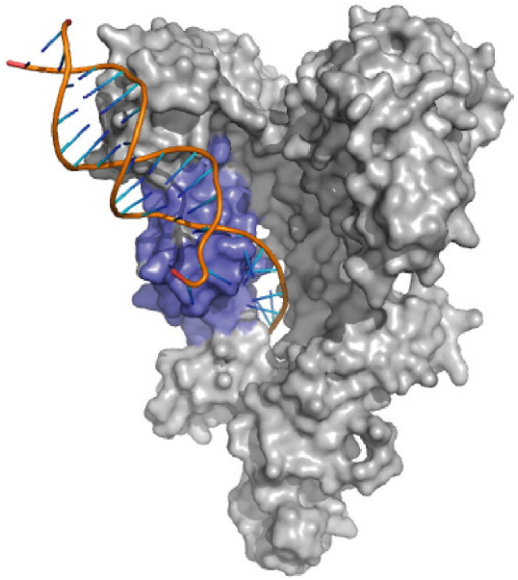

Fig. 3. Model for nucleic acid binding to Tex HtH motif. The archeal Hel308 structure (PDB accession code: 2P6R; only the DNA is shown here) was superimposed on the Tex structure (gray) by aligning HtH regions (blue). The path of the superimposed Hel308-bound ssDNA projects through a hole in the core of the Tex structure. The structure is oriented as in Fig. 1a.

proteins are predicted to be ribonucleases or resolvases based on homology to RuvC Holliday junction resolvases.[2,22,23] Like RuvC, which is structurally and biochemically well characterized, YqgF nuclease domains preserve the overall topology and the majority of structural and sequence elements characteristic of the RNase H fold.[2,24–26] The Tex YqgF domain maintains these core structural elements and aligns especially well with RuvC nucleases (PDB accession code: 1HJR, 120 C^{α}, RMSD = 3.0), although Tex does not appear to possess nuclease activity (see below).

HhH

The Tex structure contains two adjacent HhH motifs, comprising residues 502–531 and 537–557, both of which were predicted from earlier sequence analysis (Fig. 4).[5,6] The two HhH motifs are related by an approximately 90° rotation with respect to each other and pack together through extensive conserved hydrophobic interactions to generate a single, compact unit called an $(HhH)_2$ domain.[27] In contrast to a canonical $(HhH)_2$ structure in which the two HhH motifs are connected by an extra helix, the Tex $(HhH)_2$ domain makes the connection with a short five-residue loop. The typical function of $(HhH)_2$ domains is to bind dsDNA, mediated through nonspecific interactions with nitrogen atoms in the protein backbone and oxygen atoms in the DNA phosphate groups.[27] In Tex, the binding face of this domain lies on the surface of the structure and would be accessible to a potential nucleic acid substrate.

S1 domain

The Tex S1 domain (Fig. 5) adopts the canonical topology characteristic of the S1 RNA-binding domain family.[28] First identified as a motif of the ribosome essential for translational initiation, S1 domains are ubiquitous and found primarily in proteins that bind RNA and/or have nuclease activity.[29,30] The Tex S1 domain adopts the overall five-stranded antiparallel β-barrel topology representative of the ubiquitous oligonucleotide/oligosaccharide binding (OB) fold. OB-fold proteins, including S1 domains, present a common binding cleft for interaction with a variety of different ligands, the most common being nucleic acids.[3,30] This cleft runs perpendicular to the axis of the β-barrel where nucleic acids almost always bind with common polarity. The Tex S1 domain contains a short 3_{10} helix (H35) adjacent to the binding cleft that, along with a strong preference for ssRNA, distinguishes S1 domains from other OB-fold proteins.[31,32]

Evidence for flexibility

Comparison of the two crystal forms, which differ by 25 Å in *b*-axis length and each contain one molecule in the asymmetric unit, indicates that Tex displays flexibility in the disposition of its C-terminal S1 domain. The two Tex structures superimpose closely throughout (RMSD = 1.596 over 510 C^{α} atoms), with the exception of a small rotation in the YqgF domain and a 14-Å displacement of the S1 domain (Fig. 6). The S1 domain rearrangement is accomplished by rotation in the loop that tethers the domain to the rest of the Tex structure. C-terminal to the S1 domain, there is no discernable electron density for residues 731–785 in either crystal form,

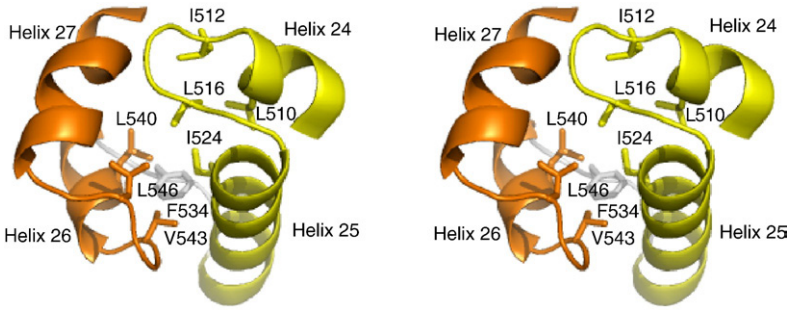

Fig. 4. The Tex $(HhH)_2$ domain stereoview. Tandem HhH motifs (yellow and orange) are linked by a short loop (gray) and pack together to form a single $(HhH)_2$ domain. Conserved hydrophobic residues that comprise the core of the HhH packing surface are indicated. The view is looking down on the surface that binds dsDNA in other structures.