Advanced Cell Biology. Lecture 23

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Outline

Questions and answers

Previous final question: the answer

What is chaperone?

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What is chaperone?

- Protein which help to fold other proteins

Gene expression and cell differentiation

- Different cells will produce different sets of proteins (except housekeeping proteins)
- Differentiated cell expressed 20–50% of existing genes

Cloning of multicellular organisms

- Organisms of “higher” evolutionary position are cloned with more and more difficulties
- Whereas plants are capable to develop new organism almost from any cell, mammals will need extremely complicated technique including transition of nucleus

Making new mammal from a cell

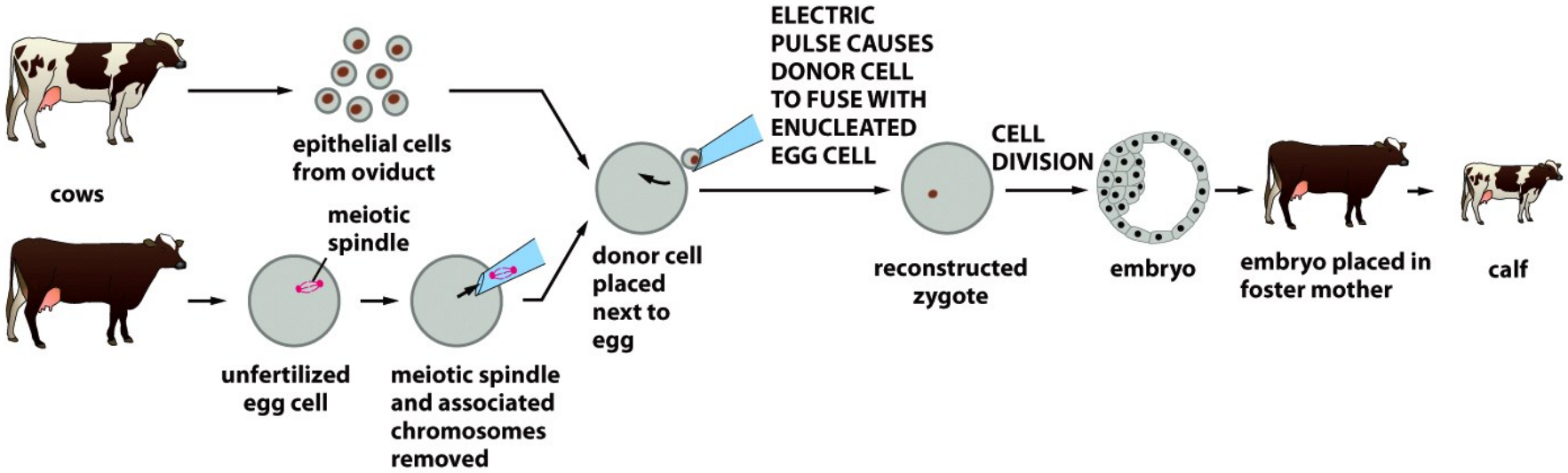


Figure 8-2c Essential Cell Biology 3/e (© Garland Science 2010)

