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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.
   If E. coli has enough tryptophan available, it does not have to make any, so the gene for its synthesis is "off". The gene turns on when there is not enough tryptophan.
2. What are the two main ways of controlling metabolism in bacterial cells?
   Activation of metabolic pathway (activity of enzymes)
   Adjustment of production & activity of 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.
   It is negative inhibition because the synthesis of tryptophan decreases as the product increases.
4. What is a *promoter*?
   A promoter is a region on DNA that binds to polymerase and initiates transcription
5. What is the *operator*? What does it do?
   Segment of DNA within promoter that controls access of RNA pol to the genes
6. What is an *operon*?
   Operator, promoter, and genes they control

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

Operator - controls access of RNA polymerase
Promoter - binds to RNA polymerase
Genes - give genetic info, serve as template

8. How does a *repressor* protein work?

Binds to operator & blocks attachment of RNA pol to promoter, preventing transcription

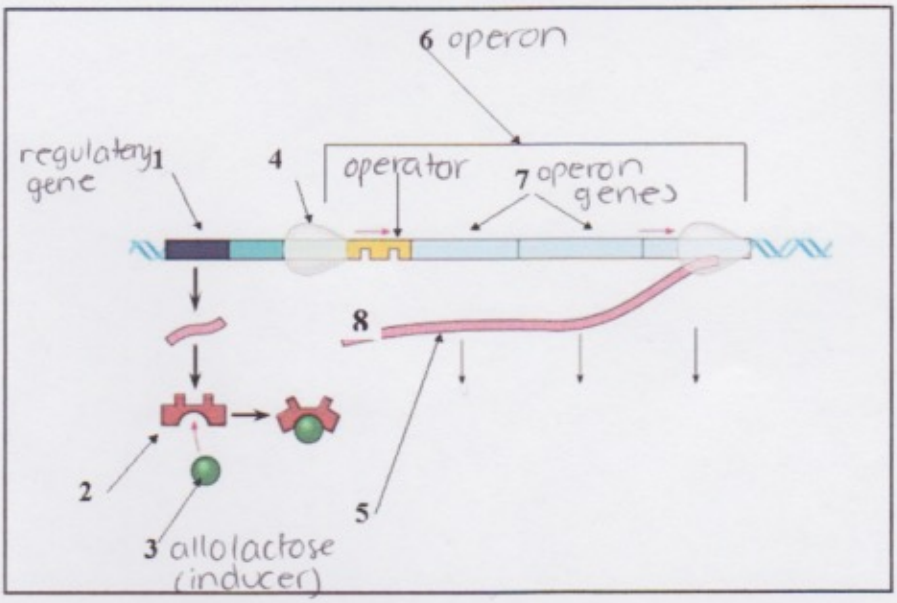
9. What are *regulatory genes*?

code for repressor protein, expressed continuously at low rate

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

INDUCIBLE: ~~usually off,~~ stimulated when molecule interacts w/ regulatory proteins, lac repressor active by itself & binds to operator to switch it off (inducer inactivates repressor)
REPRESSIBLE: activated by a corepressor and can then bind to operator & block transcription, normally off

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



Operon genes (7)
code for proteins
Operon (6)
operater, promoter, genes
RNA polymerase (4)
transcribes
mRNA (5)
codes for proteins
Repressor protein (2)
result of regulatory genes
Operator
binds to repressor
Repressor (2)
stops transcription when active
Regulatory gene (1)
makes repressor
Inducer (3)
deactivates repressor, transcription occurs

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.")
Lac & trp operons are both inhibited by repressors and make enzymes that metabolize or synthesize food. Lac operon is ~~inhibited by~~ a repressible operon and trp operon is an inducible operon b/c repressor becomes active w/ corepressor.

13. What happens when a repressor is bound to the operator?
It blocks RNA polymerase from binding and starting transcription.

14. What is *CAP*? How does *CAP* work?
CAP is a regulatory protein that activates transcription by binding to DNA when glucose ~~(+cAMP)~~ is ~~present~~ scarce. It increases affinity for RNA pol for promoter & directly stimulates gene expression.

15. Explain why CAP binding and stimulation of gene expression is *positive regulation*.
This is positive regulation because the more ~~of~~ cAMP there is and the less glucose, the more of the gene will be transcribed.

16. Describe the relationship between glucose supply, cAMP, and CAP.
When glucose supply is low, cAMP concentration increases and binds to CAP more often, which stimulates RNA pol binding to promoter.

17. How can both repressible and inducible operons be *negative regulators*?
When they bind they stop gene expression, which happens b/c the product concentration increases.

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?
Expression of different genes by cells with the same genome

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 is highly condensed and is not transcribed as easily. Euchromatin is a lightly packaged form, most active region in nucleus (transcription!).

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

Acetyl groups are added to histone tails of nucleosomes, which stops their binding. Chromatin has looser structure.

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

Bases in DNA are methylated, which inactivates the genes (usually for an extended period of time).

