30 Azuma, H. *et al.* (1993) Congenital plasminogen deficiency caused by a Ser572 to Pro mutation. *Blood* 82, 475–480
31 Geyer, M. *et al.* (1997) Structure of the Ras-binding domain of RalGEF and implications for Ras binding and signalling. *Nat. Struct. Biol.* 4, 694–699
32 Tachias, K. and Madison, E.L. (1997) Converting tissue-type plasminogen activator into a zymogen. *J. Biol. Chem.* 272, 28–31
33 Renatus, M. *et al.* (1997) Lysine 156 promotes the anomalous proenzyme activity of tPA: X-ray structure of single-chain human tPA. *EMBO J.* 16, 4797–4805
34 Bode, B. and Renatus, M. (1997) Tissue-type plasminogen activator: variants and crystal/solution structures demarcate structural determinants of function. *Curr. Opin. Struct. Biol.* 7, 865–872
35 Wang, S. *et al.* (1999) Deletion of Ile1 changes the mechanism of streptokinase: evidence for the molecular sexuality hypothesis. *Biochemistry* 28, 5232–5240
36 Stubbs, M. and Bode, W. (1995) The clot thickens: clues provided by thrombin structure. *Trends Biochem. Sci.* 20, 23–28
37 Fukao, H. and Matsuo, O. (1998) Analysis of tissue-type plasminogen activator receptor (t-PAR) in human endothelial cells. *Semin. Thromb. Hemost.* 24, 269–273
38 Banner, D. *et al.* (1996) The crystal structure of the complex of blood coagulation factor VIIa with soluble tissue factor. *Nature* 380, 41–46

TBP-associated factors (TAF_{II}s): multiple, selective transcriptional mediators in common complexes

TRANSCRIPTION SERIES

Michael R. Green

Transcription of eukaryotic structural genes requires the assembly of RNA polymerase II and the general transcription factors (GTFs) on the promoter to form a pre-initiation complex (PIC). Among these, TFIID is the major sequence-specific DNA-binding component; the other GTFs enter the PIC primarily through protein–protein interactions. TFIID is composed of the TATA-box-binding protein (TBP) and multiple TBP-associated factors (TAF_{II}s). Unexpectedly, TAF_{II}s have also been found in other multi-subunit complexes involved in transcription. Whereas TBP is a general transcription factor, a variety of *in vivo* studies have demonstrated that TAF_{II}s are highly promoter selective. Here I review studies on the role of TAF_{II}s in genome-wide transcription and their mechanism of action.

FACTORS INVOLVED IN the accurate transcription of eukaryotic structural genes by RNA polymerase II can be classified into two groups. First, general transcription factors (GTFs) are necessary and can be sufficient for accurate transcription initiation *in vitro* (reviewed in Ref. 1). These basic factors include RNA polymerase II itself and at least six GTFs: TFIID, TFIIA, TFIIB, TFIIE, TFIIF and TFIIH. The GTFs assemble on the promoter in an ordered fashion to form a pre-initiation complex (PIC). Transcriptional activity is greatly stimulated by the second class of factors, promoter-specific activator proteins (activators). In general, cellular activators are sequence-specific DNA-binding proteins whose recognition sites are present within the vicinity of their target promoters. A typical activator contains a promoter-targeting region, which comprises generally a sequence-specific DNA-binding domain and a separate activation region (reviewed in Ref. 2).

Binding of TFIID to the TATA box is the initial step of PIC assembly and is critical for the rate and efficiency of this process. TFIID was originally purified as an activity required to reconstitute a basal RNA polymerase II *in vitro* transcription reaction. The high molecular weight of partially purified TFIID immediately suggested that it was a multisubunit complex. The purification and cloning of TBP led to the subsequent identification and cloning of other TFIID subunits initially from humans and *Drosophila*. These higher eukaryotic TFIIDs were found to consist of TBP and at least 8–12 tightly bound subunits, the TBP-associated factors (TAF_{II}s; reviewed in Ref. 3).

Early studies suggested that TFIID from yeast was a single polypeptide, TBP, that is highly homologous to its human counterpart. However, subsequent studies involving affinity purification, co-immunoprecipitation with an α-TBP antibody and database searches indicated that like higher eukaryotes, yeast also contained TAF_{II}s (Ref. 3).

Figure 1 compares yeast TAF_{II}s ($yTAF_{II}$s) with those of higher eukaryotes. In almost all instances, a yeast TAF_{II} has a higher eukaryotic TAF_{II} homologue. Thus, like all other components of the transcription machinery, TAF_{II}s have been highly conserved. Studies in yeast have shown that with the exception of TAF30, all $yTAF_{II}$s are essential for viability. Thus, each essential TAF_{II}must perform at least one obligate, non-redundant function.

