Name Key Period

Chapter 18: Regulation of Gene Expression

Overview

The overview for Chapter 18 introduces the idea that while all cells of an organism have all genes in the genome, not all genes are expressed in every cell. What regulates gene expression? Gene expression in prokaryotic cells differs from that in eukaryotic cells. How do disruptions in gene regulation lead to cancer? This chapter gives you a look at how genes are expressed and modulated.

Concept 18.1 Bacteria often respond to environmental change by regulating transcription

1. All genes are not "on" all the time. Using the metabolic needs of *E. coli*, explain why not.
conservation of energy & resources (environment)
Tryp levels low, cell activates metabolic pathway to synthesize it. When level rises, it stops production

2. What are the two main ways of controlling metabolism in bacterial cells?
1. cells can adjust activities of enzymes that are present
2. cells can adjust the production levels of certain enzymes

3. *Feedback inhibition* is a recurring mechanism throughout biological systems. In the case of *E. coli* regulating tryptophan synthesis, is it *positive* or *negative inhibition*? Explain your choice.
Negative: when levels of tryptophan go up, production stops
when levels of tryptophan go down, production increases

4. What is a *promoter*?
piece of DNA that defines where transcription of a gene by DNA polymerase begins

5. What is the *operator*? What does it do?
an "on-off switch" - positioned within the promoter or between the promoter and enzyme coding genes; it controls the access of the RNA polymerase to the genes

6. What is an *operon*?
operator & promoter & genes they control

7. List the three components of an *operon*, and explain the role of each one.

operator - controls access of RNA polymerase to the genes
promoter - tells where the transcription begins
genes - stretch of DNA required for the production of the product

8. How does a *repressor* protein work?

binds to the operator and blocks attachment of RNA polymerase to the promoter, preventing transcription

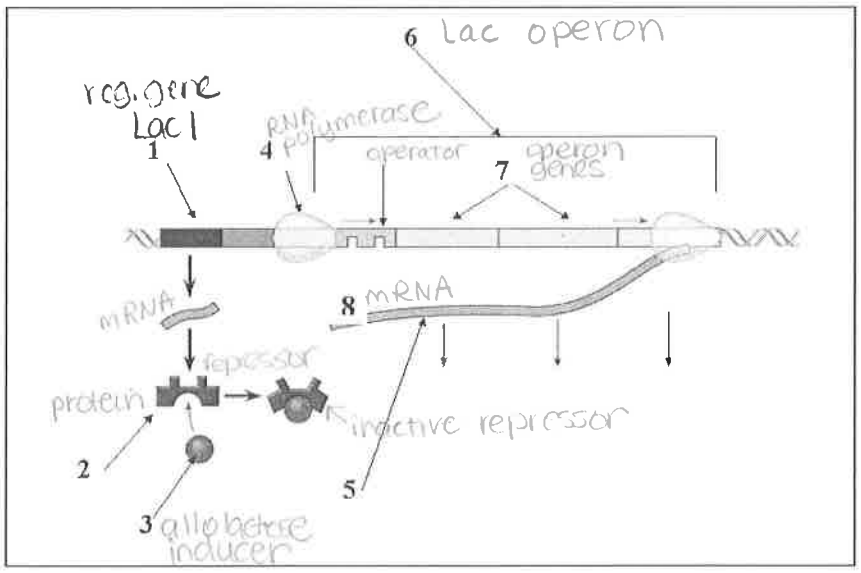
9. What are *regulatory genes*?

gene that is involved with controlling one or more other genes

10. Distinguish between *inducible* and *repressible operons*, and describe one example of each type.

repressible operon - transcription is usually (on) but can be inhibited when there is an allosteric inhibitor
inducible operon - transcription is usally off but can be stimulated when a molecule interacts with regulatory protein

11. Label this sketch of the *lac operon* with the terms at right. Know the function of each structure.



Operon genes ✓

Operon ✓

RNA polymerase ✓

mRNA ✓

Repressor protein ✓

Operator ✓

Repressor ✓

Regulatory gene ✓

Inducer ✓

12. Compare and contrast the *lac* operon and the *trp* operon. (Remember that *compare* means "to tell how they are similar," and *contrast* means "to tell how they are different.")

