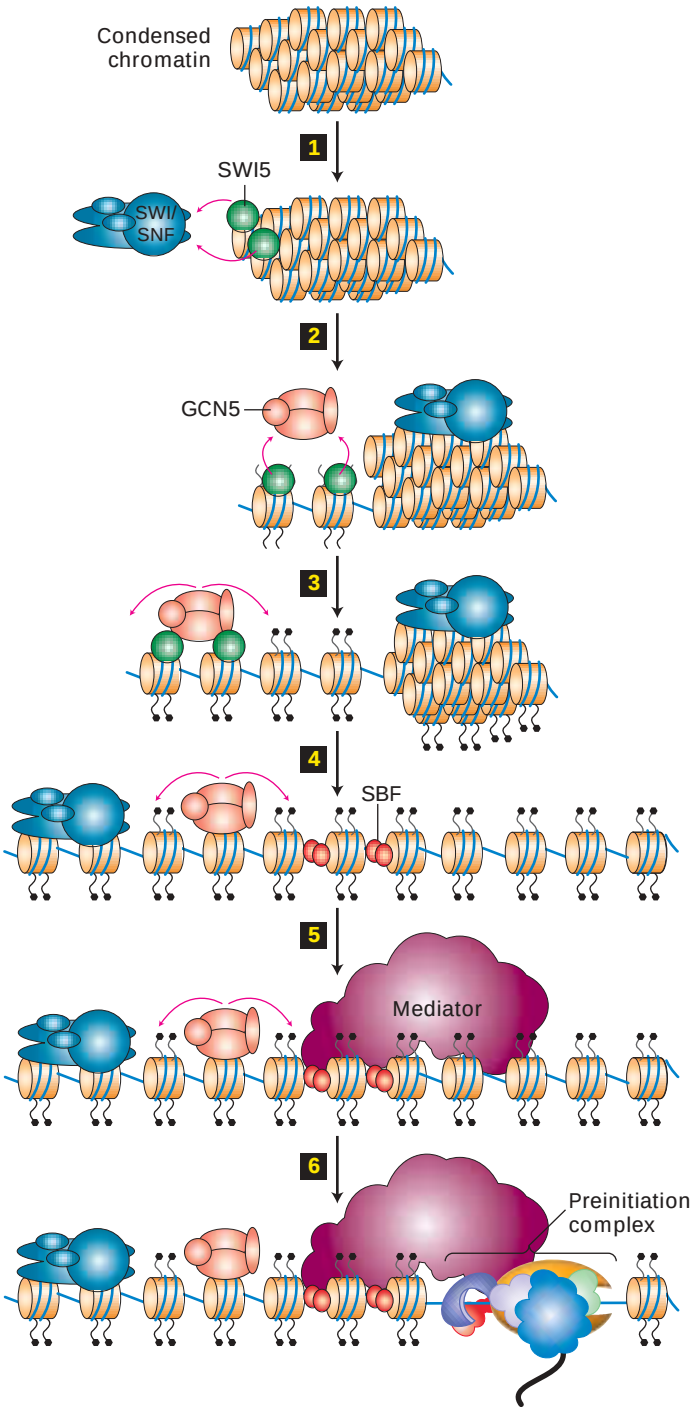
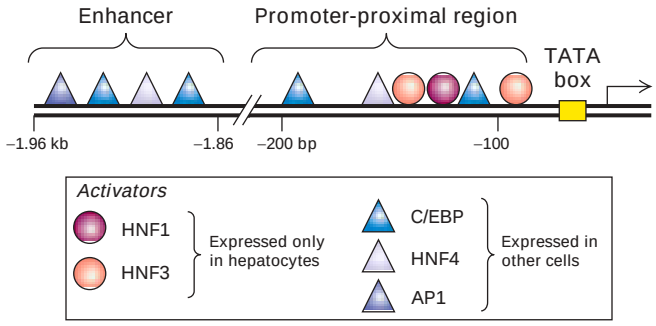


◀ FIGURE 11-37 **Ordered binding and interaction of activators and co-activators leading to transcription of the yeast *HO* gene.** Step 1: Initially, the HO gene is packaged into condensed chromatin. Activation begins when the SWI5 activator binds to enhancer sites 1200–1400 base pairs upstream of the start site and interacts with the SWI/SNF chromatin-remodeling complex. Step 2: The SWI/SNF complex acts to decondense the chromatin, thereby exposing histone tails. Step 3: A GCN5-containing histone acetylase complex associates with bound SWI5 and acetylates histone tails in the *HO* locus as SWI/SNF continues to decondense adjacent chromatin. Step 4: SWI5 is released from the DNA, but the SWI/SNF and GCN5 complexes remain associated with the *HO* control region (in the case of GCN5, by poorly understood interactions). Their action allows the SBF activator to bind several sites in the promoter-proximal region. Step 5: SBF then binds the mediator complex. Step 6: Subsequent binding of Pol II and general transcription factors results in assembly of a transcription preinitiation complex whose components are detailed in Figure 11-37. [Adapted from C. J. Fry and C. L. Peterson, 2001, *Curr. Biol.* **11**:R185. See also M. P. Cosma et al., 1999, *Cell* **97**:299, and M. P. Cosma et al., 2001, *Mol. Cell* **7**:1213.]

We can now see that the assembly of a preinitiation complex and stimulation of transcription at a promoter results from the interaction of several activators with various multiprotein co-activator complexes. These include chromatin-remodeling complexes, histone acetylase complexes, and a mediator complex. While much remains to be learned about these processes, it is clear that the net result of these multiple molecular events is that activation of transcription at a promoter depends on highly cooperative interactions initiated by several activators. This allows genes to be regulated in a cell-type-specific manner by specific combinations of transcription factors. The *TTR* gene, which encodes transthyretin in mammals, is a good example of this. As noted earlier, transthyretin is expressed in hepatocytes and in choroid plexus cells. Transcription of the *TTR* gene in hepatocytes is controlled by at least five different transcriptional activators (Figure 11-38). Even though three of these activators—HNF4, C/EBP, and AP1— are also expressed in cells of the intestine and kidney, *TTR* transcription does not occur in these cells, because all five activators are required but HNF1 and HNF3 are missing. Other hepatocyte-



▲ FIGURE 11-38 **Transcription-control region of the mouse transthyretin (*TTR*) gene.** Binding sites for the five activators required for transcription of *TTR* in hepatocytes are indicated. The complete set of activators is expressed at the required concentrations to stimulate transcription only in hepatocytes. A different set of activators stimulates transcription in choroid plexus cells. [See R. Costa et al., 1989, *Mol. Cell Biol.* **9**:1415, and K. Xanthopoulus et al., 1989, *Proc. Nat'l. Acad. Sci. USA* **86**:4117.]