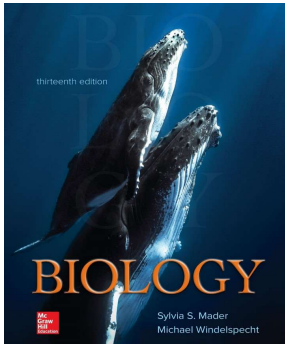


# Gene Regulation



***Biology***

Sylvia S. Mader  
Michael Windelspecht

Chapter 13  
Regulation of Gene  
Expression  
Lecture Outline

See separate FlexArt PowerPoint slides for  
all figures and tables pre-inserted into  
PowerPoint without notes.

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## Outline

13.1 Prokaryotic Regulation

13.2 Eukaryotic Regulation

13.3 Gene Mutations

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## Connection Between Gene Regulation and Physiology and Behavior in Primates

Social status can affect gene expression in macaque monkeys.

- Female monkeys have a dominance hierarchy compared with males in the wild.

The results of an experiment that established a hierarchy of higher- and lower-status female macaques:

- Showed that higher-status female macaques had stronger immune systems and genes that were expressed differently (meaning different genes were turned on and off) than lower-status female macaques.
- This shows that many factors, including social status, can control gene expression.

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# Gene Regulation

## 13.1 Prokaryotic Regulation

Bacteria do not require the same enzymes all the time.

Enzymes are produced as needed.

François Jacob and Jacques Monod (1961) proposed the **operon** model to explain regulation of gene expression in prokaryotes.

- An operon is a group of structural and regulatory genes that function as a single unit.

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## Prokaryotic Regulation (1)

An operon consists of the following components:

- **Promoter**
  - DNA sequence where RNA polymerase first attaches
  - Short segment of DNA
- **Operator**
  - DNA sequence where active repressor binds
  - Short segment of DNA
- **Structural Genes**
  - One to several genes coding for enzymes of a metabolic pathway
  - Transcribed simultaneously as a block
  - Long segment of DNA
- **A regulatory gene** that codes for a repressor protein controls the operon.
  - Regulatory gene is normally located outside the operon.
  - Repressor protein controls whether the operon is active or not.

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## Prokaryotic Regulation (2)

The *trp* Operon

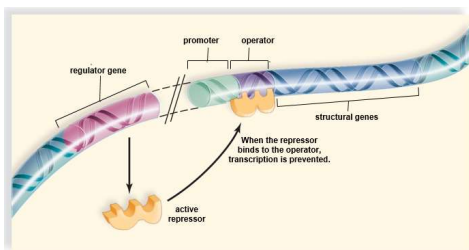
- The regulator codes for a repressor.
- If tryptophan (an amino acid) is absent:
  - The repressor is unable to attach to the operator (expression is normally "on").
  - RNA polymerase binds to the promoter.
  - Enzymes for synthesis of tryptophan are produced.
- If tryptophan is present:
  - It combines with the repressor protein as its corepressor.
  - Repressor becomes functional when bound to tryptophan.
  - Repressor blocks synthesis of enzymes in the pathway for tryptophan synthesis.

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# Gene Regulation

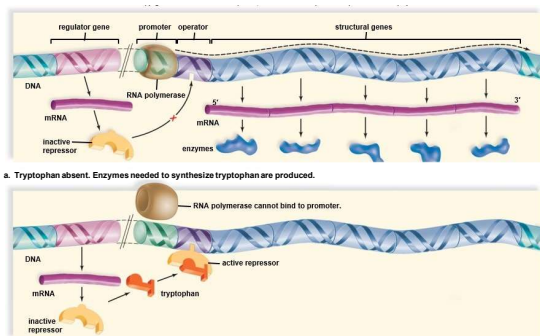
## The *trp* Operon (1)



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## The *trp* Operon (2)



a. Tryptophan absent. Enzymes needed to synthesize tryptophan are produced.

b. Tryptophan present. Presence of tryptophan prevents production of enzymes used to synthesize tryptophan.