same
- negative control of genes
- under regulation of one operator + promoter

different
trp repressor-inactive + requires tryptophan as a co-repressor
lac repressor- active by itself and switches lac operon off

13. What happens when a repressor is bound to the operator?
It is switched off and it can't bring about transcription

14. What is *CAP*? How does *CAP* work?
regulator protein - activator - binds to DNA and stimulates transcription of a gene - controls rate of transcription
- positive regulation
- regulates the lac operon

15. Explain why CAP binding and stimulation of gene expression is *positive regulation*.
Binds to the RNA polymerase to the promoter and INCREASES the rate of transcription → stimulating gene expression

16. Describe the relationship between glucose supply, cAMP, and CAP.
Glucose supply ↓, cAMP ↑
cAMP binds to CAP which becomes active and increases the rate of transcription

17. How can both repressible and inducible operons be *negative regulators*?
operons are switched off by the active form of the repressor protein.

Concept 18.2 Eukaryotic gene expression can be regulated at any stage

18. Even though all cells of an organism have the same genes, there is *differential gene expression*. What does this mean?
genes must continually be turned off/on in response to signals from the external + internal environments, also important for cell specialization

19. What percentage of the genes of a typical human cell is expressed at any given time?
20%

20. What is the common control point of gene expression for all organisms?

transcription

21. Gene expression can be regulated by modifications of the chromatin. Distinguish between *heterochromatin* and *euchromatin* as to their structure and activity.

heterochromatin - tightly coiled DNA; responsible for gene regulation + protection of chromosome integrity
euchromatin - loosely coiled DNA; aid in cell survival

22. What occurs in *histone acetylation*? How does it affect gene expression?

acetyl groups are attached to lysines in histone tails → chromatin more loose → transcription proteins have easier access ↑ transcription ↑

23. What is *DNA methylation*? What role may it play in gene expression?

Methyl groups added to the DNA keeps that segment inactive - keeps it from being expressed

24. The inactive mammalian X chromosome is heavily methylated. What is the result of this methylation?

Those genes are "turned off", or are not expressed

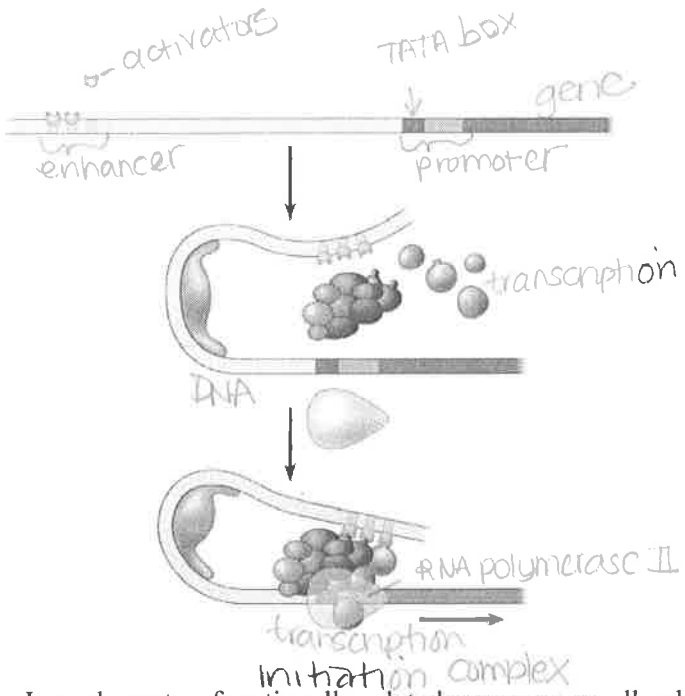
25. What is *genomic imprinting*, and how is it maintained? Give an example discussed earlier in human genetics.

