Review of gene expression by TBP-associated proteins

Tong Ihn Lee and Richard A. Young

Whitehead Institute for Biomedical Research, Cambridge, Massachusetts 02142 USA and Department of Biology, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139 USA

Transcription of rRNA, mRNA, and small RNAs in eukaryotes is accomplished by RNA polymerases I, II, and III. Much of the control of transcription occurs at the promoters, where transcriptional regulators can affect the recruitment of polymerases and their accessory factors, the rate at which the polymerases leave the promoter and the rate of transcriptional elongation. At least three levels of control must operate to ensure that regulation of the entire genome is efficiently coordinated in response to the extracellular environment and the cell cycle. There must be mechanisms that permit cells to rapidly increase or reduce the transcription of specific protein-coding genes. There must be an ability to modulate global transcription to adjust for changing levels of nutrients or growth factors, and to accommodate the demands of the cell cycle. Finally, there must be a system to coordinate the relative amounts of rRNA, mRNA, and small RNAs.

One factor that is present at promoters used by all three RNA polymerases, and is thus a likely target for all three types of control, is TATA-binding protein (TBP). TBP is associated with a variety of factors that play important roles in both general and gene-specific regulation of gene expression. Early biochemical studies in mammalian, fly, and yeast systems identified three distinct complexes containing TBP, each of which directs transcription at class I, II, or III promoters. The TBP-associated factors that bind to class I, II, and III promoters are called TAFI, TAFII, and TAFIII, respectively. There is now evidence that at least five additional factors interact with TBP. One factor that is present at promoters used by all three RNA polymerases, and is thus a likely target for all three types of control, is TATA-binding protein (TBP). TBP is associated with a variety of factors that play important roles in both general and gene-specific regulation of gene expression. Early biochemical studies in mammalian, fly, and yeast systems identified three distinct complexes containing TBP, each of which directs transcription at class I, II, or III promoters. The TBP-associated factors that bind to class I, II, and III promoters are called TAFI, TAFII, and TAFIII, respectively. There is now evidence that at least five additional factors interact with TBP. Among the eight factors that interact with TBP, four (TAFI, TAFII, and PTF/SNAPc) function in promoter selection (Fig. 1). The other four (SAGA, Mot1, NC2, and Nots) function together with TAFII to regulate expression of protein-coding genes (Fig. 2). All but one of these factors (PTF/SNAPc) is highly conserved among eukaryotes. The factors that interact with TBP in yeast are summarized in Table 1.

Here we review our current understanding of the eukaryotic TBP-associated proteins and their roles in regulation of gene expression. We describe evidence that relatively small pools of each of the TBP-associated proteins interact with and regulate a large cellular pool of TBP in yeast, and discuss its implications for genome-wide regulation. The conservation of the TBP-associated proteins suggests that the regulatory mechanisms described here apply to eukaryotes in general. Among the concepts that emerge in this discussion, we note that the TBP-associated regulatory apparatus is more complex than is typically modeled for protein-coding genes, that the means by which TBP is recruited to promoters is not yet well understood, and that there are a surprising number and variety of regulatory factors devoted to repressing TBP function.

TAFI

TAFI function as promoter selectivity factors for rRNA genes (for review, see Geiduschek and Kassavetis 1995). Three TAFI are associated with TBP in a complex called SL1 (human), TIF-IB (mouse), or CF (yeast) (Learned et al. 1985; Clos et al. 1986; Schnapp et al. 1990; Comai et al. 1992; Radebaugh et al. 1994; Zomerdijk et al. 1994; Lalo et al. 1996; Lin et al. 1996). TAFI complexes contact conserved sequences in the core promoter element of the rDNA promoter and are essential for in vitro transcription by RNA polymerase I (Learned et al. 1985; Clos et al. 1986; Bell et al. 1988; Eberhard et al. 1993; Rudloff et al. 1994; Beckmann et al. 1995; Gong et al. 1995; Lalo et al. 1996; Lin et al. 1996). TAFI complexes contact conserved sequences in the core promoter element of the rDNA promoter and are essential for in vitro transcription by RNA polymerase I (Learned et al. 1985; Clos et al. 1986; Bell et al. 1988; Eberhard et al. 1993; Rudloff et al. 1994; Beckmann et al. 1995; Gong et al. 1995; Lalo et al. 1996; Lin et al. 1996). TAFI complexes also interact with an upstream binding factor that stabilizes SL1/TIF-IB/CF binding and stimulates transcription (Beckmann et al. 1995; Steffan et al. 1996). Mutations in yeast TAFI genes result in defects in 35S rRNA transcription and led to the cloning of the three yeast TAFI, all of which are essential (Keys et al. 1994; Lalo et al. 1996; Lin et al. 1996).

TAFII

TAFII bind TBP in a complex called TFIID and have been proposed to be promoter selectivity factors and transcriptional coactivators for protein-coding genes (for review, see Goodrich and Tjian 1994; Burley and Roeder 1996; Verrijzer and Tjian 1996). TFIID complexes have been purified from mammalian, Drosophila, and yeast.

1Corresponding author.
E-MAIL young@wi.mit.edu; FAX (617) 258-0376.
cells, and 9–12 TAFIIs are found associated with TBP in these complexes. Almost all of the yeast TAFIIs are essential for viability (Henry et al. 1994; Reese et al. 1994; Verrijzer et al. 1994; Poon et al. 1995; Klebanow et al. 1996, 1997; Moqtaderi et al. 1996b; Walker et al. 1996). Several lines of evidence indicate that TAFIIs are promoter selectivity factors. TAFIIs are required to recognize sequence elements at promoters that lack the consensus sequence for TBP binding. Specific TAFIIs bind two such sites, the initiator (Inr) and downstream core promoter element (DPE), which are found at several mammalian and Drosophila TATA-less promoters (Verrijzer et al. 1994, 1995; Burke and Kadonaga 1996). Several Inr-directed in vitro transcription systems require TFII D and cannot utilize TBP (Smale et al. 1990; Pugh and Tjian 1991; Martinez et al. 1994; Purnell et al. 1994). Promoter hybrid experiments with conditional TAFII mutants in yeast indicate that the requirement for TAFII function maps to core promoter elements (Shen and Green 1997).

TAFIIIs were originally described as transcriptional co-activators, but there is conflicting evidence for this function. In reconstituted Drosophila and human in vitro systems, activated transcription does not occur with TBP alone but can be obtained with TFII D (Pugh and Tjian 1990; Dynlacht et al. 1991; Tanese et al. 1991). These results and evidence that various activators can interact directly with specific TAFIIIs led to the model that TAFIIIs mediate recruitment of TBP by activators (Chen et al. 1994; Jacq et al. 1994; Chiang and Roeder 1995; for review, see Verrijzer and Tjian 1996). However, yeast do not show global defects in class II transcription activation when TAFII function is lost in vivo (Apone et al. 1996; Moqtaderi et al. 1996a; Walker et al. 1996). Instead, yeast TAFIIIs appear to be essential for transcription of a subset of protein-coding genes, and TAFII function at these promoters is associated with core promoter elements rather than elements bound by activators (Apone et al. 1996; Moqtaderi et al. 1996a; Shen and Green 1997; Walker et al. 1997). Consistent with the in vivo observations in yeast, recent evidence indicates that activation of transcription in crude HeLa extracts can occur independent of TAFIIIs (Oelgeschlager et al. 1998). As in yeast, TAFII mutations in higher eukaryotic cells affect specific subsets of genes (Wang and Tjian 1994; Sauer et al. 1996; Suzuki-Yagawa et al. 1997; Wang et al. 1997). Metazoan TAFII function at one promoter is apparently associated with both core promoter and enhancer elements (Wang et al. 1997). A better understanding of TAFII function in core promoter recognition and activation awaits more comprehensive in vivo analysis.

