# WrbA from *Escherichia coli* and *Archaeoglobus fulgidus* Is an NAD(P)H:Quinone Oxidoreductase

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WrbA (tryptophan [W] repressor-binding protein) was discovered in *Escherichia coli*, where it was proposed to play a role in regulation of the tryptophan operon; however, this has been put in question, leaving the function unknown. Here we report a phylogenetic analysis of 30 sequences which indicated that WrbA is the prototype of a distinct family of flavoproteins which exists in a diversity of cell types across all three domains of life and includes documented NAD(P)H:quinone oxidoreductases (NQOs) from the *Fungi* and *Viridiplantae* kingdoms. Biochemical characterization of the prototypic WrbA protein from *E. coli* and WrbA from *Archaeo-globus fulgidus*, a hyperthermophilic species from the *Archaea* domain, shows that these enzymes have NQO activity, suggesting that this activity is a defining characteristic of the WrbA family that we designate a new type of NQO (type IV). For *E. coli* WrbA, the  $K_m^{NADH}$  was  $14 \pm 0.43 \mu$ M and the  $K_m^{benzoquinone}$  was  $5.8 \pm 0.12 \mu$ M. For *A. fulgidus* WrbA, the  $K_m^{NADH}$  was  $19 \pm 1.7 \mu$ M and the  $K_m^{benzoquinone}$  was  $37 \pm 3.6 \mu$ M. Both enzymes were found to be homodimeric by gel filtration chromatography and homotetrameric by dynamic light scattering and to contain one flavin mononucleotide molecule per monomer. The NQO activity of each enzyme is retained over a broad pH range, and apparent initial velocities indicate that maximal activities are comparable to the optimum growth temperature for the respective organisms. The results are discussed and implicate WrbA in the two-electron reduction of quinones, protecting against oxidative stress.

The tryptophan (W) repressor-binding protein (WrbA) from Escherichia coli (WrbA<sub>E. coli</sub>) was discovered in 1993, when it was copurified with the tryptophan repressor (TrpR) (66). Biochemical characterization of WrbA<sub>E. coli</sub> showed that the protein binds one flavin mononucleotide (FMN) molecule per monomer and is multimeric in solution (29). These results, combined with sequence analysis and homology-based structural modeling, led to the suggestion that  $WrbA_{E_{i}}$  coli is the founding member of a new family of multimeric flavodoxinlike proteins. It was predicted that the WrbA family contains an  $\alpha\beta$  twisted open-sheet fold characteristic of flavodoxins and a conserved insertion after strand  $\beta$ 4, forming an additional  $\alpha\beta$ unit (28). The presence of this fold has recently been confirmed in the published crystal structures of the Deinococcus radiodurans and Pseudomonas aeruginosa WrbA homologues (26). WrbA<sub>E. coli</sub> is the only purified and biochemically characterized WrbA protein in the literature. No enzyme activity was reported; however, it was reported that  $WrbA_{E,coli}$  enhances the development of noncovalent complexes between the TrpR holorepressor and operator DNA and that WrbA<sub>E. coli</sub> alone is not competent to interact with the DNA targets (66). Thus, it was proposed that WrbA<sub>E. coli</sub> is an accessory element which blocks TrpR-specific transcriptional events that are deleterious to cells entering stationary phase. However, it was later concluded that WrbA<sub>E, coli</sub> does not specifically affect the TrpR-DNA complex, placing the earlier proposed function in doubt (29). Thus, the function of WrbA is unknown.

Several global expression studies show that *wrbA* in *E. coli* is under the control of RpoS (the stress response sigma factor,  $\sigma^{s}$  or  $\sigma^{38}$ ). These studies report that *wrbA* is upregulated in response to stressors such as acids, salts, H<sub>2</sub>O<sub>2</sub>, and diauxie. WrbA<sub>*E. coli*</sub> is also upregulated in the early stages of the stationary phase, indicating that it could play a role in preparing the cell for long-term maintenance under stress conditions (14, 17, 31, 35, 50, 51, 59, 61). Two additional expression studies implicate WrbA<sub>*E. coli*</sub> in oxidative stress. One study shows that *E. coli wrbA* is repressed when ArcA is phosphorylated, which occurs when the quinone pool is reduced (41), and another study shows that *E. coli wrbA* is repressed by fumarate and nitrate reductase regulatory protein under anaerobic conditions (34). Aside from these findings, nothing is known about the role of WrbA in the stress response.

The most comprehensive sequence analysis of WrbA<sub>E. coli</sub> was reported in 1994 by Grandori and Carey (28). Since that time, genomic sequencing has identified more than 100 genes annotated as encoding WrbA from metabolically and phylogenetically diverse prokaryotes spanning the Bacteria and Archaea domains, consistent with a fundamental function for the WrbA family in the physiology of prokaryotes. However, WrbA<sub>E, coli</sub> is the only WrbA that has been biochemically characterized. Here we show that several biochemically characterized NAD(P)H:quinone oxidoreductases (NQOs) from the Fungi and Viridiplantae kingdoms have significant sequence identity to WrbA and belong to the same family (10, 11, 18, 33, 37, 44, 64). We also report the initial biochemical characterization of WrbA from Archaeoglobus fulgidus (WrbA<sub>A. fulgidus</sub>), a hyperthermophile and a representative of the Archaea domain, and demonstrate that WrbA<sub>E. coli</sub> and WrbA<sub>A. fulgidus</sub> exhibit robust NQO activity. The results presented are consistent with a role for WrbA

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in the oxidative stress response of diverse prokaryotes from the *Bacteria* and *Archaea* domains.

#### MATERIALS AND METHODS

**Materials and reagents.** Primers were obtained through Integrated DNA Technologies (Coralville, IA). *E. coli* K-12 MG1655 genomic DNA was a gift from Sue-Jean Hong and Kenneth Keiler (The Pennsylvania State University). All materials used to construct *E. coli* knockouts were gifts from Joe Palladino and Sarah Ades (The Pennsylvania State University). *A. fulgidus* genomic DNA was a gift from Michael W. Adams (University). *A. fulgidus* genomic DNA was a gift from Michael W. Adams (University of Georgia). All cell lines and plasmids were obtained through Novagen (Madison, WI). The chromatography resins and equipment were purchased from Amersham Biosciences, (Piscataway, NJ). F<sub>420</sub> and 2-hydroxyphenazine were gifts from Uwe Deppenmeier. All other chemicals were purchased from ICN (MP Biomedical), Sigma, or ACROS. Phenotypic analysis of the *E. coli wrbA* mutant strain was contracted to Phenotype MicroArray Services at Biolog, Inc. (Hayward, CA).

Sequence alignments and construction of the phylogenetic tree. Sequences were aligned with ClustalX (v1.83) with a BLOSUM62 matrix and default parameters. The output was edited with the Alignment Editor of MEGA (v3.1) and visualized with BioEdit (v7.0.5.2). The phylogenetic tree was constructed with the MEGA package. Distance matrices were generated in MEGA by the minimum-evolution method with the Jones-Taylor-Thornton option and the close-neighbor interchange option with a search level of 1. Gaps were deleted in a pairwise manner. The confidence limits of the nodes were estimated with the bootstrap option. Phylogenetic trees were also constructed by the parsimony method, the neighbor-joining method, and the unweighted-pair group method using average linkages available in MEGA, but the minimum-evolution method produced the tree with the greatest bootstrap values.

Cloning, expression, purification, and reconstitution. The b1004 open reading frame (ORF) was amplified by PCR from E. coli K-12 MG1655 genomic DNA with sense (ATGGCTAAAGTTCTGGTGC) and antisense (CCTCCTGTTGA AGATTAGCC) primers. The AF0343 ORF was amplified by PCR from A. fulgidus genomic DNA with sense (ATGGCCAGGATTCTTGTTATTTTCA TTCC) and antisense (CCCTTAGCAGAGCTTTTCAGCCACCTC) primers. Each PCR product was amplified and cloned into pETBlue-1 to obtain recombinant plasmids pETecb1004 from b1004 and pETaf0343 from AF0343. E. coli NovaBlue cells were used to amplify each plasmid. DNA sequencing confirmed that E. coli wrbA and A. fulgidus wrbA were intact in pETecb1004 and pETaf0343, respectively. Since the AF0343 ORF contains 12% rare codons with two rare-codon repeats, pETecb1004 and pETaf0343 were each transformed into E. coli RosettaBlue(DE3)pLacI competent cells for expression. The transformed cells were cultured at 37°C in terrific broth containing 50 µg/ml ampicillin and 34 µg/ml chloramphenicol. When the optical density at 600 nm reached 0.6, production of WrbA<sub>E. coli</sub> or WrbA<sub>A. fulgidus</sub> was induced by the addition of 0.4 mM isopropyl-β-D-thiogalactopyranoside (IPTG) at 37°C. Cells were harvested after 4 h by centrifugation and stored at  $-80^{\circ}$ C.

Initial purification and reconstitution of WrbAA. fulgidus were carried out anaerobically with an anaerobic chamber (COY Laboratory Products, Ann Arbor, MI) and at room temperature except where indicated otherwise. A comparison of the aerobic and anaerobic protocols showed no difference in the measured activities of purified protein; thus, all subsequent purifications were carried out aerobically. For WrbAA. fulgidus, thawed cells (10 g [wet weight]) were resuspended in 45 ml of 50 mM sodium phosphate buffer (pH 6.6) and lysed by three passes through a French press at 20,000 lb/in2 (137.9 MPa). Cell debris was removed by centrifugation at 65,000  $\times$  g for 45 min at 4°C, and the cleared lysate was diluted to 80 ml with 50 mM sodium phosphate buffer (pH 6.6) and incubated at 75°C for 30 min while stirring. Denatured proteins were pelleted by centrifugation at  $65,000 \times g$  for 45 min at 4°C. The supernatant was filtered and loaded onto a Q-Sepharose column equilibrated with 50 mM sodium phosphate buffer (pH 6.6). The column was developed with a 0.0 to 0.4 M NaCl linear gradient over 500 ml, applied at 2 ml/min. Yellow fractions containing WrbAA. fulgidus, monitored by sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE), were pooled, diluted fourfold with 50 mM sodium phosphate buffer (pH 7.8), and loaded onto a Q-Sepharose column equilibrated with 50 mM sodium phosphate buffer (pH 7.8). The column was developed with a 0.0 to 0.4 M NaCl linear gradient over 500 ml, applied at 2 ml/min. Yellow fractions containing WrbAA. fulgidus, monitored by SDS-PAGE, were pooled and concentrated to 1 ml with a Vivacell 70 with a 10,000 molecular weight cutoff membrane (Vivascience, Hanover, Germany). The concentrated solution was loaded onto a Sephadex-200 column equilibrated with 150 mM morpholinepropanesulfonic acid (MOPS; pH 7.2). Yellow fractions containing-WrbAA. fulgidus, monitored by SDS-PAGE, were pooled and incubated with 5 mM FMN for 16 h at 4°C. This solution was then dialyzed against 50 mM MOPS (pH 7.2)

and concentrated to 2.5 ml. Excess FMN was removed by passage through a PD-10 column, and the solution containing FMN-reconstituted WrbA<sub>A. fulgidus</sub> was stored at  $-80^{\circ}$ C.

The same protocol was used for the purification and reconstitution of  $WrbA_{E. coli}$ , except that heat denaturation was excluded from the protocol.

**Biochemical analyses.** The subunit molecular mass of each protein was estimated by 12% SDS-PAGE with low-molecular-weight markers from Bio-Rad. Native molecular mass was estimated from the elution volume from a Sephadex-S200 gel filtration fast protein liquid chromatography column calibrated with the following proteins of known molecular masses: bovine serum albumin (66 kDa), ovalbumin (45 kDa), carbonic anhydrase (31 kDa), chymotrypsinogen (25 kDa), and RNase A (13.7 kDa). The buffer (50 mM MOPS, 150 mM NaCl, pH 7.2) was applied at 0.5 ml min<sup>-1</sup>. Further oligomerization was estimated by dynamic light-scattering analyses, which were performed in triplicate with each analysis incorporating at least 10 readings.

After reconstitution, the Pierce assay was used to determine protein concentrations. Flavin/monomer ratios were calculated after quantifying the amount of FMN released by acidification (5% trichloroacetic acid) with an extinction coefficient for FMN of 12.2 mM<sup>-1</sup> cm<sup>-1</sup> at 450 nm.

The flavin cofactor of WrbA<sub>*E. coli*</sub> was previously identified as FMN (29). To identify the flavin in WrbA<sub>*A. fulgidus*</sub>, the flavin cofactor was extracted from purified protein by acidification of the protein solution with 5% trichloroacetic acid. A Hewlett-Packard model 1050 high-performance liquid chromatography system in conjunction with a Hewlett-Packard LiChrosorb C<sub>18</sub> reversed-phase column was used to identify the flavin extracted from WrbA<sub>*A. fulgidus*</sub>. Neutralized samples were injected into a mobile phase consisting of 10 mM potassium phosphate, 12.5% acetonitrile, 0.3% triethylamine, and 0.01% sodium azide at a pH of 6.5. Elution of flavin was monitored at 450 nm.

Activities. Reactions were monitored with a Varian Cary 50 spectrophotometer in combination with a Peltier thermostat-equipped accessory and an anaerobic fluorescence cuvette (2 mm by 1 cm [path length]) from Starna (Atascadero, CA). Although fluorescence was not measured, the cuvette permitted small reaction volumes under anaerobic conditions, and the 2-mm path length permitted high concentrations of NADH to be accurately determined spectroscopically. WrbA<sub>A. fulgidus</sub> activity measurements were obtained at 65°C, and WrbA<sub>E. coli</sub> activity measurements were obtained at 37°C unless indicated otherwise. Reactions were initiated by addition of the enzyme after temperature equilibration of the assay mixture. All activities were performed in triplicate, and all nonenzymatic rates were taken into account.

NADH was used as the electron donor to determine the specific activities of WrbA<sub>E. coli</sub> and WrbA<sub>A. fulgidus</sub> with a variety of electron acceptors. Reaction mixtures contained 50 mM MOPS (pH 7.2) with 800  $\mu$ M NADH, 400  $\mu$ M electron acceptor, and variable concentrations of WrbA<sub>E. coli</sub> or WrbA<sub>A. fulgidus</sub>. With 1,4-benzoquinone and 2,3-dihydroxy-5-methyl-1,4-benzoquinone, oxidation of NADH was monitored at 340 nm ( $\epsilon_{340} = 6.22$  mM<sup>-1</sup> cm<sup>-1</sup>). With menadione, NADH oxidation was monitored at 341 nm ( $\epsilon_{341} = 6.22$  mM<sup>-1</sup> cm<sup>-1</sup>), which is the isosbestic point for menadione at both 37°C and 65°C. With naphthoquinone, oxidation was measured at the appropriate isosbestic point of naphthoquinone, which shifted from 340 nm at 37°C to 341 nm at 65°C. With K<sub>3</sub>FeCN<sub>6</sub> ( $\epsilon_{420} = 1.04$  mM<sup>-1</sup> cm<sup>-1</sup>) and 2,6-dichlorophenolindophenol ( $\epsilon_{610} = 21$  mM<sup>-1</sup> cm<sup>-1</sup>), the rates of reduction were monitored at the indicated wavelengths. The initial 0 s of each progress curve was taken as the apparent initial velocity. Nonenzymatic reactions represented <8% of all enzymatic reaction conditions.

Steady-state kinetic studies were conducted with 50 mM MOPS (pH 7.2) at 37°C and various enzyme concentrations. The kinetic parameters for 1,4-benzoquinone were determined by monitoring the oxidation of 200  $\mu$ M NADH at 340 nm. The kinetic parameters for NAD(P)H were determined by monitoring the reduction of 200  $\mu$ M K<sub>3</sub>FeCN<sub>6</sub> at 420 nm. Benzoquinone and NAD(P)H concentrations were varied from 0.2 to 10 times the respective  $K_m$  values. The initial 2 to 5 s of each progress curve was taken as the apparent initial velocity, and the Michaelis-Menten equation was fitted to the data with KaleidaGraph v3.5. Non-enzymatic reactions represented <2% of all enzymatic reaction conditions.

The pH dependence of apparent initial velocities for electron transfer from NADH to menadione was measured over a wide pH range by monitoring the oxidation of NADH at 341 nm. Reaction mixtures contained 800  $\mu$ M NADH, 400  $\mu$ M menadione, and 0.1  $\mu$ M WrbA<sub>*E*</sub>. coli</sub> or 0.03  $\mu$ M WrbA<sub>*A*</sub>. fulgidus. For WrbA<sub>*E*</sub>. coli<sup>3</sup> a buffer mixture with 50 mM each Na-acetate–morpholineethanesulfonic acid (MES)–MOPS–Tris(hydroxymethyl)methylaminopropanesulfonic acid, sodium salt (TAPS) was used from pH 4.0 to 8.5. This buffer mixture (50 mM TAPS, 50 mM glycine) was used from pH 7.5 to 9.5. The initial 10 s of each progress curve was taken as the apparent initial velocity. Nonenzymatic reactions represented <8% of all enzymatic reaction conditions.

The temperature dependence of apparent initial velocities for electron transfer from NADH to menadione was determined by monitoring the oxidation of NADH at 341 nm. Reaction mixtures contained 800  $\mu$ M NADH, 400  $\mu$ M menadione, and 0.1  $\mu$ M WrbA<sub>E. coli</sub> or 0.03  $\mu$ M WrbA<sub>A. fulgidus</sub>. All reactions were performed in 50 mM sodium phosphate (pH 7.2) at 25°C. WrbA<sub>E. coli</sub> was assayed from 10°C to 60°C, and WrbA<sub>A. fulgidus</sub> was assayed from 10°C to 100°C. The initial 5 s of each progress curve was taken as the apparent initial velocity. Nonenzymatic reactions represented <8% of all enzymatic reaction conditions.

**Disruption of** *wrbA*. *E. coli* K-12 MG1655 ( $F^-$  lambda<sup>-</sup> *ilvG rfb-50 rph-1*) was used as the wild-type (WT) strain, and disruption of *wrbA* was conducted according to previously published methods (20). Primers were constructed with the pKD4 template, and kanamycin resistance genes were eliminated by with the pCP20FLP helper plasmid. Elimination of temperature-sensitive plasmids and thermal induction of the FLP recombinase synthesis were carried out with Luria broth at 43°C.

# RESULTS

**Homology, sequence analysis, and phylogeny.** The most comprehensive sequence analysis of WrbA<sub>*E. coli*</sub>, the only biochemically characterized WrbA to date, was done in 1994, when WrbA<sub>*E. coli*</sub> was suggested to be the prototype of a new family of flavoproteins (28). However, the analysis included only six sequences of putative WrbA homologues; therefore, a BLAST search of all nonredundant databases was performed with the 198-residue protein sequence of WrbA<sub>*E. coli*</sub>, encoded by locus b1004 in *E. coli* K-12 MG1655, as the query. A survey of the returned 394 sequences revealed 128 predicted WrbA proteins that had between 22% and 99% identity to WrbA<sub>*E. coli*</sub>.

The genes neighboring the loci encoding the WrbA homologues were surveyed, but no consistencies were found to suggest a common function. The returned BLAST results included 20 sequences annotated as fungal and plant quinone reductases, suggesting that these enzymes could be related to WrbA. Among the aligned data set were five documented NQOs from the Fungi and Viridiplantae kingdoms that are biochemically characterized (FQR1 from Arabidopsis thaliana, QR1 and QR2 from Gloeophyllum trabeum, QR from Phanerochaete chrysosporium, and QR2 from Triphysaria versicolor) (10, 11, 18, 33, 37, 44). These five documented quinone reductases have between 43% and 48% identity to  $WrbA_{E, coli}$ . Replicate sequences, truncated sequences, and sequences with partial alignments were removed from the BLAST results, and an initial phylogenetic tree was constructed with an alignment of the remaining 208 sequences (not shown). From the collected sequences, 30 were selected to represent the initial tree. These sequences were aligned (Fig. 1), and a bootstrapped phylogenetic tree was constructed by the minimum-evolution method with three flavodoxin sequences to root the tree (Fig. 2). The clustering of the initial phylogenetic tree indicated that all of the proteins included in the data set diverged from a common ancestor distinct from classical flavodoxins. Moreover, these results identify NQOs as members of the WrbA family. The tree contained a diverse set of organisms from all three domains of life, which included psychrophiles, mesophiles, thermophiles, animal and plant pathogens, aerobes, and anaerobes. The tree also contained 8 NQO sequences from the Fungi and Viridiplantae kingdoms and 15 and 6 WrbA sequences from the Bacteria and Archaea domains, respectively.

The PROSITE flavodoxin signature sequence (LIV)(LIVFY) (FY)X(ST)(V)X(AGC)XT(P)XXAXX(LIV), indicative of the N-terminal region that spans an FMN-binding site, was

present across all aligned sequences, with little deviation from the motif (Fig. 1). The  $\alpha\beta$  twisted open-sheet fold typical of flavodoxins is present across all sequences of the aligned data set, with an additional  $\alpha\beta$  unit previously reported for the WrbA family (28). The invariant conservation of this additional  $\alpha\beta$  unit (Fig. 1) further supports the idea that the NQO and WrbA proteins diverged from a common ancestor distinct from classical flavodoxins. These results solidify the earlier proposal (28) of a new family of flavoproteins and further extends the WrbA family to all three domains of life.

In surveying the BLAST results, it was discovered that several sequences annotated as WrbA contain a motif strictly conserved in another FMN-containing protein family called iron-sulfur flavoprotein (Isf) (2, 5, 38, 39, 67). However, the Isf family contains an unusual compact cysteine motif (CX<sub>2</sub>CX<sub>2</sub>)  $CX_{5,7}C$ ) that binds a 4Fe-4S cluster not found in the sequences of WrbA proteins or the NQO enzymes aforementioned. A sequence alignment was constructed to address the relatedness between the Isf and WrbA families. The alignment included WrbA<sub>E. coli</sub> and WrbA<sub>A. fulgidus</sub>, representing the WrbA family; three Isf sequences, including the prototype (Isf from Methanosarcina thermophila); and seven misannotated WrbA sequences that contained the compact cysteine motif. Flavodoxin 5NLL from Clostridium beijerinckii was included for comparison to characterized flavodoxins (Fig. 3). The alignment demonstrates that the misannotated WrbA sequences with the compact cysteine motif belong to the Isf family. While Fig. 3 indicates that similarity persists across the alignment, the overall identity between WrbA and Isf sequences suggests significant deviation from a common ancestor. In deviating from the common ancestor, it is possible that either Isf lost the domain containing the 4Fe-4S cluster-binding motif, giving rise to the WrbA family, or WrbA acquired the domain, giving rise to the Isf family.

