Title: PEPTIDES AND METHODS OF SCREENING IMMUNOGENIC PEPTIDE VACCINES AGAINST ALZHEIMER'S DISEASE

Abstract: The invention is in the field of immunogenicity. In one embodiment, the invention relates to method of identifying T-cell epitopes in amyloid beta peptide or homologue thereof. In another embodiment, the invention relates to a vaccine comprising an amyloid beta peptide or homologue thereof, whereby the selected peptide is a peptide which lacks certain T-cell epitopes or a peptide which is modified by deleting or modifying amino acids so as to reduce or eliminate the T-cell epitopes. The selected peptides are further assessed for reduced capacity to form fibrils, reduced cytotoxicity, and a reduced ability to induce a cellular autoimmune response. The selected peptides are further assessed for ability to induce a humoral immune response. In another embodiment, the invention relates to a method of predicting the reaction of an individual to a vaccine, which comprises amyloid beta peptide or homologue thereof, based on the HLA haplotype of the subject. In another embodiment, the invention provides a method for matching a vaccine comprising amyloid beta peptide or homologue thereof to an individual, based on the HLA haplotype of that individual. In another embodiment, the invention provides a vaccine comprising an amyloid beta peptide or homologue thereof, whereby the amyloid beta peptide or homologue thereof, lacks the ability to induce a T-cell response.
A. CLASSIFICATION OF SUBJECT MATTER
   IPC: A61K 38/00(2006.01); C07K 1/00(2006.01), 14/00(2006.01), 17/00(2006.01)
   USPC: 530/300, 350
   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.: 530/300, 350
   Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
   Electronic database consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
<thead>
<tr>
<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
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<tbody>
<tr>
<td>X</td>
<td>WO99/77944 (ATHENA NEUROSCIENCES, INC.) 10 June 1999 (10.06.1999), see full document.</td>
<td>1-36, 57</td>
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<tr>
<td>X</td>
<td>WO00/72876 (NEURALAB LIMITED) 7 December 2000 (07.12.2000), see full document.</td>
<td>1-36, 57</td>
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</table>

☐ 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
  “I” inter 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
  “E” document member of the same patent family

Date of the actual completion of the international search: 17 August 2006 (17.08.2006)
Authorised officer: Janet Andres
Telephone No. 308-1235

Date of mailing of the international search report: 27 SEP 2006

Name and mailing address of the ISA/US
Mailing PCT, Attn: ISA/US
Commissioner of Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
Facsimile No. (571) 273-3201

Form PCT/ISA/210 (second sheet) (July 1998)
### INTERNATIONAL SEARCH REPORT

**International application No.**
PCT/US03/22280

<table>
<thead>
<tr>
<th>Box I</th>
<th>Observations where certain claims were found unsrollable (Continuation of Item 1 of first sheet)</th>
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<tr>
<td>This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:</td>
<td></td>
</tr>
<tr>
<td>1.</td>
<td>Claim Nos.: because they relate to subject matter not required to be searched by this Authority, namely:</td>
</tr>
<tr>
<td>2.</td>
<td>Claim 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:</td>
</tr>
<tr>
<td>3.</td>
<td>Claim Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).</td>
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<th>Box II</th>
<th>Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)</th>
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<tr>
<td>This International Searching Authority found multiple inventions in this international application, as follows:</td>
<td></td>
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<tr>
<td>Please See Continuation Sheet</td>
<td></td>
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</table>

| 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.: 1-36 and 57 |

**Remark on Protest**

- The additional search fees were accompanied by the applicant’s protest.  
- No protest accompanied the payment of additional search fees.
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) 1-36 and 57, drawn to special technical feature beta amyloid peptide or homologue and a comprising kit.

Group II, claim(s) 37, drawn to method of determining T-cell epitopes.

Group III, claim(s) 38-41, drawn to a method of predicting the reaction of an individual to a vaccine.

Group IV, claim(s) 42-56, drawn to a method of matching a vaccine.

Group V, claim(s) 58-59, drawn to a method of preventing the formation or progression of amyloid plaques.

The inventions listed as Groups I-V 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 first appearing special technical feature beta amyloid or homologue thereof is not a contribution over the prior art. In particular, Selkoe, US 5,262,332 teaches beta-amyloid peptides and various fragments as well as beta amyloid precursor proteins corresponding to various homologues thereof as instantly claimed, see in particular Selkoe, Abstract and columns 1-2. Accordingly, unity of invention is lacking.