- variation in phenotype depending on which parent passed on the allele
- maintained as methylation patterns are passed on
- insulin growth factor

26. Explain what is meant by *epigenetic inheritance*, and give an example of epigenetic changes discussed in the text or in class.

inheritance of traits transmitted by mechanisms not directly involving the nucleotide sequence
- DNA methylation + histone deacetylation → repressing transcription

27. Use the sketch below to explain how enhancers and activators interact with transcription factors to affect gene expression. Label the following elements: *TATA box, promoter, gene, enhancer, activators, transcription factors, transcription initiation complex, RNA polymerase II,* and *DNA.* Then place your explanation to the right of the figure.



EXPLANATION

DNA is bent - allows enhancers to influence a promoter. Activators bind to the enhancer; then to mediator proteins, then transcription factors → form transcription initiation complex. This allows correct positioning of the complex on the promoter → initiate RNA synthesis

28. In prokaryotes, functionally related genes are usually clustered in a single operon. What has been found to be the case in eukaryotes?

Genes coding for enzymes of a metabolic pathway are scattered over several chromosomes

29. Operons have not been found in eukaryotic cells, and the genes coding for the enzymes of a particular metabolic pathway are often scattered over different chromosomes. What is a plausible mechanism for the *coordination of gene expression*?

- coordinate gene express depends on specific combination of control elements with ever gene
- activators recognize control elements, promoting simultaneous transcription

30. How can *alternative RNA splicing* result in different proteins derived from the same initial RNA transcript?

- different mRNA molecules are produced depending on what segments are treated as exons and which as introns
(RNA splicing – can significantly expand the repertoire of the eukaryotic genome)
↳ multiples the # of possible human proteins

31. *Posttranscriptional control* includes regulation of *mRNA degradation*. Explain how this affects translation.

How long the mRNA segments last can determine how much protein can be made
prokaryotic - quickly degrades
multicellular eukaryotes - last longer = make more protein

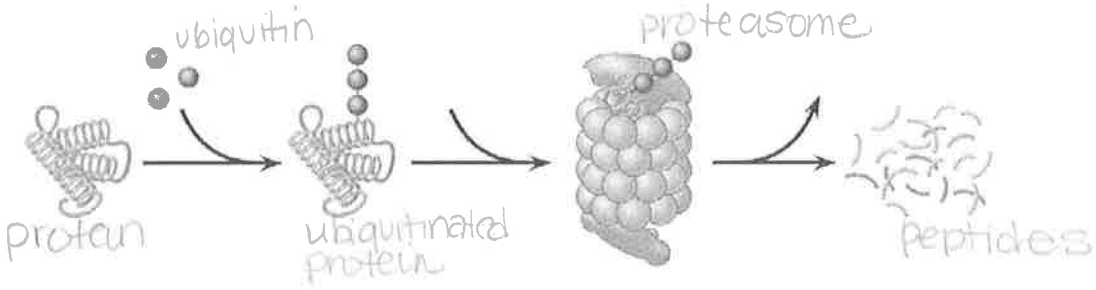
32. How can proteins be activated, processed, and degraded? Give an example or describe each process.

1. activation - cleavage or phosphorylation
2. processing - transporting, adding sugars
3. degraded - ubiquitin is attached, protein recognized by proteasome which degrades it

33. An article in *Scientific American* about *proteasomes* was entitled "Little Chamber of Horrors." Explain how proteins are targeted for degradation, and give a specific example of when this might occur.

Ubiquitin (protein) is added as a tag
Proteasome chops up unneeded proteins - proteasome + ubiquitin are recycled
Cyclins → regulate cell cycle (short lived)

34. How do these "little chambers of horrors" function? Annotate the sketch below to describe their action. Then explain their role in regulation of gene expression.



