BMC Evolutionary Biology



Open Access Research article

Molecular evolution of adenylating domain of aminoadipate reductase

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Published: 8 May 2003

BMC Evolutionary Biology 2003, 3:9

This article is available from: http://www.biomedcentral.com/1471-2148/3/9

Received: 26 November 2002 Accepted: 8 May 2003

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Abstract

Background: Aminoadipate reductase (Lys2) is a fungal-specific protein. This enzyme contains an adenylating domain. A similar primary structure can be found in some bacterial antibiotic/peptide synthetases. In this study, we aimed to determine which bacterial adenylating domain is most closely related to Lys2. In addition, we analyzed the substitution rate of the adenylating domainencoding region.

Results: Some bacterial proteins contain more than two similar sequences to that of the adenylating domain of Lys2. We compared 67 amino acid sequences from 37 bacterial and 10 fungal proteins. Phylogenetic trees revealed that the lys2 genes are monophyletic; on the other hand, bacterial antibiotic/peptide synthase genes were not found to be monophyletic. Comparative phylogenetic studies among closely related fungal lys2 genes showed that the rate of insertion/ deletion in these genes was lower and the nucleotide substitution rate was higher than that in the internal transcribed spacer (ITS) regions.

Conclusions: The lys2 gene is one of the most useful tools for revealing the phylogenetic relationships among fungi, due to its low insertion/deletion rate and its high substitution rate. Lys2 is most closely related to certain bacterial antibiotic/peptide synthetases, but a common ancestor of Lys2 and these synthetases evolutionarily branched off in the distant past.

Background

Not only fungi, but also certain prokaryotes synthesize lysine through the 2-aminoadipate pathway [1–3]. However, the prokaryotic pathway is not identical to that of fungi. The fungal process required to synthesize lysine from 2-aminoadipate differs from that of prokaryotes [4]. The first step of this fungal-specific pathway is the reduction of 2-aminoadipate.

Aminoadipate reductase converts 2-aminoadipate to 2aminoadipate 6-semialdehyde via an adenosylated derivative. In Saccharomyces cerevisiae, this reaction requires

Mg²⁺ and the participation of the products of two genes, lys2 and lys5 [5]. Recently, it has been shown that aminoadipate reductase is encoded by only lys2, and that the Lys5 protein appears to be a specific phosphopantetheinyl transferase for Lys2, converting the inactive apo-Lys2 to the active holo-Lys2 [6,7].

The lys2 gene is a fungal-specific gene and generally appears to be present in a single copy in the genome. The Lys2 protein has no extensive homologous protein in eukaryotes, with the exception of fungi, but it does possess similarity to some bacterial antibiotic/peptide synthetases [4,8–10]. Recently, *Drosophila* and mouse were found to have the analogue of Lys2, which function under degradation of lysine [11]. However, Lys2 is more similar bacterial antibiotic/peptide synthetases than the animal proteins. Lys2 has an adenylating, a peptidyl carrier, and a reductive domain. This protein has twelve conserved motifs. The adenylating domain contains nine conserved motifs [12]. In this study, we aimed to reveal which bacterial adenylating domain is the most closely related to Lys2.

In addition, in order to determine the substitution rate of *lys2*, we compared the *lys2* sequences from closely related fungi. In this study, we sequenced *lys2* fragments [13] and compared them among black-koji molds of the *Aspergillus niger* group.

Results and Discussion

The deduced amino acid sequences (each 343 amino-acids long) from Aspergillus awamori IAM 2112, A. awamori IAM 2299, A. awamori IAM 2300, A. saitoi IAM 2210, A. saitoi IAM 2215, A. saitoi IAM 14608, A. saitoi var. kagoshimaensis IAM 2190, and A. saitoi var. kagoshimaensis IAM 2191 were identical. Those from A. usamii IAM 2185 and IAM 2186 differed from the other black-koji molds by one amino acid. The nucleotide sequences from A. awamori IAM 2112, IAM 2299, and IAM 2300 were identical. Those from A. saitoi IAM 2210 and IAM 2215 were identical. Those from A. saitoi var. kagoshimaensis IAM 2190 and IAM 2191 were identical. Those from A. usamii IAM 2185 and IAM 2186 were identical. Aspergillus awamori's sequence was 10 nucleotides different from that of A. saitoi

IAM 2210 and IAM 2215, and 40 nucleotides different from that of *A. usamii*.

We deposited the sequences in the DNA Data Bank of Japan under accession numbers AB079758, AB085587, AB079759, AB085588, AB085589, AB079760, AB085590, AB079761, and AB085591 for A. awamori IAM 2299, A. awamori IAM 2300, A. saitoi IAM 2210, A. saitoi IAM 2215, A. saitoi IAM 14608, A. saitoi var. kagoshimaensis IAM 2190, A. saitoi var. kagoshimaensis IAM 2191, A. usamii IAM 2185, and A. usamii IAM 2186, respectively.

Comparisons between *A. awamori* and *Penicillium chrysogenum* (Table 1) and between *A. awamori* and *A. fumigatus* (Table 2) showed that the rate of insertion/deletion in *lys2* was lower and the nucleotide substitution rate was higher than that in ITS regions. We therefore believe that *lys2* is a more powerful tool to reveal phylogenetic relationships among fungi than are the ITS regions.

The result of the homology search using BLAST showed that Lys2 had a more similar sequence to that of certain bacterial antibiotic/peptide synthetases than did any other existing proteins. In addition, some bacterial antibiotic/peptide synthetases were shown to contain more than two homologous regions. For example, RS05859 in *Ralstonia solanacearum* GMI1000 has five homologous regions. Therefore, we obtained 57 amino acid sequences, with a value of $E < 10^{-25}$, from 39 proteins (see Materials and Methods).

Table 1: Comparison between Aspergillus awamori and Penicillium chrysogenum

Region	Alignment length (A)	Insertions/Deletions (B)	Substitutions (C)	B/A	C/(A-B)
18S rDNA	1734	3	25	1.7 × 10 ⁻³	1.4 × 10 ⁻²
ITSI	185	10	34	5.4×10^{-2}	1.9 × 10 ⁻¹
ITS2	169	5	22	3.0×10^{-2}	1.3 × 10 ⁻¹
lys2	1032	9	242	8.7×10^{-3}	2.4 × 10 ⁻¹

Table 2: Comparison between Aspergillus awamori and A. fumigatus

Region	Alignment length (A)	Insertions/Deletions (B)	Substitutions (C)	B/A	C/(A-B)
18S rDNA	1733	0	П	0	6.3 × 10 ⁻³
ITSI	188	6	23	3.2 × 10 ⁻²	1.3 × 10 ⁻¹
ITS2	170	4	22	2.4×10^{-2}	1.3 × 10 ⁻¹
lys2	1032	0	202	0	2.0 × 10 ⁻¹

The phylogenetic tree (Fig. 1ab) shows that the adenylating domains from some bacterial antibiotic/peptide synthetases are distributed quite widely, and that duplications and/or horizontal transfers occurred many times. For example, *Anabaena* sp. PCC 7120 has 12 similar sequences within itself. In this tree, these 12 sequences were distributed among at least 6 groups. The present findings indicate that duplication and/or horizontal transfer occurred in the genome of *Anabaena* sp. PCC 7120. On the other hand, the adenylating domains from Lys2 formed a monophyletic cluster. However, the neighbor-joining tree presented here did not clarify which bacterial domain was most closely related to that of Lys2.

In order to determine which bacterial domain was most closely related to that of Lys2, a maximum likelihood analysis using PHYLIP version 3.6 [14] was carried out. We selected 27 amino acid sequences from the 67 sequences used in the neighbor-joining analysis. The alignment used in maximum likelihood analysis is shown in Fig. 2. The phylogenetic tree (Fig. 3) indicates that a protein (AGR L 2311) from *Agrobacterium tumefaciens* is most closely related to a common ancestor of Lys2, but this result had only weak bootstrap support (17%). In the bootstrap consensus tree (Fig. 3), the branch points at the early stage of evolution are very weak support. Animals and plants have no Lys2. If the common ancestor of eukaryotes had a similar protein, the other eukaryotes except for fungi had lost it.

Conclusions

This study indicated that Lys2 is more closely related to certain bacterial antibiotic/peptide synthetases than it is to any other known proteins. However, in the distant past, a common ancestor of Lys2 branched off from the bacterial antibiotic/peptide synthetase. This study did not find evidence for a direct horizontal transfer (i.e., at least not a recent horizontal transfer) between bacteria and a common ancestor of fungi. The *lys2* gene has been inherited during fungal evolution. On the other hand, in the course of bacterial evolution, the duplication and/or horizontal transfer have occurred.

Materials and Methods

In this study, we used *Aspergillus awamori* IAM 2299, *A. awamori* IAM 2300, *A. saitoi* IAM 2210, *A. saitoi* IAM 2215, *A. saitoi* IAM 14608, *A. saitoi* var. *kagoshimaensis* IAM 2190, *A. saitoi* var. *kagoshimaensis* IAM 2191, *A. usamii* IAM 2185, and *A. usamii* IAM 2186. Potato dextrose agar was used for the cultivation. Genomic DNA isolation, DNA amplification, and the sequencing of *lys2* fragments were performed according to the method of An *et al.* [13].

We compared the nuclear small subunit rRNA genes (18S rDNAs), ITS1 regions, ITS2 regions, and *lys2* genes be-

tween A. awamori and Penicillium chrysogenum and between A. awamori and A. fumigatus. The following nucleotide-sequence accession numbers were used: D63695, A. awamori 18S rDNA [15]; U03518, A. awamori ITS1 [16]; U03519, A. awamori ITS2 [16]; AB076077, A. awamori lys2 [13]; M55628, P. chrysogenum 18S rDNA; AJ270768, P. chrysogenum ITS1 and ITS2 [17]; Y13967, P. chrysogenum lys2 [18]; AB008401, A. fumigatus 18S rDNA [19]; AF455542, A. fumigatus ITS1 and ITS2. The preliminary sequence of lys2 was obtained from The Institute for Genomic Research website at http://www.tigr.org.

We performed a homology search using BLAST [20] with the parameter values given in the Kyoto Encyclopedia of Genes and Genomes [21]. The query amino acid sequence was a fragment of Saitoella complicata Lys2 [13]. In this study, we phylogenetically analyzed 57 amino acid sequences (all sequences had a value of $E < 10^{-25}$, according to the BLAST search results) separately from those of fungi. Multiple alignment was created using CLUSTAL W [22] among the 57 high-scoring sequences and those of 10 fungal Lys2 proteins. A neighbor-joining phylogenetic tree was constructed using MEGA version 2.1 [23] with 1,000 bootstrap replicates. Based on this tree, we selected 27 amino acid sequences for a maximum likelihood analysis, which was performed using PHYLIP version 3.6 [14]. We used three programs (consense, proml, and seqboot) for constructing phylogenetic tree with 100 bootstrap replicates.