Figure 1. Four complexes function as class-specific promoter selectivity factors. The association of TBP with TAFIIs, TAFIIIs, TAFIIIs, and PTF/SNAPc directs TBP to different promoter classes. The distribution of TBP among these factors contributes to the global regulation of gene expression.

Figure 2. TBP function in class II transcription is regulated by diverse multisubunit complexes. TAFIIs, SAGA, Mot1, NC2, and Nots regulate the expression of protein-coding genes through diverse mechanisms.
The largest of the cloned Drosophila TAF₁ₛ has been reported to have two enzymatic activities. Two kinase domains, located at the termini of dTAF₁₂₅₀, are capable of phosphorylating subunits of general transcription factors, principally TFIIF (Dikstein et al. 1996). dTAF₁₂₅₀ also contains a highly conserved histone acetyltransferase domain that can acetylate multiple core histone subunits (Mizzen et al. 1996). The enzymatic activities of

| TAF₁ₛ | RRN6 | 102 | Y | Keys et al. (1994) |
|-------|------|-----|---|-------------------|
| RRN7  | 60   | Y   |   | Keys et al. (1994) |
| RRN11 | 59   | Y   |   | Lalo et al. (1996); Lin et al. (1996) |
| TAF₁₅₀/TSM₁ | 161 | Y | required for cell cycle progression | Verrijzer et al. (1994); Poon et al. (1995) |
| TAF₁₄₅/TAF₁₃₀ | 121 | Y | histone acetyltransferase | Reese et al. (1994); Poon et al. (1995); Mizzen et al. (1996) |
| TAF₉₀ | 89   | Y | required for cell cycle progression | Reese et al. (1994); Poon et al. (1995) |
| TAF₆₇ | 67   | Y   |   | Moqtaderi et al. (1996b) |
| TAF₆₁/TAF₆₈ | 61 | Y | similar to histone H₂B | Moqtaderi et al. (1996b); Walker et al. (1996) |
| TAF₆₀ | 58   | Y   |   | Moqtaderi et al. (1996b) |
| TAF₄₇ | 40   | Y   |   | Poon et al. (1995) |
| TAF₄₀ | 41   | Y   |   | Moqtaderi et al. (1996b); Klebanow et al. (1997) |
| TAF₃₀/ANC₁/TFG₃/SWP₂₉ | 27 | N | component of TFIIF | Henry et al. (1994) |
| TAF₂₅/TAF₂₃ | 23 | Y |   | Klebanow et al. (1996); Moqtaderi et al. (1996b) |
| TAF₁₉/FUN₈₁ | 19 | Y |   | Moqtaderi et al. (1996b) |
| TAF₁₇/TAF₂₀ | 17 | Y | similar to histone H₃ | Moqtaderi et al. (1996b) |
| TAF₁₁ₛ | BRF₁/TDS₄/PCF₄ | 67 | Y | homologous to TFIIB | Buratowski and Zhou (1992); Colbert and Hahn (1992); Lopez-de-León et al. (1992) |
| TFC₅/TFC₇ | 68 | Y | contains SANT domain | Kasavetis et al. (1995); Ruth et al. (1996) |
| SAGA | SPT₃ | 38 | N | Eisenmann et al. (1992) |
| SPT₇ | 153 | N |   | Gansheroff et al. (1995) |
| SPT₈ | 66  | N   |   | Eisenmann et al. (1994) |
| SPT₂₀/ADA₅ | 68 | N |   | Marcus et al. (1996); Roberts et al. (1996) |
| ADA₂/SWI₈ | 51 | N |   | Berger et al. (1992) |
| ADA₃/NGG₁ | 79 | N | histone acetyltransferase | Brandt et al. (1993); Pina et al. (1993) |
| GCN₅/ADA₄/SWI₉ | 51 | N | histone acetyltransferase | Georgakopoulos and Thireos (1992); Brownell et al. (1996); Grant et al. (1997) |
| Mot₁ | MOT₁/BUR₃/ADI | 210 | Y | member of SNF₂ family of ATPases | Davis et al. (1992); Piatti et al. (1992); Auble et al. (1994) |
| NC₂ | NCB₁/BUR₆ | 16 | Y | histone fold motif | Goppelt and Mielernentst (1996); Gadbois et al. (1997); Prelsch (1997) |
| NCB₂/YDR₁ | 17 | Y | histone fold motif | Goppelt and Mielernentst (1996); Gadbois et al. (1997); Kim et al. (1997) |
| Nots | NOT₁/CDC₃₉ | 240 | Y |   | Reed et al. (1980); Collart and Struhl (1993) |
| NOT₂/CDC₃₆ | 22 | N |   | Reed et al. (1980); Collart and Struhl (1994) |
| NOT₃ | NOT₄/MOT₂/SIG₁ | 94 | N | zinc finger protein | Collart and Struhl (1994) |
| NOT₅ | 66 | U | regions of homology with NOT₃ | Oberholzer and Collart (1998) |

a (U) Unknown.
TAFIIIs serve as promoter specificity factors for most this TAFII may have roles in modifying the initiation apparatus or chromatin at promoters, but further study is necessary to determine how these activities are involved in transcriptional regulation in vivo.

**TAFIIIs**

TAFIIIs serve as promoter specificity factors for most genes transcribed by RNA polymerase III (for review, see Willis 1993; Kassavetis et al. 1994; White 1994; Geiduscek and Kassavetis 1995). In yeast, two TAFIIIs are typically associated with TBP in a complex called TFIIIIB, and this complex can associate with class III promoters containing TBP binding sites (Margottin et al. 1991; Joazeiro et al. 1994). At promoters lacking strong TBP binding sites, TAFIIIs interact with general factor TFIIIC that contains TBP in a complex called TFIIIB, and this complex can associate with class III promoters containing TBP binding sites (Margottin et al. 1991; Joazeiro et al. 1994; Koo et al. 1994; Chaussevert et al. 1995; Gerlach et al. 1995). TAFIIIs interact with specific subunits of RNA polymerase III (Werner et al. 1993; Wang and Roeder 1997). The interactions that have been observed between TAFIIIs, TBP, and TFIIIC have been confirmed by genetic analysis and both yeast TAFIIIs are essential (Buratowski and Zhou 1992; Colbert and Hahn 1992; Lopez-De-Leon et al. 1992; Cormack and Struhl 1993; Werner et al. 1993; Lefebvre et al. 1994; Rameau et al. 1994; Kassavetis et al. 1995; Ruth et al. 1996; Vilalta et al. 1997).