Places of expression regulation

1. Transcription
2. RNA processing
3. RNA transport
4. RNA degradation
5. Translation
6. Protein

Control of gene expression

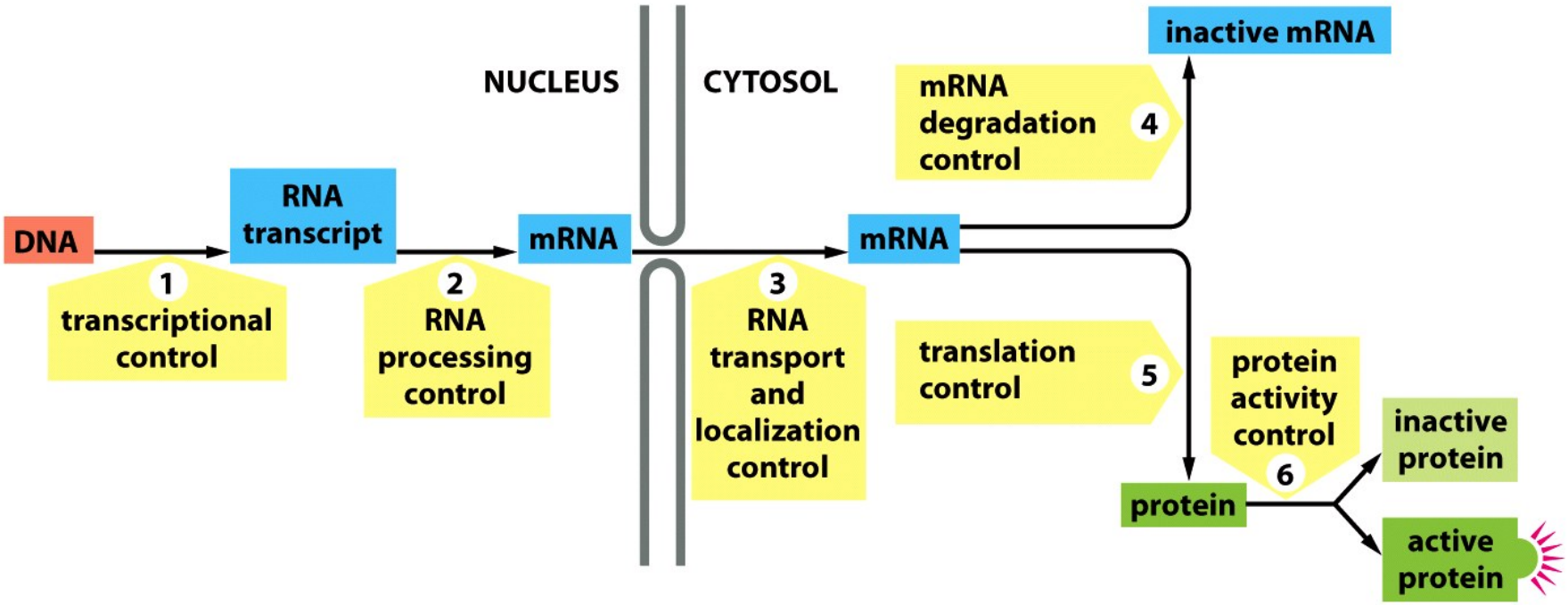


Figure 8-3 Essential Cell Biology 3/e (© Garland Science 2010)

Regulatory sequences

- Promoters + initiation sites upstream to the actual gene
- Regulatory DNA sequences upstream to the promoters
- Transcription regulators to bind with regulatory DNA sequences

