HOW AND WHY GENES ARE REGULATED

- Every somatic cell in an organism contains identical genetic instructions.
  - They all share the same genome.
  - So what makes cells different from one another?
- In **cellular differentiation**, cells become specialized in
  - structure and
  - function.
- Certain genes are turned on and off in the process of **gene regulation**.

Patterns of Gene Expression in Differentiated Cells

- In **gene expression**,
  - a gene is turned on and transcribed into RNA and
  - information flows from
    - genes to proteins and
    - genotype to phenotype.
- Information flows from DNA to RNA to proteins.
- The great differences among cells in an organism must result from the selective expression of genes.

Gene Regulation in Bacteria

- Natural selection has favored bacteria that express
  - only certain genes
  - only at specific times when the products are needed by the cell.
- So how do bacteria selectively turn their genes on and off?
- An **operon** includes
  - a cluster of genes with related functions and
  - the control sequences that turn the genes on or off.
- The bacterium *E. coli* uses the *lac* operon to coordinate the expression of genes that produce enzymes used to break down lactose in the bacterium's environment.
- The *lac* operon uses
  - a **promoter**, a control sequence where the transcription enzyme attaches and initiates transcription,
  - an **operator**, a DNA segment that acts as a switch that is turned on or off, and
  - a **repressor**, which binds to the operator and physically blocks the attachment of RNA polymerase and transcription.

Gene Regulation in Eukaryotic Cells

- Eukaryotic cells have more complex gene regulating mechanisms with many points where the process can be turned on or off.
- The multiple mechanisms that control gene expression are like the many control valves along a water supply.

The Regulation of DNA Packing

- Cells may use DNA packing for long-term inactivation of genes.
- **X chromosome inactivation**
  - takes place early in embryonic development,
  - occurs in female mammals, and
  - is when one of the two X chromosomes in each cell is inactivated at random.
- All of the descendants of each cell will have the same X chromosome turned off.
- If a female is heterozygous for a gene on the X chromosome,

  - about half her cells will express one allele and
  - the others will express the alternate allele.

The Initiation of Transcription

- The initiation of transcription is the most important stage for regulating gene expression.
- In prokaryotes and eukaryotes, regulatory proteins
  - bind to DNA and
  - turn the transcription of genes on and off.
- Transcription in eukaryotes, unlike in prokaryotes, is complex, involving many proteins, called **transcription factors**, that bind to DNA sequences called **enhancers**.
- Repressor proteins called **silencers**
  - bind to DNA and
  - inhibit the start of transcription.
- **Activators**
  - are more typically used by eukaryotes than silencers and
  - turn genes on by binding to DNA.

RNA Processing and Breakdown

- The eukaryotic cell
  - localizes transcription in the nucleus and
  - processes RNA in the nucleus.
- RNA processing includes the
  - addition of a cap and tail to the RNA,
  - removal of any introns, and
  - splicing together of the remaining exons.
- In **alternative RNA splicing**, exons may be spliced together in different combinations, producing more than one type of polypeptide from a single gene.
- A typical human gene contains about ten exons, with
  - nearly all human genes spliced in at least two different ways and
  - some spliced hundreds of different ways!
- Eukaryotic mRNAs
  - can last for hours to weeks to months and
  - are all eventually broken down and their parts recycled.

microRNAs

- Small single-stranded RNA molecules, called microRNAs (miRNAs), bind to complementary sequences on mRNA molecules in the cytoplasm.
- Some trigger the breakdown of their target mRNA, and others block translation.
- It has been estimated that miRNAs may regulate the expression of up to one-third of all human genes, yet miRNAs were unknown 20 years ago!

The Initiation of Translation

- The process of translation offers additional opportunities for regulation by regulatory molecules.

Protein Activation and Breakdown

- Post-translational control mechanisms in eukaryotes
  - occur after translation and
  - often involve cutting polypeptides into smaller, active final products.
- The selective breakdown of proteins is another control mechanism operating after translation.

Cell Signaling

- In a multicellular organism, gene regulation can cross cell boundaries.
- A cell can produce and secrete chemicals, such as hormones, that affect gene regulation in another cell.

Homeotic genes

- Master control genes called **homeotic genes** regulate groups of other genes that determine what body parts will develop in which locations.
- Mutations in homeotic genes can produce bizarre effects.
- Similar homeotic genes help direct embryonic development in nearly every eukaryotic organism examined so far.

DNA Microarrays: Visualizing Gene Expression

- A DNA microarray allows visualization of gene expression.
- The pattern of glowing spots enables the researcher to determine which genes were being transcribed in the starting cells.
- Researchers can thus learn which genes are active
  - in different tissues or
  - in tissues from individuals in different states of health.

