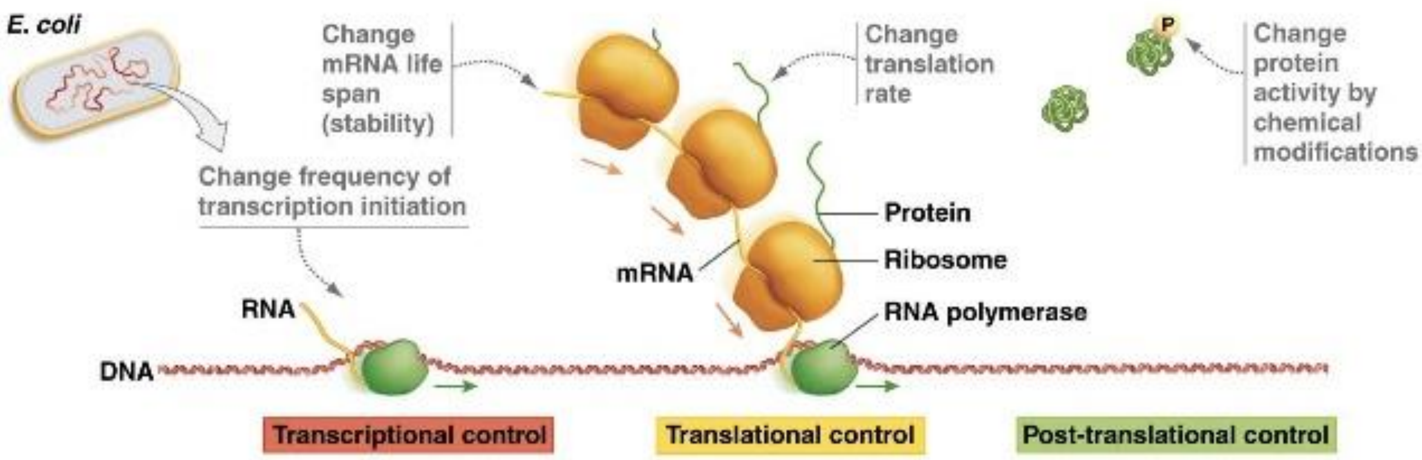
Gene Expression in Eukaryotes

Regulation of Gene Expression



- Gene expression can be regulated:
  - During transcription (transcriptional control).
  - During translation (translational control).
  - After translation (post-translational control).

Differences in gene expression between prokaryotes and eukaryotes -1

- In prokaryotes transcription and translation often occurs simultaneously and co-localized
- In eukaryotes transcription occurs in nucleus. Messenger RNA is transported outside nucleus where it is translated

Differences in gene expression between prokaryotes and eukaryotes-2

- Bacterial messenger RNA is often polycystronic i.e. encodes more than one polypeptide separately within the same RNA molecule.
- Eukaryotic messenger RNA is monocystronic

Differences in gene expression between prokaryotes and eukaryotes -3

- Bacterial messenger RNA is translated as without undergoing modifications
- Eukaryotic messenger RNA undergoes splicing and processing

Differences in gene expression between prokaryotes and eukaryotes -4

- In bacteria promoter is recognized by RNA polymerase and an associated sigma factor.
- In eukaryotes the process is more complicated, and at least seven different factors are necessary for the binding of an RNA polymerase II to the promoter.

Eukaryotic promoter

- In genetics, a promoter is a region of DNA that initiates transcription of a particular gene.
- In eukaryotes promoters have complex structure.

