EUROPEAN PATENT APPLICATION

Composition for inducing immunotolerance

The present invention provides methods of treating allergic disorders and compositions for use therein. The methods comprise administering an allergen and one or more medicaments. These medicaments are compounds that inhibit the transcription of genes involved in the initiation of innate and specific immunity, thereby promoting the development of tolerance to these allergens, through inhibition of the NF-κB and/or the MAPK/AP-1 signal transduction pathway(s). In another embodiment, the use of DNA vaccines is disclosed that incorporate a gene encoding one or more allergen sequences or fragments thereof, in combination with genes encoding proteins that inhibit the activation of the NF-κB and/or the MAPK/AP-1 pathway or in combination with small interfering RNA sequences or anti-sense sequences that inhibit the expression of NF-κB and/or AP-1 proteins.
# PARTIAL EUROPEAN SEARCH REPORT

## DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
<thead>
<tr>
<th>Category</th>
<th>Citation of document with indication, where appropriate, of relevant passages</th>
<th>Relevant to claim</th>
<th>CLASSIFICATION OF THE APPLICATION (IPC)</th>
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<tbody>
<tr>
<td>X</td>
<td>WO 95/32734 A (BARCY SERGE ;INNOGENETICS NV (BE); BOER MARK DE (NL)) 7 December 1995 (1995-12-07) * page 1, line 4 - line 18 *</td>
<td>1</td>
<td>A61K31/593 A61K31/616 A61K38/17 A61K38/19 A61K38/48 A61K93/35</td>
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<td>Y</td>
<td>* page 2, line 19 - page 3, line 12 *</td>
<td>2-4, 13-16, 18,21,22</td>
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<td>* page 4, line 12 - line 27 *</td>
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<td>* page 6, line 26 - page 7, line 7 *</td>
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<td>* page 14, line 6 - line 30; claims 1,5,6,13-15; example 6 *</td>
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## INCOMPLETE SEARCH

The Search Division considers that the present application, or one or more of its claims, does/do not comply with the EPC to such an extent that a meaningful search into the state of the art cannot be carried out, or can only be carried out partially, for these claims.

Claims searched completely:

Claims searched incompletely:

Claims not searched:

Reason for the limitation of the search:

see sheet C

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**Place of search:** Munich  
**Date of completion of the search:** 28 February 2007  
**Examiner:** Langer, Astrid

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**CATEGORY OF CITED DOCUMENTS**

- **X:** particularly relevant if taken alone
- **Y:** particularly relevant if combined with another document of the same category
- **A:** technological background
- **O:** non-written disclosure
- **P:** intermediate document

**CLASSIFICATION OF THE APPLICATION (IPC):**

- **T:** theory or principle underlying the invention
- **E:** earlier patent document, but published on, or after the filing date
- **D:** document cited in the application
- **L:** document cited for other reasons
- **A:** member of the same patent family, corresponding document
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<td>* page 633, column 2, paragraph 2 *</td>
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<td>* page 636, column 1, paragraph 2 *</td>
<td>18,21</td>
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<td>* page 638, column 1, paragraph 3 - column 2, paragraph 1 *</td>
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<td>Y</td>
<td>LARCHÉ M: &quot;SPECIFIC IMMUNOTHERAPY&quot; BRITISH MEDICAL BULLETIN, CHURCHILL LIVINGSTONE, LONDON, GB, vol. 56, no. 4, 2000, pages 1019-1036, XP001033878 ISSN: 0007-1420</td>
<td>17</td>
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<td>* page 1019, paragraph 2 - page 1020, paragraph 1 *</td>
<td>18,21</td>
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<td>* page 675, column 2, paragraph 4 - page 677, column 2, paragraph 1 *</td>
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TECHNICAL FIELDS SEARCHED (IPC)

