A. Effects of age on antibody production

- 20000
- 15000
- 10000
- 5000
- 0

Division of X maximum level

Memory
Recall

Immunizations

12 months
10 months
20 months
18 months

1* 2* 3* 1* 2* 3* 1* 2* 3*

B. Effects of age on isotype

Titer (O.D.)

1.2
1
0.8
0.6
0.4
0.2
0.0

IgA IgG1 IgG2a IgG2b IgM

Young

Old

(Continued on next page)
SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— with international search report
— before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

(88) Date of publication of the international search report:

3 March 2005
**INTERNATIONAL SEARCH REPORT**

**A. CLASSIFICATION OF SUBJECT MATTER**

| IPC | A61K39/39 | A61K39/385 | C12N15/62 |

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 | A61K | C12N |

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 database and, where practical, search terms used)

EPO-Internal, BIOSIS, WPI Data, EMBASE

**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>
</tr>
</thead>
<tbody>
<tr>
<td>Y</td>
<td>page 548; figures 1,2</td>
<td>6-10, 12, 16,18,20</td>
</tr>
<tr>
<td>Y</td>
<td>page 373, line 15 - line 46</td>
<td>6-10, 12, 16,18,20</td>
</tr>
</tbody>
</table>

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Further documents are listed in the continuation of box C. Patent family members are listed in annex.

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* 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 document 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

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Date of the actual completion of the international search

21 December 2004

Date of mailing of the international search report

07/01/2005

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk
Tel: (+31-70) 340-2040, Tx: 31 651 epo nl
Fac: (+31-70) 340-3016

Authorized officer

Lonnoy, 0
<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>
</tr>
</thead>
</table>
| Y        | KOWALCZYK D W ET AL: "Immune responses to DNA vaccines"  
CMLS CELLULAR AND MOLECULAR LIFE SCIENCES,  
vol. 55, no. 5, May 1999 (1999-05), pages 751-770, XP002311708  
ISSN: 1420-682X  
page 759, column 1, paragraph 2 | 6-10,12,  
16,18,20 |
| X        | DE 100 10 165 A (HARTMUT MERZ C O MEDIZINISCHE)  
20 September 2001 (2001-09-20)  
claims 6-10 | 1-5,11,  
13,15,17 |
| A        | SANCHEZ MARTA ET AL: "The response in old mice: Positive and negative immune memory after priming in early age"  
INTERNATIONAL IMMUNOLOGY,  
vol. 13, no. 10, October 2001 (2001-10), pages 1213-1221, XP002311709  
ISSN: 0953-8178  
cited in the application figure 6 | |
| A        | ZAFIROPOULOS A ET AL: "Induction of antigen-specific isotype switching by in vitro immunization of human naive B lymphocytes"  
JOURNAL OF IMMUNOLOGICAL METHODS, ELSEVIER SCIENCE PUBLISHERS B.V.,AMSTERDAM, NL,  
vol. 200, no. 1,  
ISSN: 0022-1759 | |
| A        | STACY SUE ET AL: "Immunological memory and late onset autoimmunity."  
MECHANISMS OF AGEING AND DEVELOPMENT. 30 APR 2002,  
vol. 123, no. 8,  
30 April 2002 (2002-04-30), pages 975-985,  
XP002311735  
ISSN: 0047-6374 | |
INTERNATIONAL SEARCH REPORT

Box No. I  Nucleotide and/or amino acid sequence(s) (Continuation of item 1.b of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the International application and necessary to the claimed invention, the international search was carried out on the basis of:
   
a. type of material
      - [x] a sequence listing
      - [ ] table(s) related to the sequence listing

   b. format of material
      - [x] in written format
      - [x] in computer readable form

   c. time of filing/furnishing
      - [ ] contained in the international application as filed
      - [ ] filed together with the international application in computer readable form
      - [x] furnished subsequently to this Authority for the purpose of search

2. [x] In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto 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

Box 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:
   Although claims 11-21 are directed to methods of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

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 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:

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.
☐ No protest accompanied the payment of additional search fees.

Form PCT/ISA/210 (continuation of first sheet (2)) (January 2004)
<table>
<thead>
<tr>
<th>Patent document cited in search report</th>
<th>Publication date</th>
<th>Patent family member(s)</th>
<th>Publication date</th>
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