# Cloning and Nucleotide Sequence of *Mycobacterium tuberculosis* gyrA and gyrB Genes and Detection of Quinolone Resistance Mutations

## HOWARD E. TAKIFF,<sup>1</sup> LEIRIA SALAZAR,<sup>1</sup> CARMEN GUERRERO,<sup>2</sup> WOLFGANG PHILIPP,<sup>3</sup> WAI MUN HUANG,<sup>4</sup> BARRY KREISWIRTH,<sup>5</sup> STEWART T. COLE,<sup>3</sup> WILLIAM R. JACOBS, JR.,<sup>6</sup> AND AMALIO TELENTI<sup>2</sup>\*

Instituto Venezolano para Investigaciones Cientificas, Caracas, Venezuela<sup>1</sup>; Institute for Medical Microbiology, University of Berne, 3010 Berne, Switzerland<sup>2</sup>; Unité de Génétique Moléculaire Bactérienne, Institut Pasteur, Paris, France<sup>3</sup>; Department of Cellular, Viral and Molecular Biology, University of Utah, Salt Lake City, Utah 84132<sup>4</sup>; Public Health Research Institute, New York, New York 10016<sup>5</sup>; and Howard Hughes Medical Institute, Albert Einstein College of Medicine, Bronx, New York 10461<sup>6</sup>

Received 3 November 1993/Returned for modification 16 December 1993/Accepted 27 January 1994

The emergence of multidrug-resistant strains of Mycobacterium tuberculosis has resulted in increased interest in the fluoroquinolones (FQs) as antituberculosis agents. To investigate the frequency and mechanisms of FQ resistance in M. tuberculosis, we cloned and sequenced the wild-type gyrA and gyrB genes, which encode the A and B subunits of the DNA gyrase, respectively; DNA gyrase is the main target of the FQs. On the basis of the sequence information, we performed DNA amplification for sequencing and single-strand conformation polymorphism analysis to examine the presumed quinolone resistance regions of gyrA and gyrB from reference strains (n = 4) and clinical isolates (n = 55). Mutations in codons of gyrA analogous to those described in other FQ-resistant bacteria were identified in all isolates (n = 14) for which the ciprofloxacin MIC was >2 µg/ml. In addition, we selected ciprofloxacin-resistant mutants of Mycobacterium bovis BCG and M. tuberculosis Erdman and H37ra. Spontaneously resistant mutants developed at a frequency of 1 in  $10^7$  to  $10^8$  at ciprofloxacin concentrations of 2 µg/ml, but no primary resistant colonies were selected at higher ciprofloxacin concentrations. Replating of those first-step mutants selected for mutants with high levels of resistance which harbored gyrA mutations similar to those found among clinical FQ-resistant isolates. The gyrA and gyrB sequence information will facilitate analysis of the mechanisms of resistance to drugs which target the gyrase and the implementation of rapid strategies for the estimation of FQ susceptibility in clinical M. tuberculosis isolates.

The resurgence of tuberculosis and its incidence in human immunodeficiency virus-positive populations in both developing countries and the industrialized world have been accompanied by the alarming emergence of virulent multidrugresistant tuberculosis (MDR-TB) strains in North American cities (7). Many of these strains have acquired resistance to almost all first- and second-line antituberculosis agents. For this reason, there is an increasing interest in the antimycobacterial actions of the fluoroquinolones (FQs). Against Mycobacterium tuberculosis, the FQs show moderate in vitro activity (4), with sparfloxacin (MIC, 0.25 to 0.5 µg/ml) perhaps being the most effective compound (17). The principal target of the quinolones is the DNA gyrase, a type II DNA topoisomerase that is composed of two A and two B subunits (30) encoded by gyrA and gyrB, respectively. Mutations in the putative FQbinding region of the A subunit have been found to confer high-level FQ resistance in several bacterial species (8, 19, 22, 31, 33). Other mutations that confer resistance to quinolones have been found in gyrB, in genes that lower the intracellular concentration of the drug (although these tend to confer lower-level resistance than do the gyrA mutations [32, 34]), or

\* Corresponding author. Mailing address: Institute for Medical Microbiology, Friedbuehlstrasse 51, 3010 Berne, Switzerland. Phone: +41.31.6328707. Fax: +41.31.3820063. Electronic mail address: telenti@imm.unibe.ch.

mapped to loci involved in uncharacterized novel mechanisms of resistance to these agents (27).

The effectiveness of the FQs in the treatment of tuberculosis may depend on the frequency and mechanisms by which *M. tuberculosis* develops resistance and the ability to determine rapidly whether the strain from a particular patient remains susceptible to FQs. Rapid susceptibility determination is especially important for the slow-growing *M. tuberculosis*, because by conventional methods it can take up to 6 to 12 weeks to determine whether the infecting strain is susceptible, a period equal to the median survival time for human immunodeficiency virus-positive patients diagnosed as having MDR-TB infections (7).

In this report we describe the cloning and sequencing of the *M. tuberculosis* genes gyrA and gyrB. On the basis of those sequences, we studied clinical *M. tuberculosis* isolates to find mutations in these genes associated with FQ resistance and then used rapid techniques to identify those mutants. In addition, we selected spontaneous FQ-resistant mutants of *Mycobacterium bovis* BCG and several *M. tuberculosis* strains and describe here the frequency and nature of these mutations.

## MATERIALS AND METHODS

Cloning of the *M. tuberculosis* DNA gyrase genes. A genomic library of *M. tuberculosis* H37Rv, constructed in the shuttle cosmid vector pYUB18, was the gift of Lisa Pascopella (15).

The library was screened by colony hybridization to a 0.9-kb BglII fragment of the novobiocin-resistant Streptomyces sphaeroides gyrB gene on plasmid pLST182, which was provided by Eric Cundliffe and Amrik Thiara (26). To confirm that the cosmids that hybridized to gyrB contained the correct region of the chromosome, they were digested with appropriate restriction enzymes and were then subjected to Southern blotting and hybridization with a series of gene-specific probes: a 1.8-kb EcoRI-BamHI fragment of the Streptomyces coelicolor dnaA gene, from plasmid pTB9018, given by Michael Calcutt (3), a 0.7-kb PCR fragment carrying the oriC locus of Streptomyces lividans supplied by Hilde Schrempf (35), and a fragment of Mycobacterium smegmatis gyrA amplified by using primers representing conserved regions of gyrase A (13). Two very similar cosmids, T776 and pIV305, hybridized to all four probes and were then used as sources of DNA to generate a series of subclones in vector pUC118 or pUC119; these were then sequenced by using the Sequenase 2.0 kit with 7-deazadGTP (United States Biochemicals, Cleveland, Ohio).

In vitro isolation of ciprofloxacin-resistant strains. *M. bovis* BCG Pasteur and *M. tuberculosis* H37Rv, H37Ra, and Erdman were grown in Middlebrook 7H9–OADC–Tween (15) (the OADC supplement was from Carr Scarborough Microbiologicals Inc., Decatur, Ga.) to a density of  $10^8$  to  $10^9$  CFU/ml, and 100 µl of culture was plated onto 7H10-OADC or 7H11-OADC plates containing concentrations of ciprofloxacin ranging from 0.25 to 3.0 µg/ml. The frequencies of selection of resistant strains were determined by simultaneously plating culture dilutions on plates without antibiotics. Individual resistant colonies formed on plates containing 0.5 to 2.0 µg of ciprofloxacin per ml were streaked onto plates containing the same concentration of ciprofloxacin for clonal purification and to new plates containing increasing concentrations of ciprofloxacin.

**Direct identification of gyrA mutations in clinical isolates.** On the basis of the sequence of gyrA, primers were designed to amplify the putative FQ-binding region of 4 reference strains, 6 ciprofloxacin-resistant laboratory mutants of the *M. tuberculosis* complex, a collection of 54 clinical isolates of *M. tuberculosis*, and 1 clinical isolate of *Mycobacterium africanum*. Strain preparation for PCR was performed by mechanical disintegration as reported previously (25). Studies of the susceptibilities of the strains to ciprofloxacin were done by radiometric methods (20).

PCR for direct sequencing and SSCP. DNA lysate preparations (2.5 µl) were used for amplification of the gyrA region with biotinylated primer GyrA1<sup>b</sup> (5'-CAGCTACATCGACTATG CGA) and GyrA2 (5'-GGGCTTCGGTGTACCTCAT). The PCR mixture (50 µl) contained 50 mM KCl; 10 mM Tris-HCl (pH 8.3); 1.5 mM MgCl<sub>2</sub>; 10% glycerol; 200 µM (each) dATP, dTTP, dCTP, and dGTP; 0.5 µM (each) primer; and 1.25 U of Taq DNA polymerase (Boehringer Mannheim). For singlestrand conformation polymorphism (SSCP) analysis, the concentration of dCTP was reduced to 100  $\mu$ M and 0.5  $\mu$ l (5  $\mu$ Ci) of  $[\alpha^{-32}P]dCTP$  was added to the reaction mixture. Amplification was performed for 40 cycles (1 min at 94°C, 1 min at 55°C, 1 min at 72°C); this was followed by a 10-min extension at 72°C to generate a 320-bp PCR product. For sequencing, PCR products were converted to single strands by using alkaline denaturation in conjunction with streptavidin-coated magnetic beads (Dynabeads M-280; Dynal, Oslo, Norway) as outlined previously (14). GyrA2 was used as the sequencing primer with T7 DNA polymerase (Sequenase). PCR-SSCP was performed as described previously (24). In addition, primers were designed for the gyrB region (5'-CCACCGACATCGGTGGATT and 5'-CTGCCACTTGAGTTTGTACA), where mutations confer-



FIG. 1. Organization of a 100-kb segment of the chromosome of M. tuberculosis encompassing the gyrB and gyrA genes (A) and the individual cosmids comprising this part of the contig (B). The position of a rare restriction site, DraI, separating two fragments of 160 and 480 kb is shown. The order and approximate positions of the genes were established by hybridization to specific probes. In the case of *oriC* and *dnaA*, the exact order is not known because these markers are on the same BamHI restriction fragment.

ring resistance to quinolones (34) have been reported to occur, and were used in PCR-SSCP analysis of 18 selected strains of M. *tuberculosis* for which ciprofloxacin MICs ranged from 0.25 to 8  $\mu$ g/ml.

Nucleotide sequence accession number. The complete nucleotide sequences of gyrA and gyrB have been deposited in GenBank under accession number L27512.

## RESULTS

M. tuberculosis DNA gyrase genes. Several screenings of mycobacterial genomic libraries with probes representing gyrA or gyrB from Escherichia coli and Bacillus subtilis were unsuccessful. However, strongly hybridizing cosmids were obtained by using the gyrB probe that was recently isolated from S. sphaeroides (26), which is phylogenetically much closer to the mycobacteria. These clones were then subjected to hybridization analysis with a set of probes for genetic loci known to be linked to gyrB in other gram-positive bacteria. Two cosmids (T776 and pIV305) with similar restriction profiles were found to hybridize with the gyrA, gyrB, oriC, and dnaA probes, whereas several others hybridized with one to three of these probes. A 5-kb BamHI fragment carried the oriC and dnaA loci, while the DNA gyrase genes appeared to be located on several BamHI fragments: 2.3 kb (gyrA), 0.9 kb (gyrBA), and 1.5 kb and two fragments of <0.5 kb (gyrB).

As part of the *M. tuberculosis* genome project, an ordered collection of cosmid clones is being established by a combination of fingerprinting and hybridization analyses and the resultant contig map is being correlated with the *DraI* macrorestriction map of the chromosome. The DNA gyrase genes are located on a 480-kb *DraI* fragment in *M. tuberculosis* H37Rv. A 100-kb segment of the contig carrying the gyrB-dnaA region is depicted in Fig. 1, where it can be seen that three

M. tuber- culosis	Frequency of resistant colonies with the following ciprofloxacin concn (µg/ml) in the plates:						
strain	0.5	1.0	2.0	3.0			
BCG	$1 \times 10^{-6} - 1 \times 10^{-7}$	$1 \times 10^{-6} - 1 \times 10^{-7}$	$1 \times 10^{-8}$	0			
H37Ra	a	$1 \times 10^{-6}$	0	0			
H37Rv		$5 \times 10^{-6}$	$1 \times 10^{-7}$	0			
Erdman		$2 \times 10^{-6}$	$1 \times 10^{-8}$	0			

"-, scant growth in patches, with occasional isolated colonies.

other known genes are located nearby (6, 19a). These encode the RecA recombinase (*recA*) and the putative thymidylate synthase (*thyS*) and sigma factor (*hrd*). Details of the construction of the map will be published elsewhere.

Nucleotide sequence analysis of DNA gyrase genes. Suitable restriction fragments from cosmids pIV305 and T776 were subcloned, and their nucleotide sequences were determined. On examination of the resultant composite DNA sequence, the gyrA gene (2,517 bp) was found to be located 36 bp downstream of gyrB (2,060 bp). The deduced M. tuberculosis GyrB protein showed 79 and 63% amino acid similarities with the S. sphaeroides and E. coli proteins, respectively (Fig. 2). The deduced GyrA protein showed 69 and 68% similarities with the E. coli and Staphylococcus aureus GyrA proteins, respectively (Fig. 3). The gyrase of M. tuberculosis also exhibited considerable homology with the type IV topoisomerase of E. coli ParC and ParE (16): 62% amino acid similarity between ParC and GyrB and 59% amino acid similarity between ParE and GyrA. The nucleotide sequence corresponding to the GyrA region associated with FQ resistance in M. tuberculosis is shown in Fig. 4.

Generation of ciprofloxacin-resistant mutants. *M. bovis* BCG was plated onto 7H11 plates with 0.5  $\mu$ g to 3.0 mg of ciprofloxacin per ml, and spontaneously resistant colonies appeared at the frequencies given in Table 1. Colonies were selected from plates with 0.5 or 1.0  $\mu$ g of ciprofloxacin per ml, and colonies from the first two restreakings were resistant to only 0.5 to 1.0  $\mu$ g of ciprofloxacin per ml. However, by the third restreaking the colonies grew well on 7H10 plates with 3  $\mu$ g of ciprofloxacin per ml. Four mutants were isolated in this way, and a fifth mutant was isolated when growth was found in a flask containing *M. bovis* BCG inoculated into Middlebrook 7H9–OADC-Tween with 1  $\mu$ g of ciprofloxacin per ml.

Spontaneous ciprofloxacin-resistant mutants were similarly selected from the avirulent strain *M. tuberculosis* H37Ra and from the virulent strains H37Rv and Erdman, and the frequencies with which they appeared are given in Table 1. The appearances of resistant colonies were roughly the same for all strains. Colonies resistant to 1.0  $\mu$ g of ciprofloxacin per ml were found 10 to 50 times more frequently than colonies resistant to 2.0  $\mu$ g of ciprofloxacin per ml. No primary resistant colonies were isolated on plates containing more than 2  $\mu$ g of ciprofloxacin per ml, even when 10<sup>8</sup> CFU per plate was used.

SSCP and sequence evaluation of reference strains, laboratory mutants, and clinical isolates. Screening of the region for FQ resistance of gyrA for polymorphisms by PCR-SSCP revealed the existence of several SSCP patterns (Fig. 5 and Table 2). Two SSCP patterns were found to be associated with susceptibility to FQs. Sequencing of this 320-bp region showed that codon 95 could present a natural polymorphism encoding either serine (in *M. tuberculosis* H37Rv and H37Ra and 11 FQ-susceptible clinical isolates) or threonine (in *M. tuberculo*sis Erdman, *M. bovis* BCG, *M. africanum*, and 28 susceptible clinical isolates). Eight different SSCP patterns were found to be associated with resistance to ciprofloxacin (MIC,  $\geq 2 \mu g/ml$ ) (Fig. 5). The corresponding mutations (Table 2) involved four codons within the well-described region of FQ resistance (Fig. 4) (31). One strain for which the ciprofloxacin MIC was 2  $\mu g/ml$  presented with a genotype of ciprofloxacin susceptibility. Without exception, all laboratory strains, laboratory mutants, and ciprofloxacin-resistant clinical isolates were evaluated by PCR-SSCP and sequenced. Ciprofloxacin-susceptible clinical isolates were characterized by PCR-SSCP, sequencing, or both. Screening of the putative gyrB quinolone resistance region previously described in *E. coli* and other bacteria resulted in a single SSCP pattern for all evaluated strains.

## DISCUSSION

Although the amino acid sequences of the DNA gyrases are well conserved in various bacteria (13), the M. tuberculosis DNA gyrase genes could not be identified by hybridization to probes from either E. coli or B. subtilis but were easily selected with a probe for the S. sphaeroides gyrB gene. These findings can be explained by the much closer dG+dC content of Mycobacterium and Streptomyces species, and this interpretation is supported by the cross-hybridization observed between their dnaA and oriC loci. Nevertheless, the putative FQ resistance-determining region of M. tuberculosis gyrA was found to be quite similar to those from other organisms; this region is located at the highly conserved (interspecies) Nterminal protein region (31), and the mutations encountered in ciprofloxacin-resistant M. tuberculosis clinical isolates and spontaneously arising ciprofloxacin-resistant BCG, Erdman, and H37Ra strains were located in codons equivalent to those

 TABLE 2. Summary of the evaluation of gyrA mutations associated with FQ resistance<sup>a</sup>

Strain (no. of indictor)	Phenotype	Genotype		
Strain (no. of isolates)	(MIC [µg/mg])	SSCP	Mutation	
Reference strains				
M. tuberculosis H37Rv (1)	S	Α	S (I)	
M. tuberculosis H37Ra (1)	S	Α	S (I)	
M. tuberculosis Erdman (1)	S	В	S (II)	
M. bovis BCG (1)	S	В	S (II)	
Laboratory mutants				
BCG mutant (3)	R (≥3)	С	Ala-90→Val	
BCG mutant (1)	R (≥3)	D	Asp-94→Asn	
Erdman mutant (1)	R (≥3)	С	Ala-90→Val	
H37Ra mutant (1)	R (≥3)́	Ε	Gly-88→Cys	
Clinical isolates				
FQ resistant (3)	R (4–8)	С	Ala-90→Val	
FQ resistant (1)	R (4)	F	Ser-91→Pro	
FQ resistant (1)	R (≥4)	G	Asp-94→His	
FQ resistant (1)	R (>8)	D	Asp-94→Asn	
FQ resistant (5)	R (>8)	Н	Asp-94→Gly	
FQ resistant (2)	R (>8)	Ι	Asp-94→Tyr	
FQ resistant (1)	R (4)	J	Asp-94→Ala	
FQ resistant (1)	M (2)	В	S (II)	
Susceptible strains (11)	S	Α	S (I)	
Susceptible strains (28)	S	В	S (II)	
M. africanum (1)	S	В	S (II)	

" S, susceptible (MIC,  $\leq 1 \ \mu g/ml$ ); S(I) and S(II), the presence of a serine or threonine polymorphism in codon 95, respectively; R, resistant; M, moderate susceptibility.