DNA-binding motifs

- Homeodomain
- Zinc finger
- Leucine zipper

Homeodomain movie

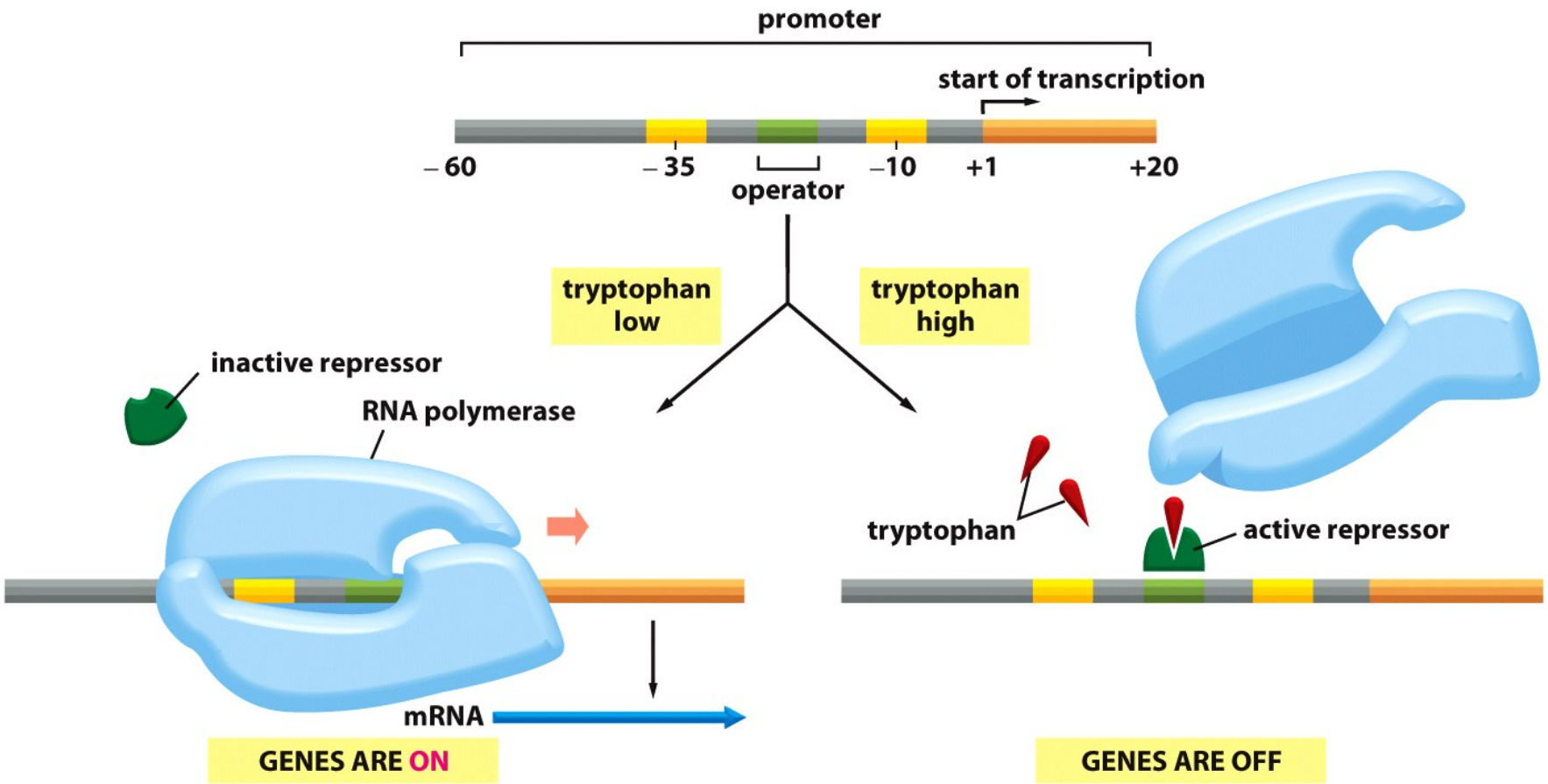
Zinc finger movie

Leucine zipper movie

Repressors

- Repressor binds to operator and blocks access of RNA polymerase to promoter
- Tryptophan repressor of *E. coli* works when concentration of tryptophane is high (activated by tryptophane)
- However, it will allow small transcription even in “off” position (constitutive expression)

Tryptophane repressor



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Activators

- Activator sequences are “sleeping promoters”, they work as promoters only if activator protein is bound to them
- *E. coli* activator CAP is activated by cyclic AMP (cAMP) which is a signal of lacking glucose; CAP activate proteins which utilize other sugars

