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WO 2003/063766 A3

(54) Title: NOVEL IMMUNOGENIC COMPOSITIONS FOR THE PREVENTION AND TREATMENT OF MENINGOCOCCAL DISEASE

(57) Abstract: The present invention relates to *Neisseria* ORF2086 proteins, crossreactive immunogenic proteins which can be isolated from nesserial strains or prepared recombinantly, including immunogenic portions thereof, biological equivalents thereof, antibodies that immunospecifically bind to the foregoing and nucleic acid sequences encoding each of the foregoing, as well as the use of same in immunogenic compositions that are effective against infection by *Neisseria meningitidis* serogroup B.

**INTERNATIONAL SEARCH REPORT**

International application No.

PCT/US02/32369

<b>A. CLASSIFICATION OF SUBJECT MATTER</b>												
IPC(7) : C07K 1/00, 2/00; A61K 39/02, 39/00, 39/095; 38/00												
US CL : 530/350, 300, 825; 424/234.1, 190.1, 184.1, 250.1, 249.1; 514/2												
According to International Patent Classification (IPC) or to both national classification and IPC												
<b>B. FIELDS SEARCHED</b>												
Minimum documentation searched (classification system followed by classification symbols) U.S. : 530/350, 300, 825; 424/234.1, 190.1, 184.1, 250.1, 249.1; 514/2												
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) Please See Continuation Sheet												
<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>												
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.										
X	WO 99/57280 A2 (CHIRON CORPORATION) 11 November 1999 (11.11.1999), entire document.	1, 6, 7, 9-38, 60-85, 100-114, 168-172, 181, 182, 194, 196-205, 213-251, 255, 257, 266-276 and 285-289										
X	WO 01/64922 A2 (CHIRON SPA) 07 September 2001 (07.09.2001), entire document.	1, 6, 7, 9-38, 60-85, 100-114, 168-172, 181, 182, 194, 196-205, 213-251, 255, 257, 266-276 and 285-289										
<input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> See patent family annex.												
<p>* Special categories of cited documents:</p> <table border="0"> <tr> <td>"A" document defining the general state of the art which is not considered to be of particular relevance</td> <td>"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</td> </tr> <tr> <td>"B" earlier application or patent published on or after the international filing date</td> <td>"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</td> </tr> <tr> <td>"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)</td> <td>"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</td> </tr> <tr> <td>"O" document referring to an oral disclosure, use, exhibition or other means</td> <td>"&amp;" document member of the same patent family</td> </tr> <tr> <td>"P" document published prior to the international filing date but later than the priority date claimed</td> <td></td> </tr> </table>			"A" document defining the general state of the art which is not considered to be of particular relevance	"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	"B" earlier application or patent published on or after the international filing date	"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	"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)	"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	"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family	"P" document published prior to the international filing date but later than the priority date claimed	
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"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family											
"P" document published prior to the international filing date but later than the priority date claimed												
Date of the actual completion of the international search 07 October 2003 (07.10.2003)		Date of mailing of the international search report <b>14 NOV 2003</b>										
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703)305-3230		Authorized officer S. Dev Ph.D. Telephone No. (703) 308-0196										

## INTERNATIONAL SEARCH REPORT

PCT/US02/32369

## C. (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 01/64920 A2 (CHIRON SPA) 07 September 2001 (07.09.2001), entire document.	1, 6, 7, 9-38, 60-85, 100-114, 168-172, 181, 182, 194, 196- 205, 213-251, 255, 257, 266-276 and 285-289

## INTERNATIONAL SEARCH REPORT

PCT/US02/32369

### 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 1, claims 2, 1, 3, 5, 9-38, 168-172, 181, 182, 194 and 196-205, drawn to a composition comprising a protein antigen of SEQ ID NO: 254, an immunogenic portion or a biological equivalent thereof.

Groups 2-6, claims 2, 1, 3, 5, 9-38, 168-172, 181, 182, 194 and 196-205, drawn to a composition comprising a protein of SEQ ID NO: 255-259 respectively.