	1								
MTbGvrB	GVRPLRRLNR	MHATPEESIR	IVAAOKKKAO	DEYGAASITI	LEGLEAVRKR	PGMYIGSTGE	.RGLHHLIWE	VVDNAVDEAM	AGYATTVNVV
SspGyrB	VAD	SGNPNENTPS	VATGENGEVT	GSYNASAITV	LEGLDAVRKR	PGMYIGSTGE	. RGLHHLVTE	VVDNSVDEAL	AGHADTIDVT
NgoGyrB			MTEOK H	FEYGADSTOV	LEGLEAVER	PGMYIGDTOD	GSGLHHMVEE	VI.DNATDEAL	ACHCOKITVT
FCOGYTB			MS	NEVDESETKV	LEGLDAVERE	PGMYIGDTDD	GTGLHHMVEF	WUNNATDEAL	ACHCKETTVT
MycGyrB			MEDNNKT	OAVDSSSIKT	LEGLEAVERE	PGMYIGSTGE	FGLHHMTWF	TIDNSTOFAM	CGEASTVKLT
HIFCVrB			MSOD	NEVGACOTOV	IECLEAVERD	DAMYICSTOR	PCLUUTVVE	WONSTDEAL	ACHCDATEVA
Conconc		• • • • • • • • • • •	M3QD	NEIGAGQIQV	LEGLEAVER	PAMIIGSIDS	CLUN E	DN DEA	AGREDATEVA
consens	01			11	L-GL-AV-KR	P-MIIG-1	GLHHE	DNDEA-	-G
	81								
MTbGyrB	LLEDGGVEVA	DDGRGIPVAT	HAS.GIPTVD	VVMTQLHAGG	KFDSDAYAIS	GGLHGVGVSV	VNALSTRLEV	EIKRDGYEWS	QVYEKSEPLG
SspGyrB	ILADGGVRVV	DNGRGIPVGI	VPSEGKPAVE	VVLTVLHAGG	KFGGGGYSVS	GGLHGVGVSV	VNALSTKVAV	EVKTDGYRWT	QDYKLGVPTR
NgoGyrB	IHADHSVSVA	DNGRGMPTGI	HPKEGRSAAE	VIMTVLHAGG	KFDNNSYKIS	GGLHGVGVSV	VNALSDWVTL	TIYRDGKEHF	VRFVRGETEE
EcoGyrB	IHADNSVSVQ	DDGRGIPTGI	HPEEGVSAAE	VIMTVLHAGG	KFDDNSYKVS	GGLHGVGVSV	VNALSQKLEL	VIQREGKIHR	QIYEHGVPQA
MycGyrB	LKDNFVTIVE	DDGRGIPVDI	HPKTNRSTVE	TVFTVLHAGG	KFDNDSYKVS	GGLHGVGASV	VNALSSSFKV	WVAREHQQYF	LAFHNGGEVI
HlfGyrB	LHEDGSVSVT	DNGRGIPVGT	HEQYDRPALE	VIMTVLHAGG	KFDNKSYQVS	GGLHGVGVTV	VNALSSELEV	EVKHDGAVWT	HRFEVGEPQV
Consens	V-	GRG-P		T-LHAGG	KFYS	GGLHGVGV	VNALS		
	171	*							
MTbGvrB	. LKOGAPTKK	TGSTVR	FWADPAVF, E	TTEYDFETVA	RRLOEMAFLN	KGLTINLTDE	RVTODEVVDE	VVSDVAEAPK	SASERAAEST
SspGyrB	RCAONEATDE	TGTTVT	FWADPDVF, E	TTEYSFETLS	RRFOEMAFLN	KGLTLKLTDE	RESAKAVVGA	DVA.GTD	SA.ETPGE
NaoGyrB	PLKTVGDSDK	KGTTVR	FLAGTETF.G	NTEYSEDILA	KRIRELSELN	NGVDIELTDE	RDGKHE		
FCOGVrB	PLAVTGETEK	TGTMVR	FWPSLETETN	VTEFEVELLA	KRIRELSELN	SGVSTRLRDK	RDGKED		
MucGurB	CDLVNECKCD	KEN GTEVE	EVEDETV ME	KODYKOTVIA	SPLOOLAFIN	KGIOIDEVDE	P		
W) fourp	EFERNARI	DCEDTCTTIE	EWDDDCIE E	TODINGIVIA	NDIDELVELN	CVETCI CDE	DTDE	•••••	• • • • • • • • • • •
AIIGYIB	EEFERVRULE	PGEDIGITIK	FWPDDG1F.E	TIEFDFRILE	NKLKELAFLN	SGVEISLSDE	RIDE	•••••	• • • • • • • • • • •
Consens		G	F		-RPLN	-GD-	R		
	261					~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~			
MTDGyrB	APHKVKSRTF	HYPGGLVDFV	KHIN. RTKNA	1HS	SIVDESGKGT	GHEVEIA	LEWNAGYSES	VHTFANT	INTHEGGTHE
SspGyrB	EPVRSVTY	YYEGGIVDFV	KYLNSRKGDL	IHP	TVIDIDAEDK	ERMLS.VEIA	MQWNSQYSEG	VYSFANT	INTHEGGTHE
NgoGyrB	SF	ALSGGVAGFV	QYMN.RKKTP	LHE	KIFYAFGEKD	GMSVECA	MQWNDSYQES	VQCFTNN	IPQRDGGTHL
EcoGyrB	HF	HYEGGIKAFV	EYLN.KNKTP	IHP	NIFYFSTEKD	GIGVEVA	LQWNDGFQEN	IYCFTNN	IPQRDGGTHL
MycGyrB	. RQNPQSFSW	KYDGGLVQYI	HHLNN.EKEP	LFEDIIFGEK	TDTVKSVSRD	ESYTIKVEVA	FQYNKTYNQS	IFSFCNN	INTTEGGTHV
HlfGyrB	SSTF	LFEGGIREFV	EYLNETKTAL	$\texttt{H} \ldots \ldots \texttt{D} \texttt{D}$	VIYYDDESEG	IEVEIA	MQATDELQGS	IHAFANN	INTREGGTHL
Consens		GG	N			VE-A		F-N-	IGGTH-
	351								
MTbGvrB	EGERSALTSV	VNKYAKDRKL	LKDKDPN, LT	GDDIREGLAA	VISVKVSEPO	FEGOTKTKLG	NTEVKSFVOK	VCNEOLTHWF	EANPTDAKVV
SspGyrB	EGERAAMTGL	VNRYAREKKE	LREKDDN, LA	GEDIREGLTA	IISVKLGEPO	FEGOTKTKLG	NTEAKTFVOK	IVHEHLTDWF	DRHPNEAADI
NgoGyrB	TALROVMTRT	INSYTEANEV	AKKAKVE. TA	GDDMREGLTC	VLSVKLPDPK	FSSOTKDKLV	SGEIGPVVNE	VINOALTDEL	EENPNEAKII
Facture	ACEDANMED	INAVMORECY	CKKYKAC TU	CDDAREGLIA	VUSVKUPDPK	FSSOTKDKLV	SSEVKSAVEO	OMNELLAEVI.	LENPTDAKTV
ECOGYIB	ECEDNALWE	INDENVENVE	IVETDEV IT	PDDICECITA	TICIKUDNDO	VECOTIKERIC	NTEVPDLVNS	TVSFIFFRFM	LENDOFANAT
MYCGYIB	EGF KNALVKI	INKEAVENKE	LABIDER. II	CEDURECIEN	VIEWKUDDO	FECOTIVETIC	NEEVECTVES	VTHOOLGTEE	FENDOWAWAT
HITGVER	THERTALTRY	VINDIANSIDM	PDDPDGDNPK	GEDVKEGLIA	VISVKHEDEQ	FEGQININDG	NSEAUGIAES	VINQQUGIFF	GENFDIAIAI
niiojio				D DOI			F 17		<b>D N</b>
Consens		-N		DEGL	S-KP-	QTK-KL-	EV		PA
Consens	441	-N		DEGL	S-KP-	QTK-KL-	EV	*	PA
Consens MTbGyrB	441 VNKAVSSAQA	-N RIAARKAREL	VRRKSATDIG	DEGL GLPGKLADCR	S-KP-	QTK-KL- # VVEGDSAGGS	EV	# AILPLRGKII	PA
Consens MTbGyrB SspGyrB	441 VNKAVSSAQA IRKSIQAATA	-N RIAARKAREL RVAARKARDL	VRRKSATDIG TRRKGLLESA	DEGL GLPGKLADCR SLPGKLSDCQ	S-KP- STDPRKSELY SNDPSKCEIF	QTK-KL- # VVEGDSAGGS IVEGDSAGGS	EV AKSGRDSMFQ AKSGRNPQYQ	# AILPLRGKII AILPIRGKIL	PA NVEKARIDRV NVEKARIDKI
Consens MTbGyrB SspGyrB NgoGyrB	441 VNKAVSSAQA IRKSIQAATA TGKIVDAARA	-N RIAARKAREL RVAARKARDL RQAARKAREI	VRRKSATDIG TRRKGLLESA TRRKGLMDGL	DEGL GLPGKLADCR SLPGKLSDCQ GLPGKLADCQ	S-KP- STDPRKSELY SNDPSKCEIF EKDPALSELY	QTK-KL- # VVEGDSAGGS IVEGDSAGGS LVEGDSAGGS	EV AKSGRDSMFQ AKSGRNPQYQ AMQGRDRKFQ	# AILPLRGKII AILPIRGKIL AILPLKGKIL	PA NVEKARIDRV NVEKARIDKI NVATLIT
Consens MTbGyrB SspGyrB NgoGyrB EcoGyrB	441 VNKAVSSAQA IRKSIQAATA TGKIVDAARA VGKIIDAARA	-N RIAARKAREL RVAARKARDL RQAARKAREI REAARRAREM	VRRKSATDIG TRRKGLLESA TRRKGLMDGL TRRKGALDLA	DEGL GLPGKLADCR SLPGKLSDCQ GLPGKLADCQ GLPGKLADCQ	S-KP- STDPRKSELY SNDPSKCEIF EKDPALSELY ERDPALSELY	QTK-KL- # VVEGDSAGGS IVEGDSAGGS LVEGDSAGGS LVEGDSAGGS	EV AKSGRDSMFQ AKSGRNPQYQ AMQGRDRKFQ AKQGRNRKNQ	# AILPLRGKII AILPIRGKIL AILPLKGKIL AILPLKGKIL	PA NVEKARIDRV NVEKARIDKI NVATLIT NVEKARFDKM
Consens MTbGyrB SspGyrB NgoGyrB EcoGyrB MycGyrB	441 VNKAVSSAQA IRKSIQAATA TGKIVDAARA VGKIIDAARA IRKTLLAQEA	-N RIAARKAREL RVAARKARDL RQAARKAREI REAARRAREM RRRSQEAREL	VRRKSATDIG TRRKGLLESA TRRKGLMDGL TRRKGALDLA TRRKSPFDSG	DEGL GLPGKLADCR SLPGKLSDCQ GLPGKLADCQ SLPGKLADCQ SLPGKLADCT	S-KP- STDPRKSELY SNDPSKCEIF EKDPALSELY ERDPALSELY TRDPSISELY	QTK-KL- # VVEGDSAGGS IVEGDSAGGS LVEGDSAGGS IVEGDSAGGT	EV AKSGRDSMFQ AKSGRNPQYQ AMQGRDRKFQ AKQGRNRKNQ AKTGRDRYFQ	# AILPLRGKII AILPIRGKIL AILPLKGKIL AILPLKGKIL AILPLRGKIL	PA NVEKARIDRV NVEKARIDKI NVATLIT NVEKARFDKM NVEKSHFEQI
Consens MTbGyrB SspGyrB NgoGyrB EcoGyrB MycGyrB HlfGyrB	441 VNKAVSSAQA IRKSIQAATA TGKIVDAARA VGKIIDAARA IRKTLLAQEA ISKAVEAARA	-N RIAARKAREL RVAARKAREL RQAARKAREI REAARRAREM RRRSQEAREL RKAAKQAEEL	VRRKSATDIG TRRKGLLESA TRRKGLMDGL TRRKGALDLA TRRKSPFDSG TRRKSALEST	DEGL GLPGKLADCR SLPGKLSDCQ GLPGKLADCQ GLPGKLADCQ SLPGKLADCT SLPGKLADCQ	S-KP- STDPRKSELY SNDPSKCEIF EKDPALSELY ERDPALSELY TRDPSISELY SRDPSESELF	QTK-KL- # VVEGDSAGGS IVEGDSAGGS LVEGDSAGGS IVEGDSAGGT IVEGDSAGGS	EV AKSGRDSMFQ AKSGRNPQYQ AMQGRDRKFQ AKQGRNRKNQ AKTGRDRYFQ AKQGRDRKFQ	AILPLRGKII AILPIRGKIL AILPLKGKIL AILPLKGKIL AILPLRGKIL AILPLKGKIL	PA NVEKARIDRV NVEKARIDKI NVATLIT NVEKARFDKM NVEKSHFEQI NVEKHRLDRI
MTbGyrB SspGyrB NgoGyrB EcoGyrB MycGyrB HlfGyrB Consens	441 VNKAVSSAQA IRKSIQAATA TGKIVDAARA VGKIIDAARA IRKTLLAQEA ISKAVEAARA -KA	-N RIAARKAREL RVAARKARDL RQAARKAREI REAARRAREM RRRSQEAREL RKAAKQAEEL RA	VRRKSATDIG TRRKGLLESA TRRKGLMDGL TRRKGALDLA TRRKSPFDSG TRRKSALEST -RRK	DEGL GLPGKLADCR SLPGKLADCQ GLPGKLADCQ SLPGKLADCT SLPGKLADCQ -LPGKL-DC-	S-KP- STDPRKSELY SNDPSKCEIF EKDPALSELY ERDPALSELY TRDPSISELY SRDPSESELF DPE	QTK-KL- # VVEGDSAGGS IVEGDSAGGS IVEGDSAGGS IVEGDSAGGT IVEGDSAGGS -VEGDSAGG-	EV AKSGRDSMFQ AKSGRNPQYQ AMQGRDRKFQ AKQGRDRKFQ AKTGRDRYFQ AGRQ	AILPLRGKII AILPIRGKIL AILPLKGKIL AILPLKGKIL AILPLRGKIL AILPLKGKIL AILPGKI-	PA NVEKARIDRV NVEKARIDKI NVATLIT NVEKARFDKM NVEKSHFEQI NVEKHRLDRI NV
Consens MTbGyrB SspGyrB NgoGyrB EcoGyrB MycGyrB HlfGyrB Consens	441 VNKAVSSAQA IRKSIQAATA TCKIVDAARA VGKIIDAARA IRKTLLAQEA ISKAVEAARA KA 531	-N RIAARKAREL RVAARKAREI RQAARKAREI REAARRAREM RRRSQEAREL RKAAKQAEEL RA	VRRKSATDIG TRRKGLLESA TRRKGLMDGL TRRKGALDLA TRRKSPFDSG TRRKSALEST -RRK	DEGL GLPGKLADCR SLPGKLSDCQ GLPGKLADCQ SLPGKLADCQ SLPGKLADCQ -LPGKL-DC-	S-KP- STDPRKSELY SNDPSKCEIF EKDPALSELY ERDPALSELY TRDPSISELY SRDPSESELF DPE	QTK-KL- # VVEGDSAGGS IVEGDSAGGS IVEGDSAGGS IVEGDSAGGS -VEGDSAGG-	EV AKSGRDSMFQ AKSGRNPQYQ AMQGRDRKFQ AKQGRNRKNQ AKTGRDRYFQ AGRQ	# AILPLRGKII AILPLRGKIL AILPLKGKIL AILPLKGKIL AILPLKGKIL AILP-GKI-	PA NVEKARIDRV NVEKARIDKI NVATLIT NVEKARFDKM NVEKSHFEQI NVEKHRLDRI NV
MTbGyrB SspGyrB NgoGyrB EcoGyrB HlfGyrB Consens MTbGyrB	441 VNKAVSSAQA IRKSIQAATA TGKIVDAARA VGKIIDAARA IRKTLLAQEA ISKAVEAARA -KA 531 LKNTEARRSS	-N RIAARKAREL RVAARKARDL RQAARKAREI REAARRAREM RRRSQEAREL RKAAKQAEEL RA RALGTGI.HD	VRRKSATDIG TRRKGLLESA TRRKGLMDGL TRRKGALDLA TRRKSPFDSG TRRKSALEST -RRK EFDIGKLRYH	DEGL GLPGKLADCR SLPGKLADCQ GLPGKLADCQ SLPGKLADCQ SLPGKLADCT SLPGKLADCQ -LPGKL-DC- KIVLMADADV	S-KP- STDPRKSELY SNDPSKCEIF EKDPALSELY ERDPALSELY SRDPSESELF DPE DGQHISTLLL	QTK-KL- # VVEGDSAGGS IVEGDSAGGS IVEGDSAGGS IVEGDSAGGS -VEGDSAGG- TLLFRFMRPL	EV AKSGRDSMFQ AKSGRNPQYQ AMQGRDRKFQ AKQGRNRKNQ AKTGRDRYFQ AKQGRDRKFQ AGRQ IENGHVFLAQ	# AILPLRGKII AILPIRGKIL AILPLKGKIL AILPLKGKIL AILPLKGKIL AILPGKI- PPLYKLKWQR	PA NVEKARIDRV NVEKARIDKI NVATLIT NVEKARFDKM NVEKSHFEQI NVEKHRLDRI NV SDPEFAYSDR
Consens MTbGyrB SspGyrB NgoGyrB EcoGyrB MycGyrB HlfGyrB Consens MTbGyrB SspGyrB	441 VNKAVSSAQA IRKSIQAATA TGKIVDAARA VGKIIDAARA IRKTLLAQEA ISKAVEAARA KA 531 LKNTEARRSS LCNTEVQALI	-N RIAARKAREL RVAARKARDL RQAARKAREI REAARRAREM RRRSQEAREL RKAAKQAEEL RA RALGTGI.HD SAFGTGV.HE	VRRKSATDIG TRRKGLLESA TRRKGLMDGL TRRKGALDLA TRRKSPFDSG TRRKSALEST -RRK EFDIGKLRYH DFDIEKLRYH	DEGL GLPGKLADCR SLPGKLADCQ GLPGKLADCQ GLPGKLADCQ SLPGKLADCT SLPGKLADCQ -LPGKL-DC- KIVLMADADV KIILMADADV	S-KP- STDPRKSELY SNDPSKCEIF EKDPALSELY TRDPSISELY SRDPSESELF DPE DGQHISTLLL DGQHINTLLL	QTK-KL- # VVEGDSAGGS IVEGDSAGGS IVEGDSAGGS IVEGDSAGGS IVEGDSAGGT IVEGDSAGG- TLLFRFMRPL TFLFRFMRPL	EV AKSGRDSMFQ AKSGRNPQYQ AMQGRDRKFQ AKQGRDRKFQ AKQGRDRKFQ AGRQ IENGHVFLAQ VEAGHVYLSR	# AILPLRGKII AILPLKGKIL AILPLKGKIL AILPLKGKIL AILPLRGKIL AILPGKI- PPLYKLKWQR PPLYKIKWGR	PA NVEKARIDRV NVEKARIDKI NVATLIT NVEKARFDKM NVEKSHFEQI NVEKHRLDRI NV SDPEFAYSDR DDFEYAYSDR
Consens MTbGyrB SspGyrB NgoGyrB EcoGyrB MycGyrB HlfGyrB Consens MTbGyrB SspGyrB NaGGyrB	441 VNKAVSSAQA IRKSIQAATA TCKIVDAARA VGKIIDAARA ISKAVEAARA ISKAVEAARA -KA 531 LKNTEARRSS LQNTEVQALI	-N RIAARKAREL RVAARKARDL RQAARKAREI REAARRAREM RRRSQEAREL RKAAKQAEEL RA RALGTGI.HD SAFGTGV.HE .ALGAGIGKE	VRRKSATDIG TRRKGLLESA TRRKGLMDGL TRRKGALDLA TRRKSPFDSG TRRKSALEST -RRK EFDIGKLRYH DFDIEKLRYH EFNPEKLRYH	DEGL GLPGKLADCR SLPGKLADCQ GLPGKLADCQ SLPGKLADCQ -LPGKLADCQ -LPGKL-DC- KIVLMADADV KIILMADADV KIILMADADV	S-KP- STDPRKSELY SNDPSKCEIF EKDPALSELY ERDPALSELY SRDPSESELF DPE DGQHISTLLL DGQHINTLLL DGAHIRTLLL	QTK-KL- # VVEGDSAGGS IVEGDSAGGS IVEGDSAGGS IVEGDSAGGT IVEGDSAGG -VEGDSAGG TLLFRFMRPL TFLFRFMRPL TFLFRFMRPL	EV AKSGRDSMFQ AKSGRNPQYQ AMQGRDRKFQ AKQGRNRKNQ AKQGRDRKFQ AGRQ IENGHVFLAQ VEAGHVYLSR VERGYIYIAQ	# AILPLRGKII AILPLRGKIL AILPLKGKIL AILPLRGKIL AILPLKGKIL AILPGKI- PPLYKLKWQR PPLYKIKWGR PPLYKAKYGK	PA NVEKARIDRV NVEKARIDKI NVATLIT NVEKARFDKM NVEKSHFEQI NVEKHRLDRI NV SDPEFAYSDR DDFEYAYSDR QERYLKDELE
MTbGyrB SspGyrB NgoGyrB EcoGyrB MycGyrB HlfGyrB Consens MTbGyrB SspGyrB NgoGyrB NgoGyrB	441 VNKAVSSAQA IRKSIQAATA TCKIVDAARA VGKIIDAARA IRKTLLAQEA ISKAVEAARA -KA 531 LKNTEARRSS LQNTEVQALI	-N RIAARKAREL RQAARKAREI REAARRAREM RRRSQEAREL RKAAKQAEEL RA RALGTGI.HD SAFGTGV.HE .ALGAGIGKE TALGCGIGRD	VRRKSATDIG TRRKGLLESA TRRKGLLESA TRRKGALDLA TRRKSPFDSG TRRKSALEST -RRK EFDIGKLRYH EFNPEKLRYH EYNPDKLRYH	DEGL GLPGKLADCR SLPGKLADCQ GLPGKLADCQ SLPGKLADCQ SLPGKLADCQ -LPGKL-DC- KIVLMADADV RIIIMTDADV SIIIMTDADV	S-KP- STDPRKSELY SNDPSKCEIF EKDPALSELY ERDPALSELY TRDPSISELY DPE DGQHISTLLL DGAHIRTLLL DGSHIRTLLL	QTK-KL- # VVEGDSAGGS IVEGDSAGGS IVEGDSAGGS IVEGDSAGGS IVEGDSAGG- TLLFRFMRPL TFFLRFMRPL TFFYRQMPDE TFFYRQMPEI	EV AKSGRDSMFQ AKSGRNPQYQ AMQGRDRKFQ AKQGRNRKNQ AKQGRDRKFQ AGRQ IENGHVFLAQ VEAGHVYLSR VERGYIYIAQ	# AILPLRGKII AILPIRGKIL AILPLKGKIL AILPLKGKIL AILPLKGKIL AILP-GKI- PPLYKLKWQR PPLYKIKWGR PPLYKVKKGK	PA NVEKARIDRV NVEKARIDKI NVATLIT NVEKARFDKM NVEKSHFEQI NV SDPEFAYSDR DDFEYAYSDR QERYLKDELE QEQYIKDDEA
MTbGyrB SspGyrB NgoGyrB MycGyrB HlfGyrB Consens MTbGyrB SspGyrB NgoGyrB EccGyrB NgoGyrB	441 VNKAVSSAQA IRKSIQAATA TGKIVDAARA VGKIIDAARA IRKTLLAQEA ISKAVEAARA KA 531 LKNTEARRSS LQNTEVQALI LSSQEVATLI ENNVEISALV	-N RIAARKAREL RVAARKARDL RQAARKAREI REAARRAREM RRRSQEAREL RKAAKQAEEL RA RALGTGI.HD SAFGTGV.HE .ALGAGIGKE TALGCGIGK	VRRKSATDIG TRRKGLLESA TRRKGLLESA TRRKGALDLA TRRKSPFDSG TRRKSALEST -RRK EFDIGKLRYH DFDIEKLRYH EFNPEKLRYH DFFLEKLRYN	DEGL GLPGKLADCR SLPGKLADCQ GLPGKLADCQ SLPGKLADCQ SLPGKLADCT SLPGKLADCQ -LPGKL-DC- KIVLMADADV KIILMADADV KIIIMTDADV SIIIMTDADV	S-KP- STDPRKSELY SNDPSKCEIF EKDPALSELY ERDPALSELY TRDPSISELY SRDPSESELF DPE DGQHISTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL	QTK-KL- # VVEGDSAGGS IVEGDSAGGS IVEGDSAGGS IVEGDSAGGS IVEGDSAGG- TLLFRFMRPL TFLFRFMRPL TFFFRMRPL TFFYRQMPDEI TFFFRFMYPL	EV AKSGRDSMFQ AKSGRDPQYQ AKQGRDRKFQ AKQGRDRKFQ AKQGRDRKFQ AGRQ IENGHVFLAQ VEAGHVYLSR VERGYIYIAQ VECGNIYIAO	# AILPLRGKII AILPIRGKIL AILPLKGKIL AILPLKGKIL AILPLKGKIL AILP-GKI- PPLYKLKWQR PPLYKIKWGR PPLYKVKGK PPLYKVSY.	PA NVEKARIDRV NVEKARIDKI NVATLIT NVEKARFDKM NVEKSHFEQI NVEKHRLDRI NV SDPEFAYSDR DDFEYAYSDR QERYLKDEE QEQYIKDDEA SNKDLYM
MTbGyrB SspGyrB NgoGyrB EcoGyrB HlfGyrB Consens MTbGyrB SspGyrB EcoGyrB NgoGyrB EcoGyrB MycGyrB	441 VNKAVSSAQA IRKSIQAATA TGKIVDAARA VGKIIDAARA IRKTLLAQEA ISKAVEAARA -KA 531 LKNTEARRSS LQNTEVQALI  LSSQEVATLI FNNVEISALV LENDEIBALI	-N RIAARKAREL RVAARKAREI REAARRAREM RRRSQEAREL RKAAKQAEEL RA RALGTGI.HD SAFGTGV.HE .ALGAGIGKE TALGGGIGRD MAVGCGIK.P TALGGGVG.D	VRRKSATDIG TRRKGLLESA TRRKGLMDGL TRRKGALDLA TRRKSPFDSG TRRKSALEST -RRK EFDIGKLRYH EFNPEKLRYH EFNPEKLRYH EFNPEKLRYH EFDIEKARYO	DEGL GLPGKLADCR SLPGKLADCQ GLPGKLADCQ SLPGKLADCQ SLPGKLADCT SLPGKL-DC- KIVLMADADV KIILMADADV KIIIMTDADV SIIIMTDADV KIIIMTDADV	S-KP- STDPRKSELY SNDPSKCEIF EKDPALSELY ERDPALSELY TRDPSISELY SRDPSESELF DPE DGQHISTLLL DGQHINTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL	QTK-KL- # VVEGDSAGGS IVEGDSAGGS IVEGDSAGGS IVEGDSAGGT IVEGDSAGGT TUEGDSAGG- TLLFRFMRPL TFFFRMRPL TFFFRMRPL TFFFRMPL TFFFRFMPL TFFFRFMPL TFFFRFMPL TFFFRFMPL	EV AKSGRDSMFQ AKSGRNPQYQ AMQGRDRKFQ AKQGRDRKFQ AKQGRDRKFQ AGRQ IENGHVFLAQ VEAGHVYLSR VERGY1YIAQ VEQGNIYIAQ VEQGNIYIAQ	# AILPLRGKII AILPLRGKIL AILPLKGKIL AILPLKGKIL AILPLKGKIL AILPLKGKIL AILPGKI- PPLYKLKWQR PPLYKLKWGR PPLYKVKKGK PPLYKVKY.	PA NVEKARIDRV NVEKARIDKI NVATLIT NVEKARFDKM NVEKSHFEQI NVEKHRLDRI NV SDPEFAYSDR DDFEYAYSDR QERYLKDELE QEQYIKDDEA SNKDLYM GNTYDAMDEA
MTbGyrB SspGyrB NgoGyrB EcoGyrB MycGyrB HlfGyrB Consens MTbGyrB SspGyrB NgoGyrB EcoGyrB MycGyrB HlfGyrB	441 VNKAVSSAQA IRKSIQAATA TCKIVDAARA VGKIIDAARA ISKAVEAARA ISKAVEAARA S31 LKNTEARRSS LQNTEVQALI LSSQEVATLI FNNVEISALV LENDEIRALI	-N RIAARKAREL RVAARKARDL RQAARKAREI REAARRAREM RRRSQEAREL RKAAKQAEEL RA RALGTGI.HD SAFGTGV.HE .ALGAGIGKE TALGCGIGRD MAVGCGIK.P TAIGGGVG	VRRKSATDIG TRRKGLLESA TRRKGLLESA TRRKSALDLA TRRKSPFDSG TRRKSALEST - RRK EFDIGKLRYH DFDIEKLRYH EFNPEKLRYH EFNPEKLRYH DFELEKLRYH EFDIEKARYQ KRY-	DEGL GLPGKLADCR GLPGKLADCQ GLPGKLADCQ SLPGKLADCQ -LPGKL-DC- KIVLMADADV KIILMADADV SIIIMTDADV SIIIMTDADV RLILMTDADV RLILMTDADV	S-KP- STDPRKSELY SNDPSKCEIF EKDPALSELY ERDPALSELY SRDPSESELF DPE DGQHISTLLL DGAHINTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL DGAHITTLLL DG-HI-TLLI	QTK-KL- # VVEGDSAGGS IVEGDSAGGS IVEGDSAGGS IVEGDSAGGT IVEGDSAGGT TLLFRFMRPL TFLFRFMRPL TFFYRQMPDL TFFYRQMPDI TFFYRQMPDI TFFYRQMPDI TLLYRHMRPL TLLYRHMRPL	EV AKSGRDSMFQ AKSGRNPQYQ AMQGRDRKFQ AKQGRDRKFQ AKQGRDRKFQ AGRQ IENGHVFLAQ VEAGHVYLSR VERGHVYIAQ VERGHVYIAQ IEAGYVYAAQ -E-G	# AILPLRGKII AILPLRGKIL AILPLKGKIL AILPLKGKIL AILPLKGKIL AILP-GKI- PPLYKLKWQR PPLYKAKYGK PPLYKAKYGK PPLYKVKKGK PPLYKVY PPLYRVRY.R	PA NVEKARIDRV NVEKARIDKI NVATLIT NVEKARFDKM NVEKSHFEQI NVEKHRLDRI NV SDPEFAYSDR QERYLKDELE QEQYIKDDEA SNKDLYM GNTYDAMDEA