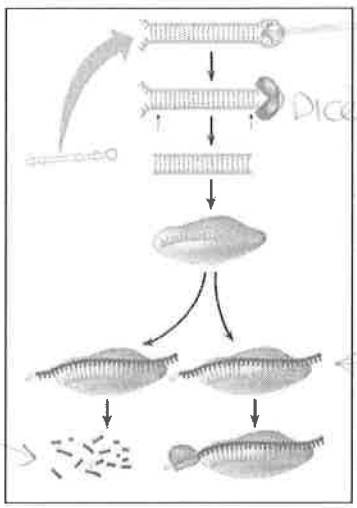
Concept 18.3 Noncoding RNAs play multiple roles in controlling gene expression

35. It is now known that much of the RNA that is transcribed is not translated into protein. these RNAs are called *noncoding RNAs*. Read carefully to discern a crucial role played by these RNAs. What is this role?

regulation of gene expression

36. One of the *noncoding RNAs* that regulate gene expression is *microRNA*. On the sketch below, follow an RNA loop, called a "hairpin," from its creation. Explain the two modes of action of *microRNAs*.

Be sure to label the location of hydrogen bonds and *Dicer*.



Concept 18.4 A program of differential gene expression leads to the different cell types in a multicellular organism

This concept deals with the regulation of gene expression in development. Animal development is also discussed in Chapter 47.

37. What three processes lead to the transformation of a zygote into the organism?

1. cell division
2. cell differentiation
3. morphogenesis

38. Explain what occurs in *cell differentiation* and *morphogenesis*.

cell differentiation - cells become specialized in structure & function

morphogenesis - physical processes that give an organism its form

39. Differential gene expression results from different activators in different cells. How do different sets of activators come to be present in two cells? Explain how each of these occurs:

a. distribution of *cytoplasmic determinants*
after fertilization, early mitotic division distribute the zygote's cytoplasm into separate cells
nuclei → exposed to different cytoplasmic determinants

b. different *inductive signals*
signals impinging on an embryonic cell from other embryonic cells in the vicinity - signals cause changes in the target cells

40. What is meant by *determination*? Explain what this means within an embryonic cell.
events the lead to the observable differentiation of a cell
cells will become the kinds of cells they are meant to be in the organism

41. What process ensures that all the tissues and organs of an organism are in their characteristic places? Where do the molecular cues that control this process arise?
regulatory genes → protein products that commit the cell to becoming a certain cell tissues

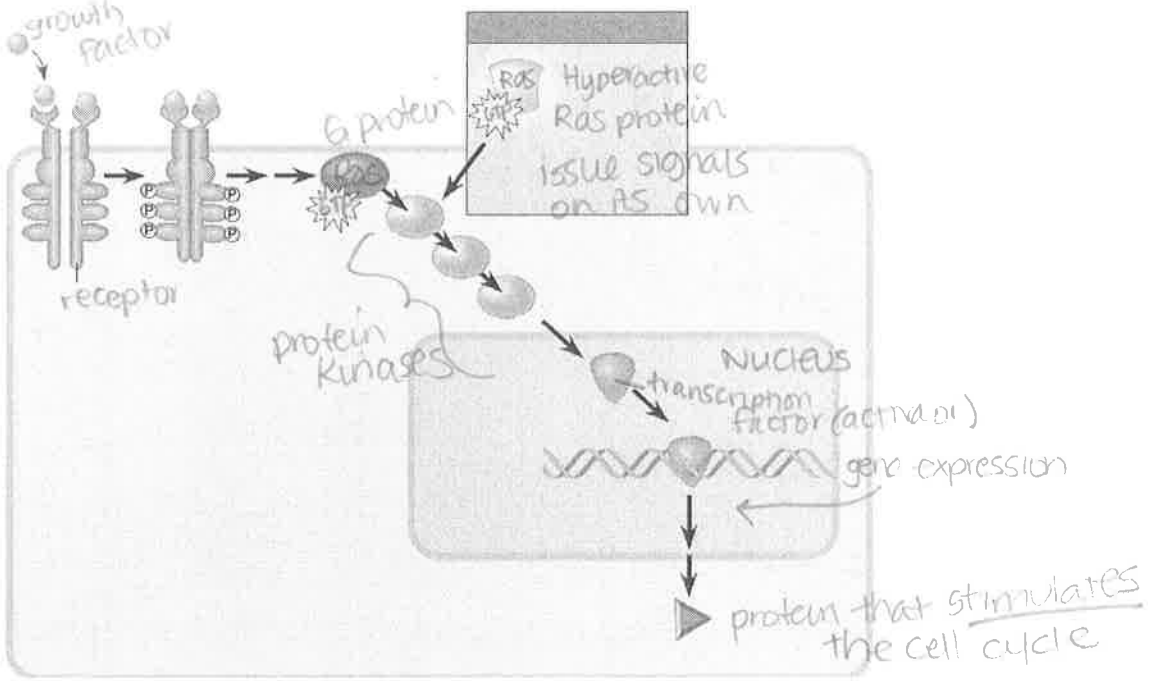
42. What is controlled by *homeotic genes*?
pattern formation in Drosophila - in the late embryo, larva + adult