The protein names used in this study are AGR_L_2311, Agrobacterium tumefaciens C58 (Cereon) AGR_L_2311; all1647, Anabaena sp. PCC 7120 peptide synthetase; all2642, Anabaena sp. PCC 7120 multifunctional peptide synthetase; all2643, Anabaena sp. PCC 7120 microcystin synthetase B; all2644, Anabaena sp. PCC 7120 peptide synthetase; all2645, Anabaena sp. PCC 7120 peptide synthetase; all2647, Anabaena sp. PCC 7120 microcystin synthetase B; all2648, Anabaena sp. PCC 7120 peptide synthetase; all2649, Anabaena sp. PCC 7120 probable non-ribosomal peptide synthetase; all1695, Anabaena sp. PCC 7120 probable peptide synthetase; Atu3682, Agrobacterium tumefaciens C58 (U.Washington/Dupont) non-ribosomal peptide synthetase; b0586, Escherichia coli K-12 MG1655 enterobactin synthetase component F; BG10168, Bacillus subtilis 168 surfactin synthetase subunit 1; BG10169, Bacillus subtilis 168 surfactin synthetase subunit 2; BG10170, Bacillus subtilis 168 surfactin synthetase subunit 3; BG10970, Bacillus subtilis 168 peptide synthetase; BG10971, Bacillus subtilis 168 peptide synthetase; BG10972, Bacillus subtilis 168 peptide synthetase; BG11243, Bacillus subtilis 168 probable non-ribosomal peptide synthetase; BG11961, Bacillus subtilis 168 peptide synthetase; ECs0625, Escherichia coli O157:H7 Sakai enterobactin synthetase component EntF; JW0578, Es-

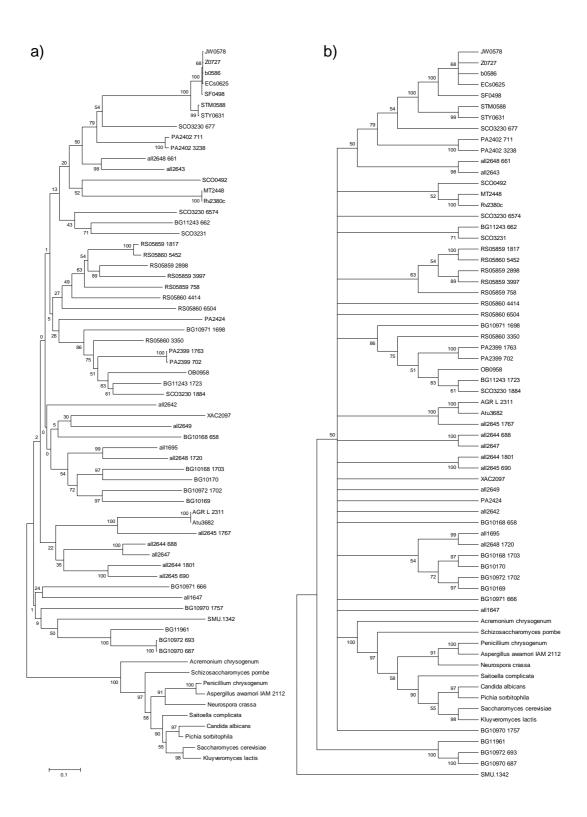


Figure I

a) Phylogenetic relationships among 67 amino acid sequences from the adenylating domain of Lys2 and bacterial antibiotic/peptide synthetase. A total of 176 amino acid sites were considered without gap regions in alignment. b) The bootstrap consensus tree. The cut-off value for consensus was 50%. Protein names were shown in Materials and Methods.