MTbGyrB SspGyrB NgoGyrB HJfGyrB Consens MTbGyrB SspGyrB NgoGyrB NgoGyrB EcoGyrB HJfGyrB EcoGyrB HJfGyrB Consens	441 VNKAVSSAQA IRKSIQAATA TCKIVDAARA VGKIIDAARA IRKTLLAQEA ISKAVEAARA ISKAVEAARA S31 LKNTEARRSS LQNTEVQALI LSSQEVATLI FNNVEISALV LENDEIRALI	-N RIAARKAREL RVAARKAREI RCAARKAREI REAARRAREM RRRSQEAREL RA RALGTGI.HD SAFGTGV.HE .ALGAGIGKE TALGCGIGRD MAVGCGIK.P TALGGGVG.D -AlG-G	VRRKSATDIG TRRKGLLESA TRRKGLLESA TRRKSALDLA TRRKSPFDSG TRRKSALEST -RRK EFDIGKLRYH DFDIEKLRYH EFNPEKLRYH EFNPEKLRYH DFELEKLRYN EFDIEKARYQ K-RY-	DEGL GLPGKLADCR SLPGKLADCQ GLPGKLADCQ SLPGKLADCQ -LPGKL-DC- KIVLMADADV RIIIMTDADV SIIIMTDADV KIIIMTDADV RLILMTDADV M-DADV	S-KP- STDPRKSELY SNDPSKCEIF EKDPALSELY ERDPALSELY TRDPSISELY DPE DGQHISTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL DG-HI-TLLL	QTK-KL- # VVEGDSAGGS LVEGDSAGGS LVEGDSAGGS LVEGDSAGGS -VEGDSAGG- TLLFRFMRPL TFFYRQMPDL TFFYRQMPDI TFFFRFMYPL TLLYRHMRPL TR	EV AKSGRDSMFQ AKSGRNPQYQ AMQGRDRKFQ AKQGRDRKFQ AGRQ IENGHVFLAQ VEAGHVYLSR VERGYIYIAQ VEQGNIYIAQ IEAGYVYAAQ -E-G	# AILPLRGKII AILPLRGKIL AILPLKGKIL AILPLKGKIL AILPLKGKIL AILPGKI- PPLYKLKWQR PPLYKLKWQR PPLYKAKYGK PPLYKVKKGK PPLYKVKY. PPLY	PA NVEKARIDRV NVEKARIDKI NVATLIT NVEKARFDKM NVEKSHFEQI NV SDPEFAYSDR DDFEYAYSDR QERYLKDELE QEQYIKDDEA SNKDLYM GNTYDAMDEA
MTbGyrB SepGyrB NgoGyrB EccGyrB HlfGyrB Consens MTbGyrB SspGyrB NgoGyrB EccGyrB NgoGyrB HlfGyrB Consens	441 VNKAVSSAQA IRKSIQAATA TGKIVDAARA VGKIIDAARA IRKTLLAQEA ISKAVEAARA KA 531 LKNTEARRSS LQNTEVQALI LSSQEVATLI FNNVEISALV LENDE IRALI 	-N RIAARKAREL RVAARKARDL RQAARKAREI REAARRAREM RRRSQEAREL RKAAKQAEEL RA RALGTGI.HD SAFGTGV.HE .ALGAGIGKE TALGCGIGRD MAVGCGIK.P TAIGGGVG.D -AlG-G	VRRKSATDIG TRRKGLLESA TRRKGLLESA TRRKGALDLA TRRKSPFDSG TRRKSALEST -RRK EFDIGKLRYH DFDIEKLRYH EFNPEKLRYH EFNPEKLRYH DFELEKLRYN EFDIEKARYQ K-RY-	DEGL GLPGKLADCR SLPGKLADCQ GLPGKLADCQ SLPGKLADCQ -LPGKL-DC- KIVLMADADV KIILMADADV KIIIMTDADV SIIIMTDADV RLILMTDADV M-DADV	S-KP- STDPRKSELY SNDPSKCEIF EKDPALSELY ERDPALSELY TRDPSISELY SRDPSESELF DPE DGQHISTLLL DGQHINTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL	QTK-KL- # VVEGDSAGGS IVEGDSAGGS IVEGDSAGGS IVEGDSAGGS IVEGDSAGGT IVEGDSAGG- TLLFRFMRPL TFFFRFMRPL TFFFRFMRPL TFFFRFMPPL TFFFRFMYPL TLLYRHMRPL TR	EV AKSGRDSMFQ AKSGRNPQYQ AMQGRDRKFQ AKQGRNRKNQ AKQGRDRKFQ AGRQ IENGHVFLAQ VEAGHVYLSR VERGYLYLAQ VERGHVYLAQ VEQGNIYIAQ IEAGYVYAAQ -E-G	# AILPLRGKII AILPIRGKIL AILPLKGKIL AILPLKGKIL AILPLKGKIL AILPLKGKI PPLYKLKWQR PPLYKLKWQR PPLYKAKYGK PPLYKVSY. PPLYRVRY.R PPLY	PA NVEKARIDRV NVEKARIDKI NVATLIT NVEKARFDKM NVEKSHFEQI NV SDPEFAYSDR DDFEYAYSDR DDFEYAYSDR QERYLKDELE QEQYIKDDEA SNKDLYM GNTYDAMDEA
MTbGyrB SspGyrB NgoGyrB MycGyrB HlfGyrB Consens MTbGyrB SspGyrB NgoGyrB EccGyrB MycGyrB HlfGyrB Consens MTbGyrB	441 VNKAVSSAQA IRKSIQAATA TGKIVDAARA VGKIIDAARA ISKAVEAARA ISKAVEAARA ISKAVEAARA S31 LKNTEARRSS LQNTEVQALI LSSQEVATLI FNNVEISALV LENDEIRALI 621 ERDGLLEAGL	-N RIAARKAREL RVAARKARDL RQAARKAREI REAARRAREM RRRSQEAREL RA RALGTGI.HD SAFGTGV.HE .ALGAGIGKE TALGCGIGRD MAVGCGIK.P TAIGGGVG.D -AlG-G KAGKKINKED	VRRKSATDIG TRRKGLLESA TRRKGLADGL TRRKSALDLA TRRKSPFDSG -RRK EFDIGKLRYH EFDIEKLRYH EFNPEKLRYH EFNPEKLRYH EFDIEKARYQ K-RY-	DEGL GLPGKLADCR SLPGKLADCQ GLPGKLADCQ SLPGKLADCQ -LPGKL-DC- KIVLMADADV KIILMADADV KIIIMTDADV SIIIMTDADV RLILMTDADV M-DADV	S-KP- STDPRKSELY SNDPSKCEIF EKDPALSELY ERDPALSELY SRDPSISELY SRDPSISELY SRDPSISELY DGQHISTLLL DGQHINTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL	QTK-KL- # VVEGDSAGGS IVEGDSAGGS IVEGDSAGGS IVEGDSAGGS IVEGDSAGGT TVEGDSAGGT TLLFRFMRPL TFFFRFMRPL TFFFRFMRPL TFFFRFMYPL TLLYRHMRPL TR	EV AKSGRDSMFQ AKSGRNPQYQ AMQGRDRKFQ AKQGRDRKFQ AKQGRDRKFQ AGRQ IENGHVFLAQ VEAGHVYLSR VERGYIYIAQ VEQGHYYIAQ IEAGYVYAAQ -E-G	# AILPLRGKII AILPLRGKIL AILPLKGKIL AILPLKGKIL AILPLKGKIL AILPLKGKIL AILPGKI- PPLYKLKWQR PPLYKLKWGR PPLYKLKWGR PPLYKVKKGK PPLYKVKY. PPLYVRY.R PPLY	PA NVEKARIDRV NVEKARIDKI NVATLIT NVEKARDKM NVEKSHFEQI NVEKHLDRI NV SDPEFAYSDR DDFEYAYSDR QERYLKDELE QEQYIKDDEA SNKDLYM GNTYDAMDEA
MTbGyrB SspGyrB NgoGyrB EcoGyrB MycGyrB HlfGyrB Consens MTbGyrB SspGyrB NgoGyrB MycGyrB HlfGyrB Consens MTbGyrB SspGyrB MycGyrB	441 VNKAVSSAQA IRKSIQAATA TCKIVDAARA VGKIIDAARA IRKTLLAQEA ISKAVEAARA ISKAVEAARA S31 LKNTEARRSS LQNTEVQALI LSSQEVATLI FNNVEISALV LENDEIRALI 	-N RIAARKAREL RVAARKAREI RQAARKAREI REAARRAREM RRRSQEAREL RKAAKQAEEL RA RALGTGI.HD SAFGTGV.HE .ALGAGIGKE TALGCGIGRD MAVGCGIK.P TAIGGGVG.D -AIG-G KAGKKINKED QNGKRI.KED	VRRKSATDIG TRRKGLLESA TRRKGLLESA TRRKGALDLA TRRKSALDLA TRRKSALEST -RRK EFDIGKLRYH DFDIEKLRYH EFNPEKLRYH EFNPEKLRYH DFELEKLRYN EFDIEKARYQ K-RY-	DEGL GLPGKLADCR SLPGKLADCQ GLPGKLADCQ SLPGKLADCQ -LPGKL-DC- KIVLMADADV KIILMADADV KIIIMTDADV SIIIMTDADV RLILMTDADV M-DADV	S-KP- STDPRKSELY SNDPSKCEIF EKDPALSELY ERDPALSELY TRDPSISELY DPE DGQHISTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL	QTK-KL- # VVEGDSAGGS IVEGDSAGGS IVEGDSAGGS IVEGDSAGGS IVEGDSAGGS -VEGDSAGG- TLLFRFMRPL TFFFRMPL TFFFRMPL TFFFRMPLI TFFFRMPLI TFFFRMPLI TLLYRHMRPL TR	EV AKSGRDSMFQ AKSGRNPQYQ AMQGRDRKFQ AKQGRDRKFQ AGRQ IENGHVFLAQ VEAGHVYLAQ VERGHVYIAQ VERGHVYIAQ VEQGNIYIAQ IEAGYVYAAQ -E-G	# AILPLRGKII AILPLRGKIL AILPLKGKIL AILPLKGKIL AILPLRGKIL AILP-GKI- PPLYKLKWQR PPLYKLKWQR PPLYKAKYGK PPLYKVKKGK PPLYKVKY. PPLYVVXY. PPLYV	PA NVEKARIDRV NVEKARIDKI NVATLIT NVEKARFDKM NVEKSHFEQI NV SDPEFAYSDR QERYLKDELE QEQYIKDDEA SNKDLYM GNTYDAMDEA 
MTbGyrB SspGyrB NgoGyrB EcoGyrB HlfGyrB Consens MTbGyrB SspGyrB EcoGyrB EcoGyrB HlfGyrB Consens MycGyrB HlfGyrB Consens MyCGyrB HlfGyrB SspGyrB NgoGyrB	441 VNKAVSSAQA IRKSIQAATA TCKIVDAARA VGKIIDAARA IRKTLLAQEA ISKAVEAARA -KA 531 LKNTEARRSS LQNTEVQALI LSSQEVATLI FNNVEISALV LENDEIRALI 621 ERDGLLEAGL ERDGLLEAGL ERDALVELGK KDQWLLGLAL	-N RIAARKAREL RVAARKAREI REAARRAREM RRRSQEAREL RA RALGTGI.HD SAFGTGV.HE .ALGAGIGKE TALGCGIGRD MAVGCGIK.P TAIGGGVG.D -AlG-G KAGKKINKED QNGKRI.KED EKAKI.V.SD	VRRKSATDIG TRRKGLLESA TRRKGLLESA TRRKSALDLA TRRKSPFDSG TRRKSALEST -RRK EFDIGKLRYH DFDIEKLRYH EFNPEKLRYH EFNPEKLRYH DFELEKLRYN EFDIEKARYQ K-RY-  GRTIEGAELA	DEGL GLPGKLADCR SLPGKLADCQ GLPGKLADCQ SLPGKLADCQ SLPGKLADCQ -LPGKL-DC- KIVLMADADV KIIIMTDADV SIIIMTDADV SIIIMTDADV RLILMTDADV M-DADV 	S-KP- STDPRKSELY SNDPSKCEIF EKDPALSELY ERDPALSELY TRDPSISELY SRDPSESELF DPE DGQHISTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL MCHI-TLLL CGHI-TLLL	QTK-KL- # VVEGDSAGGS IVEGDSAGGS IVEGDSAGGS IVEGDSAGGS IVEGDSAGGT IVEGDSAGG- TLLFRFMRPL TFFYRQMPDL TFFYRQMPDI TFFFRFMYPL TLLYRHMRPL TR VDELVLRAML	EV AKSGRDSMFQ AKSGRNPQYQ AKQGRDRKFQ AKQGRDRKFQ AGRQ IENGHVFLAQ VEAGHVYLSR VERGYIYIAQ VEQGNIYIAQ IEAGYVYAAQ -E-G HAS.P.IDLT	# AILPLRGKII AILPIRGKIL AILPLKGKIL AILPLKGKIL AILPLKGKIL AILP-GKI- PPLYKLKWQR PPLYKIKWGR PPLYKIKWGR PPLYKVKKGK PPLYKVKKGK PPLYKVKY. PPLYRVRY.R PPLY SSENADKAVA	PA NVEKARIDRV NVEKARIDKI NVATLIT NVEKARFDKM NVEKSHFEQI NV SDPEFAYSDR DDFEYAYSDR QERYLKDELE QEQYIKDEA SNKDLYM GNTYDAMDEA  ELSGLLDEKE ELSGLLDEKE
MTbGyrB SepGyrB NgoGyrB MycGyrB HlfGyrB Consens MTbGyrB SspGyrB NgoGyrB EcoGyrB HlfGyrB Consens MTbGyrB SspGyrB NgoGyrB EcoGyrB SspGyrB NgoGyrB EcoGyrB	441 VNKAVSSAQA IRKSIQAATA TGKIVDAARA VGKIIDAARA IRKTLLAQEA ISKAVEAARA KA 531 LKNTEARRSS LQNTEVQALI LSSQEVATLI FNNVEISALV LENDEIRALI 	-N RIAARKAREL RVAARKAREI REAARRAREM RRRSQEAREL RKAAKQAEEL RA RALGTGI.HD SAFGTGV.HE .ALGAGIGKE TALGCGIGRD MAVGCGIK.P TAIGGGVG.D -AlG-G KAGKKINKED QNGKRI.KED EKAKI.V.SD ALVSELNDKE	VRRKSATDIG TRRKGLLESA TRRKGLLESA TRRKSALDLA TRRKSPFDSG TRRKSALEST -RRK EFDIGKLRYH EFNPEKLRYH EFNPEKLRYH EFDIEKARYQ K-RY-  GRTIEGAELA QHGSQWKFDV	DEGL GLPGKLADCR SLPGKLADCQ GLPGKLADCQ SLPGKLADCQ -LPGKL-DC- KIVLMADADV KIILMADADV KIIIMTDADV SIIIMTDADV RLILMTDADV  DTAKQFLLA. HTNAEQNLFE	S-KP- STDPRKSELY SNDPSKCEIF EKDPALSELY ERDPALSELY TRDPSISELY SRDPSESELF DPE DGQHISTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL MGAHIRTLLL SGAHIRTLLL SGAHIRTLLL SGAHIRTLLL SGAHIRTLLL SGAHIRTLLL	QTK-KL- # VVEGDSAGGS LVEGDSAGGS LVEGDSAGGS IVEGDSAGGS IVEGDSAGGT TVEGDSAGGT TLLFRFMRPL TFFFRMPL TFFFRMPL TFFFRFMPL TFFFRFMPL TLLYRHMRPL TR VDELVLRAML DTD.YPLDHE	EV AKSGRDSMFQ AKSGRNPQYQ AMQGRDRKFQ AKQGRDRKFQ AKQGRDRKFQ AGRQ IENGHVFLAQ VEAGHVYLSR VERGYIYIAQ VEQGNIYIAQ IEAGYVYAAQ -E-G HAS.P.IDLT FITGGEYRRI	# AILPLRGKII AILPLRGKIL AILPLKGKIL AILPLKGKIL AILPLKGKIL AILPLKGKIL AILPGKI- PPLYKLKWQR PPLYKLKWQR PPLYKLKWGR PPLYKVKGK PPLYKVKGK PPLYKVKGK PPLYKVRY.R PPLY SSENADKAVA MDQYQISIAL	PA NVEKARIDRV NVEKARIDKI NVATLIT NVEKARFDKM NVEKSHFEQI NV SDPEFAYSDR DDFEYAYSDR QERYLKDELE QEQYIKDDEA SNKDLYM GNTYDAMDEA  ELSGLLDEKE DGATLHTNAS
MTbGyrB SspGyrB MycGyrB HlfGyrB Consens MTbGyrB SspGyrB NgoGyrB EccGyrB MycGyrB HlfGyrB Consens MTbGyrB SspGyrB NgoGyrB SspGyrB NgoGyrB SspGyrB NgoGyrB	441 VNKAVSSAQA IRKSIQAATA TCKIVDAARA VGKIIDAARA ISKAVEAARA ISKAVEAARA ISKAVEAARA S31 LKNTEARRSS LQNTEVQALI LSSQEVATLI FNNVEISALV LENDEIRALI CEDDEIRALI ERDGLLEAGL ERDALVELGK KDQWLLGLAL DEQTVTRWVN QTDVQLEE.	-N RIAARKAREL RVAARKARDL RQAARKAREI REAARRAREM RRRSQEAREL RKAAKQAEEL RA RALGTGI.HD SAFGTGV.HE .ALGAGIGKE TALGCGIGRD MAVGCGIK.P TAIGGGVG.D -AIG-G KAGKKINKED QNGKRI.KED QNGKRI.KED WKQQHPNLKY	VRRKSATDIG TRRKGLLESA TRRKGLLESA TRRKSALDLA TRRKSPFDSG TRRKSALEST -RRK EFDIGKLRYH DFDIEKLRYH EFNPEKLRYH EFNPEKLRYH DFELEKLRYN EFDIEKARYQ K-RY-  GRTIEGAELA QHGSQWKFDV	DEGL GLPGKLADCR GLPGKLADCQ GLPGKLADCQ SLPGKLADCQ -LPGKLADCC -LPGKL-DC- KIVLMADADV KIILMADADV KIIIMTDADV SIIIMTDADV RLILMTDADV M-DADV DTAKQFLLA. HTNAEQNLFE	S-KP- STDPRKSELY SNDPSKCEIF EKDPALSELY ERDPALSELY SRDPSESELF DPE DGQHISTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL MTVIEQESRF FIVRVRTHGV	QTK-KL- # VVEGDSAGGS IVEGDSAGGS IVEGDSAGGS IVEGDSAGGT IVEGDSAGGT TLLFRFMRPL TFFYRQMPDL TFFYRQMPDL TFFYRQMPDI TFFYRQMPDI TLLYRHMRPL TR VDELVLRAML DTD.YPLDHE 	EV AKSGRDSMFQ AKSGRNPQYQ AMQGRDRKFQ AKQGRNRKNQ AKQGRDRKFQ AGRQ IENGHVFLAQ VEAGHVYLSR VERGHVYLAQ VERGHVYIAQ VEQGNIYIAQ VEQGNIYIAQ -E-G HAS.P.IDLT FITGGEYRRI	# AILPLRGKII AILPLRGKIL AILPLKGKIL AILPLKGKIL AILPLKGKIL AILPLKGKIL AILP-GKI- PPLYKLKWQR PPLYKLKWQR PPLYKLKWGR PPLYKVKKGK PPLYKVKKGK PPLYKVKY. PPLYVRVRY.R PPLY SSENADKAVA MDQYQISIAL	PA NVEKARIDRV NVEKARIDKI NVATLIT NVEKARFDKM NVEKSHFEQI NV SDPEFAYSDR QERYLKDELE QEQYIKDEA SNKDLYM GNTYDAMDEA  ELSGLLDEKE DGATLHTNAS
Consens SspGyrB SspGyrB NgoGyrB HlfGyrB Consens MTbGyrB SspGyrB NgoGyrB HlfGyrB Consens MYCGyrB HlfGyrB SspGyrB NgoGyrB SspGyrB NgoGyrB SspGyrB NgoGyrB HlfGyrB SspGyrB NgoGyrB HlfGyrB	441 VNKAVSSAQA IRKSIQAATA TCKIVDAARA VGKIIDAARA IRKTLLAQEA ISKAVEAARA ISKAVEAARA ISKAVEAARA ISKAVEAARA S31 LKNTEARRSS LQNTEVQALI ISSQEVATLI FNNVEISALV LENDEIRALI 	-N RIAARKAREL RVAARKAREI RQAARKAREI REAARRAREM RRRSQEAREL RA RALGTGI.HD SAFGTGV.HE ALGAGIGKE TALGCGIGRD MAVGCGIK.P TAIGGGVG.D -AIG-G KAGKKINKED QNGKRI.KED EKAKI.V.SD ALVSELNDKE WKQQHPNLKY NGNPT	VRRKSATDIG TRRKGLLESA TRRKGLLESA TRRKSALDLA TRRKSPDSG TRRKSALEST -RK EFDIGKLRYH DFDIEKLRYH EFNPEKLRYH DFELEKLRYN EFDIEKARYQ K-RY-  GRTIEGAELA QHGSQWKFDV 	DEGL GLPGKLADCR SLPGKLADCQ GLPGKLADCQ SLPGKLADCQ -LPGKL-DC- KIVLMADADV KIILMADADV RIIIMTDADV SIIIMTDADV KIIIMTDADV RLILMTDADV M-DADV  DTAKQFLLA. HTNAEQNLFE 	S-KP- STDPRKSELY SNDPSKCEIF EKDPALSELY ERDPALSELY TRDPSISELY DPE DGQHISTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL KTVIEQESRF PIVRVRTHGV	QTK-KL- # VVEGDSAGGS IVEGDSAGGS IVEGDSAGGS IVEGDSAGGS IVEGDSAGGT -VEGDSAGGT TLLFRFMRPL TFFYRQMPDI TFFYRQMPDI TFFFRFMYPL TLLYRHMRPL TR VDELVLRAML DTD.YPLDHE	EV AKSGRDSMFQ AKSGRNPQYQ AMQGRDRKFQ AKQGRDRKFQ AGRQ IENGHVFLAQ VEAGHVYLAQ VEAGHVYLAQ VERGHVYIAQ VEQGNIYIAQ IEAGYVYAAQ -E-G HAS.P.IDLT FITGGEYRRI	# AILPLRGKII AILPLRGKIL AILPLKGKIL AILPLKGKIL AILPLKGKIL AILP-GKI- PPLYKLKWQR PPLYKIKWGR PPLYKAKYGK PPLYKVKKGK PPLYKVKY. PPLYKVKY. PPLYVVY.R PPLY SSENADKAVA MDQYQISIAL	PA NVEKARIDRV NVEKARIDKI NVATLIT NVEKARFDKM NVEKSHFEQI NV-EKHRLDRI NV SDPEFAYSDR DDFEYAYSDR QERYLKDELE QEQYIKDDEA SNKDLYM GNTYDAMDEA  ELSGLLDEKE DGATLHTNAS
MTbGyrB SspGyrB NgoGyrB EcoGyrB HlfGyrB Consens MTbGyrB SspGyrB EcoGyrB EcoGyrB HlfGyrB Consens MTbGyrB SspGyrB NgoGyrB SspGyrB NgoGyrB EcoGyrB NgoGyrB EcoGyrB NgoGyrB EcoGyrB NgoGyrB EcoGyrB NgoGyrB EcoGyrB NgoGyrB EcoGyrB Consens	441 VNKAVSSAQA IRKSIQAATA TCKIVDAARA VGKIIDAARA IRKTLLAQEA ISKAVEAARA -KA 531 LKNTEARRSS LQNTEVQALI LSSQEVATLI FNNVEISALV LENDEIRALI 621 ERDGLLEAGL ERDGLLEAGL ERDALVELGK KDQWLLGLAL DEQTVTRWVN QTDVQLEE. ERDRIIEECC	-N RIAARKAREL RVAARKAREI RQAARKAREI REAARRAREM RRRSQEAREL RA RALGTGI.HD SAFGTGV.HE .ALGAGIGKE TALGCGIGRD MAVGCGIK.P TAIGGGVG.D -AIG-G KAGKKINKED QNGKRI.KED EKAKI.V.SD ALVSELNDKE WKQQHPNLKY NGNPT	VRRKSATDIG TRRKGLLESA TRRKGLLESA TRRKSALDLA TRRKSPFDSG TRRKSALEST -RRK EFDIGKLRYH DFDIEKLRYH EFNPEKLRYH EFNPEKLRYH DFELEKLRYN EFDIEKARYQ K-RY-  GRTIEGAELA QHGSQWKFDV	DEGL GLPGKLADCR SLPGKLADCQ GLPGKLADCQ SLPGKLADCQ -LPGKLADCQ -LPGKL-DC- KIVLMADADV RIIIMTDADV SIIIMTDADV SIIIMTDADV RLILMTDADV M-DADV  DTAKQFLLA. HTNAEQNLFE	S-KP- STDPRKSELY SNDPSKCEIF EKDPALSELY ERDPALSELY TRDPSISELY SRDPSESELF DPE DGQHISTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL MTVIEQESRF PIVRVRTHGV	QTK-KL- # VVEGDSAGGS IVEGDSAGGS IVEGDSAGGS IVEGDSAGGS -VEGDSAGGT TLLFRFMRPL TFFYRQMPDL TFFYRQMPDL TFFFRFMYPL TLLYRHMRPL TR VDELVLRAML DTD.YPLDHE 	EV AKSGRDSMFQ AKSGRNPQYQ AKQGRDRKFQ AKQGRDRKFQ AGRQ IENGHVFLAQ VEAGHVYLSR VERGYIYIAQ VEQGNIYIAQ IEAGYVYAAQ -E-G HAS.P.IDLT FITGGEYRRI	# AILPLRGKII AILPIRGKIL AILPLKGKIL AILPLKGKIL AILPLKGKIL AILPGKI- PPLYKLKWQR PPLYKIKWGR PPLYKNKKGK PPLYKVKKGK PPLYKVKKGK PPLYKVKY.R PPLY SSENADKAVA MDQYQISIAL	PA NVEKARIDRV NVEKARIDKI NVATLIT NVEKARFDKM NVEKSHFEQI NV SDPEFAYSDR DDFEYAYSDR DDFEYAYSDR QERYLKDELE QEQYIKDEA SNKDLYM GNTYDAMDEA  ELSGLLDEKE DGATLHTNAS
Consens SepGyrB NgoGyrB EcoGyrB HlfGyrB Consens MTbGyrB SspGyrB NgoGyrB EcoGyrB MycGyrB HlfGyrB Consens MTbGyrB SspGyrB NgoGyrB EcoGyrB NgoGyrB EcoGyrB MycGyrB HlfGyrB Consens	441 VNKAVSSAQA IRKSIQAATA TGKIVDAARA VGKIIDAARA ISKAVEAARA ISKAVEAARA ISKAVEAARA S31 LKNTEARRSS LQNTEVQALI LSSQEVATLI FNNVEISALV LENDEIRALI ERDGLLEAGL ERDGLLEAGL ERDGLLEAGL ERDGLLEAGL ERDGLLEAGL DEQTVTRWVN QTDVQLEE. ERDRIIEEEC 	-N RIAARKAREL RVAARKARDL RQAARKAREI REAARRAREM RRRSQEAREL RA RALGTGI.HD SAFGTGV.HE .ALGAGIGKE TALGCGIGRD MAVGCGIK.P TAIGGCVG.D -AlG-G KAGKKINKED QNGKRI.KED EKAKI.V.SD ALVSELNDKE WKQQHPNLKY NGNPT	VRRKSATDIG TRRKGLLESA TRRKGLLESA TRRKSALDLA TRRKSPFDSG -RRK EFDIGKLRYH EFDIEKLRYH EFNPEKLRYH EFNPEKLRYH EFDIEKARYQ K-RY-  GRTIEGAELA QHGSQWKFDV	DEGL GLPGKLADCR SLPGKLADCQ GLPGKLADCQ SLPGKLADCQ -LPGKL-DC- KIVLMADADV KIILMADADV KIILMADADV SIIIMTDADV SIIIMTDADV RLILMTDADV M-DADV DTAKQFLLA. HTNAEQNLFE	S-KP- STDPRKSELY SNDPSKCEIF EKDPALSELY ERDPALSELY SRDPSISELY SRDPSISELY SRDPSISELY DGQHISTLLL DGQHISTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL MGAHIRTLLL SGAHIRTLL SGAHIRTLL SGAHIRTLLL SGAHIRTLL SGAHIRTLL SGAHIRTLLL SGAHIRTLLL SGAHIRTLLL SGAHIRTLS SGA SGAR SGAR SGAR SGAR SGAR SGAR SGAR	QTK-KL- # VVEGDSAGGS IVEGDSAGGS IVEGDSAGGS IVEGDSAGGS IVEGDSAGGT TVEGDSAGGT TLLFRFMRPL TFFFRMPL TFFFRMPL TFFFRFMPL TLLYRHMRPL TR	EV AKSGRDSMFQ AKSGRNPQYQ AMQGRDRKFQ AKQGRDRKFQ AKQGRDRKFQ AGRQ IENGHVFLAQ VEAGHVYLSR VERGYIYIAQ VEQGIYIAQ IEAGYVYAAQ -E-G HAS.P.IDLT FITGGEYRRI	# AILPLRGKII AILPLRGKIL AILPLKGKIL AILPLKGKIL AILPLKGKIL AILPLKGKIL AILPLKGKIL PPLYKLKWQR PPLYKLKWQR PPLYKLKWGR PPLYKVKKGK PPLYKVKY. PPLYVKVY. PPLY SSENADKAVA MDQYQISIAL	PA NVEKARIDRV NVEKARIDKI NVATLIT NVEKARFDKM NVEKSHFEQI NV SDPEFAYSDR DDFEYAYSDR QERYLKDELE QEQYIKDDEA SNKDLYM GNTYDAMDEA 