**PTF/SNAPc**

PTF/SNAPc is a mammalian promoter specificity factor for snRNA promoters, subsets of which are transcribed by either RNA polymerase II or RNA polymerase III (Murphy et al. 1992; Sadowski et al. 1993; Henry et al. 1995; Yoon and Roeder 1995). Purified PTF/SNAPc consists of four subunits that bind a core promoter element present at both class II and class III snRNA promoters. PTF/SNAPc is required for transcription from snRNA promoters in vitro (Henry et al. 1995; Yoon et al. 1995). Multiple subunits of PTF/SNAPc interact with TBP and TBP can be coimmunopurified with antibodies to PTF/SNAPc subunits (Henry et al. 1995, 1996; Bai et al. 1996; Sadowski et al. 1996; Yoon and Roeder 1996). PTF/SNAPc interacts with the nonconserved amino-terminal domain of TBP and stabilizes binding of TBP at snRNA promoters (Mittal and Hernandez 1997). PTF/SNAPc may also serve as the target for DNA-bound activators, which further stabilize the complex on DNA (Yoon et al. 1995; Mittal et al. 1996; Ford and Hernandez 1997; Wong et al. 1998). No obvious PTF/SNAPc homologs are encoded in the yeast genome. Consequently, PTF/SNAPc is the only TBP-associated regulator described here with no genetic evidence for a functional role in vivo.

**SAGA histone acetylation complex**

The SAGA complex regulates class II transcription at a subset of genes through its action on chromatin. Yeast SAGA is composed of Spt, Ada, and Gcn5 subunits and is capable of nucleosome acetylation (Berger et al. 1992; Eisenmann et al. 1992, 1994; Georgakopoulos and Thireos 1992; Brandl et al. 1993; Pina et al. 1993; Gan- sheroff et al. 1995; Brownell et al. 1996; Marcus et al. 1996; Roberts and Winston 1996; Grant et al. 1997). Although SAGA does not copurify with TBP (Grant et al. 1997), multiple components of SAGA (Spt3, Ada2, Ada5/Spt20) associate with TBP and genetic evidence is consistent with such an interaction (Eisenmann et al. 1992; Barlev et al. 1995; Roberts and Winston 1996, 1997; Saleh et al. 1997). If SAGA functions through an interaction with TBP, this interaction could facilitate disruption of nucleosomes near promoters to enable efficient transcription initiation or elongation. The components of the SAGA complex are not essential but have positive roles in the regulation of a subset of class II genes including amino acid synthesis, mating pheromone response, mating-type switching, and carbon source metabolism genes (Winston et al. 1984; Hirschhorn and Winston 1988; Berger et al. 1992; Horiuichi et al. 1995; Marcus et al. 1996; Pollard and Peterson 1997; Roberts and Winston 1997). Although the homologous complex has yet to be purified from mammalian cells, homologs of two SAGA components are encoded in the human genome (Candau et al. 1996; Inoue et al. 1996; Wang et al. 1997). TAFII, TAFIIIs, TAFIIIs, PTF/SNAPc, and Mot1 can be purified in association with TBP. In contrast, SAGA, NC2, and Nots have not been observed to copurify with TBP. However, the lack of copurification of these regulators and TBP does not provide evidence against such an interaction. Indeed, TAFII, TAFIIIs, PTF/SNAPc, and Mot1 can be purified independent of TBP (Keys et al. 1994; Reese et al. 1994; Yoon et al. 1995; Bai et al. 1996; Sadowski et al. 1996; Wade and Jaehning 1996; Yoon and Roeder 1996; Auble et al. 1997). The combination of genetic evidence for a functional interaction and biochemical evidence for physical binding makes it likely that SAGA, NC2, and Nots have a functional interaction with TBP.

**Mot1**

Mot1 represses transcription at a subset of class II genes by inhibiting TBP binding. The 210-kD yeast Mot1 protein binds TBP-DNA complexes and causes the dissociation of TBP from the DNA in an ATP-dependent manner (Auble and Hahn 1993; Auble et al. 1994, 1997; Wade and Jaehning 1996). TBP-Mot1 complexes have been purified from yeast and mammalian sources (Timmers and Sharp 1991; Auble and Hahn 1993; Meyers and Sharp 1993; Auble et al. 1994; Poon et al. 1994; Van Der Knaap et al. 1997). Genetic studies in yeast have linked Mot1 to TBP function in vivo (Auble et al. 1994) and have suggested that Mot1 may act with other factors to influence promoter selection by TBP (Collart 1996; Madison and Winston 1997). Yeast Mot1 is essential and affects expression from a subset of genes, including mating pheromone response, DNA synthesis, and amino acid synthe-
sis genes (Davis et al. 1992; Piatti et al. 1992; Auble et al. 1994; Madison and Winston 1997).

NC2

NC2 (Dr1/DRAP1) is a general negative regulator of class II and class III gene expression (Meisterernst and Roeder 1991; Inostroza et al. 1992; Goppelt and Meisterernst 1996; Mermelstein et al. 1996; Gadbois et al. 1997; Kim et al. 1997; Prelich 1997). It has been shown to repress transcription from a wide variety of yeast, mammalian, and viral promoters (Meisterernst and Roeder 1991; Yeung et al. 1994; Kim et al. 1995, 1996; Goppelt and Meisterernst 1996; Goppelt et al. 1996; Mermelstein et al. 1996; Gadbois et al. 1997). NC2 binds to the basic repeat domain of TBP on promoter DNA and can prevent the RNA polymerase II holoenzyme from assembling into an initiation complex (Meisterernst and Roeder 1991; Inostroza et al. 1992; Kim et al. 1995; Goppelt et al. 1996; Mermelstein et al. 1996; Gadbois et al. 1997). We have observed that yeast NC2 can bind to TBP in the absence of DNA (C. Wilson, V. Myer, and R. Young, unpubl.). This leads us to consider whether NC2 might function to regulate the association of TBP with the RNA polymerase II holoenzyme prior to promoter recruitment, thereby preventing its stable association with promoter DNA.

NC2 is composed of two subunits, NC2α (Dr1) and NC2β (DRAP1), which dimerize through histone-fold structural motifs (Arents and Moudrianakis 1995). Purified NC2 appears to be a heterotetramer composed of two NC2αβ dimers (Goppelt and Meisterernst 1996; Kim et al. 1996). Both subunits have been reported to be essential for yeast cell viability (Gadbois et al. 1997; Kim et al. 1997), although one study suggests that yeast cells can survive and grow extremely slowly without NC2 (Prelich 1997).

NOTs

NOT genes have been identified in a screen for suppressors of a defect in the GCN4 transcriptional activator and in five additional yeast genetic screens as negative regulators of cell cycle, pheromone response, and filamentous growth genes (Reed 1980; Collart and Struhl 1993, 1994; Cade and Errede 1994; Irie et al. 1994; Leberer et al. 1994; Mosch and Fink 1997; Oberholzer and Collart 1998). We recently identified a subset of NOT genes as suppressors of mutations in the general transcription apparatus, suggesting that they function as general negative regulators (T.I. Lee, J.J. Wyrick, S.S. Koh, E. Jennings, E.L. Gadbois, and R.A. Young, in prep). The protein products of these five genes form one or more complexes (Collart and Struhl 1994; Liu et al. 1998) and biochemical and genetic evidence has linked them physically and functionally to TBP (Collart and Struhl 1993, 1994; T.I. Lee, J.J. Wyrick, S.S. Koh, E. Jennings, E.L. Gadbois, and R.A. Young, in prep.), but their mechanism of action is not yet understood. NOT1 is essential and mutations in the other NOT genes cause slow growth phenotypes. A survey of sequence databases reveals that NOT genes are also encoded in metazoan genomes.

