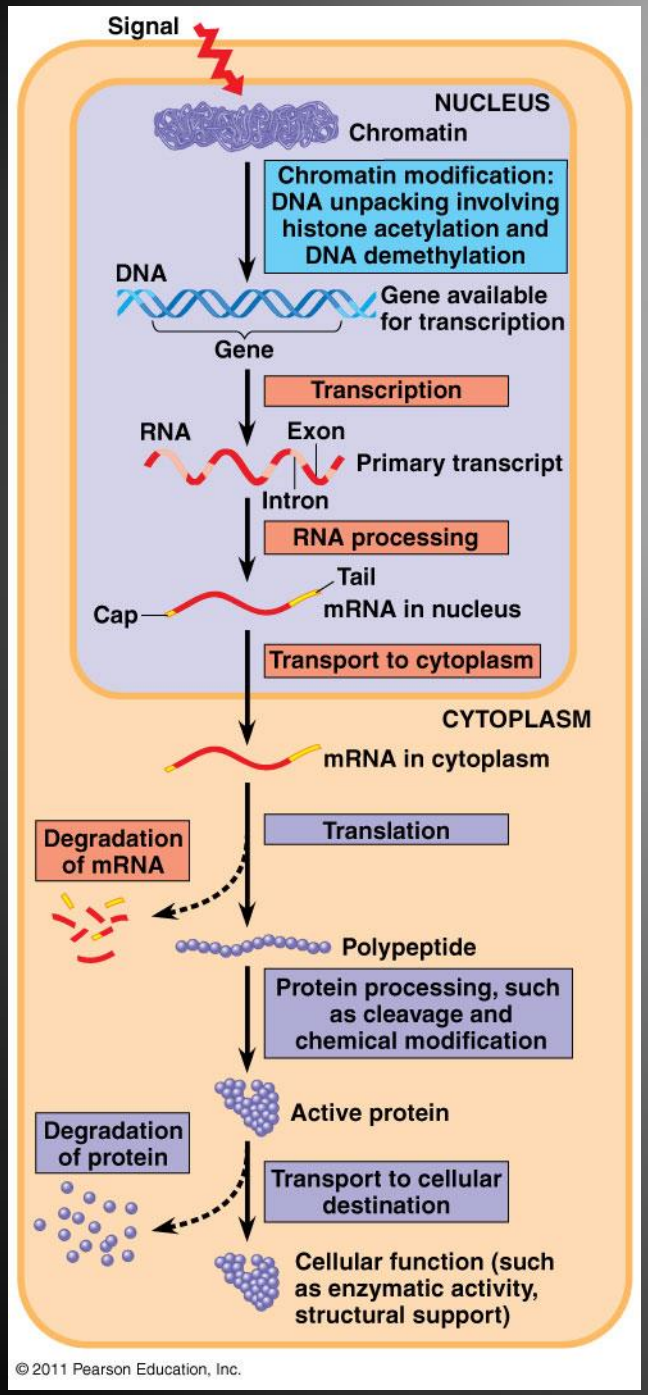
Regulation of Gene Expression by Eukaryotes

- Many stages

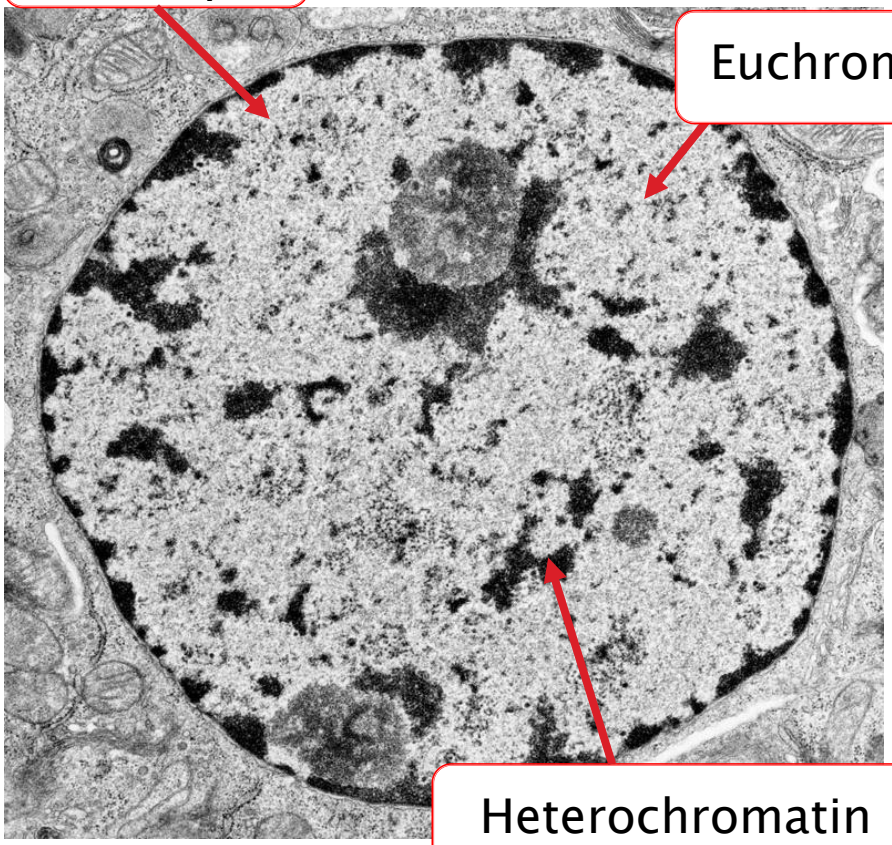
Different cells have same genome, but *express* different genes

- Typical human cell: *only 20% of genes expressed at any given time*
- Different cell types (with identical genomes) turn on different genes to carry out specific functions
- Differences between cell types is due to **differential gene expression**

