(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
2 October 2008 (02.10.2008)

(10) International Publication Number
WO 2008/118592 A3

(51) International Patent Classification:
A61K 39/10 (2006.01) C12N 7/01 (2006.01)
A61K 39/275 (2006.01) C12N 15/86 (2006.01)

(21) International Application Number:
PCT/US2008/054902

(22) International Filing Date:
25 February 2008 (25.02.2008)

(25) Filing Language:
English

(26) Publication Language:
English

(30) Priority Data:
60/891,375 23 February 2007 (23.02.2007) US

(71) Applicant (for all designated States except US):
THE PENNSYLVANIA STATE UNIVERSITY [US/US]; 304 Old Main, University Park, Pennsylvania 16802-1504 (US).

(72) Inventor: and

(75) Inventor/Applicant (for US only): HARVILL, Eric [US/US]; 304 Old Main, University Park, Pennsylvania 16802-1504 (US).

(74) Agent: LEHMAN BELL, Janae; McKee, Voorhees & Sease, PLC, 801 Grand Avenue, Suite 3200, Des Moines, Iowa 50309-2721 (US).


(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, 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:
19 March 2009

(54) Title: USE OF AN AVIRULENT BORDETELLA MUTANT AS A LIVE VACCINE VECTOR

(57) Abstract: The present invention pertains to Bordetella bacteria having a double mutation, a first mutation in a gene of the Type III secretion system and a second mutation in a gene of the adenylyl cyclase toxin (CyaA) locus of the bacteria so that the mutations result in no Type III secretion system, a non-functional Type III secretion system, no CyaA protein, or a non-functional CyaA protein or a combination thereof. The Bordetella bacteria double mutant is attenuated while maintaining the efficacy of the bacteria to elicit an immune response. The present invention also pertains to vaccine compositions and methods for treating and immunizing a mammal against a disease caused by infection of Bordetella bacteria or a disease caused by a pathogen.
**INTERNATIONAL SEARCH REPORT**

**A. CLASSIFICATION OF SUBJECT MATTER**

A61K 39/10(2006.01)i, A61K 39/275(2006.01)i, C12N 7/01(2006.01)i, C12N 15/86(2006.01)i

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 8 as above

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)

e-KIPASS(kipo internal), PubMed, STN(CAplus)

**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>X</td>
<td>US 6099848 A (FRANKEL; PORTNOY) 8 Aug. 2000 see abstract and claims</td>
<td>42</td>
</tr>
</tbody>
</table>

Further documents are listed in the continuation of Box C. See patent family annex.

*A* 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 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 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

12 JANUARY 2009 (12.01.2009)

Date of mailing of the international search report

12 JANUARY 2009 (12.01.2009)

Name and mailing address of the ISA/KR

Korean Intellectual Property Office
Government Complex-Daejeon, 139 Seonsa-ro, Seogu, Daejeon 302-701, Republic of Korea

Facsimile No. 82-42-472-7140

Authorized officer

Park, Jung Mm

Telephone No. 82-42-48 1-8291
<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>

see the whole document
**INTERNATIONAL SEARCH REPORT**

**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 1-20, 43-46**
   - because they relate to subject matter not required to be searched by this Authority, namely
   - Claims 1-20, 43-46 pertain to methods for treatment of the human or animal body by therapy, as well as diagnostic methods, and thus relate to a subject matter which this International Searching Authority is not required to search under Article 17(2)(a)(i) of the PCT and Rule 39 l(iv) of the Regulations under the PCT.

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 64(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:

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**

- **1** The additional search fees were accompanied by the applicant’s protest and, where applicable, the payment of a protest fee
- **1** 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
- **1** No protest accompanied the payment of additional search fees

Form PCT/ISA/210 (continuation of first sheet (2)) (July 2008)
## INTERNATIONAL SEARCH REPORT

**International application No:** PCT/US2008/054902

<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>
</tr>
</thead>
<tbody>
<tr>
<td>US 2003-0059442 A1</td>
<td>27.03.2003</td>
<td>AP 200202549 DO</td>
<td>30.06.2002</td>
</tr>
<tr>
<td></td>
<td></td>
<td>AU 2001-22 100 A1</td>
<td>09.07.2001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>AU 2210001 A</td>
<td>09.07.2001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>BR 0016616 A</td>
<td>29.10.2002</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CA 2395382 A1</td>
<td>05.07.2001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CN 1411468 A</td>
<td>16.04.2003</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CZ 20022444 A3</td>
<td>16.10.2002</td>
</tr>
<tr>
<td></td>
<td></td>
<td>EP 1240192 A2</td>
<td>18.09.2002</td>
</tr>
<tr>
<td></td>
<td></td>
<td>GB 9830455 DO</td>
<td>16.02.2000</td>
</tr>
<tr>
<td></td>
<td></td>
<td>HU 0203646 A2</td>
<td>28.03.2003</td>
</tr>
<tr>
<td></td>
<td></td>
<td>JP 2003-518933</td>
<td>17.06.2003</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NO 20022949 A</td>
<td>19.06.2002</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NZ 519477 A</td>
<td>30.04.2004</td>
</tr>
<tr>
<td></td>
<td></td>
<td>OA 12130 A</td>
<td>05.05.2006</td>
</tr>
<tr>
<td></td>
<td></td>
<td>US 2003-059442 A1</td>
<td>27.03.2003</td>
</tr>
<tr>
<td></td>
<td></td>
<td>WO 01-47962 A2</td>
<td>05.07.2001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>WO 01-47962 A3</td>
<td>10.05.2002</td>
</tr>
<tr>
<td></td>
<td></td>
<td>WO 01-47962 A8</td>
<td>31.10.2002</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ZA 200204725 A</td>
<td>30.07.2003</td>
</tr>
<tr>
<td>US 6099848 A</td>
<td>08.08.2000</td>
<td>AU 1999-14108 A1</td>
<td>07.06.1999</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CA 2309790 A1</td>
<td>27.05.1999</td>
</tr>
<tr>
<td></td>
<td></td>
<td>EP 1032417 A1</td>
<td>06.09.2000</td>
</tr>
<tr>
<td></td>
<td></td>
<td>US 6504020 B1</td>
<td>07.01.2003</td>
</tr>
</tbody>
</table>

Form PCT/ISA/210 (patent family annex) (May 2008)