Biochemical characterization of WrbA<sub>E. coli</sub> and WrbA<sub>A. fulgidus</sub>. WrbA<sub>E. coli</sub> is the only prokaryotic WrbA biochemically characterized; thus, WrbAA. fulgidus from the Archaea domain was heterologously produced in E. coli and characterized for comparison to WrbA<sub>E. coli</sub> from the Bacteria domain. WrbA<sub>E. coli</sub> has 43% identity and 62% similarity to WrbAA. fulgidus, encoded by locus AF0343 in A. fulgidus. WrbA<sub>E. coli</sub> and WrbA<sub>A. fulgidus</sub> were each overexpressed in E. coli and purified to homogeneity, as determined by SDS-PAGE. The identity of each protein was confirmed by N-terminal sequencing of the first five residues: AKVLV for WrbA<sub>E, coli</sub> and ARILV for WrbA<sub>A, fulgidus</sub>. SDS-PAGE revealed that the subunit molecular mass of WrbA<sub>A. fulgidus</sub> was 22.1 kDa and that of WrbA<sub>E. coli</sub> was 21.2 kDa. Size exclusion chromatography showed that WrbAA. fulgidus had a native molecular mass of 52 kDa, suggesting that WrbA<sub>A. fulgidus</sub> is able to form a dimer, as previously reported for WrbA<sub>E. coli</sub> (29). Dynamic light-scattering analyses support the idea that both WrbA<sub>E. coli</sub> and WrbA<sub>A. fulgidus</sub> participate in tetramerization. Purified WrbA<sub>E. coli</sub> had a hydrodynamic radius of 3.9  $\pm$  0.12 nm, corresponding to a molecular mass of 79  $\pm$  6.7 kDa, while purified WrbA<sub>A. fulgidus</sub> had a hydrodynamic radius of 4.1  $\pm$  0.12 nm, corresponding to a molecular mass of 89  $\pm$  8.4 kDa. Each sample was found to be monodisperse, with WrbA<sub>E. coli</sub> or WrbA<sub>A. fulgidus</sub> representing over 99.5% of the mass. During purification,  $WrbA_{E.\ coli}$  retained FMN during elution from the first Q-Sepharose column