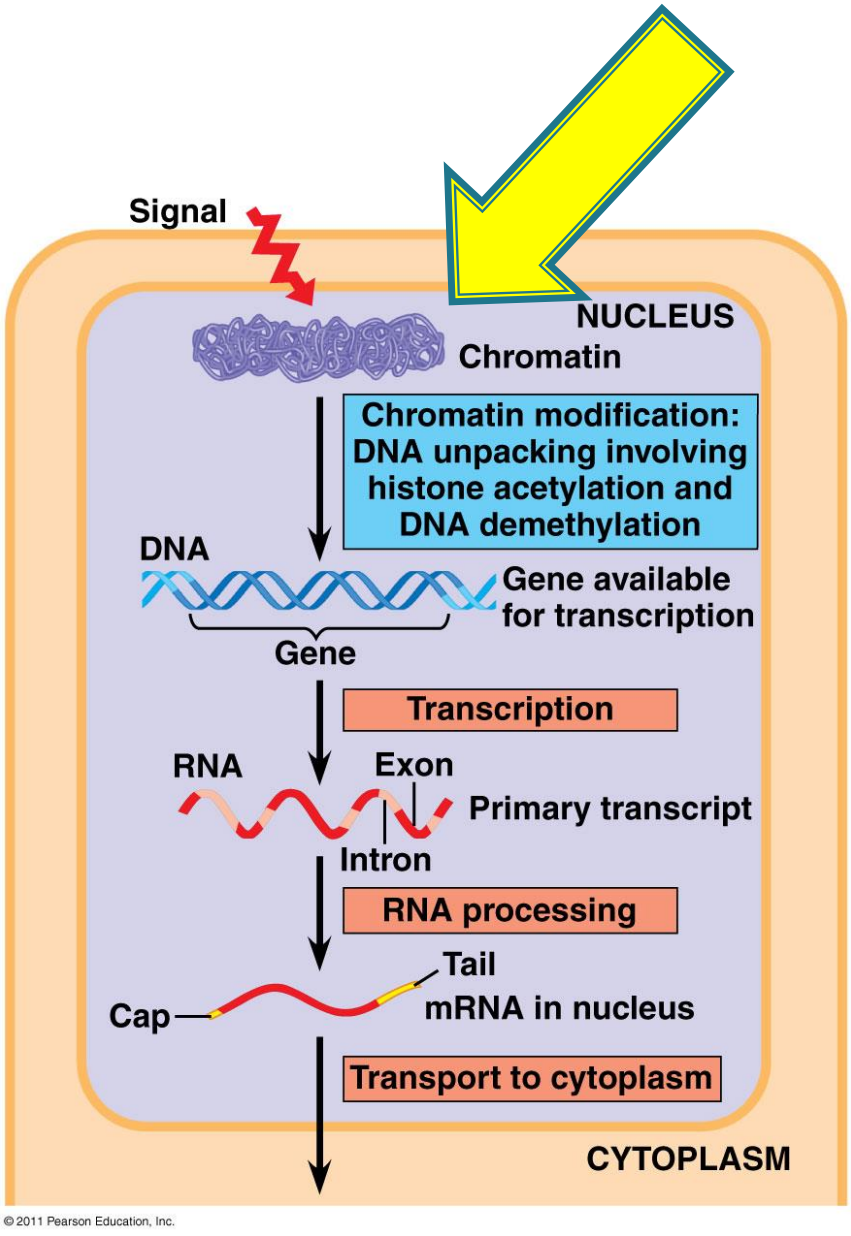


Eukaryotic gene expression regulated at many different stages

Types of Chromatin

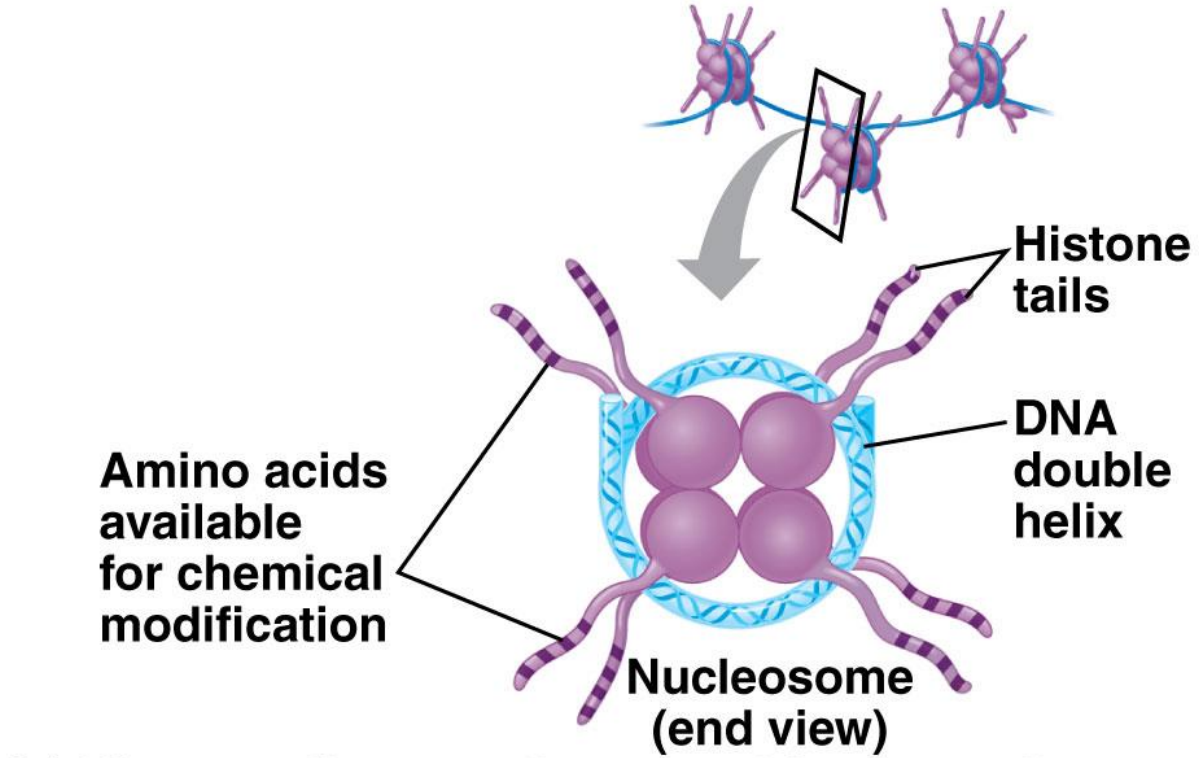


- Heterochromatin:
  - Not actively expressed (off)
  - Condensed and not available for transcription
  - High density DNA, so stains dark
- Euchromatin:
  - Loosened, uncoiled
  - Actively transcribed/ expressed
  - Low density DNA so lightly stained

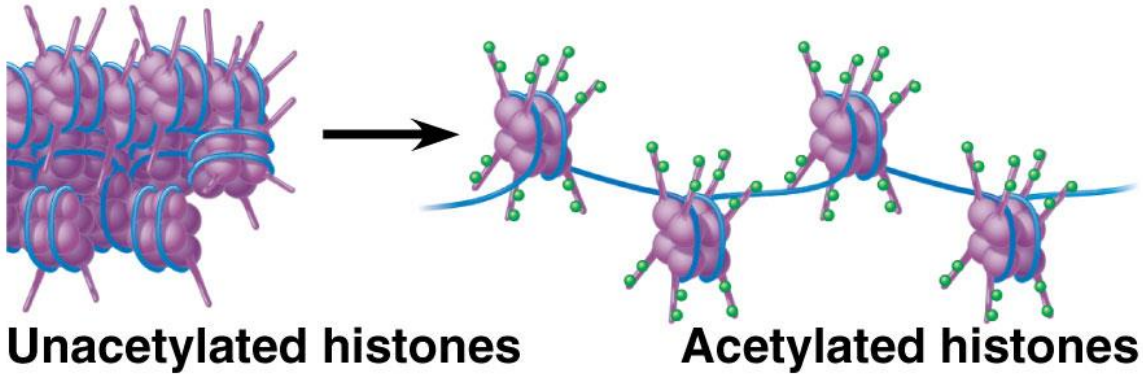


Chromatin Structure:

- Tightly bound DNA → less accessible for transcription
- **DNA methylation**: methyl groups added to DNA; tightly packed; ↓ transcription
  (turns genes off)
- **Histone acetylation**: acetyl groups added to histones; chromatin loosened; ↑ transcription
  (turns genes on)



(a) Histone tails protrude outward from a nucleosome



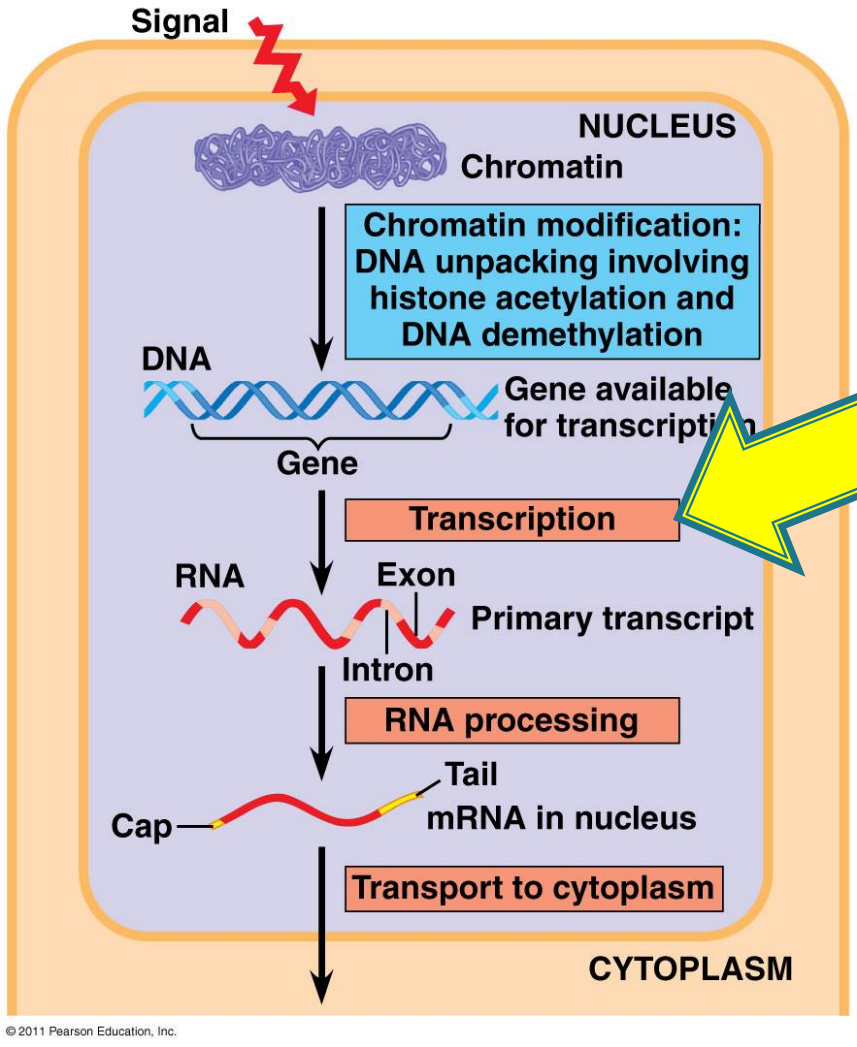
(b) Acetylation of histone tails promotes loose chromatin structure that permits transcription

Epigenetic Inheritance

- Modifications on chromatin can be passed on to future generations
- Unlike DNA mutations, these changes to chromatin *can be reversed* (de-methylation of DNA)
- Explains differences between identical twins
- Eg. DNA methylation (gene silencing), histone acetylation, X chromosome inactivation, heterochromatin (silent chromatin)

Video: The Epigenome at a Glance

- Genetic Science Learning Center

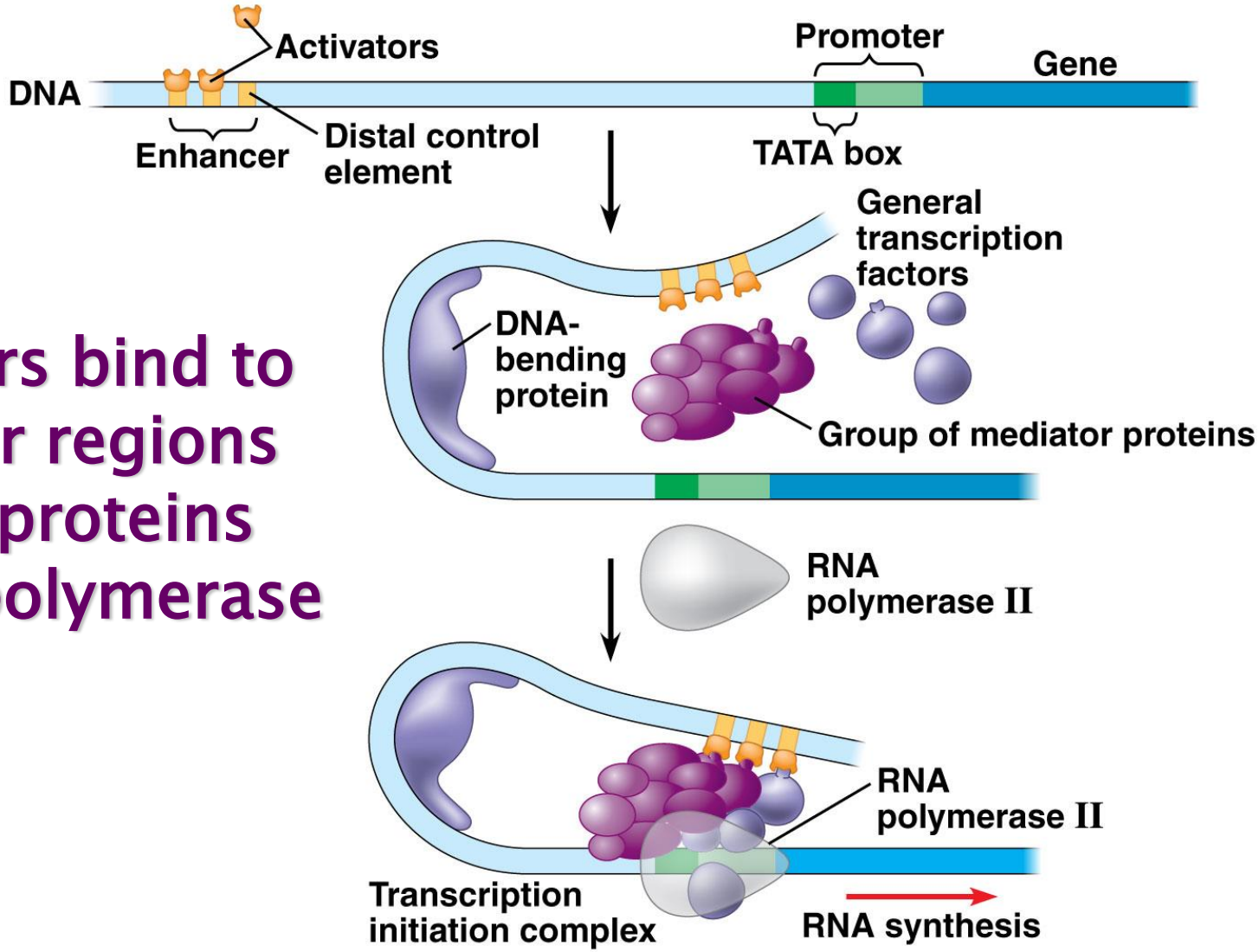


Transcription Initiation:

