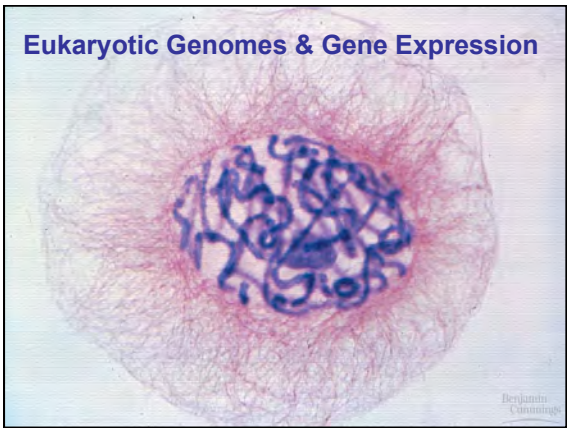
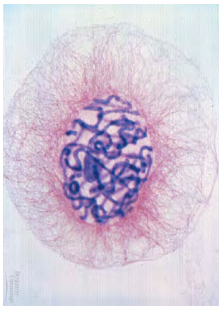
Eukaryotic Genomes & Gene Expression



Eukaryotic Cells Have Multiple Chromosomes

- Eukaryotic cells have 5–20x more DNA per cell than do bacteria.
- Divided into linear dsDNA + proteins : **chromosomes**
- Typical chromosome averages ~1.5×10^8 nucleotide pairs.
  - If straight strands would be ~ 4 cm long.
- Humans have 46 different chromosomes
  - So collectively amounts to ~ 2 m long dsDNA packed into each cell nucleus! (4 m after replication!)



Plant cell just before division

Stages in gene expression that can be regulated in eukaryotic cells

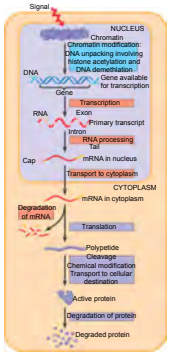
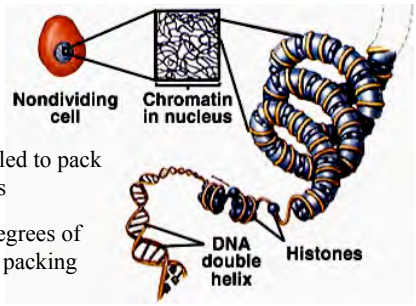


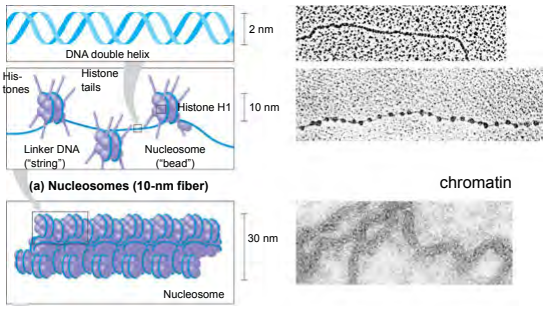
Figure 18.6

Chromatin: nondividing cells



- DNA is coiled to pack into nucleus
- Different degrees of coiling and packing

Levels of chromatin packing

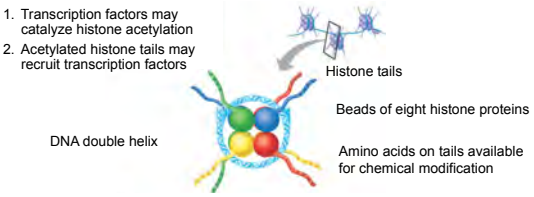


DNA remains coiled around histone "beads" except during replication.

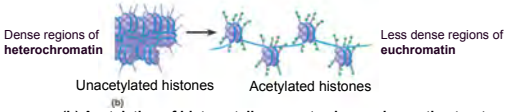
Figure 18.7

Histone tails and the effect of acetylation

1. Transcription factors may catalyze histone acetylation
2. Acetylated histone tails may recruit transcription factors



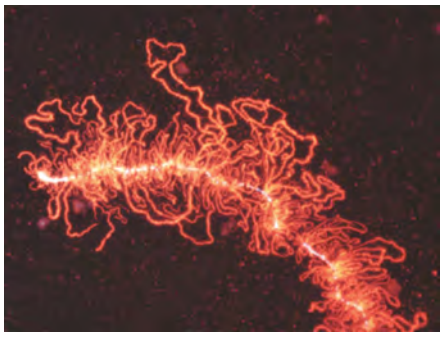
(a) Histone tails protrude outward from a nucleosome



(b) Acetylation of histone tails promotes loose chromatin structure that permits transcription

Figure 18.7

DNA in a eukaryotic chromosome from a developing salamander egg



More loosely coiled loops are available for transcription and gene expression.