Activator

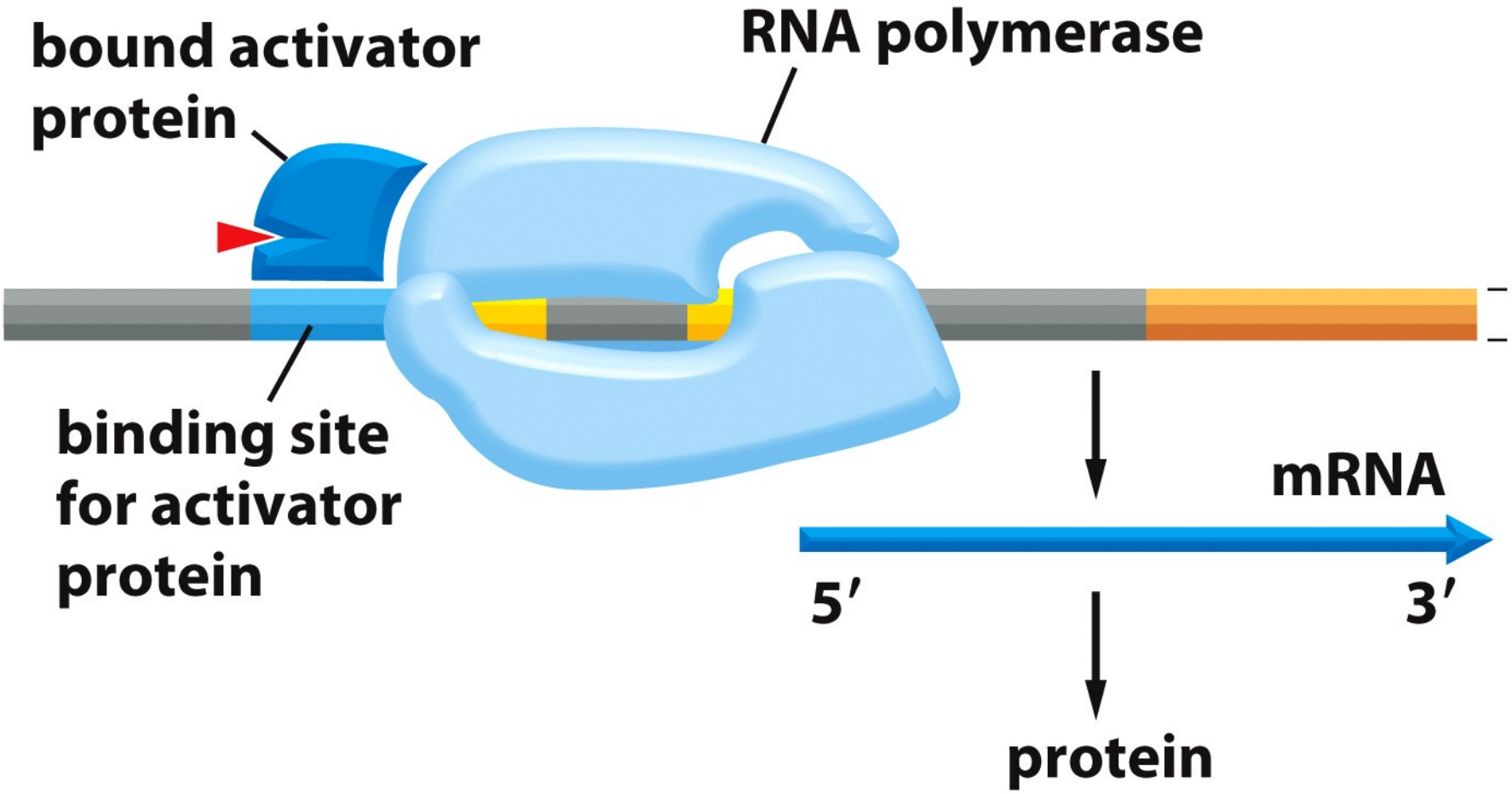


Figure 8-8 Essential Cell Biology 3/e (© Garland Science 2010)

Lac operon

- LacZ gene encodes β-galactosidase protein which breaks lactose to galactose and glucose
- Only if lactose is prsend AND glucose is absent, Lac repressor detaches from operator and CAP activator promote RNA polymerase to bind with promoter