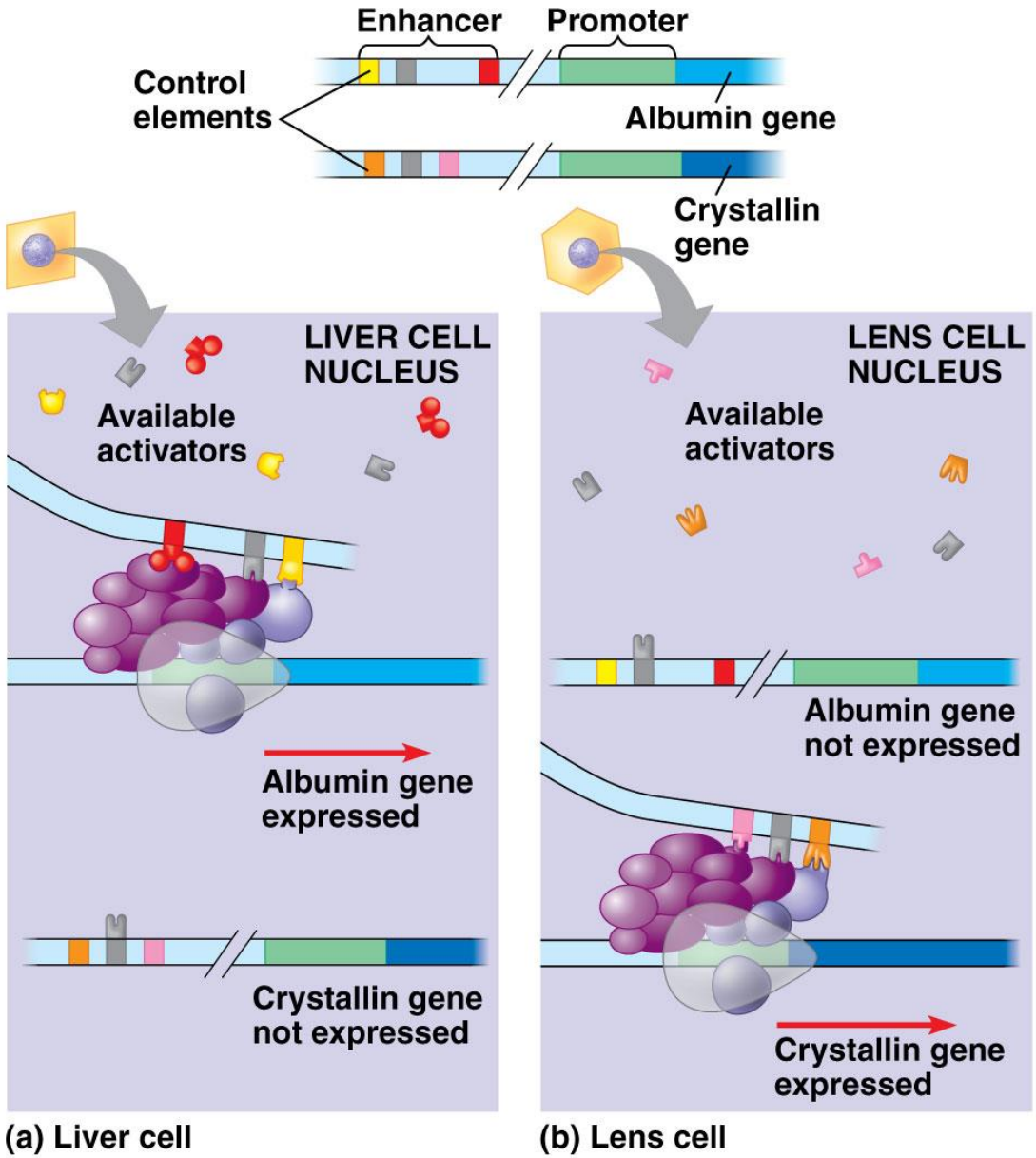
- Specific transcription factors (activators or repressors) bind to control elements (enhancer region)
- **Activators**: increase transcription
- **Repressors**: decrease transcription

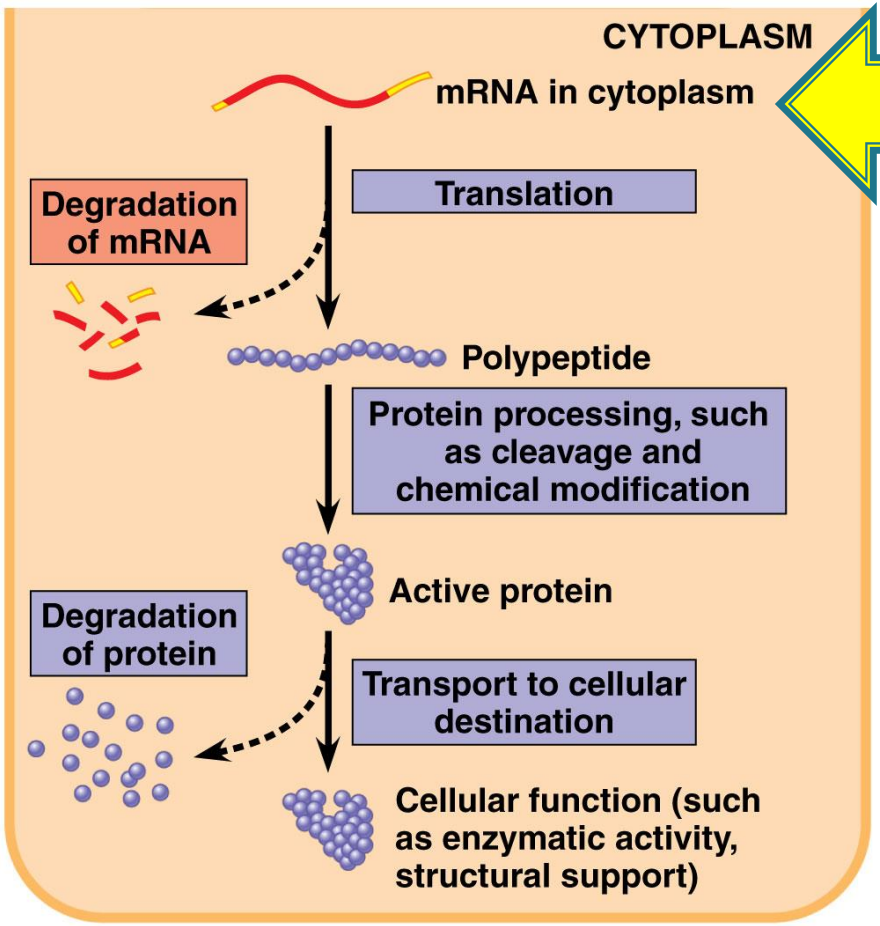
Transcription Initiation Complex

Activators bind to enhancer regions
+ other proteins
+ RNA polymerase



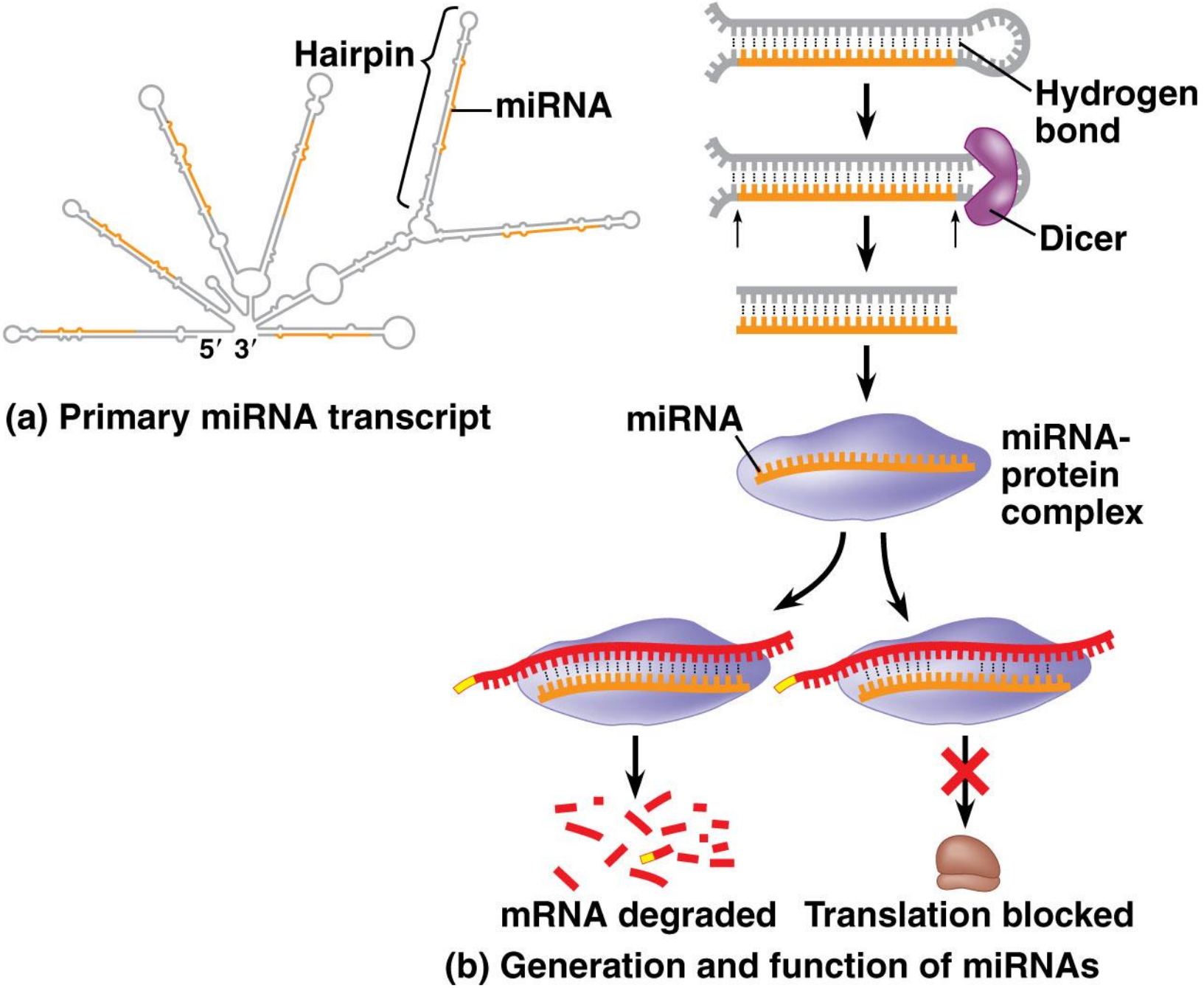
Cell type-specific transcription





Regulation of mRNA:

- **micro RNAs (miRNAs)** and **small interfering RNAs (siRNAs)** can bind to mRNA and degrade it or block translation

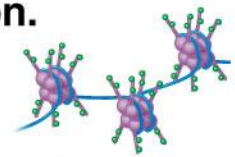


Summary of Eukaryotic Gene Expression

HHMI Biointeractive: Regulation of Eukaryotic DNA Transcription

Chromatin modification

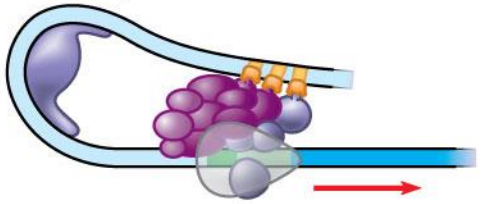
- Genes in highly compacted chromatin are generally not transcribed.
- Histone acetylation seems to loosen chromatin structure, enhancing transcription.