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PJS666WrbA	MPKVVVLYHSGYGHTQRMAQSVAQGAGA-	ELLAIDADGNLP	DGGWET	LNAADAIIMGSPTYM-	GSVSWQFKKFADASSKP-WYT	QA
EcaWrbA	MSKTVVIYHSGYGHTQRLAAAVAEGANA-	ELIAIDAEGNIS	DAEW	EKLNAADAIIFGTPTYM-	GGPTWQFKKFADASSKA-WFS	RT
BcWrbA	MSNIVIVYHSGYGHTQKLAEAVHAGAQE-AG	ATVRLLAVGDVD	DAGW	ATLDAADAIVFGAPTYM-	GGPSAQFKQFADATSKA-WFT	QK
XfWrbA	MLISIVYDSGYGHTARVAQAVAAGVQEMKG	ADVRLMAVADG	SVDW	EALEKSEAIIFGSPTYN-	GLISAKFKQFFEDSTKKAWVS	QK
NpWrbA	MPTVAIIYFSGAGHTHLMAQAIAEGATKVED	TTVELLRVT-GEQIVNGRW	KNDEGL	EKLNQADAIVFGSPTYM-	GGVAAOFKAFIDAASEV-WFR	HG
CaWrbA	TTPTCR-IFILHDHGEHVTOLAOAIGEGAAGV	TGVTVKISLP	ннатк	ADLLEADGIIIGTPNWT-	GI-KGTLKRWLDTTGDL-WEE	GS
AfWrbA	MARTLATENSTTONTMKLAKAVADGARE-GO	AEVAVKRVPETTPAETLEKNPGY	VKVRE-ELESFEVARP	ELODYDATTEGSPTRE-	SVMSSOMKOFTDMTGRL-WME	RR
PaeWrhA		FFARWRTWPAUSTECEAVAPD	TPAECAI.YATI	PDLKNCAGLALGSPTRF-	2NMASPLKYFLDGTSSL-WLT	GS .
ParWrbA				DDI KNCSCI AL CSPTHE	2NMAA DMKYEWDNEUT - NI A	CN
Falwiba Malwala 2		TEADI DEUDEUA DUEOUA EDA	IPDDCD IVCTE	DDLINGAGLALGSFIRE	SIMAAFPATEWDNIVII-WLA	GN
MOWIDA		IEARERIVPRVAPVIQVAEPA	DIPDODDLICIE		SNMAAPLAIFLDGIAIQ-WVN	GQ
Stwrda	MSCKPNILVLFYG-YGSIVELAKEIGKGAEEAGA	-EVKIRKVRETLPP-EFQS	RIPEDKVKDIPEVTL	DDMRWADGFAIGSPIRI-	JNMAGGLKTFLDTTAIL-WKD	NV
SsWrbA	MEC-PKILVLFYG-YGSIVDLAKNVAEGAKEITK	-EVKLARVKEYFPQ-EIVNKF	RIPIDTVKDIPEATL	SDLEWADGIVMGSPTRY-	GNMTGQLKLFLDQTAEL-WIK	GS
EcoWrbA	MAKVLVLYYSMYGHIETMARAVAEGASKVDG	AEVVVKRVPETMPPQLFEKAG	GKT-QTAPVATP	QELADYDAIIFGTPTRF-	GNMSGQMRTFLDQTGGL-WAS	GA
YpWrbA	-MEHREMAKILVLYYSMYGHIETLAGAIAEGARKVSG	VDVTIKRVPETMPAEAFAKAG	GKTNQQAPVATPI	HELADYDGIIFGTPTRF-	GNMSGQMRTFLDQTGGL-WAS	GA
CcWrbA	MAKVLVLYYSSYGHLEVMAKAIAEGAREA-G	ASVDIKRVPETVPLEIAKGAH	FKLDQDAPVAKV	EDLADYDAIIVGAPTRF-	GRMASQMAAFFDAAGGL-WAR	GA
MBNC1WrbA	MAKILVLYYSSWGHMEAMAMAAARGAGEAGA	-NVTIKRVPELVPEEVARKAH	YKLEQEAQIATP	LELADYDGFIFGVSTRY-	GMMSSQLKNFLDQTGPL-WAA	GK
MacWrbA	MVKVNIIFYSMYGHVYRMAEAVAAGAREVEG	AEVGIYQVPETLPEEVLEKMGA-	IETKKLFAHIPVLTREMNE	EVLAGADALIFGTPTRY-	GNMTAQMRAVLDGLGGL-WNR	DA
MmWrbA	MVKVNIIFHSVHAHIYRMAEAVAAGAREVEG	AEVGIYOVPETLPEDVLEKMGA-	IETKKLFAHIPVVTRDMYE	DVLAGADALIFGTPTRY-	GMMTAQMRAVLDGLGKL-WSE	DA
MbWrbA	MVKVNVIFHSIHGHTYKMAEAIAEGAREVEG	AEVEIYOVPETLPYEVLEKMGA-	IETKNLFAHIPVVTRSMYE	DVFAGADALIFGTPTRY-	GNMTAOMRTVFDGLGGL-WSR	DA
GtOR1 (35)	) AVMSSPKVATVTYSLYGHTAKLAEAVKSGTESAGG	-KAOTFOVPETLSEDILKLLH	APPK DYPTTTP	OLATEDAELIGIPTRY-	GNEPAOWKAEWDATGOL-WAT	GA
PCOR	MPKVAITTYSMYGHTAKLAEAEKAGIEEAGG	-SATIYOTPETLPEEVLAKMH	APPKEYPVITP	KLPEFDAFVEGIPTRY-	INFROWKAEWDATGGL-WAO	GA
G±0R2 (50)	TOTTMSSORIATUTYTMYCHVARIAFATKSCIECACC	-NASTFOVAETI SPETI NI VK		DI KNYDGET EGT PTPY-	INFOUNKAEWDSTCDI -WAS	TTA
SpObr1	MSTANTVALVIVSTVCHVVKLAFAFKAGIEKAGG	-KAUTYOFDETI SDETI EKMH		DUI TOYDAFI FOVDTRY-	STODAOFDTEWDSTOLL WVO	GA
Nelling	MADELA TUVYONYOUTDOLARAAKAGIEKAGO		ADDEDDEDUTED D	ATTREVDCELECTREDA	SHEDAOWDARWDWROGI WAM	CC
менур		-TADLIQVPETLSDEVLARMI	APPKPIDIPVIEDP	AILKEIDGFLFGIFIRI-	JNF PAQWKAP WDKIGGL-WAI	GG
тінур	PRKIAILIYSTYGHIAELARKEAEGVKAAGG	-QVDLIQVEETLSEEILKIMK	APGQPHDFKVLTPAD-VI	SVLTGIDGFLFGIPSRF-	JSFPAQWKTEWDATGGL-WAT	66
Atrori	MATKVYIVYYSMYGHVEKLAEEIRKGAASVEG	VEAKLWQVPETLHEEALSKMS	APPKS-ESPIITP	NELAEADGFVFGFPTRF-	GMMAAQFKAFLDATGGL-WRA	QA
TvQR2	MATKVYIVYYSTYGHVERLAQEIKKGAESVGN	VEVKLWQVPEILSDEVLGKMW	APPKS-DVPVITP	DELVEADGIIFGFPTRF-	GMMAAQFKAFFDSTGGL-WKT	QA
E255-15WrbA	-MSNVKLAVIYYSSTGTNHQLATWAKEAGEAAGA	-EVRLAKIKETAPAEAIASNPLW	QKHTDATRDVEEATP	DLLDWADAIIFSVPTRY-	GHVPGQFQQFLDTTGGL-WGQ	GK
DrWrbA	-MSLTAPVKLAIVFYSSTGTGYAMAQEAAEAGRAAGA	-EVRLLKVRETAPQDVIDGQDAW	KANIEAMKDVPEATP	ADLEWAEAIVFSSPTRF-	GGATSQMRAFIDTLGGL-WSS	GK
MavWrbA	MTKLAIIYYSATGHGTTMARRVAAAAESAGA	-QVRLRHVAETQDPESFAHNPAW	TANYQATKDLPAATG	DDIVWADAVIFGSPTRF-	GSPAAQLRAFLDSLGGL-WAQ	GK
	SSSSSS HHHHHHHHHHHHHHH	SSSSS		SSSSS	ннннннннн ннннн	Н
						•
	10 20 30	40 50 6	0 70 1	30 90	100 110	120
CbFldx	MKIVYWSGTGNTEKMAELIAKGIIESGK	DVNTINVSDVNI		DELLNEDILILGC-SAM-	GDEVLEESEFEPFIEETS	TK
DaEldx	MPKALIVYGSTTGNTEGVAEATAKTLN-SEG	METTVVNVADVTAP	(	SLAEGYDVVLLGCSTWG-	DDETELOEDEVPLYEDIDR	AG
EcoEldy	MATTCIFFCSDTCNTENTAKMICKOLC	KDWADWHDTAKSSK		PDIEAVDITICIPTWVV	SEAOCDWDDEEPTIEET	-D
DCOLTON	THILTOTT CODICAT DATABAT QUEDO	IID VIID VIID IIII(ODI(			SUNCEREDENT	D
PJS666WrbA EcaWrbA	# # WKDKLFAGFTNSAALDGDKMSTLNYLFTLAMOHC WSNKVFGGFTNSASLNGDKQVTLIYLQTLASOHC	GIWVSQGVLPSTSKAAQR-DDAN GIWVSINQLPSNAKAAKR-DDLN	# IYLGSY-RGAIAQSPSDAGA( INLGGS-VGLLAQTPSDASA)	GE-MFPG-DLETARSLGE DE-VVAG-DLATGKLYGQ	RVAEVAGKF <u>Q</u> R RIADIAAKLAN	31/4 27/4
PJS666WrbA EcaWrbA BcWrbA	# WKDKLFAGFTNSAALDGDKMSTLNYLFTLAMQH WSNKVFGGFTNSASLNGDKQVTLIYLQTLASQHG WKDKIAAGFTNSATMNGDKFSTIQYFVTLSMQH	GIWVSQGVLPSTSKAAQR-DDAN GIWVSINQLPSNAKAARR-DDLN MVWVGISLMPANSKAATR-NDIN	# IYLGSY-RGAIAQSPSDAGA NLGGS-VGLLAQTPSDASA IYLGGS-TGLLAQSPADSTPI	GE-MFPG-DLETARSLGE DE-VVAG-DLATGKLYGO DEGPLPG-DLETGKAFGR	RVAEVAGKFQR RIADIAAKLAN RVAEATARWVAGRG	31/4 27/4 28/4
PJS666WrbA EcaWrbA BcWrbA XfWrbA	# # WKDKLFAGFTNSAALDGDKMSTLNYLFTLAMOH WSNKVFGGFTNSAÄLNGDKQVTLIYLQTLASOH WKDKIAAGFTNSATMNGDKFSTIQYFVTLSMQH WRNKIAAGFTNSAQHEDKLNSDKSMVLFAAQHC	GTWVSQGVLPSTSKAAQR-DDAN GTWVSGVLPSNAKAAKR-DDLN WVWVGTSLMPANSKAATR-NDIN MTWVCTDLMPGNNSSTGSSDDLN	# IYLGSY-RGAIAQSPSDAGA( NLGGS-VGLLAQTPSDASA) IYLGGS-CGLLAQSPADSTP IRLGSW-LGVMTQSNNDAAPI	GE-MFPG-DLETARSLGE DE-VVAG-DLATGKLYGQ DEGPLPG-DLETGKAFGR EIAPPAS-DLKTAQHLGL	RVAEVAGKFQR RIADIAAKLAN RVAEATARWVAGRG RVAETVRRFQPV	31/4 27/4 28/4 30/4
PJS666WrbA EcaWrbA BCWrbA XfWrbA NpWrbA	# # WKDKLFAGFTNSAALDGDKMSTLNYLFTLAMQHG WSNKVFGGFTNSASLNGDKQVTLIYLQTLASQH WKDKIAAGFTNSAATMNGDKFSTJQYFVTLSMQH WRNKIAAGFTNSGAQHGDKLNSLMSMVLFAAQH WKDKIAAGFTHSSPSGDKQGTLIYLATNAGQHC	GIWVSQGVLPSTSKAAQR-DDAN GIWVSINQLPSNAKAAKR-DDLN WWVGTSLMPANSKAATR-NDLN MIWVGIDLQSFL-SGL-DDGVN	# IYLGSY-RGAIAQSPSDAGA INLGGS-VGLLAQTPSDASA IYLGGS-TGLLAQSPADSTP IRLGSW-LGVMTQSNNDAAP IRLGGF-LGVMGQSQLDMSGI	GE-MFPG-DLETARSLGE DE-VVAG-DLATGKLYGQ DEGPLPG-DLETGKAFGR SIAPPAS-DLKTAQHLGL KEPVLDSGVLTSVRFGE	RVAEVAGKFQR RIADIAAKLAN RVAEATARWVAGGG RVAETVRRFQPV RIAEATKRWNK	31/4 27/4 28/4 30/4 28/4
PJS666WrbA EcaWrbA BCWrbA XfWrbA NpWrbA CaWrbA	# WKDKIFAGFTNSAALDGDKMSTINYLFTLAMQH WSNKVFGGFTNSASLNGDKQVTLIYLQTLASOH WKDKIAAGFTNSATMNGDKFSTIQYFVTLSMQH WKDKIAAGFTNSGAQHGDKLNSLMSWVLFAAQH WKDKIAAGFTNSGAPHGDKGTLLYLATNAGOH ESGKVGAAFTSSACHSGTFFTLISVLHWMLGSG	GIWVSQGVLPSTSKAAQR-DDAN GIWVSINQLPSNAKAAKR-DDLN WVWVGTSLMPANSKAATR-NDIN MIWVGDLDHPGNNSSTGSSDDLN MIWVNVGDLQSFL-SGL-DDGVN MIVVJVGDLQSFL-SGL-DDGVN MIVVJPMSPLME	# IYLGSY-RGAIAQSPSDAGA IYLGGS-TGLLAQSPADSTP IRLGSW-LGVMTQSNNDAAP IRLGGF-LGVMGQSQLDMSGI Q-AGSYYG-ATAV-G	SE-MFPG-DLETARSLGE DE-VVAG-DLATGKLYGQ DEGPLPG-DLETGKAFGR SLAPPAS-DLKTAQHLGL KEPVLDSGDYLTSVRFGE -TITEA-DLIQARALGR	RVAEVACKFQR RIADIAAKLAN RVAEATARWVAGRG RVAETVRRFQPV RIAEATKRWNK RVAELALQLRRGAAS-	31/4 27/4 28/4 30/4 28/4 30/4
PJS666WrbA EcaWrbA BcWrbA XfWrbA NpWrbA CaWrbA AfWrbA	# # WKDKLFAGFTNSAALDGDKMSTLNYLFTLAMCH WSNKVFGGFTNSAÄLNGDKGVTLIYLQTLASCH WKDKIAAGFTNSATMNGDKFSTIQYFVTLSMQH WKDKIAAGFTNSGQHGDKLNSLMSMVLFAQH USGKVGAAFTSSAGRHSGTEFTLLSVLHWMLGS LSGKVGAVFTSNEMPHGGKEATLLSVLHWLGS LEGKVGAVFTSNEMPHGGKEATLLSVLHWLDFFAHC	GTWVSQGVLPSTSKAAQR-DDAN GTWVSINQLPSNAKAAKR-DDLN WVWVGTSLMPANSKAATR-NDIN MIWVVIGDLQSFL-SGL-DDGVN MIIVVVGDLQSFL-SGL-DDGVN MIIVGLPWSPL	# IYLGSY-RGAIAQSPSDAGA INLGGS-VGLLAQPSDASAI IYLGSS-TGLLAQSPADSTPI IRLGSW-LGVMTQSNDDAPI IRLGGF-LGVMCQSQLDMSG IQ-AGSYYG-ATAV-G R-ACSYYG-AAST-G	GE-MFPG-DLETARSLGE DE-VVAG-DLATGKLYGQ DEGPLPG-DLETGKAFGR EIAPPAS-DLKTAQHLGL KEPVLDSGDYLTSVRFGE TITEA-DLIQARALGR VPKED-DLQVAKMLGK	RVAEVAGKFQR RIADIAAKLAN RVAEATARWVAGRG RVAETVRFQPV RIAEATKRWNK RVAELALQLRRGAAS- RVAEVAEKLC	31/4 27/4 28/4 30/4 28/4 30/4 30/4 43/6
PJS666WrbA EcaWrbA BcWrbA XfWrbA NpWrbA CaWrbA AfWrbA PaeWrbA	# # WKDKLFAGFTNSAALDGDKMSTLNYLFTLAMOH WSNKVFGGFTNSASLNGDK©VTLIYLQTLASQH WKDKIAAGFTNSATMNGDKFSTOYFVTLSMQH WRNKIAAGFTNSGQHGDKLNSLMSWVLFAAQH LSGKVGAAFTSSAGHSGTFFTLISVLHWMLGS LEGKVGAVFTSNEMPHGGKBATLISMLHPILHA UVGRPAAVFTSTASLHGGOETTOLSMLLPILHHC	GIWVSQGVLPSTSKAAQR-DDAN GIWVSINQLPSNAKAAKR-DDLN WWWCTSLMPANSKAATR-NDIN MIWVGDLUPGNNSSTGSSDLN MIWVNVGDLQSFL-SGL-DDGVN MIIVGLPØSPLLY MIIVGLPØSEPLLETR	# IYLGSY-RGAIAQSPSDAGA INLGGS-VGLLAQTPSDASA IYLGGS-TGLLAQSPADSTP IRLGSW-LGVMCQSQLDMSG IRLGGF-LGVMCQSQLDMSG QAGSYYG-ATAV-G R-AGSYYG-ASTP-G G-GGTPYQ-ASTP-GADS	GE-MFPG-DLETARSLGE DE-VVAG-DLATGKLVGQ DEGPLPG-DLETGKAFGR STAPPAS-DLKTAQHLGL KEPVLDSGDVLTSVRFGE TITEA-DLIQARALGR VPKED-DLQVAKHLGK KSSLDEH-EITLCRALGK	RVAEVAGKFQR RIADIAAKLAN RVAEATARWVAGRG RVAETVRFGPV RIAEATKWNK RVAELALQIRRGAAS- RVAEVAEKLC RIAETAGKIGS	31/4 27/4 28/4 30/4 28/4 30/4 43/6 40/5
PJS666WrbA EcaWrbA BcWrbA XfWrbA NpWrbA CaWrbA AfWrbA PaeWrbA ParWrbA	WKDKLFAGFTNSAALDGDKMSTLNYLFTLAMQH WSNKVFGGFTNSASLNGDKGVTLTYLQTLASQH WKDKIAAGFTNSGAQHGDKLNSLMSWVLFAAQH WKDKIAAGFTNSGSDKGTCLLYLATNAGQH LSGKVGAAFTSSAGRGSGTFFTLSVLHWMLGS LEGKVGAVFTSNEMPHGGKBATLISMLLPLFAH LVGKPAAVFTSTSALHGQDTTLJMLPLLHH LONKPAAVFTSTGSHGGDTTLJMLPLLHH	GIWVSQGVLPSTSKAAQR-DDAN GIWVSINCLPSNAKAARR-DDLN WWWGTSLNPANSKAARR-NDIN MIWVGIDLMPGNNSSTGSSDDLN MIWVVGUQSEL-SGL-DDGVN MIVVGPV8PLME MIVUGLPPSEPLY MIVUGTPYSEPALNETT MIVUGPPAEPALNETT	# IYLGSY-RGAIAQSPSDAGAN IYLGGS-TGLLAQTPSDASAI IYLGGS-TGLLAQSPADSTP IRLGGF-LGVMGQQCDMSGI Q-AGSYYG-ATAV-G R-AGSYYG-AAST-G G-GGFPYG-ASHFAGADGI R-GGSPYG-ASHFAGADGI	3E-MFPG-DLETARSLGE DEGPLPG-DLETGKAFGR SIAPPAS-DLKTAQHLGL KEPVLDSGDVLTSVRFGE VPKED-DLQVAKMLGK KRSLDEH-EITLCRALGK KRSLDEH-EITLCRALGK	RVAEVACKFQR RVAEATARWVAGRG RVAETVRRFQPV RIAEATKRWNK RVAELALQLRRGAAS- RVAELALQLRRGAAS- RUAEVAEKLC RLAETAGKLGS RLAITASALAQANWSR	31/4 27/4 28/4 30/4 28/4 30/4 43/6 40/5 39/5
PJS666WrbA EcaWrbA ScWrbA XfWrbA NpWrbA CaWrbA AfWrbA PaeWrbA ParWrbA MdWrbA	# # WKDKLFAGFTNSAALDGDKMSTLNYLFTLAMCH WSNKVFGGFTNSAÄLNGDKQVTLIYLQTLASCH WKDKIAAGFTNSGAQHGDKLNSLMSMVLFAQH WKDKIAAGFTNSGSPGHCDKLNSLMSMVLFAQH SGKVGAAFTSSAGRHSGTEFTLLSVLHWMLGS LCGKVGAVFTSNEWHGGKEATLLSVLHWLGSL LVGKPAAVFTSTASLHGGQETTQLSMLLPLFH LQNKPAAVFTSTSSMGGQETTLLSMLLPLLHH LGKPAAVFTSTSSMGGQETTLLTMLPLLHH	GTWVSQGVLPSTSKAAQR-DDAN GTWVSINQLPSNAKAAKR-DDLN WVWVGTSLMPANSKAATR-NDIN MIWVVGDLQSFL-SGL-DDGVM MIIVGLPWSPLME MIIVGLPWSEPALLETR MUIVGIPVSEPALLETR MVL/GGPVAEPALLETR	# IYLGSY-RGAIAQSPSDAGA INLGGS-VGLLAQSPADSTP IRLGSW-LGVMTQSNNDAP IRLGSW-LGVMTQSNNDAP IRLGF-LGVMGQSQLDMSG Q-AGSYYG-ATAV-G G-GGTPYG-ASHFAGADG R-GGSPYG-ASHFAGADG T-GGTPYG-PSHLAGSDG	GE-MFPG-DLETARSLGE DE-VVAG-DLETGKAFGR BIAPPAS-DLETGKAFGR -TITEA-DLIQARALGR -VPKED-DLQVAKMLGK KRSLDEH-ELTLCRALGK QPVSAD-RELGIAQGR DQPVSAD-RELGIAQGR	RVAEVAGKFQR RIADIAAKLAN RVAEATARWVAGRG RVAETVRRFQPV RIAETARWNK RVAEUALQLRRGAAS- RVAEVAEKLC RLAETAGKLGS RLAITASALAQANWSR RLATLAKLYD	31/4 27/4 28/4 30/4 28/4 30/4 43/6 40/5 39/5 36/5
PJS666WrbA EcaWrbA BcWrbA XfWrbA OgwrbA CaWrbA AfWrbA PaeWrbA ParWrbA MdWrbA StWrbA	# WKDKIFAGFTNSAALDGDKMSTINYLFTLAMQH WSNKVFGGFTNSAJNGDKPTIJYLQTLASOH WKDKIAAGFTNSAJMNGDKFSTIQYFVTLSMQH WKDKIAAGFTNSGAQHGDKLNSLMSWVLFAAQH USGRVGAAFTSSAGRHSGTBFTLISVLHWMLGS LSGRVGAAFTSSAGRHSGTBFTLISVLHWMLGS LVGKPAAVFTSTASLHGQETTCLSMLPLLHH LVGKPAAVFTSTASLHGQETTLISVLHWLPLLHH LIRPAGVFTSTSSMHGQESTTLISMVPLLHH LIRPAGVFTSTSSMHGQESTTLISMVPLLHH LYGKPVFTBFASSWHGQESTTLISMVPLLHH	GTWVSQGULPSTSKAAQR-DDAN MVWVGTSIMPANSKAATR-NDIN MVWVGTSIMPANSKAATR-NDIN MIWVVGDLQSFL-SGL-DDGVN MIVVIGDLQSFL-SGL-DDGVN MIIVGLPØSPLMI MIVGIPPAREALHETR MVIVGGIPVAEPALHETR MVIVGGIPVAEPALHETA	# IYLGSY-RGAIAQSPSDAGA IYLGGS-TGLLAQSPADSTP IRLGSW-LGVMTQSNDAAPJ IRLGGF-LGVMTQSQLDMSGJ Q-AGSYYGATAV-G R-AGSYYGASHY-GADG R-GGSPYGASHY-SGASH IT-GGPYGSTHL-G-SI	3E-MFPG-DLETARSLGE DE-VVAG-DLATGKLYGQ DEGPLPG-DLETGKAFGR STAPPAS-DLKTAQHLGL KEPVLDSGDULTSVRFGE VPKED-DLQVAKHLGK KRSLDEH-ELTLCRALGK QQPVSAD-ERELGTAQGR TTQLSQE-EKALCVAFGK KFELDEM-BKIAEPOCK	RVAEVACKFQR RVAEATARWVAGRG RVAEATARWVAGRG RVAETVRFQPV RVAELALQLRRGAAS- RVAEVALQLRRGAAS- RVAEVAEKLC RLAETAGKLGS RLAITASALAQANWSR RLATLAKKLYD	31/4 27/4 28/4 30/4 28/4 30/4 43/6 40/5 39/5 36/5 40/5
PJS666WrbA EcaWrbA BcWrbA XfWrbA CaWrbA AfWrbA PaeWrbA ParWrbA MdWrbA StWrbA StWrbA	WKDKLFAGFTNSAALDGDKMSTLNYLFTLAMQH WSNKVFGGFTNSASLNGDKQVTLIYLQTLASQH WKDKIAAGFTNSGAQHGDKLNSLMSMVLFAAQH WKDKIAAGFTNSGAQHGDKLNSLMSMVLFAAQH SGKVGAAFTSSGRFGSFTLLYLATNAGQH LGGKVGAVFTSNEMPHGGKBATLLSMLLPLFA LQNKPAAVFTSTASLHGQETTLLTMLPLLHH LQNKPAAVFTSTSSMHGQESTLLISMLPLLHH LIGKPAGVFTSTSSMHGQESTLLISMVVPLLHH	GTWVSQGVLPSTSKAAQR-DDAN GTWVSGINLPSNAKAARR-DDLN MIWVGTDLMPANSKAARR-NDIN MIWVGTDLMPGNNSSTGSSDDLN MIWVVGTQLSL-SGL-DDGVN MIIVGLP%SPLME MIIVGLP%SPALLETR MUIVGPYAEQALLETR WUICGTPAEQALHTA MIIVPrGYGIPELFQTT	# IYLGSY-RCAIAQEPSDAGA IYLGS-VGLLAQEPSDAGA IYLGS-TGLAQEPADSTP IRLGSW-LGVMTQSNNDAAPJ IRLGSW-LGVMTQSNNDAAPJ IRLGSW-GATAV-G R-AGSYYG-AAST-G IG-GEFYG-ATAV-G IG-GEFYG-ASHSGAGSH IT-GGEPYG-ASHSGAGSH IT-GGEPYG-ASHS-G	3E-MFPG-DLETARSLGE DE-VVAG-DLATGKLYGO DEGPLPG-DLETGKAFGR EIAPPAS-DLKTAQHLGL KEPVLDSGDVLTSVFGE VPKED-DLQVAKMLGK KRSLDBH-EITLCRALGK KRSLDBH-EITLCRALGK TTQLSQE-EKALCVAFGK KEELDEM-ERKIARFOGK	RVAEVACKFQR RVAEATARWVAGRG RVAETVRRFQPV RVAEIAIQLRRGAAS- RVAELAIQLRRGAAS- RVAELALQLRRGAAS- RLAETACKLGS RLAITASALAQANWSR RLAITASKLYD RITEVAKAIKCCNK PVAFWAKLPC	31/4 27/4 28/4 30/4 43/6 40/5 39/5 36/5 40/5
PJS666WrbA EcaWrbA BcWrbA XfWrbA CaWrbA CaWrbA AfWrbA PacWrbA PawrbA MdWrbA StWrbA SsWrbA SsWrbA	# # WKDKLFAGFTNSAALDGDKMSTLNYLFTLAMCH WSNKVFGGFTNSAÄLNGDKÖVTLIYLQTLASCH WKDKIAAGFTNSGAUHODKLNSLMSMVLFAACH WKDKIAAGFTNSGAUHODKLNSLMSMVLFAACH UKDKIAAGFTNSGACHOKLNSLMSMVLFAACH LGKVGAAFTSSACHSGTEFTLLSVLLHWNLGS LCKVGAVFTSNEMHGGKEATLLSVLLHWNLGS LUGKPAAVFTSTASLHGGQETTLISMLLPLFAH LUGKPAAVFTSTASLHGGQETTLISMLLPLLHH LIGKPAGVFTSTSMHGGDESTLISMVVPLLHH LIGKPAGVFTSTSMHGGHESTILMSAVYHF	GTWVSQGVLPSTSKAAQR-DDAN GTWVSINQLPSNAKAAKR-DDLN MVWVGTSLMPANSKAATR-NDIN MIWVUGDLQSFL-SGL-DDGVM MIIVGLPWSPLMU MIIVGLPWSPL	# IYLGSY-RGAIAQSPSDAGA INLGGS-VGLLAQTPSDASAI IYLGGS-TGLLAQSPADSTP IRLGSW-LGVMGQSQLDMSG IQ-AGSYYG-ATAV-G R-AGSYYG-ATAV-G G-GCTPYG-ASHFAGADG IR-GGSPYG-ASHFAGADG IT-GGPYG-SHLAGSDG IT-GGSPYG-ASHLAGSDT IT-GGSPYG-ASHLAGSDT IT-GGSPYG-ASHLAGSDT IT-GGSPYG-ASHLAGSDT	SE-MFPG-DLETARSLGE DE-VVAG-DLATGKLYGQ DEGPLPG-DLETGKAFGR SIAPPAS-DLKTÄQHLGL VPKED-DLQARALGR VPKED-DLQARALGR VPKED-DLQAKHLGK KSLDEH-EITICRALGK DQPVSAD-ERELGIAQGR TTQLSQE-EKALCVAFGK KKELDEM-EINIAKFLGK KKELDEM-EINIAKFLGK	RVAEVAGKFQR RIADIAAKLAN RVAEATARWVAGRG RVAEITVRFGPV RIAEATKWNK RVAELALQIRRGAAS- RVAEVAEKLC RIAETAGKIGS RIATIAKKIYD RITEVAKAIKCCNK RVAEVAKKIRC RVAEVAKKIRC	31/4 27/4 28/4 30/4 43/6 40/5 39/5 36/5 40/5
PJS666WrbA EcaWrbA BCWrbA XfWrbA OgwrbA CaWrbA AfWrbA PaeWrbA ParWrbA StWrbA StWrbA StWrbA ScWrbA EcoWrbA	WKDKIFAGFTNSAALDGDKMSTINYLFTLAMOH WSNKVFGGFTNSASLNGDKQVTLIYLQTLASOH WKDKIAAGFTNSATMNGDKFSTIQYFVTLSNOH WKDKIAAGFTNSASPSGKOGTLLYLATNAGOH UKDKIAAGFTSSAGHSGTFFTLSVLHWNLGS LSGKVGAAFTSSAGHSGTFFTLSVLHWNLGS LVGKPAAVFTSTASLHGQETTLIXMLPLLHH LVGKPAAVFTSTASLHGQETTLIXMLPLLHH LIGRPAGVFTSTSSMHGQESTTLIXMVPLLHH LYGKPAVFTSTASCHHGGETTLIXMVPLLHH LYGKPVFFTEASTWHGGHSTTIIXMVYAHF LYGKPVFFTEASTWHGGHSTTIIXMXYAHF	GIWVSQGVLPSTSKAAQR-DDAN GIWVSINQLPSNAKAARR-DDLN WWVGTSLMPANSKAARR-NDIN MIWVGDLQSFL-SGL-DDGVN MIVUGDLQSFL-SGL-DDGVN MIVUGIPØSPL	# IYLGSY-RGAIAQSFSDAGA IYLGGS-TGLLAQSFADASH IYLGGS-TGLLAQSFADASH IRLGGF-LGVMTQSNNDAAP IRLGGF-LGVMGQSQLDMSGI Q-AGSYYG-ATAV-G IG-GGTPYG-ASTAFAGADGI TGGGPYG-ASHFAGADGI T-GGGPYG-ASHLAGSDG' T-GGGPYG-ATHL-G-NI T-GGSFYG-ATHL-G-NI R-GGTPYG-ATHLAG-NI	SE-MFPG-DLETARSLGE DE-VVAG-DLATGKLYGQ DEGPLPG-DLETGKAFGR ZIAPPAS-DLKTAQHLGL KEPVLDSGDVLTSVRFGE VPKED-DLQVAKHLGK KRSLDEH-ELTLCRALGK QCPVSAD-ERELGIAQGR TTQLSQE-EKALCVAFGK KEELDEM-ETMIAKFLGK SRQPSQE-ELSIARYQGE	RVAEVACKFQR RVAEATARWVAGRG RVAEATARWVAGRG RIABATKRWNK RVAEIALQIRRGAAS- RVAEVALQIRRGAAS- RVAEVALQIRRGAAS- RIAFTAGKIGS RIATTASALAQANWSR RIATLAKKIYD RITEVAKAIKCCNK RVAEVAKKIRC YVAGLAVKINC	31/4 27/4 28/4 30/4 28/4 30/4 43/6 40/5 39/5 36/5 40/5 
PJS666WrbA EcaWrbA BcWrbA XfWrbA CaWrbA AfWrbA ParWrbA ParWrbA StWrbA StWrbA StWrbA EcoWrbA PowrbA	WKDKLFAGFTNSAALDGDKMSTLNYLFTLAMOH WSNRVFGGFTNSASLNGDKGVTLTYLQTLASOH WRNKIAAGFTNSGAQHGDKLNSLMSMVLFAAQH KKDKIAAGFTNSGSPGDKGGTLLYLATNAGH LGKVGAAFTSSAGHSGTEFTLLSVLHWMLGS LGKVGAVFTSNEMPHGGKEATLLSVLHWMLGS LQKVFAAVFTSTASLHGQETTULSMLPLLHH LQNKPAAVFTSTASLHGQETTLLSMLPLLHH LGKPQVFFTTSSWHGQESTLLSMVVPLLHH LYGKPVTFTEASTWHGGHESTILSMVVPLHH LYGKPVTFTEASTWHGGHESTILSMVVPLHH LYGKASVFSSTCT-GGQEOTTTSTWTTLAHH	GTWVSQGVLPSTSKAAQR-DDAN GTWVSGINQLPSNAKAARR-DDLN MIWVGTDLMPGNNSSTGSSDDLN MIWVGTDLMPGNNSSTGSSDDLN MIWVGTDLPSL-SGL-DDGVN MIIVGLPWSPL	# YILGSY-RCAIAQSPSDAGA NILGGS-VCLLAQTPSDASA IRLGSW-LGVMTQSNNDAAPI IRLGSW-LGVMTQSNNDAAPI IRLGSW-LGVMGQSQLDMSGI Q-ASSYYG-ATAY-G R-AGSYYG-ASFAGADGI R-GGPYG-ASHYGADGI T-GGPYG-ASHYGADGI T-GGPYG-ASHL-G-SI IT-GGSPYG-ASHL-G-SI IT-GGPYG-ASHL-GCSI R-GGTPYG-ASTIAGCDGI R-GGTPYG-ATTIAGCDGI R-GGTPYG R-GGTPYG-ATTIAGCDGI R-GGTPYG R-GGTPY	3E-MFPG-DLETARSLGE DE-VVAG-DLETGKAFGR EIAPPAS-DLKTAQHLGL KEPVLDSGDVITSVFGE TITEA-DLIQARALGR VPKED-DLQVAKMLGK KRSLDEH-EITLCRALGK DQPVSAD-ERELGIAQGR TTQLSGE-EKALCVAFGK KKELDEM-ERKIARFOGK KKELDEM-ENNIARFIGK SRQPSQE-ELSIARYQGE SRQPSQE-ELSIARYQGE	RVAEVACKFQR RIADIAAKLAN RVAEATARWVAGRG RVAEIALQLRRGAAS RVAELALQLRRGAAS RVAELALQLRRGAAS RLAITASALAQANWSR RLAITASALAQANWSR RLAITASALAQANWSR RLAITASKLYD RITEVAKAIKCCNK RVAEVAKKLRC YVAGLAVKLNG HVAKITAKLKG	31/4 27/4 28/4 30/4 28/4 30/4 43/6 40/5 39/5 36/5 40/5 40/5 
PJS666WrbA EcaWrbA BcWrbA XfWrbA CaWrbA CaWrbA AfWrbA PacWrbA ParWrbA MdWrbA StWrbA StWrbA StWrbA ScWrbA CcWrbA	# WKDKIFAGFTNSAALDGDKMSTINYLFTLAMOH WSNKVFGGFTNSAINGDKPSTIOYFVTLSMOH WKDKIAAGFTNSAINNGDKFSTIOYFVTLSMOH WKDKIAAGFTNSASPSGKOGTLIYLATNAGOH USGKVGAAFTSSAGRHSGTFFTLISVLHWMLGS LSGKVGAAFTSSAGHSGTFFTLISVLHWMLGS LVGKPAAYFTSTASLHGGDETTULSWLLPLLHH UVGKPAAYFTSTASLHGGDETTULSWLLPLLHH LYGKPYFFTEASTWHGGDETTILTMNLPLLHH LYGKPYFFTEASTWHGGHETTIIMMSTXXHH LYGKPYFFTEASTWHGGHETTIIMMSTXXHH LYGKPYFFTEASTWHGGHESTIIAMANAXHH	GTWVSQGVLPSTSKAAQR-DDAN MVWVGTSLMPANSKAATR-NDIN MTWVGDLDYGNNSSGSSDDLN MIWVVGDLQSFL-SGL-DDGVN MIVVIGDLQSFL-SGL-DDGVN MIIVGLPØSPLME MIIVGPØSPLALRTT MIIVGPØSPAEPALNTT MVLGCIPXAEQALNTT MIIVPGYGIFELFQTT MIIVPGYGIKELFPVSQV VFIVPTAVAAQELFPVSQV TIVVGGDYGHAGQMTLDDI	# IYLGSY-RGAIAQSPSDAGAI INLGGS-UGLLAQTPSDASAI IYLGGS-UGVMTQSNDAAPI IRLGF-LCVMTQSOLDMSGI Q-AGSYYG-ATAV-G R-AGSYYG-ATAV-G R-GGSPYG-ASHFAGADGI R-GGSPYG-ASHFAGADGI T-GGSPYG-ASHLAGSDGI T-GGSPYG-ATHL-GSI TT-GGSPYG-ATHLAGCOS T-GGSPYG-ATTIAGCOS T-GGSPYG-ATTIAGCOS T-GGSPYG-ATTIAGCOS	SE-MFPG-DLETARSLGE DE-VVAG-DLATGKLYCO DEGPLPG-DLETGKAFGR SIAPPAS-DLKTAQHLGL TITEA-DLIQARALGR VPKED-DLQVAKHLGK KSLDEH-EITLCRALGK DQPVSAD-ERELGIAOGR TTQLSQE-EKALCVAFGK KKELDEN-EIKIARFOGK KKELDEN-EINIAKFLGK SRQPSQE-ELAIARFOGE SRQPSQE-ELAIARFOGE SRQPSQE-ELAIARFOGE	RVAEVAGKFQR RVAEATARWVAGRG RVAEATARWVAGRG RVAETVRFQPV RIAEATKRWNK RVAEUALQLRRGAAS- RVAEVAEKLG RLAITASALAQANWSR RLAITASALAQANWSR RLAITASALAQANWSR RLAITASKLGS RVAEVAKKLRC YVAGUAVKLNG HVAEITAKLKG KIAETAIKLKG	31/4 27/4 28/4 30/4 43/6 40/5 39/5 36/5 40/5 40/5 
PJS666WrbA EcaWrbA BcWrbA XfWrbA CaWrbA AfWrbA PaeWrbA PaeWrbA ParWrbA StWrbA StWrbA ScWrbA EcoWrbA YpWrbA CcWrbA MBNCLWrbA	# WKDKLFAGFTNSAALDGDKMSTLNYLFTLAMQH WSNKVFGGFTNSASLNGDKGVTLIYLQTLASQH WKDKIAAGFTNSGAQHGDKLNSLMSMVLFAAQH WKDKIAAGFTNSGAQHGDKLNSLMSMVLFAAQH UKDKJAAGFTNSGACHGDKFJTLJSULHAWLGG LSGKVGAAFTSSACHGQETTLJSULHWLGG LGKVGAVFTSNEMPHGKBATLISMLLPLFAH LJGKPAGVFTSSSMHGQESTLISMLPLLHH LJGKPAGVFTSTSMHGQESTLISMLVPLLHH LYGKVGFTFLASTWHGGHSTILMMNYAYHF LYGKVGFTFLASTWHGGHSTILMMNYAYHF LYGKVASVFSSTCT-GGQEQTITSTWTLAHH LYGKVASVFSSTCT-GGQEQTITSTWTLAHH LYGKVASVFASTCT-GGQETTISTWTLAHH LYGKVASVFASTCT-GGGQETTISTWTLAHH LYGKVASVFASTCT-GGGQETTISTWTLAHH LYGKVASVFASTCT-GGGQETTISTWTLAHH LYGKVASVFASTCT-GGGQETTISTWTLAHH LYGKVASVFASTCT-GGGQETTISTWTLAHH LYGKVASVFASTCT-GGGQETTISTWTLAHH	GIWVSQGVLPSTSKAAQR-DDAN GIWVSINQLPSNAKAAR-DDLN MIWVGIDLMPGNNSSTGSSDDLN MIWVGDLØSEL-SGL-DDGVN MIWVGSPL	# IYLGSY-RGAIAQFSDAGAN IYLGGS-TGLLAQFPSDASAI IYLGGS-TGLLAQFPSDASAI IRLGGF-LGVMTQSNNDAAPI IRLGGF-LGVMTQSNDDAAPI IRLGGFLGVMGQSQLDMSGI Q-ACSYYG-ATAV-G IG-GGFYG-ASAY-GASH T-GGFYG-ASHLAGSDG' T-GGFYG-ASHL-GNI IR-GGFYG-ASHL-G-NI IR-GGFYG-ATTIAGGDG; R-GGFYG-ATTIAGGDG; IR-GGFYG-ATTIAGGDG; IR-GGPYG-ATTIAGGDG; IR-GGPYG-ATTIAGGDG;	SE-MFPG-DLETARSLGE DE-VVAG-DLATGKLYGQ DEGPLPG-DLETGKAFGR SIAPPAS-DLKTAQHLGL KEPVLDSGDYLTSVRFGE VPKED-DLQVAKHLGK KRSLDEH-ELTLCRALGK TTQLSQE-EKALCVAFGK KRELDEM-ERKIARPGK SRQPSQE-ELSIARYQGE SRQPSQE-ELSIARYQGE SRQPSAE-ELGARFQGK	RVAEVACKFQR RIADIAAKLAN RVAEATARWVAGRG RVAELALQIRRGAAS- RVAELALQIRRGAAS- RVAELALQIRRGAAS- RUAEYAEKLC RLAITASALAQANWSR RLAITASALAQANWSR RLAITASALAQANWSR RLATLAKKLYD YVAGLAVKLNC YVAGLAVKLNC YVAGLAVKLNG RLAEITAKLVR RLAEITAKLVR	31/4 27/4 28/4 30/4 43/6 40/5 39/5 36/5 40/5 40/5 
PJS666WrbA EcaWrbA BcWrbA XfWrbA CaWrbA AfWrbA PacWrbA PacWrbA ParWrbA StWrbA SsWrbA ScWrbA ScWrbA CcWrbA MBNCLWrbA MENCLWrbA	WKDKLFAGFTNSAALDGDKMSTLNYLFTLAMOH WSNKVFGGFTNSAÄLNGDKQVTLIYLQTLASOH WKDKIAAGFTNSAÄLNGDKGVTLIYLQTLASOH WKDKIAAGFTNSAGNHOKLNSLMSMVLFAAQH SGKVGAAFTSSAGHHOKLNSLMSMVLFAAQH LGKVGAVFTSNEMPHGGKEATLISVLHWHLGS LCKVFAAVFTSTÄSLHGQETTOLSVLHWHLGS LQKVFAAVFTSTÄSLHGQETTILSVLHWHLGS LQKVFAAVFTSTÄSLHGQETTLISVLHWHLGS LYGKPAVFTATGSMHGGQETTLISVLHWHLFLH LYGKPVFFTEASTVHGGHETTILTMSTYAYHF LYGKPVFFTEASTWHGGHESTILAMNYAYHF LYGKVSFSSTCGGQQETTISTWTLAHH LYGKVAFTSTATGHGGETTLISVTTLAHH LYGKVASVFASTCT-GGQQETTIFSTTTLAHH	GTWVSQGVLPSTSKAAQR-DDAN GTWVSGINQLPSNAKAAKR-DDLN MIWVGTDLMPGNNSSTGSSDDLN MIWVGTDLMPGNNSSTGSSDDLN MIWVGTDLPSPL-SGL-DDGVN MIIVGLPWSEPME MIIVGLPYSEPALNETT MUCGIPYSEPALNETT MIIVPIGYGIPELFQTST MIIVPIGYGIKELFDVSQT FIIVPIGYGAKELFDVSQT TIIVGLDYCHAGQMTLDBL MIIVPISSEARQTMDEI	# IYLGSY-RGATAQSPSDAGA INLGGS-VGLLAQTPSDASA IYLGGS-TGLLAQTPSDASA IYLGGS-TGLLAQTPSDASA IYLGGS-UVMGQSQLDMSG IQ-AGSYYG-ATAV-G R-AGSYYG-ATAV-G SGGTPYG-ASHFAGADG IX-GGTPYG-ASHFAGADG IT-GGSPYG-ASHLAGSDG IT-GGSPYG-ATHIAGCDG IT-GGSPYG-ATTIAGCDG IT-GGSPYG-ATTIAGCDG IT-GGSPYG-ATTIAGCDG IT-GGSPYG-ATTIAGCDG IT-GGSPYG-ATTIAGCDG IT-GGSPYG-ATTIAGCDG IT-GGSPYG-ATTIAGCDG IT-GGSPYG-INTIACCDG IT-GGSPYG IT-GGSPYG-INTIACCDG IT-GGSPYG IT-G	SE-MFPG-DLETARSLGE DE-VVAG-DLATGKLVGQ DEGPLPG-DLETGKAFGR SIAPPAS-DLKTÄQHLGL VPKED-DLQARALGR VPKED-DLQARALGR VPKED-DLQAKNLGK KSSLDEH-EITICRALGK DQPVSAD-ERELGIAQGR TTQLSQE-EKALCVAFGK KKELDEM-EINIAKFLGK SRQPSQE-ELSIARYQGE SRQPSEN-ELSARYQGR SRVSAQ-ELSARYQGR SRVSAQ-ELSARYQGR	RVAEVAGKFQR RVAEATARWVAGRG RVAETVRFGPV RVAEIALQIRRGAAS- RVAEVAEKLC RLAETACKIGS RLATTAKKIGS RIATLAKKIG RVAEVAKKIRC YVAGLAVKIRG HVAKITAKLKG HVAKITAKLKG HVALTAKKIQK HVTLIAKKIQK	31/4 27/4 28/4 30/4 430/4 430/5 39/5 36/5 40/5 40/5 
PJS666WrbA EcaWrbA BCWrbA XfWrbA CaWrbA AfWrbA PaeWrbA ParWrbA ParWrbA StWrbA StWrbA StWrbA CCWrbA MENCLWrbA MacWrbA MacWrbA	WKDKIFAGFTNSAALDGDKMSTINYLFTLAMQH WSNKVFGGFTNSASINGDKQVTLIYLQTLASQH WKDKIAAGFTNSASINGDKSTIJYLQTLASQH WKDKIAAGFTNSASPSGKGGTLIYLATNAGQH UKDKIAAGFTSSAGHSGTBFTLISVLHWMLGS LSGKVGAAFTSSAGHSGTBFTLISVLHWMLGS LVGKPAAVFTSTASLHGQETTLISVLHWMLGS LUGKPAAVFTSTASLHGQETTLISVLHWMLDFAH LVGKPAVFTSTSSHGGQESTTLISMLPLLHH LYGKPAVFTSTSSHGGQESTTLISMVPLLHH LYGKPAVFTSTASLHGQESTTLISMVPLLHH LYGKPVFFTEASTWHGGHESTTIJMMVPLLHH LYGKVGFFTEASTWHGGHESTTIJMANTAYHF LYGKVASVFSSCT-GGGQENTTSTWTLAHH LYGKVAGFTSTATUHGGAETALASTQLALQHH FVGKVGSVFTSSCTQHGQESTIISHVTLLHL	GIWVSQGVLPSTSKAAQR-DDAN GIWVSINQLPSNAKAAR-DDLN WWVGTSLMPANSKAART-NDIN MIWVGDLQSFL-SGL-DDGVN MIVGD PMSPLME MIIVGLPPAKEALHETR WWIVGPTPSP	# IYLGSY-RGAIAQFSDAGAN IYLGGS-TGLLAQFFADASAI IYLGGS-TGLLAQFFADASAI IYLGGS-TGLLAQFFADASAI IRLGGF-LGVMGQSQLDMSGI Q-AGSYYG-ATAV-G G-GGTPYG-ASHYAGASHI T-GGFPYG-ASHFAGADGI T-GGSPYG-ATHIAGGDGI R-GGFPYG-ATHIAGGDGI R-GGFPYG-ATTIAGGDGI R-GGFPYG-ATTIAGGDGI T-GGSPYG-VSTIAGGDGI T-GSSPYG-VSTIAGGDGI T-GSSPYG-VSTIAGGDGI T-GSSPYG-XSTIAGGDGI	3E-MFPG-DLETARSLGE DE-VVAG-DLATGKLYGQ DEGPLPG-DLETGKAFGR ZIAPPAS-DLKTAQHIGL KEPVLDSGDULTSVRFGE VPKED-DLQVAKHIGK KRSLDEH-ELTLCRALGK OQPVSAD-ERELGIAQGR TTQLSQE-EKALCVAFGK KEELDEM-EINIAKFIGK SRQPSQE-ELSIARYQGE SRQPSEN-ELAIARFQGE SRQPSEN-ELEGARYQGK SRQPSEN-ELEMARYQGR	RVAEVACKFQR RVAEATARWVAGRG RVAEATARWVAGRG RVAETVRFQPV RIAEATKRWNK RVAELALQIRRGAAS- RVAEVALQIRRGAAS- RVAEVALGS RLAITASALAQANWSR RLATLAKKIYD RITEVAKAIKCCNK RVAEVAKKIKC RVAEVAKKIKC KIAETAIKLHG RIAEITAKLHG RIAEITAKLYR RIAEITAKLYR RIAEITAKUYR RIAEITAKUYR RIAEITAKUAGK	31/4 27/4 28/4 30/4 28/4 30/4 43/6 40/5 39/5 36/5 40/5  81/8 57/7 54/6 50/6 50/6
PJS666WrbA EcaWrbA StWrbA XfWrbA CaWrbA AfWrbA PaeWrbA ParWrbA MdWrbA StWrbA StWrbA EcoWrbA MBNC1WrbA MBNC1WrbA MacWrbA MmWrbA	WKDKLFAGFTNSAALDGDKMSTLNYLFTLAMQH WSNKVFGGFTNSASLNGDKQVTLIYLQTLASQHC WKDKIAAGFTNSGAQHGDKLNSLMSMVLFAAQH WKDKIAAGFTNSGAQHGDKLNSLMSMVLFAAQH UKDKIAAGFTNSGAQHGDKLNSLMSMVLFAAQH LSGKVGAAFTSSGTFFTLSVLHWNLGG LGKVGAVFTSNEMPHGGKEATLISMLLPLFA LQKPAAVFTSTSSMHGQESTLISMLVLHHH LIGKPAGVFTSTSSMHGQESTLISMLVPLLHH LYGKPVGFTTASTWHGGHESTILMMNYAYHF LYGKPVGFTTASTWHGGHESTILMMNYAYHF LYGKPVGFTTASTWHGGHESTILMMNYAYHF LYGKPVGFTTASTWHGGHESTILMMNYAYHF LYGKPVGFTTASTWHGGHESTILTMNIAHH LYGKPVGFTTASTWHGGHESTILTMNIAHF	GIWVSQGVLPSTSKAAQR-DDAN GIWVSQGVLPSTSKAAQR-DDAN WIWVGTLAPPANSKAATR-DDIN MIWVGDLMPGNNSSTGSSDDIN MIWVUGDLSPL-SGL-DDGVN MIWVGPAKE	# IYLGSY-RGAIAQSFSDAGAN IYLGGS-TGLLAQTPSDASAI IYLGGS-TGLLAQSFADSTPI IRLGGF-LGVMGQLDMSGI Q-ACSYYG-ATAV-G IG-GGTPYG-ATAV-G IG-GGTPYG-ASHYSGASH T-GGTPYG-ASHYSGASH T-GGTPYG-ASHYAGDGI R-GGTPYG-ASHLAGDGI R-GGTPYG-ATTIAGDGI R-GGTPYG-ATTIAGGDGI T-GSSPYG-MTTTSDTGI T-GSSPYG-XSTIAGGDGI T-GGSPYG-XSTIAGGDGI T-GSSPYG-XSTIAGGDGI	SE-MFPG-DLETARSLGE DE-VVAG-DLATGKLYGQ DEGPLPG-DLETGKAFGR SIAPPAS-DLKTAQHLGL KEPVLDSGD'LTSVRFGE VPKED-DLQVAKMLGK (RSLDBH-BITLCRALGK TTQLSQE-EKALCVAFGK KEELDEM-ERKIARFOGK SRQPSQE-ELSIARYOGE SRQPSQE-ELSIARYOGE SRQPSQH-ELCARYOGR SRQPSEN-ELCARRYOGR SRQPSEN-ELAMARYOGR RQPSEN-ELAMARYOGR	RVAEVACKFQR RVAEATARWVAGRG RVAETVRRFQPV RVAETACKRWNK RVAELALQLRRGAAS- RVAELALQLRRGAAS- RLAETAGKLGS RLAETAGKLGS RIATTASKLYD YVAGLAVKLNG YVAGLAVKLNG RLAETAKKVR RLAETAKKVR HVTLIAKKLAGK HVTQLAKKLAGK	31/4 27/4 28/4 30/4 43/6 40/5 39/5 36/5 40/5 40/5 50/6 50/6 50/6 50/6
PJS666WrbA EcaWrbA BcWrbA XfWrbA CaWrbA CaWrbA AfWrbA PacWrbA ParWrbA MdWrbA StWrbA StWrbA StWrbA ScWrbA CoWrbA MBNC1WrbA MBNC1WrbA MmWrbA MbWrbA GtQR1	<pre># # # # # # # # # # # # # # # # # # #</pre>	GTWVSQGULPSTSKAAQR-DDAN GTWVSGLPSTSKAAQR-DDAN WVWVGTSIMPANSKAATR-NDIN MTWVGLDLPGNNSTGSSDDLN MTWVVGLQSFL-SGL-DDGVN MTVVGPWSPLME MTUVGPWSPLALHTT MTUVGPYSEPALHTT MTUVGFYGEPALHTTA MTUVFGYGIKELFOYT MTUVFGYGIKELFOYT TTVGLQFAKELFOYSOT TTVGLQFKAKELFOVSOT TTVGLQFKAKELFOVSOT MTUVFSX4YQGQSGNDTV MTUVGPSKERQTMNDEI MTUVGLPYSEKRQTMNDEI MTUVGLPYSETRQTMNDEI MTUVGLPYSETRQTMNDEI MTUVGLPYSETRQTMNDEI	# IYLGSY-RGAIAQSPSDAGAI IYLGGS-TGLLAQSPADSTP IRLGSS-LGVMTQSNDAAPI IRLGF-LGVMTQSOLDMSGI Q-AGSYYG-ATAV-G R-AGSYYG-ASHYGASHI IG-GGTPYG-ASHFAGADGI R-GGSPYG-ASHLAGDGI T-GGSPYG-ASHLAGDGI T-GGSPYG-ATTIAGCDGI T-GGSPYG-ATTIAGCDGI T-GGSPYG-ATTIAGCDGI T-GGSPYG-ASTIAGCDGI T-	SE-MFPG-DLETARSLGE DE-VVAG-DLATGKLYCO DEGPLPG-DLETGKAFGR STAPPAS-DLKTAQHLGL TITEA-DLIQARALGR VPKED-DLQVAKHLGK KKSLDEH-EITLCRALGK DQPVSAD-ERELGIAOGR TTQLSGE-EKALCVAFGK KKELDEN-EINIAKFLGK SRQPSQE-ELAIARYOGE SRQPSEN-ELMARYOGE SRQPSEN-ELMARYOGE SRQPSEN-ELMARYOGE SRQPSEN-ELMARYOGE SRQPSEN-ELMARYOGE SRQPSEN-ELMARYOGE	RVAEVAGKFQR RVAEATARWVAGRG RVAEATARWVAGRG RVAETVRFQPV RVAELALQLRRGAAS- RVAEVAEKLC RLAETAGKLGS RLAITASALAQANWSR RLATLAKKLGS RVAEVAKKLRC RVAEVAKKLRC RVAEVAKKLRC RVAEVAKKLRC HVAKITAKLGG RUAETAIKLHG HVTQLAKKLAGK HVTQLAKKLAGK HVTQLAKKLAGK FYETVSKVKF	31/4 27/4 28/4 30/4 28/4 43/6 40/5 39/5 36/5 40/5 40/5  81/8 57/7 54/6 50/6 50/6 50/6 50/6
PJS666WrbA EcaWrbA BCWrbA XfWrbA OgwrbA AfWrbA PaeWrbA PaeWrbA ParWrbA StWrbA StWrbA StWrbA EcoWrbA MBNCLWrbA MBNCLWrbA MacWrbA MbWrbA MbWrbA GtQR1 PcQR	#         #           WKDKLFAGFTNSAALDGDKMSTLNYLFTLAMQH         WSNKVFGGFTNSASLNGDKQVTLTYLQTLASQH           WKDKIAAGFTNSGAQHGDKLNSLMSMVLFAAQH         WKDKIAAGFTNSGAQHGDKISTJQYUTLSNOH           WKDKIAAGFTNSGAQHGDKISTJQYUTLSNOH         WKDKIAAGFTNSGAQHGDKISTJQYULATNAQH           UKRAFANSGASTSSAGHGGCFTLTYLSNUHAWLGS         LSGKVGAAFTSSAGHGQCFTLTYLATNAQH           LSGKVGAAFTSSAGHGQCSTTLJSNLLPLHH         LIGKPAGVFTSTSSMHGQDESTLJSMLVPLHH           LYGKVQFTTACSMHGGDESTLISMMVPLLHH         LYGKVQFTSTSSMHGQDESTLISMVTLHH           LYGKVQFTTASSTNHGGHESTIJAMANYAYHF         LYGKVGSFSTCT-GGQQCTTTSTWTLAHH           LYGKVASVFSSTCT-GGQDESTIJSTWTLAHH         LYGKVGSVFTSSCT0HGGDESTIJTNUHLF           LYKNGSVFTSSCT0HGGQESTIJTNNLHL         LVKVGSVFTSSCT0HGQESTIJTHVTLLHL           LVGKVGSVFTSSCT0HGQESTIJTHVTLLHL         LVGKVGSVFTSSCT0HGQESTIJTHVTLHLL           LVGKVGSVFTSSCT0HGQESTIJTHVTLHLL	GIWVSQGVLPSTSKAAQR-DDAN GIWVSGNLPSNAKAAR-DDLN WWVGTSLMPANSKAATR-NDIN MIWVGDLMPGNNSSTGSSDDLN MIWVGDLSPL-SGL-DDGVN MIVGPVSPL	# INLGSY-RGAIAQFSDAGAN INLGGS-TGLLAQFPSDASAI INLGGS-TGLLAQFPSDASAI INLGGF-LGVMTQSNDAAPI IRLGGF-LGVMTQSNDAAPI IRLGGFLGVMGQSQLDMSGI Q-AGSYYG-ATAV-G IG-GGTPYG-ATAV-G IG-GGTPYG-ASHFAGADGI T-GGTPYG-ASHLAGSDG' T-GGTPYG-ASHL-G-NI IT-GGTPYG-ASHL-G-NI IT-GGTPYG-ASHL-G-NI IT-GGTPYG-ASHL-G-NI IT-GGTPYG-ASHLAGDGI T-GGSPYG-ASTIAGCDGI T-GGSPYG-ASTIAGCDGI T-GGSPYG-ASTIAGCDGI T-GGSPYG-ASTIAGCDGI T-GGSPYG-ASTIAGCDGI T-GGSPYG-ASTIAGCDGI T-GGSPYG-ASTIAGCDGI T-GGSPYG-ASTIAGCDGI T-GGSPYG-ASTIAGCDGI T-GGSPYG-ASTIAGCDGI T-GGSPYG-ASTIAGCDGI T-GGSPYG-ASTIAGCDGI T-GGSPYG-ASTIAGCDGI T-GGSPYG-ASTIAGCDGI T-GGSPYG-ASTIAGCDGI	GE-MFPG-DLETARSLGE DE-VVAG-DLATGKLYGQ DEGPLPG-DLETGKAFGR SIAPPAS-DLKTAQHIGL KEPVLDSGDYLTSVRFGE VPKED-DLQVAKHIGK KRSLDEH-EITLCRAIGK KRSLDEH-EITLCRAIGK KRSLDEH-EITLCRAIGK KRSLDEN-ERKIARFOGK KKELDEN-EINIAKFLGK SRQPSQE-ELSIARYOGE SRQPSQE-ELSIARYOGE SRQPSQN-ELBCARFOGK SRQPSEN-ELBCARFOGK SRQPSEN-ELBCARFOGK SRQPSEN-ELBCARFOGK SRQPSEN-ELBCARFOGK SRQPSEN-ELBCARFOGK SRQPSEN-ELBCARFOGK SRQPSEN-ELBCARFOGK SRQPSEN-ELBCARFOGK SRQPSEN-ELBCARFOGK SRQPSEN-ELBCARFOGK SRQPSEN-ELBCARFOGK	RVAEVACKFQR RIADIAAKLAN RVAEATARWVAGRG RVAETVRFQPV RIAEATKRWNK RVAELALQLRRGAAS- RVAEVALQLRRGAAS- RVAEVAKLC RIAETASLAQANWSR RIATLAKKLYD RITEVAKAIKCCNK RVAEVAKKLRC YVAGLAVKLNG HVAKITAKLKG RIAETAKLYR HVTLIAKKIAGK HVTQIAKKLAGK HVTQIAKKLAGK HVTQIAKKLAGK HVTQIAKKLAGK HVTQIAKKLAGK	31/4 27/4 28/4 30/4 43/6 40/5 39/5 36/5 40/5 40/5 36/5 36/5 50/6 50/6 50/6 43/6