Lac operon

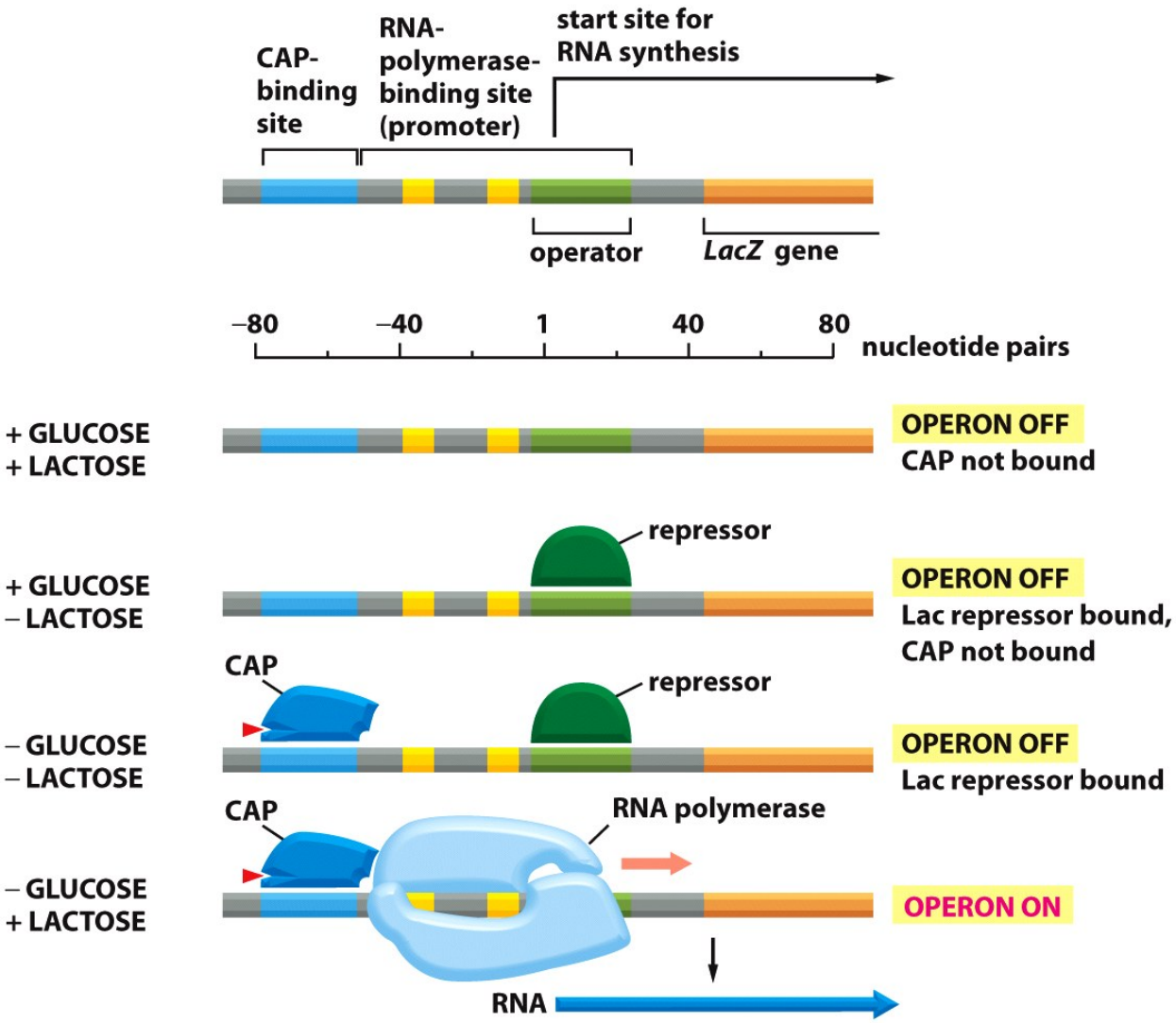


Figure 8-9 Essential Cell Biology 3/e (© Garland Science 2010)

Eukaryotic transcription regulators

- Enhancers may be located upstream or downstream from activated gene
- They work through mediators when DNA form a loop

