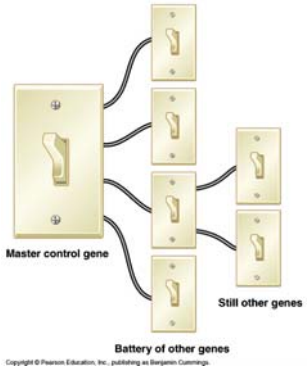
Gene Expression



•Researchers use mutants to find out what the normal (nonmutated) version of a gene does.

•Although wing formation involves many genes, this abnormality is caused by the abnormality of a single gene.

•Because that one gene controls the activity of many other genes.

The Control of Gene Expression

Gene expression- the flow of information from genes to proteins.

•Is subject to control mainly by **turning on and off genes**.

i.e.#1- If all the DNA in every cell in a developing embryo were constantly active, every cell would be like every other cell.

i.e#2.- For cells in a fruit fly's eye to develop into a lens, genes that produce lens proteins must be turned on, and other genes must be turned off.

•Cells become specialized in structure and function because only certain genes of the genome are expressed.

Genome- a complete set of an organisms genes.

•Mutant organisms give researchers clues to the function of normal genes- for example genes that direct embryonic development.

Gene Regulation in Prokaryotes

•Proteins interacting with DNA turn prokaryotic genes on or off in response to environmental changes.

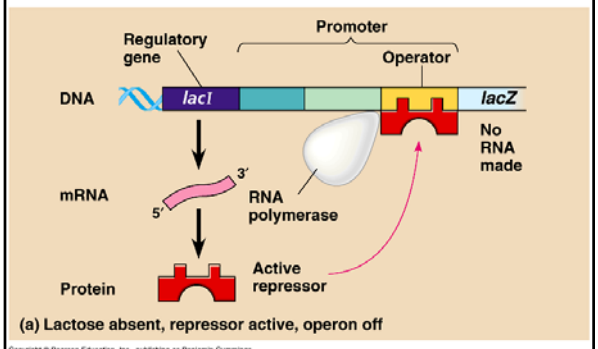
•This model of gene control was first proposed as a hypothesis in 1961 by Jacob & Monrod, for control of the **lactose** utilization enzymes in ***E. Coli***.

•An **operon** consists of several DNA sequences coding for different enzymes, all involved in the same cellular process.

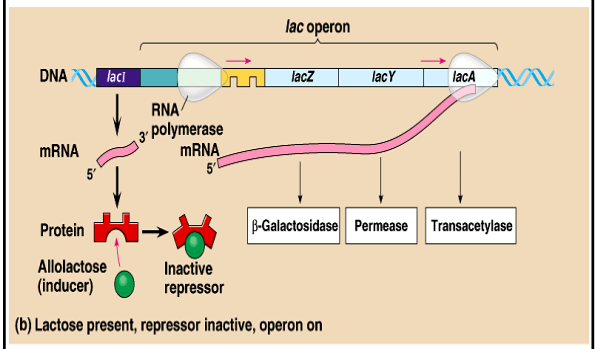
•Expression of an operon is controlled as a unit. Other DNA sequences in and near the operon control the operons expression.

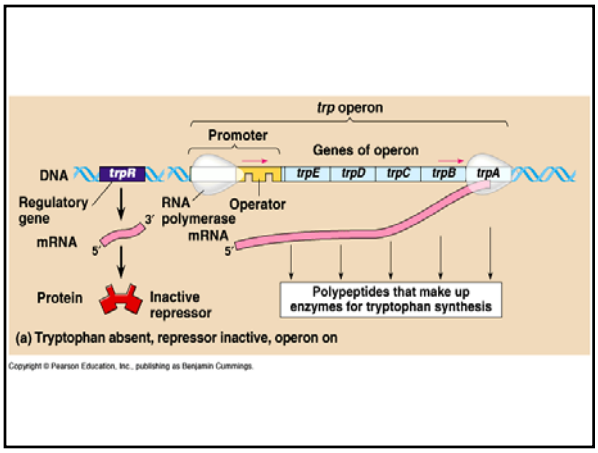
•The presence or absence of the enzyme's substrate turns on or off the controls.