BG11961									
B 0000	ELFWWPY	AGASVYLLPQ	GGEKEPEV	IAKAIEEQKI	TAMHFVPSML	HAFLEQIKYR	SVPIKTNRLK	RVFSGG	EQLGTHLVSR
Rv2380c	EIFGTLA	CGARMVIPRP	GGLTDI GY	LTALLRDEGI	TAMHEVPSLL	GLFLSLPG	VSQWRTLQ	RVPIGG	EPLPGEVADK
SC00492			GGERDP HH						
a112643			GGHQDP NY						
RS05859 18	ELFWPLL	AGARLVMARP	EGHKAPAY	LAATIEQAGI	TTLHFVPSML	QLFLDQVEAG	RCQGLR	RMLCSG	EALPHALQOR
DC05950 75	DVWVPLL	NCCDVVTTDO	DTV/I AD ED	EANAI DECOV	SVI WMTAGOE	HUANDEI TO	VEDAL D	VI MVCC	DVI DDATTAM
	LL								
RS05860 65	KNILGPLL	AGGRI HLAGP	FVPDA	LVAQIRREGI	THINLSPSAF	HALIDAAGAE	GLGGLR	RVVLGG	EPIQPARLQG
PA2424			-GQWGAEE						
XAC2097	LYLPLL	CGGTTELLPE	-RDEIEAL	LKRVCADQPL	CLVKITPAHL	DVLTQQLAAC	GGIPSVS	LFVVGG	EALHASIVKR
BG11243 66	ELYLPLI	SGAOTVTAKK	FTTRFPQA	LAGMIENEDI	NTMOATPTI W	HAI VTSFPFK	I RGI R	VI VGGF	AL PSGLLOFI
3003230_03	EMWVPLV	SUGIVVVAPP	G-HLDPAA	TIDETIMENT	TAIRLIAGEE	KVVAEEAPEC	FAGVK	EVLIGG	DVVSPAAVAK
a112644_68	EIFLPLI	VGACLVLVER	EVTLDGER	LAQAIAQHQI	TFMQATPATW	RLLLASGWEG	K-QDL	KILCGG	EALDNTLAQQ
	EIFVPLS								
a112649	LTIPLL	VGKAVILLPE	AEEIEALKNA	LOOAKNFOLV	VE I PAUL 21 L	SULLPUNYPA	G-TPQ	AFIIGG	CALICUNLER
a112642	EIIMALG	SGAKLCLAKS	ESLLPGET	LLKLLRDNAV	THITITPSAL	SLLPSADLP-	HLR	MVLVGG	EAPSPELIAK
a111695	FTWAALI	NGGKI VI MPT	NIPSLQEIG-	MATKOYHV	TTI WI TAGI F	NI MVEFOTEH	I KSI R	OLI AGG	DVI SVYHVSK
	KQIFASLL								
BG10169	EVFGALL	NGAALYPVKK	RHVLDA KQ	FAAFLREQSI	TTMWLTSPLF	NQLAAKDA	GMFGTLR	HLIIGG	DALVPHIVSK
RG10971 16	EMFGALL	NGSTI VVVSK	FTARDP - OA	FRITIKKERV	TVI NOTPTAE	YOU MI EDONH	TDHI NTR	YVIEGG	FALOPGLIOS
	LFTPLL								
all1647	EIFWTLM	SGATICPVQR	EVVLNP WE	FARWIQETQI	NVMHFVPSLF	GEFISALENE	TWSFPQLR	WLMFSG	EALPMSFIQR
JW0578			EAHRDP LA						
	FSGDLARTLT								
SMU.1342	ELFGWTF	EGAVLYFLEN	GEEKDPQR	IIELINSQNI	SKLHFVPSML	NVFLEFCERE	N-KDSLKSLS	IVFSSG	EALTKEQVIK
	DIFGPLA								
Acremonium	RDIFTPLF	LGAKITIPPA	DATAAFF	LAQWMKDNRV	IVIHLIPAMG	QILVGGAIAQ	IPSLR	NAFFVG	DLLSKKDIIR
EAEL I DW/G	- ITNSYGPTE	ATVEA ACEDO	D n	HEKI EDIDIC	KD/\HH/\DI AI	I NONO DMI	DVCCTCE! VT	VCVC//VDCA	NDDA_ IT
FHATFD-AL-	-LHNFYGPTE	TVINASRFKV	VG	PQGTRIVPIG	RPKINTTMHL	LDDSLQPV	PTGVIGEIYI	GGTHVAYGYH	RRAGLT
FRTRLD-IP-	-LYHGYGPAE	TTIGVSHVVY	RG	AAERLSTSIG	RANPNTRLYV	LDDEL RPV	PVGVGGELYA	GGLLLGRGYV	NAPGLT
	- LHNLYGPTE								
SLARFPHSE-	- LHNLYGPTE	AAIDVTAWRC	NA	EIHPGVVPIG	RPIANTQIYV	LDAYRQPV	PLGVTGEIYI	GGAGVARGYL	NRPELT
VLREGAPOH -	-LLNGYGPTE	TTTFATTHLI	QA	VAAGRGIPIG	RPIANTQIYV	LDAYQ QPV	PLGVTGEIYV	GGAGVGLGYL	NRPELT
	-MINAYGPTE								
	-FINSYGPTE								
IRQAFAPAS-	-FFNAYGPTE	TVVMPLACLA	PER-LE	EG-AASVPIG	SVVGARVAYI	LDADL ALV	PQGATGELYV	GGAGLARGYH	ERPALS
	- VVNEYGPTE								
	- VTNLYGPTE								
VLAHHPRIV-	-LRHLYGPTE	TTLCVTQHEV	TAPYEA	RGSLPVG	RATGNTRAYV	LDRYL QPV	PAGVPGELFI	SGSGLARGYL	DRPDLT
	- VWNLYGPTE								
	VYNLYGPSE								
WRSYFPQTK-	-LINEYGPTE	TVVGCCIYD-	ASQG	KSSKGNVPIG	RPIANTRLYI	LDRYL QPV	PIGVPGELYI	GGAGVARGYL	NRPELT
MOGOKK-				CNCHDI VDTT	DDCVNKUI AL	I DNVI ODV	DTCVTCEI VT	CCTCI APCVI	
							PIGVIGELYI		NRPDLT
VIEELPNCQ-	-LINGYGPTE	NTTFTCCHK-	ITVN	DLIKDSIPIG	RPIANTQVYI	LDDVLQLV	PIGIAGELYI	GGDGLARGYL	NRPDLT NKPDLT
VIEELPNCQ-	-LINGYGPTE	NTTFTCCHK-	ITVN	DLIKDSIPIG	RPIANTQVYI	LDDVLQLV	PIGIAGELYI	GGDGLARGYL	NRPDLT NKPDLT
VIEELPNCQ- FKEAGTAPR-	-LINGYGPTE -LTNVYGPTE	NTTFTCCHK- TCVDASVHPV	ITVN IPENAV	DLIKDSIPIG QSAYVPIG	RPIANTQVYI KALGNNRLYI	LDDVL QLV LDQKG RLQ	PIGIAGELYI PEGVAGELYI	GGDGLARGYL AGDGVGRGYL	NRPDLT NKPDLT HLPELT
VIEELPNCQ- FKEAGTAPR- VKQASPSLS-	-LINGYGPTE -LTNVYGPTE -LWNGYGPTE	NTTFTCCHK- TCVDASVHPV NTTFSTSFLI	IPENAV DREYGG	DLIKDSIPIG QSAYVPIG SIPIG	RPIANTQVYI KALGNNRLYI KPIGNSTAYI	LDDVLQLV LDQKGRLQ MDEQQCLQ	PIGIAGELYI PEGVAGELYI PIGAPGELCV	GGDGLARGYL AGDGVGRGYL GGIGVARGYV	NRPDLT NKPDLT HLPELT NLPELT
VIEELPNCQ- FKEAGTAPR- VKQASPSLS- WNEKYPHTD-	-LINGYGPTE -LTNVYGPTE -LWNGYGPTE -LINMYGITE	NTTFTCCHK- TCVDASVHPV NTTFSTSFLI TTVHVTFKKL	IPENAV DREYGG SAADIA	DLIKDSIPIG QSAYVPIG SIPIG KNKSNIG	RPIANTQVYI KALGNNRLYI KPIGNSTAYI RPLSTLQAHV	LDDVLQLV LDQKGRLQ MDEQQCLQ MDAHMNLQ	PIGIAGELYI PEGVAGELYI PIGAPGELCV PTGVPGELYI	GGDGLARGYL AGDGVGRGYL GGIGVARGYV GGEGVARGYL	NRPDLT NKPDLT HLPELT NLPELT NRDELT
VIEELPNCQ- FKEAGTAPR- VKQASPSLS- WNEKYPHTD-	-LINGYGPTE -LTNVYGPTE -LWNGYGPTE -LINMYGITE	NTTFTCCHK- TCVDASVHPV NTTFSTSFLI TTVHVTFKKL	IPENAV DREYGG SAADIA	DLIKDSIPIG QSAYVPIG SIPIG KNKSNIG	RPIANTQVYI KALGNNRLYI KPIGNSTAYI RPLSTLQAHV	LDDVLQLV LDQKGRLQ MDEQQCLQ MDAHMNLQ	PIGIAGELYI PEGVAGELYI PIGAPGELCV PTGVPGELYI	GGDGLARGYL AGDGVGRGYL GGIGVARGYV GGEGVARGYL	NRPDLT NKPDLT HLPELT NLPELT NRDELT
VIEELPNCQ- FKEAGTAPR- VKQASPSLS- WNEKYPHTD- NQIICPSAE-	-LINGYGPTE -LTNVYGPTE -LWNGYGPTE -LINMYGITE -LANEYGPTE	NTTFTCCHK- TCVDASVHPV NTTFSTSFLI TTVHVTFKKL NSVATTILR-	IPENAV DREYGG SAADIA	DLIKDSIPIG QSAYVPIG SIPIG KNKSNIG LNKKERITIG	RPIANTQVYI KALGNNRLYI KPIGNSTAYI RPLSTLQAHV HPIRNTKVFV	LDDVL QLV LDQKG RLQ MDEQQ CLQ MDAHM NLQ LHGN QMQ	PIGIAGELYI PEGVAGELYI PIGAPGELCV PTGVPGELYI PIGAAGELCI	GGDGLARGYL AGDGVGRGYL GGIGVARGYV GGEGVARGYL SGAGLARGYY	NRPDLT NKPDLT HLPELT NLPELT NRDELT KQQELT
VIEELPNCQ- FKEAGTAPR- VKQASPSLS- WNEKYPHTD- NQIICPSAE- WIDRHGLKTG	-LINGYGPTE -LTNVYGPTE -LWNGYGPTE -LINMYGITE -LANEYGPTE -LANLYGPTE	NTTFTCCHK- TCVDASVHPV NTTFSTSFLI TTVHVTFKKL NSVATTILR- ASIDVTCHLI	PITVN IPENAV DREYGG SAADIAH TER-PD	DLIKDSIPIG QSAYVPIG SIPIG KNKSNIG LNKKERITIG ERLTTQIPIG	RPIANTQVYI KALGNNRLYI KPIGNSTAYI RPLSTLQAHV HPIRNTKVFV KAIDNVYVKV	LDDVLQLV LDQKGRLQ MDEQQCLQ MDAHMNLQ LHGNQMQ LDGGMQPV	PIGIAGELYI PEGVAGELYI PIGAPGELCV PTGVPGELYI PIGAAGELCI QPGNMGELWL	GGDGLARGYL AGDGVGRGYL GGIGVARGYV GGEGVARGYL SGAGLARGYY GGVQLALGYL	NRPDLT NKPDLT HLPELT NLPELT NRDELT KQQELT KDPEKT
VIEELPNCQ- FKEAGTAPR- VKQASPSLS- WNEKYPHTD- NQIICPSAE- WIDRHGLKTG WQQLTGAP	- LINGYGPTE - LTNVYGPTE - LWNGYGPTE - LINMYGITE - LANEYGPTE - LANLYGPTE - LHNLYGPTE	NTTFTCCHK- TCVDASVHPV NTTFSTSFLI TTVHVTFKKL NSVATTILR- ASIDVTCHLI AAVDVSWYPA	ITVN IPENAV DREYGG SAADIAH TER-PD FGEELA	DLIKDSIPIG QSAYVPIG SIPIG KNKSNIG LNKKERITIG ERLTTQIPIG QVRGSSVPIG	RPIANTQVYI KALGNNRLYI KPIGNSTAYI RPLSTLQAHV HPIRNTKVFV KAIDNVYVKV YPVWNTGLRI	LDDVLQLV LDQKGRLQ MDEQQCLQ MDAHMNLQ LHGNQMQ LDGGMQPV LDAMMHPV	PIGIAGELYI PEGVAGELYI PIGAPGELCV PTGVPGELYI PIGAAGELCI QPGNMGELWL PPGVAGDLYL	GGDGLARGYL AGDGVGRGYL GGIGVARGYV GGEGVARGYL SGAGLARGYY GGVQLALGYL TGIQLAQGYL	NRPDLT NKPDLT HLPELT NLPELT NRDELT KQQELT KDPEKT GRPDLT
VIEELPNCQ- FKEAGTAPR- VKQASPSLS- WNEKYPHTD- NQIICPSAE- WIDRHGLKTG WQQLTGAP	- LINGYGPTE - LTNVYGPTE - LWNGYGPTE - LINMYGITE - LANEYGPTE - LANLYGPTE - LHNLYGPTE	NTTFTCCHK- TCVDASVHPV NTTFSTSFLI TTVHVTFKKL NSVATTILR- ASIDVTCHLI AAVDVSWYPA	ITVN IPENAV DREYGG SAADIAH TER-PD FGEELA	DLIKDSIPIG QSAYVPIG SIPIG KNKSNIG LNKKERITIG ERLTTQIPIG QVRGSSVPIG	RPIANTQVYI KALGNNRLYI KPIGNSTAYI RPLSTLQAHV HPIRNTKVFV KAIDNVYVKV YPVWNTGLRI	LDDVLQLV LDQKGRLQ MDEQQCLQ MDAHMNLQ LHGNQMQ LDGGMQPV LDAMMHPV	PIGIAGELYI PEGVAGELYI PIGAPGELCV PTGVPGELYI PIGAAGELCI QPGNMGELWL PPGVAGDLYL	GGDGLARGYL AGDGVGRGYL GGIGVARGYV GGEGVARGYL SGAGLARGYY GGVQLALGYL TGIQLAQGYL	NRPDLT NKPDLT HLPELT NLPELT NRDELT KQQELT KDPEKT GRPDLT