CLONING PLANTS AND ANIMALS

The Genetic Potential of Cells

- Differentiated cells
  - all contain a complete genome and
  - have the potential to express all of an organism's genes.
- Differentiated plant cells can develop into a whole new organism.
- The somatic cells of a single plant can be used to produce hundreds or thousands of identical organisms—clones from a single plant.
- Plant cloning demonstrates that cell differentiation in plants
  - is reversible and
  - does not cause irreversible changes in the DNA.
- Plant cloning is now used extensively in agriculture.
- **Regeneration**
  - is the regrowth of lost body parts and
  - occurs, for example, in the regrowth of the legs of salamanders.
- During regeneration of the leg, cells in the leg stump
  - reverse their differentiated state,
  - divide, and
  - then differentiate again to give rise to a new leg.

Reproductive Cloning of Animals

- **Nuclear transplantation** involves
  - replacing the nucleus of an egg cell with the nucleus from a differentiated cell from an adult body and
  - allowing the egg to develop into an adult.
- In 1997, Scottish researchers produced Dolly, a sheep, by replacing the nucleus of an egg cell with the nucleus of an adult somatic cell.
- This procedure is called **reproductive cloning**, because it results in the birth of a new animal.

Practical Applications of Reproductive Cloning

- Since Dolly, reproductive cloning has been used to clone many species of mammals, including mice, horses, dogs, mules, cows, pigs, rabbits, ferrets, and cats.
- Reproductive cloning has been used to restock populations of endangered species including
  - a wild mouflon (a small European sheep),
  - a banteng (a Javanese cow),
  - a gaur (an Asian ox), and
  - gray wolves.
- However, cloning does not increase genetic diversity, which may be essential to long-term species survival.

Human Cloning

- Cloning of mammals
  - has heightened speculation about human cloning and
  - is very difficult and inefficient.
- Critics raise practical and ethical objections to human cloning.

Therapeutic Cloning and Stem Cells

- The purpose of **therapeutic cloning** is
  - not to produce a viable organism but
  - to produce embryonic stem cells.

Embryonic Stem Cells

- **Embryonic stem cells (ES cells)**
  - are derived from blastocysts and
  - can give rise to all the specialized cells in the body.

Adult Stem Cells

- **Adult stem cells**
  - are cells in adult tissues and
  - generate replacements for some of the body's cells.
- Unlike embryonic ES cells, adult stem cells
  - are partway along the road to differentiation and
  - usually give rise to only a few related types of specialized cells.

Umbilical Cord Blood Banking

- Umbilical cord blood
  - can be collected at birth,
  - contains partially differentiated stem cells, and
  - has had limited success in the treatment of a few diseases.
- The American Academy of Pediatrics recommends cord blood banking only for babies born into families with a known genetic risk.

THE GENETIC BASIS OF CANCER

- Cancer is a variety of diseases in which cells
  - experience changes in gene expression and
  - escape from the control mechanisms that normally limit their growth and division.

Genes That Cause Cancer

- As early as 1911, certain viruses were known to cause cancer.
- **Oncogenes** are
  - genes that cause cancer and

  - found in viruses.

Oncogenes and Tumor-Suppressor Genes

- **Proto-oncogenes** are
  - normal genes with the potential to become oncogenes,
  - found in many animals, and
  - often genes that code for **growth factors**, proteins that stimulate cell division.
- A cell can acquire an oncogene
  - from a virus or
  - from the mutation of one of its own proto-oncogenes.
- **Tumor-suppressor genes**
  - inhibit cell division,
  - prevent uncontrolled cell growth, and
  - may be mutated and contribute to cancer.
- Researchers have identified many mutations in both tumor-suppressor and growth factor genes that are associated with cancer.

The Progression of a Cancer

- Nearly 150,000 Americans will be stricken by cancer of the colon (the main part of the large intestine) this year.
- Colon cancer, like many cancers,
  - spreads gradually and
  - is produced by more than one mutation.
- The development of a malignant tumor is accompanied by a gradual accumulation of mutations that
  - convert proto-oncogenes to oncogenes and
  - knock out tumor-suppressor genes.

"Inherited" Cancer

- Most mutations that lead to cancer arise in the organ where the cancer starts.
- In familial or inherited cancer,
  - a cancer-causing mutation occurs in a cell that gives rise to gametes and
  - the mutation is passed on from generation to generation.
- Breast cancer
  - is usually not associated with inherited mutations and
  - in some families can be caused by inherited *BRCA1* cancer genes.

Cancer Risk and Prevention

- Cancer
  - is the second leading cause of death (after heart disease) in most industrialized countries and
  - can be caused by **carcinogens**, cancer-causing agents, found in the environment, including
    - tobacco products, alcohol, and ultraviolet light from the sun.
- Exposure to carcinogens
  - is often an individual choice and
  - can be avoided.
- Some studies suggest that certain substances in fruits and vegetables may help protect against a variety of cancers.