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(54) Title: SYSTEM AND METHOD FOR AUTOMATED SELECTION OF T-CELL EPITOPES

(57) Abstract: Methodology for the automated selection and/or optimization of T-cell epitopes is disclosed. The invention provides a data processing system which utilizes sequence-based statistical pattern recognition to compute an epitope selection matrix based on the informational content of epitopes known to bind to a particular major histocompatibility class I allele. The resulting Bayes-corrected scoring matrix is used to predict the relative binding affinities of candidate T-cell epitopes derived from immunologically relevant antigens of self or foreign origin. One aspect of the invention describes an analytical method for identification of modifications in known or predicted T-cell epitopes, that confer upon the epitopes the ability to elicit stronger cellular immune response due to more efficient processing and/or presentation to T-cells. The disclosed epitope identification algorithm is applicable to the design of vaccines for infectious diseases, cancer and autoimmune diseases as well as for developing methods for the in vitro evaluation of cellular immunity.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US06/17897

A. CLASSIFICATION OF SUBJECT MATTER
IPC: **G01N 33/48**(2006.01),**33/50**(2006.01);**C12Q 1/70**(2006.01)

USPC: 702/19;703/11;435/5
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)
U.S. : 702/19; 703/11; 435/5

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)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2005/0074809 A1 (BRUSIC et al) 07 April 2005 (07.04.2005), entire document.	, 9
X	BURDEN et al. Predictive Bayesian neural network models of MHC class II peptide binding. Journal of Molecular Graphics and Modelling, June 2005 (available online 6 May 2005), Volume 23, Issue 6, pages 481-489.	1-7, 9

☐ 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 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
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03 JUL 2008

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US06/17897

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 Continuation 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 additional fees, this Authority did not invite payment of any 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.: 1-9

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.

BOX III. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

I. Claims 1-9, drawn to method for predicting T-cell epitopes that are likely to bind to an MHC class I allele of interest.

II. Claims 10-15, drawn to method for predicting whether a naturally occurring peptide sequence derived from a target protein will bind to an MHC allele of interest

III. Claims 15-17, drawn to method for the identification of an anchor-modified immunogenic analog of a native MHC class I epitope

IV. Claim 18, drawn to method for ranking a set of candidate T-cell epitopes on the basis of how efficiently a peptide is predicted to be processed or presented by antigen presenting cells by implementing a natural processing filter.

V. Claim 19, drawn to method for enhancing the immunogenicity of a target protein.

The inventions listed as Groups I-III 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: Applying Bayesian scoring matrix to evaluate MHC-binding affinities is the technical feature that links Groups I-III. This is not a contribution over the prior art because it is suggested by such references as Rognan et al (J. Med. Chem., 1999, 46500-4658) Therefore, the lack of unity is present because the linking technical feature is not a "special technical feature" as defined by PCT Rule 13.2.

Further, with regard to Groups IV, V, the methods addressed there 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: Each of the Groups IV, V claim a distinct and separate method (Gr. IV - a method for method for ranking of epitopes), Group - a method for enhancing protein immunogenecity). The methods do not share a special technical feature because each method contains specific and unique method steps which are not shared by each of the other methods and each method has a unique and distinct outcome. Thus, groups I-V do not share a corresponding special technical feature