Chapter 25: Regulating Eukaryotic Transcription

- At least 5 potential gene expression control points

Activation of gene structure

↓

Initiation of transcription

↓

Processing the transcript

↓

Transport to the cytoplasm

↓

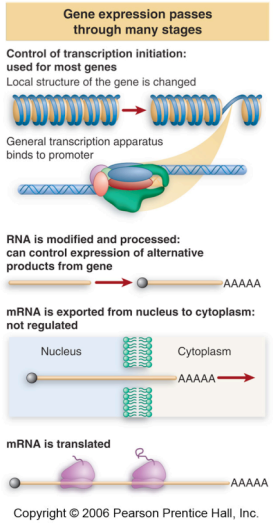
Translation of mRNA

↓

Gene expression is controlled:
• principally at the initiation of transcription

• rare for the subsequent stages to be used to determine whether a gene is expressed,

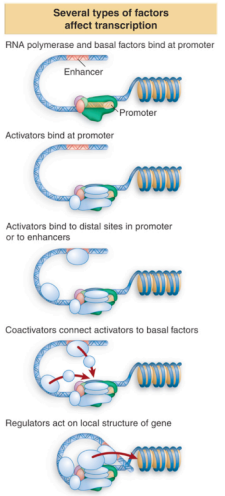
• control of processing may be used to determine which form of a gene is represented in mRNA.



25.2
There Are Several Types of Transcription Factors

- A **basal factor** is:
  - a transcription factor required by RNA polymerase II to form the initiation complex at all promoters.
  - Factors are identified as $TF_{II}X$, where X is a letter.
- An **activator** is:
  - a protein that stimulates the expression of a gene,
  - typically by acting at a promoter to stimulate RNA polymerase binding.
  - the sequence to which it binds in the promoter is called a response element.
- A **response element** is:
  - a sequence in a eukaryotic promoter or enhancer
  - is recognized by a specific transcription factor.
- **Coactivators** are:
  - factors required for transcription that do not bind DNA
  - but are required for (DNA-binding) activators to interact with the basal transcription factors.

- The basal apparatus determines:
  - the startpoint for transcription.
- Activators determine:
  - the frequency of transcription.
- Activators work by:
  - making protein–protein contacts with the basal factors.
- Activators may work:
  - via coactivators.
- local chromatin structure:
  - May be regulated or changed

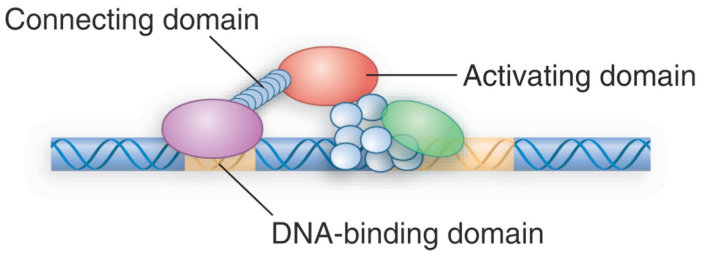


25.3
Independent Domains Bind DNA and Activate Transcription

- DNA-binding activity and transcription activation
  - are carried out by independent domains of an activator.
- The DNA-binding domain determines
  - specificity for the target promoter or enhancer.
- The role of the DNA-binding domain is to
  - bring the transcription activation domain into the vicinity of the promoter.

DNA-binding and activating functions in a transcription factor may be in independent domains of the protein.