A large pool of TBP interacts with diverse regulatory proteins in vivo

The biochemical and genetic evidence suggests that at least seven factors, TAF1s, TAF10s, TAFII15s, SAGA, Mot1, NC2, and Nots, form complexes with yeast TBP. Is the level of TBP in yeast cells sufficient to permit independent interactions with each of these TBP-binding factors? We investigated this by preparing crude cell extracts from yeast cells and carrying out Western blot analysis with serial dilutions of extract and known amounts of purified or recombinant proteins. The results indicate that there are 30,000–50,000 molecules of TBP/cell (Table 2). In contrast, there appear to be only 3000–6000 molecules of TAF1s, SAGA, Mot1, NC2, and Nots per cell. At an estimated 3000–6000 molecules per cell, there are sufficient amounts of each of these regulatory factors to regulate a significant fraction of the predicted 6275 class II genes in yeast (Goffeau et al. 1996). Previous results indicate that there are ∼200–400 molecules of TAF1s (Keys et al. 1994, 1996), 3000–6000 molecules of TAFII15s (Moqtaderi et al. 1996a; Walker et al. 1996), and

Table 2. Number of selected protein molecules in yeast cells

| Yeast protein | Molecules/cell |
|---------------|---------------|
| SRBs/RNA polymerase II holoenzyme | 2–4,000<sup>a</sup> |
| RNA polymerase II | 10-20,000<sup>b</sup> |
| TFIIF | 30–50,000 |
| TFIIB | 30–50,000 |
| TBP | 30–50,000 |
| TFIIF | 30–50,000 |
| TAF1 | 200–400<sup>c</sup> |
| TAF10 | 3–6,000<sup>c,d</sup> |
| TAFII15 | 3–6,000<sup>c,d</sup> |
| SAGA | 3–6,000 |
| Mot1 | 3–6,000 |
| NC2 | 3–6,000 |
| Nots | 3–6,000 |
| Ribosomes | 1,500,000<sup>f</sup> |
| Tubulin | 150,000<sup>e</sup> |
| ORC | 600<sup>e</sup> |

Whole cell extract was prepared from haploid, S288C wild-type yeast grown to mid-log phase in YPD at 30°C. Serial dilutions of extract were compared to known amounts of recombinant standards by Western blot analysis.

<sup>a</sup> Koleske and Young (1994).
<sup>b</sup> Keys et al. (1994).
<sup>c</sup> Moqtaderi et al. (1996a).
<sup>d</sup> Walker et al. (1996).
<sup>e</sup> I. Sethy, A Lopez-de-Leon, R. Moir, and I. Willis (pers. comm.).
<sup>f</sup> Nomura et al. (1974).
~10,000 molecules of TAFIIIs per cell (I. Sethy, A. Lopez-
de-Leon, R. Moir and I. Willis, pers. comm.). Quantitative Western analysis with epitope-tagged TBP, TAFIs, TAFIIIs, TAFIIIs, or Mot1 has generated similar estimates for these factors (P.A. Wei, Y. Bai, and A.M. Campbell, unpubl.). Thus, there is a large global pool of TBP in yeast that can interact with smaller pools of these diverse regulatory proteins in vivo.

In higher eukaryotes, it would not be surprising to find that TAFIs, TAFIIIs, TAFIIIs, PTF/SNAPc, SAGA, Mot1, NC2, and Nots also interact with and regulate a large global pool of TBP. Indeed, human TAFIs, TAFIIIs, TAFIIIs, and MOT1 can all be purified from cells in association with approximately stoichiometric amounts of TBP, suggesting that each of these factors interacts with a subset of cellular TBP.

**Implications for gene regulation**

Among the eight TBP-associated regulators discussed here, four have roles as class-specific promoter specificity factors (TAFIs, TAFIIIs, TAFIIIs, and PTF/SNAPc), two are histone acetylases with roles at class II genes (TAFIIs and SAGA), two are negative regulators of class II genes (Mot1 and Nots), and one is a general negative regulator of class II and class III genes (NC2). There are substantial levels of TBP in yeast cells, more than is necessary to associate with the promoters of all genes at one time. [Yeast have an estimated 140 RNA genes, 6275 protein-coding genes, and 315 genes for small stable RNAs (Goffeau et al. 1996)](https://genesdev.cshlp.org/article/1403). The picture that emerges from this data is that TBP is parceled out among these regulators, and this view has a number of implications for the molecular mechanisms involved in regulation of gene expression.

One critical implication of the information reviewed here is that the role of TBP in transcription of protein-coding genes cannot be described in terms of TAFIIs alone. Most models for regulated transcription initiation at protein coding genes describe a process in which TBP, tightly associated with TAFIs, is recruited to promoters. However, five factors have been identified that bind to TBP and that are clearly involved in expression of class II genes in vivo: TAFIIIs, SAGA, Mot1, NC2, and Nots (Fig. 2). The levels of TBP in yeast are approximately tenfold greater than the levels of TAFIIIs, SAGA, Mot1, NC2, and Nots. Taken together, these data argue that TBP function in class II transcription is regulated by diverse multisubunit complexes including, but not limited to, TAFIIIs.

Recent genetic evidence in yeast and metazoans indicates that individual TAFIIIs have essential roles at the promoters of specific subsets of genes but not, apparently, at promoters of all protein coding genes (Wang and Tjian 1994; Apone et al. 1996; Møgtader et al. 1996a; Sauer et al. 1996; Shen and Green 1997; Suzuki-Yagawa et al. 1997; Walker et al. 1997). Does this mean that TFIID is not part of the transcription initiation complex at the promoters of all protein coding genes? In our opinion, the available evidence does not yet permit a definitive answer to this question.

If the TAFIIs are promoter-specificity factors and do not have essential roles as targets of gene-specific activators, how is TBP recruited to promoters? TBP may be recruited to promoters through direct interactions with activators (Stringer et al. 1990; Horikoshi et al. 1991; Lee et al. 1991; Lieberman and Berk 1991; Liu et al. 1993; Truant et al. 1993; Emili et al. 1994; Kashanchi et al. 1994; Klein and Struhl 1994; Mélècher and Johnstone 1995; Wu et al. 1996; for review, see Triezenberg 1995). It is also possible that it is brought to promoters in association with RNA polymerase II holoenzyme (Ossipow et al. 1995; Pan et al. 1997). Considerable genetic and biochemical evidence indicate that activators recruit the RNA polymerase II holoenzyme to promoters through interactions with the Srb/mediator complex (Kim et al. 1994; Koleske and Young 1994; Hengartner et al. 1995; Koh et al. 1998; Miers et al. 1998). Association with the holoenzyme may thus provide another pathway to recruit TBP to promoters.

Another implication that emerges from an examination of these TBP regulators is that negative regulation of TBP is so important that three different negative regulators are critical to maintain cell viability. Transcription initiation occurs only rarely for at least half of genes in yeast cells and for an even larger fraction in human cells (Velčulescu et al. 1997). Genome packing and consequent steric hindrance may account for some general repression of gene expression, but perhaps is not adequate to completely prevent inappropriate gene expression. In this regard, Mot1, NC2, and Nots, which regulate the availability of TBP and its ability to function at specific promoters, are likely to contribute significantly to the repression of gene expression. The importance of this negative regulation is underscored by the observation that all three factors are essential for yeast cell viability.

