

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
16 March 2006 (16.03.2006)

PCT

(10) International Publication Number
WO 2006/028601 A3

(51) International Patent Classification:
C12Q 1/68 (2006.01)

(21) International Application Number:
PCT/US2005/026578

(22) International Filing Date: 26 July 2005 (26.07.2005)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/591,127 26 July 2004 (26.07.2004) US

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(81) Designated States (unless otherwise indicated, for every
kind of national protection available): AE, AG, AL, AM,

AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,
GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE,
KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,
MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ,
OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL,
SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC,
VN, YU, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every
kind of regional protection available): ARIPO (BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM,
ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),
European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI,
FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT,
RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA,
GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

- with international search report
- before the expiration of the time limit for amending the
claims and to be republished in the event of receipt of
amendments

(88) Date of publication of the international search report:
1 February 2007

For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.



WO 2006/028601 A3

(54) Title: METHOD FOR DISTINGUISHING METHICILLIN RESISTANT S. AUREUS FROM METHICILLIN SENSITIVE
S. AUREUS IN A MIXED CULTURE

(57) Abstract: The present invention provides isolated oligonucleotides and methods for detecting a methicillin resistant *Staphylococcus aureus* in a sample, including a sample that comprises nuclei acid molecules of higher biological complexity than that of amplified nucleic acid molecules.

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2005/026578

A. CLASSIFICATION OF SUBJECT MATTER
INV. C12Q1/68

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)
C12Q C12N

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, Sequence Search, WPI Data, MEDLINE, BIOSIS, EMBASE, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	SKOV R L ET AL.: "Evaluation of a new 3-h hybridization method for detecting the mecA gene in Staphylococcus aureus and comparison with existing genotypic and phenotypic susceptibility testing methods" JOURNAL OF ANTIMICROBIAL CHEMOTHERAPY, vol. 43, 1999, pages 467-475, XP002409832	5, 8-16, 19, 21, 35-41, 44-52, 55, 57, 71-79
Y	the whole document	7, 17, 22-34, 43, 53, 58-70

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

Date of the actual completion of the international search

30 November 2006

Date of mailing of the international search report

18/12/2006

Name and mailing address of the ISA/

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INTERNATIONAL SEARCH REPORT

International application No

PCT/US2005/026578

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	LEVI K AND TOWNER K J: "Detection of methicillin-resistant Staphylococcus aureus (MRSA) in blood with the EVIGENE MRSA Detection Kit" JOURNAL OF CLINICAL MICROBIOLOGY, vol. 41, August 2003 (2003-08), pages 3890-3892, XP002409833	5,8-12, 19, 39-41, 44-48, 55,75-79
Y	the whole document	7,17, 22-34, 43,53, 58-70
X	----- UBUKATA K ET AL.: "Rapid detection of the mecA gene in methicillin-resistant staphylococci by enzymatic detection of polymerase chain reaction products" JOURNAL OF CLINICAL MICROBIOLOGY, vol. 30, 1992, pages 1728-1733, XP002409834 the whole document	5,8-12, 19, 39-41, 44-48, 55,75-79
X	----- JENISON ROBERT ET AL: "Interference-based detection of nucleic acid targets on optically coated silicon" NATURE BIOTECHNOLOGY, NATURE PUBLISHING GROUP, NEW YORK, NY, US, vol. 19, no. 1, January 2001 (2001-01), pages 62-65, XP002319097 ISSN: 1087-0156 the whole document	5,12,17, 22-34, 41, 46-48, 53, 58-70, 77-79
Y	----- BRAUN E ET AL.: "DNA-templated assembly and electrode attachment of a conducting silver wire" NATURE, vol. 391, 1998, pages 775-778, XP002409835 cited in the application the whole document	17, 22-34, 53,58-70
Y	----- STORHOFF J J ET AL: "HOMOGENEOUS DETECTION OF UNAMPLIFIED GENOMIC DNA SEQUENCES BASED ON COLORIMETRIC SCATTER OF GOLD NANOPARTICLE PROBES" NATURE BIOTECHNOLOGY, NATURE PUBLISHING GROUP, NEW YORK, NY, US, vol. 22, no. 7, July 2004 (2004-07), pages 883-887, XP001204827 ISSN: 1087-0156 cited in the application the whole document	17, 22-34, 53,58-70
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INTERNATIONAL SEARCH REPORT

