Transcription factors

Transcription factors

- **Regulatory proteins**
- Three kinds of small, distinctive structural motifs: the helix-turn-helix (or HTH),
- the zinc finger(orZn-finger),
- the leucine zipper-basic region(orbZIP).

Proteins with the Helix-Turn-Helix Motif Use One Helix to Recognize DNA

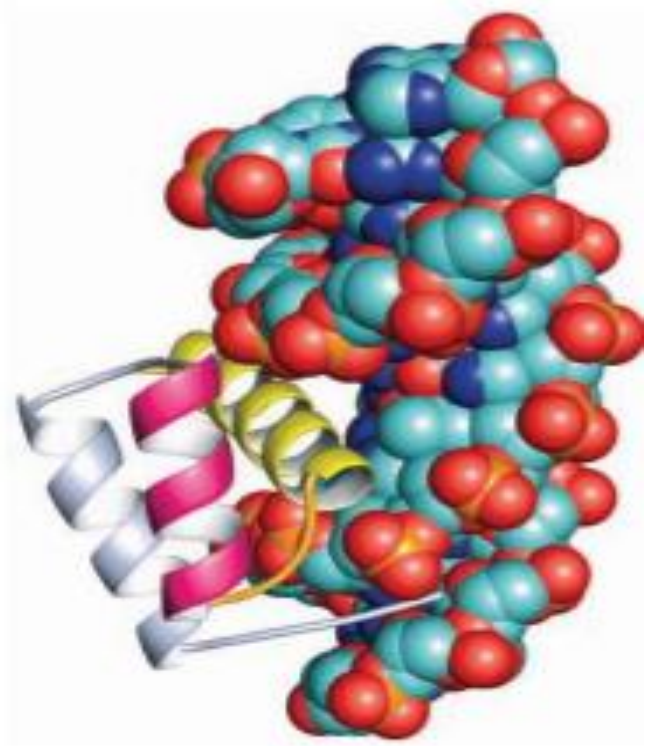
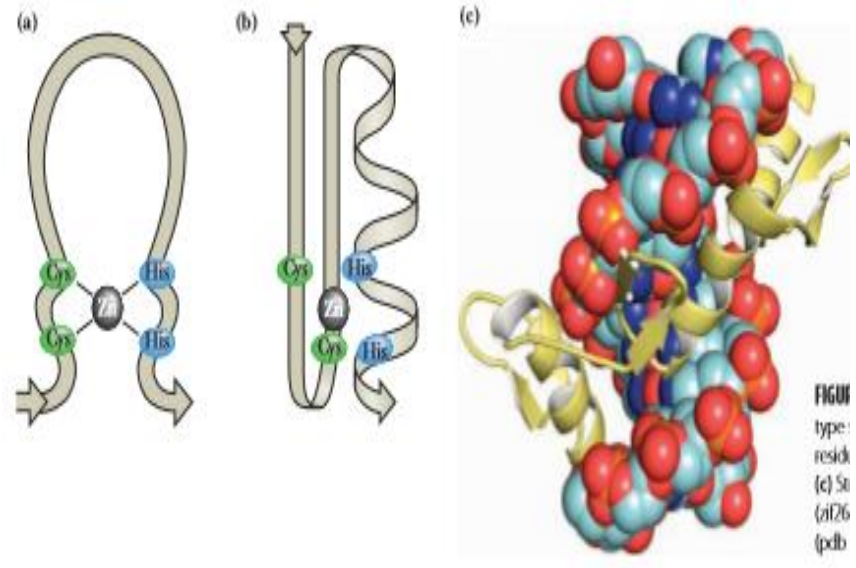


FIGURE 29.32 An HTH motif protein: *Antp* monomer bound to DNA. Helix 3 (yellow) is locked into the major groove of the DNA by helix 2 (magenta) (pdb id — 9ANT

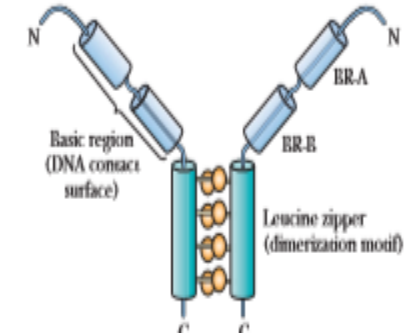
- The HTH motif is a protein structural domain consisting of two successive α -helices separated by a sharp α -turn Within this domain, the α -helix situated more toward the C-terminal end of the protein, the so-called helix 3, is the DNA recognition helix; it fits nicely into the major groove, with several of its side chains touching DNA base pairs. Helix 2, the helix at the beginning of the HTH motif, creates a stable structural domain through hydrophobic interactions with helix 3 that locks helix 3 into its DNA interface.

