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(54) Title: STREPTOCOCCUS PYOGENES VIRULENCE GENES AND PROTEINS AND THEIR USE

(57) Abstract: A series of genes from *Streptococcus pyogenes* are shown to encode products which are implicated in virulence. The identification of these genes therefore allows attenuated microorganisms to be produced. Furthermore, the genes or their encoded products can be used in the manufacture of vaccines for therapeutic application.

INTERNATIONAL SEARCH REPORT

Intern ıal Application No
PCT/GB 00/04997

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12N15/31 C07K14/315 C07K16/12 C12Q1/68 G01N33/68
A61K38/16 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)
IPC 7 C12N C07K C12Q G01N 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)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 786 519 A (HUMAN GENOME SCIENCES, INC.) 30 July 1997 (1997-07-30) contig ID NO: 52 abstract page 4, line 9 -page 21, line 44 ORF ID NO: 52-1 page 115; table 2 SEQ ID NO: 52 page 399 -page 403 page 3268 -page 3269; claims 8-11,14,15,18-24,27-29 ---	1,5,6, 13,15, 18,19
A	WO 97 13786 A (HIGHTECH RECEPTOR AB) 17 April 1997 (1997-04-17) abstract page 3, line 10 -page 20, line 10 page 46 -page 49; claims 1-15,18-24 --- -/--	1-19

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in 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.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
1 June 2001	28.8.01

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Fuchs, U

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Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Intern ıal Application No
PCT/GB 00/04997

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WESSELS, M.R. & BRONZE, M.S.: "Critical role of the group A streptococcal capsule in pharyngeal colonization and infection in mice" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, vol. 91, no. 25, 6 December 1994 (1994-12-06), pages 12238-12242, XP002168715 the whole document ---	1-19
T	FERRETTI, J.J. ET AL.: "Complete genome sequence of an M1 strain of Streptococcus pyogenes" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, vol. 98, no. 8, 10 April 2001 (2001-04-10), pages 4658-4663, XP002168716 the whole document -----	1-19

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INTERNATIONAL SEARCH REPORT

Int. ational application No.
PCT/GB 00/04997

Box I Observations where certain claims were found unsearchable (Continuation of item 1 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 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:

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.:

1-19 partially

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ 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: 1-19 partially

Invention 1

A peptide encoded by a nucleotide sequence identified herein as SEQ ID NO: 1 of S. pyogenes or a related molecule having at least 40% sequence similarity or identity at the peptide or nucleotide level in a Gram-positive bacterium or a functional fragment thereof for therapeutic or diagnostic use, said peptide comprising the amino acid sequence identified herein as SEQ ID NO: 2 (corresponding to example 1), an antibody raised against said peptide, a polynucleotide encoding said peptide for therapeutic or diagnostic use, a host transformed to express said peptide, an attenuated microorganism comprising a mutation that disrupts the expression of said nucleotide sequence, use of any of said products for the manufacture of a medicament for use in treatment or prevention of a condition associated with infection by streptococcal or Gram-positive bacteria or in a screening assay for the identification of an antimicrobial drug, a vaccine comprising said peptide or the means for its expression or said attenuated microorganism;

2. Claims: 1-19 partially

Invention 2

Idem as subject 1 but limited to SEQ ID NOS: 3 and 4 (corresponding to example 2);

3.-25. Claims: 1-19 partially

Inventions 3-25

Idem as subject 1 but limited to SEQ ID NOS: 5-62 (corresponding to examples 3-25).

INTERNATIONAL SEARCH REPORT

...ormation on patent family members

Intern al Application No
PCT/GB 00/04997

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0786519 A	30-07-1997	CA 2194411 A	06-07-1997
		JP 9322781 A	16-12-1997
WO 9713786 A	17-04-1997	AU 7233296 A	30-04-1997
		EP 0862580 A	09-09-1998
		SE 9503495 A	10-04-1997