Eukaryotic promoter – core promoter

Core promoter – the minimal portion of the promoter required to properly initiate transcription. Core promoter Includes the transcription start site (TSS) and elements directly upstream:

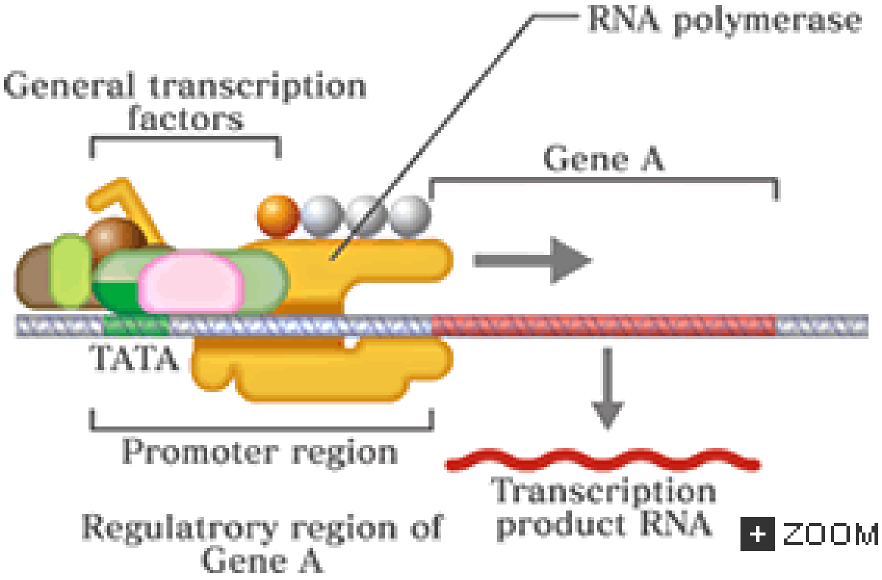
1. A binding site for RNA polymerase
   - RNA polymerase I: transcribes genes encoding 18s 5.8s 28s ribosomal RNA
   - RNA polymerase II: transcribes genes encoding messenger RNA and certain small nuclear RNAs and microRNA
   - RNA polymerase III: transcribes genes encoding transfer RNA, 5s ribosomal RNAs and other small RNAs

2. General transcription factor binding sites, e.g. TATA box.

Transcription factors

- A *transcription factor* (TF) (or sequence-specific DNA-binding factor) is a protein that controls the rate of transcription of genetic information from DNA to messenger RNA, by binding to a specific DNA sequence.