[Jump to The \*trp\* Operon \(2\) Long Description](#)

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## Prokaryotic Regulation (3)

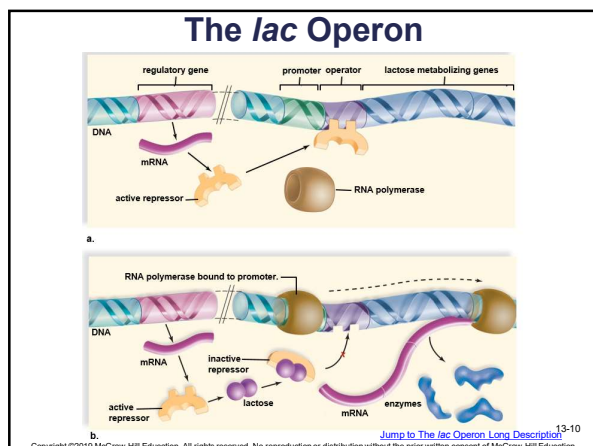
### The *lac* Operon

- The regulator codes for a repressor.
- If lactose (a sugar that can be used for food) is absent:
  - The repressor attaches to the operator.
  - The expression is normally "off."
- If lactose is present:
  - It combines with the repressor and renders it unable to bind to the operator.
  - RNA polymerase binds to the promoter.
  - The three enzymes necessary for lactose catabolism are produced.

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# Gene Regulation




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## Prokaryotic Regulation (4)

Further control of the *lac* operon

- *E. coli* preferentially breaks down glucose.
- The *lac* operon is maximally activated only in the absence of glucose.
- When glucose is absent:
  - Cyclic AMP (cAMP) accumulates.
  - cAMP binds to catabolite activator protein (CAP).
  - CAP, when bound to cAMP, binds to a site near the *lac* promoter.
  - When CAP is bound, RNA polymerase binds better to the promoter.
- The structural genes of the *lac* operon are expressed more efficiently.

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## Prokaryotic Regulation (5)

Further control of the *lac* operon

- When glucose is present
  - There is little cAMP in the cell.
  - CAP is inactive.
- The *lac* operon is not expressed maximally.

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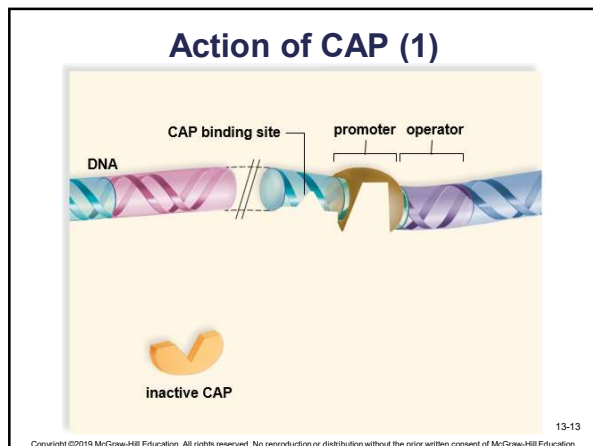
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# Gene Regulation




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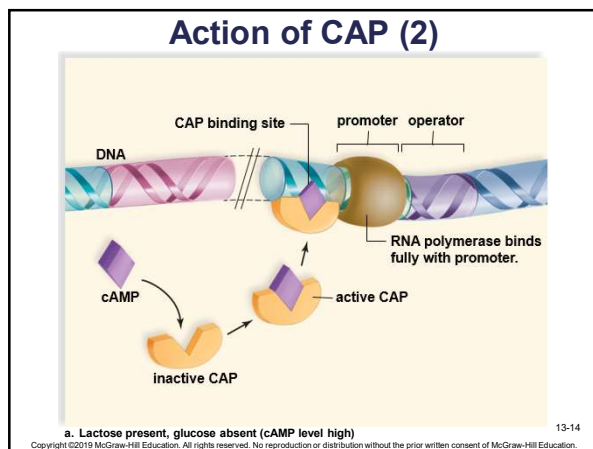
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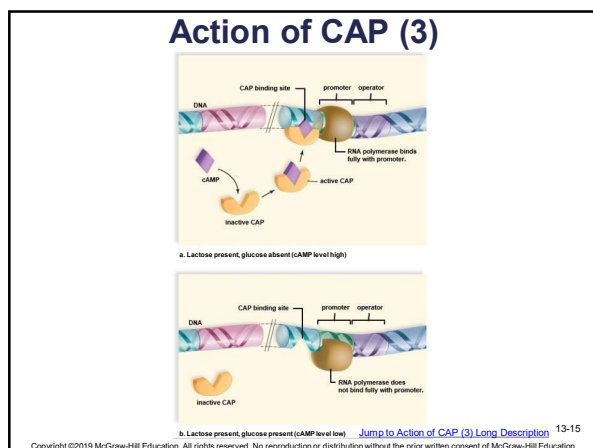
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# Gene Regulation