Consens SspGyrB SspGyrB HogGyrB HogGyrB HogGyrB Consens MTbGyrB SspGyrB HogGyrB EccGyrB MycGyrB HogGyrB SspGyrB NgoGyrB EccGyrB MycGyrB SspGyrB NgoGyrB EccGyrB MycGyrB HogGyrB HogGyrB HogGyrB HogGyrB HogGyrB	441 VNKAVSSAQA IRKSIQAATA TCKIVDAARA VGKIIDAARA ISKAVEAARA KA 531 LKNTEARRSS LQNTEVQALI LSSQEVATLI FNNVEISALV LENDEIRALI CLSSQEVATLI FNNVEISALV LENDEIRALI CALLEAGL ERDALVELGK KDQWLLGLAL DEQTVTRWVN QTDVQLEE. ERDRIIEEEC 	-N RIAARKAREL RVAARKARDL RQAARKAREI REAARRAREM RRRSQEAREL RKAAKQAEEL RA RALGTGI.HD SAFGTGV.HE .ALGAGIGKE TALGCGIGRD MAVGCGIK.P TAIGGGVG.D -AIG-G KAGKKINKED QNGKRI.KED QNGKRI.KED QNGKRI.KED WKQQHPNLKY NGNPT 	VRRKSATDIG TRRKGLLESA TRRKGLLESA TRRKSALDLA TRRKSPDSG FRK EFDIGKLRYH DFDIEKLRYH EFNPEKLRYH EFNPEKLRYH EFNPEKLRYH GRTIEGAELA QHGSQWKFDV	DEGL GLPGKLADCQ GLPGKLADCQ GLPGKLADCQ SLPGKLADCQ -LPGKL-DC- KIVLMADADV KIILMADADV KIIIMTDADV SIIIMTDADV SIIIMTDADV RLILMTDADV M-DADV DTAKQFLLA. HTNAEQNLFE	S-KP- STDPRKSELY SNDPSKCEIF EKDPALSELY ERDPALSELY SRDPSESELF DPE DGQHISTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL MTVIEQESRF PIVRVRTHGV 	QTK-KL- # VVEGDSAGGS IVEGDSAGGS IVEGDSAGGS IVEGDSAGGS IVEGDSAGGT TLLFRFMRPL TFFYRQMPDL TFFYRQMPDL TFFYRQMPDI TFFYRQMPDI TLLYRHMRPL TR VDELVLRAML DTD.YPLDHE	EV AKSGRDSMFQ AKSGRNPQYQ AMQGRDRKFQ AKQGRNRKNQ AKQGRDRKFQ AGRQ IENGHVFLAQ VEAGHVYLSR VERGHVYLAQ VERGHVYIAQ VEQGNIYIAQ VEQGNIYIAQ -E-G HAS.P.IDLT FITGGEYRRI	# AILPLRGKII AILPLRGKIL AILPLKGKIL AILPLKGKIL AILPLKGKIL AILPLKGKIL AILPLKGKIL PPLYKLKWQR PPLYKLKWQR PPLYKLKWGR PPLYKVKKGK PPLYKVKKGK PPLYKVKY. PPLYVRY.R PPLY SSENADKAVA MDQYQISIAL	PA NVEKARIDRV NVEKARIDKI NVATLIT NVEKARPDKM NVEKSHFEQI NV SDPEFAYSDR QERYLKDELE QEQYIKDDEA SNKDLYM GNTYDAMDEA  ELSGLLDEKE DGATLHTNAS
Consens SspGyrB SspGyrB NgoGyrB HlfGyrB Consens MTbGyrB SspGyrB NgoGyrB HlfGyrB Consens MTCGyrB SspGyrB NgoGyrB EcoGyrB NgoGyrB EcoGyrB NgoGyrB EcoGyrB NgoGyrB EcoGyrB MTCGyrB SspGyrB SspGyrB SspGyrB SspGyrB MycGyrB HlfGyrB Consens	441 VNKAVSSAQA IRKSIQAATA TCKIVDAARA VGKIIDAARA IRKTLLAQEA ISKAVEAARA ISKAVEAARA ISKAVEAARA ISKAVEAARA ISKAVEAARA S31 LKNTEARRSS LQNTEVQALI ISSQEVATLI FNNVEISALV LENDEIRALI 	-N RIAARKAREL RVAARKAREI RQAARKAREI REAARRAREM RRRSQEAREL RA RALGTGI.HD SAFGTGV.HE .ALGAGIGKE TALGCGIGRD MAVGCGIK.P TAIGGGVG.D -A1G-G KAGKKINKED QNGKRI.KED EKAKI.V.SD ALVSELNDKE WKQQHPNLKY NGNPT	VRRKSATDIG VRRKSATDIG TRRKGLLESA TRRKGLLESA TRRKSALDLA TRRKSPDSG TRRKSALEST -RK EFDIGKLRYH DFDIEKLRYH EFNPEKLRYH DFDLEKLRYH DFELEKLRYN EFDIEKARYQ K-RY-  GRTIEGAELA QHGSQWKFDV 	DEGL GLPGKLADCR SLPGKLADCQ GLPGKLADCQ SLPGKLADCQ -LPGKL-DC- KIVLMADADV KIILMADADV RIIIMTDADV SIIMTDADV KIIIMTDADV RLILMTDADV M-DADV DTAKQFLLA. HTNAEQNLFE	S-KP- STDPRKSELY SNDPSKCEIF EKDPALSELY ERDPALSELY TRDPSISELY DPE DGQHISTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL KTVIEQESRF PIVRVRTHGV	QTK-KL- # VVEGDSAGGS IVEGDSAGGS IVEGDSAGGS IVEGDSAGGS IVEGDSAGGT IVEGDSAGGT TLLFRFMRPL TFFYRQMPDI TFFYRQMPDI TFFFRFMYPL TLLYRHMRPL TR VDELVLRAML DTD.YPLDHE	EV AKSGRDSMFQ AKSGRNPQYQ AMQGRDRKFQ AKQGRDRKFQ AGRQ IENGHVFLAQ VEAGHVYLAQ VEAGHVYLAQ VERGHVYIAQ VEQGNIYIAQ IEAGYVYAAQ -E-G HAS.P.IDLT FITGGEYRRI	# AILPLRGKII AILPLRGKIL AILPLKGKIL AILPLKGKIL AILPLKGKIL AILP-GKI- PPLYKLKWQR PPLYKLKWQR PPLYKIKWGR PPLYKNYY.R PPLYKVKKGK PPLYKVKY. SSENADKAVA MDQYQISIAL	PA NVEKARIDRV NVEKARIDKI NVATLIT NVEKARTDKM NVEKSHFEQI NVEKHRLDRI NV SDPEFAYSDR DDFEYAYSDR QERYLKDELE QEQYIKDDEA SNKDLYM GNTYDAMDEA  ELSGLLDEKE DGATLHTNAS
Consens SspGyrB SspGyrB NgoGyrB EcoGyrB HlfGyrB Consens MTbGyrB SspGyrB EcoGyrB EcoGyrB HlfGyrB Consens MTbGyrB SspGyrB NgoGyrB EcoGyrB MycGyrB HlfGyrB Consens MTbGyrB SspGyrB NgoGyrB EcoGyrB MycGyrB HlfGyrB SspGyrB NgoGyrB	441 VNKAVSSAQA IRKSIQAATA TCKIVDAARA VGKIIDAARA IRKTLLAQEA ISKAVEAARA -KA 531 LKNTEARRSS LQNTEVQALI 	-N RIAARKAREL RVAARKAREI RQAARKAREI REAARRAREM RRRSQEAREL RA RALGTGI.HD SAFGTGV.HE ALGGGIGKE TALGCGIGRD MAVGCGIK.P TAIGGGVG.D -AIG-G KAGKKINKED QNGKRI.KED EKAKI.V.SD ALVSELNDKE WKQQHPNLKY NGNPT 	VRRKSATDIG TRRKGLLESA TRRKGLLESA TRRKGALDLA TRRKSALDLA TRRKSPFDSG TRRKSALEST -RRK EFDIGKLRYH DFDIEKLRYH EFNPEKLRYH EFNPEKLRYH DFELEKLRYN EFDIEKARYQ K-RY-  GRTIEGAELA QHGSQWKFDV  KITRKL.HGN	DEGL GLPGKLADCR SLPGKLADCQ GLPGKLADCQ SLPGKLADCQ -LPGKL-DC- KIVLMADADV KIILMADADV KIIIMTDADV SIIIMTDADV RLILMTDADV M-DADV  DTAKQFLLA. HTNAEQNLFE  VMVSYIEPKF	S-KP- STDPRKSELY SNDPSKCEIF EKDPALSELY ERDPALSELY TRDPSISELY SRDPSESELF DPE DGQHISTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL MG-HI-TLLL 	QTK-KL- # VVEGDSAGGS LVEGDSAGGS LVEGDSAGGS IVEGDSAGGS IVEGDSAGGT TVEGDSAGGT TLLFRFMRPL TFFFRMPL TFFFRMPL TFFFRFMPL TFFFRFMPL TLLYRHMRPL TR VDELVLRAML DTD.YPLDHE  QTAAALKG	EV AKSGRDSMFQ AKSGRNPQYQ AKQGRDRKFQ AKQGRDRKFQ AKQGRDRKFQ AGRQ IENGHVFLAQ VEAGHVYLSR VERGYIYIAQ VEQGNIYIAQ VEQGNIYIAQ IEAGYVYAAQ -E-G HAS.P.IDLT FITGGEYRRI 	# AILPLRGKII AILPLRGKIL AILPLKGKIL AILPLKGKIL AILPLKGKIL AILPLKGKIL AILPLKGKIL PPLYKLKWQR PPLYKLKWQR PPLYKLKWGR PPLYKVKKGK PPLYKVKY. PPLYVRY.R PPLY SSENADKAVA MDQYQISIAL  GENEYDADSF	PA NVEKARIDRV NVEKARIDKI NVATLIT NVEKARFDKM NVEKSHFEQI NV SDPEFAYSDR DDFEYAYSDR QERYLKDELE QEQYIKDDEA SNKDLYM GNTYDAMDEA  ELSGLLDEKE DGATLHTNAS  ETALDILMSV
MTbGyrB SspGyrB MycGyrB EcoGyrB MycGyrB HlfGyrB Consens MTbGyrB SspGyrB MycGyrB HlfGyrB Consens MTbGyrB SspGyrB NgoGyrB MycGyrB HlfGyrB Consens MTbGyrB SspGyrB HlfGyrB Consens MTbGyrB SspGyrB HlfGyrB Consens MTbGyrB SspGyrB HlfGyrB Consens	441 VNKAVSSAQA IRKSIQAATA TCKIVDAARA VGKIIDAARA ISKAVEAARA ISKAVEAARA ISKAVEAARA S31 LKNTEARRSS LQNTEVQALI LSSQEVATLI FNNVEISALV LENDEIRALI ERDGLLEAGL ERDALVELGK KDQWLLGLAL DEQTVTRWVN QTDVQLEE. ERDRIIEEC 	-N RIAARKAREL RVAARKARDL RQAARKAREI REAARRAREM RRRSQEAREL RKAAKQAEEL RA RALGTGI.HD SAFGTGV.HE .ALGAGIGKE TALGCGIGRD MAVGCGIK.P TAIGGGVG.D -AIG-G KAGKKINKED QNGKRI.KED EKAKI.V.SD ALVSELNDKE WKQQHPNLKY NGNPT 	VRRKSATDIG TRRKGLLESA TRRKGLLESA TRRKSALDJA TRRKSPFDSG RKKSALEST -RK EFDIGKLRYH DFDIEKLRYH EFNPEKLRYH EFNPEKLRYH OFELEKLRYN EFDIEKARYQ K-RY-  GRTIEGAELA QHGSQWKFDV  KITRKL.HGN KMINRMERRY	DEGL GLPGKLADCR SLPGKLADCQ GLPGKLADCQ SLPGKLADCQ -LPGKL-DC- KIVLMADADV KIILMADADV KIILMTDADV SIIMTDADV KIILMTDADV M-DADV DTAKQFLLA. HTNAEQNLFE 	S-KP- STDPRKSELY SNDPSKCEIF EKDPALSELY ERDPALSELY SRDPSISELY SRDPSESELF DPE DGQHISTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL DG-HI-TLLL  KTVIEQESRF FIVRVRTHGV  LNSKAYQTLT QPTLTEADLS	QTK-KL- # VVEGDSAGGS IVEGDSAGGS IVEGDSAGGS IVEGDSAGGS IVEGDSAGGS -VEGDSAGG- TLLFRFMRPL TFFFRFMRPL TFFFRFMRPL TFFFRFMPL TLLYRHMRPL TR 	EV AKSGRDSMFQ AKSGRNPQYQ AMQGRDRKFQ AKQGRDRKFQ AKQGRDRKFQ AGRQ IENGHVFLAQ VEAGHVYLSR VERGYIYIAQ VEQGHYYIAQ VEQGHYYIAQ IEAGYVYAAQ -E-G HAS.P.IDLT FITGGEYRRI  LVGEGAKLYK LUEEDAFIER	# AILPLRGKII AILPLRGKIL AILPLKGKIL AILPLKGKIL AILPLKGKIL AILPLKGKIL AILPLKGKIL AILPGKI- PPLYKLKWQR PPLYKLKWQR PPLYKLKWGR PPLYKVKKGK PPLYKVKKGK PPLYKVKY. PPLYVRVRY.R PPLY SSENADKAVA MDQYQISIAL  GENEYDADSF GERRQPVASF	PA NVEKARIDRV NVEKARIDKI NVATLIT NVEKARDKI NVEKHTLDRI NV SDPEFAYSDR DDFEYAYSDR QERYLKDELE QEQYIKDEA SNKDLYM GNTYDAMDEA 
MTbGyrB SspGyrB MycGyrB HlfGyrB Consens MTbGyrB SspGyrB NgoGyrB MycGyrB HlfGyrB Consens MTbGyrB SspGyrB HlfGyrB Consens MTbGyrB SspGyrB HlfGyrB Consens MTbGyrB SspGyrB HlfGyrB Consens MycGyrB HlfGyrB SspGyrB NgoGyrB EcoGyrB NgoGyrB SspGyrB NgoGyrB MycGyrB SspGyrB NgoGyrB MTbGyrB SspGyrB MycGyrB	441 VNKAVSSAQA IRKSIQAATA TCKIVDAARA VGKIIDAARA IRKTLLAQEA ISKAVEAARA KA 531 LKNTEARRSS LQNTEVQALI LSSQEVATLI FNNVEISALV LENDEIRALI 	-N RIAARKAREL RVAARKAREI RQAARKAREI REAARRAREM RRRSQEAREL RKAAKQAEEL RA RALGTGI.HD SAFGTGV.HE .ALGAGIGKE TALGCGIGRD MAVGCGIK.P TAIGGGVG.D -AIG-G KAGKKINKED QNGKRI.KED QNGKRI.KED QNGKRI.KED ALVSELNDKE WKQQHPNLKY NGNPT 	VRRKSATDIG TRRKGLLESA TRRKGLLESA TRRKSALDLA TRRKSALEST -RRK EFDIGKLRYH DFDIEKLRYH EFNPEKLRYH EFNPEKLRYH GFDIEKARYQ K-RY-  GRTIEGAELA QHGSQWKFDV  KITRKL.HGN KMINRMERRY	DEGL GLPGKLADCR SLPGKLADCQ GLPGKLADCQ SLPGKLADCQ -LPGKL-DC- KIVLMADADV KIILMADADV KIILMADADV KIIIMTDADV SIIIMTDADV CIIIMTDAV CIIIMTDAV CIIIMTDAV CIIIMTDAV CIIIMTDAV CIIIMTDAV CIIIMTDAV CIIIMTDAV CIIIMTDAV CIIIMTDAV CIIIMTDAV CIIIMTOAV CIIIM	S-KP- STDPRKSELY SNDPSKCEIF EKDPALSELY TRDPSISELY TRDPSISELY SRDPSESELF DPE DGQHISTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL CGAHIRTLLL SGAHIRTLLL CGAHIRTLL CGAHIRT CGAHIRTLL CGAHIRTL	QTK-KL- # VVEGDSAGGS IVEGDSAGGS IVEGDSAGGS IVEGDSAGGS IVEGDSAGGS -VEGDSAGG- TLLFRFMRPL TFFYRQMPDL TFFYRQMPDL TFFFRFMYPL TLLYRHMRPL TR VDELVLRAML DTD.YPLDHE  QTAAA.LKG CT.LGEKLRG	EV AKSGRDSMFQ AKSGRNPQYQ AMQGRDRKFQ AKQGRDRKFQ AGRQ IENGHVFLAQ VEAGHVYLSR VERGHVYLAQ VEQGNIYIAQ VEQGNIYIAQ VEQGNIYIAQ -E-G HAS.P.IDLT FITGGEYRRI 	# AILPLRGKII AILPLRGKIL AILPLKGKIL AILPLKGKIL AILPLKGKIL AILPLKGKIL AILP-GKI- PPLYKLKWQR PPLYKIKWGR PPLYKIKWGR PPLYKAKYGK PPLYKVKKGK PPLYKVKY.R PPLYV SSENADKAVA MDQYQISIAL  GENEYDADSF GERRQPVASF	PA NVEKARIDRV NVEKARIDKI NVATLIT NVEKARPDKM NVEKSHFEQI NV SDPEFAYSDR QERYLKDELE QEQYIKDDEA SNKDLYM GNTYDAMDEA  ELSGLLDEKE DGATLHTNAS  ETALDILMSV EQALDWLVKE
MTbGyrB SspGyrB NgoGyrB EcoGyrB MycGyrB HlfGyrB Consens MTbGyrB SspGyrB NgoGyrB EcoGyrB MycGyrB HlfGyrB Consens MTbGyrB SspGyrB NgoGyrB EcoGyrB MycGyrB HlfGyrB Consens MTbGyrB SspGyrB NgoGyrB HlfGyrB SspGyrB NgoGyrB HlfGyrB NgoGyrB HlfGyrB NgoGyrB HlfGyrB NgoGyrB HlfGyrB NgoGyrB HlfGyrB	441 VNKAVSSAQA IRKSIQAATA TCKIVDAARA VGKIIDAARA IRKTLLAQEA ISKAVEAARA ISKAVEAARA S31 LKNTEARRSS LQNTEVQALI LSSQEVATLI FNNVEISALV LENDEIRALI C21 ERDGLLEAGL ERDGLLEAGL ERDGLLEAGL ERDGLLEAGL ERDGLLEAGL ERDGLLEAGL ERDALVELGK KDQWLLGLAL DEQTVTRWVN QTDVQLEE. ERDRIIEEC 	-N RIAARKAREL RVAARKAREI RQAARKAREI REAARRAREM RRRSQEAREL RA RALGTGI.HD SAFGTGV.HE .ALGAGIGKE TALGCGIGRD MAVGCGIK.P TAIGGGVG.D -AIG-G KAGKKINKED QNGKRI.KED EKAKI.V.SD ALVSELNDKE WKQQHPNLKY NGNPT  H.EGHQFI KLVSEYNATQ	VRRKSATDIG TRRKGLLESA TRRKGLLESA TRRKSALDLA TRRKSPDSG TRRKSALEST -RRK EFDIGKLRYH DFDIEKLRYH EFNPEKLRYH EFNPEKLRYH DFELEKLRYN EFDIEKARYQ K-RY-  GRTIEGAELA QHGSQWKFDV  KITRKL.HGN KMINRMERRY	DEGL GLPGKLADCR SLPGKLADCQ GLPGKLADCQ SLPGKLADCQ -LPGKLADCQ -LPGKL-DC- KIVLMADADV KIIIMTDADV SIIIMTDADV SIIIMTDADV KIIIMTDADV CHILMTDADV M-DADV  DTAKQFLLA. HTNAEQNLFE  VMVSYIEPKF PKAMLKELIY	S-KP- STDPRKSELY SNDPSKCEIF EKDPALSELY ERDPALSELY TRDPSISELY DPE DGQHISTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL CGAHIRTLLL MTVIEQESRF PIVRVRTHGV  LNSKAYQTLT QPTLTEADLS 	QTK-KL- # VVEGDSAGGS IVEGDSAGGS IVEGDSAGGS IVEGDSAGGS IVEGDSAGGT IVEGDSAGGT TLLFRFMRPL TFFYRQMPDI TFFYRQMPDI TFFFRFMYPL TLLYRHMRPL TR VDELVLRAML DTD.YPLDHE  QTAAA.LKG CT.LGEKLRG	EV AKSGRDSMFQ AKSGRNPQYQ AMQGRDRKFQ AKQGRDRKFQ AGRQ IENGHVFLAQ VEAGHVYLAQ VEAGHVYLAQ VEQGNIYIAQ VEQGNIYIAQ IEAGYVYAAQ -E-G HAS.P.IDLT FITGGEYRRI  LVGEGAKLYK LLEEDAFIER	# AILPLRGKII AILPIRGKIL AILPLKGKIL AILPLKGKIL AILPLKGKIL AILP-GKI- PPLYKLKWQR PPLYKIKWGR PPLYKNKKGK PPLYKVKKGK PPLYKVKGK PPLYKVKGK PPLYKVKGK PPLYKVKGK PPLYKVKGK PPLYKVKGK PPLYKVKGK PPLYKVKGK PPLYKVSY. PPLY SSENADKAVA MDQYQISIAL  GENEYDADSF GERRQPVASF 	PA NVEKARIDRV NVEKARIDKI NVATLIT NVEKARFDKM NVEKSHFEQI NV SDPEFAYSDR DDFEYAYSDR QERYLKDELE QEQYIKDDEA SNKDLYM GNTYDAMDEA  ELSGLLDEKE DGATLHTNAS  ELSGLLDEKE DGATLHTNAS  ETALDILMSV EQALDWLVKE
Consens MTbGyrB SspGyrB NgoGyrB EcoGyrB MycGyrB HlfGyrB Consens MTbGyrB SspGyrB MycGyrB HlfGyrB Consens MTbGyrB SspGyrB MycGyrB HlfGyrB Consens MTbGyrB SspGyrB MycGyrB HlfGyrB Consens MTbGyrB SspGyrB HlfGyrB Consens MTbGyrB Consens MTCGYRB MYCGYRB MYC	441 VNKAVSSAQA IRKSIQAATA TCKIVDAARA VGKIIDAARA ISKAVEAARA ISKAVEAARA ISKAVEAARA S31 LKNTEARRSS LQNTEVQALI LSSQEVATLI FNNVEISALV LENDEIRALI 621 ERDGLLEAGL ERDALVELGK KDQWLGLAL DEQTVTRWVN QTDVQLEE. ERDRIIEEEC 711 	-N RIAARKAREL RVAARKARDL RQAARKAREI REAARRAREM RRRSQEAREL RA RALGTGI.HD SAFGTGV.HE .ALGAGIGKE TALGCGIGRD MAVGCGIK.P TAIGGCVG.D -AIG-G KAGKKINKED QNGKRI.KED EKAKI.V.SD ALVSELNDKE WKQQHPNLKY NGNPT  H.EGHQFI KLVSEYNATQ 	VRRKSATDIG TRRKGLLESA TRRKGLLESA TRRKSALDLA TRRKSPFDSG -RK EFDIGKLRYH DFDIEKLRYH EFNPEKLRYH EFNPEKLRYH EFDIEKARYQ K-RY-  GRTIEGAELA QHGSQWKFDV  KITRKL.HGN KMINRMERRY	DEGL GLPGKLADCR SLPGKLADCQ GLPGKLADCQ SLPGKLADCQ -LPGKL-DC- KIVLMADADV KIILMADADV KIILMADADV KIILMADADV KIILMADADV KIILMADADV M-DADV  DTAKQFLLA. HTNAEQNLFE  VMVSYIEPKF PKAMLKELIY 	S-KP- STDPRKSELY SNDPSKCEIF EKDPALSELY ERDPALSELY SRDPSISELY SRDPSESELF -DPE DGQHISTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL MGAHIRTLLL SCHI-TLLL KTVIEQESRF PIVRVRTHGV  LNSKAYQTLT QPTLTEADLS 	QTK-KL- # VVEGDSAGGS IVEGDSAGGS IVEGDSAGGS IVEGDSAGGS IVEGDSAGGT TVEGDSAGGT TLLFRFMRPL TFFFRFMRPL TFFFRFMPL TFFFRFMYPL TLLYRHMRPL TR VDELVLRAML DTD.YPLDHE  QTAAA.LKG CT.LGEKLRG	EV AKSGRDSMFQ AKSGRNPQYQ AMQGRDRKFQ AKQGRDRKFQ AKQGRDRKFQ AGRQ IENGHVFLAQ VEAGHVYLSR VERGYIYIAQ VERGHVYLAQ IEAGYVYAAQ -E-G HAS.P.IDLT FITGGEYRRI  LVGEGAKLYK LLEEDAFIER 	# AILPLRGKII AILPLRGKIL AILPLKGKIL AILPLKGKIL AILPLKGKIL AILPLKGKIL AILPLKGKIL PPLYKLKWQR PPLYKLKWQR PPLYKLKWGR PPLYKVKKGK PPLYKVKY. PPLYKVKY. PPLYKVKY. PPLYKVY. SSENADKAVA MDQYQISIAL 	PA NVEKARIDRV NVEKARIDKI NVATLIT NVEKARFDKM NVEKSHFEQI NV SDPEFAYSDR DDFEYAYSDR QERYLKDELE QEQYIKDEA SNKDLYM GNTYDAMDEA 
Consens SspGyrB SspGyrB HjfGyrB EcoGyrB MycGyrB HjfGyrB Consens MTbGyrB SspGyrB HjGyrB Consens MTbGyrB SspGyrB MycGyrB HjfGyrB Consens MTbGyrB SspGyrB MycGyrB HjfGyrB SspGyrB MycGyrB HjfGyrB SspGyrB HjfGyrB SspGyrB MycGyrB HjfGyrB Consens	441 VNKAVSSAQA IRKSIQAATA TCKIVDAARA VGKIIDAARA ISKAVEAARA ISKAVEAARA ISKAVEAARA ISKAVEAARA S31 LKNTEARRSS LQNTEVQALI LSSQEVATLI FNNVEISALV LENDEIRALI COLLEAGL ERDALVELGK KDQWLLGLAL DEQTVTRWVN QTDVQLEE. ERDRIIEEEC 	-N RIAARKAREL RVAARKARDL RQAARKAREI REAARRAREM RRRSQEAREL RKAAKQAEEL RA RALGTGI.HD SAFGTGV.HE .ALGAGIGKE TALGCGIGRD MAVGCGIK.P TAIGGGVG.D -AIG-G KAGKKINKED QNGKRI.KED QNGKRI.KED QNGKRI.KED WKQQHPNLKY NGNPT 	VRRKSATDIG TRRKGLLESA TRRKGLLESA TRRKSALDJA TRRKSPDSG EFDIGKLRYH DFDIEKLRYH EFNPEKLRYH EFNPEKLRYH GRTIEGAELA QHGSQWKFDV 	DEGL GLPGKLADCR SLPGKLADCQ GLPGKLADCQ SLPGKLADCQ -LPGKLADCC -LPGKL-DC- KIVLMADADV KIILMADADV KIIIMTDADV SIIMTDADV SIIMTDADV RLILMTDADV M-DADV DTAKQFLLA. HTNAEQNLFE  VMVSYIEPKF PKAMLKELIY	S-KP- STDPRKSELY SNDPSKCEIF EKDPALSELY ERDPALSELY SRDPSESELF DPE DGQHISTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL SGHIRTLLL SGHIRTLLL LG-HI-TLLL 	QTK-KL- # VVEGDSAGGS IVEGDSAGGS IVEGDSAGGS IVEGDSAGGS -VEGDSAGGT TLLFRFMRPL TFFYRQMPDL TFFYRQMPDL TFFYRQMPDI TFFYRQMPDI TFFYRQMPDI TFFYRQMPDI TFFYRQMPDI TFFYRQMPDI TFFYRQMPDI TFFYRQMPDI TFFYRQMPDI TFFYRQMPDI TLLYRHMRPL TR	EV AKSGRDSMFQ AKSGRNPQYQ AMQGRDRKFQ AKQGRNRKNQ AKQGRDRKFQ AGRQ IENGHVFLAQ VEAGHVYLSR VERGHVYLAQ VERGHVYLAQ VEQGNIYIAQ VEQGNIYIAQ VEQGNIYIAQ FE-G HAS.P.IDLT FITGGEYRRI  LVGEGAKLYK LLEEDAFIER	# AILPLRGKII AILPLRGKIL AILPLKGKIL AILPLKGKIL AILPLKGKIL AILPLKGKIL AILPLKGKIL PPLYKLKWQR PPLYKLKWQR PPLYKLKWGR PPLYKVKKGK PPLYKVKKGK PPLYKVKGK PPLYKVKGK PPLYKVKGK PPLYKVKGK SSENADKAVA MDQYQISIAL	PA NVEKARIDRV NVEKARIDKI NVATLIT NVEKARFDKM NVEKSHFEQI NV SDPEFAYSDR DDFEYAYSDR QERYLKDELE QEQYIKDEA SNKDLYM GNTYDAMDEA 