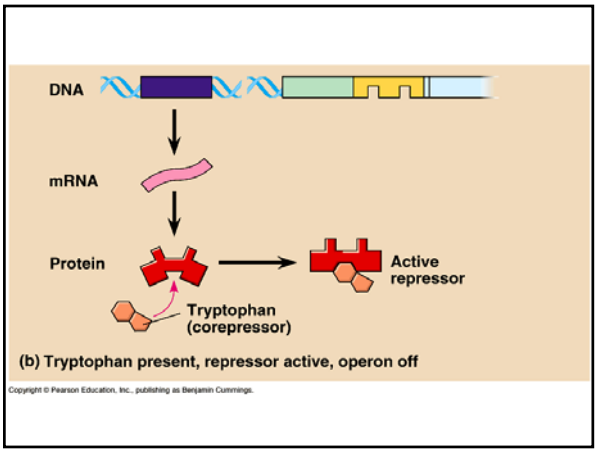
•When the ***lac*** operon is "turned off," a regulator gene continues to be transcribed and translated in to a **repressor protein**. The repressor protein binds with the operator region of the operon, repressing the transcription of the genes further along the operon.



•When the ***lac*** operon is "turned on," the regulator gene continues to be transcribed.







Cellular Differentiation and Gene Regulation in Eukaryotes

Cellular differentiation- when cells become specialized in structure & function.

Differentiation produces a variety of specialized cells in eukaryotes.

•Producing eukaryotic organelles and regulating their functions require a much more complex network of gene control.

•In multicellular eukaryotes, there is the added complexity of regulating what kinds of cells are produced when and where.

•Muscle, nerve, sperm, and blood cells (and other cell types) of a single animal are all derived from the by repeated cell divisions from the zygote.

Zygote- the fertilized egg, which is diploid, that results from the union of a sperm cell nucleus and an egg cell nucleus.

•The structure of each different cell type is visibly different, reflecting its function.

i.e.- **Muscle cells** are long with multiple nuclei, the stripes result from the arrangement of the proteins that enable the cell to contract.

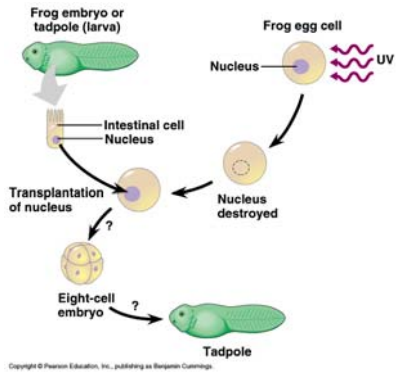
Sperm cells; their long flagella can propel them through a women's reproductive tract.

Red Blood Cells (RBCs) lack nuclei and other organelles, w/o organelles taking up space a RBC can literally be packed with oxygen carrying hemoglobin.

Specialized cells may retain all of their genetic potential

•Experimental evidence supports the retention of all a multicellular organism's DNA in each of the differentiated cells, in most cases.

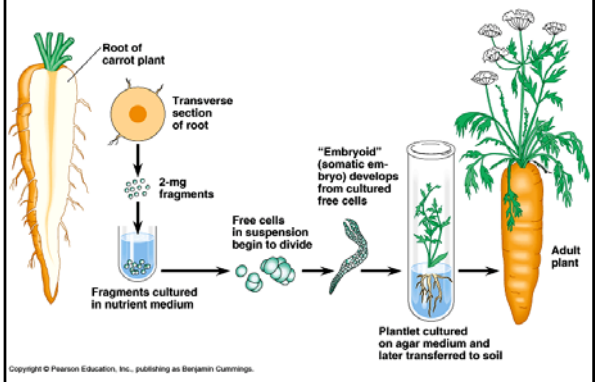
•In the 1950s, **Briggs & King** transplanted nuclei from differentiated cells lining a tadpole's intestine to unfertilized, enucleated frog eggs. Many such treated eggs developed into normal tadpoles.



•In 1997 Dolly the sheep was born. This was the first successful cloning of a mammal from a dedifferentiated nucleus. This dedifferentiated nucleus was transplanted into the enucleate egg of another sheep and implanted into the uterus of a third sheep.

•In some naturally occurring situations, differentiated cells' DNA may "dedifferentiate" to give rise to other cell types. Many animals can regenerate lost parts from differentiated cells that remain nearby.

•Many plants can regenerate completely from differentiated cells. Plant tissue culture on sterile culture media is now used widely to produce hundreds or thousands of genetic clones of domestic plants.



