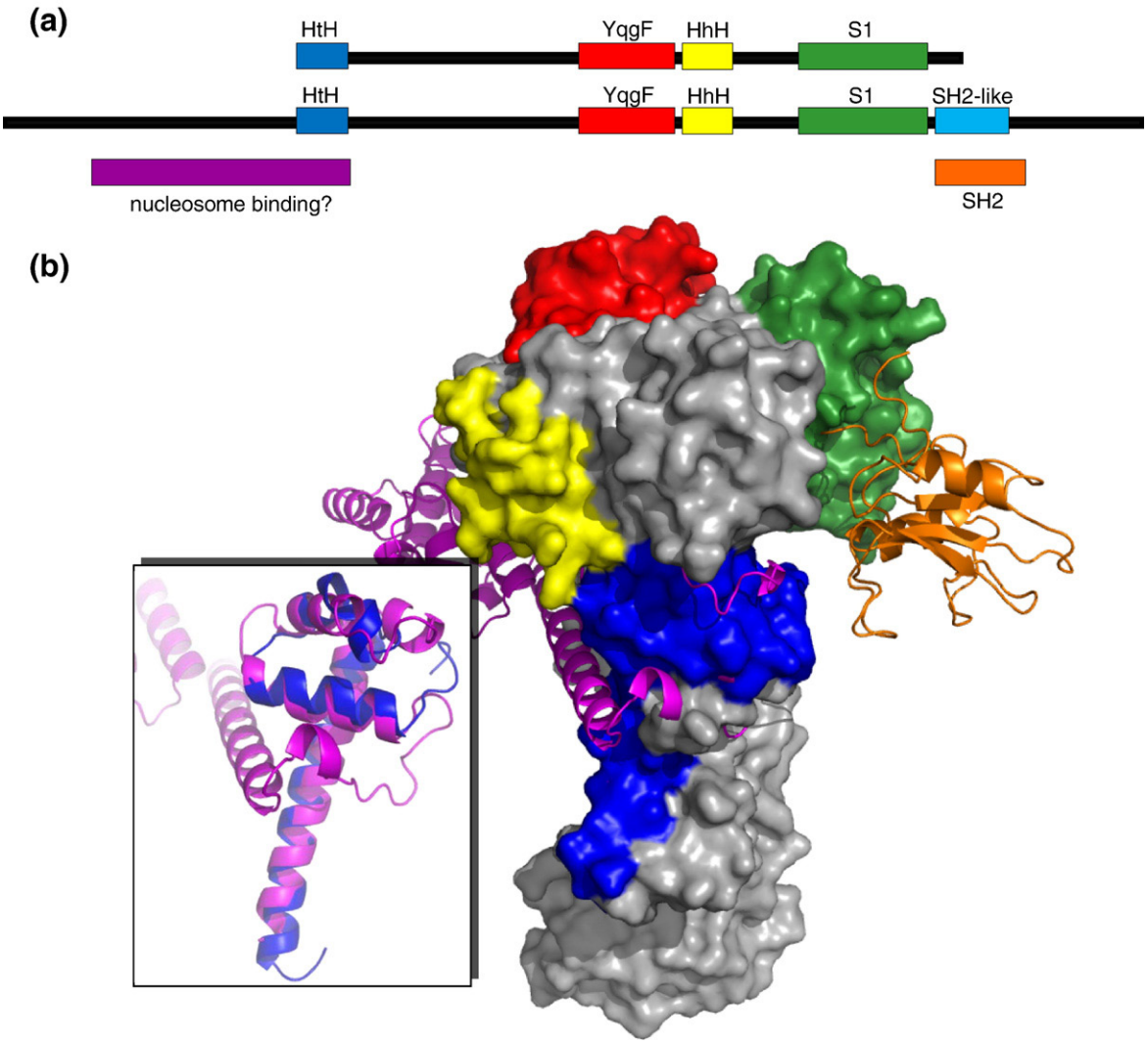

Fig. 9. Model for Spt6 structure. (a) Comparison of Tex (top) and Spt6 (bottom) domain structures. (b) The Tex structure is used to model the central portion of the Spt6 structure (surface representation). A proposed nucleosome-binding domain (magenta, inset) is modeled based on structural alignment with the C-terminal portion of the ISWI nucleosome interacting domain (PDB accession code: 1OFC). An SH2-like domain (orange, PDB accession code: 1PIC) is modeled at the C-terminal end of the S1 domain.

Structural comparisons suggest that a region toward the Spt6 N-terminus may possess histone chaperone activity. A DALI search of the Tex HtH domain identified significant structural homology (z score = 5.2, RMSD = 2.4 Å) with the nucleosome-binding SLIDE domain of ISWI (PDB accession code: 1OFC).[40] While there is insufficient sequence for Tex to form a complete SLIDE-like nucleosome-binding domain, Spt6 contains an additional sequence N-terminal to the region of Tex homology that could potentially fulfill this role. In this model, histone chaperone activity would be located on the face of Spt6 opposite from the S1 and SH2-like domains (Fig. 9).

Spt6 has demonstrated eukaryotic exosome-recruiting faculties,[12] and we have observed that Tex copurifies with RNase E and PNPase, which, in *E. coli*, are components of the RNA degradosome (I.V.-G. and S.L.D., unpublished data). This may at least partially explain why Tex appears to negatively effect transcription when overexpressed[1,2] but does not itself appear to possess ribonuclease activity in our assays; it may be coordinating the recruitment, or influencing the activities, of degradosome-associated ribonucleases. Further, Spt6 interacts with an elongating RNAP at the C-terminal domain based on elongation-specific phosphorylation.[12] The observation that Tex from *P. aeruginosa* copurifies with components of RNAP (I.V.-G. and S.L.D., unpublished data) suggests that it may be associated, either directly or indirectly, with the transcription machinery; functional parallels may therefore exist between Spt6 and Tex.

In summary, the Tex crystal structures reveal an elongated helical protein comprising several putative nucleic acid binding domains. Biochemical characterization revealed that Tex binds ssDNA, dsDNA, ssRNA, and dsRNA substrates with a preference for ssRNA, with a primary interface being mediated by interactions along the canonical OB-fold binding