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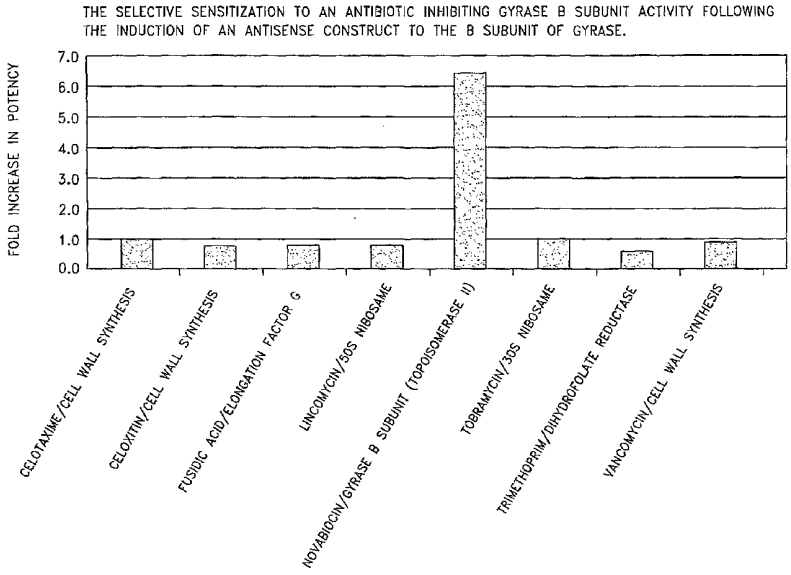
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[Continued on next page]

(54) Title: IDENTIFICATION OF ESSENTIAL GENES IN PROKARYOTES



(57) Abstract: The sequences of antisense nucleic acids which inhibit the proliferation of prokaryotes are disclosed. Cell-based assays which employ the antisense nucleic acids to identify and develop antibiotics are also disclosed. The antisense nucleic acids can also be used to identify proteins required for proliferation, express these proteins or portions thereof, obtain antibodies capable of specifically binding to the expressed proteins, and to use those expressed proteins as a screen to isolate candidate molecules for rational drug discovery programs. The nucleic acids can also be used to screen for homologous nucleic acids that are required for proliferation in cells other than *Staphylococcus aureus, Salmonella typhimurium, Klebsiella pneumoniae,* and *Pseudomonas aeruginosa*. The nucleic acids of the present invention can also be used in various assay systems to screen for proliferation required genes in other organisms.

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(81) Designated States *(national)*: AE, AG, AL, AM, AT (utility model), AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ (utility model), DE (utility model), DK (utility model), DM, DZ, EE (utility model), ES, FI (utility model), 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, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK (utility model), SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, 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, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

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INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12N15/11 C12Q1/68 C12N15/31 C07K14/195 A61K31/7088 C07K16/12

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 C07K C12N C12Q 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)
BIOSIS, EPO-Internal, SEQUENCE SEARCH

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 50555 A (HUMAN GENOME SCIENCES INC ;BARASH STEVEN C (US); DILLON PATRICK J) 12 November 1998 (1998-11-12) page 89, Table 2, contig ID 367, ORF ID 20 page 1524 -page 1531	1,2,4, 14,16, 23,33
Y	claims	18

X	DATABASE EM_PRO [Online] Accession number : L47971 (ID: BSRPLP), 2 November 1995 (1995-11-02) XP002190118 abstract & SUH, J.W. ET AL.: "Genetic and transcriptional organization of the Bacillus subtilis spc-alpha region" GENE, vol. 169, 1996, pages 17-23, XP004042981	2,4

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[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
13 February 2002	15. 05. 2002

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	ANDRES S.M.

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

INTERNATIONAL SEARCH REPORT

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PCT/US 01/09180

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 99 13893 A (NIELSEN PETER E ;GOOD LIAM (SE); ISIS PHARMACEUTICALS INC (US)) 25 March 1999 (1999-03-25) page 8, line 11 -page 9, line 3 page 12, line 7 -page 13, line 23 ---	18
A	WO 98 21366 A (Q B I ENTERPRISES LTD ;EINAT PAZ (IL); VASQUEZ IASLOP NORA CECILIA) 22 May 1998 (1998-05-22) ---	
A	WO 99 02673 A (DUGOURD DOMINIQUE ;WRIGHT JIM A (CA); YOUNG AIPING H (CA); GENESEN) 21 January 1999 (1999-01-21) ---	
A	GOOD ET AL: "Antisense inhibition of gene expression in bacteria by PNA targeted to mRNA" NATURE BIOTECHNOLOGY, vol. 16, April 1998 (1998-04), pages 355-358, XP002140166 ISSN: 1087-0156 -----	

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 01/09180

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.: 3,5-13,15,17,19-22,24-26,28-32,34-44
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 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:

see additional 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.:
1-26, 28-44 (all partially)

Remark on Protest

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

☐ No protest accompanied the payment of additional search fees.

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FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 3,5-13,15,17,19-22,24-26,28-32,34-44

Present claims 3,5-13,15,17,19-22,24-26,28-32,34-44 relate to compounds (or methods using these compounds) defined by reference to a desirable characteristic or property, namely their capacity to target the same operon as SEQ ID 8, or to be homologous to a protein whose expression is inhibited by SEQ ID 8.
The claims cover all compounds having this characteristic or property, whereas the application provides no support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compounds by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search impossible. Consequently, no search has been carried out for those claims.

The applicant's attention is drawn to the fact that claims, or parts of 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.

International Application No. PCT/US 01/09180

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

Invention 1. : Claims 1-26,28-44 (all partially)

A nucleic acid characterised by SEQ ID 8 which inhibits cellular proliferation. Fragments and variants thereof. Their uses in therapy, diagnostic and screening assays.

Inventions 2. to 3787. : Claims 1-26, 28-44 (all partially)

As for subject 1., but concerning SEQ IDs 9 to 3795 respectively.

Invention 3788. : Claim 27 partially

A purified and isolated nucleic acid (or protein ?) comprising SEQ ID 3796. Fragments and variants thereof.

Inventions 3789. to 8942. : Claim 27 partially

As for subject 3788., but concerning SEQ IDs 3797-3800, 3806-4860 and 5916-10012 respectively.

INTERNATIONAL SEARCH REPORT

Information on patent family members

Internat Application No
PCT/US 01/09180

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9850555 A	12-11-1998	AU 735444 B2	05-07-2001
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