- DNA methylation generally reduces transcription.

Transcription

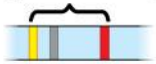
- Regulation of transcription initiation: DNA control elements in enhancers bind specific transcription factors.



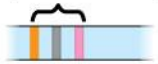
Bending of the DNA enables activators to contact proteins at the promoter, initiating transcription.

- Coordinate regulation:

Enhancer for liver-specific genes

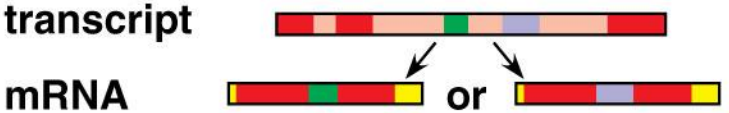


Enhancer for lens-specific genes

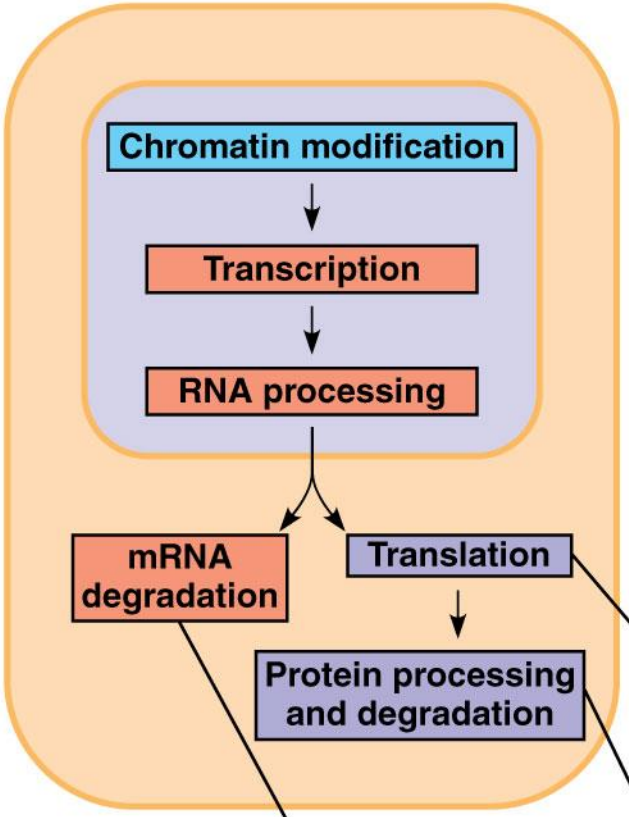


RNA processing

- Alternative RNA splicing:



In your groups, discuss how these 3 can regulate or modify gene expression in prokaryotes.



Take notes as needed

Translation

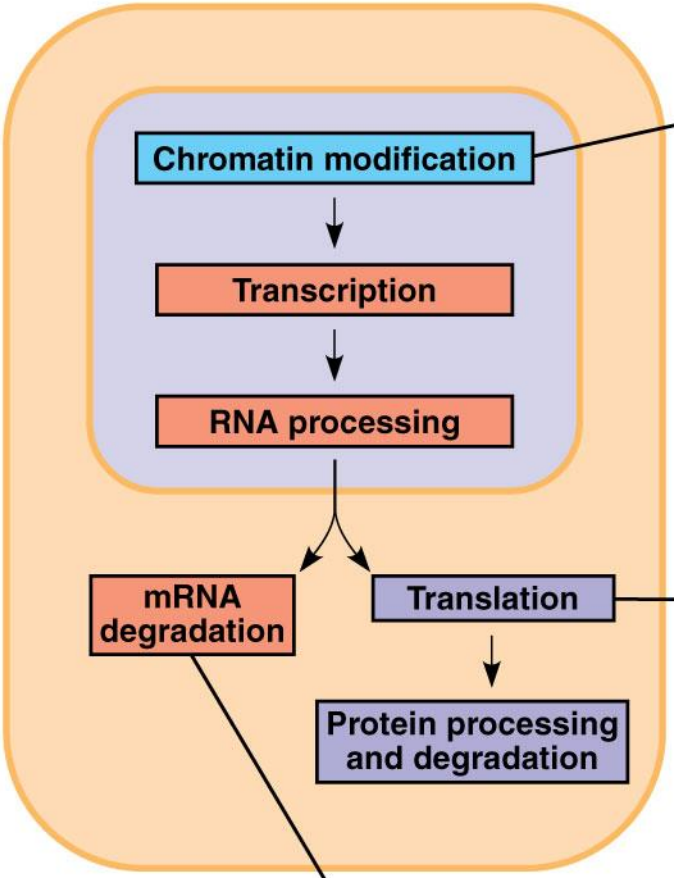
- Initiation of translation can be controlled via regulation of initiation factors.

mRNA degradation

- Each mRNA has a characteristic life span, determined in part by sequences in the 5′ and 3′ UTRs.

Protein processing and degradation

- Protein processing and degradation by proteasomes are subject to regulation.

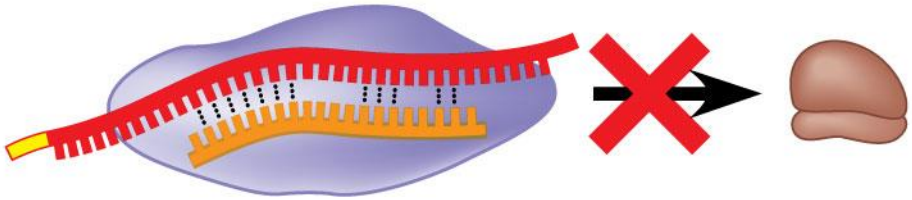


Chromatin modification

- Small or large noncoding RNAs can promote the formation of heterochromatin in certain regions, blocking transcription.

Translation

- miRNA or siRNA can block the translation of specific mRNAs.



mRNA degradation

- miRNA or siRNA can target specific mRNAs for destruction.

Add more detail!

Video: The Epigenetics of Identical Twins

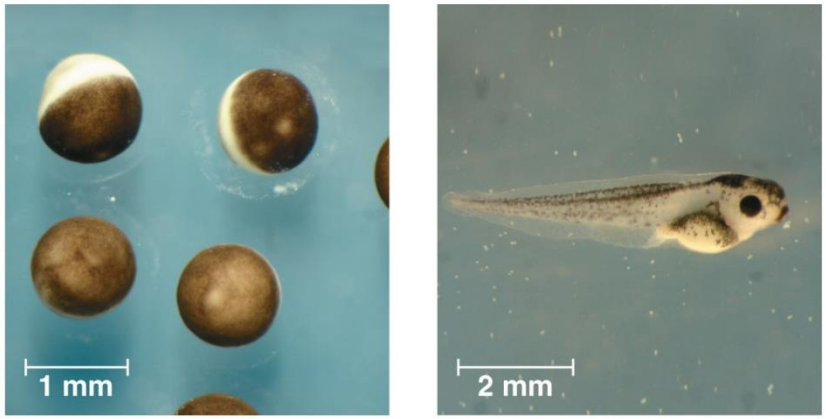
- Genetic Science Learning Center

Embryonic Development of Multicellular Organisms

- Section 18.4

Embryonic Development:

