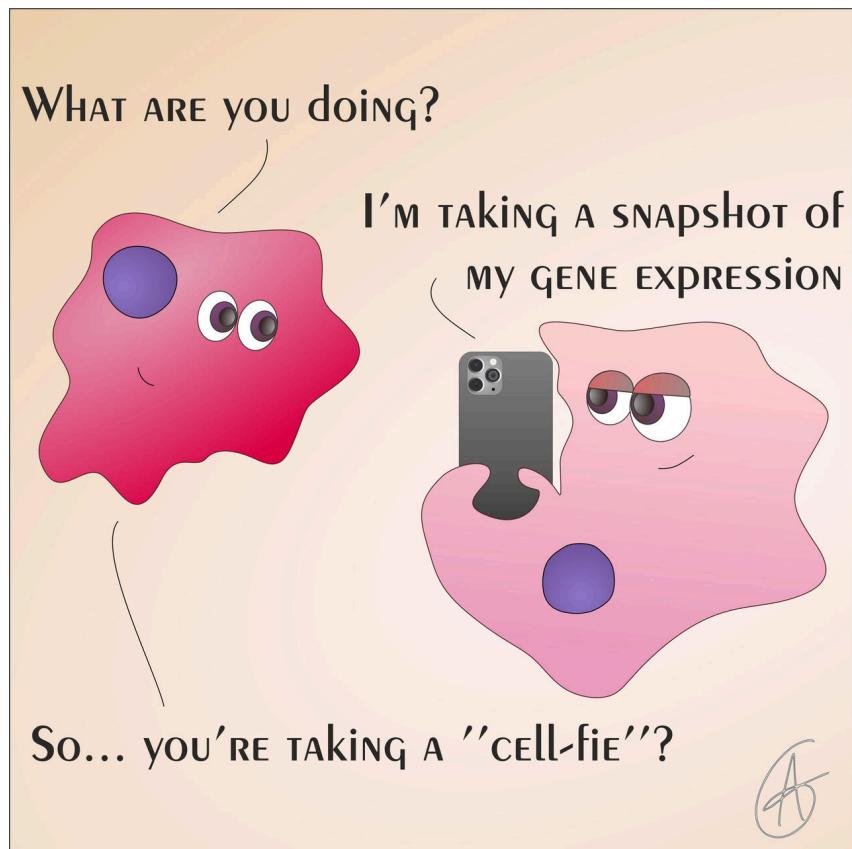


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Prokaryotic and Eukaryotic Gene Regulation

To understand how gene expression is regulated, we need to know how genes make proteins in cells. This process happens in both prokaryotic and eukaryotic cells, but in slightly different ways.

<https://study.com/academy/lesson/video/differential-gene-expression-definition-examples.html>

1. **Promoter** – A DNA sequence where RNA polymerase binds to begin transcription.
2. **ORI (Origin of Replication)** – The starting point for DNA replication.
3. **Operator** – A regulatory DNA sequence where repressor proteins bind to block transcription.
4. **Enhancer** – A distant DNA element that increases transcription when bound by activator proteins.
5. **Silencer** – A DNA sequence that represses gene expression when bound by repressors.
6. **Repressor Binding Site** – Specific DNA region (often the operator) where repressors bind to inhibit gene expression.
7. **Coding Sequence (CDS)** – The actual DNA sequence that is transcribed into mRNA and then translated into protein.
8. **Terminator** – A sequence that signals the end of transcription.
9. **TATA Box** – A specific promoter element found in eukaryotes, where transcription factors bind.
10. **Untranslated Regions (UTRs)** – Sequences at the 5' and 3' ends of mRNA that are not translated into protein but help regulate translation and mRNA stability.

