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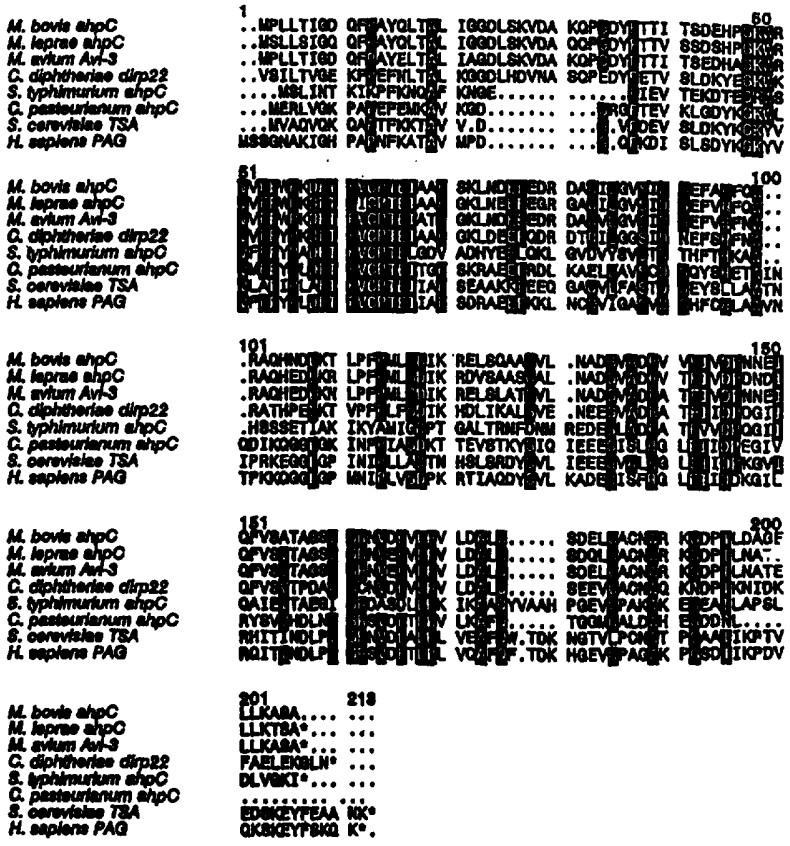
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With international search report.

(88) Date of publication of the international search report:
29 August 1996 (29.08.96)

(54) Title: METHODS AND COMPOSITIONS FOR DETECTING AND TREATING MYCOBACTERIAL INFECTIONS USING AN ahpCF OPERON

(57) Abstract

The embodiments of the invention are based upon the identification and characterization of an operon that determines mycobacterial resistance to the antibiotic isoniazid (INH) and its analogs. This operon, termed ahpCF, encodes polypeptides, AhpC and AhpF, which likely combine to form an active alkyl hydroperoxide reductase enzyme that may either be a direct target for INH or act to confer INH resistance. The sequence of the mutant ahpCF operon is provided, showing that INH resistance can be conferred by a mutation in the promoter region. Also provided are polynucleotides and polypeptides that are useful in diagnosis and treatment.



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INTERNATIONAL SEARCH REPORT

Int tional Application No
PCT/NZ 95/00133

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C12N15/52 C12N15/53 C12N9/08 C07K14/35 C12N15/11
A61K31/70 C12Q1/68 C12Q1/26 C12Q1/18 A61K39/04

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 6 C12N C07K A61K C12Q

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	INFECTION AND IMMUNITY, vol. 60, March 1992, WASHINGTON US, pages 1210-1216, XP002006470 YAMAGUCHI, R. ET AL.: "Cloning and expression of the gene for the Avi-3 antigen of Mycobacterium avium and mapping of its epitope:" see figure 2 ---	1,2,4, 6-8,21
A	WO,A,94 26312 (JACOBS WILLIAM R JR ;COLLINS DESMON) MICHAEL (NZ); BANERJEE ASESH) 24 November 1994 see page 3, line 17 - page 6, line 15 see page 19, line 6 - line 15 see claims; examples --- -/--	9-19,21

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

[X] Patent family members are listed in annex.

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1

Date of the actual completion of the international search	Date of mailing of the international search report
24 June 1996	09.07.96

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

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 BAD ORIGINAL

INTERNATIONAL SEARCH REPORT

Intr ional Application No
PCT/NZ 95/00133

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, vol. 37, October 1993, pages 2251-2253, XP000573870 ROSNER, J.: "Susceptibilities of oxyR regulon mutants of Escherichi coli and Salmonella typhimurium to isoniazid" ---	
P,X	PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1995 JUL 3) 92 (14) 6625-9, XP002006471 SHERMAN, D. ET AL.: "Disparate responses to oxidative stress in saprophytic and pathogenic mycobacteria." see figure 2 ---	1-4,6-8
P,X	MOLECULAR MICROBIOLOGY, (1995 SEP) 17 (5) 889-900, XP000572779 DERETIC, V. ET AL.: "Mycobacterium tuberculosis is a natural mutant with an inactivated oxidative-stress regulatory gene: implications for sensitivity to isoniazid." see the whole document -----	1,2,4-8, 21

1

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

INTERNATIONAL SEARCH REPORT

International application No.
PCT/NZ95/00133

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. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
Please see Further Information sheet enclosed.

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 searches 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.

INTERNATIONAL SEARCH REPORT

International Application No. PCT/NZ95/00133

FURTHER INFORMATION CONTINUED FROM PCT/ISA/210

Remark: Although claims 9-10 (as far as in vivo methods are concerned) are directed to a method of treatment of (diagnostic method practised on) the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

INTERNATIONAL SEARCH REPORT

information on patent family members

Inv tional Application No
PCT/NZ 95/00133

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
WO-A-9426312	24-11-94	AU-B-	6912194	12-12-94
		AU-B-	6949694	12-12-94
		EP-A-	0707496	24-04-96
		WO-A-	9426765	24-11-94