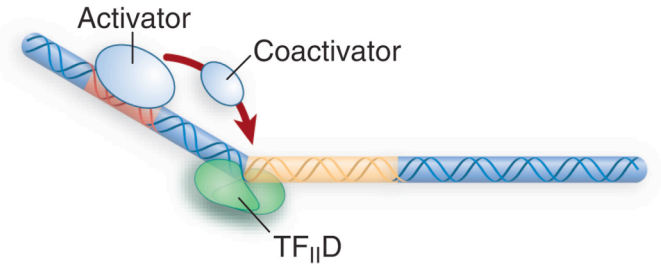
An activator has independent domains



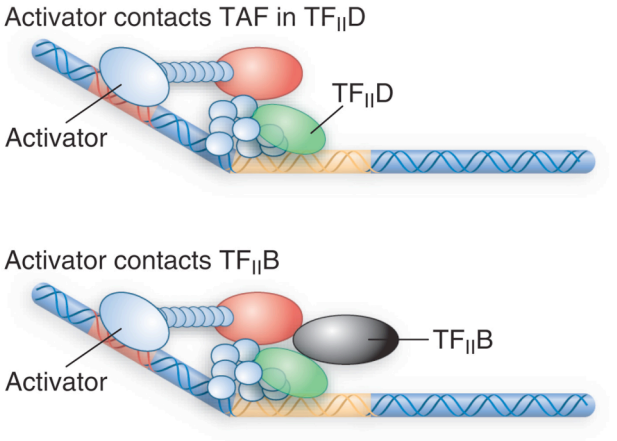
25.4 Activators Interact with the Basal Apparatus

- An activator that works directly has
  - a DNA-binding domain
  - and an activating domain.
- An activator that does not have an activating domain
  - may work by binding a coactivator that has an activating domain.
- Several factors in the basal apparatus
  - are targets with which activators or coactivators interact.
- RNA polymerase may be associated with
  - various alternative sets of transcription factors in a holoenzyme complex.
- Repression is usually achieved by
  - affecting chromatin structure,
  - but there are repressors that act by binding to specific promoters.

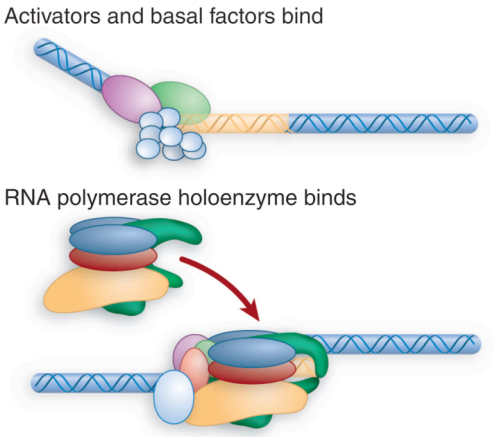
An activator may use a coactivator



Activators contact the basal apparatus



RNA polymerase exists as a holoenzyme

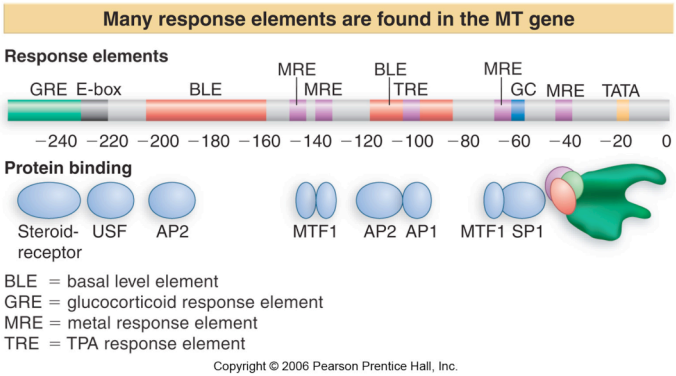


25.5
Response Elements Are Recognized by Activators

- Response elements may be located in promoters or enhancers.
- Each response element is recognized by a specific activator.
- A promoter may have many response elements, which may activate transcription independently or in certain combinations.

Common Response Elements That Are Recognized by Activators

- The **heat shock response element (HSE)** is
  - a sequence in a promoter or enhancer that is used to activate a gene by an activator induced by heat shock.
- The **glucocorticoid response element (GRE)** is
  - a sequence in a promoter or enhancer that is recognized by the glucocorticoid receptor, which is activated by glucocorticoid steroids.
- The **serum response element (SRE)** is
  - a sequence in a promoter or enhancer that is activated by transcription factor(s) induced by treatment with serum.
  - This activates genes that stimulate cell growth.
- **Heat shock genes** are a set of loci that are
  - activated in response to an increase in temperature (and other abuses to the cell).
  - All organisms have heat shock genes.
  - Their products usually include chaperones that act on denatured proteins.