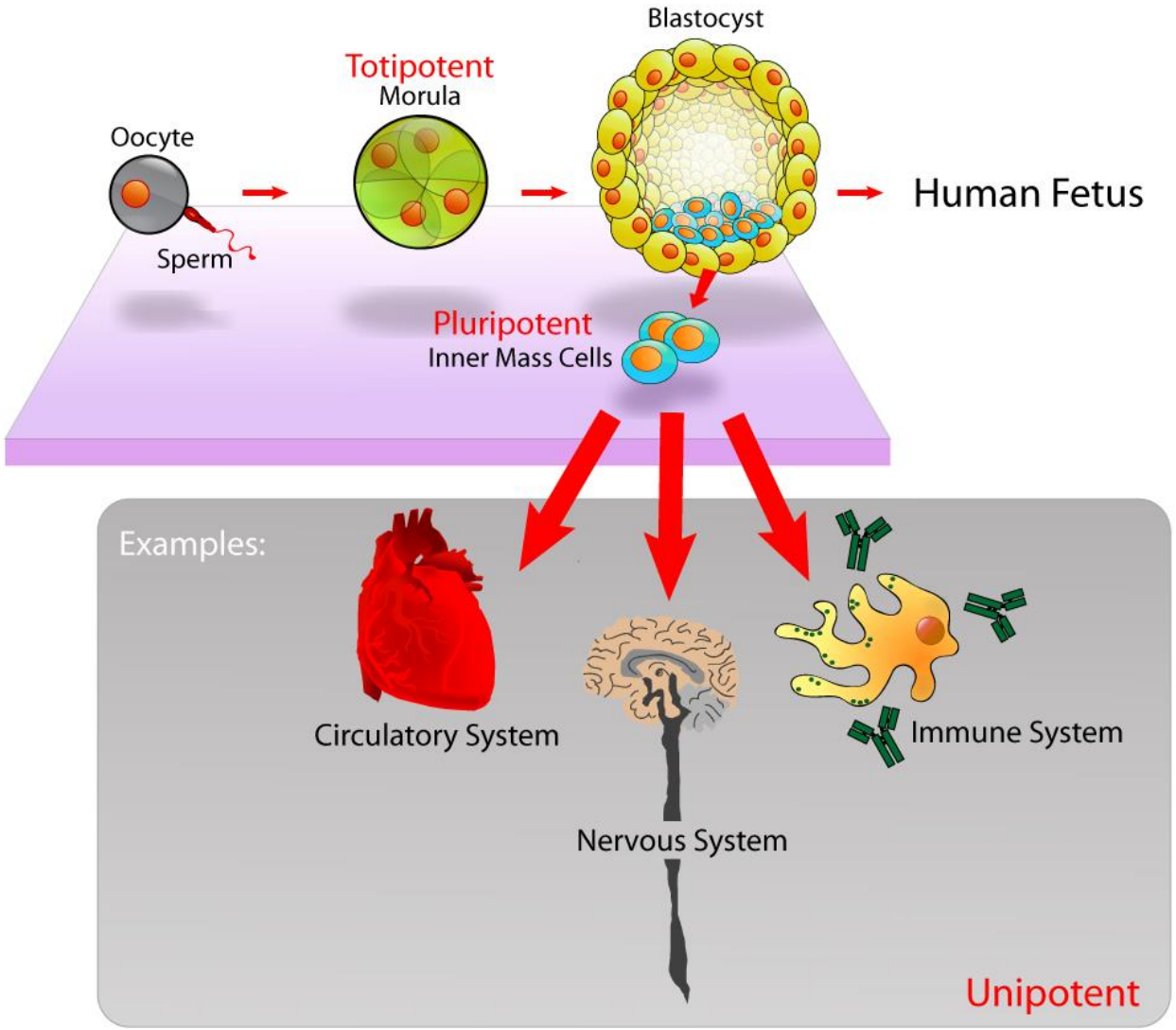
Zygote → Organism

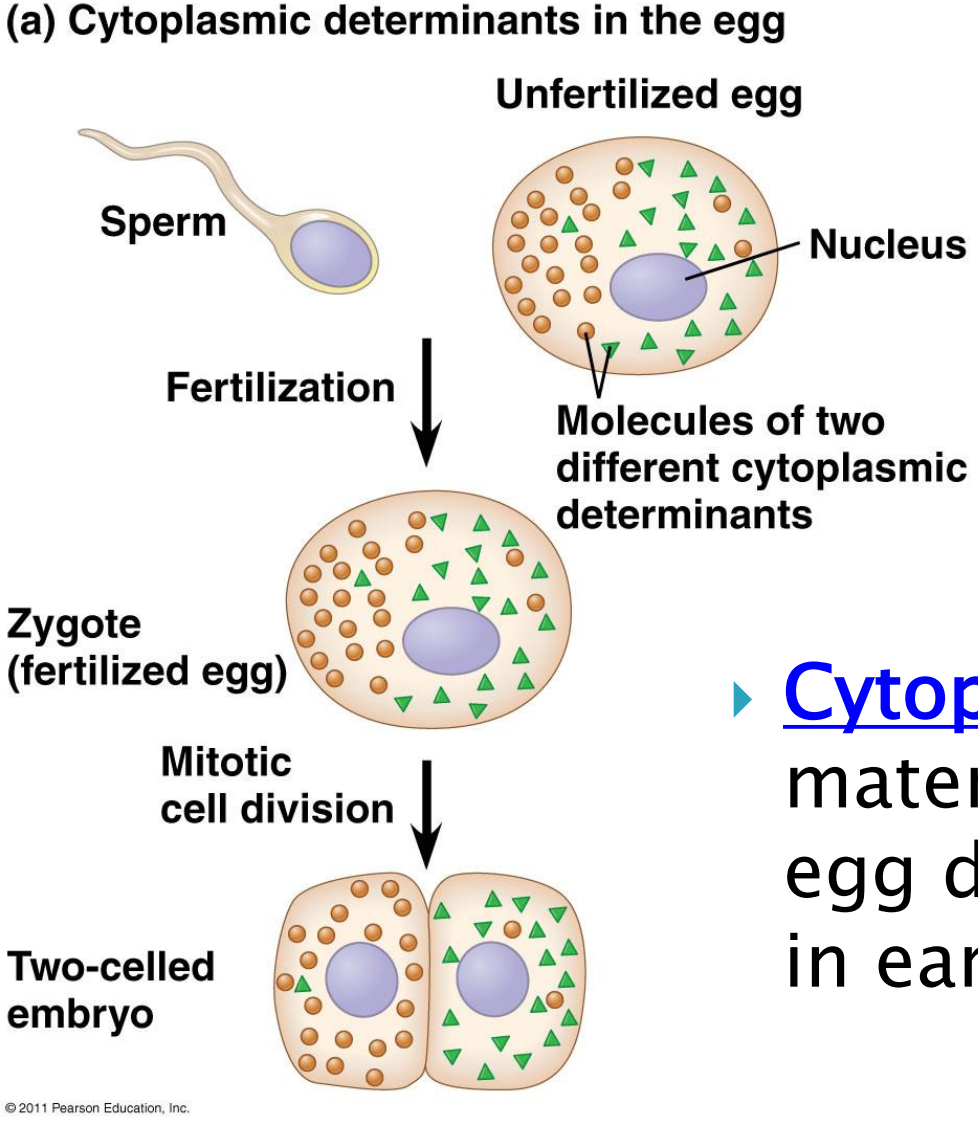


(a) Fertilized eggs of a frog (b) Newly hatched tadpole

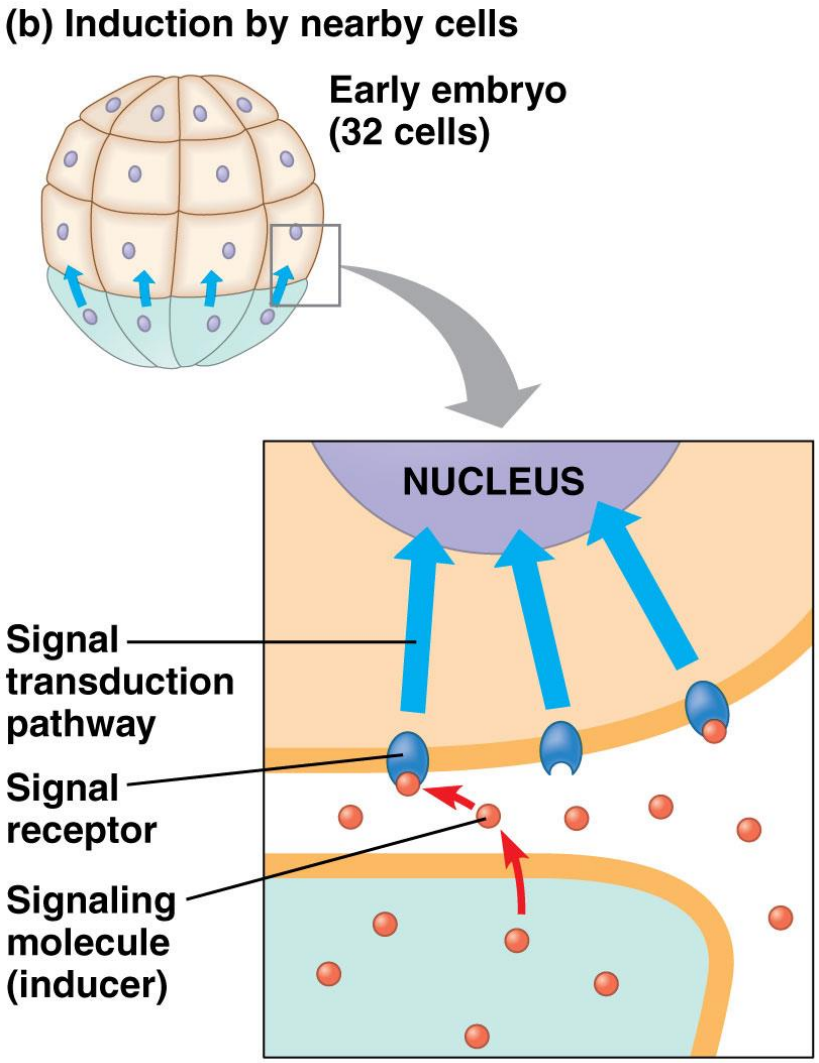
1. Cell Division: large # identical cells through mitosis
2. Cell Differentiation: cells become specialized in structure & function
3. Morphogenesis: "creation of form" – gives organism's shape