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<th>Citation of document with indication, where appropriate, of relevant passages</th>
<th>Relevant to claim</th>
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<tbody>
<tr>
<td>Y,D</td>
<td>JONULEIT H ET AL: &quot;Dendritic cells as a tool to induce anergic and regulatory T cells&quot; TRENDS IN IMMUNOLOGY, ELSEVIER, CAMBRIDGE, GB, vol. 22, no. 7, 1 July 2001 (2001-07-01), pages 394-400, XP004247295 ISSN: 1471-4906 * page 398, column 2, paragraph 2 *</td>
<td>1-4, 13-16, 18,21,22</td>
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<td>Citation of document with indication, where appropriate, of relevant passages</td>
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<td>Y</td>
<td>KIMATA M ET AL: &quot;Effects of luteolin, quercetin and baicalein on immunoglobulin E-mediated mediator release from human cultured mast cells.&quot; CLINICAL AND EXPERIMENTAL ALLERGY, vol. 30, no. 4, April 2000 (2000-04), pages 501-508, XP001154026 ISSN: 0954-7894 Abstract * page 503, column 2, paragraph 2 * * page 506, column 1, paragraph 2 - column 2, paragraph 2 * -----</td>
<td>1-4, 13-16, 18,21,22</td>
</tr>
<tr>
<td>Y,D</td>
<td>LI QIUTANG ET AL: &quot;NF-kappaB regulation in the immune system.&quot; NATURE REVIEWS IMMUNOLOGY, vol. 2, no. 10, 20 October 2002 (2002-10-20), pages 725-734, XP009015224 ISSN: 1474-1733 * page 726, column 1, paragraph 2 - column 2, paragraph 1 * * page 732, column 1, paragraph 1 * * page 732, column 2, paragraph 2 * -----</td>
<td>1-4, 13-16, 18,21,22</td>
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<tr>
<td>Y,D</td>
<td>DAYNES RAYMOND A ET AL: &quot;Emerging roles of PPARs in inflammation and immunity.&quot; NATURE REVIEWS IMMUNOLOGY, vol. 2, no. 10, 20 October 2002 (2002-10-20), pages 748-759, XP009015662 ISSN: 1474-1733 Abstract * page 752, column 1, paragraph 2 - paragraph 3; figures 2,3 * -----</td>
<td>1-4, 13-16, 18,21,22</td>
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Although claims 1-4, 15, 16, 18, 22 are directed to a method of treatment of the human/animal body (Article 52(4) EPC), the search has been carried out and based on the alleged effects of the compound/composition.

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Claim(s) searched incompletely:
1-4, 15, 16, 18, 22

Reason for the limitation of the search (non-patentable invention(s)):
Article 52 (4) EPC - Method for treatment of the human or animal body by therapy
CLAIMS INCURRING FEES

The present European patent application comprised at the time of filing more than ten claims.

☐ Only part of the claims have been paid within the prescribed time limit. The present European search report has been drawn up for the first ten claims and for those claims for which claims fees have been paid, namely claim(s):

☐ No claims fees have been paid within the prescribed time limit. The present European search report has been drawn up for the first ten claims.

LACK OF UNITY OF INVENTION

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

see sheet B

☐ All further search fees have been paid within the fixed time limit. The present European search report has been drawn up for all claims.

☐ As all searchable claims could be searched without effort justifying an additional fee, the Search Division did not invite payment of any additional fee.

☐ Only part of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the inventions in respect of which search fees have been paid, namely claims:

☐ None of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the invention first mentioned in the claims, namely claims:

1-3, 13-18, 21, 22 (partially), 4
The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

1. claims: Claims 1-3, 13-18, 21, 22 (partially), 4

   Method or composition to induce and/or increase tolerance to an allergen in a subject; DNA vaccine.

1.1. claims: Claims 1-3, 13-16, 18, 21, 22 (partially), 4

   Method or composition to induce and/or increase tolerance to an allergen in a subject, comprising inhibiting and/or preventing the production of a co-stimulator molecule in an antigen-presenting cell in the presence of an allergen by inhibiting the NF-κB and/or the MAPK/AP-1 signal transducing pathways by a ligand to a PPAR.