Sequence homologies, biochemical studies and structural analysis have revealed that a subset of TAF_{II}s have properties reminiscent of non-linker histones (i.e. the so-called core histones that form the nucleosome core)[3]. Specifically, *Drosophila* $TAF_{II}40$ ($dTAF_{II}40$), human $TAF_{II}31$ ($hTAF_{II}31$) and $yTAF_{II}17$ resemble histone H3; $dTAF_{II}62$, $hTAF_{II}80$ and $yTAF_{II}60$ resemble histone H4; and $dTAF_{II}30$, $hTAF_{II}20$ and $yTAF_{II}68$ resemble histone H2B. To date, a histone H2A homologue has not been identified. It has been proposed that these histone-like TAF_{II}s assume an octamer-like structure comprising two dimers of the histone H2B-like TAF_{II} complexed to a tetramer of the histone H3- and H4-like TAF_{II}s (Ref. 3). In addition, $hTAF_{II}18$ and $hTAF_{II}28$ heterodimerize through a histone-fold motif and have also been categorized as histone-like TAF_{II}s (Ref. 4).

TAF_{II}s in complexes other than TFIID

In both yeast and human cells, TAF_{II}s have been found in large nuclear complexes besides TFIID. In yeast, the three

M.R. Green is at the Howard Hughes Medical Institute Program in Molecular Medicine, University of Massachusetts Medical Center, Worcester, MA 01605, USA.

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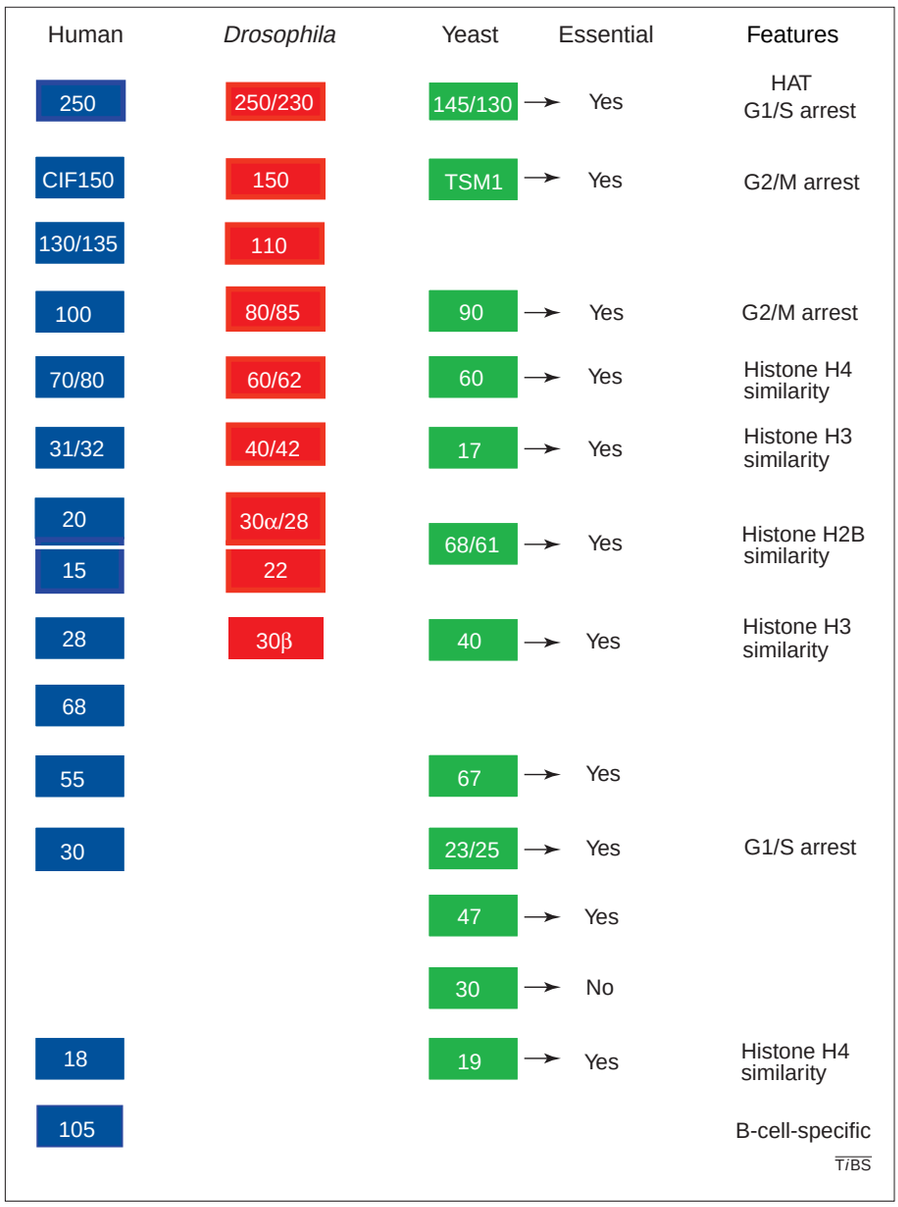