Groups 7-25, claims 4, 1, 5, 9-23, 39, 40, 168-172, 181, 182, 194 and 196-205, drawn to a composition comprising a protein antigen of SEQ ID NO: 260-278 respectively.

Groups 26-46, claims 4, 41, 42, 168-172, 194 and 196-205, drawn to a composition comprising a protein antigen of SEQ ID NO: 279-299 respectively.

Groups 47-52, claims 60-63, 72-85, 213-249, 6, 7, 1, 9-23, 255 and 257 drawn to a composition comprising an amino acid sequence of any of even numbered SEQ ID NO: 2-12 respectively.

Groups 53-58, claims 64, 60-62, 72-85, 250, 251, 213-247, 255, 257, 6, 7, 1 and 9-23, drawn to a composition comprising an amino acid sequence of any of even numbered SEQ ID NO: 14-24 respectively.

Groups 59-67, claims 65, 60-62, 72-85, 213-247, 252-255, 257, 6, 7, 1 and 9-23, drawn to a composition comprising an amino acid sequence of any of even numbered SEQ ID NO: 26-42 respectively.

Groups 68-73, claims 66, 60-62, 72-85, 213-247, 255-257, 6, 7, 1 and 9-23, drawn to a composition comprising an amino acid sequence of any of even numbered SEQ ID NO: 50-60 respectively.

Groups 74-97, claims 67, 60-62, 72-85, 213-247, 255, 257-265, 6, 7, 1 and 9-23, drawn to a composition comprising an amino acid sequence of any of even numbered SEQ ID NO: 62-108 respectively.

Groups 98-112, claims 68, 60-62, 72-85, 213-247, 255, 257, 266-270, 6, 7, 1 and 9-23, drawn to a composition comprising an amino acid sequence of any of even numbered SEQ ID NO: 110-138 respectively.

Groups 113-121, claims 69, 60-62, 72-85, 213-247, 255, 257, 271-273, 6, 7, 1 and 9-23, drawn to a composition comprising an amino acid sequence of any of even numbered SEQ ID NO: 140-156 respectively.

Groups 122-130, claims 70, 60-62, 72-85, 213-247, 255, 257, 274-276, 6, 7, 1 and 9-23, drawn to a composition comprising an amino acid sequence of any of even numbered SEQ ID NO: 158-174 respectively.

Groups 131-145, claims 71, 60-62, 72-85, 215-246, 285-289, 8-23 and 1, drawn to a composition comprising an amino acid sequence of any of even numbered SEQ ID NO: 224-252 respectively.

Groups 146-148, claims 255, 215-246, 6, 1, 9-23 and 60-62, drawn to a composition comprising an amino acid sequence of any of even numbered SEQ ID NO: 44-48 respectively.

Group 149, claims 86-89 and 93-99, drawn to a neisserial antigen that provides immunogenicity to a second neisserial species.

Group 150, claims 100-114, drawn to a composition comprising the protein of SEQ ID NO: 301.

Group 151, claims 115-127, drawn to a composition comprising the protein of SEQ ID NO: 302.

Groups 152-154, claims 277 and 247, drawn to a composition comprising an amino acid sequence having of any of even numbered SEQ ID NO: 176-180 respectively.

Groups 155-157, claims 278 and 247, drawn to a composition comprising an amino acid sequence of any of even numbered SEQ ID NO: 182-186 respectively.

Groups 158-160, claims 279 and 247, drawn to a composition comprising an amino acid sequence of any of even numbered SEQ ID NO: 188-192 respectively.

Groups 161-163, claims 280 and 247, drawn to a composition comprising an amino acid sequence of any of even numbered SEQ ID NO: 194-198 respectively.

Groups 164-166, claims 281 and 247, drawn to a composition comprising an amino acid sequence of any of even numbered SEQ ID NO: 200-204 respectively.

Groups 167-169, claims 282 and 247, drawn to a composition comprising an amino acid sequence of any of even numbered SEQ ID NO: 206-210 respectively.

Groups 170-172, claims 283 and 247, drawn to a composition comprising an amino acid sequence of any of even numbered SEQ ID NO: 212-216 respectively.

Groups 173-175, claims 284 and 247, drawn to a composition comprising an amino acid sequence of any of even numbered SEQ ID NO: 218-222 respectively.