International application No

PCT/US2005/026578

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2003/211488 A1 (MIRKIN CHAD A [US] ET AL) 13 November 2003 (2003-11-13) cited in the application * see especially e.g. [116]-[122], as well as Fig.'s 3, 5, 8 and 16 * the whole document	17, 22-31, 53,58-67
Y	WO 02/099034 A2 (INFECTIO DIAGNOSTIC INC [CA]; HULETSKY ANN [CA]; ROSSBACH VALERY [CA]) 12 December 2002 (2002-12-12) * see especially SEQ ID NO:89 * the whole document	7,43
A	ELSAYED S ET AL: "DEVELOPMENT AND VALIDATION OF A MOLECULAR BEACON PROBE-BASED REAL-TIME POLYMERASE CHAIN REACTION ASSAY FOR RAPID DETECTION OF METHICILLIN RESISTANCE IN STAPHYLOCOCCUS AUREUS" ARCHIVES OF PATHOLOGY & LABORATORY MEDICINE, CHICAGO, IL, US, vol. 127, no. 7, July 2003 (2003-07), pages 845-849, XP009025126 the whole document	
A	SHIMAOKA M ET AL.: "Development of enzyme-labeled oligonucleotide probe for detection of mecA gene in methicillin-resistant Staphylococcus aureus" JOURNAL OF CLINICAL MICROBIOLOGY, vol. 32, 1994, pages 1866-1869, XP002409836 the whole document	
A	BEKKAOUI F ET AL: "RAPID DETECTION OF THE MECA GENE IN METHICILLIN RESISTANT STAPHYLOCOCCI USING A COLORIMETRIC CYCLING PROBE TECHNOLOGY" DIAGNOSTIC MICROBIOLOGY AND INFECTIOUS DISEASES, ELSEVIER SCIENCE PUBLISHING CO., AMSTERDAM, NL, vol. 34, no. 2, 1999, pages 83-90, XP001135226 ISSN: 0732-8893 the whole document	
A	WO 91/08305 A (U GENE RESEARCH BV [NL]) 13 June 1991 (1991-06-13) the whole document	

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2005/026578

Box 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:
see FURTHER INFORMATION sheet PCT/ISA/210

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 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:

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.:

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

Continuation of Box II.2

Present claim 1 reads as: 'An isolated oligonucleotide CONSISTING of
a) a nucleic acid as set forth in (either) SEQ ID NO:1 (up to) SEQ ID NO:10; or
b) a nucleic acid sequence that hybridizes with the complement of the nucleic acid sequence as set forth as SEQ ID NO:1 (up to) SEQ ID NO:10.

Whereas part a) of claim 1 is unambiguously clear and supported, part b) refers to nucleic acid sequences described by a desired property or effect, namely their ability to hybridize to the complement of one of the SEQ ID NOS as specified under part a). Essentially, hybridizing to a complement of a sequence, inevitably means the sequence itself again, however, this time (part b)) unlimited in length, and in addition, not specifying the criteria for the hybridization conditions (?).

This results firstly, in a contradiction to the initial wording of the claim (...consisting...) which does not allow any change of a given sequence in terms of nucleotides or length (i.e. part b) refers to any sequence COMPRISING one of the sequences of part a)), and secondly, in non-compliance with the substantive provisions of Article 6 and 5 PCT, since the description does not provide support and disclosure for other sequences than the ones specified under part a) of claim 1.

Therefore, the search of claim 1 (as well as related claims 2-79) was limited to the sequences as given in part a) of claim 1.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No PCT/US2005/026578

Patent document cited in search report	Publication date	Patent family member(s)	Publication date	
US 2003211488	A1	13-11-2003	AU 2003237180 A1	11-11-2003
			CA 2483697 A1	20-11-2003
			EP 1499889 A2	26-01-2005
			JP 2005524849 T	18-08-2005
			WO 03095973 A2	20-11-2003
			US 2004086897 A1	06-05-2004
WO 02099034	A2	12-12-2002	CA 2348042 A1	04-12-2002
			DE 02740158 T1	10-02-2005
			EP 1397510 A2	17-03-2004
			ES 2223310 T1	01-03-2005
			JP 2004534537 T	18-11-2004
			US 2006252078 A1	09-11-2006
			US 2005019893 A1	27-01-2005
WO 9108305	A	13-06-1991	AU 6950791 A	26-06-1991
			NL 9002157 A	17-06-1991