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

Inactivation of the genes

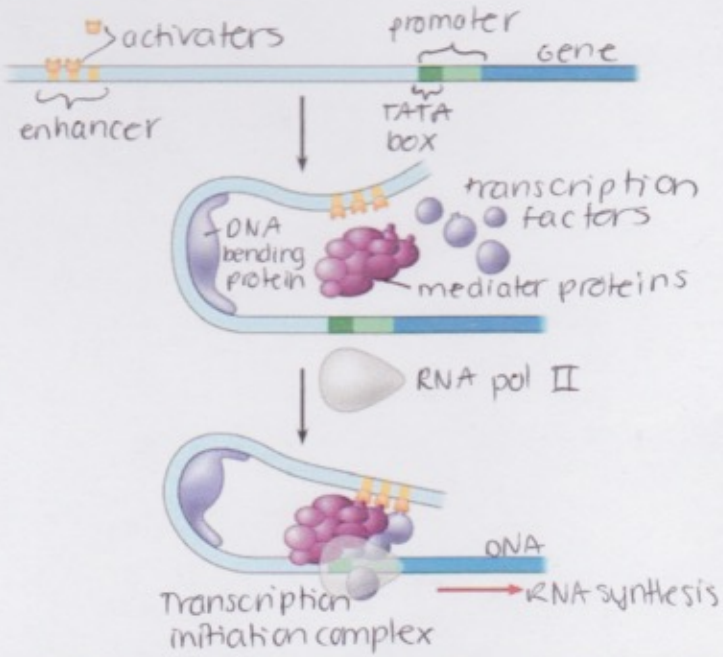
25. What is *genomic imprinting*, and how is it maintained? Give an example discussed earlier in human genetics.

Genomic imprinting is when the gene is only expressed if it comes from a certain parent. Methylation regulates expression of maternal or paternal allele. (size in mice)

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 by mechanisms not directly controlled by nucleotide sequence. Like methylation of chromosomes.

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

Activaters bind to control elements in enhancer.

DNA bending protein brings activaters close to promoter. Transcription factors, proteins, and RNA polymerase are nearby.

Activaters bind to mediators and transcription factors, which helps form an active initiation complex on promoter.

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

Related genes are dispersed throughout chromosomes, but can be activated together through the same enhancers that bind to identical activaters.

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*?

Identical enhancers and activaters (specific combo of control elements w/ every gene)

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

Depends on which segments are treated as introns and spliced away and which are treated as exons.

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

This affects translation by determining how long mRNA will be available for protein synthesis. Less time, less protein.

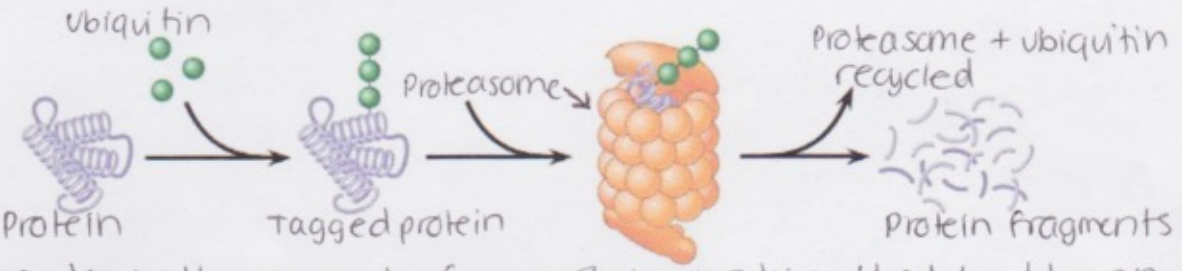
32. How can proteins be activated, processed, and degraded? Give an example or describe each process.

Many proteins undergo modifications before they can be active or be transported (addition of sugars, phosphate groups, shape change, etc.). Also, proteins are marked for destruction by ubiquitin, which shows proteasomes that they need to be degraded.

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.

They are targeted by ubiquitin, which signals proteasomes to destroy them. This might happen to cyclins during the cell cycle because they need to be short-lived for appropriate function.

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.



They lower the amount of a certain protein that had been expressed. Some mutations make cell cycle proteins immune → cancer.

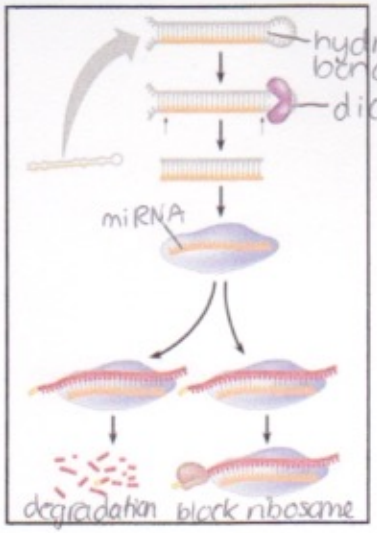
Concept 18.3 Noncoding RNAs play multiple roles in controlling gene expression

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?

Regulate expression at translation and chromatin modification and more. Can degrade or block mRNA and turn off 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*~~.



MicroRNAs can form a complex that blocks translation by a ribosome or degrades mRNA.

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?

Cell division
Cell differentiation
Morphogenesis

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

In differentiation, cells become specialized in structure and function. In morphogenesis, the shape of the organism is created.

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*

    Early divisions distribute cytoplasm into separate cells, containing different molecules.

    b. different *inductive signals*

    Signals from other embryonic cells in the vicinity cause changes in target cells

40. What is meant by *determination*? Explain what this means within an embryonic cell.

    Events that lead to observable differentiation of a cell. After determination, cell is irreversibly committed to its final fate.

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?

    Pattern formation

    Arise in the cytoplasm or outside the cell (determinants and inductive signals)

42. What is controlled by *homeotic genes*?

    Homeotic genes control pattern formation

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*.

44. What are three mechanisms for converting a proto-oncogene to an oncogene?