Figure 1

Comparison of yeast and higher eukaryotic TAF_{II}s. Homologues of TAF_{II}s are arranged in rows, human TAF_{II}s (blue), *Drosophila* TAF_{II}s (red), yeast TAF_{II}s (green). TAF_{II}s required for viability in yeast are indicated as essential. HAT, histone acetyltransferase.

histone-like TAF_{II}s (yTAF_{II}17, yTAF_{II}60 and yTAF_{II}68) and two other non-histone-like TAF_{II}s (yTAF_{II}25 and yTAF_{II}90) are integral components of the Spt-Ada-Gcn5-acetyltransferase (SAGA) complex[5]. A human TAF_{II}-containing complex, termed STAGA, is the likely human homologue of yeast SAGA (Ref. 6). Human cells also contain a p300/CBP-associated factor (PCAF) complex that includes several histone-like TAF_{II}s and other subunits bearing TAF_{II} homologies (Ref. 7). Significantly, SAGA, STAGA and PCAF each contain a single subunit with a histone acetyltransferase (HAT) activity, GCN5 and PCAF, respectively. Finally, a TBP-free TAF_{II}-containing complex (TFTC) has been reported, which also contains a human GCN5 subunit (Ref. 8). The function of TAF_{II}s in these other complexes is unknown, but has substantially complicated the interpretation of experiments analysing TAF_{II} function; if a TAF_{II} is found to have a particular activity, it is unclear in which complex that TAF_{II} is acting.

The finding that different multi-subunit complexes share common components also raises the question as to whether the functions of these complexes are unique or overlapping. For TFIID and SAGA this question has recently been investigated by genome-wide transcription analysis (see below). The expression of most genes requires one or more of the common TAF_{II} subunits, demonstrating that functions of SAGA and TFIID are required for expression of most genes. Most importantly, the histone acetylase components of SAGA and TFIID, Gcn5 and TAF_{II}145, respectively, are functionally redundant for transcription of specific genes; therefore, a large fraction of yeast genes are expressed through the action of either complex.

Requirement of TAF_{II}s for transcription

The transcriptional requirements for TAF_{II}s was assessed originally *in vitro* using transcription systems reconstituted from purified components[3]. These early studies found that TBP (which lacks TAF_{II}s) could support a 'basal' transcription reaction involving only the GTFs, but that this basal level of transcription could not be stimulated by an activator (activated transcription). Instead, TFIID (which contains TAF_{II}s) could support both basal and activated transcription. Thus, *in vitro* one or more TAF_{II}s appeared to have an obligatory 'coactivator' activity. Based upon this observation, *in vitro* interactions between activation domains and isolated TAF_{II}s, and TFIID reconstitution studies, it was proposed that TAF_{II}s are the obligatory targets of activators[3].

The discovery of yTAF_{II}s provided the opportunity to assess the role of these factors in living cells. In these *in vivo* studies TAF_{II}s have been inactivated by several experimental approaches including temperature-sensitive mutations[9–15], conditional depletion[9,10,14] and targeted protein degradation[16,17]. The effects on transcription following yTAF_{II}inactivation was then determined by analysing specific, selected genes, total poly(A)$^+$ mRNA, or the whole genome using high-density oligonucleotide arrays. The picture that has emerged from these studies is summarized in Fig. 2 and discussed below.

The striking and most important conclusion of these studies is that yTAF_{II}s are not universally required for transcription as are GTFs [e.g. the large subunit of RNA polymerase II, Srb4 and Kin28 (Ref. 15)]. Rather, each yTAF_{II} is required for the expression of a characteristic subset of genes, ranging from 3% to 67% of the genome. The broadest requirement is for yTAF_{II}17, one of the histone-like TAF_{II}s. An initial study suggested, based upon analysis of a small number of genes, that all histone-like TAF_{II}s have relatively broad transcriptional requirements, like yTAF_{II}17 (Ref. 14). However, genome-wide transcription analysis has revealed