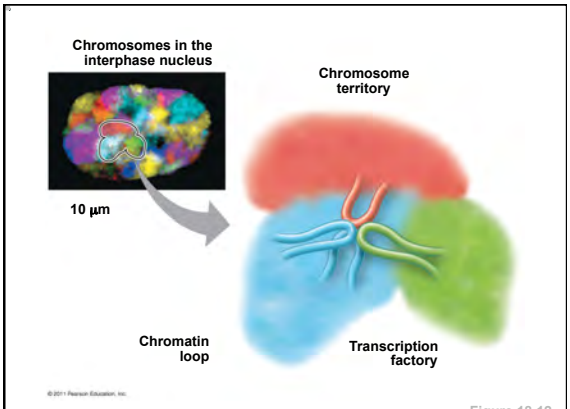
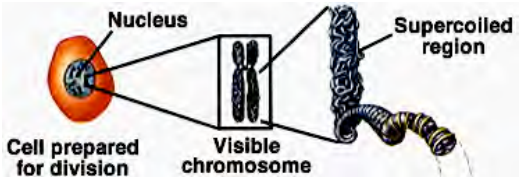


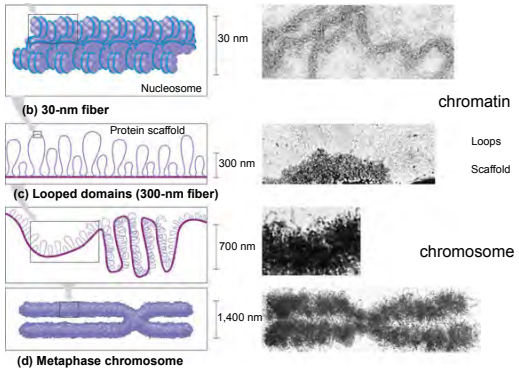
Figure 18.12

During cell division



- chromatin condenses into visible chromosomes
- Tightly wound chromosomes segregate without tangling together

Levels of chromatin packing



Cell Differentiation in Multicellular Organisms

Differential Gene Expression

- Even though every cell has the same genome, each cell type only uses a small subset of genes.
  - ~200 cell types in mammals
  - Each uses only ~20% of total genes
  - Fewer in more specialized cells
  - Unused genes may be permanently inactivated
- Histone modification
  - Methylation of histone residues may condense associated DNA into non-transcribable heterochromatin
- DNA methylation
  - Methylation of cytosines related to gene inactivation
  - Methylated DNA may attract/bind histone deacetylation enzymes
  - Epigenic inheritance — patterns of methylation passed on to daughter cells

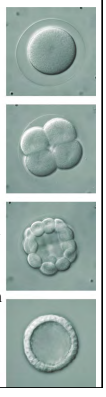


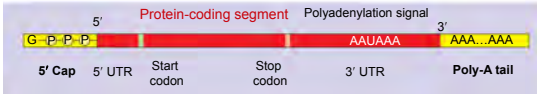
Figure 47.7 Blastulation

Processing of "primary transcript" RNA

[Review *Gene Expression* slides!]

A modified methyl-guanine nucleotide added to the 5′ end

50 to 250 adenine nucleotides added to the 3′ end by poly-A synthetase using ATPs



- Cap & tail protect mRNA from rapid degradation in the cytoplasm.
- Eukaryotic mRNA stay active for hours, or even days, in the cytoplasm.
- Prokaryotes lack cap & tail; mRNA only lasts for minutes.