•In many cases, particularly in animals, differentiated cells do not normally dedifferentiate. For instance most animals lack the ability to regenerate whole bodies from single isolated cells.

Each type of differentiated cell has a particular pattern of expressed genes

•As a developing embryo undergoes successive cell divisions, different genes are active in different cells at different times.

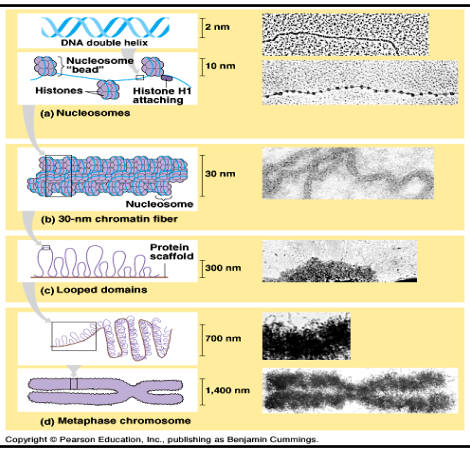
•Some genes (for example, those involved in glycolysis pathway) are active in all metabolizing cells.

•Other genes are turned on in only one cell line (for example the crystalline gene in lens cells).

DNA packing in eukaryotic chromosomes helps regulate gene expression

•The total DNA in a human cell's 46 chromosomes would stretch 3 meters. (this amount of DNA is packed in cell nuclei as small as 5 μm in diameter)

•All the DNA fits because of elaborate packing: wrapping around **histones** and other proteins into **nucleosomes**, coiling, supercoiling, and additional folding into chromosomes.



•DNA packing prevents gene expression, most likely by preventing transcription.

•An interesting known example of the role of gene packing in the control of expression is X-chromosome inactivation in the cells of female animals. Certain cell lines have one or the other X chromosome (inherited from the individual's mother or father) inactivated; thus, there can be a random mosaic of expression of these two X chromosomes, as seen in tortoiseshell

Complex assemblies of proteins control eukaryotic transcription

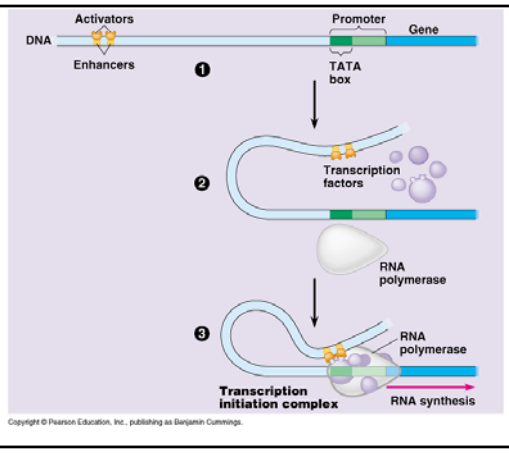
•In both prokaryotes and eukaryotes gene regulation is based on the regulation of transcription. However, whereas *prokaryotes combine several regulated genes into one operon*, **eukaryotes apparently tend to regulate individual genes**. Thus in eukaryotes there are many more regulatory proteins involved.

•Activation appears to be of greater importance in the regulation of eukaryotic gene expression than is repression. Transcription factors (of which activators are an example) interact with enhancer sites in regulating the binding of RNA polymerase to a gene's promoter.

•The binding of activators to DNA sequences called enhancers initiates transcription. Unlike prokaryotes, in eukaryotes enhancers are usually at a distance from the gene they regulate.

•Repressor protein interaction with silencer sites on DNA inhibits the start of transcription.

•Eukaryotes do not have operons and related genes are often found scattered about the genome. Regulation of functionally related genes seems to be dependent on their association with specific enhancer(s).



Eukaryotic RNA is Processed: Cap and tail are added and noncoding segments removed

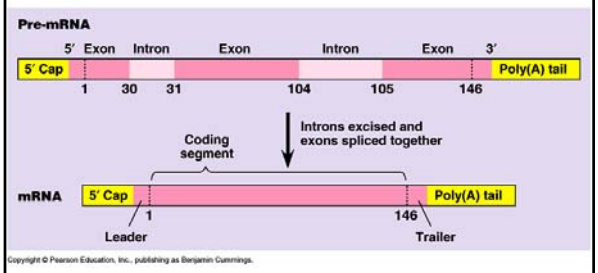
•Structural compartmentalization of eukaryotes offers opportunities for the post-transcriptional control of gene expression.