Enhancer and mediator

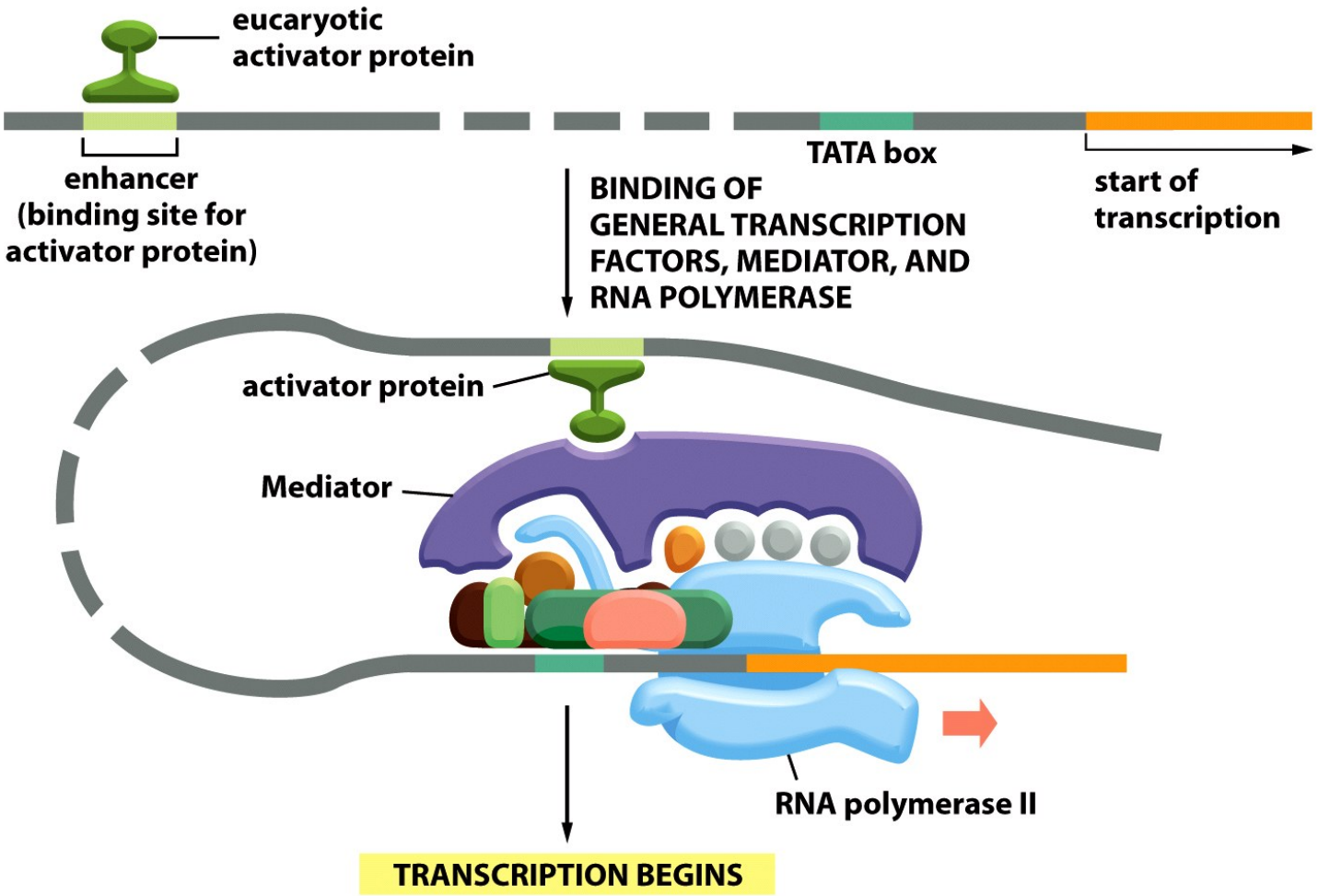


Figure 8-10 Essential Cell Biology 3/e (© Garland Science 2010)

Histones and transcription regulation

- Eukaryotic repressors and activators may work even more “distantly”, through histones and chromatin-remodeling complex
- Activators may attract histone acetylases which alter the 3D structure of histones and allow an access to some DNA parts; repressors may attract histone deacetylases

Transcription committee

- Combinatorial control means that multiple regulatory proteins will determine an expression of single gene
- In eukaryotes, each gene is controlled by dozens of regulators