Concept 18.5 Cancer results from genetic changes that affect cell cycle control

43. What mechanism is involved in the beginning of tumor growth? Discuss *oncogenes* and proto-*oncogenes*.
oncogenes - cancer-causing genes
proto-oncogenes - code for proteins that stimulate normal cell growth + division
proto-oncogene becomes an oncogene because of a genetic change

44. What are three mechanisms for converting a proto-oncogene to an oncogene?
1. movement of DNA within the genome
2. amplification of a proto-oncogene
3. point mutations in a control element or in the proto-oncogene itself

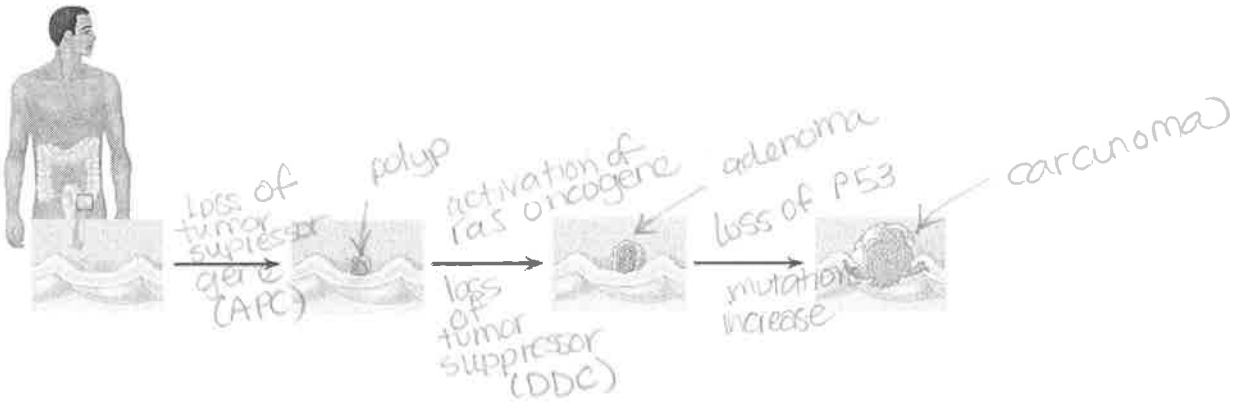
45. There seem to be two categories of genes involved in cancer: *oncogenes*, which code for proteins to regulate cell growth, and should not be stuck "on," much like the accelerator in a car; and *tumor-suppressor genes*, which work like the brakes on a car and must function! Let's begin with a look at the *ras gene*, which codes for a G protein and is an *oncogene*. Label the sketch below to explain how a *ras* mutation leads to cancer.



46. *Tumor-suppressor genes* help prevent uncontrolled cell growth. One that is found mutated (and therefore nonfunctional) in more than 50% of human cancer is *p53*. So important is the *p53 gene* that it is sometimes called the "guardian angel of the genome." Describe the double whammy that results from mutation of *p53*.

p53 activates several other genes (cell cycle halting molecules)
activates expressing of miRNAs which inhibit cell cycle
turns on genes involved in DNA repair
- cell cycle not getting inhibited AND DNA not being repaired

47. Explain the *multistep model of cancer development* by using the specific example of colorectal cancer. The figure below may be labeled to help in your explanation.



Testing Your Knowledge: Self-Quiz Answers
Now you should be ready to test your knowledge. Place your answers here:

1._____ 2._____ 3._____ 4._____ 5._____ 6._____ 7._____

8._____ 9._____ 10._____