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(54) Title: ANTIBODIES TO THE FBSA PROTEIN OF STREPTOCOCCUS AGALACTIAE AND THEIR USE IN TREATING OR PREVENTING INFECTIONS

(57) Abstract: Monoclonal and polyclonal antibodies are provided which can bind to the FbsA protein of *Streptococcus agalactiae* (GBS) and which can be used to prevent adherence of the bacteria to host cells and thus be useful in the treatment and protection against infection from *S. agalactiae*. The antibodies of the invention can also be raised against the fibrinogen binding domain of FbsA or the repeat region therein, and in addition to preventing bacterial adherence, the antibodies to FbsA are advantageous in that they can be used to prevent platelet aggregation and thrombus formation.

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US04/23701

<p>A. CLASSIFICATION OF SUBJECT MATTER IPC(7) : A61K 39/40; G01N 33/53 US CL : 424/150.1, 165.1; 435/975 According to International Patent Classification (IPC) or to both national classification and IPC</p>												
<p>B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) U.S. : 424/150.1, 165.1; 435/975 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</p>												
<p>C. DOCUMENTS CONSIDERED TO BE RELEVANT</p> <table border="1"> <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>SCHUBERT, A. et al. A fibrinogen receptor from group B Streptococcus interacts with fibrinogen by repetitive units with novel ligand binding sites. Mol. Microbiol. 2002, Vol. 2, pages 557-569, see Summary, Experimental procedures, Results, and Figure 5.</td> <td>1-16, 21-20 and 35-40</td> </tr> <tr> <td>Y</td> <td>CAMPBELL, A.M. General properties and applications of monoclonal antibodies. In: Monoclonal Antibody Technology. 1984, Elsevier Science Publishers, The Netherlands, Chapter 1, pages 1-32, see page 29, last paragraph.</td> <td>1-16, 21-30 and 35-40</td> </tr> </tbody> </table>			Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.	Y	SCHUBERT, A. et al. A fibrinogen receptor from group B Streptococcus interacts with fibrinogen by repetitive units with novel ligand binding sites. Mol. Microbiol. 2002, Vol. 2, pages 557-569, see Summary, Experimental procedures, Results, and Figure 5.	1-16, 21-20 and 35-40	Y	CAMPBELL, A.M. General properties and applications of monoclonal antibodies. In: Monoclonal Antibody Technology. 1984, Elsevier Science Publishers, The Netherlands, Chapter 1, pages 1-32, see page 29, last paragraph.	1-16, 21-30 and 35-40	
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<p><input type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> See patent family annex.</p>												
<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>"E" 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>"&" 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	"E" 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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<p>Date of the actual completion of the international search 10 February 2005 (10.02.2005)</p>		<p>Date of mailing of the international search report 05 APR 2005</p>										
<p>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</p>		<p>Authorized officer S. Devi, Ph.D. <i>[Signature]</i> Telephone No. (703) 308-0196 <i>[Signature]</i></p>										

INTERNATIONAL SEARCH REPORT

International application No.

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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.:
because they relate to subject matter not required to be searched by this Authority, namely:

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 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:
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.:

 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.: 1-16,20,21 and 35-40
- Remark on Protest** The additional search fees were accompanied by the applicant's protest.
 No protest accompanied the payment of additional search fees.

BOX III. 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, claims 1-16, 21-30 and 35-40, drawn to an isolated antibody which binds to the FbsA protein from *S. agalactiae*, a composition and a diagnostic kit comprising the same.

Group II, claim 17, drawn to a method of diagnosing an *S. agalactiae* infection using an antibody which binds to the FbsA protein from *S. agalactiae*.

Group III, claims 18 and 20, drawn to a method of treating or preventing an *S. agalactiae* infection or platelet aggregation by administering an antibody which binds to the FbsA protein from *S. agalactiae*.

Group IV, claim 19, drawn to a method of inducing an immunological response by administering the FbsA protein of *S. agalactiae*.

Group V, claims 31-34, drawn to a vaccine comprising the FbsA protein of *S. agalactiae* or the fibrinogen binding region of the protein and pharmaceutically acceptable carrier.

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 special technical features of inventions I-V are delineated above. The special technical features of inventions I and V are an antibody that binds to the FbsA protein from *S. agalactiae*, and a vaccine comprising the FbsA protein of *S. agalactiae* or the fibrinogen binding region of the protein respectively. These special technical features do not share a common structure, or immunogenic and biologic functions. Furthermore, while the FbsA protein of *S. agalactiae* is already known in the prior art, the claimed antibody is suggested by the prior art. For example, Schubert *et al.* (*Mol. Microbiol.* 2: 557-569, 2002) taught the FbsA protein encoded by the FbsA gene of *S. agalactiae*, the fibrinogen-binding region and the repeat region of the FbsA, and the fibrinogen-binding synthetic peptides derived from the repeat unit of the FbsA, contained in a buffer (see abstract; Figure 5; Experimental Procedures; and Results). Given that the FbsA protein and its fibrinogen-binding repeat regions were already disclosed in the prior art, it would have been obvious to one of ordinary skill in the art at the time the invention was made to raise a polyclonal or monoclonal antibody to the same using art-known antibody generation techniques to produce the antibody of invention I, with a reasonable expectation of success, since it is routine and conventional in the art to raise antibodies to a specific art-known protein. Therefore, the antibody product of invention I is not a unifying special technical feature. Although the product of claim 1 and the first method of using or making the same is a permitted combination under PCT Rule 13.2, in the instant case, since the product is already suggested in the art, the special technical feature does not define over the prior art. Technically, the absence of special technical feature permits the separation of the methods of using the product from the product itself. Furthermore, the antibody produce of invention I is not required to practice the method of invention IV, and the protein product of invention V is not required to practice the methods of inventions II and III. The methods of inventions II, III and IV do not share common steps and/or reagents or compositions.

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Continuation of B. FIELDS SEARCHED Item 3:
DIALOG, MEDLINE, EMBASE, WEST, BIOSIS

FbsA or fibrinogen receptor; agalactiae; (antibod? or antiser? or Ig? or immunoglobulin?); fibrinogen binding; inventors' name