Perhaps the most important implication of the observation that TBP function is controlled by a large number of regulatory factors is that much more study is needed to understand how global gene expression is regulated through TBP. The TAFIs, TAFIIIs, TAFIIIs, and PTF/SNAPc clearly provide a means to apportion TBP among the various classes of genes. However, despite knowledge that TAFIIs, SAGA, Mot1, NC2, and Nots have important functions at class II promoters, our understanding of the roles of TBP-associated regulators is incomplete. It is not yet clear whether each of these regulators interacts independently with TBP as suggested in Figure 2. Crystallographic studies show that only small surfaces of TBP are required for protein–protein contact, so simultaneous interactions with multiple regulatory factors are possible (Nikolov et al. 1995; Geiger et al. 1996). Although the regulators in Figure 2 are shown functioning at promoters, it is not certain that the action of these factors occurs exclusively on DNA. For example, global regulation of gene expression by NC2 or Nots could involve the sequestering of functional TBP off promoter DNA. It will be important to understand which factors...
Lee and Young

act generally at class II promoters and which act on a subset, and genome-wide expression monitoring technology (Lashkari et al. 1997; Wodicka et al. 1997) should provide the means to do this. And, of course, it will be interesting to learn how these regulators are regulated.

Acknowledgments

We thank S. Buratowski, M. Green, K. Struhl, P.A. Weil, F. Winston, and members of the Young laboratory for comments on this manuscript. We thank P.A. Weil and I. Willis for sharing unpublished data. This work was supported by National Institutes of Health grants to R.A.Y.

References

Arents, G. and E.N. Moudrianakis. 1995. The histone fold: A ubiquitous architectural motif used in DNA compaction and protein dimerization. Proc. Natl. Acad. Sci. 92: 11170–11174.

Auble, D.T. and S. Hahn. 1993. An ATP-dependent inhibitor of TBP binding to DNA. Genes & Dev. 7: 844–856.

Auble, D.T., K.E. Hansen, C.G. Mueller, W.S. Lane, J. Thorner, and S. Hahn. 1994. Mot1, a global repressor of RNA polymerase II transcription, inhibits TBP binding to DNA by an ATP-dependent mechanism. Genes & Dev. 8: 1920–1934.

Auble, D.T., D. Wang, K.W. Post, and S. Hahn. 1997. Molecular analysis of the SNF2/SWI2 protein family member MOT1, an ATP-driven enzyme that dissociates TATA-binding protein from DNA. Mol. Cell. Biol. 17: 4842–4851.

Bai, L., Z. Wang, J.B. Yoon, and R.G. Roeder. 1996. Cloning and characterization of the beta subunit of human proximal sequence element-binding transcription factor and its involvement in transcription of small nuclear RNA genes by RNA polymerase II and III. Mol. Cell. Biol. 16: 5419–5426.

Barlev, N.A., R. Candau, L. Wang, P. Darpino, N. Silverman, and S.L. Berger. 1995. Characterization of physical interactions of the putative transcriptional adaptor, ADA2, with acidic activation domains and TATA-binding protein. J. Biol. Chem. 270: 19337–19344.

Beckmann, H., J.L. Chen, T. O’Brien, and R. Tjian. 1995. Coactivator and promoter-selective properties of RNA polymerase I TAFs. Science 270: 1506–1509.

Bell, S.P., R.M. Learned, H.M. Jantzen, and R. Tjian. 1988. Functional cooperativity between transcription factors UBF1 and SL1 mediates human ribosomal RNA synthesis. Science 241: 1192–1197.

Berger, S.L., B. Pina, N. Silverman, G.A. Marcus, J. Agapite, J.L. Regier, Sj. Triezenberg, and L. Guarente. 1992. Genetic isolation of ADA2: A potential transcriptional adaptor required for function of certain acidic activation domains. Cell 70: 251–265.

Brandl, C.J., A.M. Furlanetto, J.A. Martin, and K.S. Hamilton. 1993. Characterization of NGG1, a novel yeast gene required for glucose repression of GAL4p-regulated transcription. EMBO J. 12: 5255–5265.

Brownell, J.E., J. Zhou, T. Ranalli, R. Kobayashi, D.G. Edmondson, S.Y. Roth, and C.D. Allis. 1996. Tetrahymena histone acetyltransferase A: A homolog to yeast Gcn5 linking histone acetylation to gene activation. Cell 84: 843–851.

Buratowski, S. and H. Zhou. 1992. A suppressor of TBP mutations encodes an RNA polymerase III transcription factor with homology to TFIIIB. Cell 71: 221–230.

Burke, T.W. and J.T. Kadonaga. 1996. Drosophil TFIIID binds to a conserved downstream basal promoter element that is present in many TATA-box-deficient promoters. Genes & Dev. 10: 711–724.

Burley, S.K. and R.G. Roeder. 1996. Biochemistry and structural biology of transcription factor IID (TFIID). Annu. Rev. Biochem. 65: 769–799.

Cade, R.M. and B. Errede. 1994. MOT2 encodes a negative regulator of gene expression that affects basal expression of phenome-responsive genes in Saccharomyces cerevisiae. Mol. Cell. Biol. 14: 3139–3149.

Candau, R.P.A. Moore, L. Wang, N. Barlev, C.Y. Ying, C.A. Rosen, and S.L. Berger. 1996. Identification of human proteins functionally conserved with the yeast putative adaptors ADA2 and GCN5. Mol. Cell. Biol. 16: 593–602.

Chaussvert, N., C. Conesa, S. Shaaban, A., and A. Sentenac. 1995. Complex interactions between yeast TFIIIB and TFIIIC. J. Biol. Chem. 270: 15353–15358.

Chen, J.L., L.D. Attardi, C.P. Verrijzer, K. Yokomori, and R. Tjian. 1994. Assembly of recombinant TFIID reveals differential coactivator requirements for distinct transcriptional activators. Cell 79: 93–105.

Chiang, C.M. and R.G. Roeder. 1995. Cloning of an intrinsic human TFIID subunit that interacts with multiple transcriptional activators. Science 267: 531–536.

Clos, J., D. Buttgereit, and I. Grummt. 1986. A purified transcription factor (TIF-IB) binds to essential sequences of the mouse rDNA promoter. Proc. Natl. Acad. Sci. 83: 604–608.

Colbert, T. and S. Hahn. 1992. A yeast TFIIB-related factor involved in RNA polymerase III transcription. Genes & Dev. 6: 1940–1949.

Collart, M.A. 1996. The NOT, SPT3, and MOT1 genes functionally interact to regulate transcription at core promoters. Mol. Cell. Biol. 16: 6668–6676.

Collart, M.A. and K. Struhl. 1993. CDC39, an essential nuclear protein that negatively regulates transcription and differentially affects the constitutive and inducible HIS3 promoters. EMBO J. 12: 177–186.

———. 1994. NOT1(CDC39), NOT2(CDC36), NOT3, and NOT4 encode a global-negative regulator of transcription that differentially affects TATA-element utilization. Genes & Dev. 8: 525–537.

Comai, L., N. Tanese, and R. Tjian. 1992. The TATA-binding protein and associated factors are integral components of the RNA polymerase I transcription factor, SL1. Mol. Cell. Biol. 12: 955–976.