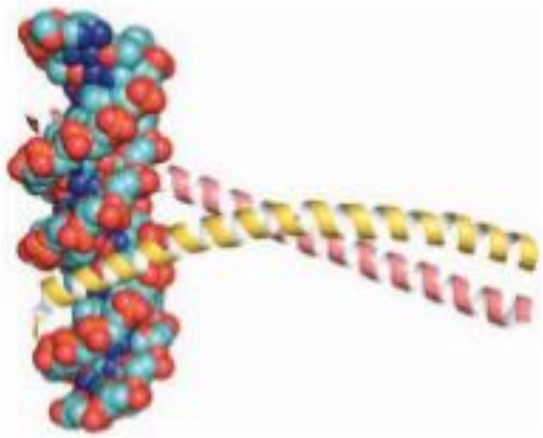
Some Proteins Bind to DNA via Zn-Finger Motifs



- There are many classes of Zn-finger motifs. The prototype Zn-finger is a structural feature formed by a pair of Cys residues separated by 2 residues, then a run of 12 amino acids, and finally a pair of His residues separated by 3 residues (Cys-x2-Cys-x12-His-x3His). This motif may be repeated as many as 13 times over the primary structure of a Zn-finger protein. Each repeat coordinates a zinc ion via its 2 Cys and 2 His residues
- The 12 or so residues separating the Cys and His coordination sites are looped out and form a distinct DNA interaction module, the so-called Zn-finger. When Zn-finger proteins associate with DNA, each Zn-finger binds in the major groove and interacts with about five nucleotides, adjacent fingers interacting with contiguous stretches of DNA. Many DNA-binding proteins with this motif have been identified. In all cases, the finger motif is repeated at least two times, with at least a 7– to 8–amino acid linker between Cys/Cys and His/His sites.

Some DNA-Binding Proteins Use a Basic Region-Leucine Zipper (bZIP)Motif





- The leucine zipper motif arises from the periodic repetition of leucine residues within this helical region. The periodicity causes the Leu side chains to protrude from the same side of the helical cylinder, where they can enter into hydrophobic interactions with a similar set of Leu side chains extending from a matching helix in a second polypeptide. These hydrophobic interactions establish a stable noncovalent linkage, fostering dimerization of the two polypeptides.
- The actual DNA contact surface of bZIP proteins is contributed by a 16-residue segment that ends exactly 7 residues before the first Leu residue of the Leu zipper. This DNA contact region is rich in basic residues and hence is referred to as the basic region. Two bZIP polypeptides join via a Leu zipper to form a Y-shaped molecule in which the stem of the Y corresponds to a coiled pair of -helices held by the leucine zipper. The arms of the Y are the respective basic regions of each polypeptide; they act as a linked set of DNA contact surfaces

Enhancers

- Enhancers Eukaryotic genes have, in addition to promoters, regulatory sequences known as enhancers. Enhancers (also called upstream activation sequences, or UAS) assist initiation. Enhancers differ from promoters in two fundamental ways.
- First, the location of enhancers relative to the transcription start site is not fixed. Enhancers may be several thousand nucleotides away from the promoter, and they act to enhance transcription initiation even if positioned downstream from the gene.
- Second, enhancer sequences are bidirectional in that they function in either orientation. That is, enhancers can be removed and then reinserted in the reverse sequence orientation without impairing their function. Like promoters, enhancers represent modules of consensus sequence. Enhancers are “promiscuous,” because they stimulate transcription from any promoter that happens to be in their vicinity. Nevertheless, enhancer function is dependent on recognition by a specific transcription factor. A specific transcription factor bound at an enhancer element stimulates transcription by interacting with RNA polymerase II at a nearby promoter.