Consens SapGyrB SapGyrB HogogyrB HogogyrB HogogyrB MycGyrB HogogyrB MycGyrB HogogyrB HogogyrB MycGyrB HogogyrB HogogyrB HogogyrB HogogyrB HogogyrB HogogyrB HogogyrB HogogyrB HogogyrB HogogyrB HogogyrB MycGyrB SapGyrB SapGyrB SapGyrB Consens MTbGyrB SapGyrB Consens MTbGyrB SapGyrB Consens	441 VNKAVSSAQA IRKSIQAATA TCKIVDAARA VGKIIDAARA IRKTLLAQEA ISKAVEAARA ISKAVEAARA ISKAVEAARA ISKAVEAARA ISKAVEAARA S31 LKNTEARRSS LQNTEVQALI ISSQEVATLI FNNVEISALV LENDEIRALI 	-N RIAARKAREL RVAARKARDL RQAARKAREI REAARRAREM RRRSQEAREL RA RALGTGI.HD SAFGTGV.HE .ALGAGIGKE TALGCGIGRD MAVGCGIK.P TAIGGGVG.D -A1G-G KAGKKINKED QNGKRI.KED EKAKI.V.SD ALVSELNDKE WKQQHPNLKY NGNPT 	VRRKSATDIG TRRKGLLESA TRRKGLLESA TRRKSALDLA TRRKSALEST -RRK EFDIGKLRYH DFDIEKLRYH EFNPEKLRYH DFDIEKLRYH DFDIEKARYQ K-RY-  GRTIEGAELA QHGSQWKFDV  KITRKL.HGN KMINRMERRY	DEGL GLPGKLADCR SLPGKLADCQ GLPGKLADCQ SLPGKLADCQ -LPGKL-DC- KIVLMADADV KIILMADADV KIIIMTDADV SIIIMTDADV KIIIMTDADV CLILMTDAV CLILMTDAV	S-KP- STDPRKSELY SNDPSKCEIF EKDPALSELY ERDPALSELY TRDPSISELY DPE DGQHISTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL CGAHIRTLLL CGAHIRTLLL LGAHIRTLLL LGAHIRTLLL LGAHIRTLLL LGAHIRTLLL LGAHIRTLLL LSKAYQTLT QPTLTEADLS	QTK-KL- # VVEGDSAGGS IVEGDSAGGS IVEGDSAGGS IVEGDSAGGS IVEGDSAGGVEGDSAGG- TLLFRFMRPL TFFYRQMPDL TFFYRQMPDL TFFFRFMYPL TLLYRHMRPL TR	EV AKSGRDSMFQ AKSGRNPQYQ AMQGRDRKFQ AKQGRDRKFQ AGRQ IENGHVFLAQ VEAGHVYLAQ VEAGHVYLAQ VEQGNIYIAQ VEQGNIYIAQ VEQGNIYIAQ IEAGYVYAAQ -E-G HAS.P.IDLT FITGGEYRRI  LVGEGAKLYK LLEEDAFIER 	# AILPLRGKII AILPLRGKIL AILPLKGKIL AILPLKGKIL AILPLKGKIL AILPLKGKIL AILPLKGKIL AILPLKGKIF PPLYKLKWQR PPLYKLKWQR PPLYKLKWQR PPLYKVKKGK PPLYKVKKGK PPLYKVKKGK PPLYKVYY.R PPLYV SSENADKAVA MDQYQISIAL SSENADKAVA MDQYQISIAL SSENADKAVA MDQYQISIAL SENEYDADSF GERRQPVASF SELDV	PA NVEKARIDRV NVEKARIDKI NVATLIT NVEKARFDKM NVEKSHFEQI NV SDPEFAYSDR QERYLKDELE QEQYIKDDEA SNKDLYM GNTYDAMDEA  ELSGLLDEKE DGATLHTNAS  ETALDILMSV EQALDWLVKE 
Consens SspGyrB SspGyrB MycGyrB HlfGyrB Consens MTbGyrB SspGyrB NgoGyrB EcoGyrB HlfGyrB Consens MTbGyrB SspGyrB NgoGyrB EcoGyrB MycGyrB HlfGyrB Consens MTbGyrB SspGyrB NgoGyrB EcoGyrB MycGyrB HlfGyrB Consens MTbGyrB SspGyrB NgoGyrB EcoGyrB NgoGyrB EcoGyrB NgoGyrB EcoGyrB NgoGyrB EcoGyrB NgoGyrB Consens MTbGyrB SspGyrB NgoGyrB EcoGyrB NgoGyrB EcoGyrB NgoGyrB SspGyrB NgoGyrB EcoGyrB NgoGyrB EcoGyrB NgoGyrB SspGyrB NgoGyrB EcoGyrB NgoGyrB EcoGyrB NgoGyrB EcoGyrB NgoGyrB EcoGyrB NgoGyrB EcoGyrB NgoGyrB EcoGyrB NgoGyrB SspGyrB SspGyrB NgoGyrB SspGyrB NgoGyrB SspGyrB SspGyrB NgoGyrB SspGyrB NgoGyrB SspGyrB NgoGyrB SspGyrB NgoGyrB SspGyr	441 VNKAVSSAQA IRKSIQAATA TCKIVDAARA VGKIIDAARA IRKTLLAQEA ISKAVEAARA -KA 531 LKNTEARRSS LQNTEVQALI 	-N RIAARKAREL RVAARKAREI RQAARKAREI REAARRAREM RRRSQEAREL RA RALGTGI.HD SAFGTGV.HE .ALGAGIGKE TALGCGIGRD MAVGCGIK.P TAIGGGVG.D -AIG-G KAGKKINKED QNGKRI.KED EKAKI.V.SD ALVSELNDKE WKQQHPNLKY NGNPT  H.EGHQ.FI KUVSEYNATQ  KGLGEMDAKE	VRRKSATDIG TRRKGLLESA TRRKGLLESA TRRKSALDLA TRRKSPDSG TRRKSALEST -RRK EFDIGKLRYH DFDIEKLRYH EFNPEKLRYH EFNPEKLRYH DFLEKLRYH OFELEKLRYN EFDIEKARYQ K-RY-  GRTIEGAELA QHGSQWKFDV  KITRKL.HGN KMINRMERRY  LWETTMDPSV	DEGL GLPGKLADCR SLPGKLADCQ GLPGKLADCQ GLPGKLADCQ SLPGKLADCQ -LPGKL-DC- KIVLMADADV KIILMADADV KIILMADADV KIILMADADV KIILMADADV KIILMADADV KIILMADADV CIILMA	S-KP- STDPRKSELY SNDPSKCEIF EKDPALSELY ERDPALSELY TRDPSISELY SRDPSESELF DPE DGQHISTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL DG-HI-TLLL  KTVIEQESRF PIVRVRTHGV  LNSKAYQTLT QPTLTEADLS  AAAADELFSI	QTK-KL- # VVEGDSAGGS IVEGDSAGGS IVEGDSAGGS IVEGDSAGGS IVEGDSAGGT TUEGDSAGGT TLLFRFMRPL TFFFRMPL TFFFRMPL TFFFRFMYPL TR VDELVLRAML DTD.YPLDHE  QTAAA.LKG CT.LGEKLRG  LMGEDVDARR	EV AKSGRDSMFQ AKSGRNPQYQ AKQGRDRKFQ AKQGRDRKFQ AKQGRDRKFQ AFGRQ IENGHVFLAQ VEAGHVYLSR VERGYIYIAQ VEQGNIYIAQ VEQGNIYIAQ IEAGYVYAAQ -E-G HAS.P.IDLT FITGGEYRRI  LVGEGAKLYK LLEEDAFIER  SFITRNAKDV SFITRNAKDV	# AILPLRGKII AILPLRGKIL AILPLKGKIL AILPLKGKIL AILPLKGKIL AILPLKGKIL AILPLKGKIL PPLYKLKWQR PPLYKLKWQR PPLYKLKWGR PPLYKVKGK PPLYKVKGK SSENADKAVA MDQYQISIAL GENEYDADSF GERRQPVASF CHDI	PA NVEKARIDRV NVEKARIDKI NVATLIT NVEKARFDKM NVEKSHFEQI NV SDPEFAYSDR DDFEYAYSDR QERYLKDELE QEQYIKDDEA SNKDLYM GNTYDAMDEA  ELSGLLDEKE DGATLHTNAS  ETALDILMSV EQALDWLVKE
Consens SspGyrB SspGyrB HlfGyrB Consens MycGyrB HlfGyrB Consens MycGyrB EccGyrB MycGyrB HlfGyrB Consens MTbGyrB SspGyrB NgoGyrB HlfGyrB Consens MTbGyrB SspGyrB HlfGyrB Consens MTbGyrB SspGyrB HlfGyrB Consens MTbGyrB SspGyrB NgoGyrB HlfGyrB SspGyrB NgoGyrB MycGyrB HlfGyrB SspGyrB MycGyrB HlfGyrB SspGyrB MycGyrB HlfGyrB Consens	441 VNKAVSSAQA IRKSIQAATA TCKIVDAARA VGKIIDAARA ISKAVEAARA KA 531 LKNTEARRSS LQNTEVQALI 	-N RIAARKAREL RVAARKARDL RQAARKAREI REAARRAREM RRRSQEAREL RA RALGTGI.HD SAFGTGV.HE .ALGAGIGKE TALGCGIGRD MAVGCGIK.P TAIGGCG.D -AIG-G KAGKKINKED EKAKI.V.SD ALVSELNDKE WKQQHPNLKY NGNPT  H.EGHQ.FI KLVSEYNATQ  KGLGEMDAKE KGLGEMDAKE	VRRKSATDIG TRRKGLLESA TRRKGLLESA TRRKSALDJA TRRKSPDSG FRK EFDIGKLRYH DFDIEKLRYH EYNPDKLRYH EFNPEKLRYH EFDIEKARYQ K-RY-  GRTIEGAELA QHGSQWKFDV  KITRKL.HGN KMINRMERRY  LWETTMDPSV LRITTMDPSV LRITTMDPSV	DEGL GLPGKLADCR SLPGKLADCQ GLPGKLADCQ SLPGKLADCQ -LPGKL-DC- KIVLMADADV KIILMADADV KIILMADADV KIILMTDADV SIIMTDADV KIILMTDADV M-DADV  DTAKQFLLA. HTNAEQNLFE  WWSYIEPKF PKAMLKELIY  RVLRQVTLDD RVLRQVTLDD RVLRQVTLDD	S-KP- STDPRKSELY SNDPSKCEIF EKDPALSELY ERDPALSELY SRDPSISELY SRDPSESELF -DPE DGQHISTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL CGAHIRTLLL DGAHIRTLLL CGAHIRTLLL CGAHIRTLLL AAAADELFSI AAQADDLFSV ANAADELFSI	QTK-KL- # VVEGDSAGGS IVEGDSAGGS IVEGDSAGGS IVEGDSAGGS IVEGDSAGGT TLLFRFMRPL TFFFRFMRPL TFFFRFMPL TLLYRHMRPL TR	EV AKSGRDSMFQ AKSGRNPQYQ AKQGRDRKFQ AKQGRDRKFQ AKQGRDRKFQ AGRQ IENGHVFLAQ VEAGHVYLSR VERGYIYIAQ VEQGHVYLSR VERGYIYIAQ VEQGHVYLAQ IEAGYVYAAQ -E-G HAS.P.IDLT FITGGEYRRI  LVGEGAKLYK LLEEDAFIER  SFITRNAKDV SFIQRNAKDV SFIQRNAKDV	# AILPLRGKII AILPLRGKIL AILPLKGKIL AILPLKGKIL AILPLKGKIL AILPLKGKIL AILPLKGKIL AILPLKGKIL PPLYKLKWQR PPLYKLKWGR PPLYKLKWGR PPLYKVKKGK PPLYKVKGK PFLYKVKGK RFLDV RFLDV RFLDV RFLDV RFLDV	PA NVEKARIDRV NVEKARIDKI NVATLIT NVEKARDKM NVEKSHFEQI NV SDPEFAYSDR DDFEYAYSDR QERYLKDELE QEQYIKDDEA SNKDYM GNTYDAMDEA
Consens SapGyrB SapGyrB HogGyrB HogGyrB HogGyrB Consens MTbGyrB SapGyrB MycGyrB HogGyrB MycGyrB HogGyrB MycGyrB HogGyrB Consens MTbGyrB SapGyrB HogGyrB HogGyrB HogGyrB SapGyrB MycGyrB HogGyrB SapGyrB SapGyrB MycGyrB HogGyrB Consens MTbGyrB SapGyrB SapGyrB HogGyrB HogGyrB HogGyrB HogGyrB SapGyrB HogGyrB SapGyrB NagGyrB HogGyrB SapGyrB SapGyrB NagGyrB NagGyrB SapGyrB SapGyrB NagGyrB SapGyrB SapGyrB SapGyrB SapGyrB SapGyrB SapGyrB SapGyrB SapGyrB SapGyrB SapGyrB SapGyrB SapGyrB SapGyrB SapGyrB SapGyrB SapGyrB SapGyrB SapGyrB	441 VNKAVSSAQA IRKSIQAATA TCKIVDAARA VGKIIDAARA IRKTLLAQEA ISKAVEAARA KA 531 LKNTEARRSS LQNTEVQALI LSSQEVATLI FNNVEISALV LENDEIRALI 	-N RIAARKAREL RVAARKAREI RQAARKAREI REAARRAREM RRRSQEAREL RKAAKQAEEL RA RALGTGI.HD SAFGTGV.HE .ALGAGIGKE TALGCGIGRD MAVGCGIK.P TAIGGGVG.D -AIG-G KAGKKINKED QNGKRI.KED QNGKRI.KED WKQQHPNLKY NGNPT  KGLGEMDAKE KGLGEMDAKE KGLGEMNAEE KGLGEMNAEE	VRRKSATDIG TRRKGLLESA TRRKGLLESA TRRKSALDJA TRRKSALDJA TRRKSPDSG EFDIGKLRYH DFDIEKLRYH EFNPEKLRYH EFNPEKLRYH OFDIEKLRYH GRTIEGAELA QHGSQWKFDV 	DEGL GLPGKLADCR SLPGKLADCQ GLPGKLADCQ GLPGKLADCQ -LPGKL-DC- KIVLMADADV KIILMADADV KIILMADADV KIILMTDADV SIIMTDADV SIIMTDADV COMPARIANCE COMPAR	S-KP- STDPRKSELY SNDPSKCEIF EKDPALSELY ERDPALSELY SRDPSESELF DPE DGQHISTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL SGHITTLLL CGHI-TLLL CGHI-TLLL CGHI-TLLL CGHI-TLLL CGHI-TLLL CGHI-TLLL CGHI-TLLL CGHI-TLLL CGHIRTLL CGHIRTLL CGHIRTLL CGHIRTLL CGHIRTLL CGHIRTLL CGHIRTLL CGHIRTLL CGHIRT CGH	QTK-KL- # VVEGDSAGGS IVEGDSAGGS IVEGDSAGGS IVEGDSAGGS IVEGDSAGGT TLLFRFMRPL TFFYRQMPDL TFFYRQMPL TFFYRQM	EV AKSGRDSMFQ AKSGRNPQYQ AMQGRDRKFQ AKQGRNRKNQ AKQGRDRKFQ AGRQ IENGHVFLAQ VEAGHVYLSR VERGHVYLAQ VERGHVYIAQ VERGHVYIAQ VEQGNIYIAQ VEQGNIYIAQ VEQGNIYIAQ VEQGNIYIAQ VEQGNIYIAQ VEQGNIYIAQ SFITRNAKDY SFITRNAKDY SFIQRNAKDY AFIENNALIA	# AILPLRGKII AILPLRGKIL AILPLKGKIL AILPLKGKIL AILPLKGKIL AILPLKGKIL AILPLKGKIL AILPLKGKIL PPLYKLKWQR PPLYKLKWQR PPLYKVKKGK PPLYKVKKGK PPLYKVKKGK PPLYKVYY. PPLYV SSENADKAVA MDQYQISIAL CSENADKAVA MDQYDI	PA NVEKARIDRV NVEKARIDKI NVEKARIDKI NVEKARDKI NVEKHEDQI NVEKHELDRI NV SDPEFAYSDR QERYLKDELE QEQYIKDEA SNKDLYM GNTYDAMDEA 
Consens SspGyrB SspGyrB MycGyrB HlfGyrB Consens MTbGyrB SspGyrB MycGyrB HlfGyrB Consens MTbGyrB SspGyrB HlfGyrB Consens MTbGyrB SspGyrB MycGyrB HlfGyrB Consens MTbGyrB SspGyrB MycGyrB HlfGyrB Consens MTbGyrB SspGyrB MycGyrB HlfGyrB SspGyrB NgoGyrB EccGyrB MycGyrB SspGyrB NgoGyrB EccGyrB MycGyrB SspGyrB NgoGyrB EccGyrB MycGyrB SspGyrB NgoGyrB EccGyrB MycGyrB SspGyrB NgoGyrB EccGyrB MycGyrB SspGyrB NgoGyrB EccGyrB MycGyrB HlfGyrB Consens	441 VNKAVSSAQA IRKSIQAATA TCKIVDAARA VGKIIDAARA IRKTLLAQEA ISKAVEAARA ISKAVEARA IS	-N RIAARKAREL RVAARKAREI RQAARKAREI REAARRAREM RRRSQEAREL RA RALGTGI.HD SAFGTGV.HE .ALGAGIGKE TALGCGIGRD MAVGCGIK.P TAIGGGVG.D -AIG-G KAGKKINKED QNGKRI.KED QNGKRI.KED EKAKI.V.SD ALVSELNDKE WKQQHPNLKY NGNPT 	VRRKSATDIG TRRKGLLESA TRRKGLLESA TRRKSALDLA TRRKSPDSG TRRKSALEST -RRK EFDIGKLRYH DFDIEKLRYH DFDIEKLRYH DFDIEKLRYH DFDIEKLRYH CYNPDKLRYH DFELEKLRYN EFDIEKARYQ K-RY-  GRTIEGAELA QHGSQWKFDV  KITRKL.HGN KMINRMERRY  KITRKL.HGN KMINRMERY LRITTMDPSV LRITTMDPSV LWETTMDPSV LWETTMDPSV	DEGL GLPGKLADCR SLPGKLADCQ GLPGKLADCQ SLPGKLADCQ SLPGKLADCQ -LPGKL-DC- KIVLMADADV KIIIMTDADV KIIIMTDADV KIIIMTDADV KIIIMTDADV COMPARIAN KIIIMTDADV COMPARIAN KIIIMTDADV COMPARIAN COMPARIA	S-KP- STDPRKSELY SNDPSKCEIF EKDPALSELY ERDPALSELY TRDPSISELY SRDPSESELF DPE DGQHISTLLL DGAHIRTLL DGAHIRTLL DGAHIRTLL DGAHIRTLL DGAHIRTLL DGAHIRTLL DGAHIRTLL DGAHIRTLL DGAHIRTLL DGAHIRTLL DGAHIRTLL DGAHIRTLL DGAHIRTLL DGAHIRTLL DGAHIRTLL DGAHIRTLL DGAHIRTLL DGAHIRTLL DGAHIRT DGAHIRT DGAHIRT DGAHIRTLL DGAHIRT DGAHIR	QTK-KL- # VVEGDSAGGS IVEGDSAGGS IVEGDSAGGS IVEGDSAGGS IVEGDSAGGF -VEGDSAGG TLLFRFMRPL TFFYRQMPDL TFFYRQMPDL TFFFRFMYPL TLLYRHMRPL TR	EV AKSGRDSMFQ AKSGRNPQYQ AMQGRDRKFQ AKQGRNRKNQ AKQGRDRKFQ AGRQ IENGHVFLAQ VEAGHVYLAQ VEAGHVYIAQ VEQGNIYIAQ VEQGNIYIAQ VEQGNIYIAQ IEAGYVYAAQ -E-G HAS.P.IDLT FITGGEYRRI  LVGEGAKLYK LLEEDAFIER  SFITRNAKDV SFIQRNAKDV AFIENNALIA AFIENNALIA	# AILPLRGKII AILPIRGKIL AILPLKGKIL AILPLKGKIL AILPLKGKIL AILPLKGKIL AILPLKGKIL AILPLKGKIL PPLYKLKWQR PPLYKLKWQR PPLYKLKWQR PPLYKVKKGK PPLYKVKKGK PPLYKVKKGK PPLYKVYY. SSENADKAVA MDQYQISIAL GENEYDADSF GERRQPVASF RFLDV RFLDI QNIDA ANIDI VNIDI	PA NVEKARIDRV NVEKARIDKI NVATLIT NVEKARDKM NVEKSHFEQI NV SDPEFAYSDR QERYLKDELE QEQYIKDDEA SNKDLYM GNTYDAMDEA  ELSGLLDEKE DGATLHTNAS  ETALDILMSV EQALDWLVKE
Consens SspGyrB SspGyrB NgoGyrB EcoGyrB HlfGyrB Consens MTbGyrB SspGyrB EcoGyrB HlfGyrB Consens MTbGyrB SspGyrB NgoGyrB EcoGyrB MycGyrB HlfGyrB Consens MTbGyrB SspGyrB NgoGyrB EcoGyrB MycGyrB HlfGyrB Consens MTbGyrB SspGyrB NgoGyrB EcoGyrB MycGyrB HlfGyrB Consens MTbGyrB SspGyrB NgoGyrB EcoGyrB MycGyrB HlfGyrB Consens	441 VNKAVSSAQA IRKSIQAATA TCKIVDAARA VGKIIDAARA ISKAVEAARA KA 531 LKNTEARRSS LQNTEVQALI  LSSQEVATLI FNNVEISALV LENDEIRALI ERDGLLEAGL ERDGLLEAGL ERDALVELGK KDQWLGLAL DEQTVTRWVN QTDVQLEE. ERDRIIEEEC 711  A. ALE. RIEG APALAGEALE  801 GIQRY SRRGLSIQRY SRRGLSIQRY NLQRY	-N RIAARKAREL RVAARKARDL RQAARKAREI RQAARKAREI REAARRAREM RRRSQEAREL RA RALGTGI.HD SAFGTGV.HE .ALGAGIGKE TALGCGIGRD MAVGCGIK.P TAIGGCG.D -AIG-G KAGKKINKED QNGKRI.KED EKAKI.V.SD ALVSELNDKE WKQQHPNLKY NGNPT 	VRRKSATDIG TRRKGLLESA TRRKGLLESA TRRKSALDLA TRRKSPDSG -RRK EFDIGKLRYH EFNPEKLRYH EFNPEKLRYH EFNPEKLRYH GFDIEKARYQ K-RY-  GRTIEGAELA QHGSQWKFDV  KITRKL.HGN KMINRMERRY  LWETTMDPSV LRITTMDPTV LWETTMDPTV LWETTMDPSS MDPKV	DEGL GLPGKLADCR SLPGKLADCQ GLPGKLADCQ SLPGKLADCQ -LPGKL-DC- KIVLMADADV KIILMADADV KIILMADADV KIILMADADV KIILMADADV KIILMADADV KIILMADADV KIILMADADV  DTAKQFLLA. HTNAEQNLFE  WVSYIEPKF PKAMLKELIY  RVLRQVTLDD RRLLKVTVED RRLLKVTVED RRLLKVTVED	S-KP- STDPRKSELY SNDPSKCEIF EKDPALSELY ERDPALSELY TRDPSISELY SRDPSESELF DPE DGQHISTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL SCHI-TLL SCHI-TLL	QTK-KL- # VVEGDSAGGS IVEGDSAGGS IVEGDSAGGS IVEGDSAGGS IVEGDSAGGT TUVEGDSAGGT TUVEGDSAGGT TFLFRFMRPL TFFYRQMPDL TFFYRQMPDL TFFYRQMPDL TFFYRQMPDL TFFYRQMPDL TFFYRQMPDL TFFYRQMPLI TFFYRQMPLI TFFYRQMPLI TFFYRQMPLI TFFYRQMPLI TFFYRQMPLI TFFYRQMPLI TFFYRQMPLI TFFYRQMPLI TFFYRQMPLI TFFYRQMPLI TFFYRQMPLI TFFYRQMPLI TCLYRMRPL TCLYRMPL TCLYRMRPL TCLYRMPL TCL	EV AKSGRDSMFQ AKSGRNPQYQ AKQGRDRKFQ AKQGRDRKFQ AKQGRDRKFQ AKQGRDKFLQ VEQGDVYLAQ VEQGNIYIAQ VEQGNIYIAQ VEQGNIYIAQ VEQGNIYIAQ VEQGNIYIAQ IEAGYVYAAQ -E-G  HAS.P.IDLT FITGGEYRRI  SFITRNAKDV SFIQRNAKDV AFIENNALIA AFIEENALKA EFIEQNARMV	AILPLRGKII AILPLRGKIL AILPLRGKIL AILPLKGKIL AILPLKGKIL AILPLKGKIL AILPLKGKIL AILPLKGKIL PPLYKLKWQR PPLYKLKWGR PPLYKLKWGR PPLYKVKKGK PPLYKVKKGK PPLYKVSY PPLYKVY SC PPLYKVK SC PPLYKVY SC PPLYKV SC PPLYKV SC PPLYKV SC PPLYKV SC PPLYKV SC PPLYKV SC PPLYKV SC PPLYKV SC PPLYKV SC PPLY SC SC SC SC SC SC SC SC SC SC SC SC SC	PA NVEKARIDRV NVEKARIDKI NVATLIT NVEKARFDKM NVEKSHFEQI NV SDPEFAYSDR DDFEYAYSDR QERYLKDELE QEQYIKDEA SNKDLYM GNTYDAMDEA 
Consens SspGyrB SspGyrB HjfGyrB EcoGyrB MycGyrB HjfGyrB Consens MTbGyrB EcoGyrB MycGyrB HjfGyrB Consens MTbGyrB SspGyrB NgoGyrB HjfGyrB Consens MTbGyrB SspGyrB NgoGyrB HjfGyrB SspGyrB NgoGyrB HjfGyrB Consens MTbGyrB SspGyrB NgoGyrB HjfGyrB Consens MTbGyrB SspGyrB HjfGyrB Consens MTbGyrB SspGyrB HjfGyrB Consens MTbGyrB HjfGyrB SspGyrB HjfGyrB SspGyrB HjfGyrB SspGyrB HjfGyrB SspGyrB HjfGyrB SspGyrB HjfGyrB SspGyrB HjfGyrB SspGyrB HjfGyrB SspGyrB HjfGyrB SspGyrB HjfGyrB SspGyrB HjfGyrB SspGyrB HjfGyrB SspGyrB HjfGyrB	441 VNKAVSSAQA IRKSIQAATA TCKIVDAARA VGKIIDAARA ISKAVEAARA ISKAVEAARA ISKAVEAARA ISKAVEAARA ISKAVEAARA S31 LKNTEARRSS LQNTEVQALI LSSQEVATLI FNNVEISALV LENDEIRALI CONTEVQALI CONTEVQALI ERDGLLEAGL ERDGLLEAGL ERDGLLEAGL ERDGLLEAGL ERDGLLEAGL ERDGLLEAGL ERDGLLEAGL ERDGLLEAGL ERDGLLEAGL ERDGLLEAGL ERDGLLEAGL CONTEV TI A. ALE. RIEG APALAGEALE CONTEV SRRGLSIQRY CONTEV CONTEX CONTEV CONTEV CONTEV CONTEV CONTEV CONTEV CONTEV CONTEX CONTEV CO	-N RIAARKAREL RVAARKARDL RQAARKAREI REAARRAREM RRRSQEAREL RA RALGTGI.HD SAFGTGV.HE .ALGAGIGKE TALGCGIGRD MAVGCGIK.P TAIGGVG.D -AIG-G KAGKKINKED QNGKRI.KED EKAKI.V.SD ALVSELNDKE WKQQHPNLKY NGNPT  H.EGHQ.FI KLVSEYNATQ  KGLGEMNPEQ KGLGEMNPEQ KGLGEMNPEQ KGLGEMNPEQ	VRRKSATDIG TRRKGLLESA TRRKGLLESA TRRKSALDJA TRRKSPDSG EFDIGKLRYH DFDIEKLRYH EFNPEKLRYH EFNPEKLRYH OFDIEKLRYH GRTIEGAELA QHGSQWKFDV 	DEGL GLPGKLADCR SLPGKLADCQ GLPGKLADCQ SLPGKLADCQ CLPGKLADCC -LPGKL-DC- KIVLMADADV KIILMADADV KIILMADADV KIILMTDADV KIILMTDADV COMPARIAN	S-KP- STDPRKSELY SNDPSKCEIF EKDPALSELY ERDPALSELY SRDPSISELY SRDPSESELF DPE DGQHISTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL DGAHIRTLLL DG-HI-TLLL MINITUR STREES STRE	QTK-KL- # VVEGDSAGGS IVEGDSAGGS IVEGDSAGGS IVEGDSAGGS IVEGDSAGGT TLLFRFMRPL TFFFRFMRPL TFFFRFMYPL TLLYRHMRPL TR	EV AKSGRDSMFQ AKSGRNPQYQ AKQGRNRKPQ AKQGRDRKFQ AKQGRDRKFQ AGRQ IENGHVFLAQ VEAGHVYLSR VERGYIYIAQ VEQGHYYIAQ VEQGHYYIAQ VEQGHYYIAQ VEQGHYYIAQ IEAGYVYAAQ -E-G  LVGEGAKLYK LLEEDAFIER  SFITRNAKDV SFIQRNAKDV SFIQRNAKDV AFIENNALIA AFIEENALKA EFIEQNARNV QFIKDHANDA	# AILPLRGKII AILPLRGKIL AILPLKGKIL AILPLKGKIL AILPLKGKIL AILPLKGKIL AILPLKGKIL AILPLKGKIL PPLYKLKWQR PPLYKLKWGR PPLYKVKKGK PPLYKVKKGK PPLYKVKGK PPLYKVGK KOUN	PA NVEKARIDRV NVEKARIDKI NVATLIT NVEKARDKM NVEKSHFEQI NV SDPEFAYSDR DDFEYAYSDR QERYLKDELE QEQYIKDEA SNKDYM GNTYDAMDEA 