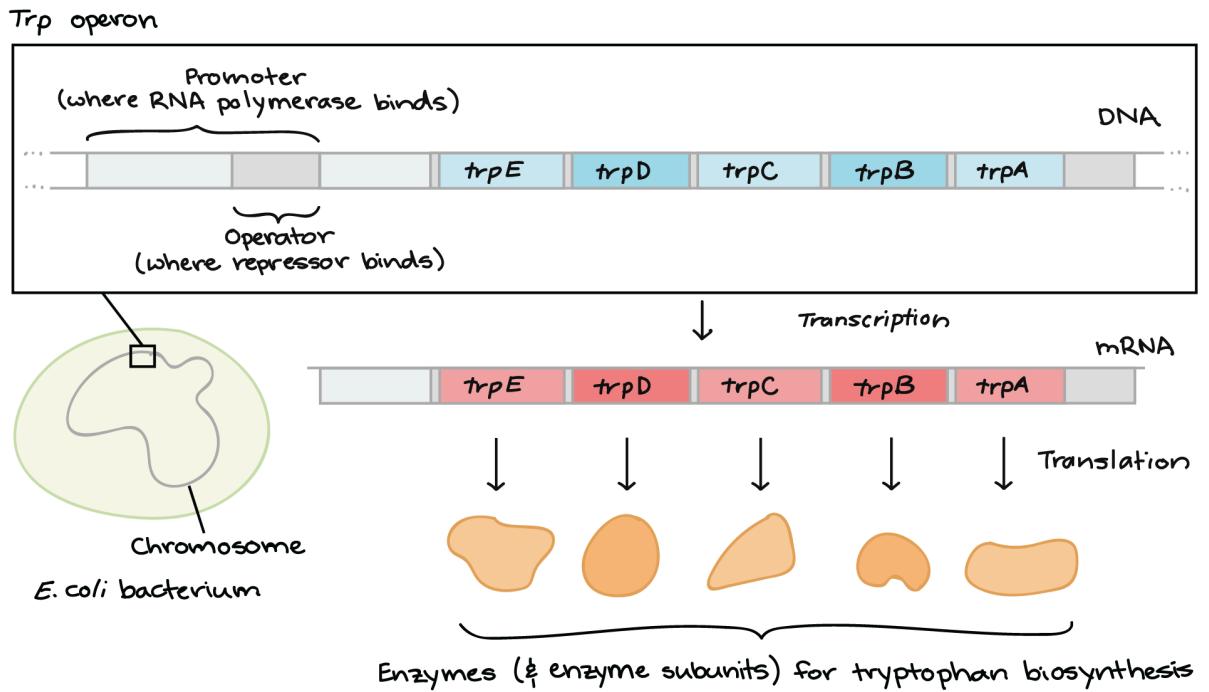
Prokaryotic Cells:

Prokaryotic cells are simple, single-celled organisms without a nucleus. Their **DNA** is free-floating in the cell's cytoplasm. In these cells, **transcription** (making RNA from DNA) and **translation** (making protein from RNA) happen almost at the same time. When a protein is no longer needed, transcription stops. The main way prokaryotic cells control which proteins are made and how much of each protein is produced is by regulating **transcription**. More transcription means more protein is made.

Component	Prokaryotes	Eukaryotes
Promoter	Yes (simpler, often includes -10 and -35 regions)	Yes (more complex, includes TATA box)
ORI (Origin of Replication)	Yes (usually one per circular genome)	Yes (multiple ORIs per linear chromosome)
Operator	Yes (part of operons)	Rare (not common in the same form)
Repressor Binding Site	Yes (operator region)	Yes (as part of silencers or regulatory elements)
Enhancer/Silencer	Rare or absent	Yes (key regulatory elements)
Coding Sequence	Yes	Yes
Terminator	Yes (simple)	Yes (can be more complex)
TATA Box	Rare	Common in promoters
UTRs (Untranslated Regions)	Yes (but shorter)	Yes (important for regulation)

E. coli bacteria need amino acids like **tryptophan** to survive. They can either get tryptophan from their environment or make it themselves using enzymes encoded by five genes. These genes are located next to each other in the **trp operon**.