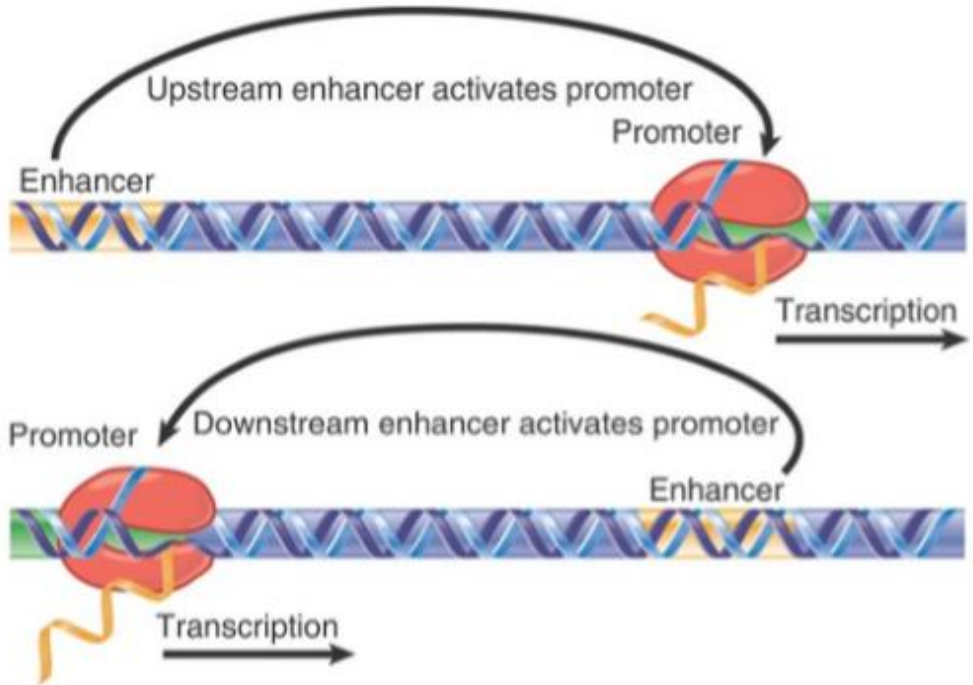


FIGURE 18.15 An enhancer can activate a promoter from upstream or downstream locations, and its sequence can be inverted relative to the promoter.

Stringent responce

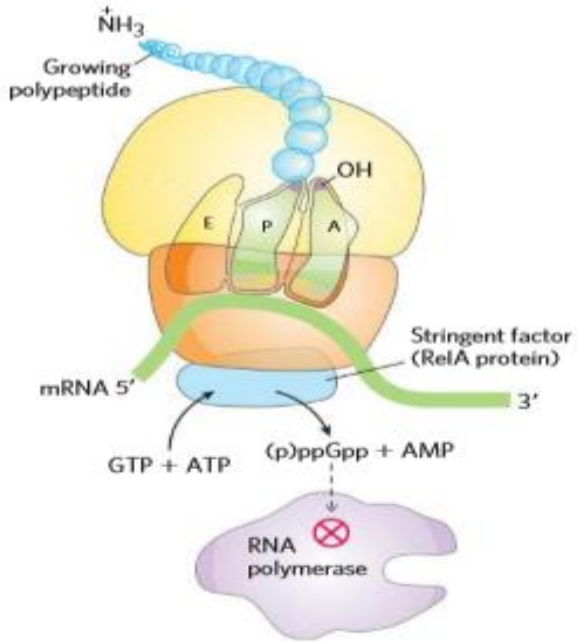


FIGURE 28–22 Stringent response in *E. coli*. This response to amino acid starvation is triggered by binding of an uncharged tRNA in the ribosomal A site. A protein called stringent factor binds to the ribosome and catalyzes the synthesis of pppGpp, which is converted by a phosphohydrolase to ppGpp. The signal ppGpp reduces transcription of some genes and increases that of others, in part by binding to the β subunit of RNA polymerase and altering the enzyme's promoter specificity. Synthesis of rRNA is reduced when ppGpp levels increase.