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Published:

- with international search report (Art. 21(3))
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))
- with sequence listing part of description (Rule 5.2(a))

(88) Date of publication of the international search report:
13 August 2009

(54) Title: MUTANT FORMS OF STREPTOLYSIN O

(57) Abstract: Forms of GAS25 (streptolysin O) which are not toxic but which still maintain the ability to induce protection against *S. pyogenes* are useful in vaccine compositions to induce protection against *S. pyogenes*.



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INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2008/003725

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07K14/315 A61K38/17 A61K39/09

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)
C07K A61K

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 practical, search terms used)

EPO-Internal, CHEM ABS Data, WPI Data, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	GB 2 233 977 A (KEHOE MICHAEL; PINKNEY MICHAEL) 23 January 1991 (1991-01-23) page 2; claims 1-7; figure 1 -----	1,5,8, 16,17
Y	WO 2005/108419 A (KIRKHAM LEA-ANN [GB]; MITCHELL TIMOTHY JOHN [GB]; COWAN GRAEME JAMES M) 17 November 2005 (2005-11-17) the entire document, particularly pages 4-7,12,16-19, claims 1-73 -----	1-23
Y	WO 93/05155 A (BECKMAN INSTRUMENTS INC [US]) 18 March 1993 (1993-03-18) page 2; claims 1-29; sequence 2 -----	1-23
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Further documents are listed in the continuation of Box C.

See patent family annex.

* 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

- *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.
- *8* document member of the same patent family

Date of the actual completion of the international search

26 May 2009

Date of mailing of the international search report

12/06/2009

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INTERNATIONAL SEARCH REPORT

International application No

PCT/IB2008/003725

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	PINKNEY M ET AL.: "The Thiol-Activated Toxin Streptolysin O Does Not Require a Thiol Group for Cytolytic Activity" INFECTION AND IMMUNITY, vol. 57, no. 8, August 1989 (1989-08), pages 2553-2558, XP002521254 abstract; figure 2; table 1 -----	1-23
Y	PALMER M ET AL: "Assembly mechanism of the oligomeric streptolysin O pore: the early membrane lesion is lined by a free edge of the lipid membrane and is extended gradually during oligomerization" THE EMBO JOURNAL, vol. 17, no. 6, 1998, pages 1598-1605, XP002529266 page 1599; figure 4 -----	1-23
A	WO 2004/078907 A (INTERCELL AG [AT]; MEINKE ANDREAS [AT]; NAGY ESZTER [AT]; WINKLER BIRG) 16 September 2004 (2004-09-16) page 1 - page 3; sequence 159 -----	
A	US 5 523 205 A (COSSART PASCALE [FR] ET AL) 4 June 1996 (1996-06-04) example 3 -----	
A	WO 99/49049 A (MOUNT SINAI HOSPITAL CORP [CA]; AZAVEDO JOYCE DE [CA]; BAST DARRIN [CA]) 30 September 1999 (1999-09-30) page 1 - page 7 -----	
P, X	WO 2008/108830 A (NOVARTIS AG [US]; SCARSELLI MARIA [IT]; BENSI GIULIANO [IT]; GRANDI GU) 12 September 2008 (2008-09-12) paragraphs [0030] - [0033], [0055]; claims 1-15 -----	1-23
P, X	WO 2007/144647 A (MITCHELL TIMOTHY JOHN [GB]; KIRKHAM LEA-ANN [AU]; COWAN GRAEME JAMES []) 21 December 2007 (2007-12-21) page 9 - page 18 -----	1-23

INTERNATIONAL SEARCH REPORT

International application No.

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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
- a sequence listing
- table(s) related to the sequence listing
- b. format of material
- on paper
- in electronic form
- c. time of filing/furnishing
- contained in the international application as filed
- filed together with the international application in electronic form
- furnished subsequently to this Authority for the purpose of search
2. 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

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:

see additional sheet

1. As all required additional search fees were timely paid by the applicant, this international search report covers allsearchable claims.
2. As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.
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 and, where applicable, the payment of a protest fee.
- 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.
- No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-23 (all partially)

mutant streptolysin O, wherein the alteration is at position P427, and its nucleic acid molecule, vaccine composition, methods, kit and use

2. claims: 1-23 (all partially)

mutant streptolysin O, wherein the alteration is at position W535, and its nucleic acid molecule, vaccine composition, methods, kit and use

3. claims: 1-23 (all partially)

mutant streptolysin O, wherein the alteration is at position C530, and its nucleic acid molecule, vaccine composition, methods, kit and use

4. claims: 1-23 (all partially)

mutant streptolysin O, wherein the alteration is at position A248, and its nucleic acid molecule, vaccine composition, methods, kit and use

5. claims: 1-23 (all partially)

mutant streptolysin O, wherein the alteration is at position D482, and its nucleic acid molecule, vaccine composition, methods, kit and use

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/IB2008/003725

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