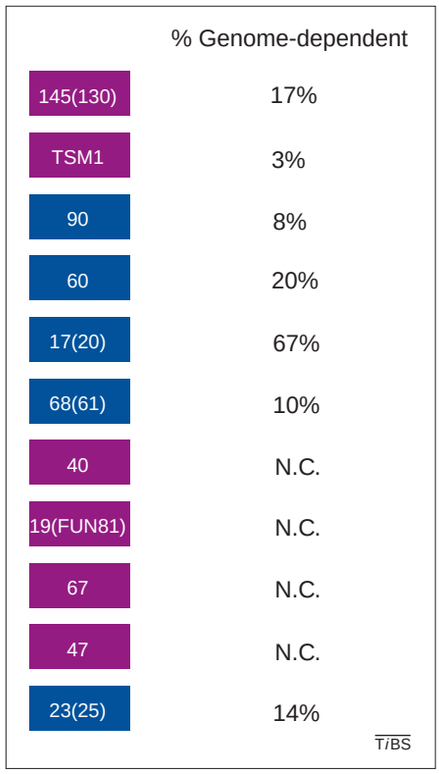

Figure 2

Dependence of genome-wide transcription on yTAF$_{II}$s. Percentage of yeast genes displaying a loss of transcription following inactivation of the indicated yTAF$_{II}$, compared with the transcriptional loss following inactivation of RNA polymerase II using the *rpb1-1* mutant allele, is indicated. (Ref. 15 and T.I. Lee *et al.*, unpublished). TFIID-specific yTAF$_{II}$s (purple), yTAF$_{II}$s in both TFIID and SAGA (blue). N.C., not completed.

substantial diversity, even among the histone-like TAF$_{II}$s (see below).

To date, seven yTAF$_{II}$s have been subjected to whole-genome expression analysis[13,15]. As a representative example, the relationship between three of these yTAF$_{II}$s is presented as Venn diagrams in Fig. 3. Significantly, each of these yTAF$_{II}$s controls a characteristic set of genes. Consider, for example, yTAF$_{II}$145 and yTAF$_{II}$60: there are genes that are yTAF$_{II}$145-dependent and yTAF$_{II}$60-independent, genes that are yTAF$_{II}$60-dependent and yTAF$_{II}$145-independent, genes that are dependent upon both of these yTAF$_{II}$s, and genes that do not require either of these yTAF$_{II}$s.

The genetic intractability of higher eukaryotes has made it challenging to assess whether the results in yeast are also applicable to higher eukaryotes. However, results from the limited studies of TAF$_{II}$ function in mammalian cells are similar to those in yeast. For example, mammalian cell lines harbouring a temperature-sensitive TAF$_{II}$250 allele do not have a global defect in RNA polymerase II transcription under non-permissive conditions[18,19]. Recently, mouse TAF$_{II}$30, the homologue of yTAF$_{II}$25 (see Fig. 1), has been subjected to targeted homologous recombination in mouse embryonic stem cells producing cells deficient in TAF$_{II}$30 (Ref. 20). The results indicate that TAF$_{II}$30 is required only for transcription of a subset of genes.

In general, higher eukaryotic TAF$_{II}$s are distributed ubiquitously, although, in several cases, they are expressed in a tissue-specific fashion. For example, there is a B-cell-specific form of hTAF$_{II}$130 (Ref. 21). The most interesting example is the *Drosophila* gene cannonball (*can*), a spermatocyte-specific form of dTAF$_{II}$80 (M. Fuller, pers. commun.) required for transcription of a group of stage- and tissue-specific target genes involved in normal spermatid differentiation[22]. Significantly, loss of *can* function leads to a G2/M arrest[23], analogous to the results with the yeast homologue yTAF$_{II}$90 (Ref. 9).

TAF$_{II}$s and cell-cycle progression

Inactivation of some yTAF$_{II}$s results in distinct cell-cycle phenotypes[9,10]. Specifically, inactivation of yTAF$_{II}$145 leads to a G1/S arrest[10], analogous to the results with its mammalian homologue, TAF$_{II}$250 (Ref. 24). Mouse cells lacking TAF$_{II}$30 also arrest in G1/S (Ref. 20). Conversely, following inactivation of yTAF$_{II}$90 (Ref. 9), yTAF$_{II}$150 (TSM1) (Ref. 10) or hTAF$_{II}$150 (Ref. 25), cells arrest in G2/M. These observations raise the possibility that TAF$_{II}$s might have a specialized role in the transcriptional control of the cell cycle and cellular-growth state and further suggest that individual yTAF$_{II}$s mediate cell-cycle progression through unique activities or targets. Consistent with this idea, yTAF$_{II}$145 is required for transcription of G1- and B-type cyclins[11], as well as other genes involved in cell-cycle progression[15]. Similarly, mouse cells lacking TAF$_{II}$30 have impaired expression of cyclin E (Ref. 20), which could explain the G1/S arrest.

Intriguingly, the TAF$_{II}$s themselves appear to be regulated by the cellular-growth state. For example, as yeast-cell growth slows down in response to high density, the levels of several yTAF$_{II}$s and TBP decrease dramatically, whereas other GTFs are unaffected[11]. Another example is as cells enter mitosis, RNA-polymerase-II-directed transcription is shut off by a mechanism involving mitosis-specific phosphorylation of TAF$_{II}$s and TBP (Ref. 26).

How do TAF$_{II}$s selectively promote transcription?