- When **tryptophan** is available, E. coli doesn't need to make it, **so the genes in the trp operon are turned off.**
- When tryptophan is scarce, the genes in the operon are turned on to make more tryptophan.



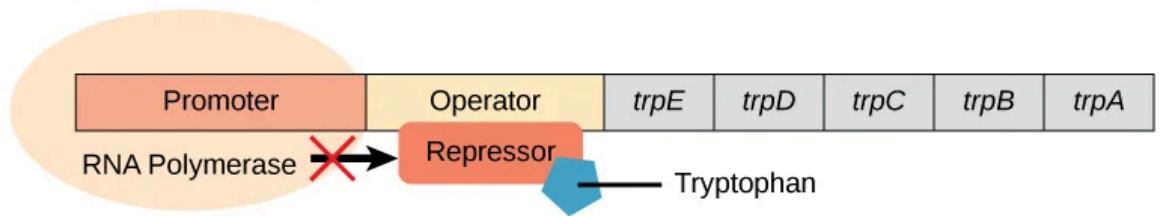
The process works like this:

- **Coding region:** The five genes needed to make tryptophan are in a sequence on the DNA, called the **coding region**.
- **Transcription start:** The **transcription start site** is where RNA polymerase (the enzyme that makes RNA) binds to start copying the DNA.
- **Promoter:** The **promoter** is a region where proteins can bind to **control transcription**.
- **An operon** is a group of genes that work together and are controlled by a single promoter

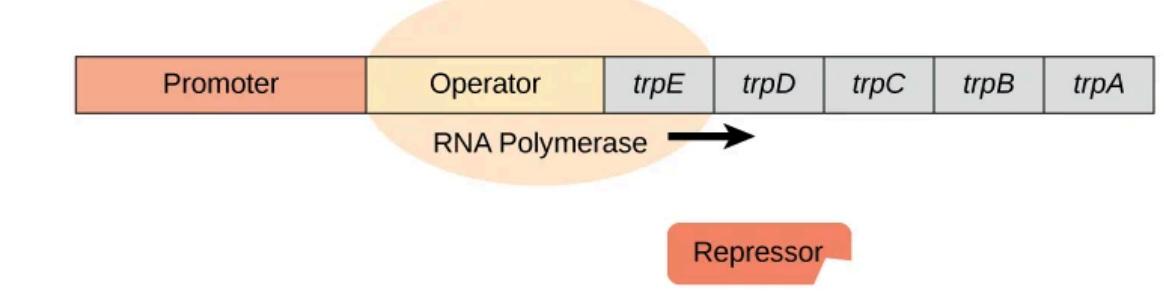
There's a sequence called the **operator** located between the promoter and the first gene in the operon. This is where a **repressor protein** can bind to stop transcription.

- **When tryptophan is present:** Two tryptophan molecules bind to the repressor, causing it to change shape and attach to the operator. This blocks RNA polymerase from transcribing the genes.
- **When tryptophan is absent:** The repressor doesn't bind to the operator, so the genes are transcribed and tryptophan is made.

When tryptophan is present, the trp repressor binds the operator, and RNA synthesis is blocked.



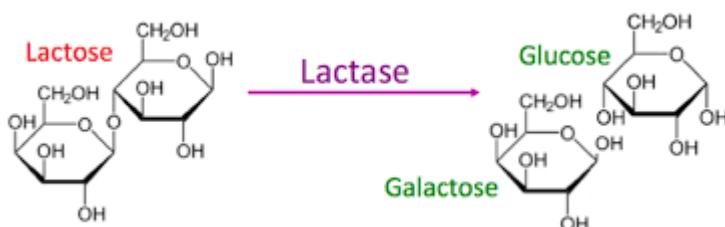
In the absence of tryptophan, the repressor dissociates from the operator, and RNA synthesis proceeds.



Since the **repressor** actively turns off the genes, the **trp operon** is **negatively regulated**. The proteins that prevent gene expression are called **negative regulators**.