General (basal) transcription factros



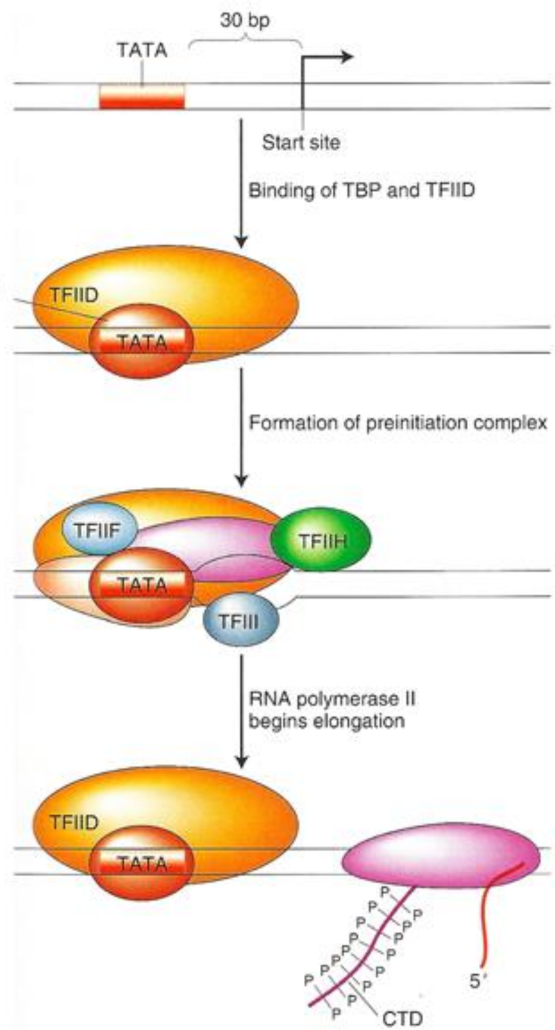
eukaryotic promoter

general transcription factors bind

TBP

preinitiation complex

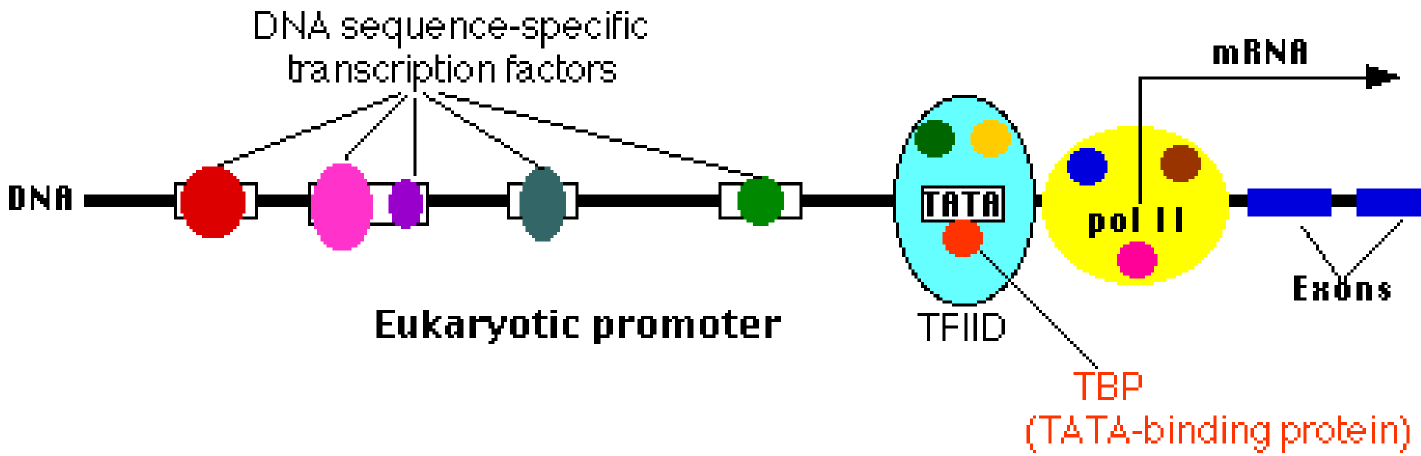
RNA pol II begins elongation



Eukaryotic promoter – proxymal promoter

- *Proximal promoter* – the proximal sequence upstream of the gene that tends to contain primary regulatory elements
- Comprises approximately 250 base pairs upstream of the start site
- Specific transcription factor binding sites

- Other transcription factors differentially regulate the expression of various genes by binding to enhancer regions of DNA adjacent to regulated genes. These transcription factors are critical to making sure that genes are expressed in the right cell at the right time and in the right amount, depending on the changing requirements of the organism.

