



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁷ : C12N 15/31, 1/21, C07K 14/245, A61K 38/16, 39/108 // (C12N 15/31, C12R 1:19)	A3	(11) International Publication Number: WO 00/28038 (43) International Publication Date: 18 May 2000 (18.05.00)																													
(21) International Application Number: PCT/GB99/03721 (22) International Filing Date: 9 November 1999 (09.11.99) (30) Priority Data: <table border="0"> <tr><td>9824569.9</td><td>9 November 1998 (09.11.98)</td><td>GB</td></tr> <tr><td>9824570.7</td><td>9 November 1998 (09.11.98)</td><td>GB</td></tr> <tr><td>9827814.6</td><td>17 December 1998 (17.12.98)</td><td>GB</td></tr> <tr><td>9827815.3</td><td>17 December 1998 (17.12.98)</td><td>GB</td></tr> <tr><td>9827816.1</td><td>17 December 1998 (17.12.98)</td><td>GB</td></tr> <tr><td>9827818.7</td><td>17 December 1998 (17.12.98)</td><td>GB</td></tr> <tr><td>9900708.0</td><td>13 January 1999 (13.01.99)</td><td>GB</td></tr> <tr><td>9900710.6</td><td>13 January 1999 (13.01.99)</td><td>GB</td></tr> <tr><td>9900711.4</td><td>13 January 1999 (13.01.99)</td><td>GB</td></tr> <tr><td>9901915.0</td><td>28 January 1999 (28.01.99)</td><td>GB</td></tr> </table> (71) Applicant (for all designated States except US): MICRO-SCIENCE LIMITED [GB/GB]; 12 St. James's Square, London SW1Y 4RB (GB). (72) Inventors; and (75) Inventors/Applicants (for US only): CROOKE, Helen, Rachel [GB/GB]; Imperial College School of Medicine at the Hammersmith Campus, Dept. of Infectious Diseases, Du Cane Road, London W12 0NN (GB). CLARKE, Enda, Elizabeth [GB/GB]; Imperial College School of Medicine	9824569.9	9 November 1998 (09.11.98)	GB	9824570.7	9 November 1998 (09.11.98)	GB	9827814.6	17 December 1998 (17.12.98)	GB	9827815.3	17 December 1998 (17.12.98)	GB	9827816.1	17 December 1998 (17.12.98)	GB	9827818.7	17 December 1998 (17.12.98)	GB	9900708.0	13 January 1999 (13.01.99)	GB	9900710.6	13 January 1999 (13.01.99)	GB	9900711.4	13 January 1999 (13.01.99)	GB	9901915.0	28 January 1999 (28.01.99)	GB	<p>at the Hammersmith Campus, Dept. of Infectious Diseases, Du Cane Road, London W12 0NN (GB). EVEREST, Paul, Howard [GB/GB]; Imperial College School of Medicine at the Hammersmith Campus, Dept. of Infectious Diseases, Du Cane Road, London W12 0NN (GB). DOUGAN, Gordon [GB/GB]; Imperial College School of Medicine at the Hammersmith Campus, Dept. of Infectious Diseases, Du Cane Road, London W12 0NN (GB). HOLDEN, David, William [GB/GB]; Imperial College School of Medicine at the Hammersmith Campus, Dept. of Infectious Diseases, Du Cane Road, London W12 0NN (GB). SHEA, Jacqueline, Elizabeth [GB/GB]; Imperial College School of Medicine at the Hammersmith Campus, Dept. of Infectious Diseases, Du Cane Road, London W12 0NN (GB). FELDMAN, Robert, Graham [GB/GB]; Imperial College School of Medicine at the Hammersmith Campus, Dept. of Infectious Diseases, Du Cane Road, London W12 0NN (GB).</p> <p>(74) Agent: GILL JENNINGS & EVERY; Broadgate House, 7 Eldon Street, London EC2M 7LH (GB).</p> <p>(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).</p> <p>Published <i>With international search report.</i></p> <p>(88) Date of publication of the international search report: 31 August 2000 (31.08.00)</p>
9824569.9	9 November 1998 (09.11.98)	GB																													
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(54) Title: VIRULENCE GENES AND PROTEINS, AND THEIR USE																															
(57) Abstract <p>The present invention is based on the identification of a series of virulence genes in <i>E. coli</i> K1, the products of which may be implicated in the pathogenicity of the organism. The identification of the genes allows them, or their expressed products, to be used in a number of ways to treat infection.</p>																															