- <https://www.youtube.com/watch?v=4Oq5RKkdO0>

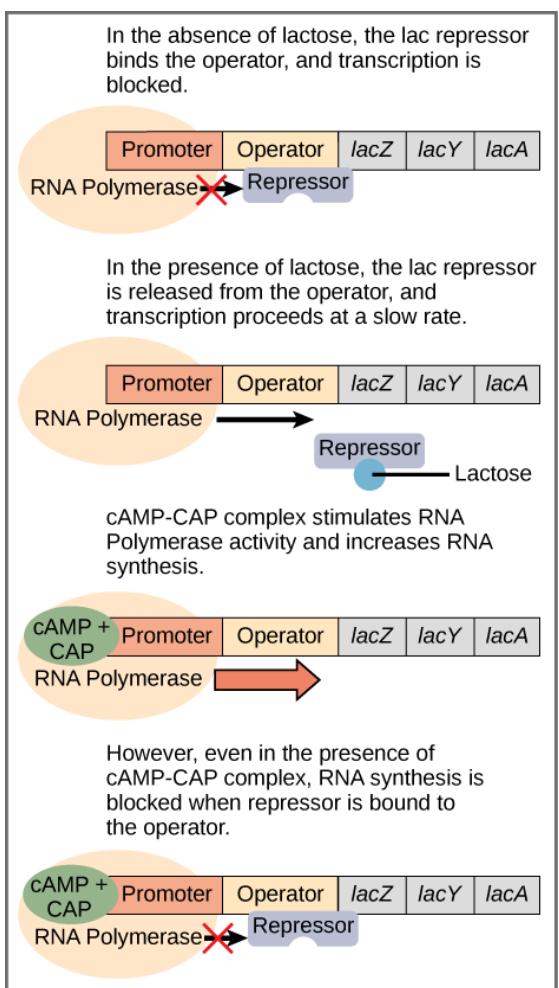
Just like the **trp operon** is turned off when tryptophan is present, there are also proteins that **turn genes on** when needed. For example, when **glucose** is low, E. coli can use other sugars for energy. This is seen in the **lac operon**, which is activated when lactose is present and glucose is absent.



- When glucose is low, the molecule **cAMP** builds up inside the cell. cAMP binds to a protein called **CAP** (Catabolite Activator Protein), which helps turn on genes needed to process other sugars like lactose.
- **CAP** binds to the promoter of the lac operon, helping **RNA polymerase** attach and start transcribing the genes needed for lactose breakdown.

So, **cAMP-CAP** works together to help *E. coli* use alternative sugars when glucose is scarce. This shows that **glucose** is easier to process than **lactose**, which is why *E. coli* prefers glucose when it's available.

In prokaryotic cells, **inducible operons** are a key way to regulate genes. These operons can either turn genes on or off depending on the **environment and the cell's needs**. The **lac operon** is a typical example.



- *E. coli* can use different sugars for energy, especially when glucose is low. One sugar source is **lactose**.

- The lac operon contains genes that help *E. coli* use lactose:
 - **lacZ** makes an enzyme that breaks down lactose.
 - **lacY** helps bring lactose into the cell.
 - **lacA** is involved in modifying lactose molecules.
 - **lacZ** and **lacY** are most important for using lactose.

For the lac operon to work, two things must happen:

1. **Glucose** must be low or absent.
2. **Lactose** must be present.(source for glucose)

When glucose is low, **CAP** binds to the lac operon and helps start transcription. But if **lactose is not available**, a **repressor protein** blocks transcription.