VIEELPNCQ- FKEAGTAPR- VKQASPSLS- WNEKYPHTD- NQIICPSAE- WIDRHGLKTG WQQLTGAP LTDRFGQSMR	-LINGYGPTE -LTNVYGPTE -LWNGYGPTE -LINMYGITE -LANEYGPTE -LANLYGPTE -LHNLYGPTE -INSYGVTE	NTTFTCCHK- TCVDASVHPV NTTFSTSFLI TTVHVTFKKL NSVATTILR- ASIDVTCHLI AAVDVSWYPA ATIDSSFYET	ITVN IPENAV DREYGG SAADIAH TER-PD FGEELA SMGG	DLIKDSIPIG QSAYVPIG SIPIG KNKSNIG LNKKERITIG ERLTTQIPIG QVRGSSVPIG ECTGDNVPIG	RPIANTQVYI KALGNNRLYI KPIGNSTAYI RPLSTLQAHV HPIRNTKVFV KAIDNVYVKV YPVWNTGLRI SPLPNVHMYV	LDDVLQLV LDQKGRLQ MDEQQCLQ MDAHMNLQ LHGNQMQ LDGGMQPV LDAMMHPV LSQTDQIQ	PIGIAGELYI PEGVAGELYI PIGAPGELCV PTGVPGELYI PIGAAGELCI QPGNMGELWL PPGVAGDLYL PIGVAGELCI	GGDGLARGYL AGDGVGRGYL GGIGVARGYV GGEGVARGYL SGAGLARGYY GGVQLALGYL TGIQLAQGYL GGAGVAKGYH	NRPDLT NKPDLT HLPELT NLPELT NRDELT KQQELT KQPEKT GRPDLT HKPDLT
VIEELPNCQ- FKEAGTAPR- VKQASPSLS- WNEKYPHTD- NQIICPSAE- WIDRHGKTG WQQLTGAP LTDRFGQSMR FYSIFDNDKP	-LINGYGPTE -LTNYYGPTE -LWNGYGPTE -LINMYGITE -LANEYGPTE -LANLYGPTE -LHNLYGPTE -IINSYGVTE QLINLYGPTE	NTTFTCCHK- TCVDASVHPV NTTFSTSFLI TTVHVTFKKL NSVATTILR- ASIDVTCHLI AAVDVSWYPA ATIDSSFYET TAIEVTYFDC	ITVN IPENAV DREYGG SAADIA	DLIKDSIPIG QSAYVPIG SIPIG KNKSNIG LNKKERITIG ERLTTQIPIG QVRGSSVPIG ECTGDNVPIG DYKSEDVPIG	RPIANTQVYI KALGNNRLYI KPIGNSTAYI RPLSTLQAHV HPIRNTKVFV KAIDNVYVKV YPVWNTGLRI SPLPNVHMYV EPLDNVEAYV	LDDVL - QLV LDQKG - RLQ MDEQQ - CLQ MDAHM - NLQ LHGN QMQ LDGGM - QPV LDAMM - HPV LSQTD - QIQ LNDKK - QKC	PIGIAGELYI PEGVAGELYI PIGAPGELCV PTGVPGELYI PIGAAGELCI QPGNMGELWL PPGVAGDLYL PIGVAGELCI PIGVVGELYI	GGDGLARGYL AGDGVGRGYL GGIGVARGYV GGEGVARGYL SGAGLARGYL TGIQLAUGYL GGAGVAKGYH GGIQVAUGYI	NRPDLT NKPDLT HLPELT NRDELT KQQELT KDPEKT GRPDLT NKEDLT NKEDAT
VIEELPNCQ- FKEAGTAPR- VKQASPSLS- WNEKYPHTD- NQIICPSAE- WIDRHGLKTG WQQLTGAP LTDRFGQSMR FYSIFDNDKP LKAQLPDAD-	-LINGYGPTE -LTNYYGPTE -LWNGYGPTE -LINMYGITE -LANEYGPTE -LANLYGPTE -LHNLYGPTE -IINSYGVTE QLINLYGPTE -LISLGGATE	NTTFTCCHK- TCVDASVHPV NTTFSTSFLI TTVHVTFKKL NSVATTILR- ASIDVTCHLI AAVDVSWYPA ATIDSSFYET TAIEVTYFDC ASIWSIFHPI	ITVN IPENAV DREYGG SAADIA	DLIKDSIPIG QSAYVPIG SIPIG KNKSNIG LNKKERITIG ERLTTGIPIG QVRGSSVPIG ECTGDNVPIG DYKSEDVPIG LRDWTSIPYG	RPIANTQVYI KALGNNRLYI KPIGNSTAYI RPLSTLQAHV HPIRNTKVFV KAIDNVYVKV KPVWNTGLRI SPLPNVHMYV EPLDNVEAYV QPLANQRWYV	LDDVL - QLV LDQKG - RLQ MDEQQ - CLQ MDAHM - NLQ LHGN QMQ LDGGM - QPV LDAMM - HPV LSQTD - QIQ LNDKK - QKC LDDQG - RPC	PIGIAGELYI PEGVAGELYI PIGAPGELCV PTGVPGELYI PIGAAGELCI PPGVAGDLYL PIGVAGELCI PIGVVGELYI PPWVTGRLFI	GGDGLARGYL AGDGVGRGYL GGIGVARGYV GGEGVARGYL SGAGLARGYL TGIQLAQGYL GGAGVAKGYH GGIQVAQGYI GGIGVARGYW	NRPDLT NKPDLT HLPELT NLPELT NRDELT KQQELT KDPEKT GRPDLT HKPDLT NKEDAT GRPQLT
VIEELPNCQ- FKEAGTAPR- VKQASPSLS- WNEKYPHTD- NQIICPSAE- WIDRHGLKTG WQQLTGAP LTDRFGQSMR FYSIFDNDKP LKAQLPDAD-	-LINGYGPTE -LTNYYGPTE -LWNGYGPTE -LINMYGITE -LANEYGPTE -LANLYGPTE -LHNLYGPTE -IINSYGVTE QLINLYGPTE	NTTFTCCHK- TCVDASVHPV NTTFSTSFLI TTVHVTFKKL NSVATTILR- ASIDVTCHLI AAVDVSWYPA ATIDSSFYET TAIEVTYFDC ASIWSIFHPI	ITVN IPENAV DREYGG SAADIA	DLIKDSIPIG QSAYVPIG SIPIG KNKSNIG LNKKERITIG ERLTTGIPIG QVRGSSVPIG ECTGDNVPIG DYKSEDVPIG LRDWTSIPYG	RPIANTQVYI KALGNNRLYI KPIGNSTAYI RPLSTLQAHV HPIRNTKVFV KAIDNVYVKV KPVWNTGLRI SPLPNVHMYV EPLDNVEAYV QPLANQRWYV	LDDVL - QLV LDQKG - RLQ MDEQQ - CLQ MDAHM - NLQ LHGN QMQ LDGGM - QPV LDAMM - HPV LSQTD - QIQ LNDKK - QKC LDDQG - RPC	PIGIAGELYI PEGVAGELYI PIGAPGELCV PTGVPGELYI PIGAAGELCI PPGVAGDLYL PIGVAGELCI PIGVVGELYI PPWVTGRLFI	GGDGLARGYL AGDGVGRGYL GGIGVARGYV GGEGVARGYL SGAGLARGYL TGIQLAQGYL GGAGVAKGYH GGIQVAQGYI GGIGVARGYW	NRPDLT NKPDLT HLPELT NLPELT NRDELT KQQELT KDPEKT GRPDLT HKPDLT NKEDAT GRPQLT
VIEELPNCQ- FKEAGTAPR- VKQASPSLS- WNEKYPHTD- NQIICPSAE- WIDRHGLKTG WQQLTGAP LTDRFGQSMR FYSIFDNDKP LKAQLPDAD-	-LINGYGPTE -LTNYYGPTE -LWNGYGPTE -LINMYGITE -LANEYGPTE -LANLYGPTE -LHNLYGPTE -IINSYGVTE QLINLYGPTE -LISLGGATE	NTTFTCCHK- TCVDASVHPV NTTFSTSFLI TTVHVTFKKL NSVATTILR- ASIDVTCHLI AAVDVSWYPA ATIDSSFYET TAIEVTYFDC ASIWSIFHPI	ITVN IPENAV DREYGG SAADIA	DLIKDSIPIG QSAYVPIG SIPIG KNKSNIG LNKKERITIG ERLTTGIPIG QVRGSSVPIG ECTGDNVPIG DYKSEDVPIG LRDWTSIPYG	RPIANTQVYI KALGNNRLYI KPIGNSTAYI RPLSTLQAHV HPIRNTKVFV KAIDNVYVKV KYPVWNTGLRI SPLPNVHMYV EPLDNVEAYV QPLANQRWYV	LDDVL - QLV LDQKG - RLQ MDEQQ - CLQ MDAHM - NLQ LHGN QMQ LDGGM - QPV LDAMM - HPV LSQTD - QIQ LNDKK - QKC LDDQG - RPC	PIGIAGELYI PEGVAGELYI PIGAPGELCV PTGVPGELYI PIGAAGELCI PPGVAGDLYL PIGVAGELCI PIGVVGELYI PPWVTGRLFI	GGDGLARGYL AGDGVGRGYL GGIGVARGYV GGEGVARGYL SGAGLARGYL TGIQLAQGYL GGAGVAKGYH GGIQVAQGYI GGIGVARGYW	NRPDLT NKPDLT HLPELT NLPELT NRDELT KQQELT KDPEKT GRPDLT HKPDLT NKEDAT GRPQLT
VIEELPNCQ- FKEAGTAFP. VKQASPSLS- WNEKYPHTD- NQIICPSAE- WIDRHGLKD WQQLTGAP LTDRFGQSMR FYSIFDNDKP LKAQLPDAD- LRSIAPNVD-	-LINGYGPTE -LTNYYGPTE -LWNGYGPTE -LINMYGITE -LANEYGPTE -LANLYGPTE -LHNLYGPTE -IINSYGVTE QLINLYGPTE -LISLGGATE -VINLYGSTE	NTTFTCCHK- TCVDASVHPV NTTFSTSFLI TTVHVTFKKL NSVATTILR- ASIDVTCHLI AAVDVSWYPA ATIDSSFYET TAIEVTYFDC ASIWSIFHPI SQRAVSFFKV	ITVN IPENAV DREYGG SAADIAH TER-PD FGEELA SMG-G SNL GEA PSRAKDPHFL	DLIKDSIPIG QSAYVPIG SIPIG KNKSNIG LNKKERITIG ERLTTQIPIG QVRGSSVPIG ECTGDNVPIG DYKSEDVPIG LRDWTSIPYG DSLPDIIPVG	RPIANTQVYI KALGNNRLYI KPIGNSTAYI RPLSTLQAHV HPIRNTKVFV KAIDNVYVKV YPVWNTGLRI SPLPNVHMYV EPLDNVEAYV QPLANQRWYV QGMQNVQLLV	LDDVL - QLV LDQKG - RLQ MDEQQ - CLQ MDAHM - NLQ LHGN QMV LDGMM - HPV LSQTD - QIQ LNDKK - QKC LDDQG - RPC VDPNDKMRLC	PIGIAGELYI PEGVAGELYI PIGAPGELCV PTGVPGELYI PIGAAGELCI QPGNMGELWL PIGVAGELCI PIGVAGELCI PIGVVGELYI PPWVTGRLFI DLGEQGELYV	GGDGLARGYL AGDGVGRGYV GGIGVARGYV GGEGVARGYL SGAGLARGYY GGVQLALGYV TGIQLAQGYL GGAGVAKGYH GGIQVAQGYI GGIGVARGYW RAAGLAEGYL	NRPDLT NKPDLT HLPELT NRDELT NRDELT KQQELT KDPEKT HKPDLT NKEDAT GRPQLT GDDEKTAELN
VIEELPNCQ- FKEAGTAPQ- VKQASPSLS- WNEKYPHTD- NQIICPSAE- WIDRHGLKTG WQQLTGAP LTDRFGQSMR FYSIFDNDKP LKAQLPDAD- LRSIAPNVD- EERFLEDPFY	-LINGYGPTE -LINVYGPTE -LWNGYGPTE -LINNYGTTE -LANEYGPTE -LANLYGPTE -LHNLYGPTE -LINLYGPTE -LINLYGPTE -LISLGGATE -VINLYGSTE ERMYKTGDVA	NTTFTCCHK- TCVDASVHPV NTTFSTSFLI TTVHVTFKKL NSVATTILR- ASIDVTCHLI AAVDVSWYPA ATIDSSFVET TAIEVTYFDC ASIWSIFHPI SQRAVSFFKV RWLPDGNVEF	ITVN IPENAV DREYGG SAADIAH TER-PD FGEELA SMG-G SNL GEA PSRAKDPHFL LGRTDDQVKI	DLIKDSIPIG QSAYVPIG QSAYVPIG KNKSNIG LNKKERITIG ERLTTQIPIG QVRGSSVPIG ECTGDNVPIG DYKSEDVPIG LRDWTSIPYG DSLPDIIPVG RGYRIEPGEI	RPIANTQVYI KALGNRLYI KPIGNSTAYI RPLSTLQAHV HPIRNTKVFV KAIDNYYKV YPVWNTGLRI SPLPNVHMYV EPLDNVEAYV QPLANQRWYV QGMQNVQLLV EAALRSIEGV	LDDVLQLV LDQKGRLQ MDEQQCLQ MDAHMNLQ LHGNQMQ LDGGMQPV LDAMM - HPV LSQTDQIQ LNDKKQKC LDDQG RPC VDPNDKMRLC REAAVTVRTD	PIGIAGELYI PEGVAGELYI PIGAPGELCV PTGVPGELYI PIGAAGELCI QPGMMGELWL PPGVAGDLYL PIGVAGELCI PIGVVGELYI PPWTGRLFI DLGEQGELYV EVRAQLER	GGDGLARGYL AGDGVGRGYL GGIGVARGYV GGEGVARGYV GGVQLALGYL TGIQLAGYL GGAGVAKGYH GGIQVAQGYI GGIGVARGYW RAAGLAEGYL LLPGYMVPAY	NRPDLT NKPDLT NKPELT NLPELT NRDELT KQQELT KDPEKT GRPDLT HKPDLT HKPDLT GDPEKTAELN MIEMEQWPV