Figure 17.9

A eukaryotic gene and its transcript

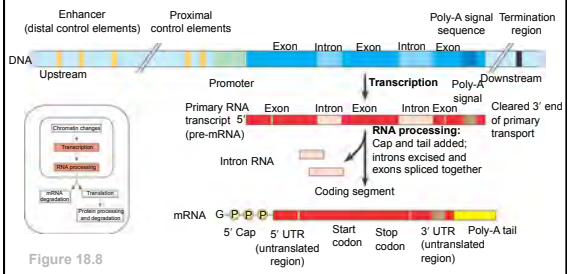


Figure 18.8

- Enhancer sequences may be several kb upstream or downstream of the gene, or within an intron.
- One gene may have several enhancers.

A model for the action of enhancers and transcription activators

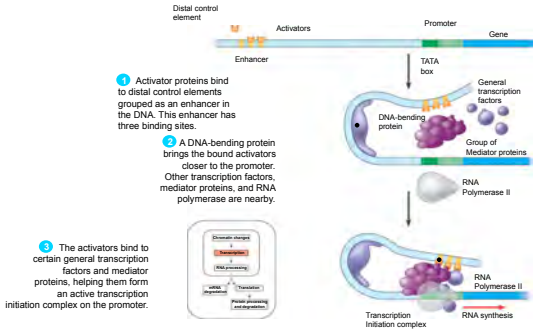


Figure 18.10

An **Activator** Protein and DNA-binding

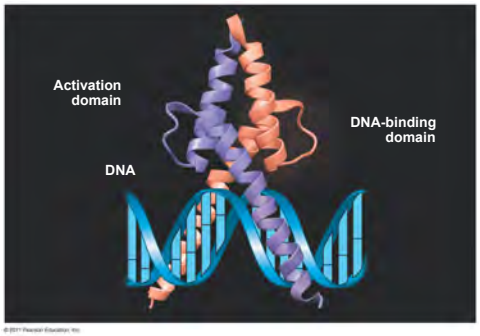


Figure 18.9

Cell type–specific transcription

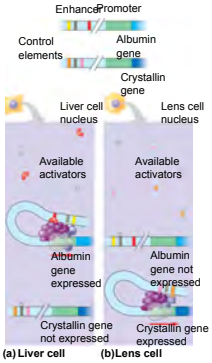


Figure 18.11

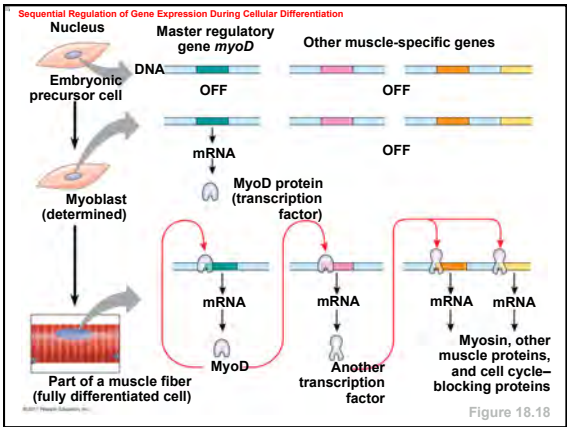


Figure 18.18

Alternative RNA splicing

- Esp. in vertebrate animals
  - >1 possible polypeptide/gene!

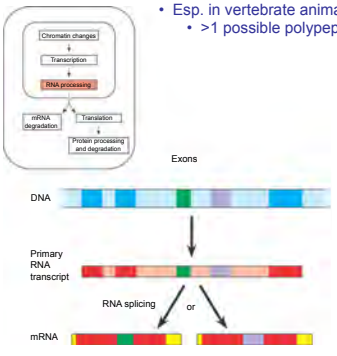


Figure 18.13

Regulation of gene expression by microRNAs (miRNAs)

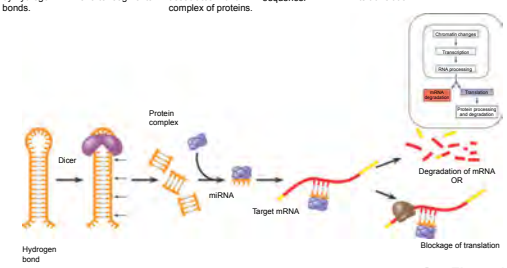
1 The **micro-RNA** (miRNA) **precursor** folds back on itself, held together by hydrogen bonds.