## 13.2 Eukaryotic Regulation

A variety of mechanisms

Five primary levels of control:

- Nuclear levels
  - Chromatin Structure
  - Transcriptional Control
  - Posttranscriptional Control
- Cytoplasmic levels
  - Translational Control
  - Posttranslational Control

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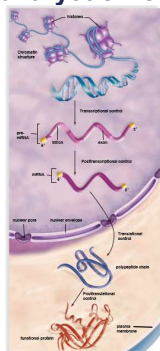
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## Levels of Gene Expression Control in Eukaryotic Cells



[Jump to Levels of Gene Expression Control in Eukaryotic Cells Long Description](#)

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## Eukaryotic Regulation (1)

Chromatin Structure

- Eukaryotic DNA is associated with histone proteins.
  - Together they make up **chromatin**.
- Nucleosomes
  - DNA is wound around groups of eight molecules of histone proteins.
  - It looks like beads on a string.
  - Each bead is called a nucleosome.
- The levels of chromatin packing are determined by the degree of nucleosome coiling.

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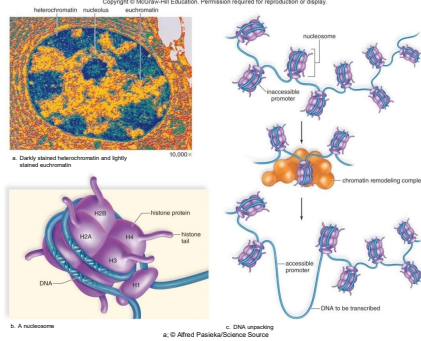
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# Gene Regulation

## Chromatin Structure Regulates Gene Expression



## Eukaryotic Regulation (2)

### Euchromatin

- Loosely coiled DNA
- Transcriptionally active

### Heterochromatin

- Tightly packed DNA
- Transcriptionally inactive

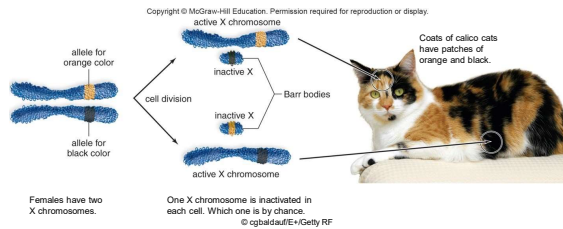
### Barr Body

- Females have two X chromosomes, but only one is active.
- The other X chromosome is tightly packed along its entire length and is inactive.
- The inactive X chromosome is called a Barr body.
  - An example is female calico cat which has patches of orange and black in its coat depending on which X chromosome is in the Barr bodies of cells in patches.

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## X-Inactivation in Mammalian Females



# Gene Regulation

## Epigenetic Inheritance

Histone modification may be linked to epigenetic inheritance in which variations in the pattern of inheritance are not due to changes in the sequence of DNA nucleotides.

Epigenetic inheritance refers to inheritance patterns not dependent on genes themselves.

Explains unusual inheritance patterns

It may also play a role in growth, aging, and cancer.

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## Eukaryotic Regulation (3)

### Transcriptional Control

- Transcription is controlled by proteins called **transcription factors**.
- Transcription factors are proteins that help regulate transcription by assisting the binding of the RNA polymerase to the promoter.
- A transcriptional activator is a DNA-binding protein that:
  - Binds to **enhancer** DNA
    - Regions of DNA where factors that regulate transcription can also bind.
  - Transcription factors are always present in the cell, but most likely have to be activated before they will bind to DNA.

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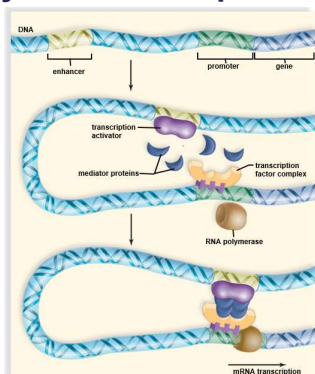
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## Eukaryotic Transcription Factors



[Jump to Eukaryotic Transcription Factors Long Description](#)

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# Gene Regulation

## Eukaryotic Regulation (4)

**Posttranscriptional control** operates on the primary mRNA transcript.

Given a specific primary transcript:

- Excision of introns can vary.
- Splicing of exons can vary.
- It determines the type of mature transcript that leaves the nucleus.