Cormack, B.P. and K. Struhl. 1993. Regional codon randomization: Defining a TATA-binding protein surface required for RNA polymerase III transcription. Science 262: 244–248.

Davis, A., G.R. Sage, L. Wilson, and K.W. Farrell. 1993. Purification and biochemical characterization of tubulin from the budding yeast Saccharomyces cerevisiae. Biochemistry 32: 8823–8835.

Davis, J.L., R. Kunisawa, and J. Thorner. 1992. A presumptive helicase (MOT1 gene product) affects gene expression and is required for viability in the yeast Saccharomyces cerevisiae. Mol. Cell. Biol. 12: 1879–1892.

Dikstein, R., S. Ruppert, and R. Tjian. 1996. TAFII250 is a bipartite protein kinase that phosphorylates the base transcription factor RAP74. Cell 84: 781–790.

Dylnacht, B.D., T. Hoey, and R. Tjian. 1991. Isolation of coactivators associated with the TATA-binding protein that mediate transcriptional activation. Cell 66: 563–576.

Eberhard, D., L. Tora, J.M. Egly, and I. Grummt. 1993. A TBP-containing multiprotein complex (TIF-IB) mediates tran-
scription specificity of murine RNA polymerase I. Nucleic Acids Res. 21: 4180–4186.
Eisenmann, D.M., K.M. Arndt, S.L. Ricupero, J.W. Rooney, and F. Winston. 1992. SPT3 interacts with TFIIID to allow normal transcription in Saccharomyces cerevisiae. Genes & Dev. 6: 1319–1321.
Eisenmann, D.M., C. Chapon, S.M. Roberts, C. Dollard, and F. Winston. 1994. The Saccharomyces cerevisiae SPT8 gene encodes a very acidic protein that is functionally related to SPT3 and TATA-binding protein. Genetics 137: 647–657.
Emili, A., J. Greenblatt, and C.J. Ingles. 1994. Species-specific interaction of the glutamine-rich activation domains of Sp1 with the TATA box-binding protein. Mol. Cell. Biol. 14: 1582–1593.
Ford, E. and N. Hernandez. 1997. Characterization of a trimeric complex containing Oct-1, SNAPc, and DNA. J. Biol. Chem. 272: 16048–16055.
Gadbois, E.L., D.M. Chao, J.C. Reese, M.R. Green, and R.A. Young. 1997. Functional antagonism between RNA polymerase II holoenzyme and global negative regulator NC2 in vivo. Proc. Natl. Acad. Sci. 94: 3145–3150.
Gansheroff, L.J., C. Dollard, P. Tan, and F. Winston. 1995. The Saccharomyces cerevisiae SPT7 gene encodes a very acidic protein important for transcription in vivo. Genetics 139: 523–536.
Geiduschek, E.P. and G.A. Kassavetis. 1995. Comparing transcriptional initiation by RNA polymerases I and III. Curr. Opin. Cell Biol. 7: 344–351.
Geiger, J.H., S. Hahn, S. Lee, and P.B. Sigler. 1996. Crystal structure of the yeast TFIIA/TBP/DNA complex. Science 272: 830–836.
Georgakopoulos, T. and G. Thireos. 1992. Two distinct yeast transcriptional activators require the function of the GCN5 acidic protein important for transcription. Mol. Cell. Biol. 15: 1455–1466.
Goffeau, A., B.G. Barrell, H. Bussey, R.W. Davis, B. Dujon, H. Hardham, D. Philippsen, G. Larsen, M. Colot et al. 1996. Life Sciences in Yeast. Nature 374: 653–656.
Hirschhorn, J.N. and F. Winston. 1988. SPT3 is required for normal levels of a-factor and alpha-factor expression in Saccharomyces cerevisiae. Mol. Cell. Biol. 8: 822–827.
Horikoshi, N., K. Maquiere, A. Kralli, E. Maldonado, D. Reinberg, and R. Weinmann. 1991. Direct interaction between adenovirus E1A protein and the TATA box binding transcription factor IID. Proc. Natl. Acad. Sci. 88: 5124–5128.
Horiuchi, J., N. Silverman, G.A. Marcus, and L. Guarente. 1995. ADA3, a putative transcriptional adaptor, consists of two separable domains and interacts with ADA2 and GCN5 in a trimeric complex. Mol. Cell. Biol. 15: 1203–1209.
Inostroza, J.A., F.H. Mermelstein, I. Ha, W.S. Lane, and D. Reinberg. 1992. Dr1, a TATA-binding protein-associated phosphoprotein and inhibitor of class II gene transcription. Cell 70: 477–489.
Inoue, M., M. Isomura, S. Ikegawa, T. Fujiwara, S. Shin, H. Moriya, and Y. Nakamura. 1996. Isolation and characterization of a human cDNA clone (GCN5L1) homologous to GCN5, a yeast transcription activator. CytoGenet. Cell Genet. 73: 134–136.
Irie, K., K. Yamaguchi, K. Kawase, and K. Matsumoto. 1994. The yeast MOT2 gene encodes a putative zinc finger protein that is involved in cell proliferation and TATA-less gene transcription. Mol. Cell. Biol. 14: 3150–3157.
Jaegle, J.A., T. Tjian. 1994. TBP-TAF complexes: Selectivity factors for eukaryotic transcription. Curr. Opin. Cell Biol. 6: 403–409.
Geiduschek, E.P., and G.A. Kassavetis. 1994. Identical components of yeast transcription factor IIIb are required and sufficient for transcription of TATA box-containing and TATA-less genes. Mol. Cell. Biol. 14: 2798–2808.
Kashanchi, F., G. Piras, M.F. Radonovich, J.F. Duvall, A. Fataey, C.M. Chiang, R.G. Roeder, and J.N. Brady. 1994. Direct interaction of human TFIID with the HIV-1 transactivator tat. Nature 367: 295–299.
Kassavetis, G.A., C. Bardwell, B. Bartholomew, B.R. Braun, C.A.P. Joazeiro, M. Pisano, and E.P. Geiduschek. 1994. Transcription by RNA polymerase III. In Transcription, mechanisms and regulation (ed. R.C. Conaway and J.W. Conaway), pp. 107–126. Raven Press, New York, NY.
Kassavetis, G.A., B.R. Braun, L.H. Nguyen, and E.P. Geiduschek. 1994. Saccharomyces cerevisiae TFIIIb is the transcription initiation factor proper of RNA polymerase III, while TFIIIA and TFIIIC are assembly factors. EMBO J. 13: 2199–2209.
Kassavetis, G.A., S.T. Nguyen, R. Kobayashi, A. Kumar, E.P. Geiduschek, and M. Pisano. 1995. Cloning, expression, and function of TFC5, the gene encoding the B” component of the Saccharomyces cerevisiae RNA polymerase III transcription factor TFIIIb. Proc. Natl. Acad. Sci. 92: 9786–9790.
Kassavetis, G.A., S.T. Nguyen, R. Kobayashi, A. Kumar, E.P. Geiduschek, and M. Pisano. 1996. Multisubunit transcription factor UAF interacts with the upstream ele-
ment of the yeast RNA polymerase I promoter and forms a stable preinitiation complex. Genes & Dev. 10: 887-903.