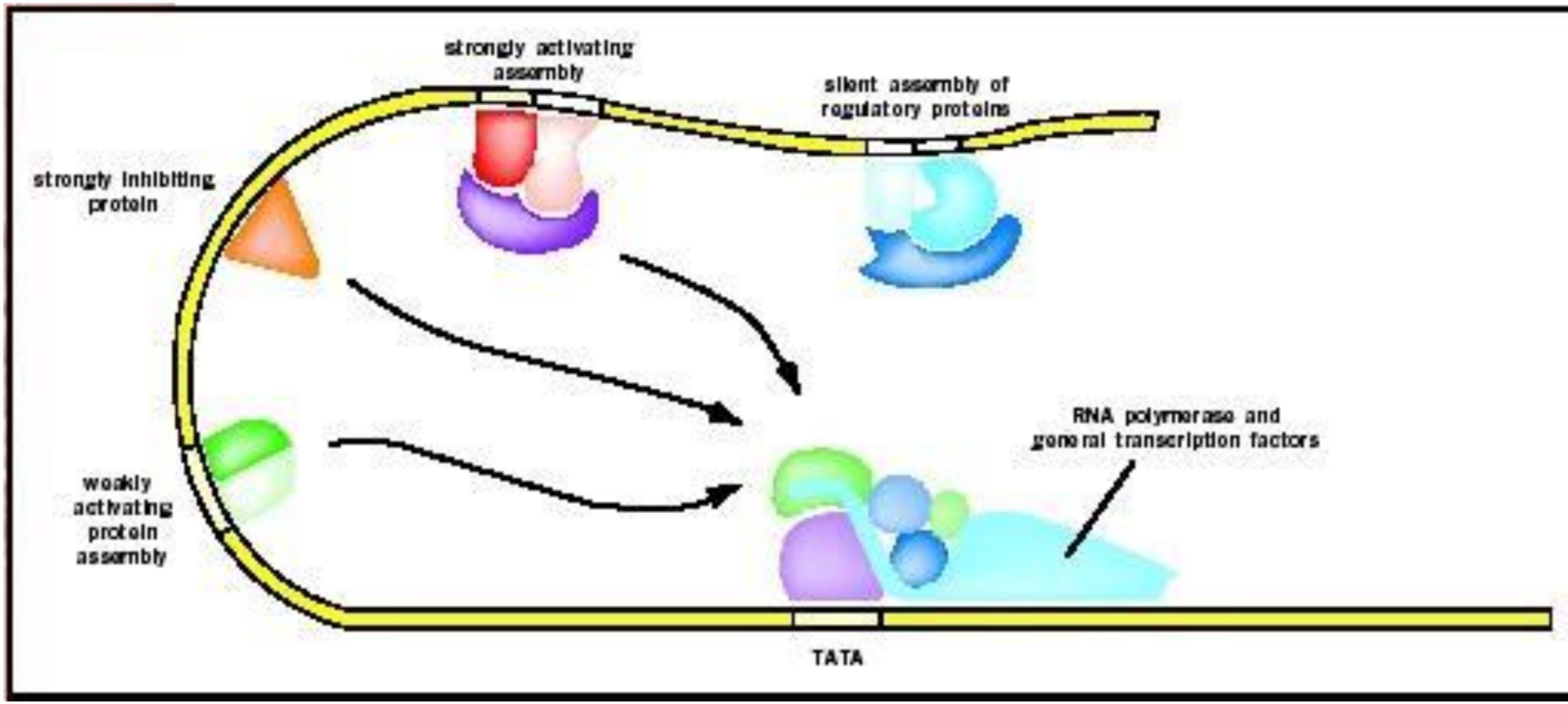


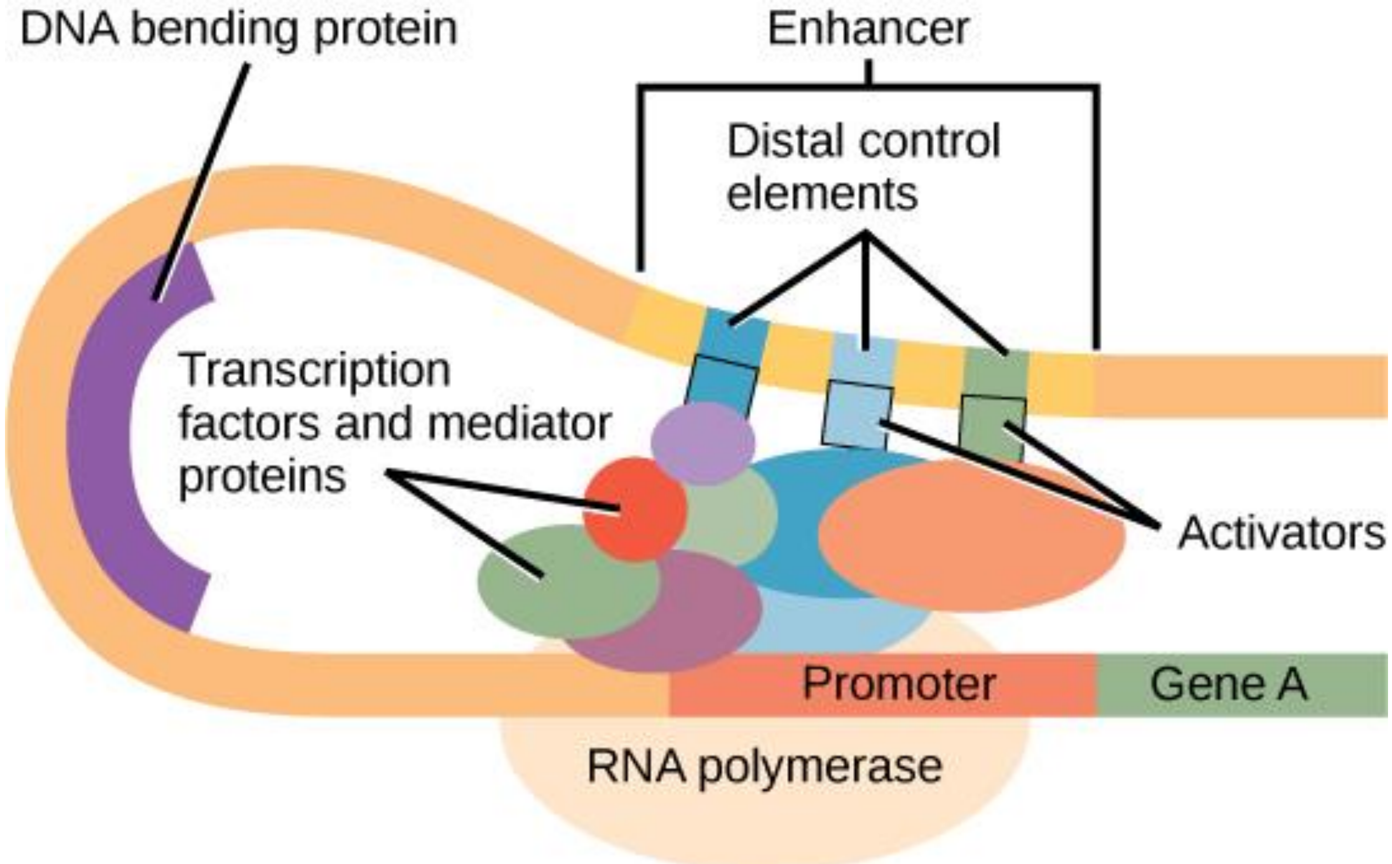
Eukaryotic promoter – distal control elements

