# Substrate RNA positioning in the archaeal H/ACA ribonucleoprotein complex

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The most complex RNA pseudouridylases are H/ACA ribonucleoprotein particles, which use a guide RNA for substrate capture and four proteins (Cbf5, Nop10, Gar1 and L7Ae/NHP2) for substrate modification. Here we report the three-dimensional structure of a catalytically deficient archaeal enzyme complex (including the guide RNA and three of the four essential proteins) bound to a substrate RNA. Extensive interactions of Cbf5 with one guide-substrate helix and a guide RNA stem shape the forked guide-substrate RNA complex structure and position the substrate in proximity of the Cbf5 catalytic center. Our structural and complementary fluorescence analyses also indicate that precise placement of the target uridine at the active site requires a conformation of the guide-substrate RNA duplex that is brought about by the previously identified concurrent interaction of the guide RNA with L7Ae and a composite Cbf5-Nop10 surface, and further identify a residue that is critical in this process.

Numerous noncoding RNAs that participate in nearly all aspects of gene expression and regulation are being discovered at a rapid rate<sup>1,2</sup>. Owing to their base-pairing potential, many noncoding RNAs act as guides in biochemical processes catalyzed by their partner proteins<sup>3</sup>. Ribonucleoprotein complexes guided by noncoding RNAs constitute an unconventional but widespread class of enzymes. One important class of these RNA-guided enzymes is the H/ACA small nucleolar (sno) RNPs that function in ribosome biogenesis in the nucleolus, isomerizing nearly 100 selected uridines to pseudouridines in human ribosomal RNA (rRNA)<sup>4–6</sup>. Many of these modified sites are within functionally critical regions of the ribosome<sup>7</sup>, and site-specific disruption of modifications impairs ribosome biogenesis or function<sup>8</sup>.

Since the role of H/ACA RNAs in rRNA pseudouridylation was first identified<sup>9,10</sup>, their known functional repertoire has expanded to include modification of small nuclear RNAs<sup>11</sup> as well as rRNA processing<sup>12</sup> and telomerase maturation<sup>13</sup>. H/ACA snoRNAs that guide rRNA modification are also found in the archaeal kingdom<sup>14</sup>, revealing the ancient evolutionary origin of H/ACA RNAs. Pseudo-uridylation contributes to RNA stability<sup>15–18</sup>, to increases in the number of available RNA functional groups<sup>19</sup> and ultimately to the cellular function of the substrate RNA<sup>7,8,20–24</sup>.

The H/ACA RNAs responsible for isomerization of uridine function with partner proteins to form complex, multicomponent pseudouridylases (H/ACA RNPs)<sup>25,26</sup>. The H/ACA RNPs contain four core proteins that are known to participate directly in pseudouridylation<sup>27–29</sup>. These are Cbf5 (dyskerin in human, NAF57 in rodents), Gar1, Nop10 and L7Ae (NHP2 in eukaryotes). Cbf5 shares close sequence and structural homology with the bacterial pseudouridylase TruB and is the catalytic subunit for H/ACA RNP-mediated pseudouridylation<sup>30</sup>. Mutations in dyskerin cause the X-linked form of the rare genetic disease dyskeratosis congenita, which is characterized by abnormal skin pigmentation, bone marrow failure and an increased predisposition to cancer<sup>31,32</sup>. Archaeal H/ACA RNPs have been reconstituted from purified components and shown to possess pseudouridylation activity *in vitro*<sup>28,29</sup>. These studies showed that the ability of Cbf5 to catalyze efficient pseudouridylation is dependent upon each of the other three core H/ACA RNP components<sup>28,29</sup>. The specific roles of Gar1, Nop10 and L7Ae in pseudouridylation are not well understood.

In contrast to stand-alone pseudouridylases, which modify one or several specific uridine nucleotides<sup>33</sup>, H/ACA RNP pseudouridylases are capable of modifying as many different sites as are specified by the H/ACA guide RNAs expressed in the organism. The pseudouridylation guide H/ACA RNAs range in size from 70 to 250 nucleotides and are comprised of one to three helix-internal loop-helix-tail units<sup>2</sup>. Each unit is sufficient for binding all four protein factors and for guiding isomerization of a target uridine in vitro<sup>28,29,34</sup>. The strictly conserved 3' tail (containing the ACA trinucleotide) and the asymmetric internal loop (pseudouridine pocket) are required for efficient binding of Cbf5 (refs. 28,29,34,35). The mechanistic details of how the target uridine of the substrate RNA is faithfully presented to the active site of Cbf5 are largely unknown. It is clear that the extensive basepairing that occurs between the single-stranded substrate RNA and complementary nucleotides of the pseudouridine pocket of the H/ACA guide RNA determines the specificity for substrate RNAs<sup>9,10,35</sup>.

Recent structural studies of archaeal H/ACA RNPs have provided significant insight into the detailed architecture of the complex. Structures of isolated Cbf5–Nop10 and Cbf5–Nop10–Gar1 complexes have been determined<sup>36–38</sup>, and a structure of the complex containing

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b а Nop10 Apical loop CGG Cbf5 catalytic SH3 Cbf5 PUA P2 G A-U SF catalytic CACACUACU 3 Chf5 PUA domain

all four proteins and a guide RNA is also available<sup>39</sup>. In addition, two structures of guide and target RNA complexes in solution were recently obtained<sup>40,41</sup>. These structures have all provided glimpses of the RNP enzyme. However, the basis for the accurate placement of target uridines in the active site of the enzyme, and for the requirement of all accessory proteins for function, is still not understood.

Toward the ultimate goal of understanding the molecular mechanism of H/ACA RNP function and the roles of the guide RNA and each protein in this process, we have determined the crystal structure of the Pyrococcus furiosus (Pf) H/ACA RNP bound to a wild-type substrate RNA for the Pf9 H/ACA guide RNA<sup>28</sup> in the absence of L7Ae at 2.87 A. To inhibit any potential chemical reaction during crystallization, we used a form of the Cbf5 protein containing an active-site mutation (D85A). The RNP structure revealed interactions between the guidetarget RNA complex and conserved residues of the Cbf5 catalytic domain, and showed that guide-target RNA base-pairing in the context of Cbf5-Nop10-Gar1 complex places the target uridine in the vicinity of the active site of Cbf5. Structural comparison with the previously determined RNP structure in the absence of the substrate RNA but in the presence of L7Ae<sup>39</sup> suggests a functional role of L7Ae in remodeling the guide RNA to further deliver the target uridine into the active site of Cbf5.

## RESULTS

#### Overall structure of the RNP

The structure of the *P. furiosus* H/ACA RNP bound to a substrate RNA in the absence of L7Ae was determined by molecular replacement methods using the previously determined crystal structure of the *P. furiosus* Cbf5–Nop10–Gar1 complex (PDB accession code 2EY4) as the search model. Details of crystallization and the structural determination processes are described in Methods. The final structure was refined to an  $R_{\rm free}$  of 30.1%, including all reflections, and to a satisfactory stereochemical quality. The refined structural model contains residues 11–340 for Cbf5 (full-length 1–343), 3–55 for Nop10 (full-length 1–60), 1–73 for Gar1 (full-length 1–97), nucleotides 4–25 and 48–72 of the guide RNA (this represents all but the last three nucleotides of the bimolecular model guide RNA) and nucleotides 5–18 of the 21-mer unmodified target RNA (**Fig. 1a**). The



predicted catalytic residue Asp85 in Cbf5 was mutated to alanine to inhibit potential pseudouridylation reactions during crystallization. For clarity, in what follows all guide RNA nucleotides are prefixed with 'g' and all target nucleotides are prefixed with 't'.

In this structure, the guide RNA is stably bound with the target RNA in the absence of the apical loop and kink-turn (**Fig. 1a**). The extended guide–target RNA helical complex adheres to an inclined plane primarily formed by the Cbf5 protein (**Fig. 1b**), which positions the target uridine close to the active site of Cbf5. The Cbf5-induced incline seems to be essential for positioning the substrate nucleotide, arguing for the importance of proteins in this process. Moreover, in this RNP structure, which lacks L7Ae, the target uridine is located  $\sim 11$  Å away from the active site of Cbf5 and is thus unavailable for modification. Previous *in vitro* reconstitution experiments had demonstrated a critical but unidentified role for L7Ae in pseudo-uridylation by the H/ACA RNP<sup>28,29</sup>. This RNP structure corroborates the biochemical data and furthermore indicates that L7Ae is also essential for target uridine placement within the active site of Cbf5.

### Structural features of the guide-target RNA complex

As is also observed in the solution structures of the RNA–RNA complexes<sup>40,41</sup>, the target RNA is bound to the guide RNA through a constrained three-way junction (**Fig. 1a,b**). The upper stem of the guide RNA (P2) and the two helices formed between the 5' and 3' halves of the pseudouridine pocket and the substrate RNA (SH1 and SH2 for substrate helices 1 and 2) constitute the three branches of the junction, whereas the lower stem of the guide RNA (P1) restricts the direction of the branches (**Fig. 1a,b**). The pseudouridine pocket of the guide RNA is an elongated opening with a distance from the apex to the base of ~40 Å (**Fig. 2**). The target RNA is bent into a V-shaped loop that fits snugly into the opening by base pairing to both sides of the pseudouridine pocket. The distance between the phosphate



**Figure 2** Structural features of the guide and target RNAs in the complex. Left, final electron density map computed as a composite omit (omitting 5% of the model each time), cross-validated and SigmaA-weighted  $3F_o - 2F_c$ . Right, guide (yellow) and target (red) RNA, respectively. The locations of the three phosphate backbone kinks are indicated with black angle brackets.



backbones of the two sides of the V-loop ranges from ~6 Å to ~14 Å (**Fig. 2**). SH1 and SH2 are each coaxial with the upper and lower stem of the guide RNA, P2 and P1, respectively (**Fig. 1a,b**), similar to what is seen in the guide–target RNA complexes formed in the absence of proteins and determined by NMR<sup>40,41</sup>. However, the two pseudo-continuous helices (P1-SH2 and P2-SH1) are inclined at a ~120° angle at junction J2, in contrast to the nearly parallel helices in the guide–target RNA-only complexes<sup>40,41</sup>. This inclination, which appears to be a consequence of interaction with Cbf5, is necessary for the substrate RNA to enter the catalytic pocket, suggesting that Cbf5 has a functional role in the placement of the substrate RNA.

The guide-target RNA complex has an unprecedented RNA architecture wherein a single RNA strand docks to an asymmetric internal loop from one side. Unique to this architecture are the structural features observed at the helical junctions between P1 and SH1 (J1) and between SH2 and P2 (J2). J2, which has more complex features than J1, includes the target uridine and makes extensive contacts with Cbf5 residues (Fig. 3a). Both junctions involve rotation of downstream nucleotides away from the upstream helical procession. In J1, gA12 rotates away from SH2 helical stack to form an AU base pair with tU17 in the substrate RNA. This creates a sharp bend at the phosphate backbone between gA12 and gG11 (Fig. 2). Nucleotide rotations in J2 occur over nucleotides 52-54 in the guide as well as nucleotides 9-10 in the target strand. As a result of its extensive interactions with Cbf5 residues, the nucleobase of gC54 rotates toward the protein and away from tG9 (Fig. 3b,c). This eases the constraint on the phosphate backbone of tG9, allowing reversal of the target chain direction at this nucleotide; the phosphate backbone flips more than  $90^{\circ}$  away from the A-form position (Fig. 3b,c). The rotation at tG9 further disrupts the Watson-Crick edge-to-edge interaction between tG9 and gC54, leaving only one potential hydrogen bond between O6 of tG9 and N4 of gC54 (Fig. 3b,c). gU53 at the center of the J2 junction, which does not pair with a nucleotide, stabilizes the unpaired tG9 by stacking on its nucleobase (Fig. 3c). The sugar-phosphate of the target uridine, tU10, further facilitates the chain reversal, but its nucleobase is disordered in our structure. Finally, gU52 rotates nearly 90° from

**Figure 3** RNA-RNA and RNA-protein interactions in the H/ACA RNP structure. (a) Detailed view of the J2 junction (see also the notations for c). (b) The RNA-protein interface involving the pseudouridine pocket. Cbf5 residues within 3.4 Å of any RNA atoms are shown in stick models and are labeled.(c) Detailed RNA-protein contacts involving the J2 junction nucleotides. In the schematic of the guide-target RNA complex, nucleotides covered by gray boxes are protected by proteins. Note that the primary protein contacts occur in the SH2 stem and that His63 forms two interactions, stacking with gU53 and hydrogen bonding with the 2'-hydroxyl group of gU52.

gU53 to pair with gG19 and initiate the P2 helix, completing the transition from SH2 to P2. The structure of J2 observed here is more open than that reported for the 3' guide-target structure of the human U65 RNA<sup>40</sup> in solution but appears to be less open than that of the 5' guide-target structure of the same RNA in solution<sup>41</sup>. Whether these differences are due to the different RNA secondary structures or to the roles of the proteins remains to be explored. However, given that each of these RNAs guides the modification of its respective substrate by the same enzyme, it is likely that a similar structure is formed in the active site of the enzyme. Therefore, H/ACA RNPs could assemble a diverse range of guide-target RNA complexes to that required for catalysis. As discussed in greater detail below, phosphate backbone bending at the two junctions may also allow parts of the phosphate backbone to act as hinges for a structural transition required to dock the target RNA into the active site of the enzyme.

### Interactions between the guide-target RNA complex and Cbf5

In the previously determined structure of the archaeal H/ACA RNP lacking target RNA, the pseudouridine pocket of the guide RNA is either disordered or stabilized by crystal packing interactions<sup>39</sup>. The primary contacts between the guide RNA and Cbf5 occur mostly in the lower stem of the RNA. Almost no interactions are observed between the pseudouridine pocket and the catalytic subunit of the pseudouridylase<sup>39</sup>. Our structure indicates that, upon association of the target RNA, the pseudouridine pocket of the guide RNA becomes ordered and forms specific contacts with conserved residues of Cbf5.

The most extensive contacts between the guide-target RNA complex and Cbf5 occur in the SH2 stem. As indicated by changes in the solvent-accessible surface areas attributable to the bound RNA, the Cbf5 residues that contact the SH2 stem are His63, Val66, Ala67, Ala68, Lys70, Gly79, His80, Thr100, Arg101, Val103, Gln104 and Lys325. Sequence alignments show that His63 and His80 are strictly conserved; homologous amino acids are found in the other positions in phylogenetically diverse organisms (Supplementary Fig. 1 online). Despite the extensive RNA-protein interface, few interactions involve nucleobases (Fig. 3a,b). This mode of interaction is consistent with the requirement that the pseudouridine pocket of the H/ACA RNA be available to interact specifically with the target RNA<sup>35,42,43</sup>. In contrast to the close interactions between SH2 and Cbf5, the SH1 stem formed between the 3' half of the target RNA and the 5' half of the pseudouridine pocket does not contact the proteins in our structure (Fig. 3b,c), which may contribute to the relatively high degree of disorder in this particular region of the RNA structure. In summary, the conservation of Cbf5 residues involved in stabilizing the pseudouridine pocket predicts the general importance of these residues in substrate binding and suggests that these interactions will be maintained in the fully assembled holoenzyme.

A mutation (S121G) in dyskerin (the human homolog of Cbf5) that affects an amino acid adjacent to the strictly conserved histidine that corresponds to Pf Cbf5 His80 (**Supplementary Fig. 1**) is associated with dyskeratosis congenita<sup>31</sup>. This is consistent with the previous



suggestion that many dyskeratosis congenita–associated mutations affect amino acids in regions important for RNA binding<sup>37,38</sup>. Protein sequence alignment shows that the mutations underlying dyskeratosis congenita do not generally affect dyskerin amino acids that are predicted to be directly involved in RNA binding<sup>39</sup> (which might cause a more severe phenotype), but rather neighboring amino acids (**Supplementary Fig. 1**). Notably, a mutation from an individual with dyskeratosis congenia was also recently mapped to human Nop10 (ref. 44) in a region expected to be involved in nonspecific binding the upper stem of the guide RNA in the holoenzyme<sup>39</sup>.

The conserved  $\beta$ 7– $\beta$ 10 loop of Cbf5, which is predicted to interact with the guide–target RNA complex<sup>37–39</sup>, is disordered and not engaged in RNA-protein interactions in our structure (**Fig. 4**, dashed line). This loop may close the active site upon correct placement of the target RNA and the triggering mechanism may rely upon residues within the active site of the enzyme. The disengagement of the analogous 'thumb loop' of TruB upon mutation of the catalytic aspartate to alanine<sup>45</sup> corroborates this possibility. Similarly, Gar1 may play a role in target RNA binding<sup>38,39</sup>, though it was not observed to interact with target RNA in our structure. Gar1 may also move closer to the target RNA when the target uridine is engaged in the active site.

#### Role of L7Ae in target RNA placement in the active site

Comparison of our *Pf* RNP structure with that of the *Pf* RNP containing L7Ae (and lacking target RNA) reveals substantial differences in the upper stem (P2) of the bound guide RNA. Structural and biochemical evidence described below suggests that these differences are attributable to L7Ae. We superimposed the Cbf5 molecules of both structures and examined the resulting positions of the other molecules. The overall structures of Cbf5, Gar1 and Nop10 are highly similar in both RNP structures (overall r.m.s. deviation 0.94 Å for 440 C $\alpha$  atoms). In addition, the structures of the P1 lower stem, including the 3' ACA trinucleotides of the guide RNAs, do not deviate substantially between the two (r.m.s. deviation 1.03 Å for 21 phosphate atoms). The largest differences between the two structures are in the pseudouridine pocket and the upper stem of the guide RNAs. Whereas the difference in the pseudouridine pockets is very likely the

**Figure 4** Guide RNA conformation and RNA-protein contacts in the presence and absence of L7Ae. (a) Comparison of the guide RNA structure in the presence of L7Ae and absence of target RNA (magenta, from ref. 39) and in the absence of L7Ae and presence of target RNA (yellow, from this study). Two orthogonal views are presented. (b) Guide RNA-protein contacts observed in the presence (magenta, from ref. 39) and absence (yellow, from this study) of L7Ae. (c) Modeled configurations of the guide and target RNAs in the presence of L7Ae. The upper stem of the guide RNA is shifted to the position observed in the presence of L7Ae. The upper stem of the guide RNA is shifted to the position observed in the presence of L7Ae, or RNA in the active site (Asp85, orange spheres). The target RNA position observed in our structure is shown in red.

result of target binding as described above, that observed between the upper stems is likely the result of L7Ae binding. In the absence of L7Ae, the upper stem is less inclined forward toward Nop10 and more bent sideways in the direction of Gar1 (Fig. 4a). As a result, the contacts established between the upper stem and the protein complex are different (Fig. 4b). For instance, the upper stem extensively contacts residues 34-38 of Nop10 in the presence but not the absence of L7Ae (Fig. 4b). Similarly, the close contact formed between the upper stem of the guide RNA and Lys87 of Cbf5 in the RNP lacking L7Ae is not found in the RNP containing L7Ae (Fig. 4b). Notably, the results of protein protection assays indicate that full-length Pf9 also contacts Cbf5 Lys87 in the absence of both L7Ae and target RNA in solution<sup>46</sup>. These findings indicate that the difference in the position of the upper stem of the guide RNA in our structure does not reflect any alteration in the model guide RNA sequence or the presence of target RNA, but rather results from the lack of L7Ae.

L7Ae seems to bend the upper stem of the guide RNA away from the active site of Cbf5 and toward Nop10 (Fig. 4a). To specifically address what effect the L7Ae-induced movement of the upper stem might have on the proximity of the target uridine to the active site of Cbf5, we superimposed the upper stems (P2) of the guide RNAs from the two structures<sup>39</sup> and allowed SH1 (which is not subject to extensive RNA-protein interaction in our structure) to follow while fixing the positions of P1 and SH2 (which are engaged in interaction with protein). Adjustments were restricted to the nucleotides in the two junction regions, J1 and J2, and were limited by steric constraints. The modeling produces an RNA configuration in which the target uridine is redirected toward the active site of Cbf5, to the position equivalent to that occupied by the target uridine in TruB-substrate RNA structures<sup>47,48</sup> (Fig. 4c). The model requires unpairing of tG11 from gC18, and possibly pairing of gC18 with gU53 to 'close' the more open pocket observed in our structure and to more closely resemble the predicted consensus guide-target RNA structure<sup>35,42,43</sup>.

To investigate the proposed role of L7Ae in the target RNA placement, we devised a fluorescence assay that monitors the conformation of the nucleotide immediately 3' of the target uridine (tG11). We replaced tG11 with the fluorescent analog of guanosine and adenosine, 2-aminopurine (2-AP), and the target uridine with 5-fluorouridine (5-FU). We believe that this target RNA mimics the rRNA substrate targeted by Pf9 RNA and that the 5-FU is converted by the enzyme to (5S,6R)-5-fluoro-6-hydroxypseudouridine (5-Fh $\Psi$ ), as has been observed in the case of the related TruB enzyme<sup>46</sup>. The fluorescence intensity of 2-AP directly reflects its stacking state and can, therefore, reveal changes in the conformational state of the RNA near the target uridine during the processes of substrate docking and the chemical reaction. The 2-AP-labeled target RNA was annealed with the guide RNA at a 1:1 molar ratio and then incubated with a ten-fold molar excess of Cbf5-Nop10-Gar1 trimeric protein complex to allow formation of an RNP similar to that observed in our crystal



**Figure 5** Effect of L7Ae on target RNA conformation. Fluorescence intensity traces of target RNA labeled with 2-AP and 2-FU and of unlabeled guide RNA assembled with a ten-fold molar excess of Cbf5–Nop10–Gar1 (+CGN), Cbf5(D85A)–Nop10–Gar1 mutant (+CmGN), L7Ae (+L7Ae), Cbf5–Nop10–Gar1 plus L7Ae (+CGN +L7Ae) or Cbf5(D85A)–Nop10–Gar1 plus L7Ae (+CmGN +L7Ae). The maximum fluorescence intensity reached as a result of L7Ae titration in the presence of Cbf5–Nop10–Gar1 trimer is designated as the 'high- fluorescence state', that reached as a result of L7Ae titration in the presence of the D85A mutant complex as the 'intermediate-fluorescence state' and that reached without L7Ae as the 'low-fluorescence state'.

structure. In the absence of the L7Ae protein, the assembled H/ACA

RNPs (either wild-type Cbf5 or the D85A mutant) showed a comparably low 2-AP fluorescence intensity, which we refer to as the 'lowfluorescence state' (Fig. 5). L7Ae was subsequently titrated into the RNP solution, which resulted in substantial increases in the 2-AP fluorescence intensity (Fig. 5), indicative of remodeling of the target RNA in the region of the target uridine. A maximum fluorescence intensity change was observed with a ten-fold molar excess of L7Ae. The change in 2-AP fluorescence required the presence of the Cbf5-Nop10-Gar1 trimeric protein complex because L7Ae titration of the guide RNA and target RNA in the absence of other proteins resulted in no change in fluorescence intensities (Fig. 5). We interpreted the L7Ae-induced change as a result of the bound 2-AP unstacking during the placement of the target RNA into the catalytic site of Cbf5 followed by conversion of 5-FU to 5-FhY. Consistent with this interpretation, when L7Ae was titrated into a solution of the 2-AP RNA bound with the trimeric protein bearing the D85A mutation in Cbf5 (the complex used for crystallization), the maximum fluorescence intensity change was substantially less than that produced by the wild-type RNP (Fig. 5), suggesting that this mutation prevents the target RNA from completing the L7Ae-induced transformation and/or the conversion of 5-FU to 5-Fh $\Psi$ . We designate the final state reached by the wild-type RNP as the 'high-fluorescence state' and that reached by the mutant RNP as the 'intermediate-fluorescence state'. Thus, both the wild-type H/ACA RNP and the mutant H/ACA RNP lacking L7Ae were effectively shifted from the low-fluorescence state to another conformational state in an active site-dependent manner by L7Ae (Fig. 5).

#### DISCUSSION

The complexity of H/ACA RNP pseudouridylase assembly has been well documented<sup>27–29</sup>. Despite the close structural homology between Cbf5 and the stand-alone pseudouridylase TruB, *in vitro* activity assays using purified archaeal components have shown that three additional proteins are required for efficient modification by Cbf5<sup>27,29</sup>. This knowledge has led to an intense and ongoing search for the molecular basis of the requirement for the accessory factors. As part of this effort, we report a crystal structure of the H/ACA RNP subcomplex containing Cbf5, Nop10, Gar1, an H/ACA RNA and a bound target RNA. Notably, we found that the guide RNA occupies a substantially different position in the absence of L7Ae than in an assembled apo H/ACA RNP structure<sup>39</sup>. The lack of L7Ae affects the locations of the upper stem and the pseudouridine pocket and thereby of the bound

target RNA. Indeed, in this subcomplex the target uridine is found about 11 Å from the catalytic aspartate residue. On the basis of the assumption that the target RNA should be fully engaged in the active site in the holoenzyme, we propose that L7Ae has an important role in the placement of the target RNA. The concurrent interaction of L7Ae with the kink-turn motif of the guide RNA and with the composite surface formed by Nop10 and Cbf5 leads to anchoring of the upper stem of the guide RNA and consequently to functional docking of the target RNA (via the complementarity to the 5' half of the pseudouridine pocket).

This proposal is supported by the results of our 2-AP fluorescence assay, which indicate that an L7Ae-induced conformational change occurs near the target uridine. In the absence of L7Ae, both the wildtype H/ACA RNP and that containing Cbf5 with an active-site mutation (D85A) stay in a low-fluorescence state that is likely to correspond to the crystal structure that we solved. L7Ae titration of both H/ACA RNPs resulted in marked increases in the fluorescence intensity, which is interpreted as a L7Ae-induced conformational change near the target uridine. However, we found that a complete L7Ae-induced conformational change (to the high-fluorescence state) requires the presence of the catalytic aspartate residue. One potential explanation for the sensitivity of the target RNA conformation to the catalytic aspartate is that conversion of 5-FU to 5-Fh $\Psi$  causes an additional change in the conformation of the target uridine. Alternatively, a critical interaction established between the catalytic aspartate of the wild-type Cbf5 and the target uridine is required for the completion of the conformational change in the target RNA.

In this work, we have demonstrated that H/ACA RNP function requires remodeling of the guide RNA structure by L7Ae, assisted by Nop10, along with Cbf5 (and its catalytic residue), to place the target uridine at the active site for pseudouridylation.