FIG. 2. Alignment of the deduced amino acid sequence of *M. tuberculosis gyrB* (MTbGyrB) with the sequences from *S. sphaeroides* (SspGyrB), *Neisseria gonorrhoeae* (NgoGyrB), *E. coli* (EcoGyrB), *Mycoplasma pneumoniae* (MycGyrB), and *Haloferax* sp. (HlfGyrB) (GenBank accession numbers Z17305, M59981, X00870, X53555, and M38373, respectively). Identical amino acids are listed on the consensus line (Consens). Marked are those positions in gyrB where mutations have been associated with resistance to coumarin (\*) or quinolone drugs (#) in *E. coli* and other bacteria (5, 34).

MTDTTLAPDD ...SLDRIEPV DIEQEMQRSY IDYAMSVIVG RALPEVRDGL KPVHRRVLYA MFDSGFRPDR SHAKSARSVA ETMGNYHPHG MTbGyrA .....MSEQ .. NTPQVREI NISQEMRTSF LDYAMSVIVS RALPDVRDGL KPVHRRILYA MNDLGMTSDK PYKKSARIVG EVIGKYHPHG BsuGyrA SauGyrA ......MAEL .. POSRINER NITSEMRESF LDYAMSVIVA RALPDVRDGL KPVHRRILYG LNEQGMTPDK SYKKSARIVG DVMGKYHPHG EcoGyrA .....MSDL ...A.REITPV NIEEELKSSY LDYAMSVIVG RALPDVRDGL KPVHRRVLYA MNVLGNDWNK AYKKSARVVG DVIGKYHPHG .....MENI FSKDSDIELV DIENSIKSSY LDYSMSVIIG RALPDARDGL KPVHRRILYA MQNDEAKSRT DFVKSARIVG AVIGRYHPHG CjeGyrA Consens \*\* \* MTDGYIA DASIYDSLVR MAQPWSLRYP LVDGQGNFGS PDNDPPAAMR YTEARLTPLA MEMLREIDEE TVDFIPNYDG RVQEPTVLPS RFPNLLANGS DSAVYESMVR MAQDFNYRYM LVDGHGNFGS VDGDSAAAMR YTEARMSKIS MEILRDITKD TIDYQDNYDG SEREPVVMPS RFPNLLVNGA BsuGyrA SauGyrA DSSIYEAMVR MAQDFSYRYP LVDGQGNFGS MDGDGAAAMR YTEARMTKIT LELLRDINKD TIDFIDNYDG NEREPSVLPA RFPNLLANGA DSAVYDTIVR MAQPFSLRYM LVDGQGNFGS IDGDSAAAMR YTEIRLAKIA HELMADLEKE TVDFVDNYDG TEKIPDVMPT KIPNLLVNGS EcoGyrA DTAVYDALVR MAQDFSMRYP SITGQGNFGS IDGDSAAAMR YTEAKMSKLS HELLKDIDKD TVDFVPNYDG SESEPDVLPS RVPNLLLNGS CjeGyrA D---Y---VR MAQ----RY- ---G-GNFGS -D-D--AAMR YTE----- -E----- T-D---NYDG ----P-V-P- --PNLL-NG-Consens 171 GGIAVGMATN IPPHNLRELA DAVFWALENH DADEEETLAA VMGRVKGPDF PTAGLIVGSQ GTADAYKTGR GSIRMRGVVE VE.EDSRGRT MTbGvrA AGIAVGMATN IPPHOLGEII DGVLAVSENP DI....TIPE LMEVIPGPDF PTAGQILGRS GIRKAYESGR GSITIRAKAE IE.QTSSGKE BsuGvrA SGIAVGMATN IPPHNLTELI NGVLSLSKNP DI....SIAE LMEDIEGPDF PTAGLILGKS GIRRAYETGR GSIQMRSRAV IE.ERGGGRQ SauGyrA SGIAVGMATN IPPHNLTEVI NGCLAYIDDE DI....SIEG LMEHIPGPDF PTAAIINGRR GIEEAYRTGR GKVYIRARAE VEVDAKTGRE EcoGyrA SGIAVGMATN IPPHSLNELI DGLLYLLDNK DA....SLEE IMOFIKGPDF PTGGIIYGKK GIIEAYRTGR GRVKVRAKTH IE..KKTNKD CjeGyrA -GIAVGMATN IPPH-L-E- ------ D------ -M----GPDF PT---I-G-- G---AY--GR G----R---- -E-----Consens 261 SLVITELPYQ VNHDNFITSI AEQVRDGKLA GISNIEDQSS DRVGLRIVIE IKRDAVAKVV INNLYKHTQL QTSFGANMLA IVDGVPRTLR MTbGvrA RIIVTELPYQ VNKAKLIEKI ADLVRDKKIE GITDLRDE.S DRTGMRIVIE IRRDANANVI LNNLYKQTAL QTSFGINLLA LVDGQPKVLT BsuGyrA RIVYTEIPFO VNKARMIEKI AELVRDKKID GITDLRDETS LRTGVRVVID VRKDANASVI LNNLYKOTPL OTSFGVNMIA LVNGRPKLIN SauGvrA TIIVHEIPYQ VNKARLIEKI AELVKEKRVE GISALRDE.S DKDGMRIVIE VKRDAVGEVV LNNLYSQTQL QVSFGINMVA LHHGQPKIMN EcoGyrA VIVIDELPYO TNKARLIEOI AELVKEROIE GISEVRDE.S NKEGIRVVIE LKREAMSEIV LNNLFKSTTM ESTFGVIMLA IHNKEPKIFS CieGvrA -----E-P-Q -N----I--I A--V------ GI----D--S ---C-R-VI- -----A----- -NNL---T-- ---FG----A -----P----Consens 351 MTbGvrA LDOLIRYYVD HOLDVIVRRT TYRLRKANER AHILRGLVKA LDALDEVIAL IRASETVDIA RAGLIE......... LKQCLEHYLD HQKVVIRRRT AYELRKAEAR AHILEGLRVA LDHLDAVISL IRNSQTAEIA RTGLIEQ...... BsuGyrA LKEALVHYLE HOKTVVRRRT OYNLRKAKDR AHILEGLRIA LDHIDEIIST IRESDTDKVA MESLOOR...... SauGvrA LKDIIAAFVR HRREVVTRRT IFELRKARDR AHIPEALAAA LANIDPIIEL IRHAPTPAEA KTALVANPWO LGNVAAMLER AGDDAARPEW EcoGyrA LLELLNLFLT HRKTVIIRRT IFELQKARAR AHILEGLKIA LDNIDEVIAL IKNSSDNNTA RDSLVAK... CjeGyrA L----- H---V--RRT ---L-KA--R AHI---L--A L---D--I-- I-----A ---L----- ------- ------Consens 441 ..... LLDIDEIQAQ AILDMQLRRL AALERQRIID DLAKIEAEIA DLEDILAKPE RQRGIVRDEL AEIVDRHGDD RRTRIIAAD. MTbGyrA BsuGyrA SauGyrA LEPEFGVRDG LYYLTEQQAQ AILDLRLQKL TGLEHEKLLD EYKELLDQIA ELLRILGSAD RLMEVIREEL ELVREQFGDK RRTEI.TANS EcoGyrA CjeGyrA Consens ------R-E-QA- AILD--L--L --LE------ -----I- -L--IL---- -----R-EL ------- R-T-I-----531 GDVSDEDLIA REDVVVTITE TGYAKRTKTD LYRSQKRGGK GVQGAGLKQD DIVAHFFVCS THDLILFFTT QGRVYRAKAY DLPEASRTAR MTbGyrA ETIEDEDLIE RENIVVTLTH NGYVKRLPAS TYRSQKRGGK GVQGMGTNED DFVEHLISTS THDTILFFSN KGKVYRAKGY EIPEYGRTAK BsuGyrA EDLEDEDLIP EEQIVITLSH NNYIKRLPVS TYRAQNRGGR GVQGMNTLEE DFVSQLVTLS THDHVLFFTN KGRVYKLKGY EVPELSRQSK SauGyrA ADINLEDLIT QEDVVVTLSH QGYVKYQPLS EYEAQRRGGK GKSAARIKEE DFIDRLLVAN THDHILCFSS RGRVYSMKVY QLPEATRGAR EcoGyrA DDIDIEDLIP NENMVVTITH RGYIKRVPSK QYEKQKRGGK GKLAVTTYDD DFIESFFTAN THDTLMFVTD RGQLYWLKVY KIPEGSRTAK CjeGyrA Consens -----EDLI- -E--V-T--- --Y-K----- -Y--Q-RGG- G------ D------ THD------ -G--Y--K-Y --PE--R---621 GQHVANLLAF QPEERIAQVI QIRGY.TDAP YLVLATRNGL VKKSKLTDFD SNRSGGIVAV NLRDNDELVG AVLCSAGDD. ..... MTbGyrA GIPIINLLEV EKGEWINAII PVTEFNAE.L YLFFTTKHGV SKRTSLSQFA NIRNNGLIAL SLREDDELMG VRLTDGTKQ. ...... GIPVVNAIEL GNDEVISTMI AVKDLESEDN FLVFATKRGV VKRSALSNFS RINRNGKIAI SFREDDELIA VRLTSGQED. ..... BsuGyrA SauGyrA GRPIVNLLPL EQDERITAIL PVTEFE.EGV KVFMATANGT VKKTVLTEFN RLRTAGKVAI KLVDGDELIG VDLTSGEDE. EcoGyrA CjeGyrA GKAVVNLINL QAEEKIMAII PTTDFD.ESK SLCFFTKNGI VKRTNLSEYQ NIRSVGVRAI NLDENDELVT AIIVQRDEDE IFATGGEENL Consens G----N-----G--A- -----DEL-- ----711 MTbGyrA BsuGyrA .....ILIGT SHASLIRFPE ST..LRPLGR TATGVKGITL REGDEVVGLD VAHANSVDEV LVVTENGYGK .....VMLFS AEGKVVRFRE SS..VRAMGC NTTGVRGIRL GEGDKVVSLI VPRGDG..AI LTATQNGYGK SauGyrA EcoGyrA ENQEIENLDD ENLENEESVS TQGKMLFAVT KKGMCIKFPL AK..VREIGR VSRGVTAIKF KEKNDELVGA VVIENDEQEI LSISAKGIGK CjeGyrA ----F-- ----F-- -----R--G- ---GV------- L----G--K Consens RTAIEEYPVQ GRGGKGVLTV MYDRRRGRLV GALIVDDDSE LYAVTSGGGV IRTAARQVRK AGRQTKGVRL MNLGEGDTLL AIARNAEESG MTbGyrA RTPAEEYRTQ SRGGKGLKTA KITENNGQLV AVKATKGEED LMIITASGVL IRMDINDISI TGRVTQGVRL IRMAEEEHVA TVALVEKNEE BsuGyrA RTPVNDYRLS NRGGKGIKTA TITERNGNVV CITTVTGEED LMIVTNAGVI IRLDVADISQ NGRAAQGVRL IRLGDDQFVS TVAKVKEDAD SauGyrA RTAVAEYPTK SRATKGVISI KVTERNGLVV GAVQVDDCDQ IMMITDAGTL VRTRVSEISI VGRNTQGVIL IRTAEDENVV GLQRVAEPVD EcoGyrA RTNAGEYRLQ SRGGKGVICM KLTEKTKDLI SVVIVDETMD LMALTSSGKM IRVDMQSIRK AGRNTSGVIV VNVENDE.VV SIAKCPKEEN CjeGyrA Consens 891 MTbGyrA DDNAVDANGA DQTGN..... BsuGyrA DENEEEQEEV ..... . EVNEDEQSTV SEDGTEQORE AVVNDETPGN AIHTEVIDSE ENDEDGRIEV RODFMDRVEE DIQQSSDEDE E SauGyrA EcoGyrA EEDLDTIDGS AAEGDDEIAP EVDVDDEPEE E...... CjeGyrA DEDELSDENF GLDLQ..... \_\_\_\_\_ Consens