•Eukaryotic mRNA is capped, tailed, and edited. These actions occur while the mRNA is still in the nucleus. Additions of cap and tail seem to help protect the mRNA from attack by cellular enzymes and may enhance translation.

•The noncoding stretches of eukaryotic genes are called **introns** (inhibited sequences), and the parts that are expressed are called **exons** (expressed sequences).

•Both introns and exons are transcribed. Before leaving the nucleus, the introns are removed from the mRNA transcript, and the remaining exons are splice together in a process known a **RNA splicing**.

•**Alternative splicing** provides a cell with several possible products from one gene region.



•It has been suggested that introns make genes longer, thereby increasing the possibility of crossovers between exons and providing another mechanism to provide genetic diversity.

Translation and later stages of gene expression are also subject to regulation

•In addition to the regulation of transcription and post-transcriptional modification, gene expression can also be regulated at the level of **mRNA degradation**, **translation initiation**, **protein activation**, and **protein breakdown**.

•The lifetime of mRNA molecules varies, controlling the amount of protein translated from a single transcription and post-transcriptional processing event. In nonmammalian vertebrates, red blood cells lose their nuclei, but not their ribosomes and mRNA, which can continue to translate into hemoglobin for a month or more.

•Some inhibitory control of the process of translation is known, such as the inhibitory action of a protein found in red blood cells when heme sub units are not available.

•Post-translational control mechanisms in eukaryotes often involve cutting polypeptides into smaller, active final products.

•Another post-translational control affects how fast protein products are degraded.

Cascades of gene expression and cell-to-cell signaling direct development of an animal

•An example of these cascades can be seen in the determination of which end of a fruit fly egg cell will become the head and which end will become the tail. These events occur within the ovaries of the mother fly and involve the following series of events.

1. The egg cell produces (gene activation) a protein that signals the adjacent follicle cells.

2. These follicle cells are stimulated (gene activation) to produce proteins that provide feedback to the egg cell.

3. As a result, microtubules within the egg cell are oriented along what will become the new fly's head-to-tail axis, with different types of mRNA located at to different ends.

4. After fertilization, repeated mitosis results in development of the embryo from the zygote. Translation of the head mRNA results in the production of a protein concentration gradient from head to tail. This protein concentration gradient corresponds to a gradient of gene expression.

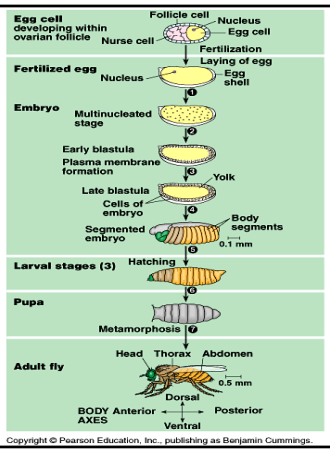
5. This gradient of gene expression results in the development of the fly's body segments.

6. The cascade continues as the gradient of gene expression results in further differentiation and specialization of the body segments.

7. The genes that regulate these major features of the body plan (body segments and the body parts that develop at each segment) are called **homeotic genes**.

8. Homeotic genes are master controls that function during embryonic development in animals to determine the developmental fates of different groups of cells destined to become different tissues.

9. Their improper functioning can lead to bizarre changes in morphology.

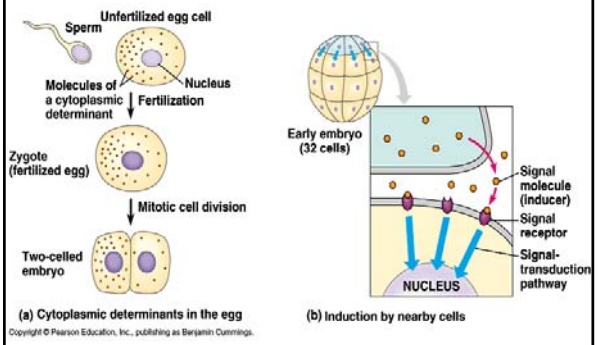


Signal-transduction pathways convert messages received at the cell surface into responses within the cell

•The gene expression of one cell can affect the gene expression of other cells. This is the result of signal transduction pathways.