Although the whole-genome expression studies have clearly revealed that individual TAF$_{II}$s function as promoter-selectivity factors, their mechanism of action remains to be elucidated. The three major proposed mechanisms of action are that TAF$_{II}$s: (1) serve as activator-binding sites, (2) mediate core-promoter recognition, or (3) provide an essential catalytic activity.

The original *in vitro* studies on TAF$_{II}$s led to the so-called 'coactivator hypothesis', which posited that TAF$_{II}$s are the obligatory targets of activators and that different activator–coactivator combinations selectively regulate transcription. The primary support for this proposal are numerous studies that have reported interactions between activation domains and isolated TAF$_{II}$s (Ref. 3). However, an isolated TAF$_{II}$ is not a physiologically relevant entity, and it will be important to demonstrate that such activation domain–TAF$_{II}$ interactions also occur with the physiologically relevant TFIID complex. The apparent, direct interaction between activators and TAF$_{II}$s could, for example, involve surfaces of TAF$_{II}$s that are not exposed in the TFIID complex. The finding that the upstream-activating sequence (UAS) is the region that confers yTAF$_{II}$17-dependence[14,17] is also consistent with, but

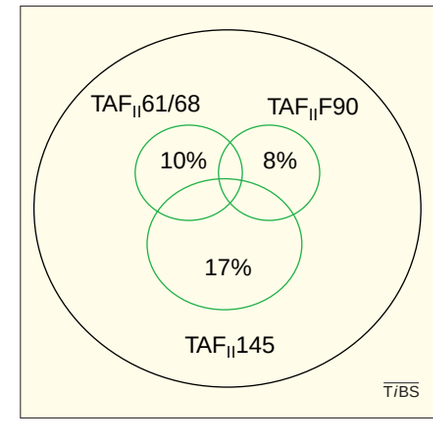

Figure 3

Comparative roles of yTAF$_{II}$145, yTAF$_{II}$61/68 and yTAF$_{II}$90 in genome-wide transcription. Percentage of yeast genes displaying a loss of transcription following inactivation of the indicated yTAF$_{II}$, compared with the transcriptional loss following inactivation of RNA polymerase II using the *rpb1-1* mutant allele, is displayed as a Venn diagram (Ref. 15 and T.I. Lee *et al.*, unpublished).

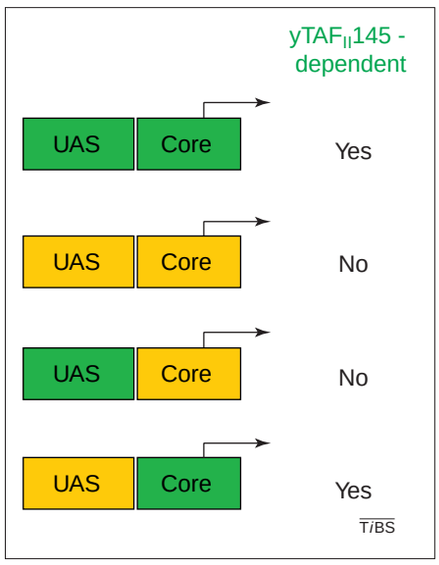

Figure 4
Experimental strategy for mapping the yTAF$_{II}$145-dependent promoter element. For detailed experimental procedures and results, see Ref. 12. Core, portion of promoter bearing the TATA box and initiation site; UAS, upstream activating sequence.

does not prove, an activator–yTAF$_{II}$17 interaction.

The second proposed mechanism of action is core-promoter recognition. Strong *in vivo* support for this proposal comes from studies with yTAF$_{II}$145. The portion of the gene that conferred yTAF$_{II}$145-dependence has been delineated[12]. The experimental strategy used was to construct a series of chimeric promoters by fusing different combinations of UASs, which harbour the activator-binding sites, with core promoters, the portion of the promoter that is recognized by the RNA polymerase II general transcription machinery (Fig. 4). Unexpectedly, the portion of these genes that rendered them yTAF$_{II}$145-dependent was the core promoter, not the UAS. In fact, a yTAF$_{II}$145-dependent promoter retained the yTAF$_{II}$145 requirement, even when its transcription was artificially driven in the absence of an activator. Taken together, these results indicate that yTAF$_{II}$145 functions in recognition and selection of core promoters by a mechanism not involving upstream activators. Significantly, in mammalian cells, temperature-sensitive inactivation of TAF$_{II}$250, the homologue of yTAF$_{II}$145, leads to loss of transcription of the cyclin D1 gene[27,28]. As in the case of yeast, it is the core promoter, and not the activator-binding sites, that is responsible for TAF$_{II}$250-dependence[28].

The results with yTAF$_{II}$145 emphasize how, in addition to the activators, the core promoter can contribute to transcriptional regulation. In this regard, a variety of studies have demonstrated differential responsiveness of various core promoters to upstream activators, perhaps reflecting differences in the rate-limiting step(s) for transcription activation.