## METHODS

**Design and purification of the components used in crystallization.** To ensure that the D85A mutant of Cbf5 could bind Pf9 RNA, electrophoretic mobility shift assays were carried out as described<sup>28</sup>. These data indicated that the D85A mutant bound guide RNA with similar affinity as the wild-type protein (D. Baker, R.M.T. and M.P.T., unpublished data). We also formed crystals with the wild-type Cbf5 and the target RNA containing 5-fluorouridine and found that they were isomorphous to those containing the D85A mutant (**Supplementary Table 1** online), suggesting that the mutant-containing complex has structural features grossly similar to those of the wild-type complex. Consistent with our observations, an aspartate-to-asparagine substitution in Cbf5's homolog, TruB, did not impair binding of its substrate RNA<sup>45</sup>. Proteins used in crystallization were purified according to published protocols<sup>38</sup>.

The model guide RNA used in crystallization contains a pseudouridine pocket identical to that of Pf9 but altered upper and lower stems, and it was assembled by hybridization of two RNA oligonucleotides. RNA oligos were purchased from Dharmacon and purified according to the manufacturer's recommended protocols.

**Crystallization.** The two guide strands and the target RNA, at a 1:1:1 molar ratio, were annealed by heating the solution for 1 min at 70 °C and then slowly cooling it. The RNA–protein complex was formed at a 1:1.2 molar ratio with a total concentration of 21.8 mg ml<sup>-1</sup>. The crystals were obtained by vapor diffusion methods in hanging drops at 30 °C. The RNA-protein mixture was mixed in an equal volume before being equilibrated with a reservoir solution containing 50 mM MES, pH 6.0, 100 mM NH<sub>4</sub>COOCH<sub>3</sub>, 5 mM MgSO<sub>4</sub> and 1.0 M NaCl. Diamond-shaped crystals were obtained in 3–5 d. Crystals were soaked stepwise in cryosolutions containing the mother liquor plus 10% (v/v) and 15% (v/v) glycerol, respectively, before being flash cooled in a liquid nitrogen stream for data collection. Data were collected at the South Eastern Consortium Access Team (SER-CAT) beamline 22ID and were processed using HKL2000 (ref. 49). The crystals are in a primitive tetragonal space group with

#### Table 1 Data collection and refinement statistics

	Cbf5(D85A)–Nop5–Gar1–RNA complex
Data collection	
Space group	P41212
Cell dimensions	
a, b, c (Å)	96.56, 96.56, 240.98
α, β, γ (°)	90.00, 90.00, 90.00
Resolution (Å)	42.5–2.8 (2.9–2.8)
R <sub>sym</sub>	11.0 (50.1)
Ι/σΙ	41.9 (2.7)
Completeness (%)	83.1 (33.2)
Redundancy	15.1 (8.1)
Refinement	
Resolution (Å)	42.5-2.87 (2.97-2.87)
Total number of reflections	29,512 (2873)
R <sub>work</sub> /R <sub>free</sub>	24.2 (35.8)/30.1 (44.3)
No. atoms	
Protein	3,711
RNA	1,293
Water/ion	1 Zn
B-factors	
Protein	49.7/50.6/40.7
Guide RNA/target RNA	68.6/84.3
r.m.s. deviations	
Bond lengths (Å)	0.016
Bond angles (°)	1.769

Data were collected from a single crystal. Values in parentheses are for highest-resolution shell.

cell dimensions a = 96.56 Å, b = 96.56 Å, c = 240.98 Å. The solvent content of the crystals was determined to be 65.4%, which was consistent with the presence of one RNP in each asymmetric unit.

Structure determination. The structure was determined by molecular replacement methods using MOLREP50 through the CCP4i interface to the CCP4 programs<sup>51</sup>, which combines rotation and translation searches in a single step. The previously determined structure of the Cbf5-Nop10-Gar1 complex was used as a search model. A single and outstanding solution was found in the space group P41212. The trimeric protein complex transformed to the correct solution was subjected to successive rigid body, minimization and simulated annealing refinement. At this stage, SigmaA-weighted  $3F_0 - 2F_c$  and  $F_0 - F_c$ electron densities were computed, which revealed the bound RNA molecules in the front surface of Cbf5-Nop10-Gar1 trimer. A molecular mask generated using a preliminary RNA model and the protein complex was then used to perform solvent flattening and flipping using initial phases computed from protein coordinates only in CNS52. The density-modified map was of sufficient quality (Supplementary Fig. 2 online) for tracing most RNA nucleotides. The real space correlation coefficients between the final model and the density modified map were 0.46 and 0.76 for RNA and proteins, respectively. Refinement of the RNP was carried out using CNS52 and REFMAC553. To account for rigid-body displacements of the complex with a reduced parameter set, the final stage of the refinement used translation-libration-screw-motion (TLS) parameters as implemented in REFMAC5. The three individual proteins and RNA strands were treated as single 'rigid-body' groups, and the final TLS parameters are listed in Supplementary Table 2 online. The refined structure has 0.45-Å coordinate error based on the maximum-likelihood method. A composite omit, cross-validated, SigmaA-weighted  $3F_0 - 2F_c$  map was computed using the final model and displayed around the RNA model (Fig. 2a) with 5% of the mode omitted at each time. The real space correlation coefficients between the final model and the composite omit  $3F_0 - 2F_c$  map are 0.87 and 0.88 for proteins and RNA, respectively. The final protein structure was assessed with Procheck<sup>54</sup> and found to be consistent with stereochemically valid models (Table 1).

Steady-state fluorescence studies. The target RNA designed for fluorescence studies contains 2-AP at position tG11 and 5-FU at position tU10. The 2-APand 5-FU-labeled target RNA was purchased from Dharmacon. The Pf9 H/ACA guide RNA was obtained by T7 transcription. The annealed targetguide RNA complex at 1 µM concentration was then incubated with 10 µM of the Cbf5-Nop10-Gar1 or Cbf5(D85A)-Nop10-Gar1 protein complex in a total volume of 100 µl. L7Ae was titrated in small increments until its final concentration reached 10-15 µM, when fluorescence intensities no longer increased. Fluorescence measurements were performed in a Cary Eclipse fluorescence spectrophotometer (Varian). The sample cuvette was maintained at 50  $^{\circ}\mathrm{C}$  using a circulating water bath. The excitation wavelength was 325 nm and the fluorescence intensity was measured at the peak of fluorescence (375 nm). The excitation and emission bandwidths were both 5 nm. For fluorescence intensity measurement after each titration, the sample was incubated for 20 min and then 8-10 accumulative scans were taken. Each titration was repeated in at least three independent experiments.

Accession codes. Protein Data Bank: Coordinates have been deposited with accession code 2RFK.

Note: Supplementary information is available on the Nature Structural & Molecular Biology website.

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#### AUTHOR CONTRIBUTIONS

B.L. designed and carried out crystallographic studies of the wild-type complex, acquired fluorescence data, and contributed to manuscript preparation; S.X. carried out crystallographic studies of the D85A mutant complex and contributed to manuscript preparation; M.P.T. and R.M.T. supplied plasmids encoding H/ ACA RNP proteins and contributed to manuscript preparation; H.L. supervised the project and contributed to manuscript preparation.

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# Substrate RNA Positioning in the Archaeal H/ACA Ribonucleoprotein Complex

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		10	20
P.furiosus		MARDEVRRI	LPADIKREVLIK
P.abyssi		MARDEVRRI	LPADIKREVIVK
P.horikoshii		MARDEVRRM	LPADIKREVLIK
T.kodakarensis		MARDEVRRI	LPADIKREVVVK
M.kandleri		MSGDKDRR	LPFDRDREMIT-
M.jannaschii		MILLEKTQ	EKKINDKEELIV
M.barkeri		MSPAG	KLPSEAERILVR
M.acetivorans		MSSAG	KLPSEIERTLVR
M.mazei		MSSAG	KLPSEVERTLVR
M.thermoautotrophicum	]		- MQVSLMANFIE
M.burtonii		MVSSK	R S P K D V N - I M V E
M.stadtmanae			MTEYEY
M.maripaludis			MELIV
M.hungatei			
A.fulgidus			MKLENFYV
N.pharaonis			
H.sp			
H.marismortui			- MATRGRHR SR T
H.walsbyi			
P.torridus			
T.acidophilum			
T.volcanium			
A.pernix	MAEEAVDAF	RGEGARFIEKV	KSICGNTSRILY
P.aerophilum			- MKC P - SR E V F S
N.equitans	MLCLSLMR   FO	SKCLEEQECP	LPWELEKYEIWV
S.cerevisiae_yeast	MSKEDFVIKPE/	AGASTDTSEW	PLLLKNFDKLLV
T.thermophila	MGKDKKKQRKQSSEVAEVEEQVVAQDFIKPS	KGGAKLDASQW	P L L L KN YD KMN I
D.melanogaster_fruitfly	MADVEVR KEKKKKKIKEEPLDGDDIGTLQKQGNFQIKPS	SKIAELDTSQW	PLLLKNFDKLNI
M.musculus_mouse	MADAEVITFPKKHKKKKDRKPLQEDDVAEIQHAEEFLIKPES	SKVAQLDTSQW	PLLLKNFDKLNV
H.sapiens_human	MADAEVIILPKKHKKKKERKSLPEEDVAEIQHAEEFLIKPES	SKVAKLDTSQW	PLLLKNFDKLNV
Interaction sites			
DC mutations		$\triangle$ $\Box$	

<u>β1'</u> - -

# Pf Cbf5

	30	40		50		60		70		8	0
P.furiosus	DENAETN	PDWGFPPEKR	PIEMHI	QFGVI	NLDK	PPGPT	SHEVV	Α <mark>ΨΙΚ</mark> ΚΙ	LNL	- EKA <mark>G</mark>	IGGTL
P.abyssi	DDKAETN	P KWG F P P D K R	PIELHI	QYGVI	NLDK	PPGPT	SHEVV	a <mark>w</mark> i kri	LNL	- EKA <mark>GH</mark>	IGGTL
P.horikoshii	DENAETN	PKWGFPPYER	PIELHI	QYGVI	NLDK	PPGPT	SHEVV	a <mark>w</mark> i kri	LNL	- EKA <mark>G</mark> F	IGGTL
T.kodakarensis	DEKAETN	PKWGFPPEKR	PIEMHI	QFGII	NLDK	PPGPT	SHEVV	a <mark>w</mark> vkr i	LNL	- N K A <mark>G</mark> F	IGGTL
M.kandleri	KAEVETD	PRYGCPPEER	PIEEYI	MKGVI	NLDK	PAGPT	SHEVV	Α <mark>W</mark> VKEI	FGL	- SKA <mark>GH</mark>	IGGTL
M.jannaschii	KEEVETN	WDYGCNPYER	KIEDLI	KYGVV	VVDK	PRGPT	S <mark>H</mark> EVS <sup>-</sup>	τ <mark>w</mark> νκκι	LNL	- D K A <mark>G F</mark>	IGGTL
M.barkeri	KSGAWTN	PSYGSYPEKR	PILEYI	EKGVV	NIDK	PKGPT	SHEVA	Α <mark>W</mark> VΚΑΙ	LGV	- STA <mark>G</mark> F	IAGSL
M.acetivorans	KSGAWTN	PVYGCAPEKR	PILEYI	EKGVV	NIDK	PSGPT	SHEVA	Α <mark>W</mark> VΚΑΙ	LGV	- N T A <mark>G</mark> F	IAGSL
M.mazei	KSGAWTN	PAYGCPPEKR	PIHEYI	EKGVV	NIDK	PRGPT	SHEVA	Α <mark>₩</mark> ٧ΚΑΙ	LGV	- H T A <mark>G</mark> H	AGSL
M.thermoautotrophicum	LKEATTN	PDYGCPPAER	DIEAHI	SMGVV	NLDK	PSGPT	SHQVD	S <mark>w</mark> vrdn	ILHV	- EKV <mark>G</mark> F	IGGTL
M.burtonii	KFHATTN	AAYGCLPQDR	PILEYI	NMGVV	NIDK	AIGPT	SHEVT	a <mark>w</mark> vrdn	1LGV	- KKA <mark>G</mark> F	ISGSL
M.stadtmanae	KCDVEVN	YDYGCHPRNR	TIEEHI	NKGII	NIDK	PSG <mark>P</mark> T	SHEVD	v <mark>w</mark> l kd i	MH V	- D K T <mark>G F</mark>	IGGTL
M.maripaludis	KEESKTD	YN YG SD P YNR	DIKTLL	NTGLV	VIDK	PSGPT	SHEVA	A <mark>W</mark> VRNN	1LNL	- VKA <mark>GH</mark>	IGGTL
M.hungatei		MERSSSFL	AHIAAH	IQGSII	LIDK	PRGPS	SHQVA	A <mark>W</mark> VR E I	TGV	- SSV <mark>G</mark> F	ITGTL
A.fulgidus	KDDASTD	ESYGCYPTKR	PMEEYI	RKGLV	СІДК	PMG P S	SHEVV	v <mark>w</mark> vrr i	LNV	- SKT <mark>G</mark> F	IAGTL
N.pharaonis		MRERGPPADR	DPETLL	EFGVI	NLDK	PPG <mark>P</mark> S	AHQVA	a <mark>w</mark> vrdn	1AG V	- EQAA	IAGTL
H.sp	MG	IRPPPGER	SPAAVL	SFGVV	NLDK	PPGPS	A <mark>H</mark> QVS/	AWIRDL	VGV	- EKAA <mark>H</mark>	IAGTL
H.marismortui	SGTSSEP	MTLRAPPDER	DLDSLR	SFGVV	NLDK	PPG <mark>P</mark> S	a <mark>h</mark> q va	a <mark>w</mark> irda	TGQ	- DR VA	IGGTL
H.walsbyi	M T E S	PRLRESPDNR	SLADIC	NFGVV	NLDK	PVG <mark>P</mark> S	AHQVS	A <mark>w</mark> vrd l	IGV	- ER A A	IAGTL
P.torridus			M S N L	NG - F I	VVDK	PKG PT	SHQID	s <mark>w</mark> irdi	TGE	- PR V <mark>G</mark> F	HIGTL
T.acidophilum					MLDK	PQG P T	SHQVDH	H <mark>W</mark> VREI	LGI	- EKVA	HIGTL
T.volcanium		M I	EEIQKL	NG - F I	VIDK	PQG <mark>P</mark> T	S <mark>H</mark> QVD'	Y <mark>W</mark> VRQI	LGT	- EKV <mark>G</mark> H	HIGTL
A.pernix	KYDEPTD	PR YG Y L PH ER	PLDVYL	RYGMI	VVDK	PPG <mark>P</mark> T	SHEVV	a <mark>w</mark> i krm	1LGV	- SR A <mark>G</mark> F	IGGTL
P.aerophilum	KFEESTN	PQWGKPPSQR	STEEYI	KYSLV	ILDK	PRGPS	SHEVA	Α <mark>₩</mark> νκκι	LGV	- ER A <mark>G</mark> H	IAGTL
N.equitans	KKEAETN	EKWGEDPYNR	PIERLL	KYSVI	NLDK	PSGPT	SHQVV	a <mark>w</mark> vrd i	VG	- VKA <mark>GH</mark>	IGGTL
S.cerevisiae_yeast	RSGHYTP	IPAGSSPLKR	DLKSYI	SSGVI	NLDK	P SN P S	SHEVV	a <mark>w</mark> i kri	LR 0	CEKT <mark>G</mark> F	ISGTL
T.thermophila	RSSHYTP	IPNGSNPLAR	PMEEHL	KYGVM	NLDK	PSN PS	SHEVV	A <mark>₩</mark> VKKL	FENITK	MEKT <mark>G</mark> H	ISGTL
D.melanogaster_fruitfly	RSNHYTP	LAHGSSPLNR	DIKEYN	IKTGFI	NLDK	(PSN <mark>P</mark> S	SHEVV	A <mark>WIK</mark> KI	LK'	V E K T <mark>G</mark> ⊦	ISGTL
M.musculus_mouse	RTAHYTP	LPCGSNPLKR	EIGDYI	RTGFI	NLDK	P SN P S	SHEVV	a <mark>w</mark> irri	LR '	VEKT <mark>G</mark>	ISGTL
H.sapiens_human	RTTHYTP	LACGSNPLKR	EIGDYI	RTGFI	NLDK	P SN P S	SHEVV	a <mark>w</mark> irri	LR '	VEKT <mark>G</mark>	ISGTL
Interaction sites						•					
DC mutations		$\Delta$									$\bigtriangleup$
Pf Cbf5			- α1'	- β1			α1			β2	