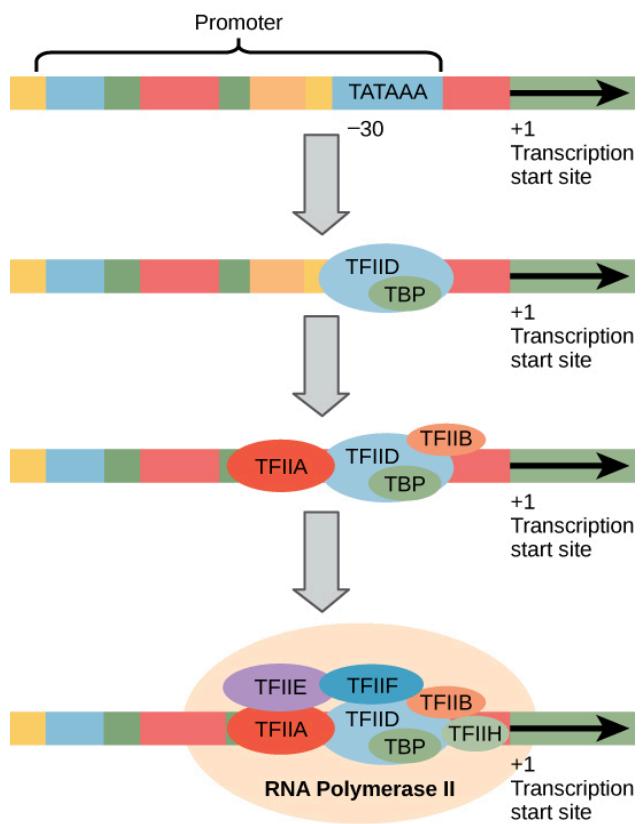
The lac operon only turns on when **both** conditions are met: low glucose and the presence of lactose. This saves the cell energy because making the proteins to process lactose would be wasteful if glucose is available or if lactose isn't around.

Eukaryotic Cells:

Eukaryotic cells are more complex and have a nucleus where their DNA is stored. In these cells, **transcription happens in the nucleus**, making RNA from DNA. The RNA then travels to the cytoplasm where **ribosomes** translate it into protein. Because transcription and translation happen in **different locations** (nucleus for transcription, cytoplasm for translation), gene expression can be regulated at many stages:

1. **Epigenetic level:** DNA is uncoiled and loosened to allow transcription factors to bind.
2. **Transcriptional level:** Regulation during RNA synthesis.

3. **Post-transcriptional level:** Regulation after RNA is made, before it is exported out of the nucleus.
4. **Translational level:** Regulation during protein synthesis.
5. **Post-translational level:** Regulation after the protein is made.



In eukaryotic cells, gene expression can be controlled at each of these steps.

Genes are organized to help control gene expression. The **promoter region** is located **just before the coding sequence of a gene**. It can be short or long, and the longer it is, the more space there is for proteins to bind and control transcription. The **length of the promoter varies between genes**, which affects how much control there is over gene expression.

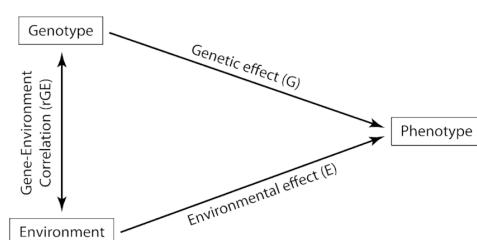
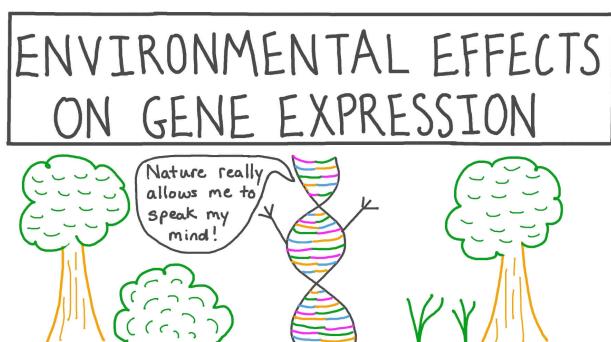
The **TATA box** is a specific sequence **within the promoter, just before the transcription start site**. It's made of repeated **thymine (T)** and **adenine (A)** pairs. This is where the transcription process begins.