Although the *in vivo* results clearly indicate that the core promoter can dictate TAF$_{II}$-dependence, the basis for recognition and selection remains to be elucidated. A variety of studies have revealed interactions between TAF$_{II}$s and the core promoter. First, whereas TBP gives rise to a discrete footprint that covers only the TATA box, the DNAse I footprint of TFIID on some core promoters is substantially larger[3]. This difference in footprinting is highly suggestive of TAF$_{II}$–DNA contacts. The occurrence of this extended footprint on only some promoters further suggests differential affinity of TAF$_{II}$s for various core promoters. Second, site-specific DNA crosslinking studies have directly demonstrated TAF$_{II}$–core promoter contacts. For example, Oelgeschlager *et al.* have shown that several TAF$_{II}$s are engaged in position-dependent contacts with the core promoter[29]. Burke and Kadonaga have shown specific photocrosslinking of dTAF$_{II}$60 and dTAF$_{II}$40 to the downstream promoter element (DPE)[30]. Third, in addition to the TATA box, several of the other core promoter elements appear to function through interactions with TAF$_{II}$s (Refs 30–34). Fourth, binding-site selection experiments indicate that TFIID interacts with the initiator element (Inr) in a sequence-specific fashion. Remarkably, this selected sequence matches a consensus deduced by comparison of *bona fide Drosophila* promoters[35]. Both dTAF$_{II}$150 and dTAF$_{II}$250 have been proposed to contact the Inr (Refs 32,34,36). Finally, the *in vitro* DNA-binding specificity of TBP–TAF$_{II}$ complexes differs from that of TBP alone[37], which is most readily explained by TAF$_{II}$–DNA contacts.

How do interactions between TAF$_{II}$s and the core promoter facilitate promoter selection? The first and most likely possibility is that the TAF$_{II}$–core promoter contacts affect the affinity or specificity of TFIID for certain core promoters. This could be particularly important *in vivo* where the amount of TFIID is probably limiting relative to the 5000–6000 actively transcribed genes. Second, TAF$_{II}$–core promoter contact might introduce allosteric effects in TFIID that modulate its activity and hence transcription. DNA-binding-induced conformational changes have been observed with several transcriptional activators, in particular nuclear hormone receptors[38]. Third, differences in chromatin structure of core promoters might affect TFIID binding and TAF$_{II}$s could be required differentially. In this regard, hTAF$_{II}$250 and its yeast homologue yTAF$_{II}$145 have intrinsic histone acetyltransferase (HAT) enzyme activity[39], which could act to overcome a repressive nucleosomal structure.

A third proposal is that TAF$_{II}$s provide a catalytic activity required for transcription. As mentioned above, hTAF$_{II}$250 and its yeast homologue yTAF$_{II}$145 have an intrinsic histone acetyltransferase (HAT) enzyme activity[39]. Although the role for the HAT activity is not clear, and there has been no direct demonstration that the HAT activity is required for function, the evolutionary conservation is highly suggestive of an important role.

hTAF$_{II}$250 has also been reported to possess a bipartite serine/threonine kinase activity that can autophosphorylate and transphosphorylate the large subunit of TFIIF (Refs 40,41). However, unlike the HAT domain, the kinase domain has not been evolutionarily conserved. Furthermore, a hTAF$_{II}$250 derivative completely lacking the kinase domains can rescue the temperature-sensitive phenotype of cell lines bearing a temperature-sensitive mutation in endogenous hTAF$_{II}$250 (Ref. 42).

In addition to their well-established roles as positive transcription factors, TAF$_{II}$s have been reported to have several other activities. For example, to couple transcription to RNA processing, TAF$_{II}$s might participate in recruiting activities such as the cleavage polyadenylation specificity factor (CPSF) to TFIID (Ref. 43). Another, somewhat paradoxical activity is negative regulation of TBP binding by dTAF$_{II}$230, the TAF$_{II}$ that makes the primary contact with TBP. This negative regulatory activity results from an interaction between the dTAF$_{II}$230 N terminus and the DNA-binding surface of TBP (Ref. 44).

In vitro approaches will be required ultimately to elucidate the detailed mechanisms of TAF$_{II}$ action. In this regard, several *in vitro* systems in yeast[45,46] and mammals[47,48] have been described in which activated transcription in the absence of TAF$_{II}$s has been achieved. The next step will be to develop an *in vitro* system that faithfully

recapitulates the selective TAF_{II}-dependence observed *in vivo*.

In summary, there is evidence to support each of the three main proposals for the mechanism of action of TAF_{II}. These three mechanisms are not mutually exclusive, and it seems likely that different TAF_{II}s will function by distinct mechanisms.