	90	10	0 1	10	120	130	140
P furiosus							
P abyaai							
P.abyssi	DPKVSGV			RETVAL	WINLINGDVP	- EDKIRAVIMKEFE	EGELIQRPERS
P.horikoshii	DPKVSGV	<sup>I</sup> PVALEKA II	RVVQALLPAG	K E Y V A L N	MHLHGDVP	- ENKLIDVMKEFE	EGETIQRPPLRS
T.kodakarensis	DPKVSGV	<sup>I</sup> PVALERATI	RVVQALLPAG	S <mark>KEYV</mark> ALN	MHLHGDVP	- ED KILAVMREFO	QGE <mark>IIQRPP</mark> LRS
M.kandleri	DPKVTGV	L PIALEKAT	KIIQTLLPAG	<mark>ΚΕΥ</mark> ΥΤΙΝ	MHLHGDVD	- EEEL ERVVKEFE	EG T I L <mark>Q</mark> R P P L R S
M.jannaschii	DPKVTGV	L P V A L E R A T	КТІРМѠНІРЯ	<sup>•</sup> KEYVCLN	MHLHRDAS	- EEDILRVFKEF1	TGR I Y <mark>Q</mark> R PPL KA
Mharkeri			KAVPALRISC	KEYVCLI	KIHKEMP		TGPLYOMPPLKS
M.oostiyoropo							
	DEKVIGL	LFILLGKAT				- FRLVRRVCEEF	
M.mazei	DPKVIGL		LAVPALRLSC	<b>KEYICHL</b>	LKLHRAMP	-QKLVRQVCEEF	IGPTYQMPPIKS
M.thermoautotrophicum	DPKVTGV	′ <mark>L</mark> PLGIDRATI	RVMQLLLEAF	° <mark>KEY</mark> VCLN	MR VHR E VD	- EERIREVLGEFO	QGK <mark>IFQIPP</mark> LKS
M.burtonii	DPHVTGL	L P V M L G R A T	KAVSALRLSO	G <mark>KEY</mark> ICVN	MHLHDDIP	- DRKIRKACKEF	TGP <mark>I</mark> YQT <mark>PP</mark> IIS
M.stadtmanae	DPKVTGV	L PVALNTAT	KSLSLLLSF	<sup>•</sup> KEYVCLN	MRLHKPVD	- EEDIISILDEF	ΓGKIYQIPPVKS
M marinaludis			KCVPIWHIPE				
M.nungaler	DPPVSGV			KETVALL		-DAELAEVIERF	IGRI IQRPPKKS
A.fulgidus	DPRVIGV		KMVKFLQESS	SKEYVCLN	MRLHGDAK	- REDVEKVMKLFV	VGRIYQRPPLKS
N.pharaonis	DPKVTGC	L P V L T G T A T I	RAAQVFDESF	R <mark>K</mark> G Y V A V L	LELHGTAP	SDLESTVAEFE	EG P L Y <mark>Q K P P</mark> R K S
H.sp	DPKVTGC	LPVLTGTAT	RIAPALLEGF	<mark>ΚΕΥ</mark> ΛΑΥΙ	LELHDDPP	RILPDVIEAF1	TGE <mark>I</mark> Y <mark>Q</mark> K <mark>PP</mark> KKS
H.marismortui	DPKVTGC		RMAQVFDNA	<mark>κεγν</mark> τνι	LELHDQAP	AD I AD I VAEFE	ETD I YQKPPRKS
H walshvi			RIAPVELEGI		FEHGPPP	SDI SMILETER	GTIYOKPPRKS
B torriduo	DRCVSCV			KEVVEVI			
	DFGV3GV					- HUST KSVFKEF	
I.acidopniium	DPNVIGV	LIMAIGKAVI	RLVDVVHESP	KEYVGVN	WRFYEDII	- EEEVRYYFKKF	IGRIYQLPPVRS
T.volcanium	D PN V TG V	′ <mark>L</mark> VMA I G K A VI	RLIDVVHEKF	° <mark>K</mark> E Y V G V N	MRFHSDIS	- EEEVREVFRKF1	T T R I YQL PP VR S
A.pernix	DPKVTGV	L PVAL ERMTI	RIIGTVMHSS	S <mark>KEYV</mark> CVN	MQLHRPVE	- EDRLREVLKLFE	EGE <mark>I</mark> Y <mark>Q</mark> KPPLRS
P.aerophilum	DPKVSGV	L P I A I A E G T	K V L M A L S R S C	κνγναν	AKFHGDVD	- EDKLRAVLQEFO	QGVIYQKPPLRS
Nequitans		PLAIGEAT	KVLOTILIAG	KEYVALN	MHIHKEVS	- EKDIIKVMSKEV	GTLIOTPPIRS
S correctione weest							
S.cerevisiae_yeast	DPKVIGC						IGALFQRPPLIS
T.thermophila	DPKVTGC	LIVCLNRATI	RLVKAQQSAG	G <mark>KEY</mark> VGIN	VRLHNDIE	SELKLAKALQQLI	TGPL FQKPPL I S
D.melanogaster_fruitfly	DPKVTGC	LIVCIDRATI	RLVKSQQSAG	S <mark>keyv</mark> aif	FKLHGAVE	SVAKVRQGLEKLF	RGAL F <mark>QR PP</mark> L I S
M.musculus_mouse	DPKVTGC	LIVCIERATI	RLVKSQQSAG	δ <mark>ΚΕΥ</mark> VGΙ \	VRLHNAIE	GGTQ <mark>L</mark> SRALETL 1	TGAL F <mark>Q</mark> R <mark>PP</mark> L I A
H.sapiens human	DPKVTGC	LIVCIERATI	RLVKSQQSAG	KEYVGI V	VRLHNALE	GGTQ <mark>L</mark> SRALETL1	TGAL F <mark>Q</mark> R PPLIA
Interaction sites							
	-	• •					
DC mutations					$\bigtriangleup$		
Df Chf5	β3	, α2		β4	、	α3	- β7
FI CDIS							
		,					,
	150	160	17(	)	180	190	200
	150	160	170	)	180	190	200
P.furiosus	150 A <mark>V</mark> KRRLR	160 TRKVYYIEV	17( L E I EGRD \	) / <mark>L F</mark> R VG VE	180 E A <mark>G</mark> T <mark>Y</mark> I <mark>R</mark> S	190 LIHH <mark>IG</mark> LAL <mark>G</mark> VGA	200 AH <mark>M</mark> SE <mark>LRR</mark> TRSG
P.furiosus P.abyssi	150 AVKRRLR AVKRRLR	160 TRKVYYIEV TRKVYYIEI	17( L E I EGRD \ L E I DGRD \	) / <mark>L F</mark> R VG V E / <b>L</b> FR VG V E	180 E A G T Y I R S E A G T Y I R S	190 LIHHIGLAL <mark>G</mark> VG7 LIHHIGLALGVG7	200 AHMSELRRTRSG AHMAELRRTRSG
P.furiosus P.abyssi P.horikoshii	150 AVKRRLR AVKRRLR AVKRRLR	160 TRKVYYIEV TRKVYYIEI TRKVYYIEI	17( L E I EGRD \ L E I DGRD \ L E I DGRD \	) / L F R V G V E / L F R V G V E / L F K V G V E	180 E AG T Y I R S E AG T Y I R S E AG T Y I R S	190 LIHHIGLALGVGA LIHHIGLALGVGA LIHHIGLALGVGA	200 AHMSELRRTRSG AHMAELRRTRSG AHMAELRRTRSG
P.furiosus P.abyssi P.horikoshii T kodakarensis	150 AVKRRLR AVKRRLR AVKRRLR AVKRRLR	160 TRKVYYIEV TRKVYYIEI TRKVYYIEI TRKVYYIDV	17( L E I EGRD \ L E I DGRD \ L E I DGRD \ L E I EGRD \	) / L F R V G V E / L F R V G V E / L F K V G V E / L F R V G V E	180 E AG T Y I R S E AG T Y I R S E AG T Y I R S E AG T Y I R S	190 LIHHIGLALGVGA LIHHIGLALGVGA LIHHIGLALGVGA	200 AHMSELRRTRSG AHMAELRRTRSG AHMAELRRTRSG AHMAELRRTRSG
P.furiosus P.abyssi P.horikoshii T.kodakarensis M kandlari	150 A V KR R L R A V KR R L R A V KR R L R A V KR R L R	160 TRKVYYIEV TRKVYYIEI TRKVYYIEI TRKVYYIDV	17( L E I EGRD \ L E I DGRD \ L E I DGRD \ L E I EGRD \ E I DGRD \	) / L FR VG V E / L FR VG V E / L FR VG V E / L FR VG V E	180 EAGTYIRS EAGTYIRS EAGTYIRS EAGTYIRS	190 LIHHIGLALGVGA LIHHIGLALGVGA LIHHIGLALGVGA	200 AHMSELRRTRSG AHMAELRRTRSG AHMAELRRTRSG AHMAELRRTRSG
P.furiosus P.abyssi P.horikoshii T.kodakarensis M.kandleri	150 AVKRRLR AVKRRLR AVKRRLR AVKRRLR AVKRRVR	160 TRKVYYIEV TRKVYYIEI TRKVYYIEI TRKVYYIDV PKKIYYIDI	17( L E I EGRD \ L E I DGRD \ L E I DGRD \ L E I EGRD \ L E I DGRD \	) / L FR VG VE / L FR VG VE / L FR VG VE / L FR VG VE / L FR VG CO	180 EAGTYIRS EAGTYIRS EAGTYIRS EAGTYIRS QAGTYIRK	190 LIHHIGLALGVGA LIHHIGLALGVGA LIHHIGLALGVGA LIHHIGLALGVGA LCHDIGEALGVGA	200 AHMSELRRTRSG AHMAELRRTRSG AHMAELRRTRSG AHMAELRRTRSG AHMAELRRTRTG
P.furiosus P.abyssi P.horikoshii T.kodakarensis M.kandleri M.jannaschii	150 A V KRR LR A V KRR LR A V KRR LR A V KRR VR A V KRR LR	160 TRKVYYIEV TRKVYYIEI TRKVYYIEI TRKVYYIDV PKKIYYIDI IRKIHELEL	17( L E I EGRD \ L E I DGRD \ L E I DGRD \ L E I EGRD \ L E I DGRD \ L D K DGKD \	) / L FR VG VE / L FR VG VE / L FR VG VE / L FR VG VE / L MR VGCO / L FR VKCO	180 EAGTYIRS EAGTYIRS EAGTYIRS EAGTYIRS QAGTYIRK QSGTYIRK	190 LIHHIGLALGVGA LIHHIGLALGVGA LIHHIGLALGVGA LIHHIGLALGVGA LCHDIGEALGVGA LCEDIGEALGTSA	200 AHMSELRRTRSG AHMAELRRTRSG AHMAELRRTRSG AHMAELRRTRG AHMAELRRTRG AHMQELRRTKSG
P.furiosus P.abyssi P.horikoshii T.kodakarensis M.kandleri M.jannaschii M.barkeri	150 A V KR R L R A V KR V I R	160 TR KVYYI EV TR KVYYI EI TR KVYYI EI TR KVYYI DV PKKI YYI DI IR KI HEL EL IR TI YYL EV	17( L E I EGRD \ L E I DGRD \ L E I DGRD \ L E I EGRD \ L E I DGRD \ L D K DGKD \ L E I EGSF \	) / L FR VG VE / L FR VG VE / L FR VG VE / L FR VG CC / L FR VKCC / L FR VKCC	180 EAGTYIRS EAGTYIRS EAGTYIRS GAGTYIRS QAGTYIRK QSGTYIRK EAGTYIRK	190 LIHHIGLALGVGA LIHHIGLALGVGA LIHHIGLALGVGA LIHHIGLALGVGA LCHDIGEALGVGA LCEDIGEALGTSA LCHDIGLALGCGG	200 AHM SE LRR TR SG AHM AE LRR TR SG AHM AE LRR TR SG AHM AE LRR TR SG AHM AE LRR TR TG AHM QE LRR TK SG GHM QE LRR TK AG
P.furiosus P.abyssi P.horikoshii T.kodakarensis M.kandleri M.jannaschii M.barkeri M.acetivorans	150 A V KR R L R A V KR V I R A V KR V I R	160 TR KVYYI EV TR KVYYI EI TR KVYYI EI TR KVYYI DV PKKI YYI DI IR KI HEL EL IR TI YYL EV VR TI YYI EV	17( L E I EGRD \ L E I DGRD \ L E I DGRD \ L E I EGRD \ L E I DGRD \ L D K DGKD \ L E I EGSF \ L E I EGMS \	) / L FR VG VE / L FR VG VE / L FR VG VE / L FR VGCC / L FR VGCE / L FR VGCE	180 EAGTYIRS EAGTYIRS EAGTYIRS QAGTYIRK QSGTYIRK EAGTYIRK EAGTYIRK	190 LIHHIGLALGVGA LIHHIGLALGVGA LIHHIGLALGVGA LIHHIGLALGVGA LCHDIGEALGVGA LCHDIGEALGCGG LCHDIGLALGCGG	200 AHM SE LRR TR SG AHM AE LRR TR SG AHM AE LRR TR SG AHM AE LRR TR SG AHM AE LRR TR SG AHM QE LRR TK SG GHM QE LRR TK AG
P.furiosus P.abyssi P.horikoshii T.kodakarensis M.kandleri M.jannaschii M.barkeri M.acetivorans M.mazei	150 A V KR R L R A V KR V I R A V KR V I R A V KR V I R	160 TR KVYYI EV TR KVYYI EI TR KVYYI EV PKKI YYI DV PKKI YYI DI IR KI HELEL IR TI YYL EV VR TI YHLEV	17( L E I EGRD \ L E I DGRD \ L E I DGRD \ L E I EGRD \ L E I DGRD \ L E I EGSF \ L E I EGMS \ L E I EGTS \	) / L FR VG VE / L FR VG VE / L FR VG VE / L FR VGC / L FR VGC E / L FR VGC E / L FR VGC E	180 EAGTYIRS EAGTYIRS EAGTYIRS QAGTYIRK QSGTYIRK EAGTYIRK EAGTYIRK	190 LIHHIGLALGVGA LIHHIGLALGVGA LIHHIGLALGVGA LIHHIGLALGVGA LCHDIGEALGTSA LCHDIGLALGCGG LCHDIGLALGCGG LCHDIGLALGCGG	200 AHM SE LRR TR SG AHM AE LRR TR SG AHM AE LRR TR SG AHM AE LRR TR SG AHM AE LRR TR SG AHM QE LRR TK SG GHM QE LRR TK AG GHM QG LRR TK AG
P.furiosus P.abyssi P.horikoshii T.kodakarensis M.kandleri M.jannaschii M.barkeri M.acetivorans M.mazei M thermoautotrophicum	150 A V KR R L R A V KR V I R	160 TR KVYYI EV TR KVYYI EI TR KVYYI DV PKKI YYI DV PKKI YYI DI IR KI HELEL IR TI YYL EV VR TI YHL EV VR TI YHL EV	17( L E I EGRD \ L E I DGRD \ L E I DGRD \ L E I EGRD \ L E I EGRD \ L E I EGSF \ L E I EGTS \ L E I EGTS \ L E I EGTS \	) / L FR VG VE / L FR VG VE / L FR VG VE / L FR VG CE / L FR VGCE / L FR VGCE / L FR VGCE / L FR VGCE	180 EAGTYIRS EAGTYIRS EAGTYIRS QAGTYIRK QSGTYIRK EAGTYIRK EAGTYIRK	190 LIHHIGLALGVGA LIHHIGLALGVGA LIHHIGLALGVGA LIHHIGLALGVGA LCHDIGEALGTSA LCHDIGLALGCGG LCHDIGLALGCGG LCHDIGLALGCGG	200 AHM SE LRR TR SG AHM AE LRR TR SG AHM AE LRR TR SG AHM AE LRR TR SG AHM AE LRR TR SG AHM QE LRR TK SG GHM QE LRR TK AG GHM QG LRR TK AG AHM AE LRR TA VG
P.furiosus P.abyssi P.horikoshii T.kodakarensis M.kandleri M.jannaschii M.barkeri M.acetivorans M.mazei M.thermoautotrophicum	150 AVKRRLR AVKRRLR AVKRRLR AVKRRLR AVKRRLR AVKRVIR AVKRVIR AVKRVIR AVKRVIR	160 TRKVYYIEV TRKVYYIEI TRKVYYIDV PKKIYYIDV PKKIYYIDI IRKIHELEL IRTIYYLEV VRTIYYLEV VRTIYHLEV VRTIYRVDI	17( L E I EGRD \ L E I DGRD \ L E I DGRD \ L E I EGRD \ L E I DGRD \ L E I EGRD \ L E I EGSF \ L E I EGMS \ L E I EGTS \ L E V DGQD \	) / L FR VG VE / L FR VG VE / L FR VG VE / L FR VGCC / L FR VGCC / L FR VGCE / L FR VGCE / L FR VGCE	180 EAGTYIRS EAGTYIRS EAGTYIRS QAGTYIRK QSGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK	190 LIHHIGLALGVGA LIHHIGLALGVGA LIHHIGLALGVGA LIHHIGLALGVGA LCHDIGEALGTSA LCHDIGLALGCGG LCHDIGLALGCGG LCHDIGLALGCGG YCHDVGEALGAGA	200 AHM SE LRR TR SG AHM AE LRR TR SG AHM AE LRR TR SG AHM AE LRR TR SG AHM AE LRR TR SG AHM QE LRR TK SG GHM QE LRR TK AG GHM QG LRR TK AG AHM AE LRR TA VG
P.furiosus P.abyssi P.horikoshii T.kodakarensis M.kandleri M.jannaschii M.barkeri M.acetivorans M.mazei M.thermoautotrophicum M.burtonii	150 AVKRRLR AVKRRLR AVKRRLR AVKRRLR AVKRRLR AVKRVIR AVKRVIR AVKRVIR AVKRVIR AVKRDLR	160 TR KVYYI EV TR KVYYI EI TR KVYYI DV PKKI YYI DI IR KI HELEL IR TI YYLEV VR TI YYLEV VR TI YHLEV VR TI YRVDI IR NI YYLDV	17( L E I EGRD \ L E I DGRD \ L E I DGRD \ L E I EGRD \ L E I EGRD \ L E I EGSF \ L E I EGMS \ L E I EGTS \ L E V DGQD \ L E I EGRE \	) / L FR VG VE / L FR VG VE / L FR VG VE / L FR VGC / L FR I ACE / L FR I ACE	180 EAGTYIRS EAGTYIRS EAGTYIRS GAGTYIRK QSGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK EAGTYRK	190 LIHHIGLALGVGA LIHHIGLALGVGA LIHHIGLALGVGA LCHDIGEALGVGA LCHDIGEALGCGC LCHDIGLALGCGC LCHDIGLALGCGC VCHDVGEALGAGA LCHDIGLALGCGC	200 AHM SE LRR TR SG AHM AE LRR TR SG AHM AE LRR TR SG AHM AE LRR TR SG AHM AE LRR TR SG AHM QE LRR TK SG GHM QE LRR TK AG GHM QG LRR TK AG AHM AE LRR TA VG GHM KQ LRR TG TG
P.furiosus P.abyssi P.horikoshii T.kodakarensis M.kandleri M.jannaschii M.barkeri M.acetivorans M.mazei M.thermoautotrophicum M.burtonii M.stadtmanae	150 A V KR R L R A V KR V I R A V KR Q L R A V KR Q L R	160 TR KVYYI EV TR KVYYI EI TR KVYYI EI TR KVYYI DV PKKI YYI DV PKKI YYI EV VRTI YYL EV VRTI YHL EV VRTI YR VDI IRNI YYL DV VRTI YEVKL	17( L E I EGRD \ L E I DGRD \ L E I DGRD \ L E I EGRD \ L E I EGRD \ L E I EGSF \ L E I EGMS \ L E I EGTS \ L E V DGQD \ L E I EGRE \ L E I R - D NQD \	) /LFRVGVE /LFRVGVE /LFRVGVE /LFRVGCE /LFRVGCE /LFRVGCE /LFRVGCE /LFRIACE /LFRIACE	180 EAGTYIRS EAGTYIRS EAGTYIRS QAGTYIRK QSGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK EAGTYLRK QSGTYIRK	190 LIHHIGLALGVGA LIHHIGLALGVGA LIHHIGLALGVGA LCHDIGEALGVGA LCHDIGEALGCGC LCHDIGLALGCGC LCHDIGLALGCGC YCHDVGEALGAGA LCHDIGLVLGCGC YCHDIGEALGCGA	200 AHMSELRRTRSG AHMAELRRTRSG AHMAELRRTRSG AHMAELRRTRSG AHMAELRRTRSG GHMQELRRTKAG GHMQALRRTKAG GHMQGLRRTKAG GHMQGLRRTAG GHMAELRRTAVG GHMAELRRTGTG
P.furiosus P.abyssi P.horikoshii T.kodakarensis M.kandleri M.jannaschii M.barkeri M.barkeri M.acetivorans M.mazei M.thermoautotrophicum M.burtonii M.stadtmanae M.maripaludis	150 A V KR R L R A V KR V I R A V KR Q L R A V KR Q L R A V KR S L R	160 TR KVYYI EV TR KVYYI EI TR KVYYI EI TR KVYYI DV PKKI YYI DV PKKI YYI EV VRTI YYL EV VRTI YHL EV VRTI YHL EV VRTI YRVDI IRNI YYL DV VRTI YEVKL IRKI YEI EI	17( L E I EGRD \ L E I DGRD \ L E I DGRD \ L E I EGRD \ L E I EGRD \ L E I EGRS \ L E I EGTS \ L E I EGRE \ L E I EGRE \ L E I EGRE \ L E I DGRD \	) /LFRVGVE /LFRVGVE /LFRVGVE /LFRVGCE /LFRVGCE /LFRVGCE /LFRIACE /LFRIACE /LFRICC LFRICC	180 EAGTYIRS EAGTYIRS EAGTYIRS QAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK EAGTYLRK QSGTYIRK QSGTYLRK	190 LIHHIGLALGVGA LIHHIGLALGVGA LIHHIGLALGVGA LCHDIGEALGVGA LCHDIGEALGCGC LCHDIGLALGCGC LCHDIGLALGCGC YCHDVGEALGAGA LCHDIGLALGCGC YCHDIGLALGCGC YCHDIGEALGCGA LCHDIGLALGCGC YCHDIGEALGCGA	200 AH M SE LRR TR SG AH M AE LRR TR SG GH MQE LRR TK AG GH MQE LRR TK AG GH MQE LRR TK AG GH MQE LRR TA VG GH M AE LRR TA VG GH M AE LRR TM AG AH M AE LRR TM AG AH M AE LRR TI SG
P.furiosus P.abyssi P.horikoshii T.kodakarensis M.kandleri M.jannaschii M.barkeri M.barkeri M.acetivorans M.mazei M.thermoautotrophicum M.burtonii M.stadtmanae M.maripaludis M.hungatei	150 A V KR R L R A V KR V I R A V KR Q L R A V KR Q L R A V KR S L R A V KR A L R	160 TR KVYYI EV TR KVYYI EI TR KVYYI EI TR KVYYI DV PKKI YYI DV PKKI YYI EV VR TI YYL EV VR TI YHL EV VR TI YHL EV VR TI YR VDI IRNI YYL DV VR TI YEVKL IRKI YEI EI IREI HEL EM	17( L E I EGRD \ L E I DGRD \ L E I DGRD \ L E I EGRD \ L E I EGRD \ L E I EGSF \ L E I EGTS \ L E I EGRE \ L E I EGRE \ L E I DGRD \ L E I DGRD \ L E I DGRD \	) /LFRVGVE /LFRVGVE /LFRVGVE /LFRVGCE /LFRVGCE /LFRVGCE /LFRIACE /LFRIACE /LFRIACE /LFRICCE	180 EAGTYIRS EAGTYIRS EAGTYIRS QAGTYIRK QAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK QSGTYIRK QSGTYIRK	190 LIHHIGLALGVGA LIHHIGLALGVGA LIHHIGLALGVGA LCHDIGEALGVGA LCHDIGEALGCGG LCHDIGLALGCGG VCHDVGEALGAGA LCHDIGLALGCGG YCHDIGLALGCGG YCHDIGEALGCGA LCHDIGLALGCGGA LCHDIGLALGCGGA LCHDIGLALGCGGA LCHDIGEALGCGA	200 AH M SE LRR TR SG AH M AE LRR TR SG GH MQE LRR TK AG GH MQE LRR TK AG GH MQE LRR TK AG GH MQE LRR TA VG GH M AE LRR TM AG AH M AE LRR TM AG AH M AE LRR TM AG AH M QE LRR TI SG GAM VE LRR TR SG
P.furiosus P.abyssi P.horikoshii T.kodakarensis M.kandleri M.jannaschii M.barkeri M.barkeri M.acetivorans M.mazei M.thermoautotrophicum M.burtonii M.stadtmanae M.maripaludis M.hungatei A.fulqidus	150 A V KR R L R A V KR V I R A V KR V I R A V KR V I R A V KR V L R A V KR Q L R A V KR S L R A V KR A L R A V K K V L R	160 TR KVYYI EV TR KVYYI EI TR KVYYI EI TR KVYYI DV PKKI YYI DV PKKI YYI EV VR TI YYL EV VR TI YHL EV VR TI YHL EV VR TI YHL EV VR TI YR VDI IRNI YYL DV VR TI YEVKL IRKI YEI EI IR EI HEL EM IR EI YEMEL	17( L E I EGRD \ L E I DGRD \ L E I DGRD \ L E I EGRD \ L E I EGRD \ L E I EGSF \ L E I EGTS \ L E I EGRE \ L E I EGRE \ L E I DGRD \	) /LFRVGVE /LFRVGVE /LFRVGVE /LFRVGCE /LFRVGCE /LFRVGCE /LFRVGCE /LFRIACE /LFRIACE /LFRIACE /LFRICCE	180 EAGTYIRS EAGTYIRS EAGTYIRS QAGTYIRK QAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK QSGTYIRK QSGTYIRK QSGTYIRK QSGTYIRK	190 LIHHIGLALGVGA LIHHIGLALGVGA LIHHIGLALGVGA LCHDIGEALGVGA LCHDIGLALGCGG LCHDIGLALGCGG VCHDVGEALGAGA LCHDIGLALGCGG YCHDIGLALGCGG YCHDIGEALGCGA LCHDIGLALGCGG LCHDIGLALGCGA LCHDIGLALGCGA LCHDIGEALGCGA LCHDIGEALGTSA	200 AHM SE LRR TR SG AHM AE LRR TR SG AHM AE LRR TR SG AHM AE LRR TR SG AHM AE LRR TK SG GHM QE LRR TK AG GHM QE LRR TK AG GHM QE LRR TA VG GHM KQ LRR TG TG AHM AE LRR TM AG AHM QE LRR TR SG AHM QE LRR TR SG
P.furiosus P.abyssi P.horikoshii T.kodakarensis M.kandleri M.jannaschii M.barkeri M.barkeri M.acetivorans M.mazei M.thermoautotrophicum M.burtonii M.stadtmanae M.maripaludis M.hungatei A.fulgidus N.pharaonis	150 A V KR R L R A V KR R V I R A V KR Q L R A V KR Q L R A V KR S L R A V KR S L R A V K R Z L R A V K R Z L R	160 TR KVYYI EV TR KVYYI EI TR KVYYI EI TR KVYYI DV PKKI YYI DV PKKI YYI EV VR TI YYL EV VR TI YYL EV VR TI YHL EV VR TI YHL EV VR TI YEVKL IR NI YYL DV VR TI YEVKL IR KI YEI EI IR EI HEL EM IR EI YEMEL	17( L E I EGRD \ L E I DGRD \ L E I DGRD \ L E I DGRD \ L E I DGRD \ L E I EGSF \ L E I EGTS \ L E I EGRE \ L E I EGRE \ L E I DGRD \ L E I ARR \	) /L FR VG VE /L FR VG VE /L FR VG VE /L FR VG CE /L FR VG CE /L FR VG CE /L FR VG CE /L FR I ACE /L FR I TCC L FR TKCC /L FR VKCE /L FR VVTE /L FR VVTE	180 EAGTYIRS EAGTYIRS EAGTYIRS QAGTYIRK QAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK CSGTYIRK QSGTYIRK QSGTYIRK CSGTYIRK	190 LIHHIGLALGVGA LIHHIGLALGVGA LIHHIGLALGVGA LCHDIGEALGVGA LCHDIGLALGCGC LCHDIGLALGCGC VCHDVGEALGAGA LCHDIGLALGCGC YCHDIGEALGCGA LCHDIGLALGCGA LCHDIGEALGCGA LCHDIGEALGCGA LCHDIGEALGCGA LCHDIGEALGTGA	200 AHMSELRRTRSG AHMAELRRTRSG AHMAELRRTRSG AHMAELRRTRSG AHMAELRRTKSG GHMQELRRTKSG GHMQELRRTKAG GHMQGLRRTKAG GHMQGLRRTAG GHMKQLRRTGTG AHMAELRRTMAG AHMAELRRTMAG AHMQELRRTSG AHMQELRRTRSG AHMQELRRTRSG
P.furiosus P.abyssi P.horikoshii T.kodakarensis M.kandleri M.jannaschii M.barkeri M.acetivorans M.mazei M.thermoautotrophicum M.burtonii M.stadtmanae M.maripaludis M.hungatei A.fulgidus N.pharaonis	150 A V KR R L R A V KR V I R A V KR V L R A V KR Q L R A V KR S L R A V KR S L R A V K R S L R A V K R L R A V K R R L R	160 TR KVYYI EV TR KVYYI EI TR KVYYI EI TR KVYYI DV PKKI YYI DV PKKI YYI DV VR TI YYL EV VR TI YYL EV VR TI YHL EV VR TI YHL EV VR TI YEVKL IR KI YEI EI IR EI HEL EM IR EI YEMEL TR TVHRL DV	17( L E I EGRD \ L E I DGRD \ L E I DGRD \ L E I DGRD \ L E I DGRD \ L E I EGRD \ L E I EGMS \ L E I EGRS \ L E I EGRD \ L E I DGRD \ L E I DGRD \ L E I DGRD \ L E I DGRD \ L E I CGRD \ L E I -	) /L FR VG VE /L FR VG VE /L FR VG VE /L FR VG CE /L FR VG CE /L FR VG CE /L FR VG CE /L FR I TCC L FR TKCC /L FR VCE /L FR VVTE /L FR VVTE /L FR VCE	180 EAGTYIRS EAGTYIRS EAGTYIRS QAGTYIRK QAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK CSGTYIRK QSGTYIRK QSGTYIRK CSGTYIRK ESGTYIRK	190 LIHHIGLALGVGA LIHHIGLALGVGA LIHHIGLALGVGA LCHDIGEALGVGA LCHDIGLALGCGC LCHDIGLALGCGC YCHDVGEALGAGA LCHDIGLALGCGC YCHDIGEALGCGA LCHDIGEALGCGA LCHDIGEALGTSA LCHDIGEALGTSA LCHDIGEVLGTGA	200 AHMSELRRTRSG AHMAELRRTRSG AHMAELRRTRSG AHMAELRRTRSG AHMAELRRTKSG GHMQELRRTKSG GHMQELRRTKAG GHMQGLRRTKAG GHMQGLRRTKAG GHMQELRRTGTG AHMAELRRTAG GHMQELRRTSG AHMQELRRTSG GHMQELRRTSG GHMQELRRTSG GHMQELRRTSG
P.furiosus P.abyssi P.horikoshii T.kodakarensis M.kandleri M.jannaschii M.barkeri M.acetivorans M.mazei M.thermoautotrophicum M.burtonii M.stadtmanae M.maripaludis M.hungatei A.fulgidus N.pharaonis H.sp	150 A V KR R L R A V KR R V I A V KR V I R A V KR V I R A V KR V I R A V KR Q L R A V KR Q L R A V KR S L R A V KR S L R A V K R L R	160 TR KVYYI EV TR KVYYI EI TR KVYYI EI TR KVYYI DV PKKI YYI DV PKKI YYI DV VR TI YYL EV VR TI YYL EV VR TI YHL EV VR TI YHL EV VR TI YHL EV VR TI YEVKL IR KI YEI EI IR EI HEL EM IR EI YEMEL TR TVHRL DV VR TI YDL DV	17( L E I EGRD \ L E I DGRD \ L E I DGRD \ L E I DGRD \ L E I EGRD \ L E I EGRD \ L E I EGNS \ L E I EGRE \ L E I DGRD \ L E I EGRD \ L E I GRD \ L E I	) /L FR VG VE /L FR VG VE /L FR VG VE /L FR VG CE /L FR VGCE /L FR VGCE /L FR VGCE /L FR VGCE /L FR I TCC L FR TKCC /L FR VKCE /L FR VKCE /L FR VKCE /L FR VKCE /L FR VFE	180 EAGTYIRS EAGTYIRS EAGTYIRS QAGTYIRS QAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK CSGTYIRK QSGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK	190 LIHHIGLALGVGA LIHHIGLALGVGA LIHHIGLALGVGA LCHDIGEALGVGA LCHDIGEALGVGA LCHDIGLALGCGC LCHDIGLALGCGC YCHDVGEALGAGA LCHDIGLALGCGA YCHDIGEALGCGA LCHDIGEALGCGA LCHDIGEALGCGA LCHDIGEALGCGA LCHDIGEALGCGA LCHDIGEALGTSA LCHHIGMACGVGC LCHDIGEALGTSA	200 AHMSELRRTRSG AHMAELRRTRSG AHMAELRRTRSG AHMAELRRTRSG AHMAELRRTKSG GHMQELRRTKSG GHMQELRRTKAG GHMQGLRRTKAG GHMQGLRRTAG GHMQELRRTAG GHMQELRRTSG AHMQELRRTSG AHMQELRRTSG AHMQELRRTSG AHMQELRRTSG AHMQELRRTSG AHMQELRRTSG
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P.furiosus P.abyssi P.horikoshii T.kodakarensis M.kandleri M.jannaschii M.barkeri M.acetivorans M.mazei M.thermoautotrophicum M.burtonii M.stadtmanae M.maripaludis M.hungatei A.fulgidus N.pharaonis H.sp H.marismortui H.walsbyi	150 A V KR R L R A V KR V I R A V KR Q L R A V KR S L R A V KR A L R A V KR A L R A V KR Q L R	160 TR K V Y Y I E V TR K V Y Y I E I TR K V Y Y I E I TR K V Y Y I D V P K K I Y Y I D V P K K I Y Y I D V V K I I Y Y I E V V R T I Y Y I E V V R T I Y Y I E V V R T I Y H L E V V R T I Y E V K L I R K I Y E I E I I R E I H E L E M I R E I Y E M E L T R T V H R L D V S R I H S L D I K R T I E T L D I	17( L E I EGRD \ L E I DGRD \ L E I DGRD \ L E I EGRD \ L E I EGRD \ L E I EGSF \ L E I EGSF \ L E I EGRS \ L E I EGRS \ L E I EGRD \ L E I DGRD \ L E I GRQ \ L E	) / L F R V G V E / L F R V G V E / L F R V G V E / L F R V G C E / L F R V K C E / L F R V V T E / L F R V V T E / L L R V R C E	180 E A G T Y I R S E A G T Y I R S E A G T Y I R S E A G T Y I R S Q A G T Y I R K Q S G T Y I R K E A G T Y I R K E A G T Y I R K E A G T Y I R K Q S G T Y I R K Q S G T Y I R K Q S G T Y I R K E S G T Y I R K	190 LIHHIGLALGVGA LIHHIGLALGVGA LIHHIGLALGVGA LCHDIGEALGVGA LCHDIGEALGCGC LCHDIGLALGCGC VCHDVGEALGAGAGA LCHDIGLALGCGC YCHDIGEALGCGC LCHDIGEALGCGA LCHDIGEALGCGA LCHDIGEALGTGA LCHDIGEALGTGA LCHDIGEALGTGA LCHDIGEALGTGA	200 AHM SE LRR TR SG AHM AE LRR TR SG AHM AE LRR TR SG AHM AE LRR TR SG AHM AE LRR TK SG AHM QE LRR TK SG GHM QE LRR TK AG GHM QE LRR TK AG GHM QE LRR TK AG AHM AE LRR TA VG GHM KQ LRR TG TG AHM QE LRR TR SG AHM QE LRR TA TG AHM GD LRR TG TT
P.furiosus P.abyssi P.horikoshii T.kodakarensis M.kandleri M.jannaschii M.barkeri M.acetivorans M.mazei M.thermoautotrophicum M.burtonii M.stadtmanae M.maripaludis M.hungatei A.fulgidus N.pharaonis H.sp H.marismortui H.walsbyi P.torridus	150 A V KR R L R A V KR V I R A V KR Q L R A V KR S L R A V KR A L R A V KR R L R A V KR Q L R A V S R L R	160 TR KVYYI EV TR KVYYI EI TR KVYYI EI TR KVYYI DV PKKI YYI DV PKKI YYI DV VRTI YYI EV VRTI YYL EV VRTI YHL EV VRTI YEVKL IRKI YEI EI IREI HEL EM IREI YEMEL TR TVHRL DV TR TVHRL DV SRRIHSL DI KRTI ETL DI IREI YNL EL	17( L E I EGRD \ L E I DGRD \ L E I DGRD \ L E I EGRD \ L E I EGRD \ L E I EGSF \ L E I EGSF \ L E I EGRS \ L E I EGRS \ L E I EGRD \ L E I DGRD \ L E	/ L FR VG VE / L FR VG VE / L FR VG VE / L FR VG VE / L FR VG CE / L FR VC CE / L FR VC CE / L R VC CE	180 EAGTYIRS EAGTYIRS EAGTYIRS EAGTYIRK QAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK QSGTYIRK QSGTYIRK QSGTYIRK QSGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK	190 LIHHIGLALGVGA LIHHIGLALGVGA LIHHIGLALGVGA LCHDIGEALGVGA LCHDIGEALGCGA LCHDIGLALGCGA LCHDIGLALGCGA YCHDVGEALGAGA LCHDIGLALGCGA LCHDIGLALGCGA LCHDIGLALGCGA LCHDIGLALGCGA LCHDIGLALGTAA LCHDIGLAVGTGA LCHDIGLAAGTGA	200 AHM SE LRR TR SG AHM AE LRR TK SG GHM QE LRR TK AG GHM QE LRR TK AG GHM QE LRR TK AG GHM QE LRR TA SG AHM AE LRR TA SG AHM QE LRR TR SG AHM QE LRR TA SG AHM ZE LRR TA SG AH
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P.furiosus P.abyssi P.horikoshii T.kodakarensis M.kandleri M.jannaschii M.barkeri M.barkeri M.acetivorans M.mazei M.thermoautotrophicum M.burtonii M.stadtmanae M.maripaludis M.hungatei A.fulgidus N.pharaonis H.sp H.marismortui H.walsbyi P.torridus T.acidophilum T.volcanium	150 A V KR R L R A V KR V I R A V KR Q L R A V S R L R A V S R L R A V S R K V R	160 TR KVYYI EV TR KVYYI EI TR KVYYI EI TR KVYYI DV PKKI YYI DV PKKI YYI DV VRTI YYL EV VRTI YYL EV VRTI YHL EV VRTI YEVKL IRNI YYL DV VRTI YEVKL IRKI YEI EI IREI YEMEL TR TVHRL DV TR TVYDL DV SRRI HSL DI KRTI ETL DI IREI YNL EL IKT YEL DM	17( L E I EGRD \ L E I DGRD \ L E I DGRD \ L E I EGRD \ L E I EGRD \ L E I EGRT \ L E I DGRD \ L E I GRQ \ L E I GRQ \ L E I GRQ \ L E I GRQ \ L E I DFRI \ L E I DFRI \ L E I DFRI \ L E I DFRI \ L E I CRR \ L E	/ L FR VG VE / L FR VG VE / L FR VG VE / L FR VG VE / L FR VG CE / L FR VG CE / L FR VG CE / L FR VG CE / L FR I ACE / L FR VG CE / L FR VC CE / L FR VC CE / L FR VC CE / L FK VC CE / L FK VC CE / L FK VC CE / L FK VC CE	180 EAGTYIRS EAGTYIRS EAGTYIRS CAGTYIRS CAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK CSGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK	190 LIHHIGLALGVGA LIHHIGLALGVGA LIHHIGLALGVGA LCHDIGEALGVGA LCHDIGEALGCGG LCHDIGLALGCGG YCHDVGEALGAGA LCHDIGLALGCGG YCHDIGLALGCGG LCHDIGLALGCGG LCHDIGLALGCGG LCHDIGLALGCGG LCHDIGLALGTGA LCHDIGLAGTGA LCHDIGLAGTGA LCHDIGLAGTGA LCHDIGLAGTGA LCHDIGLAGTGA LCHDIGLAGTGA	200 AH M SE LRR TR SG AH M AE LRR TK AG GH MQE LRR TK AG GH MQE LRR TK AG AH M AE LRR TA VG GH MQE LRR TA VG GH MQE LRR TA SG AH M AE LRR TR SG AH M AE LRR TR SG AH MQE LRR TR SG AH MGD LRR TA TG GH MGD LRR TS TG GQM AE LRR TS TG GQM VD LRR TS TG GQM VD LRR TS TG
P.furiosus P.abyssi P.horikoshii T.kodakarensis M.kandleri M.jannaschii M.barkeri M.barkeri M.acetivorans M.mazei M.thermoautotrophicum M.burtonii M.stadtmanae M.maripaludis M.hungatei A.fulgidus N.pharaonis H.sp H.marismortui H.walsbyi P.torridus T.acidophilum T.volcanium A pernix	150 A V KR R L R A V KR R V I A V KR V I R A V KR Q L R A V S R R L R A V S R R L R A V S R R L R A V S R K V R S V K P A L R	160 TR KVYYI EV TR KVYYI EI TR KVYYI EI TR KVYYI DV PKKI YYI DV PKKI YYI DV VRTI YYL EV VRTI YYL EV VRTI YYL EV VRTI YEV VRTI YEV VRTI YEV VRTI YEV VRTI YEV TR YEL IR I YENEL TR TVHRLDV TR TVYDLDV SRRIHSLDI KRTI ETLDI IR EI YNL EL IKTVYSLDL	17( L E I EGRD \ L E I DGRD \ L E I DGRD \ L E I EGRD \ L E I EGRD \ L E I EGRD \ L E I EGSF \ L E I EGRS \ L E I EGRS \ L E I EGRD \ L E I EGRD \ L E I DGRD \ L E I GRQ \ L E I CGRQ \ L	/ L FR VG VE / L FR VG VE / L FR VG VE / L FR VG VE / L FR VG CE / L FR VC CE / L FR VC CE / L FR VC CE / L FN VC CE / L FN VC CE / L FN VC CE / L FN VC CE	180 EAGTYIRS EAGTYIRS EAGTYIRS EAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK	190 LIHHIGLALGVGA LIHHIGLALGVGA LIHHIGLALGVGA LCHDIGEALGVGA LCHDIGEALGCGG LCHDIGLALGCGG YCHDVGEALGAGA LCHDIGLALGCGG YCHDIGLALGCGG LCHDIGLALGCGG LCHDIGLALGCGG LCHDIGLALGCGG LCHDIGLALGCGG LCHDIGLAGTGA LCHDIGLAGTGA LCHDIGLAGTGA LCHDIGLAGTGA LCHDIGLAGTGA LCHDIGLAGTGA LCHDIGLAGTGA LCHDIGLAGTGA LCHDIGLAGTGA	200 AH M SE LRR TR SG AH M AE LRR TK AG GH MQE LRR TK AG GH MQE LRR TK AG GH MQE LRR TK AG AH M AE LRR TA VG GH MQE LRR TG TG AH M AE LRR TA SG AH M AE LRR TR SG AH MQE LRR TR SG AH MQE LRR TR SG AH MQE LRR TR SG AH MQE LRR TR TG GH MGD LRR TA TG AH MGD LRR TA TG AH MGD LRR TS TG GQM VD LRR TS TG GQM VD LRR IS TG GQM VD LRR IS TG