Determination: irreversible series of events that lead to cell differentiation

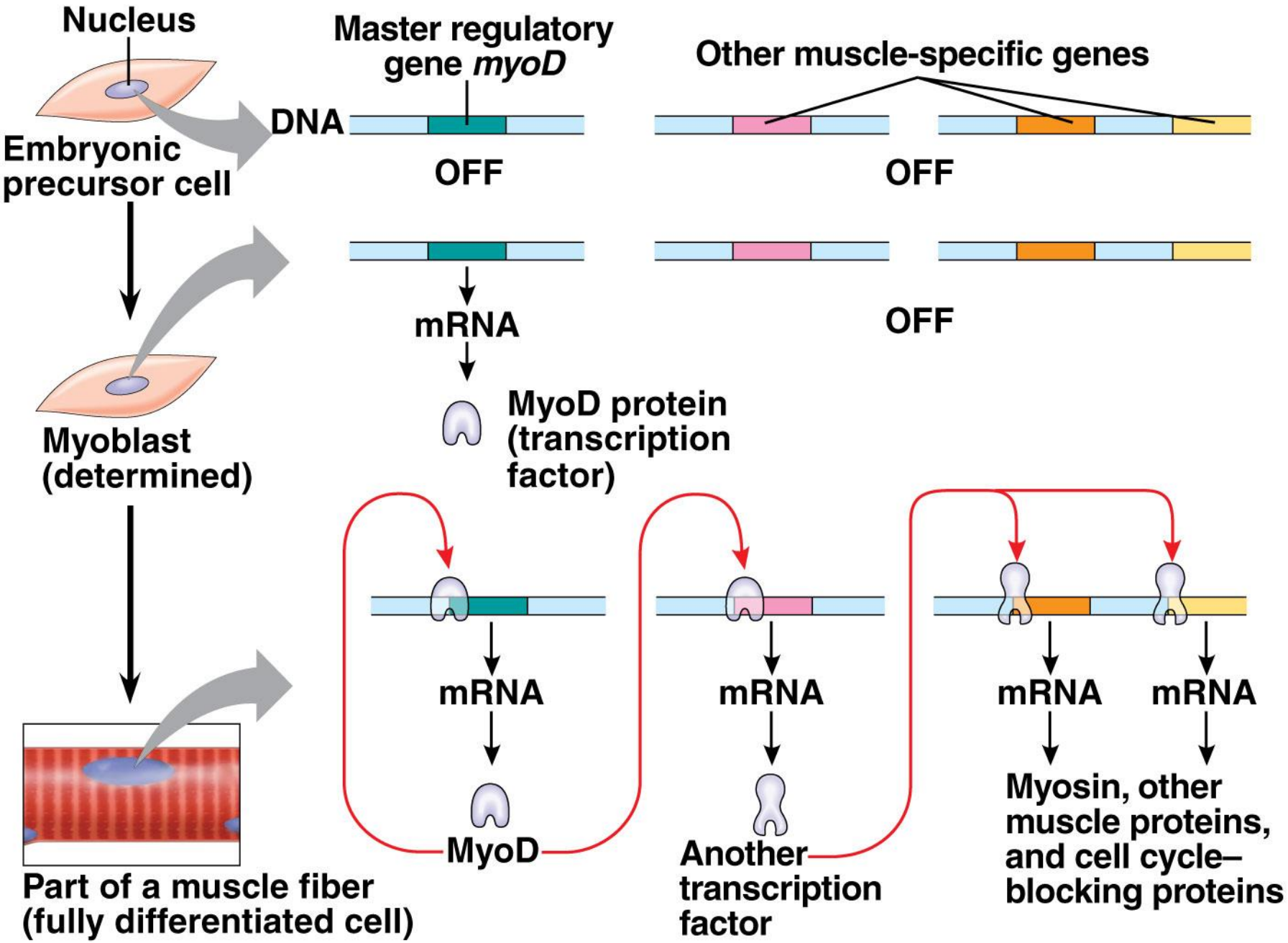




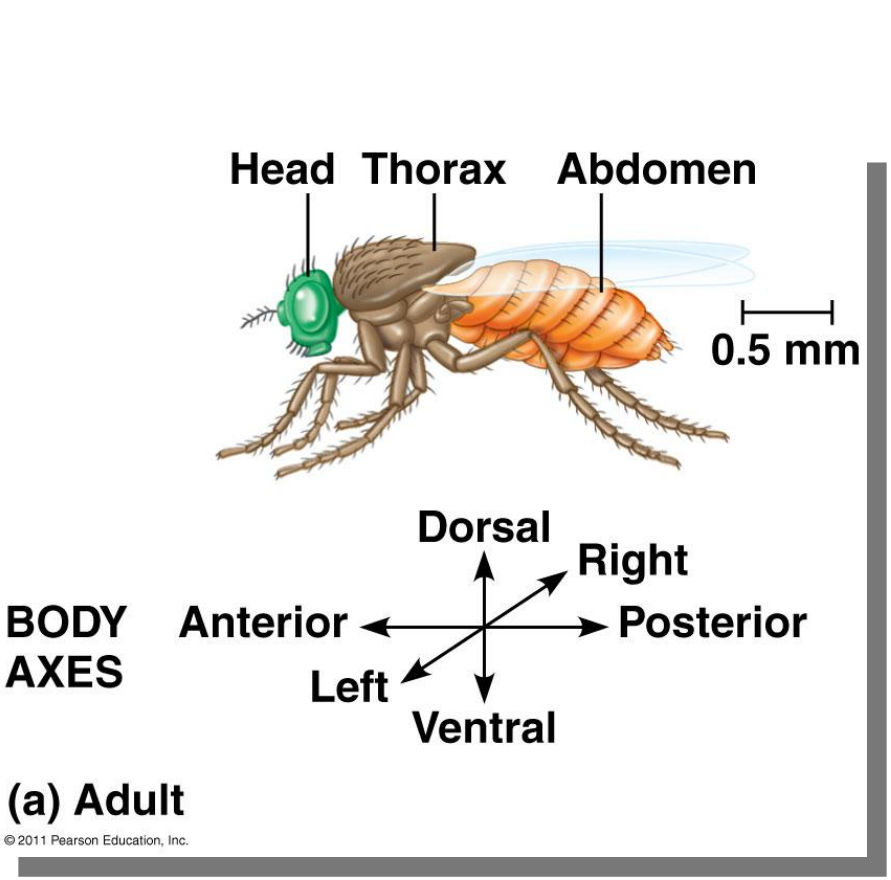
- Cytoplasmic determinants: maternal substances in egg distributed unevenly in early cells of embryo

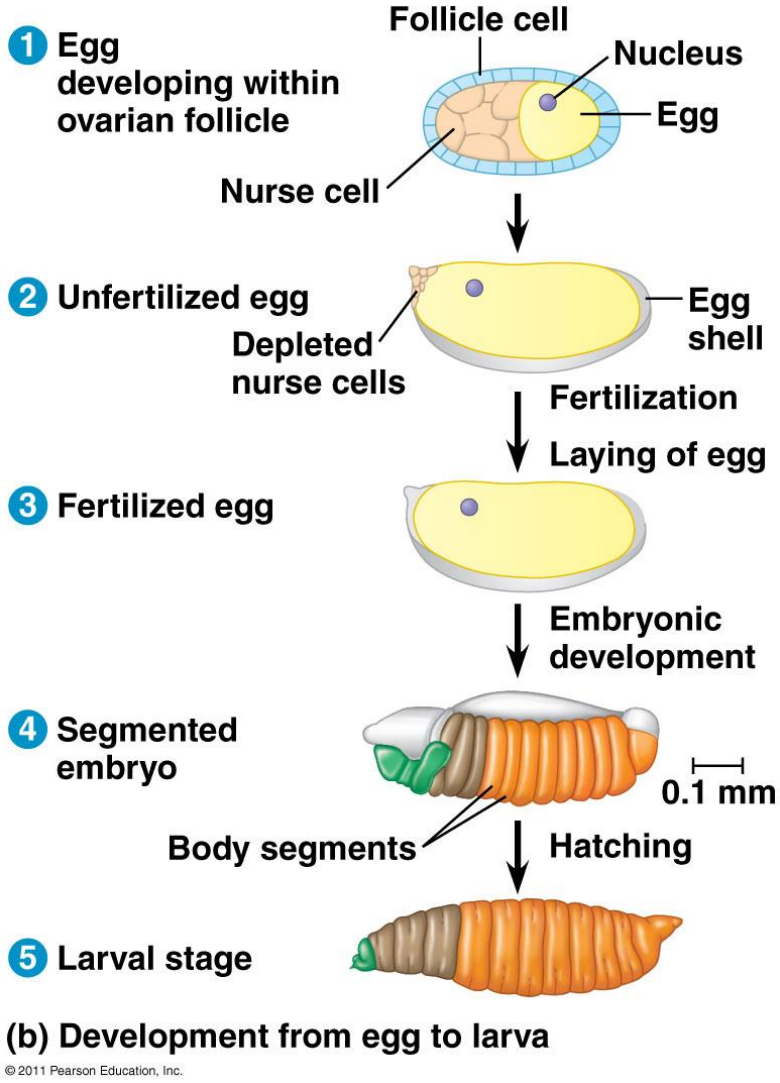


- **Cell-Cell Signals**: molecules produced by one cell influences neighboring cells
  - Eg. Growth factors
- **Induction**: cells triggered to differentiate

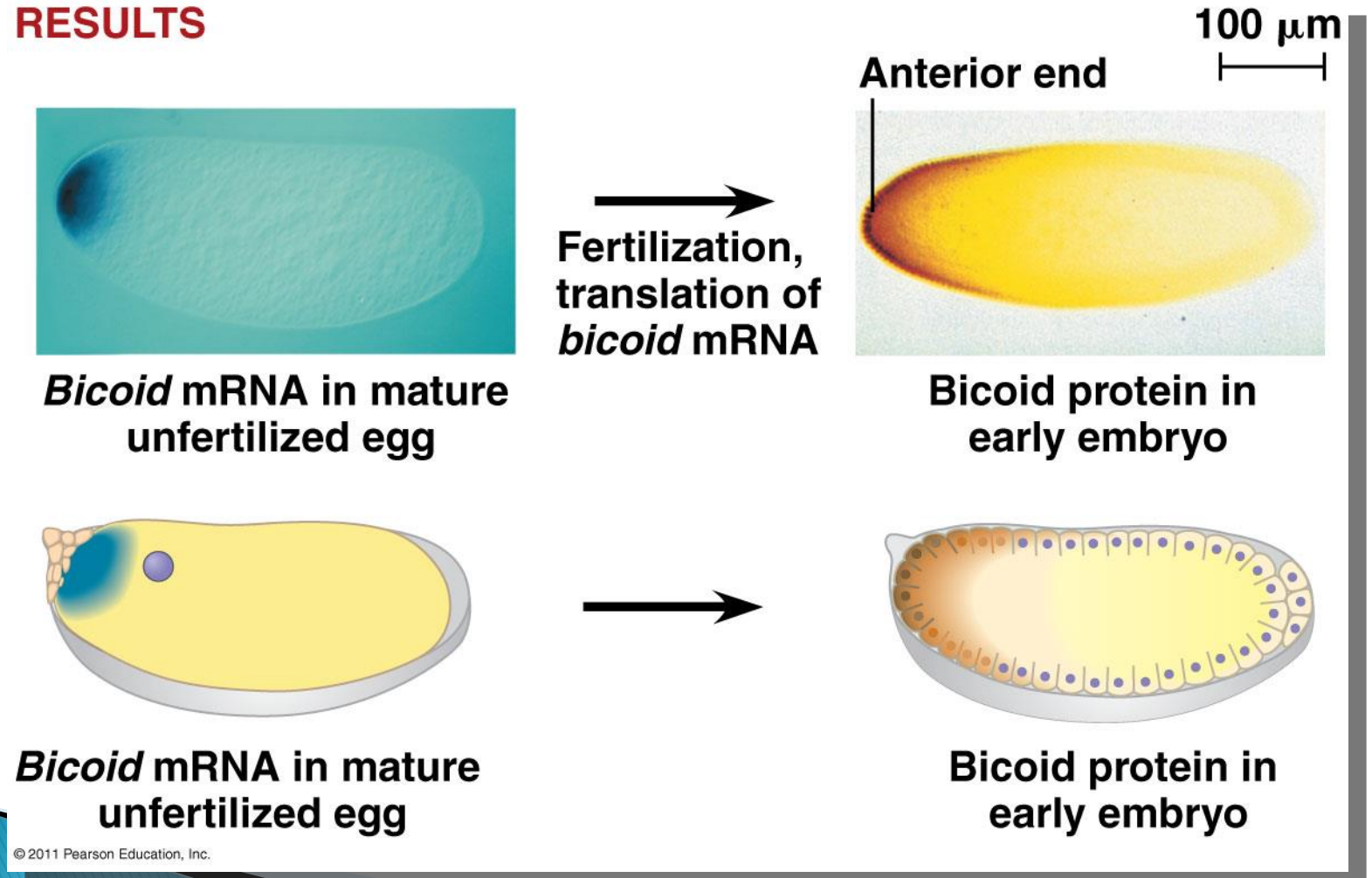


Pattern formation: setting up the body plan (head, tail, L/R, back, front)