VIEELPNCQ- FKEAGTAPR- VKQASPSLS- WNEKYPHTD- NQIICPSAE- WIDRHGLKTG WQQLTGAP LTDRFGQSMR FYSIFDNDKP LKAQLPDAD- LRSIAPNVD- EERFLEDPFY AERFVADPFN	-LINGYGPTE -LTNVYGPTE -LWNGYGPTE -LWNGYGPTE -LANLYGPTE -LANLYGPTE -LHNLYGPTE -LISLGGATE -VINLYGSTE -VINLYGSTE -WYNTGDVA SRMYRSGDLA	NTTFTCCHK- TCVDASVHPV NTTFSTSFLI TTVHVTFKKL NSVATTILR- ASIDVTCHLI AAVDVSWYPA ATIOSSFYET TAIEVTYFDC SQRAVSFFKV RWLPDGNVEF RRNADGDIEF	ITVN IPENAV IPENAV IPEYGG SAADIA	DLIKDSIPIG QSAYVPIG QSAYVPIG KNKSNIG LNKKERITIG ERLTTQIPIG QVRGSSVPIG ECTEDNVPIG DYKSEDVPIG DYKSEDVPIG DSLPDIIPVG RGYRIEPGEI RGFRIELGDV	RPIANTQVYI KALGNNRLYI RPISTLQAHV HPIRNTKVFV KAIDNVYVKV YPWNTGLRI SPLPNVHMYV EPLDNVEAYV QPLANQRWYV QGMQNVQLLV EAALRSIEGV AAAIAVDPTV	LDDVL - QLV LDQKG - RLQ MDEQQ - CLQ MDAHM - NLQ LHGM QMQ LDGKM - QPV LDAHM - HPV LSQTD - QIQ LNDKK - QKC VDPNDKMRLC REAAVTVRTD GQAVVVVSDL	PIGIAGELYI PEGVAGELYI PEGVAGELYI PIGAPGELCV PTGVPGELYI PIGAAGELCI QPGNMGELWL PIGVAGELCI PIGVVGELYI DLGEQGELYVEVRAQLERRIRARVAA	GGDGLARGYL AGDGVGRGYL GGGIGVARGYV GGEGVARGYV GGAGLARGYY TGIQLAGGYL GGAGVAKGYH GGIQVARGYW RAAGLAEGYL LLPGYMVPAY ALPEYMLPAA	NRPDLT NKPDLT NKPDLT NLPELT NRDELT NRDELT KDPEKT GRPDLT NKEDLT NKEDAT GRPQLT GRPQLT MEMEQWPV YVVLDEIPI
VIEELPNCQ- FKEAGTAPR- VKQASPSLS- WNEKYPHTD- NQIICPSAE- WIDRHGLKTG WQQLTGAP LTDRFGQSMR FYSIFDNDKP LKAQLPDAD- LRSIAPNVD- EERFLEDPFY AERFVADPFN	-LINGYGPTE -LTNVYGPTE -LWNGYGPTE -LWNGYGPTE -LANLYGPTE -LANLYGPTE -LHNLYGPTE -LISLGGATE -VINLYGSTE -VINLYGSTE -WYNTGDVA SRMYRSGDLA	NTTFTCCHK- TCVDASVHPV NTTFSTSFLI TTVHVTFKKL NSVATTILR- ASIDVTCHLI AAVDVSWYPA ATIOSSFYET TAIEVTYFDC SQRAVSFFKV RWLPDGNVEF RRNADGDIEF	ITVN IPENAV IPENAV IPEYGG SAADIA	DLIKDSIPIG QSAYVPIG QSAYVPIG KNKSNIG LNKKERITIG ERLTTQIPIG QVRGSSVPIG ECTEDNVPIG DYKSEDVPIG DYKSEDVPIG DSLPDIIPVG RGYRIEPGEI RGFRIELGDV	RPIANTQVYI KALGNNRLYI RPISTLQAHV HPIRNTKVFV KAIDNVYVKV YPWNTGLRI SPLPNVHMYV EPLDNVEAYV QPLANQRWYV QGMQNVQLLV EAALRSIEGV AAAIAVDPTV	LDDVL - QLV LDQKG - RLQ MDEQQ - CLQ MDAHM - NLQ LHGM QMQ LDGKM - QPV LDAHM - HPV LSQTD - QIQ LNDKK - QKC VDPNDKMRLC REAAVTVRTD GQAVVVVSDL	PIGIAGELYI PEGVAGELYI PEGVAGELYI PIGAPGELCV PTGVPGELYI PIGAAGELCI QPGNMGELWL PIGVAGELCI PIGVVGELYI DLGEQGELYVEVRAQLERRIRARVAA	GGDGLARGYL AGDGVGRGYL GGGIGVARGYV GGEGVARGYV GGAGLARGYY TGIQLAGGYL GGAGVAKGYH GGIQVARGYW RAAGLAEGYL LLPGYMVPAY ALPEYMLPAA	NRPDLT NKPDLT NKPDLT NLPELT NRDELT NRDELT KDPEKT GRPDLT NKEDLT NKEDAT GRPQLT GRPQLT MEMEQWPV YVVLDEIPI
VIEELPNCQ- FKEAGTAPR- WKQASPSLS- WNEKYPHTD- NQIICPSAE- WIDRHGLKTG WQQLTGAP LTDRFGQSMR FYSIFDNDKP LKAQLPDAD- LRSIAPNVD- EERFLEDPFY AERFVADPFN ASRFVANPFA	-LINGYGPTE -LTNVYGPTE -LWNCYGPTE -LWNCYGPTE -LANLYGPTE -LANLYGPTE -LHNLYGPTE -LHNLYGPTE -LINSYGVTE -LISLGGATE -VINLYGSTE -VINLYGSTE -VINLYGSTE -VINLYGSTE -VINLYGSTE -VINLYGSTGATGATGATGATGATGATGATGATGATGATGATGATGAT	NTTFTCCHK- TCVDASVHPV NTTFSTSFLI TTVHVTFKKL NSVATTILR- ASIDVTCHLI AAVDVSWYPA ATIDSSFYET TAIEVTVFDC ASIWSIFHPI SQRAVSFFKV RWLPDGNVEF RRNADGDIEF RRNADGDIEF RFAPDGSLDF	IPENAV DREYGG SAADIA	DLIKDSIPIG QSAYVPIG SIPIG KNKSNIG LNKKERITIG ERLTTQIPIG QVRGSSVPIG ECTGDNVPIG DYKSEDVPIG LRDWTSIPYG DSLPDIIPVG RGYRIEPGEI RGFRIELGDV RGMRLEIEDV	RPIANTQVYI KALGNNRLYI KPIGNSTAYI RPLSTLQAHV HPIRNTKVFV KAIDNYVKW YPWNNTGLRI SPLPNVHMYV EPLDNVEAYV QPLANQRWYV QGMQNVQLLV EAALRSIEGV AAAIAVDPTV EVGLAEHPRV	LDDVL QLV LDQKG RLQ MDAMH NLQ LHGN QMV LDGCM QPV LDAMM HPV LSQTD Q1Q LDDGC RPC VDPNDKMRLC REAVTVRTD GQAVVVSDL RHTCVVARKN	PIGIAGELYI PEGVAGELYI PIGAPGELCV PIGYPGELYI PIGAAGELUI PIGAMGELWL PIGVAGELVI PIGVAGELYI PIGVYGELYI PIGVYGELYI PEWTGRLFI DLGEQGELYV EVRAQLER RIRARVAAA	GGDGLARGYL AGDGVGRGYL GGIGVARGYV GGEGVARGYV GGEGVARGYV GGVQLALGYL GGIQVAQGYI GGIQVAQGYI GGIQVAQGYI GGIQVARGYW RAAGLAEGYL LLPGYMVPAY HMVEYMVPTH	NRPDLT NKPDLT NKPDLT NLPELT NRDELT KQQELT KDPEKT GRPDLT NKEDAT GRPQLT GDDEKTAELN MIEMGWPV YVVMTEFPL
VIEELPNCQ- FKEAGTAPR- WKQASPSLS- WNEKYPHTD- WQITCPSAE- WIDRHGLKTG WQQLTGAP LTDRFGQSMR FYSIFDNDKP LKAQLPDAD- LRSIAPNVD- EERFLEDPFY AERFVADPFA ASRFVANPFA TERFVGGLGT	-LINGYGPTE -LTNVYGPTE -LWNCYGPTE -LWNCYGPTE -LINMYGITE -LANLYGPTE -LHNLYGPTE -LHNLYGPTE -LINSYGVTE -LISLGGATE -VINLYGFTE -VINLYGFTE ERMYKTGDVA SRLYREGDLA STLYKTGDLA	NTTFTCCHK- TCVDASVHPV NTTFSTSFLI TTVHVTFKKL NSVATTILR- ASIDVTCHLI AAVDVSWYPA ATIDSSFYET TAIEVTYFDC ASIWSIFHPI SQRAVSFFKV RWLPDGNVEF RRNADGDIEF RRNADGDIEF RYLPDGNLEY	ITVN IPENAV DREYGG SAADIA	DLIKDSIPIG QSAYVPIG QSAYVPIG KNKSNIG LNKKERITIG ERLTTQIPIG QVRGSSVPIG ECTGDNVPIG DYKSEDVPIG LRDWTSIPYG DSLPDIIPVG RGYRIEPGEI RGFRIELGDV RGGRRLEIGDV RGIRIELGEI	RPIANTQVYI KALGNNRLYI KALGNNRLYI RPLSTLQAHV HPIRNTKVFV KAIDNVYVKV YPVWNTGLRI SPLPNVHNYV QPLANQRWYV QGMQNVQLLV EAALRSIEGV AAATAVDPTV EVGLAEHPRV EAVINQHPDV	LDDVL QLV LDQKG RLQ MDAHM NLQ LHGM QMV LDGKM QPV LDAMM HPV LSQTD QIQ LNDKK QKC LDDQG RPC VDPNDKMRLC REAAVTVRTD GQAVVVVSDL RHTCVVARKN QQAVVILDSK	PIGIAGELYI PEGVAGELYI PIGAPGELCV PTGVPGELLYI PIGAAGELCI QPGMMGELLYI PPGVAGELLYI PIGVVGELIYI PPWYTGRLFI DLGEQGELYV EVRAQLER EIRARVAA EVKAWAGE ELEKLLAS	GGDGLARGYL AGDGVGRGYL GGGIGVARGYV GGEGVARGYL SGAGLARGYY TGIQLAQGYL GGAGVAKGYH GGIQVAQGYI GGIQVARGYW RAAGLAEGYL LLPGYMVPAY ALPEYMLPAA HMVEYMVPTH QLPEYMLPSV	NRPDLT NKPDLT NLPELT NLPELT NRDELT KQQELT KDPEKT GRPDLT HKPDLT HKPDLT GDDEKTAELN MIEMEQWPV YVVLDEIPI VVMTEFPL FVMLSELPL
VIEELPNCQ- FKEAGTAPR- WKQASPSLS- WNEKYPHTD- NQIICPSAE- WIDRHGLKTG- WQQLTGAP LTDRFGGSMR FYSIFDNDKP LKAQLPDAD- LRSIAPNVD- EERFLEDPFY AERFVADPFN ASRTVANPFA TAERFVVGPFT AERFVVGPFT	-LINGYGPTE -LTNVYGPTE -LWNGYGPTE -LWNGYGPTE -LANLYGPTE -LANLYGPTE -LHNLYGPTE -LINSYGVTE -LISLGGATE -VINLYGSTE	NTTFTCCHK- TCVDASVHPV NTTFSTSFLI TTVHVTFKKL NSVATTILR- ASIDVTCHI AAVDVSWYPA ATIOSSFYET TAIEVTYFDC RWLPDGNVEF RRNADGDIEF RFAPDGSLDF RYLPDGNLEY RWLPDGSLEY		DLIKDSIPIG QSAYVPIG QSAYVPIG KNKSNIG LNKKERITIG ERLTTQIPIG QVRGSSVPIG ECTGDNVPIG DYKSEDVPIG DYKSEDVPIG RGYRIEPGEI RGFRIELGDV RGMRLEIEDV RGMRLEIEDV RGFRIELGEI	RPIANTQVYI KALGNNRLYI KPIGNSTAYI RPLSTLQAHV HPIRNTKYFV YPWNTGLRI SPLPNVHMYV EPLDNVEAYV QFMQNVQLLV EAALRSIEGV AAAIAVDPTV EVGLAEHPRV EAVINQHPDV EARLSQCAGV	LDDVL - QLV LDQKG RLQ MDEQQ CLQ MDAHM - NLQ LHGM QMQ LDGKM - QPV LDAHM - HPV LSQTD - QIQ LNDKK - QKC VDPNDKMRLC REAAVTVRTD GQAVVVVSDL RHTCVVARKN QQAVVILDSK SEAVVAMRED	PIGIAGELYI PEGVAGELYI PEGVAGELYI PIGAPGELCV PTGVPGELYI PIGAAGELCI QPGMMGELWL PIGVAGELCI PIGVVGELYI DLGEQGELYVEVRAQLERRIRARVAAEVKAWAGEELELLASTLREQLQA	GGDGLARGYL AGDGVGRGYL GGIGVARGYV GGEGVARGYL GGAGLARGYY GGYQLALGYL TGIQLAQGYL GGAGVAKGYH GGIQVARGYW RAAGLAEGYL LLPGYMVPAY ALPEYMLPAA HMVEYMVPTH QLEYMLPAA LSPEYMLPAA LSPEYMLPAA LSPEYMLPAA LSPEYMLPAA LSPEYMLPAA LSPEYMLPAA	NRPDLT NKPDLT NKPDLT NLPELT NLPELT NRDELT KDPEKT GRPDLT NKEDLT NKEDAT GRPQLT WEDDEKTAELN MIEMEQWPV YVVLDEIPI VVMTEFPL FVMLSELPL VNRLEHLPL