P.furiosus P.abyssi P.horikoshii T.kodakarensis M.kandleri M.jannaschii M.barkeri M.barkeri M.acetivorans M.mazei M.thermoautotrophicum M.burtonii M.stadtmanae M.maripaludis M.hungatei A.fulgidus N.pharaonis H.sp H.marismortui H.walsbyi P.torridus T.acidophilum T.volcanium A.pernix	150 A V KR R L R A V KR R V I A V KR V I R A V KR Q L R A V S R R L R A V S R S L R A V S R K V R A V S R K R L R A V S R K L R	160 TR KVYYI EV TR KVYYI EI TR KVYYI EI TR KVYYI DV PKKI YYI DV PKKI YYI DV VRTI YYI EV VRTI YYL EV VRTI YHLEV VRTI YHLEV VRTI YEVKL IRKI YEIEI IREI HELEM IREI YEMEL TR TVHRLDV TR TVYDLDV SRRI HSLDI KRTI ETLDI IREI YNLEL IKT YSLDL IKT YELDM TRR VFRI EL	17( L E I EGRD \ L E I DGRD \ L E I DGRD \ L E I EGRD \ L E I EGRD \ L E I EGRD \ L E I EGSF \ L E I EGSF \ L E I EGRS \ L E I EGRD \ L E I EGRD \ L E I DGRD \ L E I GRQ \ L E I	/ L FR VG VE / L FR VG VE / L FR VG VE / L FR VG VE / L FR VG CE / L FR VC CE / L FR VC CE / L FR VC CE / L FR VC CE / L FN VC CE	180 EAGTYIRS EAGTYIRS EAGTYIRS EAGTYIRS CAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK CSGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK	190 LIHHIGLALGVGA LIHHIGLALGVGA LIHHIGLALGVGA LCHDIGEALGVGA LCHDIGEALGCGG LCHDIGLALGCGG YCHDVGEALGAGA LCHDIGLALGCGG YCHDVGEALGAGA LCHDIGLALGCGG YCHDIGEALGCGA LCHDIGLALGCGG LCHDIGLALGCGG LCHDIGEALGTGA LCHDIGLAGTGA LCHDIGLAGTGA LCHDIGLAGTGA LCHDIGLAGTGA LCHDIGLAGTGA LCHDIGLAGTGA LCHDIGLAGTGA LCHDIGLAGTGA LCHDIGLAGTGA	200 AH M SE LRR TR SG AH M AE LRR TR SG GH M QE LRR TK AG GH M QE LRR TR SG AH M QE LRR TR SG GH M GD LRR TS TG GG M VD LRR TS TG GG M VD LRR IS TG
P.furiosus P.abyssi P.horikoshii T.kodakarensis M.kandleri M.jannaschii M.barkeri M.barkeri M.acetivorans M.mazei M.thermoautotrophicum M.burtonii M.stadtmanae M.maripaludis M.hungatei A.fulgidus N.pharaonis H.sp H.marismortui H.walsbyi P.torridus T.acidophilum T.volcanium A.pernix P.aerophilum	150 A V KR R L R A V KR V I R A V KR Q L R A V SR R L R A V SR R L R A V SR K V R S V KR Q L R A V SR K V R	160 TR KVYYI EV TR KVYYI EI TR KVYYI EI TR KVYYI DV PKKI YYI DV PKKI YYI DV VRTI YYL EV VRTI YYL EV VRTI YHL EV VRTI YHL EV VRTI YHL EV VRTI YEVKL IRKI YEI EI IREI HEL EM IREI YEMEL TR TVHRL DV SRRI HSL DI KRTI ETL DI IREI YNL EL IKT YSL DL IKTI YEL DM TRR VFRI EL TRR VYSL DL	17( L EI EGRD \ L EI DGRD \ L EI DGRD \ L EI EGRD \ L EI EGRD \ L EI EGRD \ L EI EGSF \ L EI EGTS \ L EI EGRT \ L EI EGRD \ L EI DGRD \ L EI DGRD \ L EI DGRD \ L EI DGRD \ L EI GRQ \ L EI GRQ \ L EX CRR \ L EWD SD AQQ \ L EWD SD AQQ \ L EW DEKF \ L EK - KDKI \ L EY - TGKY \ L EY TGKY \ L EY DGRY \ L EY DGRY \ L EY CRY \ L EY CY	/ L FR VG VE / L FR VG VE / L FR VG VE / L FR VG VE / L FR VG CE / L FR VC CE / L FR VC CE / L FR VC CE / L FN VC CE	180 EAGTYIRS EAGTYIRS EAGTYIRS EAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRT ESGTYIRT ESGTYIRT	190 LIHHIGLALGVGA LIHHIGLALGVGA LIHHIGLALGVGA LCHDIGEALGVGA LCHDIGEALGCGG LCHDIGLALGCGG VCHDVGEALGAGAGA LCHDIGLALGCGG YCHDVGEALGAGAGA LCHDIGLALGCGG YCHDIGEALGCGA LCHDIGLALGCGG LCHDIGLALGCGG LCHDIGEALGTGA LCHDIGEALGTGA LCHDIGEALGTGA LCHDIGEALGTGA LCHDIGEALGTGA LCHDIGEALGTGA LCHDIGEALGTGA LCHDIGEALGTGA LCHDIGEALGTGA LCHDIGEALGTGA LCHDIGEALGTGA LCHDIGEALGTGA LCHDIGEALGTGA LCHDIGEALGTGA LCHDIGEALGTGA	200 AH M SE L RR TR SG AH M AE L RR TK SG GH MQE L RR TK AG GH MQE L RR TA VG GH MQE L RR TA SG AH MQE L RR TR SG AH MQE L RR TR TG GH MGP L RR TR TG GH MGP L RR TR TG GH MGD L RR TA TG GAM VE L RR TR TG GAM VE L RR TS TG GQM VD L RR TS TG GQM VD L RR I STG AH MRE L RR I AVS
P.furiosus P.abyssi P.horikoshii T.kodakarensis M.kandleri M.jannaschii M.barkeri M.acetivorans M.mazei M.thermoautotrophicum M.burtonii M.stadtmanae M.maripaludis M.hungatei A.fulgidus N.pharaonis H.sp H.marismortui H.walsbyi P.torridus T.acidophilum T.volcanium A.pernix P.aerophilum N.equitans	150 A V KR R L R A V KR V I R A V KR Q L R A V KR AL R A V KR Q L R A V KR Q L R A V SR R L R A V SR K V R A V SR K V R A V SR K V R A V SR K R A V SR R L R A V SR K R A V SR R L R A V SR K R A V SR R L R A V SR K R R A V SR R R R A V SR K R R A V SR R R R R A V SR R R R R R R R R R R R R R R R R R	160 TR KVYYI EV TR KVYYI EI TR KVYYI EI TR KVYYI DV PKKI YYI DV PKKI YYI DV VRTI YYL EV VRTI YHLEV VRTI YHLEV VRTI YHLEV VRTI YHLEV VRTI YEVKL IRKI YEIEI IREI HELEM IREI YEMEL TR TVHRLDV TR TVYDLDV SRRI HSLDI KRTI ETLDI IREI YNLEL IKTI YELDM TRR VFRI EL TRR VYSLDL KKKVYCI KI	17( L EI EGRD \ L EI DGRD \ L EI DGRD \ L EI DGRD \ L EI EGRD \ L EI EGRD \ L EI EGSF \ L EI EGTS \ L EI EGRD \ L EI DGRD \ L EX KDR L \ L EK KDR L \ L EK KDR L \ L EK CGRY \ L EI DGRY \ L EI DGRY \ L EN DGRY \ L EN L CKY \ L EN L CKY \ L EN L CKY \ L EN DGKY \ L EI DGKD \	/ L FR VG VE         / L FR VG VE         / L FR VG VE         / L FR VG CE         / L FR VC CE         / L FR VC CE         / L FN VC CE	180 EAGTYIRS EAGTYIRS EAGTYIRS CAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK CSGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRT ESGTYIRT ESGTYIRT	190 LIHHIGLALGVGA LIHHIGLALGVGA LIHHIGLALGVGA LIHHIGLALGVGA LCHDIGEALGTSA LCHDIGLALGCGG LCHDIGLALGCGG YCHDVGEALGAGAGA LCHDIGLALGCGG YCHDIGEALGCGA LCHDIGLALGCGG YCHDIGEALGTSA LCHDIGLAGTGA LCHDIGLAVGTGG LCHDIGLAVGTGG LCHDIGLAGTGA LCHDIGLAGTGA LCHDIGLAGTGA LCHDIGLAGTGA LCHDIGLAGTGA LCHDIGLAGTGA LCHDIGLAGTGA LCHDIGLAGTGA LCHDIGLAGTGA LCHDIGLAGTGA LCHDIGLAGTGA LCHDIGLAGTGA LCHDIGLAGTGA LCHDIGVVGKGG LCTDIGVVGKGGA LCHDIGLVLGVGA	200 AH M SE LRR TR SG AH M AE LRR TK AG GH MQE LRR TK AG GH MQE LRR TK AG GH MQE LRR TK AG GH MQE LRR TA SG AH MAE LRR TA SG AH MQE LRR TR SG AH MQE LRR TR SG AH MQE LRR TR SG AH MQE LRR TR TG GAM VE LRR TR TG GAM VE LRR TR TG GAM VE LRR TR TG AH MGD LRR TA TG GQM VD LRR TS TG GQM VD LRR I STG GQM VD LRR I STG AH MRE LRR I AVS AH MQE LRR I KSG
P.furiosus P.abyssi P.horikoshii T.kodakarensis M.kandleri M.jannaschii M.barkeri M.acetivorans M.mazei M.thermoautotrophicum M.burtonii M.stadtmanae M.maripaludis M.hungatei A.fulgidus N.pharaonis H.sp H.marismortui H.walsbyi P.torridus T.acidophilum T.volcanium A.pernix P.aerophilum N.equitans S.cerevisiae_yeast	150 A V KR R L R A V KR V I R A V KR Q L R A V KR AL R A V KR AL R A V KR R L R A V KR R L R A V SR R L R A V SR R L R A V SR K V R A V SR K R A V SR AL R A V KR Q L R A V KR Q L R	160 TR KVYYI EV TR KVYYI EI TR KVYYI EI TR KVYYI DV PKKI YYI DV PKKI YYI DV VRTI YYL EV VRTI YYL EV VRTI YHL EV VRTI YHL EV VRTI YHL EV VRTI YHL EV VRTI YEVKL IRKI YEI EI IREI HEL EM IREI YEMEL TR TVHRL DV TR TVHRL DV SRRIHSL DI KRTI ETL DI IREI YNL EL IKTI YEL DM TRRVFRIEL TRRVFRIEL TRRVYSL DL KKKVYCI KI VRTI YESNL	17( L E I EGRD \ L E I DGRD \ L E I DGRD \ L E I DGRD \ L E I EGRD \ L E I EGRS \ L E I EGSF \ L E I EGTS \ L E I EGRS \ L E I DGQD \ L E I DGQD \ L E I DGQD \ L E I DGRD \ L E V DEKF \ L E K KDR L \ L E K KDR L \ L E K TGKY \ L E I - DGRD \ L E I DGRD \ L E I DGRD \ L E I DGRD \ L E I DGKD \ L E I	/ L FR VG VE         / L FR VG CE         / L FR VC CE         / L FR VS CE         / L FR VS CE         / L FR VS CE	180 EAGTYIRS EAGTYIRS EAGTYIRS CAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK CSGTYIRK CSGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRT ESGTYIRT ESGTYIRT ESGTYIRT	190 LIHHIGLALGVGA LIHHIGLALGVGA LIHHIGLALGVGA LIHHIGLALGVGA LCHDIGEALGVGA LCHDIGLALGCGG LCHDIGLALGCGG VCHDVGEALGAGA LCHDIGLALGCGG VCHDIGLALGCGG VCHDIGLALGCGG LCHDIGLALGCGG LCHDIGLALGTGA LCHDIGLAVGTGG LCHDIGLAVGTGG LCHDIGLAVGTGG LCHDIGLAVGTGG LCHDIGLAVGTGG LCHDIGLAVGTGG LCHDIGLAVGTGG LCHDIGLAGTGA LCHDIGLAGTGA LCHDIGLAGTGA LCHDIGLAGTGA LCHDIGLAGTGA LCHDIGLAGTGA LCHDIGVVGGKGG LCTDIGVVGGKGG LCTDIGVVGGKGG LCHDIGLVGVGA	200 AHM SE LRR TR SG AHM AE LRR TK SG GHM QE LRR TK AG GHM QE LRR TK AG GHM QE LRR TK AG GHM QE LRR TA VG GHM KQ LRR TG TG GHM KQ LRR TG TG GAM VE LRR TR SG AHM QE LRR TR SG AHM QE LRR TR SG AHM QE LRR TR TG GAM VE LRR TS TG AHM GD LRR TS TG GAM VE LRR I STG AHM RE LRR I AVS AHM QE LRR VR SG
P.furiosus P.abyssi P.horikoshii T.kodakarensis M.kandleri M.jannaschii M.barkeri M.acetivorans M.mazei M.thermoautotrophicum M.burtonii M.stadtmanae M.maripaludis M.hungatei A.fulgidus N.pharaonis H.sp H.marismortui H.walsbyi P.torridus T.acidophilum T.volcanium A.pernix P.aerophilum N.equitans S.cerevisiae_yeast T.thermophila	150 A V KR R L R A V KR V I R A V KR Q L R A V KR AL R A V KR AL R A V KR AL R A V KR Q L R A V SR R L R A V SR R L R A V SR R L R A V SR K V R A V SR K R A V SR C A V SR C C A V SR C C A V SR C C C C C C C C C C C C C C C C C C C	160 TR K V Y Y I E V TR K V Y Y I E I TR K V Y Y I E I TR K V Y Y I D V PKKI YY I D V PKKI YY I D V VR TI YY L E V VR TI YY L E V VR TI YY L E V VR TI YHLE V VR TI YHLE V VR TI YE V KL I R I Y E V L E I I R E I HE L E M I R E I YE K L I R T V H R L D V VR T I YE V L D V SR R I H S L D I KR T I E T L D I I R E I YN L E L I K T VY S L D L I K T Y S L D L I K T Y S L D L KK K V Y C I K I VR T I YE S K L	17( L EI EGRD \ L EI DGRD \ L EI DGRD \ L EI EGRD \ L EI EGRD \ L EI EGSF \ L EI EGSF \ L EI EGSF \ L EI EGRS \ L EI EGRS \ L EI DGRD \ L EI DGRD \ L EI DGRD \ L EI DGRD \ L EN DGRD \ L EX CRQ \ L EVD SD AQQ \ L EWD SD AQQ \ L EW TGKY \ L EK KDR L \ L EK KDR L \ L EK CGR \ L EN - DGRD \ L EN - DGRD \ L EN - DGRD \ L EN - CGRD \ L EN	/ L FR VG VE / L FR VG VE / L FR VG VE / L FR VG VE / L FR VG CE / L FR VC CE	180 EAGTYIRS EAGTYIRS EAGTYIRS CAGTYIRS CAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK CSGTYIRK CSGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRT ESGTYIRT EAGTYMRT EAGTYRT	190 LIHHIGLALGVGA LIHHIGLALGVGA LIHHIGLALGVGA LCHDIGEALGVGA LCHDIGEALGVGA LCHDIGLALGCGG LCHDIGLALGCGG YCHDVGEALGAGA LCHDIGLALGCGG YCHDIGEALGCGA LCHDIGLALGCGG CYCHDIGEALGTGA LCHDIGLALGTGA LCHDIGLAVGTGG LCHDIGLAGTGA LCHDIGLAGTGA LCHDIGLAGTGA LCHDIGLAGTGA LCHDIGLAGTGA LCHDIGVVGSKGG LCHDIGVVGSKGG LCTDIGYVGSKGG LCTDIGYVGGKGG LCTDIGYVG	200 AHM SE LRR TR SG AHM AE LRR TK SG GHM QE LRR TK AG GHM QE LRR TA SG AHM QE LRR TR SG AHM QE LRR TR SG AHM QE LRR TR SG GHM QE LRR TR SG GHM GP LRR TR TG GHM GD LRR TA TG GHM GD LRR TA TG GGM VD LRR TS TG GGM VD LRR I STG GGM VD LRR I STG GGM VD LRR I STG GGM VD LRR I STG GGM VD LRR I STG GAM RE LRR I AVS GHM QE LRR VR SG GHM QE LRR VR SG
P.furiosus P.abyssi P.horikoshii T.kodakarensis M.kandleri M.jannaschii M.barkeri M.acetivorans M.mazei M.thermoautotrophicum M.burtonii M.stadtmanae M.maripaludis M.burtonii M.stadtmanae M.maripaludis M.hungatei A.fulgidus N.pharaonis H.sp H.marismortui H.walsbyi P.torridus T.acidophilum T.volcanium A.pernix P.aerophilum N.equitans S.cerevisiae_yeast T.thermophila D melanogaster fruitfly	150 A V KR R L R A V KR V I R	160 TR KVYYI EV TR KVYYI EI TR KVYYI EI TR KVYYI DV PKKI YYI DV PKKI YYI DV PKKI YYI EV VR TI YYL EV VR TI YYL EV VR TI YHL EV VR TI YHL EV VR TI YEVKL IR KI YEI EI IR EI HEL EM IR EI YENEL TR TVHRL DV TR TVYD LD V SRR I HSL DI KR TI ETL DI IR EI YNL EL IKT VYSL DL IKT YSL DL KKKVYC I KI VR TI YESKL VR TI YESKL	17( L EI EGRD \ L EI DGRD \ L EI DGRD \ L EI EGRD \ L EI EGRD \ L EI EGSF \ L EI EGSF \ L EI EGSF \ L EI EGRS \ L EV DGRD \ L EI EGRE \ L EI DGRD \ L EI DGRD \ L EI DGRD \ L EI DGRD \ L EX ARR \ L EVD SD AQQ \ L EWD SD AQQ \ L EW TGKY \ L EK KDR L \ L EK KDR L \ L EK CGR \ L EY TGKY \ L EI DGRD \ L EY - TGKY \ L EI DGRD \ L EY - TGKY \	/ L FR VG VE / L FR VG VE / L FR VG VE / L FR VG VE / L FR VG CE / L FR VC CE	180 EAGTYIRS EAGTYIRS EAGTYIRS EAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK CSGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRT ESGTYIRT ESGTYIRT ESGTYIRT	190 LIHHIGLALGVGA LIHHIGLALGVGA LIHHIGLALGVGA LCHDIGEALGVGA LCHDIGEALGCGA LCHDIGLALGCGA LCHDIGLALGCGA LCHDIGLALGCGA YCHDVGEALGAGA LCHDIGLALGCGA LCHDIGLALGCGA LCHDIGLALGCGA LCHDIGLALGCGA LCHDIGLALGCGA LCHDIGLALGCGA LCHDIGEALGTAA LCHDIGLAAGTAA LCHCAA	200 AHM SE LRR TR SG AHM AE LRR TK SG GHM QE LRR TK SG GHM QE LRR TK AG GHM QE LRR TK AG GHM QE LRR TK AG GHM QE LRR TK AG GHM QE LRR TA SG AHM QE LRR TR SG AHM QE LRR TR SG AHM QE LRR TR SG GHM QE LRR TR SG GHM QE LRR TR SG GHM GD LRR TA TG GHM GD LRR TA TG GHM GD LRR TA TG GGM VD LRR TS TG GGM VD LRR I STG GGM QE LRR VR SG GGM QE LRR VR SG
P.furiosus P.abyssi P.horikoshii T.kodakarensis M.kandleri M.jannaschii M.barkeri M.acetivorans M.mazei M.thermoautotrophicum M.burtonii M.stadtmanae M.maripaludis M.hungatei A.fulgidus N.pharaonis H.sp H.marismortui H.walsbyi P.torridus T.acidophilum T.volcanium A.pernix P.aerophilum N.equitans S.cerevisiae_yeast T.thermophila D.melanogaster_fruitfly	150 A V KR R L R A V KR V I R A V KR Q L R	160 TR KVYYI EV TR KVYYI EI TR KVYYI EI TR KVYYI DV PKKI YYI DV PKKI YYI DV PKKI YYI EV VR TI YYLEV VR TI YYLEV VR TI YHLEV VR TI YEVKL IR KI YEI EI IR EI HELEM IR EI HELEM IR EI YENEL TR TVHRLDV TR TVHRLDV SRR I HSLDI KR TI ETLDI IR EI YNLEL IKT YSLDL KK VYCI KI VR TI YESNL VR TI YESNL VR TI YESKL VR TI YESKL	17( L E I EGRD \ L E I DGRD \ L E I DGRD \ L E I EGRD \ L E I EGRD \ L E I EGSF \ L E I EGSF \ L E I EGST \ L E I EGRT \ L E I EGRD \ L E I DGRD \ L E X KDR \ L E VD SD AQQ \ L E X KDR \ L E X KDR \ L E X TGKY \ L E X TGKY \ L E X TGKY \ L E X DGRD \ L E X DGRD \ L E X CGR \	/ L FR VG VE / L FR VG VE / L FR VG VE / L FR VG VE / L FR VG CE / L FR VC CE	180 EAGTYIRS EAGTYIRS EAGTYIRS EAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK CSGTYIRK CSGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRT ESGTYIRT ESGTYIRT ESGTYIRT ESGTYRT EAGTYMRT EAGTYMRT	190 LIHHIGLALGVGA LIHHIGLALGVGA LIHHIGLALGVGA LCHDIGEALGVGA LCHDIGEALGCGA LCHDIGLALGCGA LCHDIGLALGCGA LCHDIGLALGCGA LCHDIGLALGCGA YCHDVGEALGAGA LCHDIGLALGCGA LCHDIGLALGCGA LCHDIGLALGCGA LCHDIGLALGCGA LCHDIGLALGCGA LCHDIGLALGCGA LCHDIGLALGCGA LCHDIGLACGTA LCHDIGLAAGTA LCHO LCHDIGLAAGTA LCHO	200 AH M SE LRR TR SG AH M AE LRR TK AG GH MQE LRR TK AG GH MQE LRR TK AG GH MQE LRR TK AG GH MQE LRR TA VG GH MQE LRR TA SG AH MAE LRR TR SG AH MQE LRR TR SG GQM VD LRR TS TG GQM VD LRR TS TG GQM VD LRR TS TG GQM VD LRR TS TG GQM VD LRR SG GH MQE LRR VR SG GH MQE LRR VR SG GH MQE LRR VR SG GH M ELRR VR SG GH M ELRR VR SG GH M ELRR VR SG GQM LE LRR VR SG
P.furiosus P.abyssi P.horikoshii T.kodakarensis M.kandleri M.jannaschii M.barkeri M.barkeri M.acetivorans M.mazei M.thermoautotrophicum M.burtonii M.stadtmanae M.maripaludis M.hungatei A.fulgidus N.pharaonis H.sp H.marismortui H.walsbyi P.torridus T.acidophilum T.volcanium A.pernix P.aerophilum N.equitans S.cerevisiae_yeast T.thermophila D.melanogaster_fruitfly M.musculus_mouse	150 A V KR R L R A V KR V I R A V KR Q L R A V SR R L R A V SR C L R A V KR Q L R	160 TR KVYYI EV TR KVYYI EI TR KVYYI EI TR KVYYI DV PKKI YYI DV PKKI YYI DV PKKI YYI EV VR TI YYL EV VR TI YYL EV VR TI YYL EV VR TI YEVKL IRKI YEI EI IREI HELEM IREI YEMEL TR TVHRLDV VR TI YEVKL IRKI YEI EI IREI YEMEL TR TVHRLDV SRR I HSLDI KR TI ETLDI IREI YNLEL IKT YSLDL KKT YSLDL KKVYCI KI VR TI YESNL VR TI YESKL VR TI YESKL VR TI YESKL	17( L E I EGRD \ L E I DGRD \ L E I DGRD \ L E I EGRD \ L E I EGRD \ L E I EGRS \ L E I EGSF \ L E I EGSF \ L E I EGSF \ L E I EGRS \ L E I EGRS \ L E I DGRD \ L E I	/ L FR VG VE / L FR VG VE / L FR VG VE / L FR VG VE / L FR VG CE / L FR VG CE	180 EAGTYIRS EAGTYIRS EAGTYIRS EAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK CSGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRT EAGTYARK EAGTYART EAGTYART EAGTYART EAGTYART EAGTYART	190 LIHHIGLALGVGA LIHHIGLALGVGA LIHHIGLALGVGA LCHDIGEALGVGA LCHDIGEALGCGA LCHDIGLALGCGA LCHDIGLALGCGA LCHDIGLALGCGA LCHDIGLALGCGA LCHDIGLALGCGA LCHDIGLALGCGA LCHDIGLALGCGA LCHDIGLALGCGA LCHDIGLALGCGA LCHDIGLALGCGA LCHDIGLALGCGA LCHDIGLALGTA LCHDIGLAGTA LCHDIGLAGTA LCHDIGLAGTA LCHDIGLAGTA LCHDIGLAGTA LCHDIGLAGTA LCHDIGLAGTA LCHDIGLAGTA LCHDIGLAGTA LCHDIGLAGTA LCHDIGLAGTA LCHDIGVGGA LCHDIGVGGA LCHDIGLAGTA LCHDIGVGGA LCHDIGVGGA LCHDIGVGGA LCHDIGVGGA LCHDIGVGGA LCHDIGVGGA LCHDIGVGGA LCHLGCGA LCHLGCGA LCHLGALGGA LCHLGALGGA LCHLGALGGA LCHLGALGGA LCHLGALGGA LCHLGALGAA	200 AH M SE LRR TR SG AH M AE LRR TR SG GH MQE LRR TK AG GH MQE LRR TK AG GH MQE LRR TK AG GH MQE LRR TK AG AH MAE LRR TA VG GH MQE LRR TR SG AH MAE LRR TA SG AH MQE LRR TR SG GM VD LRR SATT GQ M AE LRR TR SG GM VD LRR SG AH MQE LRR VR SG GH MEE LRR VR SG GM LE LRR VR SG GQ M LE LRR VR SG GQ M LE LRR VR SG GQ M LE LRR VR SG
P.furiosus P.abyssi P.horikoshii T.kodakarensis M.kandleri M.jannaschii M.barkeri M.barkeri M.acetivorans M.mazei M.thermoautotrophicum M.burtonii M.stadtmanae M.maripaludis M.hungatei A.fulgidus N.pharaonis H.sp H.marismortui H.walsbyi P.torridus T.acidophilum T.volcanium A.pernix P.aerophilum N.equitans S.cerevisiae_yeast T.thermophila D.melanogaster_fruitfly M.musculus_mouse H.sapiens_human	150 A V KR R L R A V KR V I R A V KR Q L R A V SR R L R A V SR C L R A V KR Q L R	160 TR KVYYI EV TR KVYYI EI TR KVYYI EI TR KVYYI DV PKKI YYI DV PKKI YYI DV VRTI YYL EV VRTI YYL EV VRTI YYL EV VRTI YEVKU IRNI YYL DV VRTI YEVKL IRKI YEI EI IREI HELEM IREI YEMEL TR TVHRL DV TR TVYDL DV SRRIHSL DI KRTI ETL DI IREI YNL EL IKTVYSL DL KRTI ETL DI IREI YNL EL IKTVYSL DL KKVYCI KI VRTI YESNL VRTI YESKL VRTI YESKM VRTI YESKM	17( L E I EGRD \ L E I DGRD \ L E I DGRD \ L E I EGRD \ L E I EGRD \ L E I EGRT \ L E I DGRD \ L E I -	/ L FR VG VE / L FR VG VE / L FR VG VE / L FR VG VE / L FR VG CE / L FR VC CE	180 E A G T Y I R S E A G T Y I R S E A G T Y I R S E A G T Y I R S C A G T Y I R S C A G T Y I R K E A G T Y I R K E A G T Y I R K E A G T Y I R K C S G T Y I R K C S G T Y I R K E S G T Y I R T E A G T Y N R T E A G T Y I R T	190 LIHHIGLALGVGA LIHHIGLALGVGA LIHHIGLALGVGA LIHHIGLALGVGA LCHDIGEALGVGA LCHDIGEALGCGC LCHDIGLALGCGC VCHDIGLALGCGC YCHDVGEALGAGAGA LCHDIGLALGCGC YCHDIGEALGCGC YCHDIGEALGTGA LCHLGEALGTGA LCHLGEALGTGA LCHLGEALGTGA LCHLGALLGTGA LCHLGALLGTGA LCHLGALLGTGA LCHLGALLGTGA LCHLGALLGTGA LCHLGALLGTGA LCHLGALLGTA LCHLGALLGTA LCHLGALLGAAGTGA	200 AH M SE LRR TR SG AH M AE LRR TR SG GH MQE LRR TK AG GH MQE LRR TK AG GH MQE LRR TK AG GH MQE LRR TK AG AH MAE LRR TA VG GH MQE LRR TA SG AH MAE LRR TR SG AH MQE LRR TR SG AH MQE LRR TR SG GH MGP LRR TR SG GH MGD LRR TS TG GAM VE LRR TR SG GAM VE LRR SG GAM VE LRR TR SG GAM VE LRR TR SG GAM VE LRR VR SG GAM VE LRR VR SG GAM E LRR VR SG
P.furiosus P.abyssi P.horikoshii T.kodakarensis M.kandleri M.jannaschii M.barkeri M.barkeri M.acetivorans M.mazei M.thermoautotrophicum M.burtonii M.stadtmanae M.maripaludis M.hungatei A.fulgidus M.hungatei A.fulgidus N.pharaonis H.sp H.marismortui H.walsbyi P.torridus T.acidophilum T.volcanium A.pernix P.aerophilum N.equitans S.cerevisiae_yeast T.thermophila D.melanogaster_fruitfly M.musculus_mouse H.sapiens_human Interaction sites	150 A V KR R L R A V KR V I R A V KR Q L R A V SR R L R R L R A V SR R L R R L R A V SR R L R R L R R R R R R R R R R R R R	160 TR KVYYI EV TR KVYYI EI TR KVYYI EI TR KVYYI DV PKKI YYI DV PKKI YYI DV VRTI YYL EV VRTI YYL EV VRTI YYL EV VRTI YEV VRTI YEV VRTI YEV VRTI YEV VRTI YEV VRTI YEV VRTI YEV VRTI YEU IR I YEL IR VFRI EL TR VFRI EL TR VFRI EL TR VFRI EL VRTI YES KL VRTI YES KL VRTI YES KM VRTI YES KM	17( L E I EGRD \ L E I DGRD \ L E I DGRD \ L E I EGRD \ L E I EGRD \ L E I EGRD \ L E I EGRS \ L E I EGRD \ L E I DGRD \ L E I -	/ L FR VG VE / L FR VG VE / L FR VG VE / L FR VG VE / L FR VG CE / L FR VC CE	180 EAGTYIRS EAGTYIRS EAGTYIRS EAGTYIRS EAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRT EAGTYMRT EAGTYMRT EAGTYIRT EAGTYIRT EAGTYIRT	190 LIHHIGLALGVGA LIHHIGLALGVGA LIHHIGLALGVGA LCHDIGEALGVGA LCHDIGEALGCGG LCHDIGLALGCGG VCHDIGLALGCGG YCHDVGEALGAGAGA LCHDIGLALGCGG YCHDIGEALGCGG LCHDIGLALGCGG LCHDIGLALGCGG LCHDIGLALGCGG LCHDIGEALGTGA LCHDIGEALGTGA LCHDIGLAGTGA LCHDIGLAGGTGA LCHLGLAGGTGA	200 AH M SE LRR TR SG AH M AE LRR TR SG GH MQE LRR TK AG GH MQE LRR TK AG GH MQE LRR TK AG GH MQE LRR TK AG AH M AE LRR TA VG GH MQE LRR TA SG AH M AE LRR TR SG AH M AE LRR TR SG AH MQE LRR TR SG GH MGP LRR TR SG GH MGP LRR TR TG GH MGD LRR TA TG GH MGD LRR TA TG GH MGD LRR TS TG GAM VD LRR TS TG GAM VD LRR TS TG GAM VD LRR IS TG GAM NE LRR I AVS AH MQE LRR VR SG GH MEE LRR VR SG GH MEE LRR VR SG GGM QE LRR VR SG
P.furiosus P.abyssi P.horikoshii T.kodakarensis M.kandleri M.jannaschii M.barkeri M.acetivorans M.mazei M.thermoautotrophicum M.burtonii M.stadtmanae M.maripaludis M.hungatei A.fulgidus N.pharaonis H.sp H.marismortui H.walsbyi P.torridus T.acidophilum T.volcanium A.pernix P.aerophilum N.equitans S.cerevisiae_yeast T.thermophila D.melanogaster_fruitfly M.musculus_mouse H.sapiens_human Interaction sites DC mutations	150 A V KR R L R A V KR R V I A V KR V I R A V KR Q L R A V SR R L R R R L R A V SR R L R R R R R R R R R R R R R R R R	160 TR KVYYI EV TR KVYYI EI TR KVYYI EI TR KVYYI DV PKKI YYI DV PKKI YYI DV VRTI YYL EV VRTI YYL EV VRTI YHLEV VRTI YHLEV VRTI YEVKL IRKI YEIEI IREI HELEM IREI YEMEL TRTVHRLDV TRTVYDLDV SRRIHSLDI KRTI ETLDI IREI YNLEL IKTVYSLDL IKTI YELDM TRR VFRIEL TRR VFRIEL TRR VFRIEL TRR VFRIEL KKVYCI KI VRTI YESKL VRTI YESKM VRTI YESKM	17( L E I EGRD \ L E I DGRD \ L E I DGRD \ L E I EGRD \ L E I EGRD \ L E I EGRD \ L E I EGRS \ L E I DGRD \ L E S ARR \ L E VD SD AQQ \ L E WD SD AQQ \ L E WD SD AQQ \ L E W DGKD \ L E Y - TGKY \ L E I DGKD \ L E Y N PEKKMO I E YN PEKKMO I E YD PERR L O I E YD PERR L O	/ L FR VG VE / L FR VG VE / L FR VG VE / L FR VG VE / L FR VG CE / L FR VC CE	180 E A G T Y I R S E A G T Y I R S E A G T Y I R S E A G T Y I R S C A G T Y I R K E S G T Y I R T E S G T Y	190 LIHHIGLALGVGA LIHHIGLALGVGA LIHHIGLALGVGA LCHDIGEALGVGA LCHDIGEALGCGG LCHDIGLALGCGG VCHDIGLALGCGG YCHDVGEALGAGA LCHDIGLALGCGG YCHDIGLALGCGG YCHDIGLALGCGG LCHDIGLALGCGG LCHDIGLALGCGG LCHDIGLALGCGG LCHDIGLALGTGA LCHDIGLAGTGA LCHDIGLAGTGA LCHDIGLAGTGA LCHDIGLAGGTGA LCHLGLAGTGA LCHLGCGGA LCHLGLLGGTGGA LCHLGLLGGTGGA LCHLGLLGGTGGA	200 AH M SE LRR TR SG AH M AE LRR TK AG GH MQE LRR TK AG GH MQE LRR TK AG GH MQE LRR TK AG GH MQE LRR TA VG GH MQE LRR TA SG AH M AE LRR TR SG AH M AE LRR TR SG AH MQE LRR TR SG AH MQE LRR TR SG AH MQE LRR TR TG GH MGD LRR TS TG GH MGD LRR TS TG GAM VE LRR SA TT SQM AE LRR I AV S GAM VE LRR SG GAM ME LRR VR SG GAM QE LRR VR SG
P.furiosus P.abyssi P.horikoshii T.kodakarensis M.kandleri M.jannaschii M.barkeri M.barkeri M.acetivorans M.mazei M.thermoautotrophicum M.burtonii M.stadtmanae M.maripaludis M.hungatei A.fulgidus N.pharaonis H.sp H.marismortui H.walsbyi P.torridus T.acidophilum T.volcanium A.pernix P.aerophilum N.equitans S.cerevisiae_yeast T.thermophila D.melanogaster_fruitfly M.musculus_mouse H.sapiens_human Interaction sites DC mutations	150 A V KR R L R A V KR R V I A V KR V I R A V KR Q L R A V SR R L R A V KR Q L R	160 TR KVYYI EV TR KVYYI EI TR KVYYI EI TR KVYYI DV PKKI YYI DV PKKI YYI DV VRTI YYL EV VRTI YYL EV VRTI YHLEV VRTI YHLEV VRTI YEV VRTI YEV KTI YEL IR I YELEI IR EI HELEM IR EI YEMEL TR TVHRLDV TR TVYDLDV SRRI HSLDI KRTI ETLDI IREI YNLEL IKT VYSLDL IKTI YELDM TRR VFRI EL TRR VYSLDL KKVYCI KI VRTI YESKL VRTI YESKL VRTI YESKM VRTI YESKM	17( L E I EGRD \ L E I DGRD \ L E I DGRD \ L E I EGRD \ L E I EGRD \ L E I EGRS \ L E I DGRD \ L E I -	/ L FR VG VE / L FR VG VE / L FR VG VE / L FR VG VE / L FR VG CE / L FR I ACE / L FR VG CE / L FR VG CE / L FR VG CE / L FR VC CE	180 EAGTYIRS EAGTYIRS EAGTYIRS EAGTYIRS EAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRT EAGTYARK EAGTYARK EAGTYARK EAGTYAR ESGTYIRT EAGTYAR EAGTYIRT EAGTYIRT	190 LIHHIGLALGVGA LIHHIGLALGVGA LIHHIGLALGVGA LCHDIGEALGVGA LCHDIGEALGCGG LCHDIGLALGCGG VCHDIGLALGCGG YCHDVGEALGAGA LCHDIGLALGCGG YCHDIGLALGCGG LCHDIGLALGCGG LCHDIGLALGCGG LCHDIGLALGCGG LCHDIGLALGCGG LCHDIGLALGTGA LCHDIGLAVGTGG LCHDIGLAVGTGG LCHDIGLAVGTGG LCHDIGLAGTGA LCHDIGLAGGTGA LCHDIGLAGGTGA LCHDIGLAGGTGA LCHDIGLAGGTGA LCHDIGLAGGTGA LCHDIGLAGGTGA LCHDIGLAGGTGA LCHDIGLAGGTGA LCHDIGLAGGTGA LCHDIGLAGGTGA LCHDIGLAGGTGA LCHDIGLAGGTGA LCHDIGLAGGTGA LCHDIGLAGGTGA LCHDIGLAGGTGA LCHDIGLAGGTGA LCHDIGLAGGTGA LCHDIGLAGGTGA LCHLGLAGGTGA	200 AH M SE LRR TR SG AH M AE LRR TK AG GH MQE LRR TK AG GH MQE LRR TK AG GH MQE LRR TK AG GH MQE LRR TA VG GH MQE LRR TA SG AH MAE LRR TR SG AH MQE LRR TR SG AH MQE LRR TR SG AH MQE LRR TR TG GH MGP LRR TR TG GH MGP LRR TR TG GAM VE LRR T
P.furiosus P.abyssi P.horikoshii T.kodakarensis M.kandleri M.jannaschii M.barkeri M.barkeri M.acetivorans M.mazei M.thermoautotrophicum M.burtonii M.stadtmanae M.maripaludis M.burtonii M.stadtmanae M.maripaludis M.hungatei A.fulgidus N.pharaonis H.sp H.marismortui H.walsbyi P.torridus T.acidophilum T.volcanium A.pernix P.aerophilum N.equitans S.cerevisiae_yeast T.thermophila D.melanogaster_fruitfly M.musculus_mouse H.sapiens_human Interaction sites DC mutations	150 A V KR R L R A V KR R V I A V KR V I R A V KR Q L R A V SR R L R A V KR Q L R	160TR KVYYIEITR KVYYIEITR KVYYIEITR KVYYIEITR KVYYIEVPKKIYYIEVPKKIYYIEVVRTIYYLEVVRTIYYLEVVRTIYKLIRNIYYLDVVRTIYEVVRTIYKLIRNIYYLDVVRTIYEVVRTIYELEUIRNIYYLDVVRTIYELEIIREIYENELTRTVHRLDVSRRIHSLDIKRTIYELDUKRTIYELDUKRTYSLDLKKVYCIKIVRTIYESNLVRTIYESKLVRTIYESKMVRTIYESKMKRTIYESKMA10	17( L E I EGRD \ L E I DGRD \ L E I DGRD \ L E I EGRD \ L E I EGRD \ L E I EGRD \ L E I EGRS \ L E I EGRS \ L E I EGRS \ L E I EGRS \ L E I DGRD \ L E I GRQ \ L E I DGRD \ L E I DGRD \ L E I DGRD \ L E S ARR \ L E VD SD AQQ \ L E WD SD AQQ \ L E WD SD AQQ \ L E W DGRT \ L E W	/ L FR VG VE / L FR VG VE / L FR VG VE / L FR VG VE / L FR VG CE / L FR VC CE	180 EAGTYIRS EAGTYIRS EAGTYIRS EAGTYIRS EAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK EAGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRK ESGTYIRT EAGTYARK EAGTYARK EAGTYARK EAGTYAR EAGTYAR EAGTYAR EAGTYIRT EAGTYIRT	190 LIHHIGLALGVGA LIHHIGLALGVGA LIHHIGLALGVGA LIHHIGLALGVGA LCHDIGEALGVGA LCHDIGEALGCGG LCHDIGLALGCGG VCHDIGLALGCGG YCHDVGEALGAGAGA LCHDIGLALGCGG YCHDIGEALGCGA LCHDIGLALGCGG LCHDIGLALGCGG LCHDIGEALGTGA LCHDIGLAVGTGG LCHDIGLAVGTGG LCHDIGLAVGTGG LCHDIGLAVGTGG LCHDIGLAGTGA LCHDIGLAGGTGA LCHDIGLAGGTGA LCHDIGLAGGTGA LCHDIGLAGGTGA LCHDIGLAGGTGA LCHDIGLAGGTGA LCHDIGLAGGTGA LCHDIGLAGGTGA LCHDIGLAGGTGA LCHDIGLAGGTGA LCHDIGLAGGTGA LCHDIGLAGGTGA LCHDIGLAGGTGA LCHDIGLAGGTGA LCHDIGLAGGTGA LCHDIGLAGGTGA LCHDIGLAGGTGA LCHDIGLAGGTGA LCHLGLAGGTGA LCHLGLAGGTGA	200 AH M SE L RR TR SG AH M AE L RR TK AG GH MQE L RR TA VG GH MQE L RR TA VG GH MQE L RR TR SG AH MAE L RR TR SG AH MQE L RR TR SG GH MGP L RR TR TG GH MGP L RR TR TG GAM VE L RR TR TG G

