SPT15 encodes TATA-binding protein, an essential general transcription factor involved in directing the transcription of genes by the three nuclear RNA polymerases, I, II, and III. TBP is a component of the polymerase I core factor, TFIID, and TFIIIB, which are complexes required for delivering polymerases I, II, and III, respectively, to transcription start sites. TBP localizes to promoter sites either by direct binding to a TATA box motifAN; 11, 12) or through recruitment by other complexes such as UAF, SAGA, or TFIIIC.TBP is one of the few transcription factors highly conserved among all eukaryotes and archaea, though it is not found in eubacteria. Across eukaryotes, the 180-residue core domain shares 80% sequence identity. In humans, trinucleotide expansions in TBP lead to the Huntington-like neurological disorder Spinocerebellar Ataxia-17.In S. cerevisiae, the TBP polypeptide is a 240-residue molecule with a 60 amino acid N-terminal region that is divergent among eukaryotes, and a highly-conserved C-terminal core domain. The N-terminal domain has been suggested to inhibit TBP/DNA interaction and to mediate TBP/protein interaction. The C-terminus is pseudo-symmetric and saddle-shaped, with amino and carboxyl-terminal stirrups flanking a concave/convex surface. The concave side of TBP primarily binds to the minor groove of DNA, which unwinds the double-helix and induces a dramatic bend in the DNA. The convex side is the site of interaction for many transcriptional activators and repressors. The C-terminal stirrup and the concave side of TBP are involved in the formation of TBP homodimers, which serves as a self-regulatory mechanism as these dimers are inactive and must disassociate before the protein is able to bind DNA.Levels of transcription are often regulated by targeting TBP. For example, dimer disassociation and TBP/promoter association are considered the rate-limiting steps in the formation of transcriptional pre-initiation complexes; the slow rate of this process serves to prevent unregulated gene expression. Many transcriptional activators, such as the SAGA and mediator complexes, stimulate transcription by facilitating TBP binding to the TATA boxwhile transcriptional repressors such as histones, Mot1p, and negative cofactor 2 impede this interaction.As a component of the polymerase I core factor, TFIID, and TFIIIB, TBP is essential for positioning the appropriate RNA polymerase at the transcription start site. Polymerase I, which directs the transcription of rRNA, localizes to the promoters of ribosomal genes bound by the upstream activating factorand the core factor. UAF binds to a pol I promoter in a sequence-specific manner and then recruits CF to a site in the promoter known as the core domain. The core domain overlaps the site of transcription initiation so CF is able to position pol I over the transcription start site and facilitate multiple rounds of transcription. Along with TBP, CF is comprised of the subunits Rrn6p, Rrn7p, and Rrn11p. Although initial TBP association with CF is functional but not stable, this interaction is stabilized upon contact with UAF, which is mediated by protein-protein interaction between TBP and the UAF subunit Rrn9p.TFIID is a transcription factor complex that is required for RNAPII-mediated transcription of protein-coding genes and some small nuclear RNAs. The complex is composed of Spt15pand 14 TBP-associated factors: Taf1p, Taf2p, Taf3p, Taf4p, Taf5p, Taf6p, Taf7p, Taf8p, Taf9p, Taf10p, Taf11p, Taf12p, Taf13p, Taf14p. The TFIID complex is required for basal transcription, but some individual subunits regulate the activated transcription of a subset of genes. Recognition of promoter DNA by the TFIID complex is required for the formation of the preinitation complexduring transcription initiation. The interaction between the TFIID complex and the promoter is stabilized by TFIIA. The recruitment of TFIID to promoters is dependent on an upstream activating sequence in the promoter region.The TFIIIB complex is a initiation factor for RNA polymerase III, which transcribes tRNAs, most small nuclear RNAs, and 5S rRNA. TFIIIB, comprised of TBP, Brf1p, and Bdp1p, directs pol III to the transcriptional start site of these genes and is itself recruited to a location immediately upstream of the transcriptional start site by the TFIIIC complex. TFIIIB binds to TFIIIC mainly through contact between TFIIIB subunits Brf1p and Bdp1p and the TFIIIC subunit Tfc4p, and between TBP and the TFIIIC subunit Tfc8p. The TFIIIB footprint on promoter DNA is influenced by the DNA-binding site preferences of the TBP subunit and by the non-histone chromatin proteins Nhp6Ap and Nhp6bp. TFIIIB function is also important for promoter opening, reinitiation of pol III transcription, and targeting and efficiency of Ty3 retrotransposition. TFIIIB is also the target of Maf1-mediated repression of pol III transcription.