To start transcription:

1. The **TFIID transcription factor** binds to the TATA box first.
2. Other transcription factors (**TFIIB, TFIIE, TFIIF, TFIIH**) are then recruited.
3. The **RNA polymerase** enzyme binds to the promoter with the help of these factors.
4. RNA polymerase gets activated and starts transcription in the right direction.

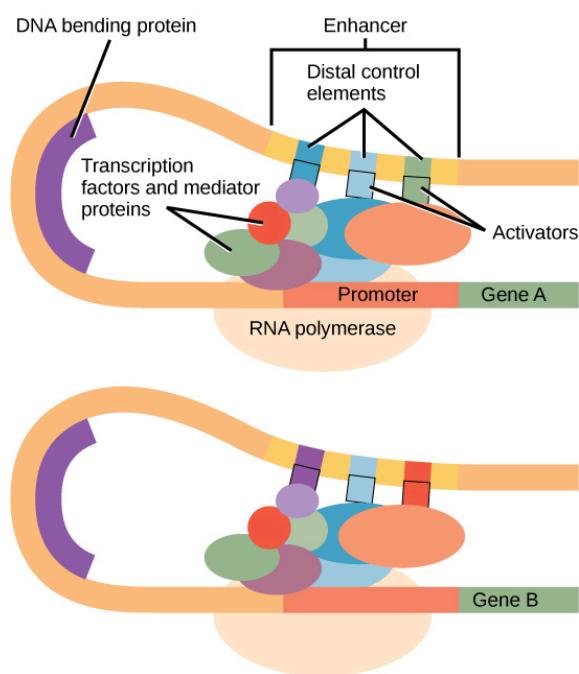
A **DNA-bending protein** helps bring the enhancer (which can be far from the gene) into contact with the transcription factors, further helping the transcription process.

Transcription factors respond to **environmental signals**, which help them find their binding sites and start transcription of the necessary gene.



In addition to the general transcription factors, there are other transcription factors that bind to specific promoters to control gene expression. These factors don't bind to every gene but are only recruited to specific genes. There are many transcription factors in a cell, each

binding to a particular DNA sequence. When they bind to the promoter of a gene, they are called **cis-acting elements (enhancers)** because they are on the same chromosome, near the gene. The specific spot where a transcription factor binds is called the **transcription factor binding site**. Some genes have special regions called **enhancers** that help **increase transcription**. These enhancers aren't always close to the gene—they can be located far away, either upstream, within the gene, or downstream.

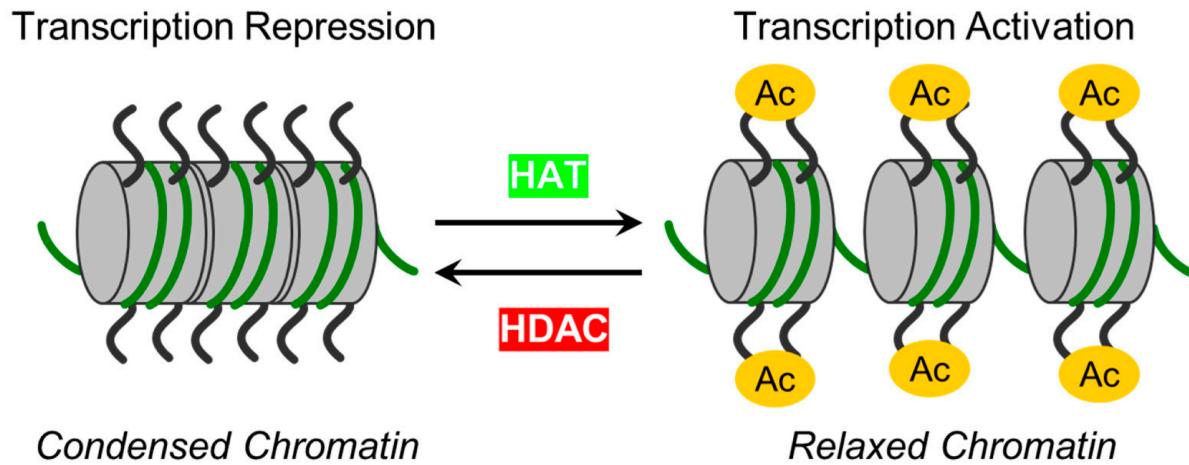


Enhancers have binding sites for transcription factors. When a **DNA-bending protein binds to an enhancer, it changes the DNA shape**. This shape change allows the enhancer to interact with the promoter region and help the transcription factors and RNA polymerase start transcription. **Even if the enhancer is far away from the gene, the DNA can fold and bring it close to the promoter to help start transcription.**