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 99/03721

A. CLASSIFICATION OF SUBJECT MATTER
 IPC 7 C12N15/31 C12N1/21 C07K14/245 A61K38/16 A61K39/108
 //(C12N15/31,C12R1:19)

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 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	SARGENT F. ET AL.: "Overlapping functions of components of a bacterial Sec-independent protein export pathway" EMBO J., vol. 17, no. 13, 1 July 1998 (1998-07-01), pages 3640-3650, XP002133191 the whole document	1-4
X	-& DATABASE SPTREMBL [Online] Accession No. 065938, 1 August 1998 (1998-08-01) "tatA protein (mttA1)" XP002133194 the whole document	1-4
X	-& DATABASE SPTREMBL [Online] Accession No. 069415, 1 August 1998 (1998-08-01) "tatB protein (mttA2)" XP002133195 the whole document	1-4
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Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

° Special categories of cited documents :

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- *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
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Date of the actual completion of the international search

15 March 2000

Date of mailing of the international search report

26. 06. 2000

Name and mailing address of the ISA

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Galli, I

INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB 99/03721

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	-& DATABASE SWISSPROT [Online] Accession No. P27857, 15 July 1998 (1998-07-15) "tatC protein (mttB)" XP002133196 the whole document	1-4
P,X	-& DATABASE GENBANK [Online] Accession No. AJ005830, 29 March 1999 (1999-03-29) SARGENT: "E. coli tatABCD operon" XP002133197 cited in the application the whole document	1-4
X	--- DATABASE GENBANK [Online] Accession No. P25895, 1 November 1997 (1997-11-01) CHUNG E.: "E. coli protein YBEC from CRB-LIPA intergenic region" XP002133198 the whole document	1-4
A	--- WEINER J.H. ET AL.: "A novel and ubiquitous system for membrane targeting and secretion of cofactor-containing proteins." CELL, vol. 93, 3 April 1998 (1998-04-03), pages 93-101, XP002133192 the whole document	1-11
A	--- BOGSCH E.G. ET AL.: "An essential component of a novel bacterial protein export system with homologues in plastids and mitochondria" J. BIOL. CHEM., vol. 273, no. 29, 17 July 1998 (1998-07-17), pages 18003-19006, XP002133193 the whole document	1-11
A	--- CIESLEWICZ M. & VIMR E.: "Thermoregulation of kpsF, the First Region 1 gene in the kps locus for polysialic acid biosynthesis in E. coli K1" J. BACTERIOLOGY, vol. 178, no. 11, June 1996 (1996-06), pages 3212-3220, XP000877094 the whole document	1-11
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INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 99/03721

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>VANN W.F. ET AL.: "Purification and characterization of the Escherichia coli K1 neuB gene product N-acetylneuraminic acid synthase" GLYCOBIOLOGY, vol. 7, no. 5, 1997, pages 697-701, XP000877095 the whole document</p> <p style="text-align: center;">---</p>	1-11
A	<p>BOYD E.F. & HARTL D.L.: "Chromosomal regions specific to pathogenic isolates of Escherichia coli have a phylogenetically clustered distribution" J. BACTERIOL., vol. 180, no. 5, March 1998 (1998-03), pages 1159-1165, XP002133065 the whole document</p> <p style="text-align: center;">-----</p>	1-11

INTERNATIONAL SEARCH REPORT

International application No.
PCT/GB 99/03721

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.:

see additional sheet, invention 1.

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: (1-11) - partially, where applicable

A peptide encoded by an operon including *tatA*, *tatB*, *tatC*, *tatD* or by an operon including *tatE* (Seq. IDs 11-14,16,18,19,21) obtainable from *E. coli* K1, or a homologue thereof in a Gram-negative bacterium, or a functional fragment thereof, for therapeutic use.

Corresponding polynucleotide, recombinant host cells, vaccine containing said polypeptide, vaccine containing an attenuated pathogen in which the virulence gene encodes said peptide is mutated. Use in screening for potential drugs or detection of virulence; use in manufacture of medicament.

2. Claims: (1-11) - partially, where applicable

Idem as subject matter 1, but limited to *mdoG* (seq. ID 2).

3. Claims: (1-11) - partially, where applicable

Idem as subject-matter 1, but limited to *creC* (Seq. ID 5).

4. Claims: (1-11) - partially, where applicable

Idem as subject-matter 1, but limited to *recG* (Seq. ID 7).

5. Claims: (1-11) - partially, where applicable

Idem as subject-matter 1, but limited to *yggN* (Seq. ID 9).

6. Claims: (1-11) - partially, where applicable

Idem as subject-matter 1, but limited to *eck1* (Seq. IDs 23-26).

7. Claims: (1-11) - partially, where applicable

Idem as subject-matter 1, but limited to *iroC*, *iroD* and *iroE* (Seq. IDs 28,29,31,32).

8. Claims: (1-11) - partially, where applicable

Idem as subject-matter 1, but limited to *aslA/hemY* (Seq. ID 33).

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

9. Claims: (1-11) - partially, where applicable

Idem as subject-matter 1, but limited to mtd2/ms1-16 (Seq. IDs 35-48).