Implications for the function of multicomponent transcription complexes

Multisubunit transcription complexes have been generally believed to mediate a single activity, for example PIC assembly for TFIID and chromatin modification for SAGA. The results with $yTAF_{II}$s underscore the unexpected diversity of the individual subunits of these complexes. There are also striking differences in the properties of individual subunits of other complexes, such as the Srb/Mediator complex, both with regard to requirements for viability and transcriptional effects[49]. These observations raise the possibility that it could be the intrinsic activity of the subunits, rather than their presence in a single complex, that is critical. Perhaps, components such as TAF_{II}s are present in a complex not to provide a common activity, but for other reasons, such as co-regulation or efficient co-recruitment to the promoter.

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References

1 Orphanides, G. *et al.* (1996) The general transcription factors of RNA polymerase II. *Genes Dev.* 10, 2657–2683
2 Ptashne, M. (1988) How eukaryotic transcription activators work. *Nature* 335, 683–689
3 Burley, S.K. and Roeder, R.G. (1996) Biochemistry and structural biology of transcription factor IID (TFIID). *Annu. Rev. Biochem.* 65, 769–799
4 Birck, C. *et al.* (1998) Human TAF(II)28 and TAF(II)18 interact through a histone fold encoded by atypical evolutionary conserved motifs also found in the SPT3 family. *Cell* 94, 239–249
5 Grant, P.A. *et al.* (1998) A subset of TAFIIs are integral components of the SAGA complex required for nucleosome acetylation and transcriptional stimulation. *Cell* 94, 45–53
6 Martinez, E. *et al.* (1998) A human SPT3-TAFII31-GCN5-L acetylase complex distinct from transcription factor IID. *J. Biol. Chem.* 273, 23781–23785
7 Ogryzk, V.V. *et al.* (1998) Histone-like TAFs within the PCAF histone acetylase complex. *Cell* 94, 35–44
8 Brand, M. *et al.* (1999) Identification of TATA-binding protein-free TAFII-containing complex subunits suggests a role in nucleosome acetylation and signal transduction. *J. Biol. Chem.* 274, 18285–18289
9 Apone, L.M. *et al.* (1996) Yeast $TAF_{II}90$ is required for cell-cycle progression through G_2/M but not for general transcription activation. *Genes Dev.* 10, 2368–2380
10 Walker, S.S. *et al.* (1996) Transcription activation in cells lacking TAF_{II}s. *Nature* 383, 185–188
11 Walker, S.S. *et al.* (1997) Yeast $TAF_{II}145$ required for transcription of G1/S cyclin genes and regulated by the cellular growth state. *Cell* 90, 607–614
12 Shen, W-C. and Green, M.R. (1997) Yeast $TAF_{II}145$ functions as a core promoter selectivity factor, not a general coactivator. *Cell* 90, 615–624
13 Apone, L.M. *et al.* (1998) Broad, but not universal, transcriptional requirement for yTAFII17, a histone H3-like TAFII present in TFIID and SAGA. *Mol. Cell* 2, 653–661
14 Michel, B. *et al.* (1998) Histone-like TAFs are essential for transcription *in vivo*. *Mol. Cell* 2, 663–673
15 Holstege F.C. *et al.* (1998) Dissecting the regulatory circuitry of a eukaryotic genome. *Cell* 95, 717–728
16 Moqtaderi, Z. *et al.* (1996) TBP-associated factors are not generally required for transcriptional activation in yeast. *Nature* 383, 188–191
17 Moqtaderi, Z. *et al.* (1998) The histone H3-like TAF is broadly required for transcription in yeast. *Mol. Cell* 2, 675–682
18 Liu, H.T. *et al.* (1985) Expression of thymidine kinase and dihydrofolate reductase genes in mammalian ts mutants of the cell cycle. *J. Biol. Chem.* 260, 3269–3274
19 Hirschhorn, R.R. *et al.* (1984) Cell-cycle-specific cDNAs from mammalian cells temperature sensitive for growth. *Proc. Natl. Acad. Sci. U. S. A.* 81, 6004–6008
20 Metzger, D. *et al.* (1999) Mammalian TAF(II)30 is required for cell cycle progression and specific cellular differentiation programmes. *EMBO J.* 18, 4823–4834
21 Dikstein, R. *et al.* (1996) Human TAFII 105 is a cell type-specific TFIID subunit related to hTAFII130. *Cell* 87, 137–146
22 White-Cooper, H. *et al.* (1998) Transcriptional and post-transcriptional control mechanisms coordinate the onset of spermatid differentiation with meiosis I in *Drosophila*. *Development* 125, 125–134