FIG. 3. Alignment of the deduced amino acid sequence of *M. tuberculosis gyrA* (MTbGyrA) with the sequences from *B. subtilis* (BsuGyrA), *S. aureus* (SauGyrA), *E. coli* (EcoGyrA), and *Campylobacter jejuni* (CjeGyrA) (modified from reference 31). Identical amino acids are listed on the consensus line (Consens). Codons where mutations in *M. tuberculosis* or other bacteria have been associated with resistance are marked with an asterisk. Tyrosine-122 (#), the active site which links to DNA, was found to be fully conserved among the tested species.



FIG. 4. Nucleotide sequence of the gyrA FQ resistance region amplified with primers GyrA1 and GyrA2 (underlined) corresponding to nucleotides 78 to 397 in *M. tuberculosis gyrA*. The deduced amino acid sequence is shown together with mutations in codons 88, 90, 91, and 94 (boldface type), which were found to be associated with ciprofloxacin resistance. Codon 95 may display a serine or a threonine in ciprofloxacin-susceptible strains. An asterisk indicates two additional positions were mutations associated with FQ resistance have been reported in other bacteria. The complete nucleotide sequences of gyrA and gyrB are deposited in GenBank under accession number L27512.

in the gyrA genes of other ciprofloxacin-resistant bacteria (8, 19, 22, 31, 33). Similarly, the regions of gyrB where mutations have been described in *E. coli* (5, 34) and which lead to resistance to coumarin compounds (coumermycin A1, novobiocin, and clorobiocin) and to the quinolone compound nalidixic acid were found to be highly conserved among *M. tuberculosis* and other bacteria.