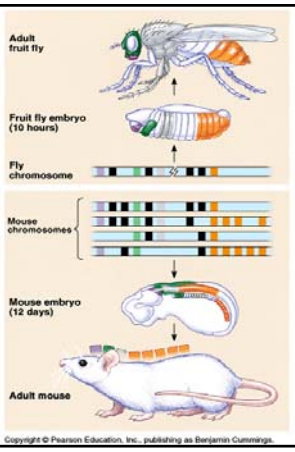
The main components of a signal transduction pathway are:

- the signaling cell secretes signal molecules.
- the signal molecules bind to the receptors on the target cell's plasma membrane.
- this results in a cascade of events that leads to the activation of a specific transcription factor.
- the transcription factor activates a specific gene, resulting in the expression of a protein for which the gene codes.



Key developmental genes are very ancient

- Virually every homeotic gene found in fruit flies contains a common 180 nucleotide sequence. Very similar sequences have been found in virtually all eukaryotic organisms studied.
- These nucleotide sequences called **homeoboxes**, translate into a small polypeptide sequence that binds to specific DNA sequences and thereby regulate their expression.

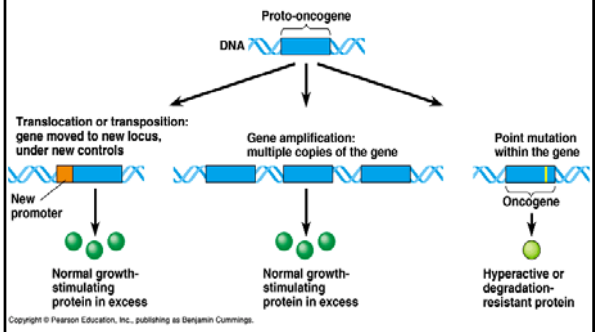


The Genetic Basis of Cancer

- Cancer results from mutations in genes that control cell division.
- In all its forms, cancer is a disease of gene expression.
- Viruses can cause cancer by inserting cancer-causing genes (**oncogenes**) into the host genome.

  i.e.- STD Viruses can cause cervical cancer.

- A normal gene with the potential to become an oncogene is called a **proto-oncogene**. Proto-oncogenes usually code for proteins that stimulate cell division or affect growth-factor synthesis or function. A mutation that results in a failure to regulate the production of these proteins will result in the conversion of a proto-oncogene into an oncogene.
- Most cancers occur in somatic cells, thus they are not inherited.
- **Mutations in tumor-suppressor genes**, genes whose products inhibit cell division, also contribute to uncontrolled cell division.



Oncogene proteins and faulty tumor-suppressor proteins can interfere with normal signal transduction pathways

•In response to a growth factor, a signal-transduction pathway can act to stimulate cell division. In response to a growth-inhibiting factor a signal transduction pathway can act to inhibit cell division.

•A mutation in a proto-oncogene may produce an oncogene that in turn may produce a hyperactive version of a protein that stimulates cell division , even in the absence of growth factor. Moreover, abnormal amounts or versions of growth factor, transcription factor, and so on could all result in the abnormal excess production of proteins that stimulate cell division.

•Faulty tumor-suppressor genes produce faulty tumor-suppressor proteins that may fail to inhibit cell division.

Multiple genetic changes underlie the development of cancer

•More than one somatic mutation is required to produce a significant cancer.

•Colon cancer first appears as an unusually high rate of cell division occurring in apparently normal cells. Next a benign tumor (**polyp**)appears, followed by the development of this benign tumor into a malignant tumor.

•Underlying these changes are changes at the DNA level (that are passed on to daughter cell via the cell cycle) to proto-oncogenes and tumor-suppressor gene (including tumor suppressor genes that code for proteins involved in the repair of damaged DNA). That several mutations required explains why some cancers can take a long time to develop.

Changes in lifestyle can reduce the risk of cancer

•There is much evidence that the tendency to get certain cancers is hereditary.

•Cancer-causing agents other than viruses are called **carcinogens**.

•Mutagenic chemicals cause mutations. In general, mutagens are carcinogens.
i.e.- X-rays and UV radiation

- The largest group of carcinogens are mutagenic chemical compounds. Substances from **tobacco** are known to cause more cases and types of cancer than any other single agent.

- Exposure to carcinogens is **additive**, so long term exposure to these agents is more likely to cause cancer.

- Tissues in which cells have a high rate of cell division are more likely to become cancerous.