23 Lin, T-Y. *et al.* (1996) Coordinate developmental control of the meiotic cell cycle and spermatid differentiation in *Drosophila* males. *Development* 122, 1331–1341
24 Talavera, A. and Basilico, C. (1977) Temperature sensitive mutants of BHK cells affected in cell cycle progression. *J. Cell. Physiol.* 92, 425–436
25 Martin, J. *et al.* (1999) Human transcription factor hTAF(II)150 (CIF150) is involved in transcriptional regulation of cell cycle progression. *Mol. Cell Biol.* 19, 5548–5556
26 Segil, N. *et al.* (1996) Mitotic regulation of TFIID: inhibition of activator-dependent transcription and changes in subcellular localization. *Genes Dev.* 10, 2389–2400
27 Suzuki-Yagawa, Y. *et al.* (1997) The ts13 mutation in the TAF(II)250 subunit (CCG1) of TFIID directly affects transcription of D-type cyclin genes in cells arrested in G1 at the nonpermissive temperature. *Mol. Cell. Biol.* 17, 3284–3294
28 Sekiguchi, T. *et al.* (1998) Overexpression of D-type cyclins, E2F-1, SV40 large T antigen and HPV16 E7 rescue cell cycle arrest of tsBN462 cells caused by the CCG1/TAF(II)250 mutation. *Oncogene* 18, 1797–1806
29 Oelgeschlager, T. *et al.* (1996) Topology and reorganization of a human TFIID-promoter complex. *Nature* 382, 735–738
30 Burke, T.W. and Kadonaga, J.T. (1997) The downstream core promoter element DPE, is conserved from *Drosophila* to humans and is recognized by $TAF_{II}60$ of *Drosophila*. *Genes Dev.* 11, 3020–3031
31 Nakatani, Y. *et al.* (1990) A downstream initiation element required for efficient TATA box binding and *in vitro* function of TFIID. *Nature* 348, 86–88
32 Smale, S.T. *et al.* (1998) The initiator element: a paradigm for core promoter heterogeneity within metazoan protein-coding genes. *Cold Spring Harbor Symp. Quant. Biol.* 63, 21–31
33 Martinez, E. *et al.* (1995) Core promoter-specific function of a mutant transcription factor TFIID defective in TATA-box binding. *Proc. Natl. Acad. Sci. U. S. A.* 92, 11864–11868
34 Verrijzer, C.P. *et al.* (1994) *Drosophila* TAFII150: Similarity to yeast gene TSM-1 and specific binding to core promoter DNA. *Science* 264, 933–941
35 Purnell, B.A. *et al.* (1994) TFIID sequence recognition of the initiator and sequences further downstream in *Drosophila* class II genes. *Genes. Dev.* 8, 830–842
36 Chalkley, G.E. and Verrijzer, C.P. (1999) DNA binding site selection by RNA polymerase II TAFs: a TAF(II)250–TAF(II)150 complex recognizes the initiator. *EMBO J.* 18, 4835–4845
37 Verrijzer, C.P. *et al.* (1995) Binding of TAFs to core elements directs promoter selectivity by RNA polymerase II. *Cell* 81, 1115–1125
38 Lefstin, J. and Yamamoto, K. (1998) Allosteric effects of DNA on transcriptional regulators. *Nature* 392, 885–888
39 Mizzen, C.A. *et al.* (1996) The $TAF_{II}250$ subunit of TFIID has histone acetyltransferase activity. *Cell* 87, 1261–1270
40 Dikstein, R. *et al.* (1996) Allosteric effects of DNA on transcriptional regulators. *Cell* 84, 781–790
41 O'Brien, T. and Tjian, R. (1998) Functional analysis of the human TAFII250 N-terminal kinase domain. *Mol. Cell* 1, 905–911
42 Noguchi, E. *et al.* (1994) Minimum essential region of CCG1/TAFII250 required for complementing the temperature-sensitive cell cycle mutants, tsBN462 and ts13 cells, of hamster BHK21 cells. *Somat. Cell Mol. Genet.* 20, 505–513
43 Dantonel, J.C. *et al.* (1997) Transcription factor TFIID recruits factor CPSF for formation of 3′ end of mRNA. *Nature* 389, 399–402
44 Liu, D. *et al.* (1998) Solution structure of a TBP–TAF(II)230 complex: protein mimicry of the minor groove surface of the TATA box unwound by TBP. *Cell* 94, 573–583
45 Kim, Y-J. *et al.* (1994) A multiprotein mediator of transcriptional activation and its interaction with the C-terminal repeat domain of RNA polymerase II. *Cell* 77, 599–608
46 Koleske, A.J. and Young, R.A. (1994) An RNA polymerase II holoenzyme responsive to activators. *Nature* 368, 466–469
47 Oelgeschlager, T. *et al.* (1998) Transcription activation via enhanced preintiation complex assembly in a human cell-free system lacking TAF_{II}s. *Mol. Cell* 1, 925–931
48 Wu, S.Y. *et al.* (1998) TAFII-independent activation mediated by human TBP in the presence of the positive cofactor PC4. *EMBO J.* 17, 4478–4490
49 Myers, L.C. *et al.* (1998) The Med proteins of yeast and their function through the RNA polymerase II carboxy-terminal domain. *Genes Dev.* 12, 45–54