VIEELPNCQ- FKEAGTAPR- WKQASPSLS- WNEKYPHTD- NQIICPSAE- WIDRHGLKTG- WQQLTGAP LTDRFGGSMR FYSIFDNDKP LKAQLPDAD- LRSIAPNVD- EERFLEDPFY AERFVADPFN ASRTVANPFA TAERFVVGPFT AERFVVGPFT	-LINGYGPTE -LTNVYGPTE -LWNCYGPTE -LWNCYGPTE -LINMYGITE -LANLYGPTE -LHNLYGPTE -LHNLYGPTE -LINSYGVTE -LISLGGATE -VINLYGFTE -VINLYGFTE ERMYKTGDVA SRLYREGDLA STLYKTGDLA	NTTFTCCHK- TCVDASVHPV NTTFSTSFLI TTVHVTFKKL NSVATTILR- ASIDVTCHI AAVDVSWYPA ATIOSSFYET TAIEVTYFDC RWLPDGNVEF RRNADGDIEF RFAPDGSLDF RYLPDGNLEY RWLPDGSLEY		DLIKDSIPIG QSAYVPIG QSAYVPIG KNKSNIG LNKKERITIG ERLTTQIPIG QVRGSSVPIG ECTGDNVPIG DYKSEDVPIG DYKSEDVPIG RGYRIEPGEI RGFRIELGDV RGMRLEIEDV RGMRLEIEDV RGFRIELGEI	RPIANTQVYI KALGNNRLYI KPIGNSTAYI RPLSTLQAHV HPIRNTKYFV YPWNTGLRI SPLPNVHMYV EPLDNVEAYV QFMQNVQLLV EAALRSIEGV AAAIAVDPTV EVGLAEHPRV EAVINQHPDV EARLSQCAGV	LDDVL - QLV LDQKG RLQ MDEQQ CLQ MDAHM - NLQ LHGM QMQ LDGKM - QPV LDAHM - HPV LSQTD - QIQ LNDKK - QKC VDPNDKMRLC REAAVTVRTD GQAVVVVSDL RHTCVVARKN QQAVVILDSK SEAVVAMRED	PIGIAGELYI PEGVAGELYI PEGVAGELYI PIGAPGELCV PTGVPGELYI PIGAAGELCI QPGMMGELWL PIGVAGELCI PIGVVGELYI DLGEQGELYVEVRAQLERRIRARVAAEVKAWAGEELELLASTLREQLQA	GGDGLARGYL AGDGVGRGYL GGIGVARGYV GGEGVARGYL GGAGLARGYY GGYQLALGYL TGIQLAQGYL GGAGVAKGYH GGIQVARGYW RAAGLAEGYL LLPGYMVPAY ALPEYMLPAA HMVEYMVPTH QLEYMLPAA LSPEYMLPAA LSPEYMLPAA LSPEYMLPAA LSPEYMLPAA LSPEYMLPAA LSPEYMLPAA	NRPDLT NKPDLT NKPDLT NLPELT NLPELT NRDELT KDPEKT GRPDLT NKEDLT NKEDAT GRPQLT WEDDEKTAELN MIEMEQWPV YVVLDEIPI VVMTEFPL FVMLSELPL VNRLEHLPL
VIEELPNCQ- FKEAGTAPR- WKQASPSLS- WNEKYPHTD- WIICPSAE- WIDRHGLKTG WQQLTGAP LTDRFGQSMR FYSIFDNDKP LKAQLPDAD- LRSIAPNVD- EERFLEDPFY AERFVADPFN ASRFVANPFA TERFVGGLGT AERFVVNPFH AERFVVNPFH AERFVVNPFH	-LINGYGPTE -LTNVYGPTE -LWNCYGPTE -LWNCYGPTE -LANLYGPTE -LANLYGPTE -LHNLYGPTE -LINLYGPTE -LISLGGATE -VINLYGSTE	NTTFTCCHK- TCVDASVHPV NTTFSTSFLI TTVHVTFKKL NSVATTILR- ASIDVTCHLI AAVDVSWYPA ATIDSSFYET TAIEVTYFDC ASIWSIFHPI SQRAVSFFKV RWLPDGNUEF RRNADGDIEF RFAPDGSLEY RWLPDGSLEY RWLPDGSLEY RWLPDGSLEY RWLPDGSLEY	ITVN DRENAV DREYGG SAADIA	DLIKDSIPIG QSAYVPIG QSAYVPIG KNKSNIG LNKKERITIG QVRGSSVPIG ECTGDNVPIG DYKSEDVPIG LRDWTSIPYG DSLPDIIPVG RGYRIEPGEI RGFRIELGDV RGRRELIEDV RGRRELIEDV RGRRELIEDEI RGFRIELGEI RGFRIELGEI	RPIANTQVYI KALGNNRLYI KALGNNRLYI RPLSTLQAHV HPIRNTKVFV YPWNNTGLRI SPUNNHYV EPLDNVEAYV QPLANQRWYV QGMQNVQLLV EAALRSIEGV EAALAUADPTV EAVINQHPDV EAVINQHPDV EAVINQHPDV EAVINQHPDV EAVINQHPDV EAVINQHPDV EAVINQHPDV EAXLSQCAGV	LDDVL QLV LDQKG RLQ MDAMH NLQ LHGN QPV LDGMM QPV LDAMM HPV LSQTD Q1Q LNDKK QKC LDDQG RPC VDPNDKMRLC REAAVTVRTD GQAVVVSDL RHTCVVARKN QQAVVILDSK SEAVVAMRED SEAVVAMRED SEAVVIRED	PIGIAGELYI PEGVAGELYI PEGVAGELYI PIGAPGELCV PTGVPGELYI PIGAAGELCI PIGAAGELCI PIGAAGELWI POWAGDLYL PIGVAGELYI PIGVAGELYI PIGVYGELYI PWYTGRLFI DLGEQGELYVEVRAQLERRIRARVAAAEVKAWAGEELEKLLASTLREQLQAALREQLQA	GGDGLARGYL AGDGVGRGYL GGIGVARGYV GGEGVARGYV GGGVQLALGYL TGIQLAQGYL GGIQVAQGYI GGIQVAQGYI GGIGVARGYW RAAGLAEGYL LLPGYMVPAY ALPEYMLPAA HMVEYMVPTH QLPEYMLPSV SLPEYMVPAA SLPEYMVPAA	NRPDLT NKPDLT NKPDLT NLPELT NLPELT NRDELT KDPEKT GRPDLT NKEDAT GRPQLT GDDEKTAELN MIEMEQWPV VVVLDEIPI VVVMTEFPL FVMLSELPL VVKLERLPL
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VIEELPNCQ- FKEAGTAPR- WKGASPSLS- WNEKYPHTD- NQIICPSAE- WIDRHGLKTG WQQLTGAP LTORFGGSMR FYSIFDNDKP LKAQLIPDAD- LKSIAPNVD- EERFLEDPFY AERFVANPFA ASRFVANPFA AERFVVNPFH AERFVVNPFH AERFWNPFA GACFLADPFH	-LINGYGPTE -LTNVYGPTE -LWNCYGPTE -LWNCYGPTE -LWNCYGPTE -LANLYGPTE -LANLYGPTE -LHNLYGPTE -LISLGGATE -VINLYGSTE	NTTFTCCHK- TCVDASVHPV NTTFSTSFLI TTVHVTFKKL NSVATTILR- ASIDVTCHI AAVDVSWYPA ATIDSSFYET TAIEVTYFDC RWLPDGNVEF RRNADGDIEF RFAPDGSLDF RYLPDGNLEY RWLPDGSLEY RWLPDGSLEY RWLPDGSLEY RWLPDGSLEY RWLPDGSLEY RWLPDGSLEY RWLPDGSLEY RWLPNGSLEY RWLPNGSLEY RWLPNGSLEY RWLPNGSLEY RWLPNGSLEY	ITVN DREYGG SAADIA	DLIKDSIPIG QSAYVPIG QSAYVPIG KNKSNIG LNKKERITIG QVRGSSVPIG ECTGDNVPIG DYKSEDVPIG DYKSEDVPIG RGYRIEPGEI RGFRIELGDV RGMRLEIEDV RGRIELGEI RGFRIELGEI RGFRIELGEI RGFRIELGEI RGFRIELGEI RGFRIELGEI RGFRIELGEI RGFRIELGEI	RPIANTQVYI KALGNNRLYI KALGNNRLYI RPLSTLQAHV HPIRNTKYFV KAIDNVYVKV YPVWNTGLRI SPLPNVHMYV QFLANQRWYV QFLANQRWYV QFLANQRWYV EAALRSIEGV AAAIAVDPTV EVGLAEHPRV EAVINQHPDV EARLSQCAGV EASLSQCAGV GASLARCDGV GASLARCDGV	LDDVLQLV LDQKGRLQ MDEQQCLQ MDAHMNLQ LHGMQPV LDGMMQPV LDAMMHPV LSQTDQIQ LNDKKQKC VDPNDKMRLC REAAVTVRTD GQAVVUSDL RHTCVVARKN QQAVVILDS SEAVVAMRED SEAVVIVRED SEAVVIVRED REAAVLARED	PIGIAGELYI PEGVAGELYI PEGVAGELYI PIGAPGELCV PTGVPGELYI PIGAAGELCI PPGVAGDLYL PIGVAGELLI PPGVAGDLYL PIGVVGELYI DLGEQGELYV EVRAQLERRIRARVAAEVKANAGETLREQLQAALREQLQAALREQLQAALRENIMQA	GGDGLARGYL AGDGVGRGYL GGIGVARGYV GGEGVARGYL GGAGLARGYY GGAGUALGYL TGIQLAQGYL GGIQVAQGYI RAAGLAEGYL LLPGYMVPAY ALPEYMLPAA HMVEYMYPTH ALPEYMLPSV SLPEYMVPAA SLPEYMVPAA QLPEHMVPAA QLPEHMVPAA	NRPDLT NKPDLT NKPDLT NLPELT NLPELT NRDELT KDPEKT GRPDLT NKEDAT GRPQLT NKEDAT GRPQLT VVVLDEIPI VVVMTEPL FVMLSELPL VVRLEHLPL VVRLEHLPL VVRLEHLPL
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VIEELPNCQ- FKEAGTAPR- WKQASPSLS- WNEKYPHTD- NQIICPSAE- WIDRHGLKTG WQQLTGAP LTDRFGQSMR FYSIFDNDKP LKAQLPDAD- LRSIAPNVD- EERFLEDPFY AERFVADPFN ASRFVANPFA TERFVOGLGT AERFVVNPFH AERFVNPFH AERFWNPFA AERFWADPFN AERFMANPFA GACFLADPFH AERFMANPFA GACFLADPFH AERFMANPFA GACFLADPFH AERFMANPFA	-LINGYGPTE -LTNVYGPTE -LWNCYGPTE -LWNCYGPTE -LINYGITE -LANLYGPTE -LHNLYGPTE -LINLYGPTE -LISLGGATE -VINLYGSTE -	NTTFTCCHK- TCVDASVHPV NTTFSTSFLI TTVHVTFKKL NSVATTILR- ASIDVTCHLI AAVDVSWYPA ATIDSSFYET TAIEVTYFDC ASIWSIFHPI SQRAVSFFKV RWLPDGNUEF RRNADGDIEF RYLPDGNLEY RWLPDGSLEY RWLPDGGYEY RULCDNGQVEY	ITVN DREYGG SAADIA	DLIKDSIPIG QSAYVPIG QSAYVPIG KNKSNIG LNKKERITIG QVRGSSVPIG ECTGDNVPIG QVRGSSVPIG LRDWTSIPYG DSLPDIIPVG RGYRIEPGEI RGFRIELGDI RGFRIELGEI RGFRIELGEI RGFRIELGEI RGFRIELGEI RGFRIELGEI RGFRIELGEI RGFRIELGEI	RPIANTQVYI KALGNNRLYI KALGNNRLYI RPLSTLQAHV HPIRNTKVFV YPVNNTGLRI SPLDNVHMYV QPLANQRWYV QPLANQRWYV QGMQNVQLLV EAALRSIEGV AAAIAVDPTV EAYLNQHPDV EARLSQCAGV EARLSQCAGV GASLARCDGV GASLARCDGV GASLARCDGV GARLEHPQV EARLLEHPQV	LDDVL QLV LDQKG RLQ MDAMH NLQ LHGN QPV LDGMM QPV LDAMM HPV LSQTD Q1Q LNDKK QKC LDDQG RPC VDPNDKMRLC REAAVTVRTD GQAVVVSDL KHTCVVARKN QQAVVILDSK SEAVVINRED SEAVVINRED SEAVVINRED SEAVVINRED REAAVLARED REAAVLALDS	PIGIAGELYI PEGVAGELYI PEGVAGELYI PIGAPGELCV PTGVPGELYI PIGAAGELCI PIGVAGELWI PIGVAGELWI PIGVAGELYI PIGVVGELYI PIGVVGELYI PWYTGRLFI DLGEQGELYVEVRAQLERRIRARVAAAEVKAWAGEELEKLLASTLREQLQATLREQLQATLREQLQSALRRHMQAALKRHMQAALKRHHKQAALKRHMQA	GGDGLARGYL AGDGVGRGYL GGIGVARGYV GGEGVARGYV GGGVQLALGYL TGIQLAQGYL GGIQVARGYH GGIQVARGYH RAGLAEGYL LLPGYMVPAY ALPEYMLPAY ALPEYMLPAY ALPEYMLPSV SLPEYMVPAA RLPEYMVPAA RLPEYMVPAA RLPEYMVPAA QLPEYMVPAA QLPEHMVPAA QLPEHMVPAA	NRPDLT NKPDLT NKPDLT NLPELT NLPELT NRDELT KDPEKT GRPDLT NKEDAT GRPQLT GDDEKTAELN MIEMEGWPV VVVLDEIPI VVVLDEIPI VVVLEHLPL VVKLEHLPL VVKLEHLPL LLLLASLPL