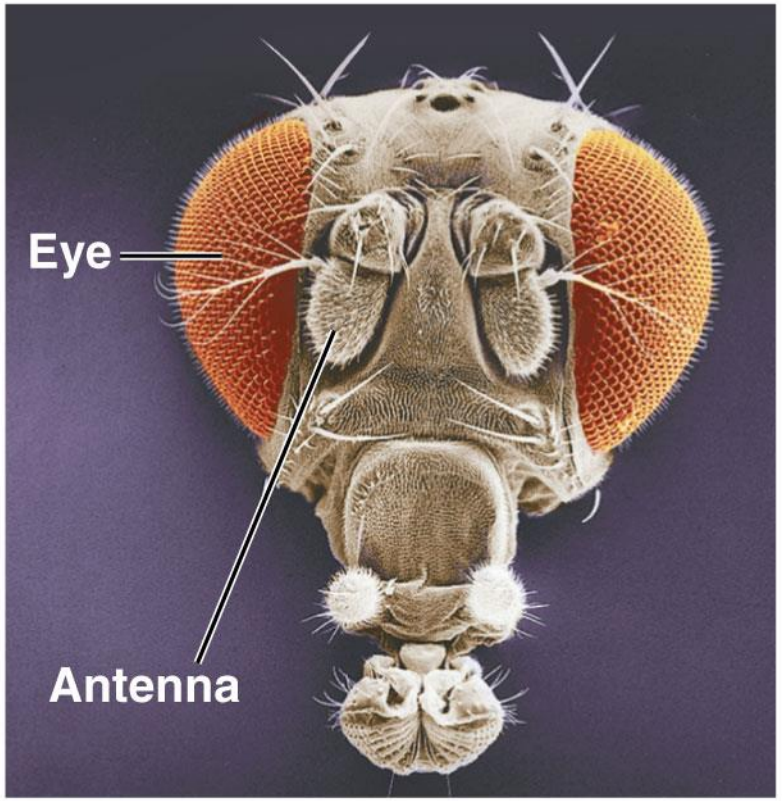




Morphogens: substances that establish an embryo's axes



Homeotic genes: master control genes that control pattern formation (eg. Hox genes)



Wild type

Mutant

Evolving Switches, Evolving Bodies

- Close Read the Intro
  HHMI Short Film

HHMI Biointeractive: Regulation of Eukaryotic DNA Transcription

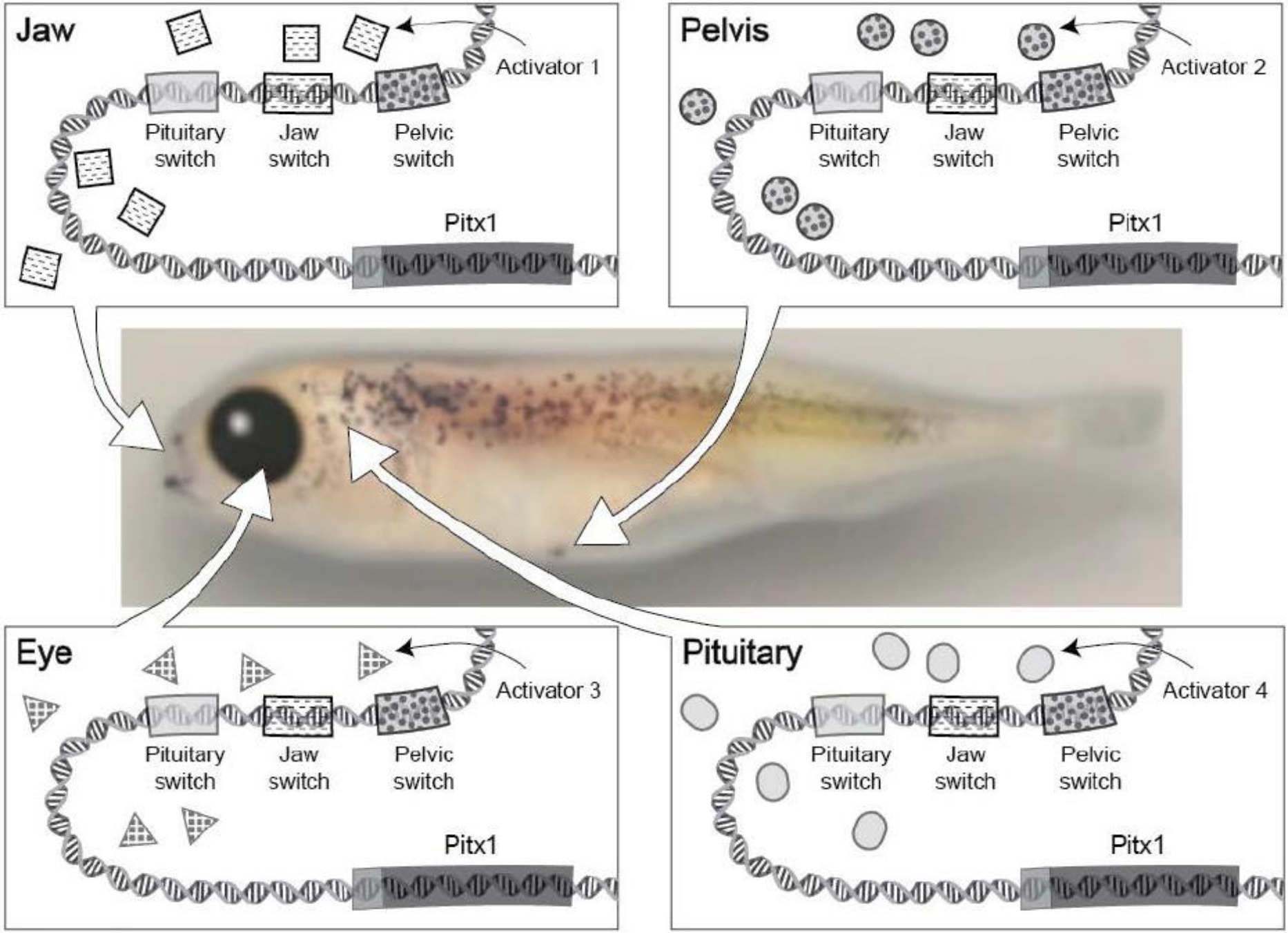
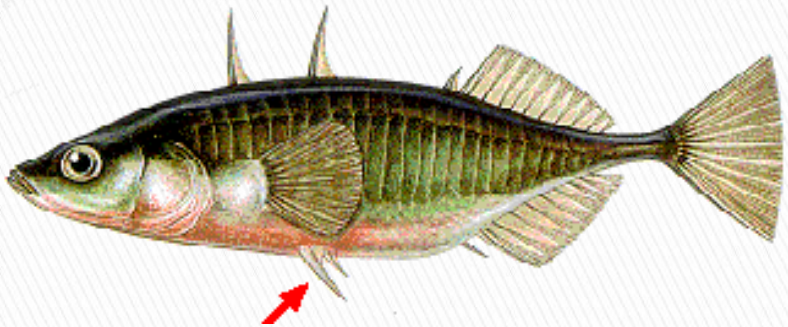

Jaw
Activator 1
Pituitary switch
Jaw switch
Pelvic switch
Pitx1
Pelvis
Activator 2
Pituitary switch
Jaw switch
Pelvic switch
Pitx1
Eye
Activator 3
Pituitary switch
Jaw switch
Pelvic switch
Pitx1
Pituitary
Activator 4
Pituitary switch
Jaw switch
Pelvic switch
Pitx1

Figure 2

Pitx1 Gene = Homeotic/Hox Gene

Stickleback Fish

- Development of pelvic bone

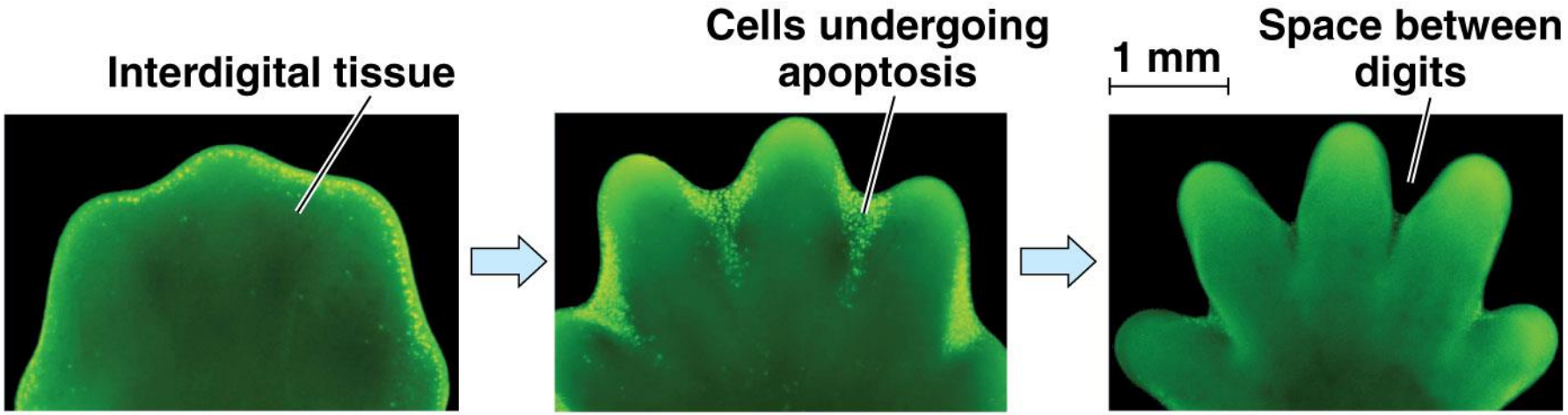


Humans

- Development of anterior structures, brain, structure of hindlimb
- Mutation may cause clubfoot, polydactyly (extra fingers/toes), upper limb deformities

Role of Apoptosis

- Most of the embryonic cells are produced in excess
- Cells will undergo *apoptosis* (programmed cell death) to sculpture organs and tissues