Eukaryotic transcription regulators

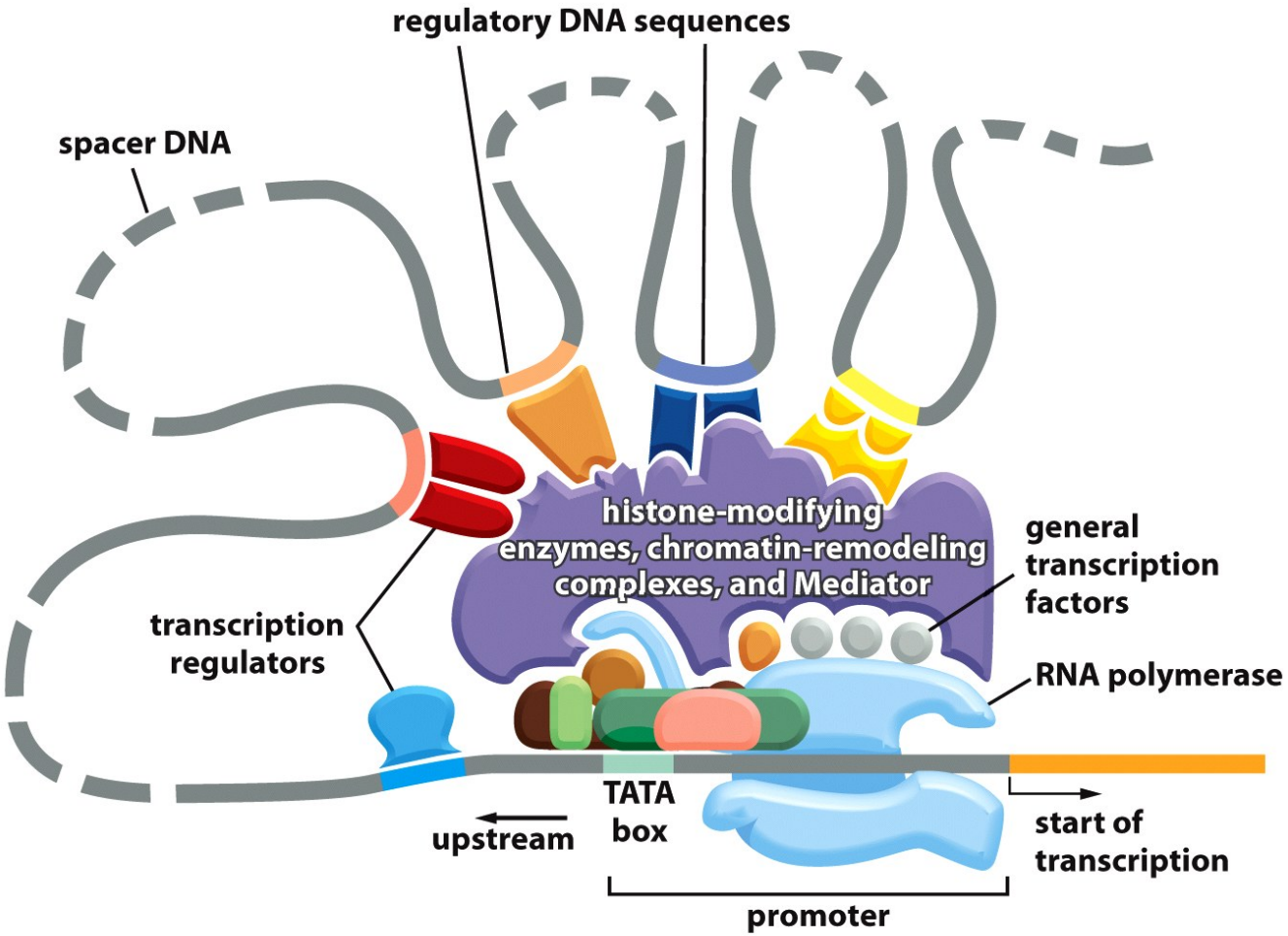


Figure 8-12 Essential Cell Biology 3/e (© Garland Science 2010)