	210	220		230		
P.furiosus	PFK <mark>E</mark> DE - T	LITLHDL	VDYYYF	WKEDGIE		
P.abyssi	PFK <mark>E</mark> DE - T	LVTLHDL	VD Y Y H F	WK ED G I E		
P.horikoshii	PFKEDE - T	LVTLHDL	VDYYHF	WKEDGIE		
1.kodakarensis M.kandlori	PFKEDE-I		VD Y YH F AD A V E E	WKEDGVE		
M.kanulen M iannaschii	CEEEK D		DAYVE	WKEDGDE		
M.barkeri	PFTEE T		<pre>CDATVL</pre>	WKEDGDE		
M.acetivorans	PFT <mark>E</mark> KT	LVTLHEL	<pre>KDAYVF</pre>	WKEDGDE		
M.mazei	PFT <mark>E</mark> KT	LITLHELI	<pre>KDAYVF</pre>	WKEDGDE		
M.thermoautotrophicum	PFT <mark>E</mark> EG	LVTLHDL	<dayqf< td=""><td> WVEDGDE</td><td></td><td></td></dayqf<>	WVEDGDE		
M.burtonii	PFRED T	LVSLYDL	<pre></pre>	WQ ED GD E		
M.stadtmanae	SFLEDD - I			YKEDGDE		
M.manpaluuis M.hungatei	PFIENE	CVTLHTLI	- DATIF RDAVEK			
A.fulaidus	KFGED M	CYTLQDL	_DAYVE	WKEEGEE		
N.pharaonis	GFDDRT	LVTFEDF	ADGLAF	WRDHDDP		
H.sp	PFD <mark>D</mark> TD	LVTLHDL	AD A V A W	LRD TDD T	E P P D	A P A
H.marismortui	TFDDGS	LSTMHDL	VDALAF	AADGDE -		
H.walsbyi	PFSDTN	LISTADL	TDAVVFTLEE	IVRANQTQIN	DAPDDSTAAYSLLH	KINTANIDPNSTSPT
P.torridus	PFDESM	CHTLQEV	SDAFKL	KSMGNE		
T.acidopniium T.volcanium	PFSEDR					
A pernix	PESEDSGL	MVRIDDV	4YAVIR	WR F F G K D		
P.aerophilum	CYTED E	AVTLQDI	ADAYYI	WKH YGDD		
N.equitans	PFH <mark>E</mark> N N	SVYLQDI	VDSLYF	WKEEGNE		
S.cerevisiae_yeast	ALS <mark>E</mark> ND-N	MVTLHDVI	MD AQWV	YDN TRD E		
T.thermophila	I LD <mark>E</mark> NQ - Y	LVTMHDV	<d i="" s="" td="" wr<=""><td> YQH F KD E</td><td></td><td></td></d>	YQH F KD E		
D.melanogaster_fruitfly	IQSERD-G	MVTMHDV	_DAMWL	YENHKDE		
M.musculus_mouse	VMSEKD-H		DAQWL	YDNHKDE		
Interaction sites			_DAQWL			
DC mutations						
		α6		α6		
Pf Cbf5						
	240	250	260	270	280	290
D furia qua	240	250	260			
P.furiosus P.abyssi	240 EYFRKAIQ EYIRKAIO	250 PMEKAVE PMEKAVE	260 HLPKVWIKDS	270 AVAAVTHGAD	280 L AVP <mark>G I</mark> AKLH	290 AG I KRGD L VA I MT AG I KKGD I VA I MT
P.furiosus P.abyssi P.horikoshii	240 EYFRKAIQ EYIRKAIQ KYLRRAIQ	250 PMEKAVEI PMEKAVEI PMEKAVEI	260 H L P K V W I K D S H L P K I W I K D S H L P K I W I K D S	270 A V A A V T H <mark>G</mark> A D A V A A V A H G A N A V A A V A H G A N	280 L A V P <mark>G I</mark> A K L H L T V P G I V K L N L T V P G I V K L N	290 AG I KRGD L VA I MT AG I KKGD L VA I MT VG I KRGD L VA I MT
P.furiosus P.abyssi P.horikoshii T.kodakarensis	240 EYFRKAIQ EYIRKAIQ KYLRRAIQ EYFRKAIQ	250 PMEKAVEI PMEKAVEI PMEKAVEI PMEKAVEI	260 H L P K VW I KD S H L P K I W I KD S H L P K I W I KD S H L P K VW I RD S	270 A V A A V T H G A D A V A A V A H G A N A V A A V A H G A N A V A A V T H G A D	280 L AVP <mark>G I</mark> AKLH L TVPG I VKLN L TVPG I VKLN L AVPGVVKLH	290 AG I KRGDL VA I MT AG I KKGDL VA I MT VG I KRGDL VA I MT KG I KKGDL VA I MT
P.furiosus P.abyssi P.horikoshii T.kodakarensis M.kandleri	240 EYFRKAIQ EYIRKAIQ KYLRRAIQ EYFRKAIQ EPLRHVVR	250 PMEKAVEI PMEKAVEI PMEKAVEI PMEKAVEI PMEEGLEI	260 H L P K V W I K D S H L P K I W I K D S H L P K I W I K D S H L P K V W I R D S H L P R I E I R D T	270 AVAAVTHG AD AVAAVAHG AN AVAAVAHG AN AVAAVTHG AD AVDAICHG AN	280 L AVPGI AKLH L TVPGI VKLN L TVPGI VKLN L AVPGVVKLH L AAPGI VR VE	290 AG I KRGD L VA I MT AG I KKGD L VA I MT VG I KRGD L VA I MT KG I KKGD L VA I MT KG I Q PGD L VA I F T
P.furiosus P.abyssi P.horikoshii T.kodakarensis M.kandleri M.jannaschii	240 EYFRKAIQ EYIRKAIQ KYLRRAIQ EYFRKAIQ EPLRHVVR EELRRVIK	250 PMEKAVEI PMEKAVEI PMEKAVEI PMEKAVEI PMEEGLEI PMEYGLRI	260 H L P K V W I K D S H L P K I W I K D S H L P K I W I K D S H L P K V W I R D S H L P R I E I R D T H L K K V V V K D S	270 AVAAVTHGAD AVAAVAHGAN AVAAVAHGAD AVAAVTHGAD AVDAICHGAN AVDAICHGAD	280 L AVP G I AKLH L TVP G I VKLN L TVP G I VKLN L AVP G VVKLH L AAP G I VR VE V YVR G I AKLS	290 AG I KRGDL VA I MT AG I KKGDL VA I MT VG I KRGDL VA I MT KG I KKGDL VA I MT KG I QPGDL VA I FT KG I GKG ET VL VET
P.furiosus P.abyssi P.horikoshii T.kodakarensis M.kandleri M.jannaschii M.barkeri	240 EYFRKAIQ EYIRKAIQ KYLRRAIQ EYFRKAIQ EPLRHVVR EELRRVIK SEIRRVIM	250 PMEKAVEI PMEKAVEI PMEKAVEI PMEKAVEI PMEEGLEI PMEYGLRI PMETAVSI	260 HLPKVWIKDS HLPKIWIKDS HLPKIWIKDS HLPKVWIRDS HLPRIEIRDT HLKKVVVKDS HLPKIILRDS	270 AVAAVTHGAD AVAAVAHGAN AVAAVAHGAN AVAAVTHGAD AVDAICHGAN AVDAICHGAD AVDAICGAA	280 L AVP G I AKLH L TVP G I VKLN L TVP G I VKLN L AVP G VVKLH L AAP G I VR VE VYVR G I AKLS L AVP G I TSLD	290 AG I KRGDL VA I MT - AG I KKGDL VA I MT - VG I KRGDL VA I MT - KG I KKGDL VA I MT - KG I QPGDL VA I FT - KG I GKG ET VL VET - ANL KKG EL I AL FT
P.furiosus P.abyssi P.horikoshii T.kodakarensis M.kandleri M.jannaschii M.barkeri M.acetivorans	240 EYFRKAIQ EYIRKAIQ KYLRRAIQ EYFRKAIQ EPLRHVVR EELRRVIK SEIRRVIM SELRRVIR	250 PMEKAVEI PMEKAVEI PMEKAVEI PMEEGLEI PMEEGLEI PMEYGLRI PMESAVSI	260 1 L P K V W I K D S 1 L P K I W I K D S 1 L P K I W I K D S 1 L P K V W I R D S 1 L P K I V V V K D S 1 L P K I I L R D S 1 L P K I I L R D S	270 A V A A V T H G A D A V A A V A H G A N A V A A V A H G A N A V A A V T H G A D A V D A I C H G A D A V D A I C H G A D A V D A I C S G A A A V D A V C S G A S	280 L AVP G I AKLH L TVP G I VKLN L TVP G I VKLN L AVP G VVKLH L AAP G I VR VE VYVR G I AKLS L AVP G I TSLD L AVP G I TSLD	290 AG I KRGDL VAIMT - AG I KKGDL VAIMT - VG I KRGDL VAIMT - KG I KKGDL VAIMT - KG I QPGDL VAIFT - KG I GKGET VL VET - ANL KKGEL I ALFT - SSL AEGEL AALFT
P.furiosus P.abyssi P.horikoshii T.kodakarensis M.kandleri M.jannaschii M.barkeri M.acetivorans M.mazei M thermoautotrophicum	240 EYFRKAIQ EYIRKAIQ KYLRRAIQ EYFRKAIQ EPLRHVVR EELRRVIK SEIRRVIK SELRRVIR SELRRVIR	250 PMEKAVEI PMEKAVEI PMEKAVEI PMEEGLEI PMEYGLRI PMETAVSI PMESAVSI PMESAVSI PMESAVSI	260 1 L P K V W I K D S 1 L P K I W I K D S 1 L P K I W I K D S 1 L P K I W I K D S 1 L P K I I L R D S 1 L P K I L P K I L R D S 1 L P K I R D	270 AVAAVTHGAD AVAAVAHGAN AVAAVAHGAN AVAAVTHGAD AVDAICHGAN AVDAICHGAD AVDAICSGAS AVDAICSGAS	280 L AVP G I AKLH L TVP G I VKLN L AVP G VKLH L AVP G VKLH L AAP G I VR VE VYVR G I AKLS L AVP G I TSLD L AVP G I TSLD L AVP G I TSLD	290 AG I KRGDL VAIMT - AG I KKGDL VAIMT - VG I KRGDL VAIMT - KG I KKGDL VAIMT - KG I QPGDL VAIFT - KG I G KG ET VL VET - ANL KKG EL I ALFT - SSL AEG EL AALFT - SNL AEG EL TGLFT - DN I AWGDT VAIMT
P.furiosus P.abyssi P.horikoshii T.kodakarensis M.kandleri M.jannaschii M.barkeri M.acetivorans M.mazei M.mazei M.thermoautotrophicum M.burtonii	240 EYFRKAIQ EYIRKAIQ EYFRKAIQ EPLRHVVR EELRRVIK SEIRRVIM SELRRVIR SELRRVIR TFLRECIL SELRKLVR	250 PMEKAVEI PMEKAVEI PMEKAVEI PMEKAVEI PMEGLEI PMEGLEI PMESAVSI PMESAVSI PMEFAVGI PMEFAVGI	260 1 L P K V W I K D S 1 L P K I W I K D S 1 L P K I W I K D S 1 L P K V W I R D S 1 L P K I E I R D T 1 L K K V V V K D S 1 L P K I I L R D S 1 L P K I I L R D S 1 L P K I I L R D S 1 L P K I I R D S	270 AVAAVTHGAD AVAAVAHGAN AVAAVAHGAN AVDAICHGAD AVDAICHGAD AVDAICSGAS AVDAICSGAS AVDAICSGAS AVDAICHGAD	280 L AVP G I AKLH L TVP G I VKLN L AVP G VVKLH L AVP G VVKLH L AVP G I VR VE L AVP G I TSLD L AVP G I TSLD L AVP G I TGLD L AVP G I AGLD L AVP G I VSF S	290 AG I KRGDL VA I MT - AG I KKGDL VA I MT - VG I KRGDL VA I MT - KG I QPGDL VA I MT - KG I GKG ET VL VET - ANL KKG EL I AL FT - SSL AEG EL AAL FT - SNL AEG EL TGL FT - DN I AWGDT VA I MT - KC I QKDD K I AVFT
P.furiosus P.abyssi P.horikoshii T.kodakarensis M.kandleri M.jannaschii M.barkeri M.barkeri M.acetivorans M.mazei M.thermoautotrophicum M.burtonii M.stadtmanae	240 EYFRKAIQ EYIRKAIQ KYLRRAIQ EYFRKAIQ EPLRHVVR EELRRVIK SEIRRVIK SELRRVIR SELRRVIR SELRRVIR TFLRECIL SELRKLVR TLLRKLIQ	250 PMEKAVEI PMEKAVEI PMEKAVEI PMEKAVEI PMEEGLEI PMEYGLRI PMESAVSI PMESAVSI PMESAVSI PMEFAVGI PMEEGLSI PMEHTTK	260 1 L P K V W I K D S 1 L P K I W I K D S 1 L P K I W I K D S 1 L P K I W I K D S 1 L P K I E I R D T 1 L K K V V V K D S 1 L P K I I L R D S 1 L P K I I L R D S 1 L P K I I L R D S 1 L P K I I I R D S 1 L P K I I I R D S 1 L P K I I I R D S 1 L P K I I I R D S 1 L P K I I I R D S 1 L P K I I V K D T	270 AVAAVTHGAD AVAAVAHGAN AVAAVAHGAN AVAAVTHGAD AVDAICHGAN AVDAICHGAN AVDAICSGAS AVDAICSGAS AVDAICSGAS AVDAICHGAD AVDAICHGAD	280 L AVP G I AKLH L TVP G I VKLN L AVP G VVKLH L AVP G VVKLH L AVP G I VR VE L AVP G I TSLD L AVP G I TSLD L AVP G I TGLD L AVP G I AGLD L AVP G I VSFS L AVP G I VSFS	290 AG I KRGDL VAIMT - AG I KKGDL VAIMT - VG I KRGDL VAIMT - KG I QPGDL VAIFT - KG I GKGET VL VET - ANL KKGEL I ALFT - SSL AEGEL AALFT - SNL AEGEL TGLFT - DN I AWGDT VAIMT - KC I QKDD KIAVFT - NQ I HENNT VAVMT
P.furiosus P.abyssi P.horikoshii T.kodakarensis M.kandleri M.jannaschii M.barkeri M.acetivorans M.mazei M.thermoautotrophicum M.burtonii M.stadtmanae M.maripaludis	240 EYFRKAIQ EYIRKAIQ KYLRRAIQ EYFRKAIQ EPLRHVVR EELRRVIK SELRRVIK SELRRVIR SELRRVIR TFLRECIL SELRKLVR TLLRKLIQ EELRKIVK	250 PMEKAVEI PMEKAVEI PMEKAVEI PMEEGLEI PMEEGLEI PMEEGLEI PMESAVSI PMESAVSI PMEFAVGI PMEEGLSI PMEHTTK PLEYGLQI	260 1 L P K V W I K D S 1 L P K I W I K D S 1 L P K I W I K D S 1 L P K I W I K D S 1 L P K I I L R D S 1 L P K I I L R D S 1 L P K I I L R D S 1 L P K I I L R D S 1 L P K I I L R D S 1 L P K I I K D S 1 L K K I I K D S	270 A V A A V T H G A D A V A A V A H G A N A V A A V A H G A N A V A A V T H G A D A V D A I C H G A D A V D A I C H G A D A V D A I C S G A S A V D A I C S G A S A V D A I C H G A D A V D A I C H G A D A V D A I C H G A D A V D A I C H G A D A V D A I C H G A D A V D A V C H G A T	280 L AVP G I AKLH L TVP G I VKLN L TVP G I VKLN L AVP G VVKLH L AAP G I VR VE VYVR G I AKLS L AVP G I TSLD L AVP G I TSLD L AVP G I TGLD L AVP G I AGLD L AVP G I AGLD L AVP G I VSFS L AVS G I SKIE	290 AG I KRGDL VAIMT - AG I KKGDL VAIMT - VG I KRGDL VAIMT - KG I KKGDL VAIMT - KG I G KG ET VL VET - ANL KKG EL IAL FT - SSL AEG EL AAL FT - SNL AEG EL TGL FT - DN I AWGDT VAIMT - KC I Q KDD KIAVFT - NQ I HENNT VAVMT - KGLGTD EVVL I ET
P.furiosus P.abyssi P.horikoshii T.kodakarensis M.kandleri M.jannaschii M.barkeri M.acetivorans M.mazei M.thermoautotrophicum M.burtonii M.stadtmanae M.maripaludis M.hungatei	240 EYFRKAIQ EYIRKAIQ KYLRRAIQ EYFRKAIQ EPLRHVVR EELRRVIK SELRRVIK SELRRVIR SELRRVIR TFLRECIL SELRKLVR TLLRKLIQ EELRKIVK TYLRKIIR	250 PMEKAVEI PMEKAVEI PMEKAVEI PMEEGLEI PMEYGLRI PMESAVSI PMESAVSI PMESAVSI PMEFAVGI PMEEGLSI PMEHTTK PLEYGLQI SPLEALHO	260 1 L P K V W I KD S 1 L P K I I L R D S 1 L P K I I L R D S 1 L P K I I L R D S 1 L P K I I L R D S 1 L P K I I L R D S 1 L P K I I I K D S 1 L P K I I I K D S 3 F P R I Q M K E S	270 A V A A V T H G A D A V A A V A H G A N A V A A V A H G A N A V A A V T H G A D A V D A I C H G A D A V D A I C H G A D A V D A I C H G A S A V D A I C H G A D A V D A I C H G A S A V D A I C H G A S A V D A V C H G A S A V D A V C H G A S A V D A V C H G A S A V D A V C H G A S A V D A V C H G A S A V D A V C H G A S A V D A V C H G A S A V D A V C H G A S A V D A V C H G A S	280 L AVP G I AKLH L TVP G I VKLN L TVP G I VKLN L AVP G VVKLH L AVP G I VR VE L AVP G I TSLD L AVP G I TSLD L AVP G I TSLD L AVP G I TGLD L AVP G I XSLS L ASS G VVKLD L SSR G VVSHD	290 AG I KRGDL VAIMT - AG I KKGDL VAIMT - VG I KRGDL VAIMT - KG I KKGDL VAIMT - KG I QPGDL VAIFT - KG I G KG ET VL VET - ANL KKG EL I ALFT - SSL AEG EL AALFT - SNL AEG EL TGLFT - DN I AWGDT VAIMT - KC I QKDD KIAVFT - NQ I HENNT VAVMT - KGLGTD EVVL I ET - TFQMEDL VVMLA
P.furiosus P.abyssi P.horikoshii T.kodakarensis M.kandleri M.jannaschii M.barkeri M.acetivorans M.mazei M.thermoautotrophicum M.burtonii M.stadtmanae M.maripaludis M.hungatei A.fulgidus	240 EYFRKAIQ EYIRKAIQ KYLRRAIQ EYFRKAIQ EPLRHVVR EELRRVIK SELRRVIR SELRRVIR SELRRVIR SELRRVIR TFLRECIL SELRKLVR TLLRKLIQ EELRKIVK TYLRKIIR	250 PMEKAVEI PMEKAVEI PMEKAVEI PMEEGLEI PMEYGLRI PMESAVSI PMESAVSI PMESAVSI PMEFAVGI PMEEGLSI PMEHTTK PLEYGLQI SPLEVAAA	260 1 L P K V W I K D S 1 L P K I W I K D S 1 L P K I W I K D S 1 L P K I W I K D S 1 L P K I I L R D S 1 L P K I I L R D S 1 L P K I I L R D S 1 L P K I I L R D S 1 L P K I I L R D S 1 L P K I I L R D S 1 L P K I I L R D S 5 L P K I V V K D T 1 L K K I I I K D S 5 F P K I V K D S 2 L P K I V K D S 2 L P K I V K D S 3 L P K I V K D S 4 L P K V V K D S 5	270 AVAAVTHGAD AVAAVAHGAN AVAAVAHGAN AVAAVHGAN AVDAICHGAD AVDAICHGAD AVDAICSGAS AVDAICSGAS AVDAICHGAD AVDAVCRGAS AVDAVCRGAS AVDSICHGAT AVDAVCHGAT AVDAICHGAN	280 L AVP G I AKLH L TVP G I VKLN L TVP G I VKLN L AVP G VVKLH L AVP G I VR VE L AVP G I TSLD L AVP G I SLD L AVP G I VSFS L SSR G VVKLD L SVR G VVSHD	290 - AG I KRGDL VAIMT - AG I KKGDL VAIMT - VG I KRGDL VAIMT - KG I KKGDL VAIMT - KG I QPGDL VAIFT - KG I G KG ET VL VET - ANL KKG EL I ALFT - SSL AEGEL AALFT - SNL AEGEL TGLFT - DN I AWGDT VAIMT - KC I QKDD KI AVFT - NQ I HENN T VAVMT - KGLGTD E VVL I ET - TF QKEDL VVML A - KN VKKD ST VAIFT
P.furiosus P.abyssi P.horikoshii T.kodakarensis M.kandleri M.jannaschii M.barkeri M.acetivorans M.mazei M.thermoautotrophicum M.burtonii M.stadtmanae M.maripaludis M.hungatei A.fulgidus N.pharaonis	240 EYFRKAIQ EYIRKAIQ KYLRRAIQ EYFRKAIQ EPLRHVVR EELRRVIK SELRRVIR SELRRVIR SELRRVIR SELRKIVR TFLRECIL SELRKLVQ EELRKIVK TYLRKIIR KYLREIIK ELCDVVA	250 PMEKAVEI PMEKAVEI PMEKAVEI PMEKAVEI PMEEGLEI PMEYGLRI PMESAVSI PMESAVSI PMESAVSI PMEFAVGI PMEEGLSI PMEHTTK PLEYGLQI SPLEALHO PAERALEO	260 1 L P K V W I K D S 1 L P K I W I K D S 1 L P K I W I K D S 1 L P K I W I K D S 1 L P K I E I R D T 1 L K K V V V K D S 1 L P K I I L R D S 1 L P K I I L R D S 1 L P K I I L R D S 1 L P K I I K D S 1 L P K I I K D S 5 F P R I Q M K E S 5 L P K I V I K D S 3 L P R I V R I V R I V R I V R I V R I V R I V R I V R I V R I V R I V	270 AVAAVTHGAD AVAAVAHGAN AVAAVAHGAN AVAAVHGAN AVDAICHGAD AVDAICHGAD AVDAICHGAD AVDAICSGAS AVDAICSGAS AVDAICHGAD AVDAVCRGAS AVDAICHGAN AVDAVCHGAT AADAICHGAN AVDAICHGAN	280 L AVP G I AKLH L TVP G I VKLN L AVP G VKLH L AVP G VKLH L AVP G I VR VE L AVP G I TSLD L SSG VVKLD L SSR G VVSHD L SSR G VVSHD L SVR G VAYVE L SVR G VAYVE	290 - AG I KRGDL VAIMT - AG I KKGDL VAIMT - VG I KRGDL VAIMT - KG I KKGDL VAIMT - KG I GKGET VL VET - KG I GKGET VL VET - ANL KKGEL I ALFT - SSL AEGEL AALFT - SNL AEGEL TGLFT - DN I AWGDT VAIMT - KC I QKDD KI AVFT - NQ I HENNT VAVMT - KGLG TD E VVL I ET - TFQMEDL VVMLA - KN VKKD ST VAIFT DGAD - EGSL VACYT
P.furiosus P.abyssi P.horikoshii T.kodakarensis M.kandleri M.barkeri M.barkeri M.acetivorans M.mazei M.thermoautotrophicum M.burtonii M.stadtmanae M.maripaludis M.hungatei A.fulgidus N.pharaonis H.sp H marismortui	240 EYFRKAIQ EYIRKAIQ EYFRKAIQ EPLRHVVR EELRRVIK SEIRRVIK SELRRVIR SELRRVIR TFLRECIL SELRKLVR TLLRKLIQ EELRKIVK TYLRKIIR KYLREIIK ELLCDVVA DALRAAVQ	250 PMEKAVEI PMEKAVEI PMEKAVEI PMEKAVEI PMEEGLEI PMEEGLEI PMETAVSI PMESAVSI PMESAVSI PMEFAVGI PMEEGLSI PMEHTTK PLEYGLQI SPLEALHO PMEVAAA PAERALEO PAERALI	260 1 L P K V W I KD S 1 L P K I E I R D T 1 L K K V V V KD S 1 L P K I I L R D S 1 L P K I I L R D S 1 L P K I I L R D S 1 L P K I I K D S 1 L P K I I K D S 5 L P K I V K D S 5 L P K I V K D S 5 L P K I V K D S 1 L P K I V K D S 5 L P K I V K D S 1 L P K I V K D S 5 L P K I V K D S 1 L P K I V K	270 A V A A V T H G A D A V A A V A H G A N A V A A V A H G A N A V A A V A H G A N A V D A I C H G A D A V D A I C H G A D A V D A I C H G A D A V D A I C H G A S A V D A I C H G A S A V D A I C H G A S A V D A I C H G A S A V D A I C H G A S A V D A I C H G A S A V D A I C H G A S A V D A I C H G A S A V D A I C H G A S A V D A I C H G A S A V D A I C H G A S A V D A I C H G A S A V D A I C H G A S A V D A I C H G A S A V D A I C H G A S A V D A I C H G A S A V D A I C H G A S A A S E I A N G A P A A H E V A F G A P	280 L AVP GI AKLH L TVP GI VKLN L TVP GI VKLN L AVP GVVKLH L AAP GI VR VE L AAP GI TSLD L AVP GI TSLD L AVP GI TGLD L AVP GI TGLD L AVP GI XSFS L AVP GI SKIE L SSR GVVKLD L SSR GVVFD L SVR GVAYVE VYAP GVLAH EL VAP GVLAH EL	290 AG I KRGDL VAIMT - AG I KKGDL VAIMT - VG I KRGDL VAIMT - KG I KKGDL VAIMT - KG I QPGDL VAIFT - KG I GKGETVL VET - ANL KKGEL I ALFT - SSL AEGEL AALFT - SNL AEGEL TGLFT - DN I AWGDT VAIMT - KC I QKDD KIAVFT - NQ I HENN TVAVMT - KGLG TD EVVL I ET - TFQMEDL VVML A - KN VKKD ST VAIFT DGAD - EG SL VACYT - TPPADGAL VACYT
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P.furiosus P.abyssi P.horikoshii T.kodakarensis M.kandleri M.jannaschii M.barkeri M.acetivorans M.mazei M.thermoautotrophicum M.burtonii M.stadtmanae M.maripaludis M.hungatei A.fulgidus N.pharaonis H.sp H.marismortui H.walsbyi P.torridus	240 EYFRKAIQ EYIRKAIQ EYFRKAIQ EYFRKAIQ EPLRHVVR EELRRVIK SELRRVIR SELRRVIR SELRRVIR TFLRECIL SELRKLVR TLLRKLIQ EELRKIVK TYLRKIR KYLREIIK ELLCDVVA DALRAAVQ AQLREIIQ DHLRNVIS KLFKNIFI	250 PMEKAVEI PMEKAVEI PMEKAVEI PMEKAVEI PMEEGLEI PMEYGLRI PMESAVSI PMESAVSI PMESAVSI PMEFAVGI PMEFAVGI PMEHTTK PLEYGLQI SPLEALHO PAERALEO PAERALEO PAERALOI PAERALQI PMDFIFI	260 1 L P K V W I KD S 1 L P K I I L R D S 1 L P K I I L R D S 1 L P K I I L R D S 1 L P K I I L R D S 1 L P K I I L R D S 1 L P K I V I L D S 3 L P R I Q M K E S 5 L P R I Q M K E S 5 L P R I Q M K E S 1 L P R V I A P S 1 L P R V I I A P S 1 L P R V I V K E T 1 L P K V I V K E T	270 AVAAVTHGAD AVAAVAHGAN AVAAVAHGAN AVAAVAHGAN AVDAICHGAD AVDAICHGAD AVDAICHGAD AVDAICHGAD AVDAICHGAS AVDAICHGAS AVDAICHGAN AVDAVCRGAS AVDAICHGAN AVDAVCHGAT AADAICHGAN AASEIANGAP AAAEVAMGAP AAAEVAMGAP ALKNIAHGSD	280 L AVP G I AKLH L TVP G I VKLN L TVP G I VKLN L AVP G VKLH L AVP G I VR VE L AVP G I TSLD L SVR G VAY VE L SVR G VAY VE V Y AP G V L AH EL V Y AP G V I E TG PAE V V Y AP G V I E FD SAAG I Y P A G I H A I TG	290 AG I KRGDL VAIMT - AG I KKGDL VAIMT - VG I KRGDL VAIMT - KG I KKGDL VAIMT - KG I QPGDL VAIFT - KG I G KG ET VL VET - AN L KKG EL I ALFT - SSL AEGEL AALFT - SNL AEGEL TGLFT - DN I AWGDT VAIMT - KC I QKDD KI AVFT - NQ I HENNT VAVMT - KGLGTD EVVL I ET - TFQMEDL VVMLA - KN VKKD ST VAIFT DGAD - EG SL VACYT - TPPADGAL VACYT GD AT PE I D SQ VVS VT NTHD I TD SAL VSCHT - SPKKGD VVAVYT
P.furiosus P.abyssi P.horikoshii T.kodakarensis M.kandleri M.jannaschii M.barkeri M.acetivorans M.mazei M.thermoautotrophicum M.burtonii M.stadtmanae M.maripaludis M.hungatei A.fulgidus N.pharaonis H.sp H.marismortui H.walsbyi P.torridus T.acidophilum	240 EYFRKAIQ EYIRKAIQ EYFRKAIQ EYFRKAIQ EPLRHVVR EELRRVIK SELRRVIR SELRRVIR SELRRVIR TFLRECIL SELRKLVR TLLRKLIQ EELRKIVK TYLRKIIR KYLREIIK ELLCDVVA DALRAAVQ AQLREIIQ DHLRNVIS KLFKNIFI	250 PMEKAVEI PMEKAVEI PMEKAVEI PMEKAVEI PMEEGLEI PMEYGLRI PMESAVSI PMESAVSI PMESAVSI PMEFAVGI PMEFAVGI PMEFAVGI PMEHTTK PLEYGLQI SPLEALAI PAERALEI PAERALEI PAERALSI PAERALQI PMEFIFI DMTYAFKI	260 1 L P K V W I KD S 1 L P K I I L R D S 1 L P K I I L R D S 1 L P K I I L R D S 1 L P K I I L R D S 1 L P K I I L R D S 1 L P K I V V K D S 5 L P K I V V K D S 5 L P R I Q M K E S 5 L P R I Q M K E S 5 L P R I V I KD S 6 L P R V I V K E S 1 L P R V I V K E T 5 Y P K I V V K S	270 AVAAVTHGAD AVAAVAHGAN AVAAVAHGAN AVAAVHGAN AVDAICHGAD AVDAICHGAD AVDAICHGAD AVDAICSGAS AVDAICSGAS AVDAICHGAD AVDAVCRGAS AVDAICHGAN AVDAVCHGAT AVDAVCHGAT AVDAVCHGAT AVDAVCHGAT AADAICHGAN AVDAICHGAN AVDAVCHGAT AADAICHGAN AASEIANGAP AAAEVAAGAP AAAEVAAGAP AAAEVAMGAP AAARNIAHGSD	280 L AVP G I AKLH L TVP G I VKLN L TVP G I VKLN L AVP G VVKLH L AVP G I VR VE VYVR G I AKLS L AVP G I TSLD L AVP G I SKI E L AVP G I VSFS L AVP G VKLD L SSR G VVSHD L SSR G VVSHD L SSR G V AYVE VYAP G V LAH EL V AP G V I D TTALP - V YAP G V I ETG PAEV V YAP G V I EFD SAAG I YPAG I KI I DG	290 - AG I KRGDL VAIMT - AG I KKGDL VAIMT - VG I KRGDL VAIMT - KG I KKGDL VAIMT - KG I QPGDL VAIFT - KG I G KG ET VL VET - ANL KKG EL I ALFT - SSL AEGEL AALFT - SNL AEGEL TGLFT - DN I AWGDT VAIMT - KC I QKDD KIAVFT - KG LG TD E VVL I ET - KN VKKD ST VAIFT DG AD - EG SL VACYT GD AT PE I D SQ VVS VT NTHD I TD SAL VSCHT - SPKKGD VVAVYT - KFR KG ER VAVIS
P.furiosus P.abyssi P.horikoshii T.kodakarensis M.kandleri M.jannaschii M.barkeri M.acetivorans M.mazei M.thermoautotrophicum M.burtonii M.stadtmanae M.maripaludis M.hungatei A.fulgidus N.pharaonis H.sp H.marismortui H.walsbyi P.torridus T.acidophilum T.volcanium	240 EYFRKAIQ EYIRKAIQ EYFRKAIQ EYFRKAIQ EPLRHVVR EELRRVIK SELRRVIR SELRRVIR SELRRVIR TFLRECIL SELRKLVR TFLRECIL SELRKLVR TYLRKIIR KYLREIIK ELLCDVVA DALRAAVQ AQLREIIQ DHLRNVIS KLFKNIFI KLLRDHIL ELFRSHFL	250 PMEKAVE PMEKAVE PMEKAVE PMEKAVE PMEKAVE PMEGLE PMEYGLE PMEYGLE PMESAVS PMESAVS PMEFAVG PMEFAVG PMEFAVG PMEFAVG PMEFAVG PMEFAVG PMEFAVG PMEFAVG PMEFAVG PMEFAVG PMEFAVG PMEFAVG PMEFAVG PMEFAVG PMEFAVG PMEFAVG PMEFAVG PMEFAVG PAERALC PAERALC PAERALC PAERALC PAERALC PAERALC PAERALC	260 1 L P K V W I KD S 1 L P K I I L R D S 1 L P K I I L R D S 1 L P K I I L R D S 1 L P K I I L R D S 1 L P K I V V K D S 1 L P K I V K S 5 L P K S 5 L P K I V K S 5 L P K S	270 AVAAVTHGAD AVAAVAHGAN AVAAVAHGAN AVAAVAHGAN AVDAICHGAD AVDAICHGAD AVDAICHGAD AVDAICSGAS AVDAICSGAS AVDAICHGAN AVDAVCRGAS AVDAICHGAN AVDAVCRGAS AVDAICHGAN AVDAVCRGAS AVDAICHGAN AVDAVCRGAS AVDAICHGAN AVDAVCRGAS AVDAICHGAN AAAEVANGAP AAAEVAMGAP AAAEVAMGAP AAAEVAMGAP AARNIAHGSD AVENIAHGSD	280 L AVP G I AKLH L TVP G I VKLN L AVP G VVKLH L AVP G VVKLH L AVP G I VR VE VYVR G I AKLS L AVP G I TSLD L AVP G I TSLD L AVP G I TGLD L AVP G I TGLD L AVP G I SLD L AVP G I TSLD L AVP G I TSLD L AVP G I TSLD L AVP G I TSLD L SSR G VVKLD L SSR G VVKLD L SSR G VVSHD L SSR G VVSHD L SSR G VVSHD L SSR G VLAH EL VYAP G VLAH EL VYAP G VLAH L YAG G I HAITG L YAG G K I DG	290 - AGIKRGDLVAIMT - AGIKKGDLVAIMT - VGIKRGDLVAIMT - KGIKRGDLVAIMT - KGIQPGDLVAIFT - KGIGKGETVLVET - ANLKKGELIALFT - SSLAEGELAALFT - SNLAEGELTGLFT - DNIAWGDTVAIMT - KCIQKDDKIAVFT - NQIHENNTVAVMT - KGLGTDEVVLIET - TFQMEDLVVMLA - KNVKKDSTVAIFT DGAD - EGSLVACYT GDATPEIDSQVVSVT NTHDITDSALVSCHT - SPKKGDVVAVYT - KFRKGERVAVIS - NFQKGDRVCVLS
P.furiosus P.abyssi P.horikoshii T.kodakarensis M.kandleri M.jannaschii M.barkeri M.acetivorans M.mazei M.thermoautotrophicum M.burtonii M.stadtmanae M.maripaludis M.hungatei A.fulgidus N.pharaonis H.sp H.marismortui H.walsbyi P.torridus T.acidophilum T.volcanium A.pernix	240 EYFRKAIQ EYIRKAIQ EYFRKAIQ EYFRKAIQ EPLRHVVR EELRRVIK SEIRRVIR SELRRVIR SELRRVIR TFLRECIL SELRKLVR TLLRKLIQ EELRKIVK TYLRKIIR KYLREIIK ELLCDVVA DALRAAVQ AQLREIIQ DHLRNVIS KLFKNIFI KLLRDHIL ELFRSHFL DLLRRVVI	250 PMEKAVE PMEKAVE PMEKAVE PMEKAVE PMEEGLE PMEEGLE PMETAVS PMESAVS PMESAVS PMEFAVG PMEEGLS PMEHTTK PLEYGLQ SPLEALHO PMEVAAA PAERALEO PAERALEO PAERALS PAERALO PAERALS PAERALO	260 1 L P K V W I KD S 1 L P K I I L R D S 1 L P K I I L R D S 1 L P K I I L R D S 1 L P K I I L R D S 1 L P K I V V K D S 1 L P K I V V K D S 5 L P K I V V K D S 5 L P K I V I KD S 5 L P K I V K K S 1 L P K V I V K S 1 L P K V V K S 1	270 A V A A V T H G AD A V A A V A H G AN A V A A V A H G AN A V A A V A H G AN A V D A I C H G AD A VD A I C H G AD A A H E V A T G AP A A H E V A T G AP A A A E V A E G AP A A A E V A E G AP A A A E V A H G SD A W E S L T H G AQ	280 L AVP G I AKLH L TVP G I VKLN L TVP G I VKLN L AVP G VVKLH L AVP G VVKLH L AVP G I VR VE VYVR G I AKLS L AVP G I TSLD L AVP G I TSLD L AVP G I TGLD L AVP G I VSFS L AVP G I VSFS L SSR G VVKLD L SSR G VVKLD L SVR GVAYVE VYAP G V I ETGPAEV V AP G V I EFD SAAG I YPAG I KI I DG L YVG G VKLI DG L YVG G VAAVE	290 - AG I KRGDL VAIMT - AG I KKGDL VAIMT - VG I KRGDL VAIMT - KG I KKGDL VAIMT - KG I QPGDL VAIFT - KG I G KG ET VL VET - AN L KKG EL I ALFT - SSL AEGEL AALFT - SNL AEGEL TGLFT - DN I AWGDT VAIMT - KC I Q KDD KIAVFT - NQ I HENN T VAVMT - KGLG TD E VVL I ET - TFQMEDL VVML A - KN VKKD ST VAIFT DGAD - EG SL VACYT GDATPE I D SQ VVS VT NTHD I TD SAL VSCHT - SPKKGDR VCVL S - NFQ KGDR VCVL S - NFQ KGDR VCVL S
P.furiosus P.abyssi P.horikoshii T.kodakarensis M.kandleri M.jannaschii M.barkeri M.acetivorans M.mazei M.thermoautotrophicum M.burtonii M.stadtmanae M.maripaludis M.hungatei A.fulgidus N.pharaonis H.sp H.marismortui H.walsbyi P.torridus T.acidophilum T.volcanium A.pernix P.aerophilum	240 EYFRKAIQ EYIRKAIQ EYFRKAIQ EYFRKAIQ EPLRHVVR EELRRVIK SELRRVIM SELRRVIM SELRRVIR TFLRECIL SELRKLVR TLLRKLIQ EELRKIVK TYLRKIIR KYLREIIK ELLCDVVA DALRAAVQ AQLREIIQ DHLRNVIS KLFKNIFI KLLRDHIL ELFRSHFL DLLRRVVI	250 PMEKAVEI PMEKAVEI PMEKAVEI PMEKAVEI PMEEGLEI PMEYGLRI PMEYGLRI PMEYGLRI PMEYGLRI PMEYGLRI PMEYGLRI PMEYGLQI SPLEALSI PMEHTTK PLEYGLQI SPLEALHO PAERALEO PAERALEO PAERALEO PAERALOI PAERALOI PAERALOI PAERALOI PAERALOI PAERALOI PAERALOI PAERALOI PAERALOI PAERALOI PAERALOI PAERALOI PAERALOI PAERALOI PAERALOI PAERALOI PAERALOI PAERALOI PAERALOI	260 1 L P K V W I KD S 1 L P K I V V V KD S 1 L P K I I L R D S 1 L P K I I L R D S 1 L P K I I L R D S 1 L P K I V V KD S 3 L P R V I D S 3 L P R V I V K S 3 L P R V I V K S 4 L P R V I V K S 4 L P R V I V K S 4 L P R V I V K S 5 L P K I V V K S 4 L P R V I V K S 4 L P K V V V K S 5 L P K I V K S 5 L P K I V V K S 5 L P K I V K S 5 L P K	270 A V A A V T H G AD A V A A V A H G AN A V A A V A H G AN A V A A V T H G AD A V D A I C H G AD A V D A V C H G A A V D A I C H G AD A V D A V C H G A A V D A I C H G AN A A S E I AN G AP A A H E V A T G AP A A H E V A T G AP A A A E V A B G AP A A A E V A B G AP A A A E V A B G AP A A H E V A T G AP A A A E V A B G A A C V A B A C A A C V A A C A A C V A A C A A C V A A C A A C V A A C A A C V A A C A A C V A A A C V A A C A A C V A A C A A C V A A A C	280 L AVP G I AKLH L TVP G I VKLN L TVP G I VKLN L AVP G VKLH L AVP G VKLH L AVP G I TSLD L YSS G I SKI E L SVR G VAYVE L SVR G V AYVE L YAP G V I ETG PAEV V YAP G V I EFD SAAG I YPA G I HA I TG L YAG G I KI I DG L YAG G V KL I DG L AAP G V AAVE L AAP G I SKFE	290 - AGIKRGDLVAIMT - AGIKKGDLVAIMT - VGIKRGDLVAIMT - KGIQRGDLVAIMT - KGIQRGDLVAIFT - KGIGKGETVLVET - ANLKKGELIALFT - SSLAEGELAALFT - SNLAEGELTGLFT - DNIAWGDTVAIMT - KCIQKDDKIAVFT - NQIHENNTVAVMT - KGLGTDEVVLIET - TFQMEDLVVMLA - KNVKKDSTVAIFT DGAD - EGSLVACYT GDATPEIDSQVVSVT NTHDITDSALVSCHT - SPKKGDVVAVYT - KFRKGERVAVIS - NFQKGDRVCVLS - EGVEKGGMVALMT
P.furiosus P.abyssi P.horikoshii T.kodakarensis M.kandleri M.jannaschii M.barkeri M.acetivorans M.mazei M.thermoautotrophicum M.burtonii M.stadtmanae M.maripaludis M.burtonii M.stadtmanae M.maripaludis M.hungatei A.fulgidus N.pharaonis H.sp H.marismortui H.walsbyi P.torridus T.acidophilum T.volcanium A.pernix P.aerophilum N.equitans	240 EYFRKAIQ EYIRKAIQ EYFRKAIQ EYFRKAIQ EPLRHVVR EELRRVIK SELRRVIR SELRRVIR SELRRVIR TFLRECIL SELRKLVR TLLRKLIQ EELRKIVK TYLRKIIR KYLREIIK ELLCDVVA DALRAAVQ AQLREIIQ DHLRNVIS KLFKNIFI KLLRDHIL ELFRSHFL DLLRRVVI TYLRRVLL	250 PMEKAVEI PMEKAVEI PMEKAVEI PMEKAVEI PMEEGLEI PMEYGLRI PMESAVSI PMESAVSI PMESAVSI PMEFAVGI PMEFAVGI PMEFAVGI PMEEGLSI PMEHTTK PLEYGLQI SPLEALHO PAERALCI	260 1 L P K V W I KD S 1 L P K I I L R D S 1 L P K I I L R D S 1 L P K I I L R D S 1 L P K I I L R D S 1 L P K I I L R D S 1 L P K I V V K D S 1 L P K I V V K D S 1 L P K I V V K D S 3 L P R I Q M K E S 5 L P R I Q M K E S 5 L P R I Q M K E S 5 L P R I V I K D S 1 L P R V I I A P S 1 L P K I V V K E T 0 Y P K I V V K E T 0 Y P K I V V K E S 1 L P K I W V R D S 1 L P K I W V R D S 1 L P K I W V R D S 1 L P K I W V R D S 1 L P K I W V R D S 1 L P K I W V R D S 1 L P K I W V R D S 1 L P K I W V R D S 1 L P K I W V R D S 1 L P K I W V R D S 1 L P K I W V R D S 1 L P K I W V R D S 1 L P K I W V R D S 1 L P K I W V R D S 1 L P K I W V R D S 1 L P K I W V R D S 1 L P K I W V R D S 1 L P K I W V V K D S 1 L P K I W V R D S 1 L P K I W V R D S 1 L P K I W V R D S 1 L P K I W V V K D S 1 L P K I W V K D S 1 L P K I W V K D S 1 L P K I W V L V R D S 1 L P K I W V K D S 1 L P K I W V K D S 1 L P K I W V K D S 1 L P K I W V K D S 1 L P K I W V L V R D S 1 L P K I W V K D S 1 L P K V V K D S 1 L P K I W V K D S 1 L P K V V K D S 1 L	270 A V A A V T H G AD A V A A V A H G AN A V A A V A H G AN A V A A V A H G AN A V D A I C H G AD A V D A I C H G AS A V D A I C H G AS A V D A I C H G AN A V D A V C H G AN A V D A V C H G AN A V D A I C H G AN A V D A I C H G AN A V D A I C H G AN A A S E I A N G AP A A H E V A T G AP A A H E V A T G AP A A A E V A M G AP	280 L AVP G I AKLH L TVP G I VKLN L TVP G I VKLN L AVP G VKLH L AVP G VKLH L AVP G I TSLD L YSS G I SKI E L SVR G VAYVE L SVR G VAYVE L YAP G V I ETG PAEV V Y AP G V I ETG PAEV V Y AP G V I EFD SAAG I Y PA G I HA I TG L YAG G I KI I DG L AAP G V AAVE L AAP G V AAVE L AAP G I SKFE L AVP G I AKLY	290 - AGIKRGDLVAIMT - AGIKKGDLVAIMT - VGIKRGDLVAIMT - VGIKRGDLVAIMT - KGIQPGDLVAIFT - KGIGKGETVLVET - ANLKKGELIALFT - SSLAEGELAALFT - SNLAEGELTGLFT - DNIAWGDTVAIMT - KCIQKDDKIAVFT - NQIHENNTVAVMT - KGLGTDEVVLIET - TFQMEDLVVMLA - KNVKKDSTVAIFT DGAD - EGSLVACYT GDATPEIDSQVVSVT NTHDITDSALVSCHT - SPKKGDVVAVYT - KFRKGERVAVIS - NFQKGDRVCVLS - EGVEKGGMVALMT - SNIKKGDLVSIHT - SNIKKGDLVSIHT
P.furiosus P.abyssi P.horikoshii T.kodakarensis M.kandleri M.jannaschii M.barkeri M.acetivorans M.mazei M.thermoautotrophicum M.burtonii M.stadtmanae M.maripaludis M.burtonii M.stadtmanae M.maripaludis M.hungatei A.fulgidus N.pharaonis H.sp H.marismortui H.walsbyi P.torridus T.acidophilum T.volcanium A.pernix P.aerophilum N.equitans S.cerevisiae_yeast	240 EYFRKAIQ EYIRKAIQ EYFRKAIQ EYFRKAIQ EPLRHVVR EELRRVIK SELRRVIR SELRRVIR SELRRVIR TFLRECIL SELRKLVR TLLRKLIQ EELRKIVK TYLRKIIR KYLREIIK ELCDVVA DALRAAVQ AQLREIIQ DHLRNVIS KLFKNIFI KLLRDHIL ELFRSHFL DLLRRVVI TYLRRVLL EYIRKVFL SYLRSIIQ	250 PMEKAVEI PMEKAVEI PMEKAVEI PMEKAVEI PMEEGLEI PMEYGLRI PMESAVSI PMESAVSI PMEFAVGI PMEFAVGI PMEFAVGI PMEHTTK PLEYGLQI SPLEALAI PAERALEI PAERALEI PAERALEI PAERALI	260 1 L P K V W I KD S 1 L P K I I L R D S 1 L P K I I L R D S 1 L P K I I L R D S 1 L P K I I L R D S 1 L P K I V V K D S 1 L P K I V V K D S 5 L P K I V K K S 5 L P K I V K K S 5 L P K I V K K S 6 L P K I V K K S 6 L P K I V K K S 7 V K V V K S 6 L P K I V K K S 7 V K I V V K S 6 L P K I V K K S 7 V K I V V K S 6 L P K I V V K S 7 V V K	270 AVAAVTHGAD AVAAVAHGAN AVAAVAHGAN AVAAVAHGAN AVAAVTHGAD AVDAICHGAD AVDAICHGAD AVDAICHGAD AVDAVCSGAS AVDAICHGAD AVDAVCRGAS AVDAICHGAN AVDAVCHGAT AVDAVCHGAT AVDAVCHGAN AVDAVCHGAN AVDAICHGAN AVDAICHGAN AVDAICHGAN AVDAICHGAN AVDAICHGAN AVDAICHGAN AVDAICHGAN AVDAICHGAN AVDAICHGAN AVDAICHGAN AVDAICHGAN AVDAICHGAN AASEIANGAP AAAEVAAGAP AAAEVAGAP AAAEVAGAP AAAEVAGAP AAAEVAGAP AAAEVAGAP	280 L AVP G I AKLH L TVP G I VKLN L TVP G I VKLN L AVP G VKLH L AVP G I VR VE L AVP G I TSLD L AVP G I SLD L AVP G I TSLD L YSS G I SKI E L YAP G V I DTTALP - V YAP G V I ETG PAEV V YAP G V I ETG PAEV V YAP G V I ETG SAAG I YPAG I HA I TG L YAG G I KI I DG L AAP G V AAVE L AAP G I SKFE L AVP G I AKLY L AVP G I AKLY	290 - AGIKRGDLVAIMT - AGIKKGDLVAIMT - VGIKRGDLVAIMT - VGIKRGDLVAIMT - KGIQPGDLVAIFT - KGIGKGETVLVET - ANLKKGELIALFT - SSLAEGELAALFT - SNLAEGELTGLFT - DNIAWGDTVAIMT - KCIQKDDKIAVFT - NQIHENNTVAVMT - KGLGTDEVVLIET - TFQMEDLVVMLA - KNVKKDSTVAIFT DGAD - EGSLVACYT GDATPEIDSQVVSVT NTHDITDSALVSCHT - SPKKGDVVAVYT - SPKKGDVVAVYT - KFRKGERVAVIS - NFQKGDRVCVLS - EGVEKGGMVALMT - TPFSKGDLVAMFT - SNIKKGDLVSIHT - SNIKKGDLVSIHT - SNIKKGDLVSIHT
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P.furiosus P.abyssi P.horikoshii T.kodakarensis M.kandleri M.jannaschii M.barkeri M.barkeri M.acetivorans M.mazei M.thermoautotrophicum M.burtonii M.stadtmanae M.maripaludis M.hungatei A.fulgidus N.pharaonis H.sp H.marismortui H.walsbyi P.torridus T.acidophilum T.volcanium A.pernix P.aerophilum N.equitans S.cerevisiae_yeast T.thermophila D.melanogaster_fruitfly M.musculus_mouse H.sapiens_human Interaction sites DC mutations	240 EYFRKAIQ EYIRKAIQ EYFRKAIQ EYFRKAIQ EPLRHVVR EELRRVIK SELRRVIR SELRRVIR SELRRVIR TFLRECIL SELRKLVR TFLRECIL SELRKLVR TFLRECIL SELRKIVK TYLRKIR KYLREIIK ELCDVVA DALRAAVQ AQLREIIQ DHLRNVIS KLFKNIFI KLLRDHIL ELFRSHFL DLLRRVVI SYLRRVVL SYLRRVVL SYLRRVVL SYLRRVVY SYLRRVVY	250 PMEKAVE PMEKAVE PMEKAVE PMEKAVE PMEEGLE PMEYGLR PMESAVS PMESAVS PMESAVS PMEFAVG PMEEGLS PMEHTTK PMEVAAA PAERALE	260 1 L P K V W I KD S 1 L P K I I L R D S 1 L P K I I L R D S 1 L P K I I L R D S 1 L P K I I L R D S 1 L P K I I L R D S 1 L P K I V V K D S 1 L P K I V V K D S 5 P R I Q M K E S 5 L P K I V K D S 1 L P K I V I K D S 5 L P K I V K D S 1 L P K V I V K E S 1 L P K V I V K E S 1 L P K V V V K D S 1 L P K V V V K D S 1 L P K V V V K D S 1 L P K V V V K D S 1 L P K V V V K D S 1 L P K V V V K D S 1 L P K V V V K D S 1 L P K V V V K D S 1 L P K V V V K D S 1 L P K V V V K D S 1 L P K V V V K D S 1 L P K V V V K D S 3 K K I V V K D S 5 F P R I V V K D S 5 F P R I V V K D S 5 H K R L V M K D S 5 H K R L V R R L	270 A V A A V T H G AD A V A A V A H G AN A V A A V A H G AN A V A A V T H G AD A V D A I C S G AS A V D A I C S G AS A V D A I C S G AS A V D A I C H G AD A V D A V C H G AT A V D A I C H G AD A A H E V A H G S D A A H E V A H G S D A A H E V A H G S D A A H E V A H G S D A A H E V A H G S D A V D A I C H G AN A V N A I C Y G A K A V N A I C Y G A K A V N A I C Y G A K	280 L AVP G I AKLH L TVP G I VKLN L AVP G VKLN L AVP G VKLH L AVP G VKLH L AVP G I TSLD L AVP G V AVE L YAG G I KI I DG L AVP G I AKL I DG L AVP G I AKL I L AVP G V L R YE L M I P G V L R YE L M I P G V L R YE L M I P G V L R YE L AVP G V L R YE L M I P G V L R YE	290 - AG I KRGDL VAIMT - AG I KKGDL VAIMT - VG I KRGDL VAIMT - VG I KRGDL VAIMT - KG I QPGDL VAIFT - KG I G KG ET VL VET - ANL KKG EL I ALFT - SSL AEGEL AALFT - SSL AEGEL TGLFT - DN I AWGDT VAIMT - KC I QKDD KI AVFT - NQ I HENN TVAVMT - KGLG TD EVVL I ET - TFQMEDL VVMLA - KN VKKD ST VAIFT DGAD - EG SL VACYT GDATPE I D SQ VVSVT NTHD I TD SAL VSCHT - SPKKGD VVAVYT - SPKKGD VVAVYT - KFR KG ER VAVIS - SPKKGD L VAMFT - SN I KKGDL VSIHT - SN I KKGDL VSIHT - SN I KKGDL VSIHT - SN I KKGDL VVIT - DG I E VNQE I VVIT
P.furiosus P.abyssi P.horikoshii T.kodakarensis M.kandleri M.jannaschii M.barkeri M.acetivorans M.mazei M.thermoautotrophicum M.burtonii M.stadtmanae M.maripaludis M.hungatei A.fulgidus N.pharaonis H.sp H.marismortui H.walsbyi P.torridus T.acidophilum T.volcanium A.pernix P.aerophilum N.equitans S.cerevisiae_yeast T.thermophila D.melanogaster_fruitfly M.musculus_mouse H.sapiens_human Interaction sites DC mutations	240 EYFRKAIQ EYIRKAIQ EYFRKAIQ EYFRKAIQ EPLRHVVR EELRRVIK SELRRVIR SELRRVIR SELRRVIR TFLRECIL SELRKLVR TLLRKLIQ EELRKIVK TYLRKIIR KYLREIIK ELLCDVVA DALRAAVQ AQLREIIQ DHLRNVIS KLFKNIFI KLLRDHIL ELFRSHFL DLLRRVVI TYLRRVLL EYIRKVFL SYLRSIIQ SYLRRVVY SYLRRVVY	250 PMEKAVE PMEKAVE PMEKAVE PMEKAVE PMEEGLE PMEYGLR PMESAVS PMESAVS PMESAVS PMEFAVG PMEFAVG PMEFAVG PMEHTTK PLEYGLQ SPLEALHO PAERALE PAERALE PAERALE PAERALE PAERALS PAERALO PAERALS PAERALO PAERALS PAERALO PAERALS PAERALO PAERALS PAERALO PAERALS PAERALO PAERALS PAERALO PAERALS PAERALO	260 1 L P K V W I KD S 1 L P K I I L R D S 1 L P K I I L R D S 1 L P K I I L R D S 1 L P K I I L R D S 1 L P K I V V K D S 1 L P K I V V K D S 5 L P K I V V K C S 5 L P K I V K C	270 A V A A V T H G AD A V A A V A H G AN A V A A V A H G AN A V A A V T H G AD A VD A I C H G AD A VD A V C H G AD A A H E V A H G AD A V D A I C H G AD A A H E V A H G AD A A H E V A H G AD A A H E V A H G AD A V D A I C H G A H H H H H H H H H H H H H H H H H	280 L AVP GI AKLH L TVP GI VKLN L TVP GI VKLN L AVP GVVKLH L AVP GVVKLH L AVP GI TSLD L AVP GI TSLD L AVP GI TSLD L AVP GI TGLD L AVP GI TGLD L AVP GI VSFS L ASS GVVKLD L SSR GV VSHD L SSR GV VSHD L SSR GV VSHD L SVR GVAYVE L SVR	290 - AGIKRGDLVAIMT - AGIKKGDLVAIMT - VGIKRGDLVAIMT - VGIKRGDLVAIMT - KGIQRGDLVAIFT - KGIQRGETVLVET - ANLKKGELIALFT - SSLAEGELAALFT - SSLAEGELAALFT - DNIAWGDTVAIMT - KCIQKDDKIAVFT - NQIHENNTVAVMT - KGLGTDEVVLIET - TFQMEDLVVMLA - KNVKKDSTVAIFT DGAD - EGSLVACYT GDATPEIDSQVVSVT NTHDITDSALVSCHT - SPKKGDVVAVYT - SPKKGDVVAVYT - KFRKGERVAVIS - NFQKGDRVCVLS - EGVEKGGMVALMT - SNIKKGDLVSIHT - SNIKKGDLVSIHT - SNIKKGDLVSIHT - SNIKKGDLVSIHT - OGIELDQEIVVIT