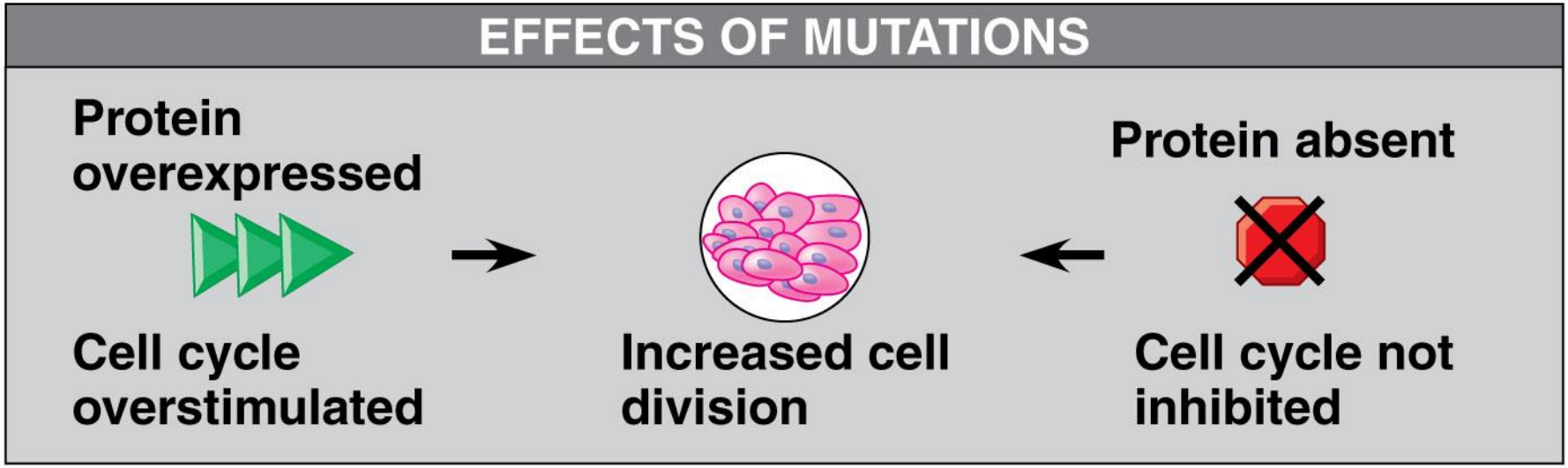
Cancer results from genetic changes that affect cell cycle control

- Section 18.5

Control of Cell Cycle:

1. **Proto-oncogene** = stimulates cell division
2. **Tumor-suppressor gene** = inhibits cell division

- Mutations in these genes can lead to cancer



(c) Effects of mutations

Proto-Oncogene

- Gene that stimulates <u>normal</u> cell growth & division

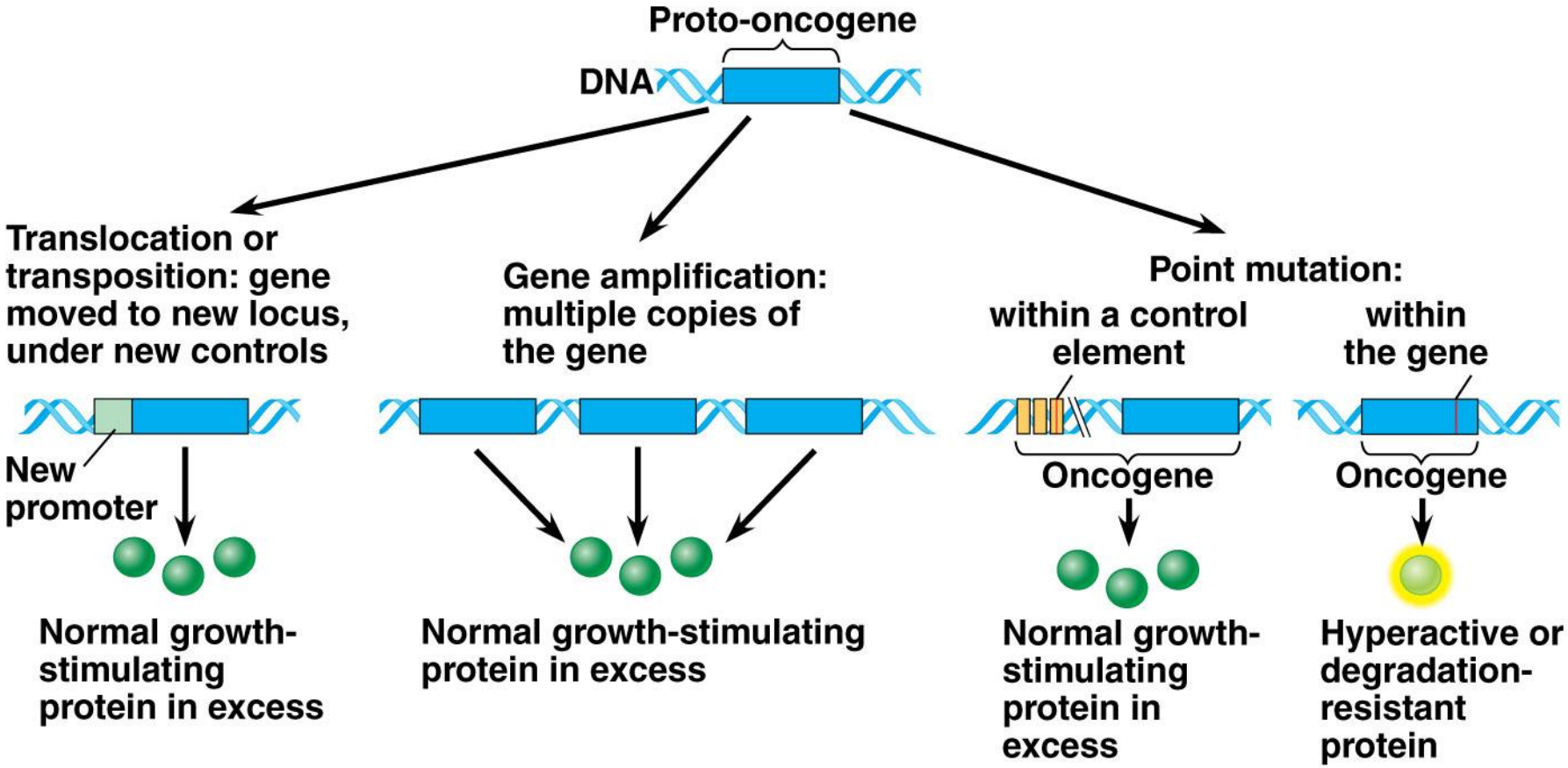
Oncogene

- Mutation in proto-oncogene
- Cancer-causing gene

Effects:

- Increase *product* of proto-oncogene
- Increase *activity* of each protein molecule produced by gene

Proto-oncogene → Oncogene



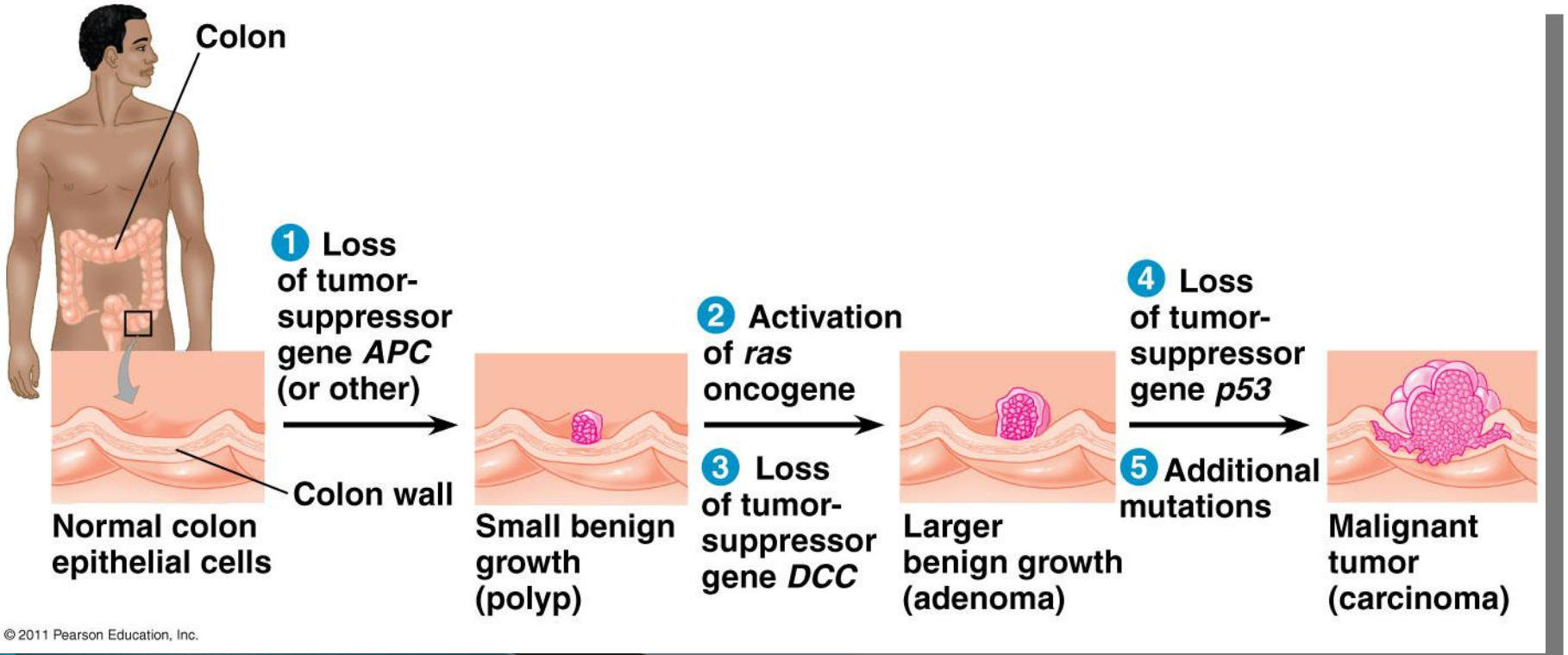
Genes involved in cancer:

- ***Ras* gene**: stimulates cell cycle (proto-oncogene)
  - Mutations of *ras* occurs in 30% of cancers

- ***p53* gene**: tumor-suppressor gene
  - Normal anti-cancer functions:
    - Activate p21 gene, whose product halts cell cycle for DNA repair
    - Activate miRNAs to inhibit cell cycle
    - turn on DNA repair genes
    - activate apoptosis (cell suicide) if DNA repair not possible
  - Mutations of *p53* in 50+% of cancers

http://www.hhmi.org/biointeractive/p53

- Cancer results when mutations accumulate (5–7 changes in DNA)
- Active oncogenes + loss of tumor-suppressor genes
- The longer we live, the more likely that cancer might develop



Summary

- *Embryonic development* occurs when gene regulation proceeds correctly
- *Cancer* occurs when gene regulation goes awry