May also control the speed of mRNA transport from nucleus to cytoplasm

- It will affect the number of transcripts arriving at rough ER and, therefore, the amount of gene product realized per unit time.

Example: The hypothalamus and thyroid gland produce a protein hormone called calcitonin, but the mRNA that leaves the nucleus is not the same in both types of cells.

- The thyroid and hypothalamus therefore release different versions of the hormone.

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## Small RNA (sRNA) Molecules Regulate Gene Expression (1)

The noncoding transcribed DNA is used to form small RNA (**sRNA**) molecules.

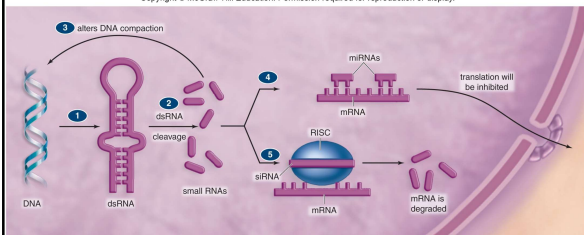
- These are involved in gene regulation and function at multiple levels of gene expression.
- Some of the sRNA molecules regulate transcription and others regulate translation.
- sRNA molecules are the source of **microRNAs** (miRNAs) regulating translation by causing the destruction of mRNAs before they can be translated.
- They also are the source of **small-interfering RNAs** (siRNAs) that form a silencing complex that targets specific mRNAs for breakdown, preventing their expression.
- This is referred to as **RNA interference**.

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## Small RNA (sRNA) Molecules Regulate Gene Expression (2)

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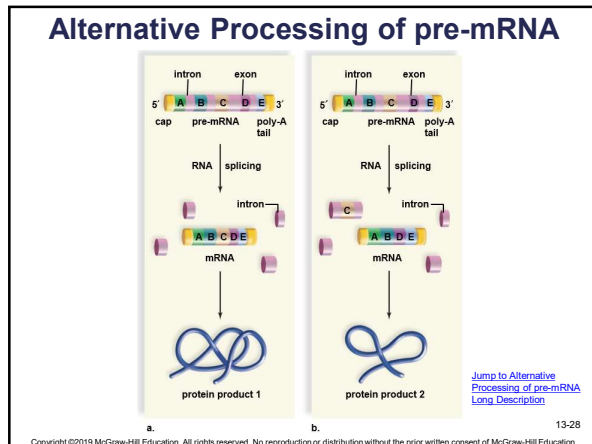


[Jump to Small RNA \(sRNA\) Molecules Regulate Gene Expression \(2\) Long Description](#)

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## Gene Regulation



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## Eukaryotic Regulation (5)

**Translational control** determines the degree to which mRNA is translated into a protein product.

Features of the mRNA affect whether translation occurs and how long the mRNA remains active.

- Presence of 5 prime cap
- Length of poly-A tail on 3 prime end

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## Eukaryotic Regulation (6)

**Posttranslational control** affects the activity of a protein product.

Posttranslational control is accomplished by regulating

- Activation
- Degradation rate

Proteases are enzymes that break down proteins, and by doing so they help regulate gene expression.

- They regulate how long a protein remains active in the cell.
- They are confined to proteasomes or lysosomes to protect the cell.

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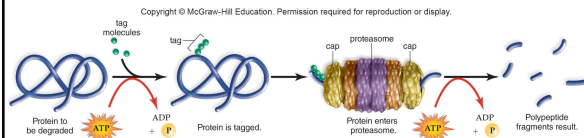
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# Gene Regulation

## Eukaryotic Regulation (7)



[Jump to Eukaryotic Regulation \(7\) Long Description](#)

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## 13.3 Gene Mutations

A **gene mutation** is a permanent change in the sequence of bases in DNA.

The effects of a gene mutation can range from

- No effect on protein activity to
- Complete inactivation of the protein

Germ-line mutations occur in sex cells.

Somatic mutations occur in body cells.