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P.furiosus	LKDEL	ALGK	AMMTS	QEML	EKTKG	IAVD	VEKV	FMPRC	WYPK	LWEK	RDRS-			
P.abyssi	LKDEL	ALGK	AMMST	QEMI	ERSKG	IAVD	VEKV	FMPRC	WYPK	LW				
P.horikoshii	LKDEL	ALGK	AMMTS	QEMN	/QR S KG	IAVD	VEKV	FMPRC	WYPK	LW				
T.kodakarensis	LKDEL	ALGK	АММ Т Т	GEML	QKSKG	IAVD	VDKV	FMPRC	WYPK	LWKE	KE			
M.kandleri	LKGEA	/ALGV/	ΑΚΑΤΝ	KEML	HADRG	I MVD	T KR V	LMEPG	ТҮРК	AWGL	KTPGE			
M.jannaschii	LKGEA	/ A V G K /	ALMN T	KEIL	N AD KG	VAVD	VERV	YMDRG	TYPR	MWKR	KK			
M.barkeri	LKGEL	/ A L A K /	AEMST	EELL	KASTG	LAATS	SVRI	MMEIG	БТҮРК	GWTK	KEYG	/ES		
M.acetivorans	LKGEL	/ A L A K /	ΑΕΜΝ Τ	EEIL	KASAG	IAASI	PIRV	LMEAG	ТҮРК	GWTK	KEESV	/RL		
M.mazei	LKGEL	/ A L A K /	<u>акмтт</u>	EEIL	KASAG	IAASI	PIRV	LMEAG	6 T Y PR	GWTK	KEEK V	/QL		
M.thermoautotrophicum	LKGEL	/GV <mark>G</mark> E/	ASMSA	LDIA	AADGG	LVIE	TRKV	FMEPG	6 T Y PR	MWR -				
M.burtonii	LKGEA	/ALCR	S F MN A	DELE	ENESHG	I AC I '	T ER V	IMDAA	A I Y PR	CWKA	K			
M.stadtmanae	LKEELL	A I G T (	СМҮЅТ	NDII	NSDTK	IIVD	IQKV	FILPN	ІТҮРК	MWK -				
M.maripaludis	LKGEA	/ A V G K I	P L MN T	KDML	KTEEG	EVVE	ITRV	IMEPG	SIYPR	IWKK	(RN KN D	KSKPEL	<u> </u>	
M.hungatei	G - DD F I	GIGE	ALVSS	;	- SRIV	PGEK	GLVV	APR		L VMG	!	DIGVYF	PAVWKAH	łΚΡ
A.fulgidus	LKNEL	/ A I GR /	ALMD A	EDIY	(R L K KG	IAAD	I QR V	MMERG	ЗVYPK	VWKS	SSD			
N.pharaonis	PDGAA	/CLGWI	_ VGD P	·	DAADG	ΤΥΑΕΙ	L ER V	LV						
H.sp	AGGTA	/CLGRI	_ VGD P	·	D AD AG	VVVAI	L ER V	LV						
H.marismortui	PDGAA	/CLGTI	VSD P	·	DADSG	LVVEI	LDRM	LV						
H.walsbyi	PD E T A V	/CLGR	VSGPL		DAESG	EVISI	L ER V	LV						
P.torridus	EKNEL	/ A T G T I	MM VN A	DEIY	/DLKVI	DIDN	VLIE	TGDND	GKDS	LVRK	DNRW	(D I P V Q F	<pre>K<pre>K<pre>K<pre>K<pre>K<pre>L<pre>F</pre></pre></pre></pre></pre></pre></pre>	IGN
T.acidophilum	EDNDL	/GTGI/	AMC S S	DNIF	- MKVV	DFDH	IFLE	ADD	GKDN	VVR I	6	GKEAVQK	< SG SG L F	ΙKD
T.volcanium	EDNELL	.GTGI	ARCDS	SNLF	- MKVV	DFDH	IFVE	AKH	GKGD	VVRD	F	REKDVQF	RPGQQVH	IRN
A.pernix	LKGELI	GLGK	ALASA	QEML	EAERG	IVVSI	PTRI	IMERG	BLYPR	MWKR	QQAPC	QGA		
P.aerophilum	LKGELI	GIGR	ALVGS	SEEVK	KMERG	LVAR	TDRV	VMRRG	БТҮРА	MWKR	KAKSC	QSDSA		
N.equitans	LKGEL	/AIGI/	ALMDS	KEML	EKKRG	IAVD	I ER V	FMKPG	6 L Y P K	MWVS	QG			
S.cerevisiae_yeast	TKGEAI	AVAL	AQMST	VDLA	SCDHG	VVAS	VKRC	IMERD	LYPR	RWGL	GPVAC	Q K K K Q M F	KADGKLD	) K Y
T.thermophila	TKGEAI	AVAV	ΑQΜΤΤ	SELA	ATCDHG	I VCK	T KR V	IMDRD	LYPK	RWGL	GPRAL	RKKNLI	KEGLLD	) KH
D.melanogaster_fruitfly	TKGEAI	CLAI	ALMTT	ATMA	SCDHG	VVAK	I KR V	IMERD	TYPR	KWGL	GPKAS	SAKKALI	AAGKLD	) K F
M.musculus_mouse	TKGEAI	CMAI	ALMTT	AVIS	STCDHG	ΙVΑΚ	I KR V	IMERD	TYPR	KWGL	GPKAS	SQKKMMI	KQGLLD	) KH
H.sapiens_human	TKGEAI	CMAI	ALMTT	AVIS	STCDHG	ΙVΑΚ	I KR V	IMERD	TYPR	KWGL	GPKAS	SQKKLMI	KQGLLD	) KH
Interaction sites					••	• •		•	•	•••	•			
DC mutations					$\bigtriangleup$						$\triangle$ $\triangle$		$\bigtriangleup$	
Pf Chf5	<u>β</u> 16	6	α	2' -		β17								
110013														