PJS666WrbA EcaWrbA BcWrbA XfWrbA CaWrbA CaWrbA ParWrbA ParWrbA ParWrbA StWrbA ScWrbA ScWrbA CcWrbA MENCLWrbA MENCLWrbA MacWrbA McWrbA GtQR1 PcQR GtQR2	WKDKLFAGFTNSAALDGDKMSTLNYLFTLAMOH WSNKVFGGFTNSAŠLNGDKGVTLĪYLQTLASOH WKDKIAAGFTNSĞNGDKFJTIQYLQTLASOH WKDKIAAGFTNSĞNGDKFJTIQYLTLATNAGQH UKDKIAAGFTNSĞRDGDKTLIYLATNAGQH LGKVGAVFTSNGAHGGCSTLIYLATNAGQH LGKVGAVFTSÄĞHGGQETTLIXMLPLLHH LQNKPAAVFTSTÄĞLHGQETTLISMLPLLHH LQNKPAVFTSTSMHGQESTLISMVVLLHH LYKKASVFSTCT-GGQDCTTISTMTTLAHH LYKKASVFSTCT-GGQDCTTISTMTTLAHH LYKKASVFSTCT-GGQDETTIFSTTTLAHH LYKKASVFSTCT-GGQDETTIFSTTTLAHH LYKKASVFSTCT-GGQDETTIFSTTTLAHH LYKKASVFSTCT-GGQDETTIFSTTTLAHH LYKKASVFSTCT-GGQDETTIFSTTTLAHH LYKKASVFSTCT-GGQDETTIFSTTTLAHH LYKKASVFSTCT-GGQDESTIJFHVTLLH FVKWGSVFTSSCT0HGQDESTIJSTMTTLAHH LUKNKSVFSTCT-GGQDESTIJSTMTLAHH LUKKVGSVFTSSCT0HGQDESTIJSTMTLLH LAKYAGLFVSTSCT0HGQDESTIJSTMTLH LAKYAGLFVSTSCT0HGQDESTIJSTTTTLH LAKYAGLFVSTCFPGGQDESTJATAMSTLVHH	GTWVSQGVLPSTSKAAQR-DDAN GTWVSQGVLPSTSKAAQR-DDAN GTWVSINQLPSNAKAARR-DDLN MIWVGDLMPGNNSSTGSSDDLN MIWVGDLSPSL-SGL-DDGVN MIWVGDLSPSPME MIIVGLPPAEPALLETR MIVUCGIPYAEQALLETR MIVUCGIPYAEQALHTTA MIVUFGYGIPELFPVSQV FIVUFGYGKEELFPVSQV FIVUFGYGKELFPVSQV FIVUFGYGAKGQSCNDTV MILVGLPYSEKRQTHMDEI MIVUCGIPYSEKRQTHMDEI LIYVPLGYKHTFAQLANLSEV VIVUFLGYKHTFAQLANLESV	# IYLGSY-RCAIAQSPSDAGA INLGGS-VGLAQTPSDASA IYLGGS-TGLLAQTPSDASA IYLGGS-TGLLAQTPSDASA IYLGGS-TGLAQSPADSTP IRLGF-LCVMCQSQLDMSG IQ-AGSYYG-ATAV-G R-AGSYYG-ATAV-G SGCPYG-ASHFAGADG IX-GGTPYG-ASHFAGADG IX-GGTPYG-ASHFAGADG IX-GGTPYG-ASHIAGSDG IX-GGSPYG-ATTIAGCDG IX-GGSPYG-ATTIAGCDG IX-GGSPYG-ATTIAGCDG IX-GGSPYG-ATTIAGCDG IX-GGSPYG-ASTIAGCDG IX-GGSPYG-ASTIAGCDG IX-GGSPYG-ASTIAGCDG IX-GGSPWG-ASTIAGCDG IX-GGSPWG-ASTIAGCDG IX-GGSPWG-ASTIAGCDG IX-GGSPWG-ASTIAGCDG IX-GGSPWG-ACTFAGADG	SE-MFPG-DLETARSLGE DE-VVAG-DLATGKLYGQ DEGPLPG-DLETGKAFGR SIAPPAS-DLKTÄQHLGL VPKED-DLQARALGR VPKED-DLQARALGR VPKED-DLQAKALGK KSLDEH-EITLCRALGK OQPVSAD-ERELGIAQGR TFQLSQE-EKALCVAFGK KKELDEM-EINIAKFLGK SRQPSEN-EISIARYGGE SRQPSEN-ELSARYGGR SRQPSEN-ELEGARYGGR SRQPSEN-ELEMARYGGR SRQPSEN-ELAMARYGGR SRQPSEN-ELAMARYGGR SRQPFL-ELEVATIGGK SRQPTPL-ELEVATIGGK	RVAEVAGKFQR RVAEATARWVAGRG RVAETVRFGPV RVAEIALQIRRGAAS- RVAEVAEKLC RLAETACKIGS RLATTAKKLGS RTEVAKAIKCCNK RVAEVAKKRC VAGLAVKIRG HVAKITAKLKG HVAKITAKLKG HVTLIAKKIAGK HVTLIAKKIAGK HVTLIAKKIAGK IFYETVSKVKF IFYETVSKVKF IFYETVSKVKF IFYETVSKVKF	31/4 27/4 28/4 30/4 43/6 40/5 36/5 36/5 36/5 54/6 50/6 50/6 50/6 50/6 48/6 48/6 44/6
PJS666WrbA EcaWrbA BcWrbA XfWrbA OgwrbA AfWrbA PacWrbA PacWrbA ParWrbA StWrbA StWrbA StWrbA CcWrbA CcWrbA MBNCIWrbA MacWrbA MmWrbA MbWrbA GtQR1 PcQR GtQR2 SpObr1	WKDKIFAGFTNSAALDGDKMSTINYLFTLAMOH WSNKVFGGFTNSAZNMCDKFSTIOYLFTLAMOH WKDKIAAGFTNSAZNMCDKFSTIOYFVTLSMCH WKDKIAAGFTNSAZNMCDKFSTIOYFVTLSMCH WKDKIAAGFTNSACHSCTFFTLSVLHWMLGS LSGKVGAAFTSSACHSGTFFTLSVLHWMLGS LVGKPAAVFTSTASLHGQETTLISVLHWMLGS LVGKPAAVFTSTASLHGQETTLISVLHWMLGS LVGKPAVFTSTASLHGQETTLISVLHWMLGH LVGKPAVFTSTASLHGQETTLISVLHWLLHH LYGKPVFFTEASTWHGGHESTIIXMVPLLHH LYGKVGFFTEASTWHGGHESTIIXMVPLLHH LYGKVGFFTEASTWHGGHESTIIXMVTLHH LYGKVGFFTEASTWHGGBESTIISTWTLAHH LYGKVGSVFTSSCTOHGQESTIISTWTLAHH FVGKVGSVFTSSCTOHGQESTIITNVLHLH FVGKVGSVFTSSCTOHGQESTIITSWTLAHH LAGKYAGLFVSTASPGGQESTIITSWTLLH LAGKYAGLFVSTASPGGQESTIITSWTLLH LAGKYAGLFVSTASPGGQESTIISSISTIH LAGKYAGLFVSTASPGGQESTINSISTIHH LAGKYAGLFVSTASPGGQESTIMMANSTVHH	GIWVSQGVLPSTSKAAQR-DDAN GIWVSGNQLPSTSKAAQR-DDAN MIWVGTSLMPANSKAARR-DDLN MIWVGDLQSFL-SGL-DDGVN MIVGDLØSFL-SGL-DDGVN MIVGLPØSPL	# IYLGSY-RGAIAQSPSDAGAN IYLGS-TGLLAQTPSDAGAI IYLGGS-TGLLAQSPADSTP IRLGSH-LGVMTQSNDAAP] IRLGGF-LGVMTQSNDAAP] IRLGGF-LGVMGQSQLDMSGI Q-AGSYYG-ATAV-G G-GGTPYG-ASHYAGABI T-GGTPYG-ASHYAGABI T-GGTPYG-ATTIAGGDG: T-GGSPYG-ATTIAGGDG: T-GGSPYG-ATTIAGGDG: T-GGSPYG-ASTIAGABGI T-GGSPYG-ASTIAGGDG: T-GGSPYG-ASTIAGGDG: T-GGSPYG-ASTIAGGDG: T-GGSPYG-ASTIAGGDG: T-GGSPYG-ASTIAGGDG: T-GGSPYG-AGTIAGGDG: T-GGSPYG-AGTIAGADG: T-GGSPYG-AGTAGADG: T-GGSPYG-AGADG: T-GGSPYG-AGTAGADG: T-GGSPYG-A	3E-MFPG-DLETARSLGE DE-VVAG-DLATGKLYGO DEGPLPG-DLETGKAFGR TIAPPAS-DLKTAQHIGL KEPVLDSGDULTSVRFGE VPKED-DLQVAKHIGK KRSLDEH-ELTLCRALGK OQPVSAD-ERELGIAQGR TTQLSQE-EKALCVAFGK KKELDEN-EINIAKFLGK KKELDEN-EINIAKFLGK SRQPSE-ELAIARFOGE SRQPSEN-ELATARFOGE SRQPSEN-ELAMARYOGR SRQPSEN-ELAMARYOGR SRQPSEN-ELEMARYOGR SRQPSEN-ELEMARYOGR SRQPSEN-ELEMARYOGR SRQPSEN-ELEMARYOGR SRQPFL-ELEVATLOGK SRQPFL-ELEIATAQGK	RVAEVACKFQR RVAEATARWVAGRG RVAEATARWVAGRG RVAETVRFQPV RIAEATKRWNK RVAELALQIRRGAAS- RVAEVALQIRRGAAS- RVAEVALQIRRGAAS- RVAEVAKIC RIAITASALAQANWSR RLATTASLAQANWSR RLATTAKICS RVAEVAKKICC VAEVAKKICC VAEVAKKICC RUAETAIKLIG RIAETAKLIG HVTQIAKKIAGK HVTQIAKKIAGK HVTQIAKKIAGK YFWIIIKVAF SFYEYVARVKW	31/4 22/4 28/4 30/4 43/6 39/5 39/5 39/5 39/5 336/5 40/5 39/5 57/7 50/6 50/6 50/6 50/6 43/6 43/6 43/6 44/6
PJS666WrbA EcaWrbA XfWrbA XfWrbA CaWrbA AfWrbA PaeWrbA PaeWrbA ParWrbA StWrbA StWrbA StWrbA ScWrbA EcoWrbA MBNC1WrbA MBNC1WrbA MBNC1WrbA MbWrbA GtQR1 PcQR GtQR2 SpObr1 NcHyp	WKDKLFAGFTNSAALDGDKMSTLNYLFTLAMQH WSNKVFGGFTNSASLNGDKQVTLTYLQTLASQH WKDKIAAGFTNSGAQHGDKLNSLMSMVLFAAQH WKDKIAAGFTNSGAQHGDKLNSLMSMVLFAAQH UKDKIAAGFTNSGAQHGDKLNSLMSMVLFAAQH LSGKVGAAFTSSGRFGTFTLSVLHAWLGG LGKVQAAVFTSNEMPHGKBATLISMLLPLFAH LQNKPAAVFTSTSMHGQESTFLTNMLPLLHH LIGKPAGVFTSTSSMHGQESTLISMLVPLLHH LIGKPAGVFTSTSMHGQESTLISMMVPLLHH LYGKVQFTFTEASTWHGGHSTILMMANYAYHF LYGKVGSVFTSSCT-GGGQEQTITSTWTLAHH LYGKVGSVFTSSCT-GGGQEQTITSTWTLAHH LYGKVGSVFTSSCT-GGGQESTIISTWTLAHH LYGKVGSVFTSSCT-GGGQESTIITSWTLAHH LYGKVGSVFTSSCT-GGGQESTIITSWTLAHH	GIWVSQGVLPSTSKAAQR-DDAN GIWVSQGVLPSTSKAAQR-DDAN GIWVSINQLPSNAKAAR-DDLN MIWVGDLMPGNNSSTGSSDDLN MIWVGDLSPSSTGSSDDLN MIWVGDL9SL-SGL-DDGVN MIVGPYBSP	# IYLGSY-RGAIAQ5F5DAGAA IYLGSY-RGAIAQ5F5DAGAA IYLGGS-TGLLAQ5F2DASAI IYLGGS-TGLAQ5F2DASAI IYLGGS-TGLAQ5F2DASAI IYLGGS-TGLAQ5F2DASAI RLGGFLGVMC9QLDMSG1 G-AGSYYG-ATAV-G G-GGFYG-ASHFAGADG1 T-GGSFYG-ASHLAG5DG1 T-GGSFYG-ASHLAG5DG2 T-GGSFYG-ASHLAG5DG3 R-GGAPYG-ASHLAG5DG3 R-GGAPYG-ASHLAG5DG3 R-GGAPYG-ASHLAG5DG3 R-GGAPYG-ASHLAG5DG3 R-GGSFYG-ASHLAG5DG3 R-GGSFYG-ASHLAG5DG3 R-GGSFYG-ASHLAG5DG3 R-GGSFYG-ASHLAG5DG3 R-GGSFYG-ASHLAG5DG3 R-GGSFYG-ASHLAG5DG3 R-GGSFYG-ASHLAG5D3 R-GGSFYG-ASHLAG5 R-GG5FYG-ASHLAG5 R-GG5FYG-ASHLAG5 R-GG5FYG R-GG5FYG-ASHLAG5 R-GG5FYG R-G5FYG R-G5FYG R-G5FYG R-G5FYG R-G5FYG R-G5FYG R-G5FYG R-G5F	SE-MFPG-DLETARSLGE DE-VVAG-DLATGKLYGQ DEGPLPG-DLETGKAFGR SIAPPAS-DLKTAQHLGL KEPVLDSGDYLTSVRFGE VPKED-DLQVAKMLGK KRSLDBH-EITLCRALGK KRSLDBH-EITLCRALGK KRSLDBH-EITLCRALGK KRSLDBH-EITLCRALGK SRQPSQE-EISIARYGGE SRQPSQE-EISIARYGGE SRQPSQE-EISIARYGGE SRQPSQE-EISIARYGGE SRQPSQE-ELGARFYGGK SRQPSD-ELEMARYGGR SRQPSD-ELEMARYGGR SRQPSD-ELEMARYGGR SRQPSD-ELEMARYGGR SRQPSD-ELEMARYGGR SRQPTL-ELEIANLGGK SRQPTL-ELEIANLGGK SRQPSD-ELEMARIGGE	RVAEVACKFQR RVAEATARWVAGRG RVAEATARWVAGRG RVAELALQIRRGAAS- RVAELALQIRRGAAS- RVAELALQIRRGAAS- RVAEVAEKLC RLAITASALQQANWSR RLAITASALQANWSR RLAITASALQANWSR RLAITASALQANWSR RLAITAKKLYD YVAGLAVKLNG YVAGLAVKLNG HVAEVAKKLC HVAEVAKKLG HVTQIAKLAGK HVTQIAKKLG FFYETVSKVRF SFYEYVARVKW SFYEYVARVKW FFYETVEK	31/4 27/4 28/4 30/4 43/6 40/5 40/5 50/6 50/6 50/6 50/6 50/6 43/6 50/6 50/6 43/6 44/6 44/6 48/6
PJS666WrbA EcaWrbA BcWrbA XfWrbA CaWrbA CaWrbA AfWrbA ParWrbA ParWrbA MdWrbA StWrbA SsWrbA CcWrbA CcWrbA MBNC1WrbA MBNC1WrbA MbWrbA MbWrbA MbWrbA GtQR1 PcQR GtQR2 SpObr1 NcHyp Y1Hyp	WKDKIFAGFTNSAALDGKMSTINYLFTLAMOH WSNKVFGGFTNSAINGDKPSTINYLFTLAMOH WKDKIAAGFTNSATMNGDKFSTIOYFVTLSMOH WKDKIAAGFTNSAGAHGKUSTIYLQTLASOH UKDKIAAGFTNSAGAHGKUSTIYLQTLANAGGH USGKVGAAFTSSAGHGGTFTLISVLHWMLGS LEGKVGAYFTSTAGHGGCETTLISVLHWMLGS UVGKPAAYFTSTAGHGGCETTLISVLHWLDLHH UVGKPAAYFTSTAGHGGCETTLISVLHWLLHLH LIGKPAGVFTSTAGHGGDETTLISVLHWLLHH LYGKPVFFTEASTWHGGHETTIIMMSTXYHF LYGKPVFFTEASTWHGGHETTIIMMSTXYHF LYGKPVFFTEASTWHGGHETTIIAMSTXYHF LYGKVSFSTGT-GGGDETTFSTTTLAHH UVKKPAAYFSTSGTGGGDETTIFNTTLAHH UVKVAGAFTSTATQHGGDETTIFSTITMTLAHH UVKVGSVFTSSCTGHGGDESTIISFWTLLHL VGKVGSVFTSSCTGHGGDESTIISFWTLLHL UVGKVGSVFTSSCTGHGGDESTIISFWTLLHL LAGKYAGLFVSTSGFGGGDESTNINSISTITH LGKYAGLFVSTSCFGGGDESTNINSISTITH LGKYAGLFVSTSCFGGGDESTNINSISTIHH	GTWVSQGVLPSTSKAAQR-DDAN GTWVSGDLPSTSKAAQR-DDAN WVWVGTSLMPANSKAATR-NDIN MTWVGDLQSFL-SGL-DDGVN MTVGLPQSFL-SGL-DDGVN MTVGLPQSFL-SGL-DDGVN MTVGLPQSFLALHTT MTVGCPYAEPALHTTA MTVGGPYAEPALHTTA MTVGTPTAVAAQELFPVSQU MTVFVGVGIFELFPVSQU MTVFVGVGCKELFPVSQU MTVGDYGAKELFPVSQU MTVGLPYAEKQUMTLDEL MTVGLPYAEKQUMTLDEL MTVGLPYAEKQUMTLDEL TVFVGVSTFFAQLANLSEV VTVFVGVSTTFAQLANLSEV VTVFVGVSTTFAQLANLSEV VTVFVGVSTFFAQLANLSEV VTVFVGVSTFFAQLANLSEV MTVFUGVAKVFGELSDLSAV	# IYLGSY-RCAIAQSPSDAGA IYLGSS-TGLLAQSPSDASA IYLGSS-TGLLAQSPADSTP IRLGSS-LGVMCQSLDMSG Q-AGSYYG-ATAV-G R-AGSYYG-ASHFAGADG IQ-GSPYG-ASHFAGADG IC-GGSPYG-ASHFAGADG IT-GGSPG-ASHLAGSDG IT-GGSPG-ATHLAGSDG IT-GGSPG-ATHLAGDG IT-GGSPG-ATTIAGCDG IT-GSSYG-ATTIAGCDG IT-GSSYG-VSTIAGCDG IT-GSSYG-ASTIAGCDG IT-GSSYG IT-GSSYG-ASTIAGCDG IT-GSSYG IT-GSS	SE-MFPG-DLETARSLGE DE-VVAG-DLATGKLVGQ DEGPLG-DLETGKAFGR STAPPAS-DLKTAQHLGL -TITEA-DLIQARALGR -VPKED-DLQVAKHGK KKSLDEH-EITLCRALGK DQPVSAD-ERELGIAQGR TTQLSGE-EKALCVAFGK KKELDEN-EIKIARFQGK KKELDEN-EIKIARFQGK SRQPSEN-ELGARFQGK SRQPSEN-ELGARFQGK SRQPSEN-ELGARFQGK SRQPSEN-ELGARFQGK SRQPSEN-ELGARFQGK SRQPSEN-ELGARFQGK SRQPSEN-ELGARFQGK SRQPSEN-ELGARFQGK SRQPSEN-ELGARFQGK SRQPSEN-ELGARFQGK SRQPSEN-ELGARFQGK SRQPFL-ELELATAQGK SRQPSEL-ELELATAQGK SRVPSED-ELEIARLQGF SRQPSES-ELKVAGIQGE	RVAEVACKFQR         RVAEATARWVAGRG         RVAEATARWVAGRG         RVAETVRFQPV         RIAEATKRWNK         RVAEVAEKLC         RLAETACKIGS         RLAITASALAQANWSR         RLAITASALAQANWSR         RLAITASALAQANWSR         RLAITASALAQANWSR         RUAEVAKKIGS         WYAGLAVKING         WAGLAVKING         HVAKITAKLKG         HVAKITAKLAGK         HVTLIAKKIACK         HVTQIAKKIAGK         HVTQIAKKIAGK         HVTQIAKKIAGK         HVTQIAKKIAGK         HVTQIAKKIAGK         FYEYIXWKW         FYEYIXWKW         FYFEVILKWAF         FYFEVILKWAF	31/4 27/4 28/4 30/4 43/6 40/5 33/5 53/6 50/6 50/6 50/6 50/6 50/6 43/6 48/6 45/5 44/6
PJS666WrbA EcaWrbA BcWrbA XfWrbA CaWrbA AfWrbA PaeWrbA PaeWrbA ParWrbA StWrbA StWrbA StWrbA ScWrbA CoWrbA MBNCLWrbA McWrbA MBCLWrbA MbWrbA GtQR1 PcQR GtQR2 SpObr1 NcHyp YlHyp AtFOB1	WKDKIAGFTNSAALDGDKMSTINYLFTLAMOH WSNKVFGGFTNSASINGDKSTINYLFTLAMOH WRNKIAAGFTNSASNNGDKFSTIQYFVTLSMOH WRNKIAAGFTNSASNSGDFSTIQYFVTLSMOH WKDKIAAGFTNSASPSGKOGTLIYLATNAGH LSGKVGAAFTSSAGHSGTEFTLISULHMMLGS LSGKVGAAFTSSAGHSGTEFTLISULHMMLGS LUGKPAAVFTSTASLHGQETTLIXMLPLLHH LUGKPAAVFTSTASLHGQETTLIXMLPLLHH LUGKPAAVFTSTASLHGQETTLIXMLPLLHH LYGKPAVFTSTSSMHGGPSTLIXMMVPLLHH LYGKPAVFTSTGSMHGGPSTLIXMMVPLLHH LYGKVGFFTEASTWHGGHSTIIXMVTLAHH LYGKVGSVFTSSGT-GGGDETTTSTWTLAHH LYGKVGSVFTSSGT-GGGDESTIISTWTLAHH LYGKVGSVFTSSGT0HGGAETLASTQLALOHH LYGKVGSVFTSSGT0HGGDESTIISFWTLLHL LUKVGSVFTSSGT0HGGDESTIISFWTLLHL LAGKYAGFVSTASPGGQESTIISFWTLLHL LAGKYAGFVSTASPGGQESTIISFWTLLHL LGCKYAGLFVSTASPGGQESTIISTWTLHL LGCKYAGLFVSTASPGGQESTIISTWTLH	GIWVSQGVLPSTSKAAQR-DDAN GIWVSINQLPSTSKAAQR-DDAN MIWVGTSLMPANSKAATR-NDIN MIWVGDLQSFL-SGL-DDGVN MIVGDLQSFL-SGL-DDGVN MIVGD PMSP	# IYLGSY-RGAIAQSFSDAGAN IYLGS-TGLLAQTFSDASAI IYLGGS-TGLLAQTFSDASAI IYLGGS-TGLLAQSFADATP  IRLGSH-LGVMTQSNDAAP  IRLGGF-LGVMTQSNDAAP  IRLGGF-LGVMTQSNDAAP  IRLGGF-GATAV-G GG-GTPYG-ATAV-G GG-GTPYG-ASHLAGSDG' IT-GGSPYG-ASHLAGSDG' IT-GGSPYG-ATTIAGCDG' IT-GGSPYG-ATTIAGCDG' IT-GGSPYG-ATTIAGCDG' IT-GGSPYG-ASTIAGCDG' IT-GGSPWG-ACTFAGADG' IT-GGSPW	SE-MFPG-DLETARSLGE DE-VVAG-DLATGKLYGQ DEGPLPG-DLETGKAFGR ZIAPPAS-DLKTAQHIGL KEPVLDSGDJLTSVRFGE VPKED-DLQVAKHIGK KRSLDEH-ELTLCRALGK OQPVSAD-ERELGIAQGR TTQLSQE-EKALCVAFGK KEELDEM-ETNIAKFIGK SRQPSQE-ELSIARYQGE SRQPSQE-ELSIARYQGE SRQPSQN-ELFGARYQGK SRQPSQN-ELEMARYQGR SRQPSDN-ELEMARYQGR SRQPSDN-ELEMARYQGR SRQPSDN-ELEMARYQGR SRQPSDN-ELEMARYQGR SRQPSDN-ELEMARYQGR SRQPSDN-ELEMARYQGR SRQPTPL-ELEIATLQGK SRQPTPL-ELEIATLQGK SRQPTPL-ELEIATLQGK SRQPSDSN-ELEMARYQGR SRQPSDN-ELEMARYQGR SRQPTPL-ELEIATLQGK SRQPSDN-ELEMARYQGR SRQPSDN-ELEMARYQGR SRQPSDN-ELEMARYQGR SRQPTPL-ELEIATLQGK SRQPTPL-ELEIATLQGK SRQPSDSN-ELEMARIGGE SRQPSSN-ELEMARIGGE SRQPSSN-ELEMARIGGE SRQPSSN-ELEMARIGGE	RVAEVACKFQR RVAEVACKFQR RVAEATARWVAGRG RVAETVRFQPV RIAEATKRWNK RVAELALQIRRGAAS- RVAEVALQIRRGAAS- RUAETAGKIGS RIAITASALAQANWSR RIAITASALAQANWSR RIAITAKLYO RIAEVAKIKCONK RVAEVAKKICC VVAGIAVKING HVARITAKIAGK HVTLIAKKIAGK HVTLIAKKIAGK HVTQIAKKIGC IFYETVSKVKF IFYETVSKVF FFFKTVFRK EFYNTLSKITASQPKP(35) VTEVLIKAEGAAGA(147)	31/4 27/4 28/4 30/4 40/5 40/5 40/5 51/7 54/6 55/6 55/6 55/6 55/6 48/6 48/6 48/6 48/6 48/6 48/6
PJS666WrbA EcaWrbA BcWrbA XfWrbA CaWrbA AfWrbA ParWrbA ParWrbA ParWrbA StWrbA StWrbA ScWrbA ScWrbA CcWrbA MENCLWrbA MENCLWrbA MENCLWrbA MENCLWrbA GtQR1 FcQR GtQR2 SpObr1 NcHyp YLHyp AtFQR1 Twr022	WKDKLFAGFTNSAALDGDKMSTLNYLFTLAMQH WSNKVFGGFTNSAŠLNGDKQVTLIYLQTLASQH WKDKIAAGFTNSGAQHGDKLNSLMSMVLFAAQH WKDKIAAGFTNSGAQHGDKLNSLMSMVLFAAQH UKDKIAAGFTNSGAQHGDKLNSLMSMVLFAAQH LGGKVGAVFTSNEMPHGGKEATLISMLVLATNAGQH LGKVGAVFTSSASGTFFTLSVLHWNLGS LUGKPAQVFTSSSMHGQDSTLISMLVLHHH LIGKPAGVFTSSSMHGQDSTLISMLVLHHH LIGKPAGVFTSTSMHGQDSTLISMNVPLLHH LYGKPVGFTTASSMHGGDSTTLISMNVPLLHH LYGKPVGFTTASSMHGGESTILTMSTXAYHF LYGKPVGFTTASSTHGGHSTILMMANYAYHF LYGKPVGFTTASSTHGGBSTILTMSTXAYHF LYGKPVGFTTASSTUGGBSTIISTWTLAHH GUNFAAVFTSGCGGGDSTLISTWTLAHH LYGKPVGFTSSCTG-GGGQBQTITSTWTLAHH CHGKVAGAFTSTATQHGGDSTIISTWTLAHH CUNKPATVMSTATQHGGDSTIISTWTLAHH FVGKVGSVFTSSCTQHGQDSSTIITTHVTLHL CLAGKYAGLFVSTSSTQHGGQESTIISTUTTLAHH LGCKYAGLFVSTSGFGGGQSSTATAMSTLYHH LGCKYAGLFVSTSGFGGGQSSTATAMSTLYHH LHGKYGQFFSTCTLGGGQBSTATAMSTLYHH	GIWVSQGVLPSTSKAAQR-DDAN GIWVSQGVLPSTSKAAQR-DDAN GIWVSINQLPSNAKAAR-DDLN MIWVGDLMPGNNSSTGSSDDLN MIWVGDLMPGNNSSTGSSDDLN MIWVGDL9PSL-SGL-DDGVN MIVGJPYSPALETR MIVGJPYSP	# IYLGSY-RCAIAQSPSDAGA INLGGS-VGLLAQTPSDASA IYLGGS-TGLLAQTPSDASA IYLGGS-TGLLAQTPSDASA IYLGGS-TGLAQSPADSTP IRLGF-LCVMCQSQLDMSG Q-AGSYYG-ATAV-G R-AGSYYG-ATAV-G SGCPYG-ASHFAGADG IX-GGPYG-ASHFAGADG IX-GGPYG-ASHFAGADG IX-GGPYG-ASHIAGSDG T-GGSPYG-ATTIAGCDG T-GGSPYG-ATTIAGCDG T-GGSPYG-ATTIAGCDG T-GGSPYG-ATTIAGCDG T-GGSPYG-ATTIAGCDG T-GGSPYG-ATTIAGCDG T-GGSPYG-ATTIAGCDG T-GGSPYG-ASTIAGCDG IX-GGSPYG-ASTIAGCDG R-GGSPWG-AGTFAGADG R-GGSPWG-AGTFAGADG R-GGSPWG-AGTFAGADG H-GGSPWG-AGTFAGADG H-GGSPWG-AGTFAGDG H-GGSPWG-AGTFAGDDG IX-GSPWG-AGTFAGDDG IX-GSPWG IX-GSPWG-AGTFAGDDG IX-GSPWG IX-GSPWG IX-GSPWG IX-GSPWG IX-GSPWG IX-GSPWG IX-GSPWG IX-G	SE-MFPG-DLETARSLGE DE-VVAG-DLATGKLVGQ DEGPLPG-DLETGKAFGR SIAPPAS-DLKTÄQHLGL VPKED-DLQARALGR VPKED-DLQARALGR VPKED-DLQVAKHLGK KSLDEH-EITLCRALGK OQPVSAD-ERELGIAQGR TTQLSQE-EKALCVAFGK KKELDEM-EINIAKFLGK SRQPSQE-ELSIARYQGE SRQPSEN-ELSIARYQGE SRQPSEN-ELSARYQGR SRQPSEN-ELESARYQGR SRQPSEN-ELEMARYQGR SRQPSEN-ELAMARYQGR SRQPSEN-ELAMARYQGR SRQPSEN-ELAMARYQGR SRQPSEL-ELEVATIQGK SRSPSAL-ELEIATAQGK SRQPTPL-ELEVATIQGS SRQPSES-ELAMARYQGR SRQPTPL-ELEIATAQGK SRNSDD-ELEIATAQGK SRNSDD-ELEIATAQGK SRNSDD-ELEIATAQGK SRDYSDD-ELEIATAQGK SRDYSDD-ELEIATAQGK SRDYSDD-ELEIATAQGK SRDYSDD-ELEIATAQGK SRDYSDD-ELEIATAQGK SRDYSDD-ELEIATAQGK SRDYSDD-ELEIATAQGK SRDYSDD-ELEIATAQGK SRDYSDD-ELEIATAQGK SRDYSDD-ELEIATAQGK SRDYSDD-ELEIATAQGK	RVAEVAGKFQR RVAEVAGKFQR RVAEATARWVAGRG RVAEIALQIRRGAAS RVAEIALQIRRGAAS RVAEIALQIRRGAAS RVAEVAEKCG RLAETAGKIGS RLATIAKKIVG RVAEVAKKIGC VVAGLAVKING HVAKITAKLKG HVAKITAKLKG HVTLIAKKIAGK HVTLIAKKIAGK HVTLIAKKIAGK IFYETVSKVFF IFYETVSKVFF IFYETVSKVFF IFYETVSKVFF IFYETVSKVFF IFYETVSKVF IFYETVSKVF7	31/4 27/4 28/4 30/4 43/6 40/5 36/5 53/6 55/7 54/6 40/5 50/6 40/5 50/6 43/6 48/6 48/6 48/6 48/6 48/6 48/6
PJS666WrbA EcaWrbA BcWrbA XfWrbA OgwrbA AfWrbA PacWrbA ParWrbA ParWrbA StWrbA StWrbA StWrbA StWrbA CcWrbA CcWrbA CcWrbA CcWrbA MBNC1WrbA McWrbA MbWrbA GtQR1 PcQR GtQR2 Spobr1 NcHyp Y1Hyp AtFQR1 TvQR2	WKDKIAGFTNSAALDGDKMSTINYLFTLAMQH WSNKVFGGFTNSATMNGDKFSTIOYFVTLSMQH WKDKIAAGFTNSATMNGDKFSTIOYFVTLSMQH WKDKIAAGFTNSAGAHGDKINSLMSWVLFAAQH USGKVGAAFTSSAGHSGTBFTLISVLHWMLGS LSGKVGAAFTSSAGHSGTBFTLISVLHWMLGS LUGKPAAVFTSTASLHGQETTQISMLPLLHH LUGKPAAVFTSTASLHGQETTLISMLPLLHH LUGKPAAVFTSTASLHGQETTLISMLPLLHH LYGKPVFFTEASTWHGGHESTILMMVPLLHH LYGKPVFFTEASTWHGGHESTILMMVPLLHH LYGKPVFFTEASTWHGGHESTILMMVANAHF LYGKVYFSTSGCGGGDETTTSTWTLAHH LYGKVSFSTGTGGGDETTTSTWTLAHH LYGKVSFSTGT-GGGDESTISTWTLAHH LYGKVSFTSCT-GGGDESTISTWTLAHH LYGKVSFTSCT-GGGDESTISTWTLAHH LYGKVSFTSCT-GGGDESTISTWTLAHH LYGKVSSFTSCT-GGGDESTISTWTLAHH LYGKVSSFTSCT-GGGDESTISTWTLAHH LUGKVAGFTSCT-GGGDESTISTWTLAHH LUGKVAGFTSCT-GGGDESTISTWTLAHH LUGKVAGFTSCT-GGGDESTISTWTLAH LUGKVGSVFTSSCT-GGGDESTISTWTLAH LAGKYAGLFVSTSCT-GGGDESTISTSTUFN LAGKYAGLFVSTSCT-GGGDESTISTSTUH	GTWVSQGVLPSTSKAAQR-DDAN GTWVSGLVPSTSKAAQR-DDAN WWVGTSLMPANSKAARR-DDLN WIWVGDLQSFL-SGL-DDGVN MIWVIGDLQSFL-SGL-DDGVN MIVGLPWSP	# VILGSY-RGAIAQSPSDAGAN VILGS-TGLIAQTPSDAGAN VILGS-TGLIAQSPADSTP RLGSW-LGVMTQSNDAAPI RLGSW-LGVMTQSNDAAPI RGGSYG-ASTWGQAQLMSGI GGSTYG-ASTHAGADGI R-GGSPYG-ASTHAGADGI T-GGSPYG-ASTHAGADGI T-GGSPYG-ATTIAGCDGI T-GGSPYG-ATTIAGCDGI T-GGSPYG-ATTIAGCDGI T-GGSPYG-ATTIAGCDGI T-GGSPYG-ASTIAGCDGI T-GGSPYG-ASTIAGCDGI T-GGSPYG-ASTIAGCDGI T-GGSPYG-ASTIAGCDGI T-GGSPYG-ASTIAGCDGI T-GGSPYG-ACTFAGADGI R-GGSPWG-ACTFAGADGI R-GGSPWG-ACTFAGADGI R-GGSPWG-ACTFAGADGI H-GGSPWG-ACTFAGADGI K-GGSPYG-ACTFAGADGI K-GGSPYG-ACTFAGADGI K-GGSPYG-ACTFAGADGI CH-GSSWG-ACTFAGADGI CH-GSSWG-AGTFAGADGI CH	SE-MFPG-DLETARSLGE DE-VVAG-DLATGKLYGQ DEGPLPG-DLETGKAFGR STAPPAS-DLKTAQHLGL TITEA-DLIQARALGR VPKED-DLQVAKHLGK KKSLDEH-ELTICRALGK DQPVSAD-ERELGIAQGR TTQLSQE-EKALCVAFGK KKELDEN-EINIAKFLGK SRQPSQE-ELSIARYGGE SRQPSEN-ELMARFQGR SRQPSEN-ELMARFQGR SRQPSEN-ELMARFQGR SRQPSEN-ELMARFQGR SRQPSEN-ELMARFQGR SRQPSEN-ELMARFQGR SRQPSEN-ELMARFQGR SRQPSEN-ELMARFQGR SRQPSEN-ELEMARFQGR SRQPSEN-ELEMARFQGR SRQPSEN-ELEMARFQGR SRQPSEN-ELEMARFQGR SRQPSEN-ELEMARFQGR SRQPSEN-ELEMARFQGR SRQPSEN-ELEMARFQGR SRQPSEN-ELEMARFQGR SRQPSEN-ELEMARFQGR SRQPSEN-ELEMARFQGR SRQPSEN-ELEMARFQGR SRQPSEN-ELEMARFQGR SRQPSEN-ELEMARFQGR SRQPSEN-ELEMARFQGR SRQPSEN-ELCQAFHCGM	RVAEVAGKFQR RVAEVAGKFQR RVAEATARWVAGRG RVAETVRFQPV RVAELALQLRGAAS- RVAELALQLRGAAS- RVAEVAEKLC RLAETAGKLGS RLAITASALAQANWSR RLATTASALAQANWSR RLATTASKLGS RVAEVAKKLGC RVAEVAKKLRC RVAEVAKKLRC RVAEVAKKLRC RVAEVAKKLGC HVTQIAKKLGG HVTQIAKKLAGK HVTQIAKKLAGK HVTQIAKKLAGK FYFITVSKF SFYEVARVKW FFYITVSKF FFYITVSKFAC FFYITVSKFAC FFYITVSKKF304(147) YFEVLIKAEGGAAGA(147) YIASITKKLKGSTA	31/4 27/4 28/4 30/4 40/5 39/5 40/5 50/6 50/6 50/6 43/6 50/6 43/6 44/6 42/6 42/6 42/6 28/6 28/6 28/6 28/6 28/6 28/6
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PJS666WrbA EcaWrbA BcWrbA XfWrbA CaWrbA CaWrbA AfWrbA ParWrbA ParWrbA SwrbA StWrbA SsWrbA CcWrbA MBNC1WrbA MBNC1WrbA MBNC1WrbA MBNC1WrbA MBWrbA GtQR1 PcQR GtQR1 PcQR SpObr1 NcHyp Y1Hyp AtFQR1 TvQR2 E255-15WrbA DrWrbA	WKDKIFAGFTNSAALDGDKMSTINYLFTLAMOH WSNKVFGGFTNSAINGDKDVTLIYLQTLASOH WKDKIAAGFTNSATMNGDKFSTIQYFVTLSMQH WKDKIAAGFTNSAGAHGDKLNSLMSWVLFFAQH UKDKIAAGFTNSAGNHGCHSTLIYLATNAQH LSGKVGAAFTSSAGHSGTBFTLISVLHWMLGS LOKWFAAVFTSTASLHGGDETOLSWLPLLHH LQKPAVFTSTASLHGGDETTLISVLHWMLGS LQKPAVFTSTASLHGGDETTLISVLHWLLHLH LQKPAVFTSTASLHGGDETTLISVLHWLLHLH LQKPAVFTSTASLHGGDETTLISVLHWLLHH LYGKPVFFTEASTWHGGBETTIIMMSYAYHH LYGKPVFFTEASTWHGGBETTIIAMNYAYHH LYGKPVFFTEASTWHGGBETTIIAMNYAYHH LYGKVSFSTGT-GGGDETTISTWTLAHH LYGKVSFSTSCT-GGGDETTISTWTLAHH LYGKVSFSTSCT-GGGDESTIISHVTLHLH LYGKVSFTSSCT0HGQDESTIIFHVTLHLH LYGKVSFTSSCT0HGQDESTIIFHVTLHLH LUKKVGSVFTSSCT0HGQDESTIIFHVTLHLH LGKYAGIFVSTSGTOHGGDESTIISHVTLHLH LGKYAGIFVSTSGTOHGGDESTIITHVTLHLH LAGKYASUFVSTCTCIGGCDESTNINSTSTHTH LHGKYGOFFSCTLGGGDESTNINSTSTHH LHGKYGOFSCTGGGDESTALAMSTFAHH LHGKYGOFSCTGGGDESTALAMSTFAHH LHGKYGFVSSCTGGGGDESTALAMSTFHH LHGKYGFVSSCTGGGDESTALAMSTLAHH LHGKYGFVSSCTGGGGDESTALAMSTLAHH LHGKYGFVSCTGGGGDESTALAMSTLAHH LHGKYGSVFSCTGUGGGDESTALAMSTLAHH LHGKYGGFSCTGUGGDESTALAMSTLAHH LHGKYGGFVSCTGUGGDESTALAMSTLAHH	GIWVSQGULPSTSKAAQR-DDAN GIWVSQGULPSTSKAAQR-DDAN WVWVGTSLMPANSKAATR-NDIN MIWVGLDLMPGNNSTGSSDDLN MIWVVGLDLYSLME MIVGLPSPLME MIVGPYSPLALHTT MIVGTPYSPLALHTT MIVGTYSPAEPALHTT MIVGTYGYGIFELFOYT MIVFGYGIFELFOYT MIVFGYGISKELFOVSOU MIVFGACKELFOVSOU MIVFGACKELFOVSOU MIVGLPYSEKQUTLDEL MIVGLPYSEKQUTLDEL MIVGLPYSEKQUTMDEL MIVGLPYSETAQLANLSEV MIFVPLGYKTFAQLANLSEV MIFVPLGYKTFAQLANLSEV MIFVPLGYKTFSLANLYSI MIVFJGYKTFSLANLYSI MIVFJGYFGAGMFEMENV MIFVPLGYTFGAGMFEMENV MIFVPLGYTFGAGMFEMENV MIFVPLGYTFGAGMFEMENV MIFVPLGYTFGAGMFEMENV MIFVPLGYTFGADMFNMEKI	# YLGSY-RCAIAOSPSDAGA YLGSTCLLAOTPSDAGA YLGSTCLLAOTPSDASA YLGSTCLLAOTPSDASA YLGSTCLAOSPADSTP RLGSTLOWCOSOLDMSG Q-AGSYYG-ATAV-G R-AGSYYG-ASHFAGADG R-GGSPYG-ASHFAGADG R-GGSPYG-ASHFAGADG R-GGTPYG-ATHLAGDG T-GGSPYG-ATHLAGDG R-GGTPYG-ATTLAGCDG R-GGTPYG-ATTLAGCDG R-GGPYG-ATTLAGCDG R-GGPYG-ATTLAGCDG R-GGSPYG-ATTLAGCDG R-GGSPYG-ASTLAGCDG R-GSSYG-ASTLAGCDG R-GSSPG-ASTLAGCDG R-GSSWG-ACTTAGADG R-GSSWG-ACTTAGADG R-GSSWG-ACTTAGADG R-GSSWG-ACTTAGADG R-GSSWG-ACTTAGADG R-GSSWG-ACTTAGADG R-GSSWG-ACTTAGADG R-GSSYG-ACTTAGADG R-GSNYG-ACTTAGADG R	SE-MFPG-DLETARSLGE DE-VVAG-DLATGKLVGQ DEGPLPG-DLETGKAFGR SIAPPAS-DLKTÄQHLGL VPKED-DLQVAKHGK KSPULBSGDVLTSVRFGE UPKED-DLQVAKHGK KSLDEH-EITICRALGK DQPVSAD-ERELGIAQGR TTQLSGE-EKALCVAFGK KELDEM-EINIAKFLGK SRQPSDE-ELSIARYGGE SRQPSEN-ELMARYGGR SRQPSEN-ELGARYGGR SRQPSEN-ELMARYGGR SRQPSEN-ELMARYGGR SRQPSEN-ELMARYGGR SRQPSEN-ELENARYGGR SRQPSEN SRQPSEN-ELENARYGGR SRQPSEN SRQPSE	RVAEVACKFQR RIADIAAKLAN RVAEATARWVAGRG RVAETVPRFQPV RVAELALQIRRGAAS- RVAEVAEKLC RLATTASALAQANWSR RLATTASKLGS RLATTASKLGS RVAEVAKKLRC VYAGLAVKLNG HVAKITAKLKG HVAKITAKLKG HVAKITAKLKG HVTLIAKKIACK HVTQIAKKIACK HVTQIAKKIACK HVTQIAKKIACK FFYETVSKVFP FFFKTVFRK FFKTVFRK	31/4 227/4 28/4 28/4 43/6 40/5 39/5 39/5 39/5 39/5 50/6 50/6 50/6 50/6 48/6 45/5 50/6 48/6 48/6 48/6 48/6 48/6 43/5 53/3 43/5 35/5 43/5
PJS666WrbA EcaWrbA BcWrbA XfWrbA OgwrbA AfWrbA PacWrbA PacWrbA ParWrbA StWrbA StWrbA StWrbA CcWrbA CcWrbA MBNCIWrbA MSWrbA GtQR1 PcQR GtQR1 PcQR GtQR2 SpObr1 NcHyp Y1Hyp AtFQR1 TvQR2 E255-15WrbA MavHyp	WKDKIAGFTNSAALDGDKMSTLNYLFTLAMOH WSNKVFGGFTNSAKNNGDKSTLNYLFTLAMOH WKDKIAAGFTNSAKNNGDKSTIJYLQTLASOH WKDKIAAGFTNSASPSGNGGTFTLISVLHWMLGS UKDKIAAGFTSSAGHSGTBFTLSVLHWMLGS LSGKVGAAFTSSAGHSGTBFTLSVLHWMLGS LUGKPANFTSTASLHGQETTLISVLHWMLGS LUGKPANFTSTASLHGQETTLISVLHWMLGS LYGKPAVFTSTASLHGQETTLISVLHWMLGS LYGKPAVFTSTASLHGQETTLISVLHWMLGH LYGKPAVFTSTASLHGQETTLISVLHWLLHH LYGKPAVFTSTASLHGQETTLISVLHWLHLH LYGKVGSFTSSGTHGGDETTLISVLHWLHH LYGKVGSFTSSGTHGGOESTLISMVTLLHH LYGKVGSFTSSGTHGGOESTLISMVTLLHH LYGKVGSFTSSGTHGGQESTLISTNTLAHH LYGKVGSVFTSSGTHGGQESTLISTNTLAHH LYGKVGSVFTSSGTHGGQESTIITHVTLLH LAGKYAGLFVSTASPGGQESTIITSTVTLAHH LAGKYAGLFVSTASPGGQESTIITSTVTLLH LGKYAGLFVSTASPGGQESTIITSTVTLLH LGKYAGLFVSTASPGGQESTLISSTVTHSISTLH LGKYAGLFVSTASPGGQESTLAMSTSLHH LGKYAGLFVSTASPGGGGSTALAMSTLAH	GIWVSOGVLPSTSKAAQR-DDAN GIWVSINQLPSTSKAAQR-DDAN MIWVGTSLMPANSKAATR-NDIN MIWVGDLQSFL-SGL-DDGVN MIVGDLQSFL-SGL-DDGVN MIVGLPMSP	# IYLGSY-RGAIAQSPSDAGAN IYLGS-TGLLAQTPSDAGAN IYLGGS-TGLLAQTPSDAGAN IYLGGS-TGLLAQSPADJTPI RLGSW-LGVMTQSNDAAPI RLGSW-LGVMTQSQLDMSGI Q-AGSYYG-ATAV-G G-GGTPYG-ASHYAGABH IT-GGTPYG-PSHLAGSDG' T-GGSPYG-ATHIAGGGG' T-GGSPYG-ATHIAGGGG' T-GGSPYG-ATTIAGGGG' T-GGSPYG-ATTIAGGGG' T-GGSPYG-ATTIAGGDG' T-GGSPYG-ATTIAGGDG' T-GGSPYG-ASTIAGABG' T-GGSPYG-ASTIAGABG' T-GGSPYG-ASTIAGABG' T-GGSPYG-ASTIAGABG' T-GGSPYG-ASTIAGABG' T-GGSPYG-ASTIAGABG' T-GGSPYG-ASTIAGABG' T-GGSPYG-ASTIAGABG' T-GGSPYG-AGTAGGDG' T-GGSPYG-AGTAGGDG' T-GGSPYG-ASTIAGABG' T-GGSPYG-ASTIAGABG' T-GGSPYG-AGTAGGDG' T-GGSPYG-AGTAGGDG' T-GGSPYG-AGTAGABG' T-GGSPYG-AGTAABBC' T-GGSPYG-AGTAGABG' T-GGNPYG-ASTABBC' T-GGSPYG-AGTAGABG' T-GGNPYG-AGTAGABG' T-GNPYG-AGTAGABG' T-GNPYG-ASTABBC' T-GNPYG-ASTABBC' T-GNPYG-AGTAGABG' T-GNPYG' T-TVDDD' T-GNPYG' T-TVD' T-GNPYG' T-TVD' T-TTTG' T-GNPYG' T-TVD' T-TTTTG' T-GNPYG' T-TTTTTG' T-GNPYG' T-TTTTTG' T-GNPYG' T-TTTTTTTTG' T-TTTTG' T-GNPYG' T-TTTTTTG' T-TTTTTTTTTTTTTTTTTTTTTTTT	SE-MFPG-DLETARSLGE DE-VVAG-DLATGKLYGO DEGPLPG-DLETGKAFGR TAPPAS-DLKTAQHIGL KEPVLDSGDULTSVRFGE VPKED-DLQVAKHIGK KRSLDEH-ELTLCRALGK OQPVSAD-ERELGIAQGR TTQLSQE-EKALCVAFGK KKELDEM-EINIAKFLGK SRQPSCE-ELSIARYGGE SRQPSEN-ELMARYGGR SRQPSEN-ELMARYGGR SRQPSEN-ELMARYGGR SRQPSEN-ELMARYGGR SRQPSEN-ELEMARYGGR SRQPSEN-ELEMARYGGR SRQPSEN-ELEMARYGGR SRQPSEN-ELEMARYGGR SRQPSEN-ELEMARYGGR SRQPFL-ELEVATIGGK SRQPSEL-ELEVATIGGK SRQPSEL-ELEVATIGGS SRQPSEL-ELQAFHOGG SRQPSEL-ELQAFHOGG SRQPSDI-ELQAFHOGG SRQPSDI-ELQAFHOGG SRQPSDI-ELQAFHOGG SRQPSDI-ELQAFHOGG SRQPSDI-ELQAFHOGG SRQPSDI-ELQAFHOGG SRQPSDI-ELQAFHOGG SRQPSDI-ELQAFHOGG SRQPSDI-ELQAFHOGG SRQPSDI-ELSAFHOGG SRQPSDI-ELSAFHOGG SRQPSDI-ELSAFHOGG SRQPSDI-ELSAFHOGG SRQPSDI-ELSAFHOGG SRQPSDI-ELSAFHOGG SRQPSDI-ELSAFHOGG SRQPSDI-ELSAFHOGG SRQPSDI-ELSAFHOGG SRQPSDI-ELSAFHOGG SRQPSDAFHOGG SRQPSDI-ELSAFHOGG SRQPSDI-SAFHOGG SRQPSDI-SAFHOGG SRQPSDI-SAFHOGG SRQPSDI-SAFHOGG SRQPSDI-SAFHOGG SRQPSDI-SAFHOGG SRQPSDI-SAFHOGG SRQPSDI-SAFHOGG SRQPSDI-SAFHOGG SRQPSDI-SAFHOGG SRQPSDI-SAFHOGG SRQPSDI-SAFHOGG SRQPSDI-SAFHOGG SRQPSDI-SAFHOGG SRQPSDI-SAFHOGG SRQPSDI-SAFHOGG SRQPSDI-SAFHOGG SRQPSDI-SAFHOGG SRQPSDI-SAFHOGG SRQPSDI SRDSDI SAFHOGG SRQPSDI SRDSDI SAFHOGG SRQPSDI SRDSDI S	RVAEVACKFQR RVAEVACKFQR RVAEATARWVAGRG RVAETVRFQPV RIAEATKRWNK RVAELALQLRRGAAS- RVAEVALQLRRGAAS- RVAEVALQLRRGAAS- RLATTASLAQANWSR RLATTASLAQANWSR RLATTAKLYN RLAETAKLYN RVAEVAKKLKC RVAEVAKKLKC RIEVAKIAKCC RIETAKLKG HVTQIAKKIAGK HVTQIAKKIAGK HVTQIAKKIAGK FYFTVSKVKF SFYEYVARVKW FFFNTFKK EFYNTLSKLTASQPKP(35) VFTEVLIKAEGAAGA(147) YIASITKKIKGSTA RVVDIASRIKG RVDIASRIKG RVDIASRIKG	31/4 28/4 28/4 30/4 43/6 40/5 50/6 50/6 50/6 50/6 50/6 43/6 48/6 48/6 48/6 28/6 28/6 28/6 28/6 28/6 28/6 28/6 2
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PJS666WrbA EcaWrbA BcWrbA XfWrbA NpWrbA CaWrbA AfWrbA ParWrbA ParWrbA StWrbA StWrbA StWrbA ScWrbA CcWrbA CcWrbA CcWrbA CCWrbA MBNC1WrbA McWrbA McWrbA MbWrbA GtQR1 PcQR GtQR2 SpObr1 NcHyp Y1Hyp AtFQR1 TvQR2 E255-15WrbA MavHyp	WKDKIAGFTNSAALDGDKMSTINYLFTLAMQH WSNKVFGGFTNSATMNGDKFSTIQYFVTLSMQH WKDKIAAGFTNSAGNHOKDKSTIQYFVTLSMQH WKDKIAAGFTNSAGNHOKDKSIMSWVLFAAQH UKDKIAAGFTNSAGNHSGTFFTLSVLHWMLGS LSGKVGAAFTSSAGHSGTFFTLSVLHWMLGS LUGKPAAVFTSTASLHGQETTQISMLPLLHH LUGKPAAVFTSTASLHGQETTLISMLPLLHH LUGKPAAVFTSTASLHGQETTLISMLPLLHH LYGKPVGFTEASTWHGGHESTILMMVPLLHH LYGKPVGFTEASTWHGGHESTILMMVPLLHH LYGKVGFFTEASTWHGGHESTILMMVTLHH LYGKVGFFTEASTWHGGBESTLSMVVLLHH LYGKVAGFTSTATUHGGESTILTMNLPLLHH LYGKVAGFTSTATUHGGESTILTMNLPLHH LYGKVAGFTSTATUHGGASILASTQLALQHH FVGKVGSVFTSSGTUHGQESTILFNVTLLHL FVGKVGSVFTSSGTUHGQESTILSFHVTLLHL FVGKVGSVFTSSGTUHGQESTILSFHVTLLHL LAGKYAGLFVSTASPGGGSSTMIAMSTLAHH LAGKYAGLFVSTASPGGGSSTMIAMSTLAHH LGGKYAGLFVSTASPGGGSSTMIATSTVHH LAGKPAGIFTSTGTUGGGSSTMIATSTVHH	G IWVSCGVLPSTSKAAQR-DDAN G IWVSCGVLPSTSKAAQR-DDAN MIWVGTDLVGPNAKAAKR-DDLN MIWVGTDLWGNNSTGSSDDLN MIWVGTDLVSGL-SGL-DDGVN MIVGLPWSPLML MIVGJPPAKE	#           YLGSY-RGAIAQSPSDAGA           NILGGS-UCLLAQTPSDASA           NILGSTCLAQTPSDASA           YLGSTCLAQSPADATP           RLGSTCLAQSPADATP           RLGSTCLAQSPADATP           RLGSTCLAQSPADATP           QAGSYYG-ATAV-G           R-ACSYYG-ASHAGADG           GCPYG-ASHFAGADG           R-GSPYG-ASHLAGSDG           GCPYG-ASHLAGSDG           T-GGPYG-ASHLAGSDG           T-GGPYG-ATTIAGCDG           T-GGPYG-ATTIAGCDG           T-GGPYG-ATTIAGCDG           T-GGSPYG-ATTIAGCDG           T-GGSPYG-ATTIAGCDG           T-GSSPYG-ASTIAGCDG           T-GSSPYG-ATTIAGCDG           T-GSSPYG-ASTIAGCDG           T-GSSPYG-ASTIAGCDG           T-GSSPYG-ASTIAGCDG           R-GSSPWG-ACTFAGADG           R-GSSPWG-ACTFAGADG           R-GSSPWG-ACTFAGADG           K-GSSPYG-ACTFAGADG           K-GSSPYG-ACTFAGADG           K-GSSPYG-ACTFAGADG           SSSSSSSS                    SSSSSSSS	SE-MFPG-DLETARSLGE DE-VVAG-DLATGKLYGQ DEGPLPG-DLETGKAFGR STAPPAS-DLKTAQHLGL TITEA-DLIQARALGR VPKED-DLQVAKHLGK KKSLDEH-ELTICRALGK DQPVSAD-ERELGIAQGR TTQLSQE-EKALCVAFGK KKELDEN-EINIAKFLGK SRQPSQE-ELSIARYGGE SRQPSE-ELAIARFOGE SRQPSE-ELAIARFOGE SRQPSEN-ELMARYGGR SRQPSEN-ELMARYGGR SRQPSEN-ELMARYGGR SRQPSEN-ELMARYGGR SRQPSEN-ELEMARYGGR SRQPSEN-ELAMARYGGR SRQPSEN-ELAMARYGGR SRQPSEN-ELAMARYGGR SRQPSEN-ELEMARYGGR SRQPSEN-ELAMARYGGR SRQPSEN-ELAMARYGGR SRQPSEN-ELAMARYGGR SRQPSEN-ELAMARYGGR SRQPSEN-ELEMARYGGR SRQPSEN-ELAMARYGGR SRQPSEN-ELAMARYGGR SRQPSEN-ELEMARYGGR SR	RVAEVACKFQR RVAEVACKFQR RVAEATARWVAGRG RVAETVRFQPV RVAELALQLRRGAAS- RVAELALQLRGAAS- RVAEVAEKLC RLAITASALAQANWSR RLAITASALAQANWSR RLAITASKLGS RVAEVAKKLGC RVAEVAKKLRC RVAEVAKKLRC RVAEVAKKLRC RVAEVAKKLRG RVAEVAKKLGST HVTQIAKKIAGK HVTQIAKKIAGK FYFIVSKF SFYEVARVKW FFYITYSKKFS SFYEVARVKW FFYITYSKLGSTA RTVDIASRIKG RTVDIASRIKG RTVDIASRIKG RUVEITAKLLGGS RUVETACRLAS HHHHHHHH	31/4 227,4 28/4 30/4 43/6 40/5 36/5 50/6 50/6 50/6 50/6 50/6 50/6 50/6 48/6 48/6 48/6 48/6 48/6 48/6 48/6 28/6 35/5 41/5 ns/n
PJS666WrbA EcaWrbA BcWrbA XfWrbA CaWrbA AfWrbA ParWrbA ParWrbA ParWrbA StWrbA SsWrbA EcoWrbA YpWrbA CcWrbA MBNCLWrbA MBNCLWrbA MBNCLWrbA MBNCLWrbA MBNCLWrbA MBNCLWrbA MBNCLWrbA MBNCLWrbA MBNCLWrbA MbWrbA GtQR1 PcQR GtQR2 SpObr1 NcHyp Y1Hyp AtFQR1 TvQR2 E255-15WrbA DrWrbA MavHyp CbFldx DgFldx	WKDKLFAGFTNSAALDGDKMSTLNYLFTLAMQH WSNKVFGGFTNSASLNGDKQVTLTYLQTLASQH WKDKIAAGFTNSGAQHGDKLNSLMSMVLFAAQH WKDKIAAGFTNSGAQHGDKLNSLMSMVLFAAQH UKDKIAAGFTNSGAQHGDKLNSLMSMVLFAAQH LSGKVGAAFTSSAFAGGDETLIYLATNAQG LSGKVGAAFTSSAFAGGQETTLIXLHNWLGG LUGKPAAVFTSTSMHGGDETTLIMLPLLHH LUGKPAAVFTSTSMHGGDETTLIMLPLLHH LIGKPAGVFTSTSMHGGDETTLIMMLPLLHH LIGKPAGVFTSTSMHGGDETTLIMMLPLLHH LIGKPAGVFTSTSMHGGDETTLIMMTYAHF LYGKVGFTEASTMHGGHESTILMMNYAYHF LYGKVGFTTSSGHGGQESTLISMVTLLHH LYGKVGFTSSTD-GGQDETTFSTWTLAHH LYGKVGSFTSSCT-GGGDETTISTWTLAHH LYGKVGSFTSSCTHGGQESTIITTNVTLH LYGKVGSFTSSCTHGGQESTIISSNTTLH LAGKYASGFTSTATOHGGDESTIISSNTTLHL LAGKYAGFTSTATOHGGDESTLISSNTTLHL LGKYAGLFVSTSSCTHGGQESTLISSNTTLHL LGKYAGLFVSTSSCTHGGQESTLISSNTTLH LGKYAGLFVSTSCTGGGQESTLMANSTSLHH LAGKYAGLFYSTGSCGGGGESTMAANSTLHH LAGKYAGLFYSTGSCGGGDESTLMANSTLHH LAGKYAGLFYSTSGCGGGDESTLMANSTLHH LAGKYAGLFYSTSGCGGQESTLMAANSTLHH LAGKYAGLFYSTSGCGGCDESTLMANSTLHH LAGKYAGLFYSTSGCGGCDESTLMANSTLHH LAGKYAGLFYSTSGCGGDESTLMANSTLHH LAGKYAGLFYSTSGCGGDESTLMANSTLHH	GIWVSQGVLPSTSKAAQR-DDAN GIWVSINQLPSTSKAAQR-DDAN WWVGTSLNPANSKAATR-NDIN MIWVGDLMPGNNSSTGSSDDIN MIWVGDLSPSP	#           YILGSY-RGAIAQFSDAGA           NILGGS-VGLIAQTPSDASA           YILGSY-TGLIAQFSDADSTP           YILGSTCLIAQFSDADSTP           RRAGN-GUMGQSQLDMSGI           Q-AGSYYG-AATAV-G           ''''''''''''''''''''''''''''''''''''	SE-MFPG-DLETARSLGE DE-VVAG-DLATGKLYGQ DEGPLPG-DLETGKAFGR ZIAPPAS-DLKTAQHIGL KEPVLDSGDYLTSVRFGE VPKED-DLQVAKHIGK KRSLDEH-ELTLCRALGK OQPVSAD-ERELGIAQGR TTQLSQE-EKALCVAFGK KEELDEM-ETNIAKFLGK SRQPSD-ELSIARYGGE SRQPSD-ELSIARYGGE SRQPSD-ELAIARFGGE SRQPSD-ELAIARFGGE SRQPSD-ELAARFGGE SRQPSD-ELAARFGGE SRQPSD-ELAMARYGGR SRQPSD-ELAMARYGGR SRSPSAL-ELEVATIGK SRSPSL-ELEVATIGK SRQPSD-ELEVATIGGE SRQPSD-TANALDHLAR HHHHHHHHH	RVAEVACKFQR RIADIAAKIAN RVAEATARWVAGRG RVAEATARWVAGRG RVAEIALQIRRGAAS- RVAEVALQIRRGAAS- RVAEVALQIRRGAAS- RVAEVALQIRRGAAS- RIAFTASALAQANWSR RIAFTASALAQANWSR RIAFTASALAQANWSR RIAFTAKIKGS RITEVAKAIKCCNK RVAEVAKKIRC HVAKIAKKCCNK RVAEVAKKIRC HVAKIAKKG HVAKIAKKG HVTLIAKKIAGK HVTLIAKKIAGK HVTLIAKKIAGK FYETVSKVKF FFFTVFSKTASCAAG(147) YIASITKKIKGSTA RTVDIASRIKG RVVETAKIAGSA RVVETAKIAGSA RVVETAKIAGSA RVVETACRLAS RVVETACRLAS HHHHHHHH 	31/4 28/4 30/4 28/4 43/6 40/5 336/5 50/6 50/6 50/6 43/6 44/5 50/6 50/6 43/6 44/6 44/6 48/6 48/6 48/6 48/6 43/5 41/5 ns/n ns/n