2 An enzyme called Dicer moves along the double-stranded RNA, cutting it into shorter segments.

3 One strand of each short double-stranded RNA is degraded; the other strand (**miRNA**) then associates with a complex of proteins.

4 The bound miRNA can base-pair with any target mRNA that contains the complementary sequence.

5 The **miRNA-protein complex** prevents gene expression either by **degrading** the target mRNA or by **blocking** its translation.



See Figure 18.15

Degradation of a protein by a proteasome

1 Multiple ubiquitin molecules are attached to a protein by enzymes in the cytosol.

2 The ubiquitin-tagged protein is recognized by a proteasome, which unfolds the protein and sequesters it within a central cavity.

2 Enzymatic components of the proteasome cut the protein into small peptides, which can be further degraded by other enzymes in the cytosol.

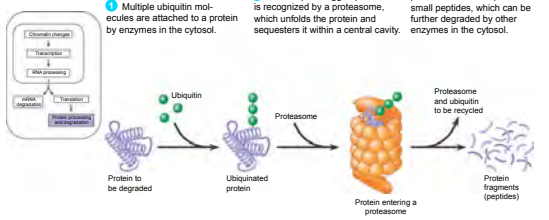
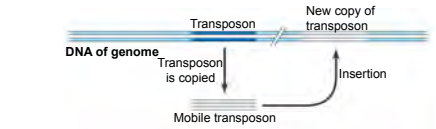


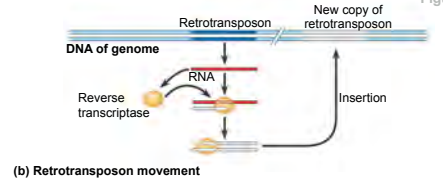
Figure 18.14

Movement of eukaryotic transposable elements



(a) Transposon movement ("copy-and-paste" mechanism)

Figure 21.9



(b) Retrotransposon movement

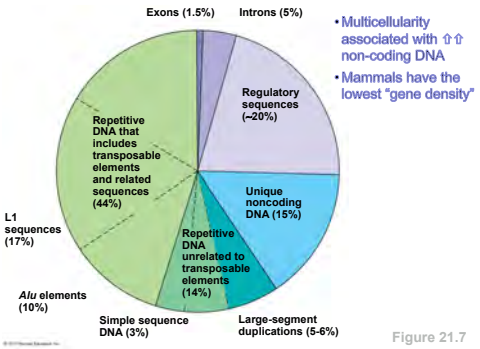
Figure 21.10

The effect of transposable elements on corn kernel color

Barbara McClintock's breeding experiments with Indian corn

Figure 21.8

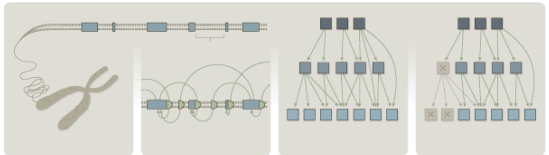
Types of DNA sequences in the human genome



- Multicellularity associated with ⇧⇧ non-coding DNA
- Mammals have the lowest "gene density"

Figure 21.7

Encode Project: Rethinking 'Junk' DNA



GENES
Each human cell contains about 10 feet of DNA, coiled into a dense tangle. But only a very small percentage of DNA encodes genes, which control inherited traits like eye color, blood type and so on

"JUNK" DNA
["DARK MATTER"]
Stretches of DNA around and between genes seemed to do nothing, and were called junk DNA. But now researchers think that the junk DNA contains a large number of tiny genetic switches, controlling how genes function within the cell.

REGULATION
The many genetic regulators seem to be arranged in a complex and redundant hierarchy. Scientists are only beginning to map and understand this network, which regulates how cells, organs and tissues behave.

DISEASE
Errors or mutations in genetic switches can disrupt the network and lead to a range of diseases. The new findings will spur further research and may lead to new drugs and treatments.

Over half of the human genome is gene switches.

Bits of Mystery DNA, Far From 'Junk,' Play Crucial Role
By GINA KOLATA; September 5, 2012, NY Times

ENCODE
National Human Genome Research Institute
Encyclopedia Of DNA Elements