25.6 There Are Many Types of DNA-Binding Domains

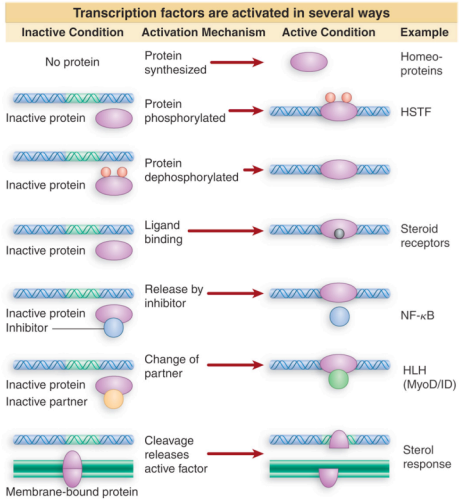
- Activators are classified according to the type of DNA-binding domain.
- Members of the same group have sequence variations of a specific motif that confer specificity for individual target sites.

25.6 There Are Many Types of DNA-Binding Domains

- The **zinc finger** is
  - a DNA-binding motif that typifies a class of transcription factor (TF).
- **Steroid receptors** are
  - TFs that are activated by binding of a steroid ligand.
- The **helix-turn-helix** motif describes
  - an arrangement of two α-helices that form a site that binds to DNA,
  - one fitting into the major groove of DNA and other lying across it.
- The **homeodomain** is
  - a DNA-binding motif that typifies a class of TFs.
  - The DNA sequence that codes for it is called the homeobox.
- The **helix-loop-helix (HLH)** motif is
  - responsible for dimerization of a class of TFs called HLH proteins.
  - has a basic DNA-binding sequence close to the dimerization motif.
- The **leucine zipper** is
  - a dimerization motif adjacent to a basic DNA-binding region

Transcription factors are activated in several ways

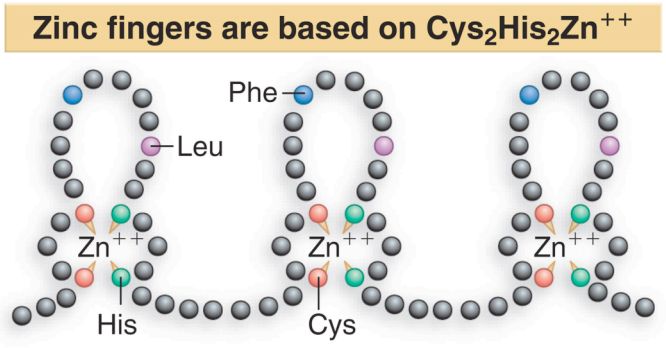
- The activity of a regulatory transcription factor may be controlled by
  - synthesis of protein
  - covalent modification of protein
  - ligand binding
  - or binding of inhibitors that sequester the protein or affect its ability to bind to DNA.

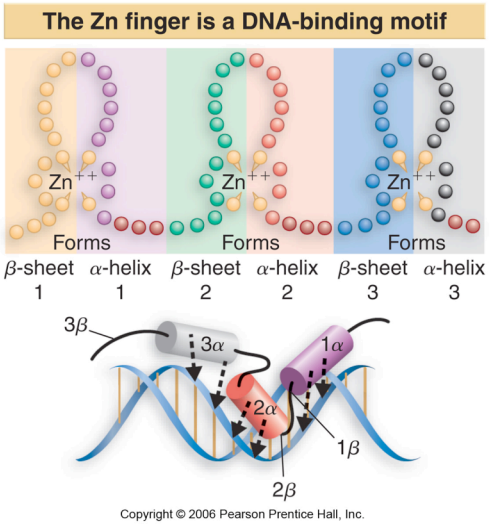


25.7 A Zinc Finger Motif Is a DNA-Binding Domain

- A zinc finger is a loop of ~23 amino acids that
  - protrudes from a zinc-binding site formed by His and Cys amino acids.
- A zinc finger protein usually has multiple zinc fingers.
- The C-terminal part of each finger forms
  - an α-helix that binds one turn of the major groove of DNA.
- Some zinc finger proteins bind
  - RNA instead of or as well as DNA.

Transcription factor SP1 has a series of three zinc fingers, each with a characteristic pattern of cysteine and histidine residues that constitute the zinc-binding site. (Cys_2/His_2)





25.8
Some Steroid Hormone Receptors Are Transcription Factors

- Steroid receptors are examples of ligand-responsive activators that are activated by
  - binding a steroid (or other related molecules).
- There are separate DNA-binding and ligand-binding domains.
- A variety of hydrophobic ligands activate these transcription factors
- Several types of hydrophobic small molecules activate these transcription factors.