Keys, D.A., L. Vu, J.S. Steffan, J.A. Dodd, R.T. Yamamoto, Y. Nog, and M. Nomura. 1994. RRN6 and RRN7 encode subunits of a multiprotein complex essential for the initiation of rDNA transcription by RNA polymerase I in Saccharomyces cerevisiae. Genes & Dev. 8: 2349-2362.

Khoo, B., B. Brophy, and S.P. Jackson. 1994. Conserved functional domains of the RNA polymerase III general transcription factor BRF. Genes & Dev. 8: 2879-2890.

Kim, J., J.D. Parvin, B.M. Shykard, and P.A. Sharp. 1996. A negative cofactor containing Dr1/p19 modulates transcription with TFIIA in a promoter-specific fashion. J. Biol. Chem. 271: 18405-18412.

Kim, S., J.G. Na, M. Hampsay, and D. Reinberg. 1997. The Dr1/DRAP1 heterodimer is a global repressor of transcription in vivo. Proc. Natl. Acad. Sci. 94: 820-825.

Kim, T.K., Y. Zhao, H. Ge, R. Bernstein, and R.G. Roeder. 1995. TATA-binding protein residues implicated in a functional interplay between negative cofactor N/C2 (Dr1) and general factors TFIIA and TFIIIB. J. Biol. Chem. 270: 10976-10981.

Kim, Y.J., S. Bjerkund, Y. Li, M.H. Suyre, and R.D. Kornberg. 1994. A multiprotein mediator of transcriptional activation and its interaction with the C-terminal repeat domain of RNA polymerase II. Cell 77: 599-608.

Klebanow, E.R., D. Poon, S. Zhou, and P.A. Weil. 1996. Isolation and characterization of TAF25, an essential yeast gene that encodes an RNA polymerase II-specific TATA-binding protein-associated factor. J. Biol. Chem. 271: 13706-13715.

Klebanow, E.R., D. Poon, S. Zhou, and P.A. Weil. 1997. Cloning and characterization of an essential Saccharomyces cerevisiae gene, TAF40, which encodes yTAF40, an RNA polymerase II-specific TATA-binding protein-associated factor. J. Biol. Chem. 272: 9436-9442.

Klein, C. and K. Struhl. 1994. Increased recruitment of TATA-binding protein to the promoter by transcriptional activation domains in vivo. Science 266: 280-282.

Koh, S.S., A.Z. Ansari, M. Ptashne, and R.A. Young. 1998. An activator target in the RNA polymerase II holoenzyme. Mol. Cell 1: (in press).

Koleske, A.J. and R.A. Young. 1994. An RNA polymerase II holoenzyme responsive to activators. Nature 368: 466-469.

Lalo, D., J.S. Steffan, J.A. Dodd, and M. Nomura. 1996. RRN1 encodes the third subunit of the complex containing Rrn6 and Rrn7 that is essential for the initiation of rDNA transcription by yeast RNA polymerase I. J. Biol. Chem. 271: 21062-21067.

Lashkari, D.A., J.L. DeReiisi, J.H. McCusker, A.F. Namath, C. Gentile, S.Y. Hwang, P.O. Brown, and R.W. Davis. 1997. Yeast microarrays for genome wide parallel genetic and gene expression analysis. Proc. Natl. Acad. Sci. 94: 13057-13062.

Learned, R.M., S. Cordes, and R. Tjian. 1985. Purification and characterization of a transcription factor that confers promoter specificity to human RNA polymerase I. Mol. Cell. Biol. 5: 1385-1369.

Leberer, E., D. Dignard, D. Harcus, M. Whiteway, and D.Y. Thomas. 1994. Molecular characterization of SIG1, a Saccharomyces cerevisiae gene involved in negative regulation of G-protein-mediated signal transduction. EMBO J. 13: 3050-3064.

Lee, W.S., C.C. Kao, G.O. Bryant, X. Liu, and A.J. Berk. 1991. Adenovirus E1A activation domain binds the basic repeat in the TATA box transcription factor. Cell 67: 365-376.

Lefebvre, O., J. Ruth, and A. Sentenac. 1994. A mutation in the largest subunit of yeast TFIIIC affects RNA and 5 S RNA synthesis. Identification of two classes of suppressors. J. Biol. Chem. 269: 23374-23381.

Lieberman, P.M. and A.J. Berk. 1991. The Zta trans-activator protein stabilizes TFIIID association with promoter DNA by direct protein–protein interaction. Genes & Dev. 5: 2441-2454.

Lin, C.W., B. Moorefield, J. Payne, P. Aprikian, K. Mitomo, and R.H. Reeder. 1996. A novel 66-kilodalton protein complexes with Rrn6, Rrn7, and TATA-binding protein to promote polymerase I transcription initiation in Saccharomyces cerevisiae. Mol. Cell. Biol. 16: 6436-6443.

Liu, H.Y., V. Badarinarayana, D.C. Audino, J. Rappaport, M. Mann, and C.L. Denis. 1998. The NOT proteins are part of the CR4 transcriptional complex and affect gene expression both positively and negatively. EMBO J. 17: 1096-1106.

Liu, X., C.W. Miller, P.H. Koeffler, and A.J. Berk. 1993. The p53 activation domain binds the TATA box-binding polypeptide in Holo-TFIIID, and a neighboring p53 domain inhibits transcription. Mol. Cell. Biol. 13: 3291-3300.

Lopez-De-Leon, A., M. Librizzi, K. Puglia, and I.M. Willius. 1992. PCF4 encodes an RNA polymerase III transcription factor with homology to TFIIIB. Cell 71: 211-220.

Madison, J.M. and F. Winston. 1997. Evidence that Spt3 functionally interacts with Mot1, TFIIA, and TATA-binding protein to confer promoter-specific transcriptional control in Saccharomyces cerevisiae. Mol. Cell. Biol. 17: 287-295.

Marcus, G.A., J. Horiuchi, N. Silverman, and L. Guarente. 1996. ADA/SPT20 links the ADA and SPT genes, which are involved in yeast transcription. Mol. Cell. Biol. 16: 3197-3205.

Margottin, F., G. Dujardin, M. Gerard, J.M. Egly, J. Huet, and A. Sentenac. 1991. Participation of the TATA factor in transcription of the yeast U6 gene by RNA polymerase C. Science 251: 424-426.

Martinez, E., C.M. Chiang, H. Ge, and R.G. Roeder. 1994. TATA-binding protein-associated factor(s) in TFIIID function through the initiator to direct basal transcription from a TATA-less class II promoter. EMBO J. 13: 3115-3126.

Meisterernst, M. and R.G. Roeder. 1997. Family of proteins that interact with TFID and regulate promoter activity. Cell 67: 557-567.

Melcher, K. and S.A. Johnston. 1995. GAL4 interacts with TATA-binding protein and coactivators. Mol. Cell. Biol. 15: 2839-2848.

Mermelstein, F., K. Yeung, J. Cao, J.A. Inostroza, H. Erdjument-Bromage, K. Eagleson, D. Landsman, P. Levitt, P. Tempst et al. 1996. Requirement of a corepressor for Dr1-mediated repression of transcription. Genes & Dev. 10: 1033-1048.

Meyers, R.E. and P.A. Sharp. 1993. TATA-binding protein and associated factors in polymerase II and polymerase III transcription. Mol. Cell. Biol. 13: 7953-7960.