FIG. 1. Alignment of WrbA, NAD(P)H:quinone oxidoreductase, and flavodoxin sequences. Numerical values at the C terminus indicate percent identity/percent similarity to WrbA<sub>E. coli</sub>: ns, not significant; #, completely conserved residue. Shaded residues indicate that a conservation of similar residues persists across at least 60% of the alignment. = = = = = =, region of the flavodoxin signature motif. JPred at ExPASy's Proteomic Tools was used to predict  $\alpha$ -helix (HHHH) and  $\beta$ -sheet (SSSS) sequences with the alignment (flavodoxin sequences were excluded). The additional  $\alpha\beta$  unit that is discussed is indicated in bold below the secondary-structure prediction. Organisms and ORF designations from the corresponding genomic sequence: *A. fulgidus* WrbA (gi: 11497955), *A. thaliana* FQR1 (gi: 21539481), *Burkholderia cepacia* WrbA (gi: 46310790), *Chloroflexus aurantiacus* WrbA (gi: 53798190), *Caulobacter crescentus* WrbA (gi: 13422034), *C. beijerinckii* Fldx (gi: 1941945), *Desulfovibrio gigas* Fldx (gi: 40801), *D. radiodurans* WrbA (gi: 58177611), *Exiguobacterium* sp. strain 255-15 WrbA (gi: 6845352), *Erwinia carotovora* WrbA (gi: 49613050), *E. coli* WrbA (gi: 41409133), *Methanosarcina barkeri* WrbA (gi: 31793946) and Fldx (gi: 72396729), *Mezorhizobium* sp. strain BNC1 WrbA (gi: 68191386), *Microbulbifer degredans* WrbA (gi: 48860599), *Methanosarcina mazei* WrbA (gi: 21228326), *Neurospora crassa* Hyp (gi: 38566940), *Nostoc punctiforme* WrbA (gi: 23129682), *Psychrobacter arcticum* WrbA (gi: 71038102), *P. chrysosporium* QR (gi: 15899861), *Sulfolobus todakii* WrbA (gi: 22126332). *Sylelabacter* (gi: 2462689), *Sulfolobus solfataricus* WrbA (gi: 15899861), *Sulfolobus todakii* WrbA (gi: 22126332). *Xylella fastidiosa* WrbA (gi: 22993897), *Yarrowia lipolytica* Hyp (gi: 49647887), and *Yersinia pestis* WrbA (gi: 22126332).