We found gyrA mutations in all strains for which the ciprofloxacin MIC was >2  $\mu$ g/ml, a level which appears to be useful in the evaluation of clinical isolates and which has been proposed as a cutoff for clinical resistance (9). The development of acquired resistance has been described after single-drug therapy of the rapidly growing mycobacterium *M. fortuitum*, and resistant strains have been isolated in vitro from *M. fortuitum* and *M. smegmatis* at frequencies of  $10^{-5}$  to  $10^{-7}$  (22a, 29). Spontaneously resistant mutants of *M. bovis* of BCG and *M. tuberculosis* H37Ra, H37Rv, and Erdman have been



FIG. 5. Evaluation by PCR-SSCP of the FQ resistance region. The control strains *M. tuberculosis* H37Rv (lanes A), *M. bovis* BCG (lanes B), and *M. tuberculosis* Erdman (lane C) represent the two SSCP polymorphisms for FQ-susceptible strains. FQ-resistant laboratory mutants are strains of BCG with a Val-90 mutation (lane 1) and an Asn-94 mutation (lane 2) and a strain of *M. tuberculosis* H37Ra displaying a Cys-88 mutation (lane 3). An isolate from a patient (lane 4) had a mixed pattern, reflecting the presence of a mixed population: a Val-90 mutant and a susceptible organism. The other clinical isolates (lanes 5 to 7) contained the mutations Pro-91, His-94, and Asn-94, respectively.

isolated at frequencies ranging from  $10^{-6}$  to  $10^{-8}$ . These frequencies appear to be slightly higher than those seen in the enteric bacteria (11).

Are these the only mutations in these strains involved in their resistance to ciprofloxacin? The initial level of ciprofloxacin at which the resistant mutants were selected, 0.5 to 2.0  $\mu$ g/ml, is only two to eight times the reported MIC range (0.25 to 1.0 µg/ml) for M. tuberculosis (9). Primary mutants resistant to more than 2 µg of ciprofloxacin per ml were not obtained in the initial selection. Difficulties in obtaining high-level resistance in a single step and the need for repeated subculturing in low concentrations of FQs for the selection of high-level FQ-resistant strains have been described for other bacteria (1, 12, 18). In S. aureus, resistance to quinolones is achieved in two sequential steps: a first event resulting in a moderate increase in MICs and a second step in which a mutation in gyrA takes place (12). Accumulation of additional mutations in the FQ resistance region of gyrA may lead to even higher levels of resistance (10). Thus, in vitro data suggest that more than one step is required for the development of high-level resistance, and such multistep development of resistance may occur during therapy (21). We did not determine the MICs for our preliminary mutants and we did not look for gyrA mutations in our preliminary mutants prior to replating of the mutants in higher concentrations of ciprofloxacin. Those mutants are no longer available for testing, and thus, we cannot rule out the possibility that, as in S. aureus, our method would first select for mutations involving drug uptake or other resistance mechanisms which result in a lower level of resistance (27, 32) and that the gyrA mutations were a subsequent event (12). It is also possible that the M. bovis BCG and M. tuberculosis mutants or clinical isolates contained other mutations in their DNA gyrase genes. However, we screened by SSCP the region where mutations that confer quinolone resistance most commonly arise in E. coli gyrB (34) in 18 M. tuberculosis isolates (ciprofloxacin MIC range, 0.25 to 8 µg/ml) and found no polymorphisms suggestive of the presence of mutations.

The technique used in the present study to amplify and analyze the presumed FQ-binding region, PCR-SSCP, is easy and rapid and should be useful in estimating whether clinical *M. tuberculosis* isolates are resistant to FQs. One of the advantages of this method is that material can be used from minimally grown cultures and that SSCP can be performed in an automated, nonradioactive fashion (24). In addition, it is possible to amplify and establish the gyrA genotypes of mycobacteria directly from sputum specimens, in which significant numbers of acid-fast bacilli are present (24). At least 10 SSCP patterns were identified (2 among susceptible strains and 8 among FQ-resistant isolates), and the identities of the mutations were established by DNA sequencing. No FQ-resistant isolates with a wild-type SSCP pattern were encountered.

Will the FQs be useful in treating MDR-TB? Although we found that the tested organisms developed a relatively high frequency of resistance developed in vitro, the frequency of emergence of resistant strains should be lower in the clinical setting, where the FQs will be part of a multidrug regimen. However, the use of FQs in a regimen that is failing or in noncompliant patients will facilitate the emergence of resistant strains. This is illustrated by two of the clinical isolates investigated here: MDR-TB strains from New York City, which shared the same rifampin resistance rpoB mutation (23) and appeared to be clonal on the basis of fingerprint analysis (28). However, they were found to have different gyrA mutations, which suggests that both of the patients from whom the two isolates were obtained were infected with the same MDR-TB organism and, later on, developed FQ resistance independently.

May specific mutations predict the level of resistance? In *E. coli*, different *gyrA* substitutions are associated with different ciprofloxacin MICs (33). This could be the case in *M. tuberculosis*, because our preliminary assessment of clinical isolates identified some mutations which were associated with ciprofloxacin MICs of 4 to 8  $\mu$ g/ml, and others were associated with MICs of >8  $\mu$ g/ml. It is also conceivable that not all mutations will result in resistance to different compounds from the same family; *M. tuberculosis* displays discrepant susceptibility patterns to rifabutin and rifampin that are dependent on the type and location of the mutation within the rifampin resistance region of *rpoB* (2). However, because resistance to FQs results from more than one mutational event, it may not be possible to establish a firm relationship between specific *gyrA* mutations, ciprofloxacin MICs, and variable susceptibilities to other FQs.

The knowledge of the nucleotide and amino acid sequences of the gyrases and the delineation of the antibiotic resistance regions (to quinolones and coumarin drugs) provided by the results of the present study will serve as useful bases for the assessment of the mechanisms of action and the molecular basis of resistance to new compounds of those families or other drugs which putatively target the gyrase.

## ACKNOWLEDGMENTS

We thank T. Bodmer for susceptibility testing; M. Calcutt, J. Colston, E. Cundliffe, J. Dale, H. Schrempf, and A. Thiara for kindly providing probes; L. Pascopella for the genomic library; Sang Jae Kim from the Korean Institute of Tuberculosis for providing ciprofloxacinresistant strains; P. Imboden for help with sequence data; and Carmen Rios, Mary Avalle, and Amanda Brown for collaboration.

This investigation received financial support from the STD3 program of the European Community (grant ERB3504PL921516), the Institut Pasteur, the Association Française Raoul Follereau, CONICIT (grant S1-2519), the National Institutes of Health (grant GM 21960), and the Swiss National Science Foundation (grant 32-32406.91).

#### REFERENCES

- Barry, A. L., and R. N. Jones. 1984. Cross-resistance among cinoxacin, ciprofloxacin, DJ-6783, enoxacin, nalidixic acid, and oxolinic acid after in vitro selection of resistant populations. Antimicrob. Agents Chemother. 25:775–777.
- Bodmer, T., G. Zürcher, P. Imboden, and A. Telenti. Submitted for publication.

- Calcutt, M. J., and F. J. Schmidt. 1992. Conserved gene arrangement in the origin region of the *Streptomyces coelicolor* chromosome. J. Bacteriol. 174:3220–3226.
- Chen, C. H., J. F. Shih, P. J. Lindholm-Levy, and L. B. Heifets. 1989. Minimal inhibitory concentrations of rifabutin, ciprofloxacin, and ofloxacin against Mycobacterium tuberculosis in patients in Taiwan. Am. Rev. Respir. Dis. 140:987–989.
- Contreras, A., and A. Maxwell. 1992. gyrB mutations which confer coumarin resistance also affect DNA supercoiling and ATP hydrolysis by *Escherichia coli* DNA gyrase. Mol. Microbiol. 6:1617–1624.
- 6. Davis, E. O., S. G. Sedgwick, and M. J. Colston. 1991. Novel structure of the *recA* locus of *Mycobacterium tuberculosis* implies processing of the gene product. J. Bacteriol. 173:5653–5662.
- Fischl, M. A., G. L. Daikos, R. B. Uttamchadani, R. B. Poblete, J. N. Moreno, R. R. Reyes, A. M. Boota, L. M. Thompson, S. A. Cleary, S. A. Oldham, M. J. Saldana, and S. Lai. 1992. Clinical presentation and outcome of patients with HIV infection and tuberculosis caused by multiple drug resistant bacilli. Ann. Intern. Med. 117:184–190.
- Goswitz, J. J., K. E. Willard, C. E. Fasching, and L. R. Peterson. 1992. Detection of gyrA gene mutations associated with ciprofloxacin resistance in methicillin resistant *Staphylococcus aureus*: analysis by polymerase chain reaction and direct DNA sequencing. Antimicrob. Agents Chemother. 36:1166–1169.
- Heifets, L. B., and P. J. Lindholm-Levy. 1990. MICs and MBCs of Win 57273 against Mycobacterium avium and Mycobacterium tuberculosis. Antimicrob. Agents Chemother. 34:770-774.
- Heisig, P., H. Schedletzky, and H. Falkenstein-Paul. 1993. Mutations in the gyrA gene of a highly fluoroquinolone-resistant clinical isolate of *Escherichia coli*. Antimicrob. Agents Chemother. 37: 696–701.
- Hirai, K., H. Aoyoma, S. Suzue, T. Irikura, S. Iyobe, and S. Mitsuhashi. 1986. Isolation and characterization of norfloxacinresistant mutants of *Escherichia coli* K-12. Antimicrob. Agents Chemother. 30:248–253.
- Hori, S., Y. Ohshita, Y. Utsui, and K. Hiramatsu. 1993. Sequential acquisition of norfloxacin and ofloxacin resistance by methicillinresistant and -susceptible *Staphylococcus aureus*. Antimicrob. Agents Chemother. 37:2278–2284.
- Huang, W. M. 1993. Multiple gyrase-like genes in eubacteria, p. 37-46. In T. Andoh, H. Ideda, and M. Oguro (ed.), Molecular biology of DNA topoisomerases and its application to chemotherapy. CRC Press, Inc., Boca Raton, Fla.
- 14. Imboden, P., S. Cole, T. Bodmer, and A. Telenti. 1993. Detection of rifampicin resistance mutations in *Mycobacterium tuberculosis* and *Mycobacterium leprae*, p. 519–526. In D. H. Persing, T. F. Smith, F. C. Tenover, and T. J. White (ed.), Diagnostic molecular microbiology. American Society for Microbiology, Washington, D.C.
- Jacobs, W. R., G. V. Kalpana, J. D. Cirillo, L. Pascopella, S. B. Snapper, R. A. Udani, W. Jones, R. G. Barletta, and B. R. Bloom. 1991. Genetic systems in mycobacteria. Methods Enzymol. 204: 537-555.
- Kato, J., Y. Nishimura, R. Imamura, H. Niki, S. Hiraga, and H. Suzuki. 1990. New topoisomerase essential for chromosome segregation in *E. coli*. Cell 63:393–404.
- Lalande, V., A. Truffot-Pernot, A. Paccaly-Moulin, and J. Grosset. 1993. Powerful activity of sparfloxacin (AT 4140) against Mycobacterium tuberculosis in mice. Antimicrob. Agents Chemother. 37:407-413.
- Limb, D. I., D. J. W. Dabbs, and R. C. Spencer. 1987. In vitro selection of bacteria resistant to the 4-quinolone agents. J. Antimicrob. Chemother. 19:65–71.
- 19. Oram, M., and L. M. Fisher. 1991. 4-Quinolone resistance mutations in the DNA gyrase of *Escherichia coli* clinical isolates identified using the polymerase chain reaction. Antimicrob. Agents Chemother. 35:387–389.
- 19a.Philipp, W., et al. Unpublished data.
- Siddiqi, S., J. Libonati, and G. Middlebrook. 1981. Evaluation of a rapid method for drug susceptibility testing in *Mycobacterium* tuberculosis. J. Clin. Microbiol. 13:908–912.
- 21. Silver, L. L., and K. A. Bostian. 1993. Discovery and development of new antibiotics: the problem of antibiotic resistance. Antimi-

crob. Agents Chemother. 37:377-383.

- 22. Sreedharan, S., M. Oram, B. Jensen, L. Petersen, and L. Fisher. 1990. DNA gyrase gyrA mutations in ciprofloxacin-resistant strains of *Staphylococcus aureus*: close similarity with quinolone resistant mutations in *Escherichia coli*. J. Bacteriol. 172:7260–7262.
- 22a. Takiff, H. Unpublished data.
- Telenti, A., P. Imboden, F. Marchesi, D. Lowrie, S. Cole, M. J. Colston, L. Matter, K. Schopfer, and T. Bodmer. 1993. Detection of rifampicin-resistance mutations in *Mycobacterium tuberculosis*. Lancet 341:647-650.
- Telenti, A., P. Imboden, F. Marchesi, T. Schmidheini, and T. Bodmer. 1993. Direct, automated detection of rifampin-resistant mutants of *Mycobacterium tuberculosis* by PCR and single-strand conformation polymorphism. Antimicrob. Agents Chemother. 37: 2054-2058.
- Telenti, A., F. Marchesi, M. Balz, F. Bally, E. Böttger, and T. Bodmer. 1993. Rapid differentiation of mycobacteria to the species level by polymerase chain reaction and restriction enzyme analysis. J. Clin. Microbiol. 31:175–178.
- Thiara, A. S., and E. Cundliffe. 1988. Cloning and characterization of a DNA gyrase B gene from *Streptomyces sphaeroides* that confers resistance to novobiocin. EMBO J. 7:2255-2259.
- Trucksis, M., J. S. Wolfson, and D. C. Hooper. 1991. A novel locus conferring fluoroquinolone resistance in *Staphylococcus aureus*. J. Bacteriol. 173:5854–5860.
- Van Embden, J. D. A., M. D. Cave, J. T. Crawford, J. W. Dale, K. D. Eisenach, B. Gicquel, P. Hermans, C. Martin, R. McAdam, T. M. Shinnick, and P. M. Small. 1993. Strain identification of

Mycobacterium tuberculosis by DNA fingerprinting—recommendations for a standardized methodology. J. Clin. Microbiol. 31: 406–409.

- 29. Wallace, R. J., G. Bedsole, G. Sumter, C. V. Sanders, L. C. Steele, B. A. Brown, J. Smith, and D. R. Graham. 1990. Activities of ciprofloxacin and ofloxacin against rapidly growing mycobacteria with demonstration of acquired resistance following single-drug therapy. Antimicrob. Agents Chemother. 34:65-70.
- Wang, J. C. 1985. DNA topoisomerases. Annu. Rev. Biochem. 54:665–697.
- 31. Wang, Y., W. M. Huang, and D. E. Taylor. 1993. Cloning and nucleotide sequence of the *Campylobacter jejuni gyrA* gene and characterization of quinolone resistance mutations. Antimicrob. Agents Chemother. 37:457-463.
- 32. Wolfson, J. S., and D. C. Hooper. 1989. Bacterial resistance to quinolones. Rev. Infect. Dis. 11(Suppl. 5):S960-S968.
- 33. Yoshida, H., M. Bogaki, M. Nakamura, and S. Nakamura. 1990. Quinolone resistance-determining region in the DNA gyrase gyrA gene of *Escherichia coli*. Antimicrob. Agents Chemother. 34:1271– 1272.
- 34. Yoshida, H., M. Bogaki, M. Nakamura, L. M. Yamanaka, and S. Nakamura. 1991. Quinolone resistance-determining region in the DNA gyrase gyrB gene of *Escherichia coli*. Antimicrob. Agents Chemother. 35:1647–1650.
- Zakrzewska-Czerwinska, J., and H. Schrempf. 1992. Characterization of an autonomously replicating region from the *Streptomyces lividans* chromosome. J. Bacteriol. 174:2688–2693.