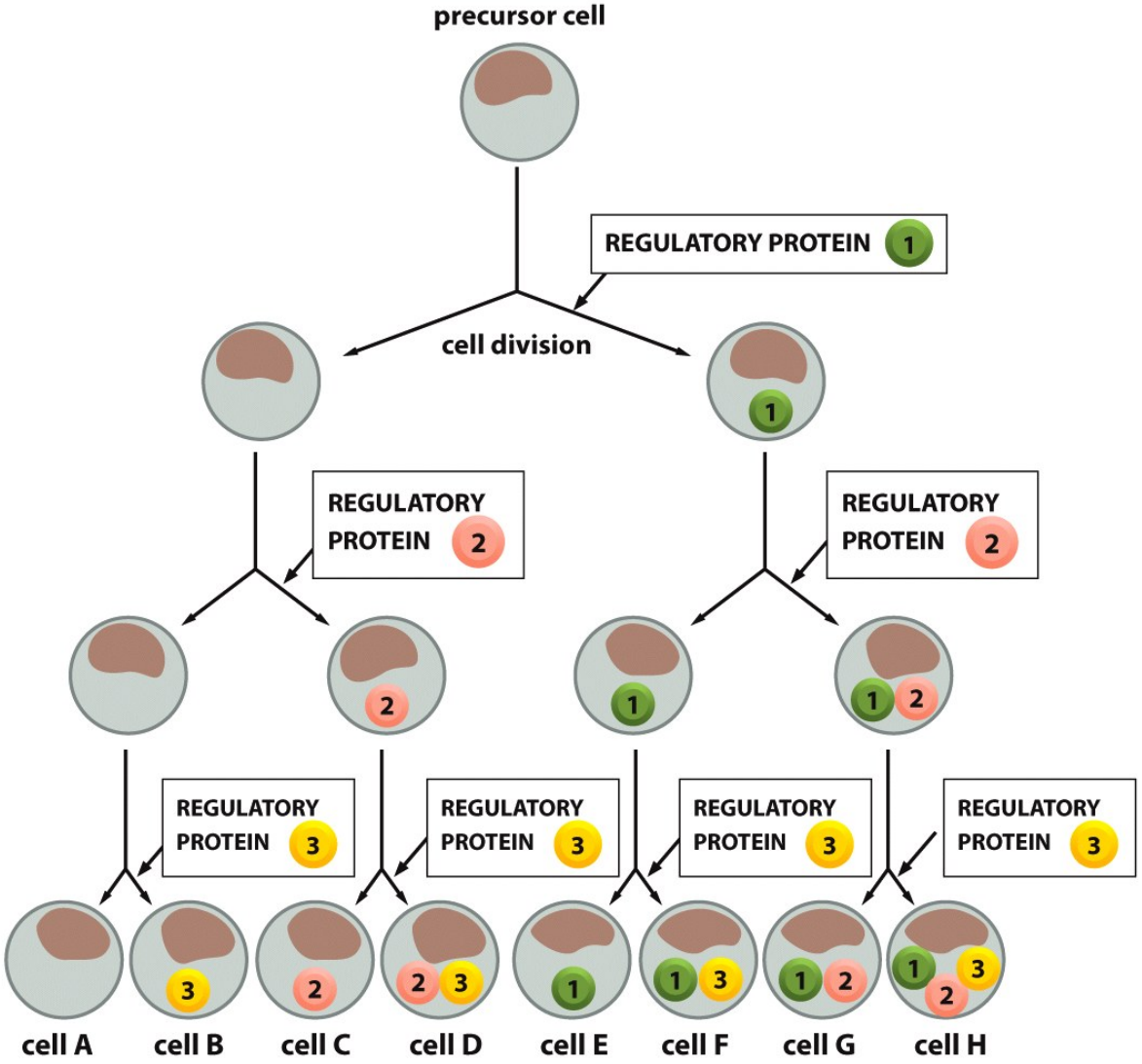
One-to-many regulators

- Glucocorticoid receptor protein forms a complex with hormone (e.g., cortisol)
- This complex works simultaneously as activator for many genes

Combinatorial control and cell differentiation

- Skin fibroblasts could be turned in muscle cells (myoblasts) with MyoD regulator
- Different combinations of regulators will result in different kinds of cells

Differentiation through combination



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Final question (1 point)

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How many signals control the *Lac* operon?

Summary

- Cell differentiation is a result of nonuniform gene expression
- Activators and repressors could switch transcription on and off
- Different combinations of transcription regulators activate gene expression in different places and in different ways

For Further Reading

A. Shipunov.
Advanced Cell Biology [Electronic resource].
2011—onwards.
Mode of access: http://ashipunov.info/shipunov/school/biol_250.

B. Alberts et al.
Essential Cell Biology. 3rd edition.
Garland Science, 2009.
Chapter 8, pp. 270–286.