VIEELPNCQ- FKEAGTAPR- WKQASPSLS- WNEKYPHTD- NQIICPSAE- WIDRHGLKTG WQQLTGAP LTDRFGQSMR FYSIFDNDKP LKAQLPDAD- LRSIAPNVD- EERFLEDPFY AERFVADPFN ASRFVANPFA TERFVGGLGT AERFVVNPFH AERFVVNPFH AERFVVNPFH AERFVDPFH	-LINGYGPTE -LTNVYGPTE -LWNCYGPTE -LWNCYGPTE -LWNCYGPTE -LANLYGPTE -LANLYGPTE -LHNLYGPTE -LINSYGVTE -LISLGGATE -VINLYGSTE ERMYKTGDVA SRLYRTGDLA STLYKTGDLA ERMYRTGDLG ERMYRTGDLG ARMYKTGDLG ARMYKTGDLG CRMYRTGDLG ARMYKTGDLG CRMYRTGDLG CRMYCSGDLA	NTTFTCCHK- TCVDASVHPV NTTFSTSFLI TTVHVTFKKL NSVATTILR- ASIDVTCHLI AAVDVSWYPA ATIDSSFYET TAIEVTYFDC ASIWSIFHPI SQRAVSFFKV RWLPDGNLEY RKAPDGSLEY RWLDGGYEY RWLDGGYEY RWMPDGTLEY	ITVN DREYGG SAADIA	DLIKDSIPIG QSAYVPIG QSAYVPIG KNKSNIG LNKKERITIG QVRGSSVPIG ECTGDNVPIG DYKSEDVPIG LRDWTSIPVG RGYRIEPGEI RGFRIELGDIV RGMRLEIDV RGLRIELGEI RGFRIELGEI	RPIANTQVYI KALGNNRLYI KALGNNRLYI RPLSTLQAHV HPIRNTKVFV KAIDNVYVKV YPVWNTGLRI SPLPNVHMYV QFMQNVQLLV EAALRSIEGV AAALAVDPTV EVGLAEHPRV EAVINQHPDV EARLSQCAGV EASLSQCAGV EASLSQCAGV EASLSQCAGV EASLSQCAGV SSRILDHPLV SSRILDHPLV	LDDVL QLV LDQKG RLQ MDAMH NLQ LHGM QPV LDGM QPV LDGM QPV LDDKK QKC LDDQG RPC VDPNDKMRLC REAAVTVRTD GQAVVVSDL RHTCVVARKN QQAVVILDSK SEAVVIWED SEAVVIV	PIGIAGELYI PEGVAGELYI PEGVAGELYI PIGAPGELCV PTGVPGELYI PIGAAGELCI PIGAAGELCI PIGAAGELCI PIGAAGELCI PIGAAGELCI PIGVAGELVI PIGVAGELYI PIGVYGELYI PIGVYGELYI PEWYTGRLFI DLGEQGELYVEVRAQLERRIRARVAAAELEKLLASTLREQLQAALREQLQATLREQLQAALREQLQA	GGDGLARGYL AGDGVGRGYL GGIGVARGYV GGEGVARGYL GGAGLARGYY GGAQLALGYL TGIQLAQGYL GGIQVAQGYI GGIQVARGYW RAAGLAEGYL LLPGYMVPAY ALPEYMLPAA HWVEYMVPTH QLPEYMLPAA SLPEYMVPAA RLPEYMVPAA QLPEHMVPAA QLPEYMVPAA QLPEYMVPAA QLPEYMVPAA	NRPDLT NKPDLT NKPELT NLPELT NRDELT KQQELT KQPEKT GRPDLT NKEDAT GRPQLT GDDEKTAELN MIEMEQWPV YVVLDEIPI VVMTEFPL FVMLSELPL YVKLERLPL YVKLERLPL YVKLEHLPL YVKLEHLPL YVKLEHLPL YVKLEHLPL YIKHELPL YIKHELPL YIKHELPL YIKHELPL YIKHDLPM
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VIEELPNCQ- FKEAGTAPR- WKQASPSLS- WNEKYPHTD- NQILCPSAE- WIDRHGLKTG WQQLTGAP LTDRFGQSMR FYSIFDNDKP LKAQLPDAD- LRSIAPNVD- EERFLEDPFY AERFVADPFA ASRFVANPFA TERFVGGLGT AERFVVNPFH AERFVVNPFH AERFVVNPFH AERFVADPYG GACFLADPFH AERFVADPYG	-LINGYGPTE -LTNVYGPTE -LWNCYGPTE -LWNCYGPTE -LWNCYGPTE -LANLYGPTE -LANLYGPTE -LHNLYGPTE -LINSYGVTE -LISLGGATE -VINLYGSTE	NTTFTCCHK- TCVDASVHPV NTTFSTSFLI TTVHVTFKKL NSVATTILR- ASIDVTCHLI AAVDVSWYPA ATIDSSFYET TAIEVTYFDC ASIWSIFHPI SQRAVSFFKV RWLPDGSLEY RWLPDGSLEY RWLPDGSLEY RWLPDGSLEY RWLPDGSLEY RWLPDGSLEY RWLPDGSLEY RWLPDGSLEY RWLPDGSLEY RWLPDGSLEY RWLPDGSLEY RWLPDGSLEY RWLPDGSLEY RWLPDGSLEY RWLDGGEY RWLDGSLEY RWLDGGEY RYLDGGKLEY	ITVN DRENAV DREYGG SAADIA	DLIKDSIPIG QSAYVPIG QSAYVPIG KNKSNIG LNKKERITIG QVRGSSVPIG ECTGDNVPIG DYKSEDVPIG LRDWTSIPVG RGYRIEPGEI RGFRIELGDV RGGRIELGEI RGFRIELGEI	RPIANTQVYI KALGNNRLYI KALGNNRLYI RPLSTLQAHV HPIRNTKVFV KAIDNVYVKV YPVWNTGLRI SPLPNVHMYV QFMQNVQLLV EAALRSIEGV AAALAVDPTV EVGLAEHPRV EAVINQHPDV EARLSQCAGV EASLSQCAGV EASLSQCAGV EASLSQCAGV EASLSQCAGV SSRILDNPLV DAVLANHPHI EAVLATRPEL EAVLATRPEL EAVLATRPEL EAVLATRPEL EAVLATRPEL	LDDVL QLV LDQKG RLQ MDAMH NLQ LHGN QPV LDGM QPV LDAMM HPV LSQTD QIQ LNDKK QKC LDDQG RPC VDPNDKMRLC REAAVTVRTD GQAVVVVSDL RHTCVVARKN QQAVVILDSK SEAVVIVRED SEAVVIVRED SEAVVTRED REAAVLARED SADAAVVIHTA EQAAVVVRED AQAAVVVRED SQAVVVVRED SQAVVVVSQED	PIGIAGELYI PEGVAGELYI PEGVAGELYI PIGAPGELCV PTGVPGELYI PIGAAGELCI PIGAAGELCI PIGAAGELCI PIGAAGELCI PIGAAGELCI PIGVAGELVI PIGVAGELYI PIGVYGELYI PIGVYGELYI PIGVYGELYI PEWYTGRLFI DLGEQGELYVEVRAQLERRIRARVAAAELEKLLASTLREQLQAALREQLQAALREQLQAALREQLQAALREALQQELRAYMGAALREQLQQELRAYMGAALREALQQELRAYMGAALREALQQELRAYMGAALREALQQELRAYMGAALREALQQELRAYMGAALREALQQ	GGDGLARGYL AGDGVGRGYL GGIGVARGYV GGEGVARGYV GGEGVARGYV GGAGLARGYV TGIQLAQGYL GGAGVAKCYH GGIQVAQGYI GGIGVARGYW RAAGLAEGYL LLPGYMVPAY ALPEYMLPAA HWVEYMVPTH QLPEYMLPAA RLPEYMVPAA RLPEYMVPAA RLPEYMVPAA RLPEYMVPAA RLPDYMVPAH	NRPDLT NKPDLT NKPDLT NLPELT NRDELT KQQELT KQPEKT GRPDLT NKEDAT GRPQLT GDDEKTAELN MIEMEQWPV YVVLDEIPI VVNLEHLPL YVKLEHLPL
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VIEELPNCQ- FKEAGTAPR- WKQASPSLS- WNEKYPHTD- WQITCPSAE- WIDRHGLKTG WQQLTGAP LTDRFGQSMR FYSIFDNDKP LKAQLPDAD- LRSIAPNVD- EERFLEDPFY AERFVADPFN AERFVADPFN AERFVADPFN AERFVADPFN AERFVNDFFG AERFVNDFFG AERFVADPYG AERFLAQGS- DERFIKQS DERFIKQS AERFIRDWGL	-LINGYGPTE -LTNVYGPTE -LWNCYGPTE -LWNCYGPTE -LWNCYGPTE -LANLYGPTE -LANLYGPTE -LANLYGPTE -LINLYGPTE -LINLYGPTE -LINLYGPTE -LISLGGATE -VINLYGSTE	NTTFTCCHK- TCVDASVHPV NTTFSTSFLI TTVHVTFKKL NSVATTILR- ASIDVTCHLI AAVDVSWYPA ATIDSSFYET TAIEVTYFDC ASIWSIFHPI SQRAVSFFKV RWLPDGSLEY RWLPDGTIEF RWLPDGTIEF RWLPDGTIEF RWLPDGTIEF RWLPDGTIEF KRISNGELEY RFLPDGTIEY KELPDGTIEY KELPDGTIEY RWLDDGJEY RWLDDGJEY RWLDDGJEY RWLDDGJEY RWLDDGJEY RWLPDGTIEY	IPPENAV DREYGG SAADIA	DLIKDSIPIG QSAYVPIG QSAYVPIG KNKSNIG LNKKERITIG QVRSSSVPIG ECTGDNVPIG ECTGDNVPIG DYKSEDVPIG LRDWTSIPYG DSLPDIIPVG RGYRIEPGEI RGFRIELGEI	RPIANTQVYI KALGNNRLYI KALGNNRLYI RPLSTLQAHV HPIRNTKVFVV KAIDNVYVKV YPWNNTGLRI SPLPNVHYVV EPLDNVENYV EPLDNVENYV EPLDNVENYV EPLDNVENYV EPLDNVENYV EPLDNVENYV EVGLAEHPRV EANLINGLES EARLSQCAGV EARLCQAGV EARLCQAGV EARLCQAGV EARLCQAGV EARLCQAGV EARLCQAGV EARLCQAGV EARLCAGV	LDDVL QLV LDQKG RLQ MDAMH NLQ LHGN QPV LDAMM HPV LDGM QPV LDAMM HPV LSQTD QIQ LNDKK QKC LDDQG RPC VDPNDKMRLC REAAVTVRTD GQAVVVYSDL RHTCVVARKN QQAVVILDSK SEAVVAMRED SEAVVIVRED SEAVVIVRED SEAVVIVRED SEAVVIVRED REAAVLALDS ADAAVVIHTA EQAAVVVRED AQAAVVIRED AQAAVITRAD KEAAVILARPD TEAAVILARPD TEAAVILARDV REAAVILARDV REAAALAAVDY EQAVTHACVI EQAVTHACVI	PIGIAGELYI PEGVAGELYI PEGVAGELYI PIGAPGELCV PTGVPGELYI PIGAAGELCI PIGAMGELWL PPGVAGDLYL PIGVAGELYI	GGDGLARGYL AGDGVGRGYL GGIGVARGYV GGEGVARGYV GGEGVARGYV GGGVALGYL TGIQLAQGYI GGIGVARGYW GGIGVARGYW GGIGVARGYW GGIGVARGYW GAGLAGYL LLPGYMVPAY ALPEYMLPAA HMVEYMVPTH QLPEYMVPAA SLPEYMVPAA RLPEYMVPAA RLPEYMVPAA QLPEHMVPAA QLPEHMVPAA RLPDYMVPAH RLPDYMVPAH RLPDYMVPAH RLPDYMVPAH RLPDYMVPAH RLPDYMVPAS KLPYMIPGV KLPAYMLPSA KLPYMPFA KLPYMPFA KLPYMPFA KLPYMPFA KLPYMPFA KLPYMPFA KLPYMPFA KLPYMPFA KLPYMPFA KLPYMIPGA	NRPDLT NKPDLT NKPDLT NLPELT NLEDLT VYULEHLPL VYVLEHLPL VYRLEHLPL VYRLEHLP VYRLEHLPL VYRLEHL
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Figure 2
Alignment of the selected 27 amino acid sequences. This alignment was used in the maximum likelihood analysis. Protein names were shown in Materials and Methods.