1.2. claim: Claim 17

   A DNA vaccine comprising a gene encoding an allergen.
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2. claims: Claims 1-3, 5, 13-16, 18, 21, 22 (partially)

   Method or composition to induce and/or increase tolerance to an allergen in a subject, comprising inhibiting and/or preventing the production of a co-stimulator molecule in an antigen-presenting cell in the presence of an allergen by inhibiting the NF-κB and/or the MAPK/AP-1 signal transducing pathways by an anti-oxidant compound.
   ---

3. claims: Claims 1-3, 5, 13-16, 18, 21, 22 (partially)

   Method or composition to induce and/or increase tolerance to an allergen in a subject, comprising inhibiting and/or preventing the production of a co-stimulator molecule in an antigen-presenting cell in the presence of an allergen by inhibiting the NF-κB and/or the MAPK/AP-1 signal transducing pathways by a proteasome and/or protease inhibitor.
   ---

4. claims: Claims 1-3, 5, 13-16, 18, 21, 22 (partially)

   Method or composition to induce and/or increase tolerance to an allergen in a subject, comprising inhibiting and/or preventing the production of a co-stimulator molecule in an antigen-presenting cell in the presence of an allergen by inhibiting the NF-κB and/or the MAPK/AP-1 signal transducing pathways by an IκBa phosphorylation and/or degradation inhibitor.
   ---

5. claims: Claims 1-3, 13-16, 18, 21, 22 (partially), 6-8, 10, 11
Method or composition to induce and/or increase tolerance to an allergen in a subject, comprising inhibiting and/or preventing the production of a co-stimulator molecule in an antigen-presenting cell in the presence of an allergen by inhibiting the NF-kB and/or the MAPK/AP-1 signal transducing pathways by miscellaneous inhibitors (e.g. glucocorticoids, pyridinylimidazole compounds).

6. claims: Claims 1-3, 13-16, 18, 21, 22 (partially), 9

Method or composition to induce and/or increase tolerance to an allergen in a subject, comprising inhibiting and/or preventing the production of a co-stimulator molecule in an antigen-presenting cell in the presence of an allergen by inhibiting the NF-kB and/or the MAPK/AP-1 signal transducing pathways by cAMP-elevating compounds.

7. claims: Claims 1-3, 13-16, 18, 21, 22 (partially), 12

Method or composition to induce and/or increase tolerance to an allergen in a subject, comprising inhibiting and/or preventing the production of a co-stimulator molecule in an antigen-presenting cell in the presence of an allergen by inhibiting the NF-kB and/or the MAPK/AP-1 signal transducing pathways by an NF-kB and/or AP-1 decoy oligonucleotide.

8. claims: Claims 1-3, 13-16, 18, 21, 22 (partially), 20

Method or composition to induce and/or increase tolerance to an allergen in a subject, comprising inhibiting and/or preventing the production of a co-stimulator molecule in an antigen-presenting cell in the presence of an allergen by inhibiting the NF-kB and/or the MAPK/AP-1 signal transducing pathways by a small interfering RNA sequence and/or antisense sequence that inhibits the expression of the NF-kB and/or AP-1 protein.

Please note that all inventions mentioned under item 1, although not necessarily linked by a common inventive concept, could be searched without effort justifying an additional fee.
ANNEX TO THE EUROPEAN SEARCH REPORT
ON EUROPEAN PATENT APPLICATION NO.

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report. The members are as contained in the European Patent Office EDP file on 28-02-2007.
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

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<th>Publication date</th>
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<td>WO 9532734 A</td>
<td>07-12-1995</td>
<td>AU 2670995 A</td>
<td>21-12-1995</td>
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<td>CA 2188812 A1</td>
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For more details about this annex: see Official Journal of the European Patent Office, No. 12/82