Mittal, V. and N. Hernandez. 1997. Role for the amino-terminal region of human TBP in U6 snRNA transcription. Science 275: 1136-1140.

Mittal, V., M.A. Cleary, W. Herr, and N. Hernandez. 1996. The Oct-1 POU-specific domain can stimulate small nuclear RNA gene transcription by stabilizing the basal transcription complex SNAPc. Mol. Cell. Biol. 16: 1955-1965.

Mizzen, C.A., X.J. Yang, T. Kokubo, J.E. Brownell, A.J. Bannister, T. Owen-Hughes, J. Workman, L. Wang, S.L. Berger, T. Kouzianides et al. 1996. The TAF(II)250 subunit of TFIID has transcriptional activation and its interaction with the C-terminal repeat domain of RNA polymerase II. Cell 77: 599-608.

Lee and Young

Lee and Young
growth by transposon mutagenesis in Saccharomyces cerevisiae. Genetics **145**: 671–684.

Murphy, S., J.B. Yoon, T. Gerster, and R.G. Roeder. 1992. Oct-1 and Oct-2 potentiate functional interactions of a transcription factor with the proximal sequence element of small nuclear RNA genes. Mol. Cell. Biol. **12**: 3247–3261.

Myers, L.C., C.M. Gustafsson, D.A. Bushnell, M. Lui, H. Erdjument-Bromage, P. Tempst, and R.D. Birnberg. 1998. The N and S proteins of yeast and their function through the RNA polymerase II carboxy-terminal domain. Genes & Dev. **12**: 45–54.

Nikolov, D.B., H. Chen, E.D. Halay, A.A. Usheva, K. Hisatake, Oelgeschlager, T., Y. Tao, Y.-K. Kang, and R.G. Roeder. 1998. TATA box-binding protein (TBP) is a constituent of the polymerase I-specific transcription initiation factor TIF-IB (SL1) bound to the RNA promoter and shows differential sensitivity to TBP-directed reagents in polymerase I, II, and III transcription factors. Mol. Cell. Biol. **14**: 597–605.

Oberholzer, U. and M.A. Collart. 1998. Characterization of NOT5 that encodes a new component of the NOT protein complex. Gene **207**: 61–69.

Pan, G., T. Aso, and J. Greenblatt. 1997. Interaction of elongation factors TFIIS and elon G with a human RNA polymerase II holoenzyme capable of promoter-specific initiation and responsive to transcriptional activators. J. Biol. Chem. **272**: 24563–24571.

Plati, S., R. Tazzi, A. Pizzagalli, P. Plevani, and G. Lucchini. 1992. Control of DNA synthesis genes in budding yeast: Involvement of the transcriptional modulator MOT1 in the expression of the DNA polymerase alpha gene. Chromosoma **102**: S107–113.

Pina, B., S. Berger, G.A. Marcus, N. Silverman, J. Agapite, and L. Piatti, S., R. Tazzi, A. Pizzagalli, P. Plevani, and G. Lucchini. 1994. TFIID transcription activation via enhanced preinitiation assembly in a human cell-free system lacking TAF_{170}. Mol. Cell. (in press).

Radebaugh, C.A., X. Gong, B. Bartholomew, and M.R. Paule. 1997. Identification of previously unrecognized common elements in eukaryotic promoters. A ribosomal RNA gene initiator element for RNA polymerase I. J. Biol. Chem. **272**: 3141–3144.

Radebaugh, C.A., J.L. Matthews, G.K. Geiss, F. Liu, J.M. Wong, E. Bateman, S. Camier, A. Sentenac, and M.R. Paule. 1994. TATA box-binding protein (TBP) is a constituent of the polymerase I-specific transcription initiation factor TIF-IB (SL1) bound to the RNA promoter and shows differential sensitivity to TBP-directed reagents in polymerase I, II, and III transcription factors. Mol. Cell. Biol. **14**: 597–605.

Rameau, G., K. Puglia, A. Crowe, I. Sethy, and I. Willis. 1994. A mutation in the second largest subunit of TFIIFC increases a rate-limiting step in transcription by RNA polymerase III. Mol. Cell. Biol. **14**: 822–830.

Reed, S.I. 1980. The selection of S. cerevisiae mutants defective in the start event of cell division. Genetics **95**: 561–577.

Roberts, S.M. and F. Winston. 1996. SPT20/ADA5 encodes a novel protein functionally related to the TATA-binding protein and important for transcription in Saccharomyces cerevisiae. Mol. Cell. Biol. **16**: 3206–3213.

Rowley, A., J.H. Cocker, J. Harwood, and J.F. Diffley. 1995. Initiation complex assembly at budding yeast replication origins begins with the recognition of a bipartite sequence by limiting amounts of the initiator, ORC. EMBO J. **14**: 2631–2641.

Sadowski, C.L., R.W. Henry, R. Kobayashi, and N. Hernandez. 1996. The SNA45 subunit of the small nuclear RNA (snRNA) activating protein complex is required for RNA polymerase I transcription. EMBO J. **15**: 2611–2616.

Rudloff, U., D. Eberhard, L. Tora, H. Stunnenberg, and I. Grummt. 1994. TBP-associated factors interact with DNA and govern species specificity of RNA polymerase I transcription. EMBO J. **13**: 2611–2616.

Ruth, J., C. Conesa, G. Dieci, O. Lefebvre, A. Dusterhoff, S. Ottonello, and A. Sentenac. 1996. A suppressor of mutations in the class III transcription system encodes a component of yeast TFIIIB. EMBO J. **15**: 1941–1949.

Sadowski, C.L., R.W. Henry, K. Kobayashi, and N. Hernandez. 1996. The SNA45 subunit of the small nuclear RNA (snRNA) activating protein complex is required for RNA polymerase II and III snRNA gene transcription and interacts with the TATA box binding protein. Proc. Natl. Acad. Sci. **93**: 4289–4293.

Sadowski, C.L., R.W. Henry, S.M. Lobo, and N. Hernandez. 1993. Targeting TBP to a non-TATA box cis-regulatory element: A TBP-containing complex activates transcription from snRNA promoters through the PSE. Genes & Dev. **7**: 1535–1548.

Saleh, A., V. Lang, R. Cook, and C.J. Brandl. 1997. Identification of native complexes containing the yeast coactivator/repressor proteins NGG1/ADA3 and ADA2. J. Biol. Chem. **272**: 5571–5578.

Sauer, F., D.A. Wasserman, G.M. Rubin, and R. Tjian. 1996. TAF(II)145 mediates activation of transcription in the Drosophila embryo. Cell **87**: 1271–1284.

Schmuck, A., J. Clo, W. Hadde, R. Schreck, A. Cvekel, and I. Grummt. 1990. Isolation and functional characterization of TIF-IB, a factor that confers promoter specificity to mouse RNA polymerase I. Nucleic Acids Res. **18**: 1385–1393.

Shen, W.C. and M.R. Green. 1997. Yeast TAF(II)145 functions as a core promoter selectivity factor, not a general coactivator.
Regulation of gene expression by TBP-associated proteins

Tong Ihn Lee and Richard A. Young

Genes Dev. 1998, 12:
Access the most recent version at doi:10.1101/gad.12.10.1398

References

License

Email Alerting Service
Receive free email alerts when new articles cite this article - sign up in the box at the top right corner of the article or click here.