1999 PNAS Vol. 96, No. 4, pages 1615-1620) teach a peptide (Table 1, tenth from the top, GNAEKYDKMDEPQHYGKS) that meets the limitation of Group V (a P. falciparum peptide with the same residue requirements as Group I except that it is not an influenza peptide). Note that PCT Rule 13 does not provide for multiple products or methods within a single application. Because the technical feature of Group I is not a special technical feature, unity of invention is lacking.

INTERNATIONAL SEARCH REPORT	PCT/US03/08990
Continuation of B. FIELDS SEARCHED Item 3: Sequence search of replikin motif, WEST, MEDLINE terms- influenza, p falciparum, replication	

Form PCT/ISA/210 (second sheet) (July 1998)