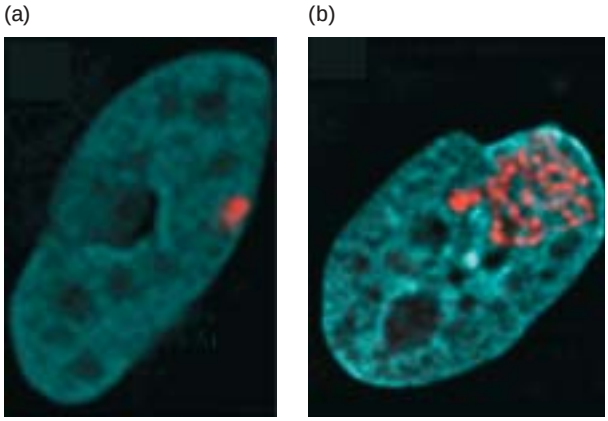


▲ EXPERIMENTAL FIGURE 11-34 **Expression of fusion proteins demonstrates chromatin decondensation in response to an activation domain.** A cultured hamster cell line was engineered to contain multiple copies of a tandem array of *E. coli lac operator* sequences integrated into a chromosome in a region of heterochromatin. (a) When an expression vector for the *lac* repressor was transfected into these cells, *lac* repressors bound to the *lac* operator sites could be visualized in a region of condensed chromatin using an antibody against the *lac* repressor (red). DNA was visualized by staining with DAPI (blue), revealing the nucleus. (b) When an expression vector for the *lac* repressor fused to an activation domain was transfected into these cells, staining as in (a) revealed that the activation domain causes this region of chromatin to decondense into a thinner chromatin fiber that fills a much larger volume of the nucleus. Bar = 1 μm. [Courtesy of Andrew S. Belmont, 1999, *J. Cell Biol.* **145**:1341.]

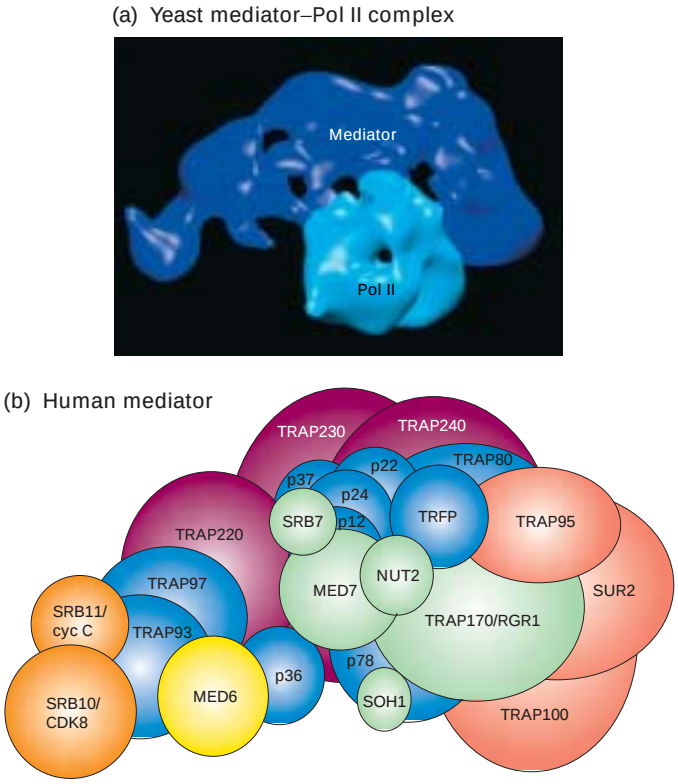
higher-order chromatin structures. The net result of such chromatin remodeling is to facilitate the binding of transcription factors to DNA in chromatin. Some activation domains have been shown to bind to the SWI/SNF complex, and this binding stimulates in vitro transcription from chromatin templates (DNA bound to nucleosomes). Thus the SWI/SNF complex represents another type of co-activator complex. Other multi-protein complexes with similar chromatin-remodeling activities have been identified in yeast, raising the possibility that different chromatin-remodeling complexes may be required by distinct families of activators (see chapter opening figure).

Higher eukaryotes also contain multiprotein complexes with homology to the yeast SWI/SNF complex. These complexes isolated from nuclear extracts of mammalian and *Drosophila* cells have been found to assist binding of transcription factors to their cognate sites in nucleosomal DNA in an ATP-requiring process. The experiment shown in Figure 11-34 dramatically demonstrates how an activation domain can cause decondensation of a region of chromatin. This is thought to result from the interaction of the activation domain with chromatin remodeling and histone acetylase complexes.

Surprisingly, SWI/SNF complexes are also required for the repression of some genes, perhaps because they help expose histone tails to deacetylases or because they assist in the folding of chromatin into condensed, higher-order structures. Much remains to be learned about how this important class of co-activators and co-repressors alters chromatin structure to influence gene expression.

The Mediator Complex Forms a Molecular Bridge Between Activation Domains and Pol II

Still another type of co-activator, the multiprotein mediator complex, assists more directly in assembly of Pol II preinitiation complexes (Figure 11-35). Some of the ≈20 mediator subunits binds to RNA polymerase II, and other mediator subunits bind to activation domains in various activator proteins. Thus mediator can form a molecular bridge between



▲ FIGURE 11-35 **Structure of yeast and human mediator complexes.** (a) Reconstructed image of mediator from *S. cerevisiae* bound to Pol II. Multiple electron microscopy images were aligned and computer-processed to produce this average image in which the three-dimensional Pol II structure (light blue) is shown associated with the yeast mediator complex (dark blue). (b) Diagrammatic representation of mediator subunits from human cells. Subunits shown in the same color are thought to form a module. Subunits in orange, yellow, and green are homologous with subunits in the yeast mediator complex. Genetic studies in yeast show that mutations in one of the subunits in a module inhibit the association of other subunits in the same module with the rest of the complex. [Part (a) courtesy of Francisco J. Asturias, 2002, *Mol. Cell* **10**:409. Part (b) adapted from S. Malik and R. G. Roeder, 2000, *Trends Biochem. Sci.* **25**:277.]