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US02/32369

## Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claim Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
  
2.  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:
  
3.  Claim Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of Item 2 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 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.: Please See Continuation Sheet
  
  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.

## INTERNATIONAL SEARCH REPORT

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Groups 176-181, claim 128-131 and 133, drawn to a composition comprising an antibody specific to a protein of SEQ ID NO: 254-259 respectively.

Group 182, claims 134 and 135, drawn to an antibody composition specific to SEQ ID NO: 300.

Groups 183-308, claim 136, drawn to an antibody composition specific to an even numbered amino acid sequence of SEQ ID NO: 2-252 respectively.

Group 309, claims 137-146, drawn to a polynucleotide that encodes a neisserial cross-reactive protein.

Groups 310-354, claims 147-154 and 330, a composition and a transformed cell comprising a polynucleotide that encodes a protein of SEQ ID NO: 254-299 respectively.

Group 355, claims 155, 156 and 173-175, drawn to a composition comprising a polynucleotide encoding the protein of SEQ ID NO: 300.

Groups 356-481, claims 157-167, 176, 178-180, 183-193, 225-228 and 331-338, drawn to a composition and a transformed cell comprising an odd-numbered polynucleotide of SEQ ID NO: 1-253 respectively.

Groups 482-961, claims 290-296, drawn to the use of a composition of any of claims 1-289 respectively.

Groups 962-967, claims 297-303, 326 and 327, drawn to a method of preparing a protein of SEQ ID NO: 254-299 respectively.

Groups 968-1447, claims 306-312, 314 and 315, drawn to a method of inducing an immune response by administering a composition of claims 1-289 respectively.

Groups 1448-1573, claims 316-322, a method of expressing any of odd numbered nucleic acid sequences of SEQ ID NO: 1-253 respectively.

Group 1574, claims 323-325, a method of preparing a composition comprising a protein of SEQ ID NO: 300.

Groups 1575-1745, claims 326 and 327, drawn to a method of preparing a protein of SEQ ID NO: 254-299, or any of the even numbered SEQ ID NO: 2-252 respectively.

Groups 1746-1916, claims 328 and 329, drawn to a method of using a protein of any of the even numbered SEQ ID NO: 2-252, or any of SEQ ID NO: 254-299 respectively to prepare an antibody.

Group 1917, claim 339, drawn to a method of identifying an immunogenic protein using antisera.

Group 1918, claim 340, drawn to a method of detecting a polynucleotide using a nucleic acid probe.

The inventions listed as Groups 1-1918 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 special technical feature of invention 1 is a protein antigen of SEQ ID NO: 254, an immunogenic portion or a biological equivalent thereof. This special technical feature is already disclosed in the prior art. For example, the WIPO publication WO 200164920 A2 disclosed a portion of the neisserial protein comprising SEQ ID NO: 254, i.e., GLADA, which qualifies as a biologic (antigenic) equivalent of, or an immunogenic fragment of an immunogenic portion of SEQ ID NO: 254. See the enclosed sequence alignment. Therefore, the special technical feature is not a unifying feature. Although the protein antigen of invention 1 and the first method of using or making the product is a permitted combination under PCT Rule 13.2, in the instant case, since the product of invention 1 is already disclosed in the art, the special technical feature is not a unifying feature. Technically, the absence of special technical feature permits the separation of the methods of using or making the product from the product itself. The special technical features of the rest of the inventions are delineated above. The various products of inventions 2-481 do not share significant structural elements, whereas the methods of inventions 1917 and 1918 do not share common steps and/or active reagents. The inventions lack unity since the special technical feature(s) does not define over the prior art.

### Continuation of Box II Item 3:

1,6,7,9-38,60-85,100-114,168-172,181,182,194,196-205,213-251,255,257,266-276 and 285-289 (in part)

### Continuation of B. FIELDS SEARCHED Item 3:

DIALOG, WEST, MEDLINE, BIOSIS, EMBASE

Neisseria, meningitidis, SEQ ID NO: 12, 24, 42, 48, 60, 108, 138, 156, 174, 252, 254 and 301