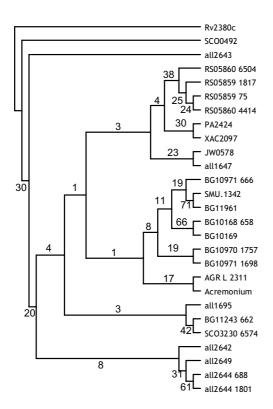


Figure 3
The bootstrap consensus tree among the selected 27 amino acid sequences based on the maximum likelihood analysis.
The JTT model was used as the model of amino acid substitution. Number of times of bootstrap replicates was 100.
Number of times to jumble in the proml program was 5. Protein names were shown in Materials and Methods.

cherichia coli K-12 W3110 Enterochelin synthetase component F; MT2448, Mycobacterium tuberculosis CDC1551 peptide synthetase; OB0958, Oceanobacillus iheyensis HTE831 monomodular nonribosomal peptide synthetase; PA2399, Pseudomonas aeruginosa PA01 pyoverdine synthetase D; PA2402, Pseudomonas aeruginosa PA01 probable non-ribosomal peptide synthetase; PA2424, Pseudomonas aeruginosa PA01 probable non-ribosomal peptide synthetase; RS05859, Ralstonia solanacearum GMI1000 probable peptide synthetase protein; RS05860, Ralstonia solanacearum GMI1000 probable peptide synthetase protein; Rv2380c, Mycobacterium tuberculosis H37Rv mbtE; SCO0492, Streptomyces coelicolor A3(2) putative peptide synthetase; SCO3230, Streptomyces coelicolor A3(2) CDA peptide synthetase I; SCO3231, Streptomyces coelicolor A3(2) CDA peptide synthetase II; SF0498, Shigella flexneri 301 (serotype 2a) ATP-dependent serine activating enzyme; SMU.1342, Streptococcus mutans UA159

(serotype C) putative bacitracin synthetase 1; STM0588, *Salmonella typhimurium* LT2 enterobactin synthetase, component F (nonribosomal peptide synthetase); STY0631, *Salmonella typhi* enterobactin synthetase component F; XAC2097, *Xanthomonas axonopodis* pv. *citri* 306 ATP-dependent serine activating enzyme; Z0727, *Escherichia coli* O157:H7 EDL933 enterobactin synthetase component F.

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