FIG. 2. Phylogenetic tree of selected WrbA, NAD(P)H:quinone oxidoreductase, and flavodoxin sequences. The full alignment of these sequences is shown in Fig. 1. The scale represents the average number of amino acid substitutions per site. WrbA<sub>E. coli</sub> and WrbA<sub>A. fulgidus</sub> are in bold type. Organisms and ORF designations from the corresponding genomic sequence: A. fulgidus WrbA (gi: 11497955), A. thaliana FQR1 (gi: 21539481), B. cepacia WrbA (gi: 46310790), C. aurantiacus WrbA (gi: 53798190), C. crescentus WrbA (gi: 13422034), C. beijerinckii Fldx (gi: 1941945), D. gigas Fldx (gi: 40801), D. radiodurans WrbA (gi: 58177611), Exiguobacterium sp. strain 255-15 WrbA (gi: 68054352), E. carotovora WrbA (gi: 49613050), E. coli WrbA (gi: 148264) and Fldx (gi: 145986), G. trabeum QR1 (gi: 30027749) and QR2 (gi: 33668045), M. acetivorans WrbA (gi: 19915027), M. avium WrbA (gi: 41409133), M. barkeri WrbA (gi: 31793946), Mesorhizobium sp. strain BNC1 WrbA (gi: 68191386), M. degradans WrbA (gi: 48860599), M. mazei WrbA (gi: 21228326), N. crassa WrbA (gi: 38566940), N. punctiforme WrbA (gi: 23129682), P. arcticum WrbA (gi: 71038102), P. chrysosporium QR (gi: 4454993), Polaromonas sp. strain JS666 WrbA (gi: 67847813), P. aeruginosa WrbA (gi: 9946855), S. pombe Obr1 (gi: 2462689), S. solfataricus WrbA (gi: 15899861), S. todakii WrbA (gi: 15621890), T. versicolor QR2 (gi: 12484052), X. fastidiosa WrbA (gi: 22993897), Y. lipolytica WrbA (gi: 49647887), and Y. pestis WrbA (gi: 22126332).