P.furiosus	
P.abyssi	
P.horikoshii	
T.kodakarensis	
M.kandleri	
M.jannaschii	
M.barkeri	
M.acetivorans	
M.mazei	
M.thermoautotrophicum	]
M.burtonii	
M.stadtmanae	
M.maripaludis	
M.hungatei	KR E K S
A.fulgidus	
N.pharaonis	
H.sp	
H.marismortui	
H.walsbyi	
P.torridus	LQGSQEWKDTGNRGNPKRGGTGSKGFSSGFRKRKAKR
T.acidophilum	I QR SEGR KD T R TGWYGRD TG PE K T ADR VWKG KN KGR V Y PR SG AD KGGGG K ER HGRD HQ
T.volcanium	IRDAAHGPDSRTGRGRKETGPQIAPNRVRKLQNKTGVHRRPGSH
A.pernix	
P.aerophilum	
N.equitans	
S.cerevisiae_yeast	GRVNENTPEQWKKEYVPLDNAEQSTSSSQETKETEEEPKKAKEDSLIKEVETEKEEVKEDDSKK
T.thermophila	GKPNDQTPNDWTVFYVNEENNNIPKPEEN
D.melanogaster_fruitfly	GRPNENTPKEWLTGYVDYN AKKPAAQEVSPTNGSSEPSKRKLSTSSVEETAAAAVSEETPSK
M.musculus_mouse	GKPTDNTPATWKQDYIDYSDSGKNTLVTEAVQAPQLAAEAVNVIKRKRDSESESDETP-TVPQL
H.sapiens_human	GKPTDSTPATWKQEYVDYSESAKKEVVAEVVKAPQVVAEAAKTAKRKRESESESDETPPAAPQL
Interaction sites	
DC mutations	$\Delta$ $\Delta\Delta$

