

▲ **FIGURE 11-46 In vitro assembly of the yeast Pol I transcription initiation complex.** UAF and CF, both multimeric general transcription factors, bind to the upstream element (UE) and core element, respectively, in the promoter DNA. TBP and a monomeric factor (Rrn3p) associated with RNA polymerase I (Pol I) also participate in forming the initiation complex. [Adapted from N. Nomura, 1998, in R. M. Paule, *Transcription of Ribosomal RNA Genes by Eukaryotic RNA Polymerase I*, Landes Bioscience, pp. 157–172.]

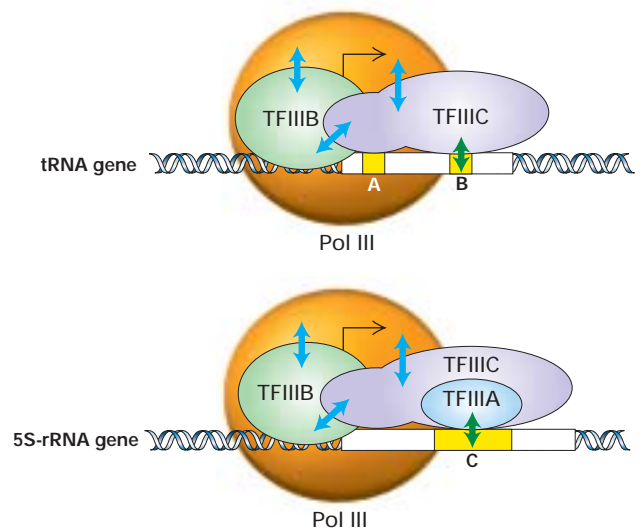
Assembly of a fully active Pol I initiation complex begins with binding of a multimeric upstream activating factor (UAF) to the upstream element (Figure 11-46). Two of the six subunits composing UAF are histones, which probably participate in DNA binding. Next, a trimeric core factor binds to the core element together with TBP, which makes contact with both the bound UAF and the core factor. Finally, a preformed complex of Pol I and Rrn3p associates with the bound proteins, positioning Pol I near the start site. In human cells, TBP is stably bound to three other polypeptides, forming an initiation factor called *SL1* that binds to the core promoter element and is functionally equivalent to yeast core factor plus TBP.

Initiation by Pol III Unlike protein-coding genes and pre-rRNA genes, the promoter regions of tRNA and 5S-rRNA genes lie entirely within the transcribed sequence (Figure 11-47). Two such *internal* promoter elements, termed the *A box* and *B box*, are present in all tRNA genes. These highly conserved sequences not only function as promoters but also encode two invariant portions of eukaryotic tRNAs that are required for protein synthesis. In 5S-rRNA genes, a single internal control region, the *C box*, acts as a promoter.

Three general transcription factors are required for Pol III to initiate transcription of tRNA and 5S-rRNA genes *in vitro*. Two multimeric factors, TFIIB and TFIIC, participate in initiation at both tRNA and 5S-rRNA promoters; a third factor, TFIIA, is required for initiation at 5S-rRNA promoters. As with assembly of Pol I and Pol II initiation complexes, the Pol III general transcription factors bind to promoter DNA in a defined sequence.

The N-terminal half of one TFIIB subunit, called *BRF* (for TFIIB-related factor), is similar in sequence to TFIIB (a Pol II factor). This similarity suggests that BRF and TFIIB perform a similar function in initiation, namely, to direct the polymerase to the correct start site. Once TFIIB has bound to either a tRNA or 5S-rRNA gene, Pol III can bind and initiate transcription in the presence of ribonucleoside triphosphates. The BRF subunit of TFIIB interacts specifically with one of the polymerase subunits unique to Pol III, accounting for initiation by this specific nuclear RNA polymerase.

Another of the three subunits composing TFIIB is TBP, which we can now see is a component of a general transcription factor for all three eukaryotic nuclear RNA polymerases. The finding that TBP participates in transcription initiation by Pol I and Pol III was surprising, since the promoters recognized by these enzymes often do not contain TATA boxes. Nonetheless, recent studies indicate that the TBP subunit of TFIIB interacts with DNA similarly to the way it interacts with TATA boxes.



▲ **FIGURE 11-47 Transcription-control elements in genes transcribed by RNA polymerase III.** Both tRNA and 5S-rRNA genes contain internal promoter elements (yellow) located downstream from the start site and named A-, B-, and C-boxes, as indicated. Assembly of transcription initiation complexes on these genes begins with the binding of Pol III-specific general transcription factors TFIIA, TFIIB, and TFIIC to these control elements. Green arrows indicate strong, sequence-specific protein-DNA interactions. Blue arrows indicate interactions between general transcription factors. Purple arrows indicate interactions between general transcription factors and Pol III. [From L. Schramm and N. Hernandez, 2002, *Genes Dev.* 16:2593.]