developed at pH 6.6, as indicated by the yellow color of the fractions containing WrbA<sub>E. coli</sub>. However, the WrbA<sub>E. coli</sub> protein that eluted from the second Q-Sepharose column developed at pH 7.8 did not contain FMN, indicating that binding of FMN in WrbA<sub>E coli</sub> is pH dependent. After reconstitution with FMN, a ratio of  $1.04 \pm 0.03$  FMN molecules per monomer was obtained, suggesting 1 FMN molecule per monomer, consistent with a previous report (29). The reconstituted protein exhibited a spectrum characteristic of oxidized flavoproteins (Fig. 4). Other than an initial heat denaturation step, WrbAA. fulgidus was purified in the same way as WrbA<sub>E. coli</sub>, although WrbA<sub>A. fulgidus</sub> retained FMN through all steps of the purification, with a ratio of 0.87  $\pm$ 0.05 FMN molecule per monomer upon elution from the second Q-Sepharose column developed at pH 7.8. After reconstitution, a ratio of  $1.10 \pm 0.04$  FMN molecules per monomer was obtained, suggesting 1 FMN molecule per monomer, and the reconstituted protein exhibited a spectrum characteristic of oxidized flavoproteins. Differences in the UV-visible spectra at the peak centered on 450 nm suggest that the FMN environment is somewhat different in WrbA<sub>E. coli</sub> than in WrbA<sub>A. fulgidus</sub> (Fig. 4). The ratio of absorbance of  $WrbA_{E.\ coli}$  at 274 nm/450 nm was 4.7, with an extinction coefficient of  $\epsilon_{450} = 11.6 \text{ mM}^{-1} \text{ cm}^{-1}$ . The ratio of absorbance of WrbAA. fulgidus at 274 nm/457 nm was 3.7, with an extinction coefficient of  $\tilde{\epsilon}_{457} = 14.0 \text{ mM}^{-1} \text{ cm}^{-1}$ .