- *Distal promoter* – the distal sequence upstream of the gene that may contain additional regulatory elements, often with a weaker influence than the proximal promoter
- *Enhancers* and other distal regulatory regions influence gene transcription in a "positional/orientation independent " manner. The action of these elements depends on the 3-dimentional structure of chromatin.

Transcription factors use a variety of mechanisms for the regulation of gene expression. These mechanisms include:

- Stabilize or block the binding of RNA polymerase to DNA
- recruit co-activator or co-repressor proteins to the transcription factor DNA complex


strongly activating assembly
silent assembly of regulatory proteins
strongly inhibiting protein
weakly activating protein assembly
RNA polymerase and general transcription factors
TATA


DNA bending protein
Enhancer
Distal control elements
Transcription factors and mediator proteins
Activators
Promoter
Gene A
RNA polymerase

- There are approximately 2600 proteins in the human genome that contain DNA-binding domains, and most of these are presumed to function as transcription factors. Therefore, approximately 10% of genes in the genome code for transcription factors, which makes this family the single largest family of human proteins.

Example of a transcription factor – steroid hormone receptor

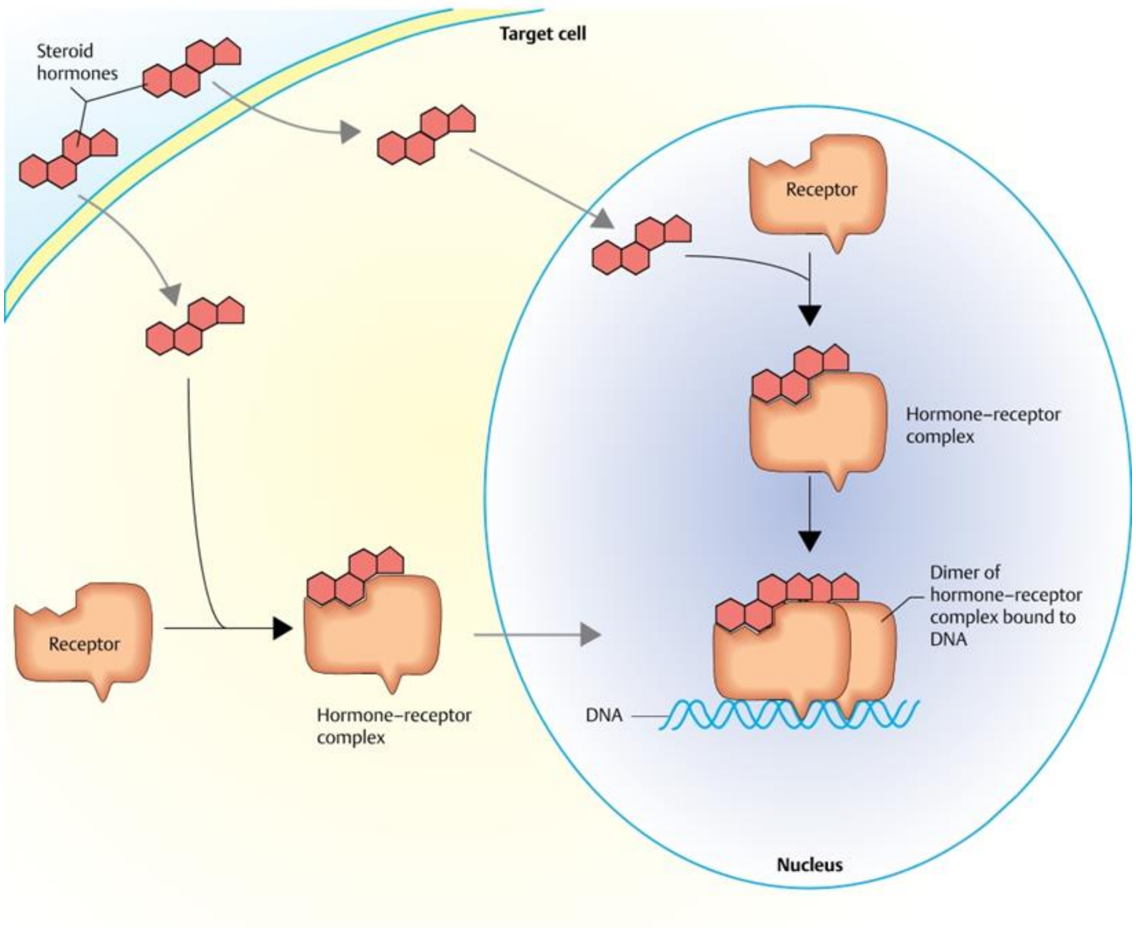
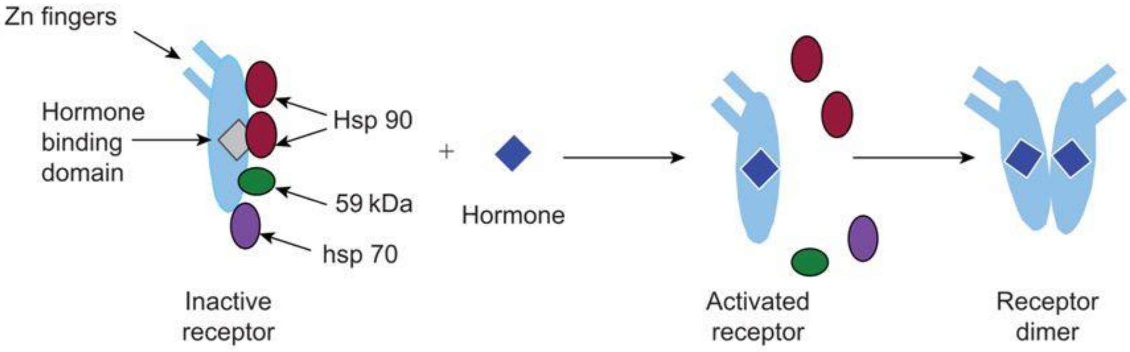


Fig. 14.13

Activation of Steroid Hormone Receptors



- Inactive receptors associated with other proteins react with hormone, shed their associated proteins, and change their conformation
- They can then form dimers that bind DNA and a variety of nuclear peptide regulators of gene transcription