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## Gene Mutations (1)

### Spontaneous mutations

- Chemical changes in DNA that lead to mispairing during replication
- Movement of transposons from one chromosomal location to another
- Replication Errors
  - DNA polymerase
    - Proofreads new strands
    - Generally corrects errors
  - Overall mutation rate is 1 in 1,000,000,000 nucleotide pairs replicated.

### Induced mutations

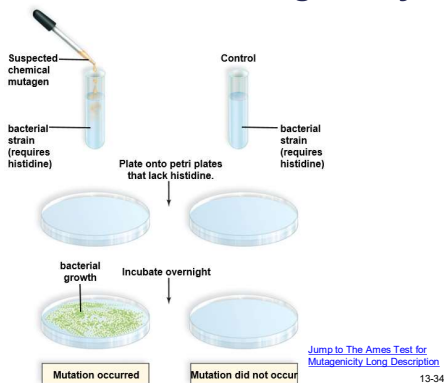
- Caused by **mutagens** such as radiation and organic chemicals
- Many mutagens are also **carcinogens** (cancer-causing).
- Environmental Mutagens
  - Ultraviolet radiation
  - Tobacco smoke

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# Gene Regulation

## The Ames Test for Mutagenicity



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## Gene Mutations (2)

### Point Mutations

- One type of point mutation is a base substitution.
- Involves a change in a single DNA nucleotide
- Change one codon to a different codon.
- Effects on the protein vary:
  - Nonfunctional
  - Reduced functionality
  - Unaffected

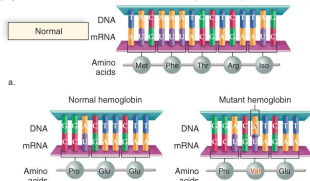
### Frameshift Mutations

- One or two nucleotides are either inserted or deleted from DNA.
- The protein is always rendered nonfunctional.
  - Normal: THE CAT ATE THE RAT
  - After deletion: THE ATA TET HER AT
  - After insertion: THE CCA TAT ETH ERA T

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## Point Mutations (1)

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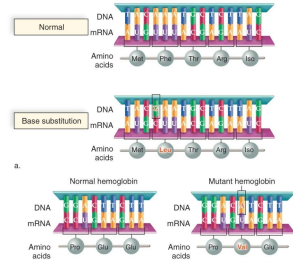
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# Gene Regulation

## Point Mutations (2)

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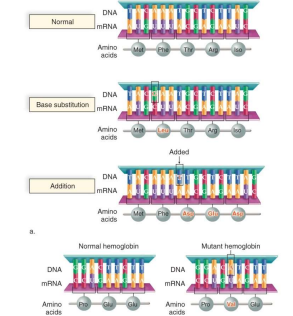
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## Point Mutations (3)

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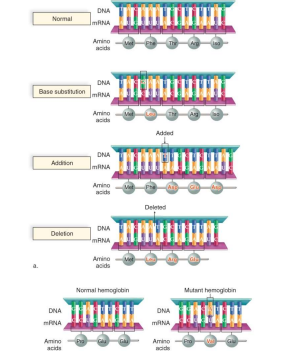
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## Point Mutations (4)

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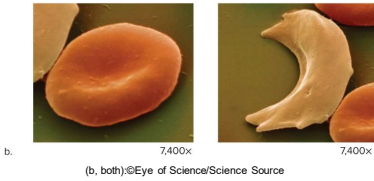
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# Gene Regulation

## Point Mutation in Hemoglobin

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[Jump to Point Mutation in Hemoglobin Long Description](#)

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## Gene Mutations (3)

Development of cancer involves a series of accumulating mutations.

Proto-oncogenes – Stimulate cell division

- Mutated proto-oncogenes become oncogenes that are always active.

Tumor suppressor genes – inhibit cell division

Mutations in oncogene and tumor suppressor genes:

- Stimulate the cell cycle uncontrollably
- Lead to tumor formation

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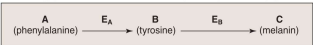
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## Nonfunctional Proteins

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If a faulty enzyme is inserted into a metabolic pathway, a person may be unable to convert one molecule to another with serious consequences.

In the disorder phenylketonuria (PKU), phenylalanine builds up in the system and the excess causes an intellectual disability.

In androgen insensitivity, cells are unable to respond to testosterone due to a faulty receptor for testosterone.

- Female instead of male genitals form, and female instead of male secondary sex characteristics occur at puberty.

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