Pf Cbf5

P. abyssi P. horikoshi C. kodakarensis M. kandleri K. kodakarensis M. kandleri M. jannaschii M. bankeri M. acetivorans M. marzei M. marzei M. thermoautotrophicum M. burtonii M. stadtmanae M. maripaludis M. hungatei A. fulgidus N. pharaonis H. sp H. marismortui H. walsbyi P. torridus T. acidophilum A. pernix P. aerophilum A. pernix E. KKEKKD - KKEKKEKKEKKEKKEKKEKKEKKEKKEKKEKKEKKEKKE	P.furiosus	
P.horikoshii T.kodakarensis M.kandleri M.kandleri M.kandleri M.jannaschii M.barkeri M.acetivorans M.mazei M.mazei M.thermoautotrophicum M.thermoautotrophi	P.abyssi	
T.kodakarensis M.kandleri M.jannaschii M.barkeri M.barkeri M.acetivorans M.mazei M.mazei M.thermoautotrophicum M.burtonii M.burt	P.horikoshii	
M.kandleri M.jannaschii M.jannaschii M.acetivorans M.mazei M.mazei M.thermoautotrophicum M.burtonii M.stadtmanae M.marjaludis M.marjaludis M.hungatei A.fuljidus M.hungatei A.fuljidus M.hungatei A.fuljidus M.hungatei A.fuljidus M.hungatei A.fuljidus M.hungatei A.fuljidus M.hungatei A.fuljidus M.hungatei A.fuljidus M.hungatei A.fuljidus M.hungatei A.fuljidus M.hungatei A.fuljidus M.hungatei A.fuljidus M.hungatei A.fuljidus M.hungatei A.fuljidus M.hungatei A.fuljidus M.hungatei A.fuljidus M.hungatei A.fuljidus H.sap Interaction sites DC mutations Pf Cbf5	T.kodakarensis	
M. Jannaschii M. Jankrei M. Aactivorans M. Mazei M. Mazei M. Thermoautotrophicum M. thermoautotrophicum M. thermoautotrophicum M. burtonii M. burtonii	M.kandleri	
M.barkeri M.acetivorans M.mazei M.mazei M.thermoautotrophicum M.burtonii M.stadtmanae M.maripaludis M.stadtmanae M.maripaludis M.hungatei A.fulgidus N.pharaonis H.sp H.marismortui H.sp H.marismortui H.walsbyi P.torridus T.acidophilum T.acidophilum N.penrix P.aerophilum N.equitans S.cerevisiae_yeast E.KKEKKD - KKEKKEKKEKKEKKEKKEKKEKKEKKEKKEKKEKKEKKE	M.jannaschii	
M.acetivorans M.mazei M.thermoautotrophicum M.burtonii M.stadtmanae M.maripaludis M.hungatei A.fulgidus M.hungatei A.fulgidus N.pharaonis H.sp H.marismortui H.marismortui H.maismortui H.KEKKKKK - KHKGD EAPEAAEEEAEPVEKEKKKKKKKKKKKKKKKKKKKKKKKK	M.barkeri	
M.mazei M.thermoautotrophicum M.stadtmanae M.maripaludis M.maripaludis M.hungatei A.fulgidus N.pharaonis H.sp H.sp H.marismontui H.walsbyi P.torridus T.acidophilum T.acidophilum P.torridus T.acidophilum N.equitans S.cerevisiae_yeast EKKEKKD - KKEKKEKKEKKEKKEKKEKKEKKEKKEKKEKKEKKEKKE	M.acetivorans	
M.thermoautotrophicum - M.burtonii M.stadtmanae M.maripaludis M.hungatei A.fulgidus N.pharaonis H.sp H.marismortui H.walsbyi P.torridus T.acidophilum T.volcanium A.pernix P.aerophilum S.cerevisiae_yeast S.cerevisiae_yeast EKKEKKD - KKEKKEKKEKKEKKEKKEKKEKKEKKEKKEKKEKKEKKE	M.mazei	
M.burtonii M.stadtmanae M.maripaludis M.hungatei A.fulgidus N.pharaonis H.sp H.sp H.marismortui H.walsbyi P.torridus T.acidophilum T.acidophilum T.volcanium A.pernix P.aerophilum N.equitans S.cerevisiae_yeast EKKEKKD - KKEKKEKKEKKEKKEKKEKKEKKEKKEKKEKKEKKEKKE	M.thermoautotrophicum	)
M.stadtmanae M.maripaludis M.hungatei A.fulgidus N.pharaonis H.sp H.marismortui H.walsbyi P.torridus T.acidophilum T.acidophilum T.volcanium A.pernix P.aerophilum N.equitans S.cerevisiae_yeast EKKEKKD - KKEKKEKKEKKEKKEKKEKKEKKEKKEKKEKKEKKEKKE	M.burtonii	
M.maripaludis M.hungatei A.fulgidus N.pharaonis H.sp H.marismortui H.walsbyi P.torridus T.acidophilum T.acidophilum M.equitans S.cerevisiae_yeast S.cerevisiae_yeast EKKEKKD - KKEKKEKKEKKEKKEKKEKKEKKEKKEKKEKKEKKEKKE	M.stadtmanae	
M.hungatei A.fulgidus N.pharaonis H.sp H.marismortui H.walsbyi P.torridus T.acidophilum T.acidophilum A.pernix P.aerophilum N.equitans S.cerevisiae_yeast EKKEKKD - KKEKKEKKEKKEKKEKKEKKEKKEKKEKKEKKEKKEKKE	M.maripaludis	
A.fulgidus N.pharaonis H.sp H.marismortui H.walsbyi P.torridus T.acidophilum T.acidophilum T.volcanium A.pernix P.aerophilum N.equitans S.cerevisiae_yeast S.cerevisiae_yeast EKKEKKD - KKEKKEKKEKKDKKEKKEKKEKKEKKEKKEKKEKKEKKEK	M.hungatei	
N.pharaonis         H.sp         H.marismortui         H.walsbyi         P.torridus         T.acidophilum         T.acidophilum         T.volcanium         A.pernix         P.aerophilum         N.equitans         S.cerevisiae_yeast         EKKEKKD - KKEKKEKKEKKEKKEKKEKKEKKEKKEKKEKKEKKEKKE	A.fulgidus	
H.sp H.marismortui H.walsbyi P.torridus T.acidophilum T.acidophilum A.pernix P.aerophilum N.equitans S.cerevisiae_yeast EKKEKKD - KKEKKEKKEKKEKKEKKEKKEKKEKKEKKEKKEKKEKKE	N.pharaonis	
H.marismortui H.walsbyi P.torridus T.acidophilum T.volcanium A.pernix P.aerophilum N.equitans S.cerevisiae_yeast EKKEKKD - KKEKKEKKEKKEKKEKKEKKEKKEKKEKKEKKEKKEKKE	H.sp	
H.walsbyi P.torridus T.acidophilum T.volcanium A.pernix P.aerophilum N.equitans S.cerevisiae_yeast EKKEKKD - KKEKKEKKEKKEKKEKKEKKEKKEKKEKKEKKEKKEKKE	H.marismortui	
P.torridus	H.walsbyi	
T.acidophilum         T.volcanium         A.pernix         P.aerophilum         N.equitans         S.cerevisiae_yeast         EKKEKKD - KKEKKEKKEKKEKKEKKEKKEKKEKKEKKEKKEKKEKKE	P.torridus	
T.volcanium         A.pernix         P.aerophilum         N.equitans         S.cerevisiae_yeast         EKKEKKD - KKEKKEKKEKKEKKEKKEKKEKKEKKEKKEKKEKKEKKE	T.acidophilum	
A.pernix       P.aerophilum         P.aerophilum       N.equitans         S.cerevisiae_yeast       EKKEKKD - KKEKKEKKEKKEKKEKKEKKEKKEKKEKKEKKEKKEKKE	T.volcanium	
P.aerophilum       N.equitans         N.equitans       EKKEKKD         S.cerevisiae_yeast       EKKEKKD - KKEKKEKKEKKEKKEKKEKKEKKEKKEKKEKKEKKEKKE	A.pernix	
N.equitans       EKKEKKD         S.cerevisiae_yeast       EKKEKKD         T.thermophila       EKKEKKD         D.melanogaster_fruitfly       DKKKKKK-         M.musculus_mouse       KEKKKKK         H.sapiens_human       IKKEKKKSKKDKKAKAGLESGAEPGDGDSDTTKKKKKKKKKKKKKKKKKKKKKKKKKKKKKKKK	P.aerophilum	
S.cerevisiae_yeast       EKKEKKD - KKEKKEKKEKKEKKEKKEKKEKKEKKEKKEKKEKKEKKE	N.equitans	
T.thermophila       D.melanogaster_fruitfly         D.melanogaster_fruitfly       D KKKKKKK - KH KGD EEAPEAAEEEAEPVEKEKKKKKKKK KK KD KDRDRDEAQE         M.musculus_mouse       KEKKKKK D KKPKTVL ESGG ETGDGDNDTTKKKKKKKKK - VKVVEEMSE         H.sapiens_human       I KKEKKKSKKDKKAKAGL ESGAEPGDGD SDTTKKKKKKKKKKKKKKEVELVSE         Interaction sites       DC mutations         Pf Cbf5	S.cerevisiae_yeast	EKKEKKD - KKEKKEKKEKKDKKEKKEKKEKKRKSEDGDSEEKKSKKSKK
D.melanogaster_fruitfly D.KKKKKK - KHKGDEEAPEAAEEEAEPVEKEKKKKKKKKKKKDKDRDRDEAQE M.musculus_mouse KEKKKKK DKKPKTVLESGGETGDGDNDTTKKKKKKKK - VKVVEEMSE H.sapiens_human IKKEKKKSKKDKKAKAGLESGAEPGDGDSDTTKKKKKKKKKKKKKEVELVSE Interaction sites DC mutations Pf Cbf5	T.thermophila	
M.musculus_mouse       KEKKKKK DKKPKTVLESGGETGDGDNDTTKKKKKKKK - VKVVEEMSE         H.sapiens_human       IKKEKKKSKKDKKAKAGLESGAEPGDGDSDTTKKKKKKKKKKKKKEVELVSE         Interaction sites       DC mutations         Pf Cbf5	D.melanogaster_fruitfly	DKKKKKKKHKGDEEAPEAAEEEAEPVEKEKKKKKKKKDKDRDRDEAQE
H.sapiens_human IKKEKKKSKKDKKAKAGLESGAEPGDGDSDTTKKKKKKKKKKKKKKEVELVSE Interaction sites DC mutations Pf Cbf5	M.musculus_mouse	KEKKKKK DKKPKTVLESGGETGDGDNDTTKKKKKKK - VKVVEEMSE
Interaction sites DC mutations Pf Cbf5	H.sapiens_human	I KKEKKKSKKDKKAKAGLESGAEPGDGDSDTTKKKKKKKKAKEVELVSE
DC mutations Pf Cbf5	Interaction sites	
Pf Cbf5	DC mutations	
	Pf Cbf5	

**Figure S1.** Sequence alignment of Cbf5 and sites of interactions with the pseudouridine pocket (red triangle for SH1 or SH2 stem) and with the guide RNA alone (yellow diamond for P2 and yellow circle for P1 stem). Residues interacting with both guide RNA (P2 or P1) and the pseudouridine pocket (SH1 or SH2) are labeled by red squares. Sites of interactions are defined as those that have more than 2  $Å^2$  decrease in solvent accessible surface as result of RNA binding. Mutations in human Cbf5 that cause dyskeratosis congenita (DC) are also indicated with open squares (multiple families) or triangles (single family).



**Figure S2.** Density modified map  $(3F_0-2F_c)$  computed prior to modeling of RNA and using protein coordinates for phases only. The map is displayed around the RNA as indicated by the stick models (guide RNA is in yellow and target RNA is in red).

**Table S1.** Diffraction data statistics of the crystals containing the wild-type Cbf5-Nop10-Gar1 complex bound with the bi-molecular guide RNA and the target RNA containing 5-fluorouridine at the target site. Values in parentheses refer to those of the highest resolution shell.

Space group*	P4 <sub>1</sub> 2 <sub>1</sub> 2
Unit-cell parameters (Å)	
a	96.629
b	96.629
с	238.951
Resolution range (Å)	50-8.0 (8.3-8.0)
No. of unique reflections	2309 (230)
Redundance	6.4 (6.7)
Completeness (%)	98.7 (100.0)
Ι/σ(Ι)	41.1 (21.8)
R <sub>sym</sub> (%)	7.9 (15.5)

\*the space group is assumed to be the same as the Asp85Ala mutant-containing complex

Group 1. C	bf5								
T(Å <sup>2</sup> )	-0.0205	-0.0707	0.3184	-0.3764	-0.2188	0.1242			
L(° <sup>2</sup> )	1.876	1.7205	4.9607	0.1261	0.5403	-1.2868			
S(Å2)	0.0846	-0.4581	0.3734	-0.1793	-0.2675	-0.515	0.4228	-0.5061	1.0077
Group 2. N	lop10								
T(Ų)	-0.1567	-0.273	0.1119	-0.2459	-0.1013	-0.1515			
L(° <sup>2</sup> )	7.6412	3.1016	11.2289	1.7167	1.1447	-3.4687			
S(Å2)	0.0143	-0.1582	0.1439	1.0323	-0.3755	-0.2104	-0.2068	0.2505	0.6775
Group 3. G	ar1								
T(Ų)	0.5526	0.9082	0.8904	-0.6972	-0.2446	0.4869			
L(° <sup>2</sup> )	14.0046	6.7073	10.2546	2.7106	1.6742	-4.3765			
S(Å2)	-0.3504	0.2738	0.0766	1.7614	1.3078	0.2559	-0.4432	-1.0284	1.1234
Group 4. 5	' guide RNA s	strand							
T(Ų)	0.5429	0.4862	0.2118	-0.19	-0.0595	0.2529			
L(° <sup>2</sup> )	1.9926	4.708	17.4169	-0.8017	5.7773	-4.0332			
S(Å2)	0.1349	0.1396	-0.2746	-0.6752	0.5955	0.4962	0.8044	-2.6099	-0.9471
Group 5. 3	' guide RNA s	strand							
T(Ų)	0.5869	0.0952	-0.0135	-0.5015	-0.3204	-0.0524			
L(° <sup>2</sup> )	2.6505	2.7531	7.8963	-1.5719	0.9959	-3.3112			
S(Å2)	0.0247	0.0135	-0.0381	-0.6623	0.0124	-0.1304	0.7577	-1.2759	-0.0453
Group 6. ta	arget RNA								
T(Ų)	0.671	0.1768	0.2631	-0.7094	-0.4597	-0.0996			
L(° <sup>2</sup> )	17.8313	30.3146	0	12.1335	0	0			
S(Å2)	-0.4621	0.3104	0.1516	-0.3801	1.0859	0.6757	0.1528	-0.7902	-1.283

 Table S2. Elements of T, L, S tensors for the six groups in the orthogonal coordinate system used in TLS refinement