Hydrophobicity plots were produced with TMpred (available at ExPASy's Proteomic Tools) to clarify whether WrbA is localized at the membrane. The plots indicated two hydrophobic regions. The first of these overlaps with the flavodoxin signature motif, suggesting that this region binds the flavin and contributes to stabilization of the  $\alpha\beta$  twisted open-sheet fold typical of flavodoxin-like proteins. The second hydrophobic span, predicted to be a transmembrane region, overlaps the unique additional  $\alpha\beta$  unit (Fig. 1). Gorman and Shapiro found that this unique hydrophobic region significantly contributes to tetramerization and is located at the core of the tetramer (26). Thus, WrbA proteins do not appear to be integral membrane proteins, although it is unclear whether WrbA proteins are membrane associated.

Since sequence comparisons indicated that WrbA<sub>E. coli</sub> and WrbAA. fulgidus are related to fungal and plant NQOs, this activity was determined for both WrbA<sub>E. coli</sub> and WrbA<sub>A. fulgidus</sub>. As shown in Table 1, both  $WrbA_{E. \ coli}$  and  $WrbA_{A. \ fulgidus}$  were able to couple electron transfer from NADH to several quinones. There was significantly less activity with cytochrome c(<1%) and no activity with benzyl viologen, methyl viologen (paraquat), FMN, flavin adenine dinucleotide (FAD), F<sub>420</sub>, 2-hydroxyphenazine, 2-hydroxynaphthoquinone, or 9,10-anthroquinone-2,6-disulfonate (data not shown). The apparent kinetic parameters determined for WrbA<sub>E. coli</sub> or WrbA<sub>A. fulgidus</sub> catalyzing electron transfer from NAD(P)H to 1,4-benzoquinone or to  $K_3$ FeCN<sub>6</sub> (Table 2) support the idea that the activities are physiological. Both WrbA<sub>E. coli</sub> and WrbA<sub>A. fulgidus</sub> preferred NADH over NADPH, which suggests that the enzyme does not play a role in biosynthesis since NADPH is the preferred electron donor in biosynthetic pathways of prokaryotes.

The pH dependence of electron transfer from NADH to menadione was measured for both  $WrbA_{E. \ coli}$  and  $WrbA_{A. \ fulgidus}$ (Fig. 5). Apparent initial velocities showed that  $WrbA_{E. \ coli}$  retained nearly 95% activity over a pH range of 6.0 to 8.0 and

	# ## • • #
AfWrbA	MARILVIFHSITGNTMKLAKAVADGA-REGGAEVAVKRVPETIPAEILEKNPGYVKVREELESFEVARPEELQDYDAI
EcWrbA	MAKVLVLYYSMYGHIETMARAVAEGASKVDGAEVVVKRVPETMPPQLFEKAGGKTQTAPVATPQELADYDAI
MtIsf	$-MKITGISGSPRKGQNCEKIIGAALEVAKER-GFETDTVFISNEEVAP\mathbf{C}KA\mathbf{C}GA\mathbf{C}RDQDF\mathbf{C}VIDDDMDEIYEKMRAADGI$
AfIsf	-MKLLAINGSPN-KRNTLFLLEVIAEEVKKL-GHEAEIIHLKDYEIKECKGCDACLK-GDCSQKDDIYKVLEKMQEADAI
MjIsf	-MKVIGISGSPRPEGNTTLLVREALNAIAEE-GIETEFISLADKELNPCIGCNMCKEEGKCPIIDDVDEILKKMKEADGI
MkWrbA	MILGISGSPR-EGNTEYLVRIALEAAEEVSGEETEFITVRDLDISP <b>C</b> EACGECLETGECAIDDDMQDVYELMRECDGM
CaWrbA	MSKIVIFKGSPRKNGYTAKLLEQVAKGAKSK-GAEVIEFDLNNPGIRGCQGCFYCRTHDGCAVNDYLQPMYEDIKEADAI
	· · · · ·   · · · ·   · · · ·   · · · ·
CbFlax	-MKIVYWSGTGNTEKMAELIAKGIIES-GKDVNTINVSDVNIDELLNE-DIL
	# #
AfWrbA	
EcWrbA	IFGTPTRFGNMSGQMRTFLDQTGGLW-ASGALYGKLASVFSSTGTG-GGQEQTITSTWTTLAHHGMVIVPIAYAAQELFD
MtIsf	IVAAPVYMGNYPAQLKALFDRSVLLRRKNFALKNKVGAALSVGGSRNGGQEKTIQSIHDWMHIHGMIVVGDNSHFG-
AfIsf	VIGTPTYFGNVTGIVKNLIDRSRMARMGNYRLRNRVFAPVVTSGLRNGGAEYAAMSLIVYALGQAMLPVSIVENPITTGT
MjIsf	ILGSPVYFGGVSAQLKMLMDRSRPLR-IGFQLRNKVGGAVAVGASRNGGQETTIQQIHNFFLIHSMIVVGDNDPTAHYGG
MkWrbA	IVGSPVYYGGVSAQLKALIDRTRPLR-INWELKDKVGGAIAIGGARNGGQEHTLRDIQNFFMIHAMIVVGDSDPTAHFGG
CaWrbA	$\tt VFGSPIYYYKITGQSKIWFDRTFPMTGNDYKPKYPGKKLITVFAQGNPDPKIGAEGVKFANDMLEELGWKLEDSINYCG-$
	·····
	90 100 110 120 130 140 150 160
CbFldx	ILGCSAMGDEVLEESEFEPFIEEISTKISGKKVALFGSYGWGDGKWMRDFEERMNGYGCVVVETPLIVQNEP-
AfWrbA	RAGSYYGAASTGVPKEDDLQVAKMLGKRVAEVAEKLC
EcWrbA	VSQVRGGTPYGATTIAGGDGSRQPSQEELSIARYQGEYVAGLAVKLNG 43/63
MtIsf	GITWNPAEEDTVGMQTVSETAKKLCDVLELIQKNRDK 29/49
AfIsf	FPVGVIQGDAGWRSVKKDEIAINSAKALAKRIVEVAEATKNLRES 31/50
MjIsf	TGVGKAPGDCKNDDIGLETARNLGKKVAEVVKLIKK 30/47
MkWrbA	AGVGLEPGDVEEDETGIETARNTGRRVGEVVKLIKG 28/45
CaWrbA	30/45
Chrldy	1/0 $180$ $190$ $200$ $210$
ODLTAV	

FIG. 3. Sequence alignment with WrbA sequences, Isf sequences, and misannotated WrbA sequences that have a compact cysteine motif. Numerical values at the C terminus indicate percent identity/percent similarity to *E. coli* WrbA. ns, not significant; #, completely conserved residues; = = = = =, region of the flavodoxin signature motif;  $\blacktriangle$ , compact cysteine motif. Organisms and ORF designations from the corresponding genomic sequence: *A. fulgidus* Isf (gi: 11499480), *A. fulgidus* WrbA (gi: 11497955), *Clostridium acetotrophicum* WrbA (gi: 15896732), *E. coli* WrbA (gi: 148264), *C. beijerinckii* Fldx (gi: 1941945), *Methanosarcina jannaschii* Isf (gi: 15669271), *Methanopyrus kandleri* WrbA (gi: 20094374), and *M. thermophila* Isf (gi: 2246438).



FIG. 4. UV-visible light spectra of reconstituted, oxidized WrbA<sub>*E. coli*</sub> and WrbA<sub>*A. fulgidus*</sub>. Comparison of WrbA-bound FMN versus free FMN. WrbA<sub>*A. fulgidus*</sub>, —; WrbA<sub>*E. coli*</sub>, —; free FMN, - - -.

WrbA<sub>A. fulgidus</sub> retained at least 95% activity from pH 5.0 to 8.5. The temperature dependence of electron transfer from NADH to menadione was measured for both WrbA<sub>E. coli</sub> and WrbA<sub>A. fulgidus</sub>. The apparent initial velocities reflect the optimal growth temperatures of the respective species. In the linear range of highest activity, Arrhenius plots of the apparent initial velocities show that the  $E_a$  for WrbA<sub>A. fulgidus</sub> is 3.63

TABLE 1. Specific activities of WrbA<sub>E. coli</sub> and WrbA<sub>A. fulgidus</sub>

Electron accenter	Avg sp act ( $U^a mg^{-1}$ ) ± SD			
	WrbA <sub>E. coli</sub>	WrbA <sub>A. fulgidus</sub>		
1,4-Benzoquinone	$990 \pm 30$	$25,000 \pm 850$		
1,4-Naphthoquinone	$560 \pm 30$	$8,900 \pm 260$		
Menadione	$430 \pm 10$	$1,300 \pm 10$		
2,3-Dihydroxy-5-methyl-1,4-benzoquinone	$930 \pm 60$	$6,700 \pm 140$		
Potassium ferricyanide	$50 \pm 1.6$	$1,400 \pm 80$		
Dichloroindolphenol	$160\pm3.0$	$1,400 \pm 70$		

<sup>a</sup> Micromoles of NADH oxidized per minute.

Substrate	WrbA <sub>E. coli</sub>			WrbA <sub>A. fulgidus</sub>			
	$k_{\rm cat}^{\rm app}/K_m^{\rm app} ({\rm M}^{-1} {\rm s}^{-1})$	$k_{\rm cat}^{\rm app}$ (s <sup>-1</sup> )	$K_m^{\mathrm{app}}(\mu\mathrm{M})$	$k_{\rm cat}^{\rm app}/K_m^{\rm app} ({\rm M}^{-1} {\rm s}^{-1})$	$k_{\rm cat}^{\rm app}$ (s <sup>-1</sup> )	$K_m^{\rm app}$ (µM)	
NADH <sup>a</sup> NADPH <sup>a</sup> 1,4-Benzoquinone <sup>b</sup>	$\begin{array}{c} 6.4\times10^5\pm0.20\times10^{5c}\\ 3.5\times10^4\pm0.26\times10^4\\ 6.4\times10^7\pm0.14\times10^7\end{array}$	$\begin{array}{c} 8.9 \pm 0.064 \\ 6.0 \pm 0.15 \\ 370 \pm 1.7 \end{array}$	$14 \pm 0.43$ $170 \pm 12$ $5.8 \pm 0.12$	$\begin{array}{c} 6.3\times 10^6 \pm 0.59\times 10^6 \\ 5.5\times 10^6 \pm 0.33\times 10^6 \\ 8.6\times 10^7 \pm 0.090\times 10^7 \end{array}$	$120 \pm 2.9$ $170 \pm 2.4$ $3,200 \pm 130$	$19 \pm 1.7$ $31 \pm 1.8$ $37 \pm 3.6$	

TABLE 2. Apparent kinetic parameters of WrbA<sub>E. coli</sub> and WrbA<sub>A. fulgidus</sub>

<sup>a</sup> K<sub>3</sub>FeCN<sub>6</sub> was the electron acceptor.

<sup>b</sup> NADH was the electron donor.

<sup>c</sup> Values are averages and standard deviations.

kcal/mol and that for WrbA<sub>*E. coli*</sub> is 1.88 kcal/mol (Fig. 6). The Arrhenius plots also suggest that the kinetic system undergoes a temperature-dependent shift that increases the activation energy of the rate-limiting steps when the temperature dips below 30°C.

Under aerobic conditions, auto-oxidation took about 20 min for 10  $\mu$ M reduced WrbA<sub>*E*, coli</sub> or WrbA<sub>*A*, fulgidus</sub> (not shown). Despite this low activity with O<sub>2</sub>, all activity assays were conducted anaerobically to prohibit electron acceptors from interacting with O<sub>2</sub> to produce ROS, which might affect the rates.

**Phenotypic screening at Biolog, Inc.** A *wrbA* knockout was constructed from *E. coli* K-12 MG1655, and the knockout and WT strains were submitted to Biolog, Inc., for phenotypic analyses. The growth of the *wrbA* mutant strain was compared to the growth of the WT strain at  $37^{\circ}$ C in Luria broth with nearly 2,000 phenotypes tested. (Phenotypes tested are available from Biolog, Inc., at http://www.biolog.com/phenoMicro.html.) No phenotypes were gained; however, *N*-trichloromethyl-mercapto-4-cyclohex-ene-1,2-dicarboximide and 8-hydroxyquinoline significantly inhibited the growth of the *wrbA* knockout relative to the WT, which is consistent with a role for WrbA in protecting against environmental stressors through its quinone reductase activity.

## DISCUSSION

 $WrbA_{E.\ coli}$  was previously proposed to play a role as an accessory element in blocking TrpR-specific transcriptional processes (66); however, this role has been questioned (29) and the function is unknown. Further,  $WrbA_{E.\ coli}$  was the only biochemically characterized member of the WrbA family and

no enzyme activity has been reported. Here, we demonstrate that WrbA<sub>*E. coli*</sub> has NAD(P)H-dependent redox activity and reduces quinones. We also report the characterization of WrbA<sub>*A. fulgidus*</sub>, a homologue from a hyperthermophilic archaeon, and show that it has the same redox activity. Phylogenetic analyses indicate that several characterized fungal and plant NQOs belong to the WrbA family, which suggests that this enzyme activity is a defining characteristic common to the WrbA family. Further, the activities and kinetic constants of WrbA<sub>*E. coli*</sub> and WrbA<sub>*A. fulgidus*</sub> reported here correlate well with those reported for NQO homologues in *G. trabeum* (33) and *P. chrysosporium* (11).

At least six other protein families with NQO activity are known, three of which have been designated type I through type III. Other than activity, the WrbA family bears no sequence similarity to and has unique structural characteristics not present in any of the six other protein families; in addition to the unique  $\alpha\beta$  unit, WrbA has one FMN molecule per monomer and participates in a dimer-tetramer equilibrium. Thus, we adopt the nomenclature initiated by type I through type III and designate the WrbA family type IV. Types I to III are more commonly referred to as NADH dehydrogenases. Perhaps the best-characterized type I protein is NADH-dependent complex I, the H<sup>+</sup>/Na<sup>+</sup>-transporting integral membrane complex composed of up to 46 subunits that participates in electron transfer in prokaryotes from the *Bacteria* domain during respiration (46, 65). Type II NADH dehydrogenase is usu-



FIG. 5. pH dependence of apparent initial velocities. Activities were obtained at  $37^{\circ}$ C with WrbA<sub>*E*</sub> *coli* ( $\bigcirc$ ) and at  $65^{\circ}$ C with WrbA<sub>*A*</sub> *fulgidus* ( $\blacktriangle$ ).



FIG. 6. Arrhenius plot of apparent initial velocities. Activities were obtained at pH 7.2. WrbA<sub>A. fulgidus</sub>,  $\bigstar$ ; WrbA<sub>E. coli</sub>,  $\bigcirc$ .

ally a single polypeptide and does not generate a chemical gradient (46). The Na<sup>+</sup>-transporting (type III) NAD(P)H dehydrogenase is composed of six or seven subunits and is responsible for generating an Na<sup>+</sup> potential that can be used for flagellar movement or for substrate transfer (8, 46). There is no standard nomenclature for the remaining three protein families with NQO activity. The first of these three families is eukaryotic DT-diaphorase-NQO1, a dimeric FAD-containing protein that reduces antitumor quinones with NAD(P)H (15, 57). The second family is FAD-containing NQO2, which has sequence similarity to NOO1, uses dihydronicotinamide riboside as the electron donor, and is resistant to typical inhibitors of DT-diaphorases (15). The third family is  $\zeta$ -crystalline and is a major protein present in some mammalian ocular lenses which participates in the one-electron reduction of quinones (52).

Possible physiological roles for type IV NQOs. Several NQOs from the Fungi and Viridiplantae kingdoms identified here as belonging to the WrbA family have been suggested to function in reducing quinones to the hydroquinone state to prevent interaction of the semiquinone with O<sub>2</sub> and production of superoxide. Quinoid compounds are essential to organisms from all domains of life. Quinones are generally tethered to the plasma membrane or freely traverse the lipid bilayer and function in electron transport chains, in cell signaling, and in protection from environmental oxidizers through direct reduction (6, 45). Although they usually serve as electron mediators by cycling between the oxidized (hydroquinone) state and the two-electron reduced (hydroquinol) state, quinones can also participate in deleterious redox cycling through direct interactions with single electron acceptors such as O2. This oneelectron redox cycling leads to the accumulation of reactive oxygen species (ROS) such as superoxide, hydrogen peroxide, and the hydroxyl radical (1, 3, 7, 9–13, 22, 24, 32, 33, 44, 53, 64). Intracellular production of ROS can result in the peroxidation of lipids, the destruction of cofactors, and the hydroxylation of proteins and nucleic acids (1, 16, 21, 23, 24, 40, 55, 63). Several reports suggest that in order to guard against the production of ROS from one-electron redox cycling, a wide diversity of cells have evolved NQOs to maintain quinones in the fully reduced state (1, 10, 11, 15, 30, 32, 33, 42, 47, 54, 58, 64).

A role for the type IV NQO family in alleviating and recovering from oxidative stress through quinone reduction fits the available data, and both WrbA<sub>E. coli</sub> and WrbA<sub>A. fulgidus</sub> derive from organisms that synthesize quinones; E. coli synthesizes ubiquinone-8 and menaquinone-8, while A. fulgidus produces a menaquinone with a fully saturated heptaprenyl side chain (60). However, NQO activity could also suggest a role in cell signaling, as has been proposed for a type IV NQO found in yeast (Schizosaccharomyces pombe Obr1 in Fig. 2) (19, 48, 56, 62). Numerous studies have shown that the redox status of the quinone pool is tightly coupled to cell signaling and cell growth of diverse cell types (4, 27, 36, 49). More specifically, the ArcA-ArcB two-component system of E. coli, which regulates cellular transcription in response to external electron acceptors, is one method by which E. coli controls expression in response to redox changes (25, 43). As previously reported, E. coli wrbA is repressed by phosphorylated ArcA, which is phosphorylated when the quinone pool is reduced (41). Further, WrbA is upregulated when E. coli enters the stationary phase

and in the presence of a variety of stressors, such as acids, salts,  $H_2O_2$ , and diauxie, under the control of RpoS (the stress response sigma factor,  $\sigma^{s}$  or  $\sigma^{38}$ ) (14, 17, 31, 35, 50, 51, 59, 61). Another study demonstrated that, under anaerobic conditions, E. coli wrbA is also repressed by fumarate and nitrate reductase regulatory protein, suggesting that WrbA<sub>E. coli</sub> does not function during anaerobiosis (34). Cumulatively, these expression studies suggest that WrbA<sub>E. coli</sub> functions in response to environmental stress when various electron transfer chains are affected or when the environment is highly oxidizing. Although the idea is speculative, WrbA<sub>E. coli</sub> could function in cell signaling by reducing the quinone pool, which would subsequently signal redox sensors such as the ArcA modulon. Chang and coworkers speculated about a similar mechanism for an  $\zeta$ -crystalline type of NQO that is expressed under stress and reduces the quinone pool, ultimately phosphorylating ArcA and inducing a shift from respiratory metabolism to fermentative metabolism (14).

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