Turning Genes Off: Transcriptional Repressors

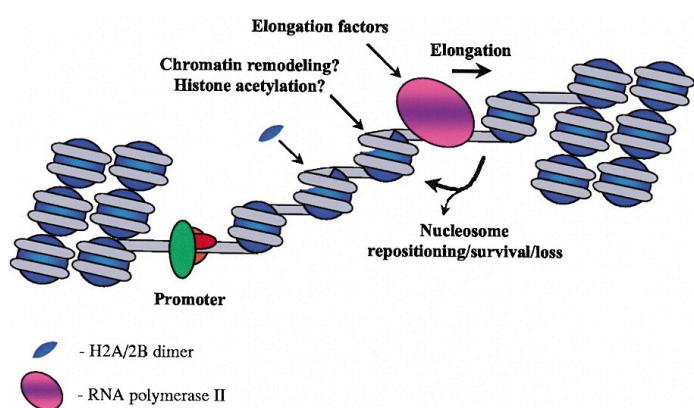
Just like in prokaryotic cells, eukaryotic cells can also stop transcription. **Transcriptional repressors** bind to the promoter or enhancer regions of genes and block transcription. These repressors respond to external signals to prevent activator proteins from starting transcription.

A **corepressor** is a protein that helps decrease gene expression. It works by binding to a transcription factor, which can't bind DNA on its own. The **corepressor can stop transcription** by recruiting an enzyme called **histone deacetylase**, which removes acetyl groups from histones. This makes the histones more positively charged, causing them to hold onto the DNA more tightly, making it harder for transcription to happen. histone acetyltransferases (HATs), histone deacetylases (HDACs).



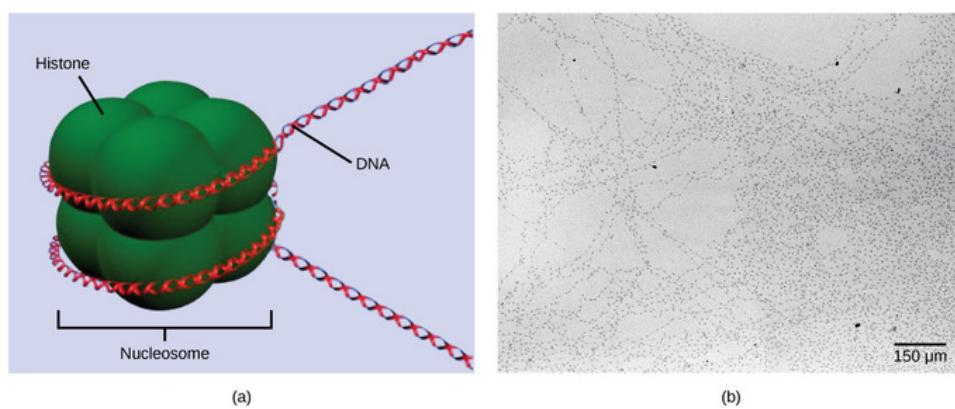
The human genome has over 20,000 genes, packed into 23 pairs of chromosomes in the nucleus. This DNA is tightly wound and organized so that only the necessary parts are accessible to specific cell types.

The first level of DNA organization is the winding of DNA around **histone proteins**, forming structures called **nucleosomes**. These nucleosomes control how accessible different parts of the DNA are. The histones can move along the DNA and change its structure, regulating access to specific genes.

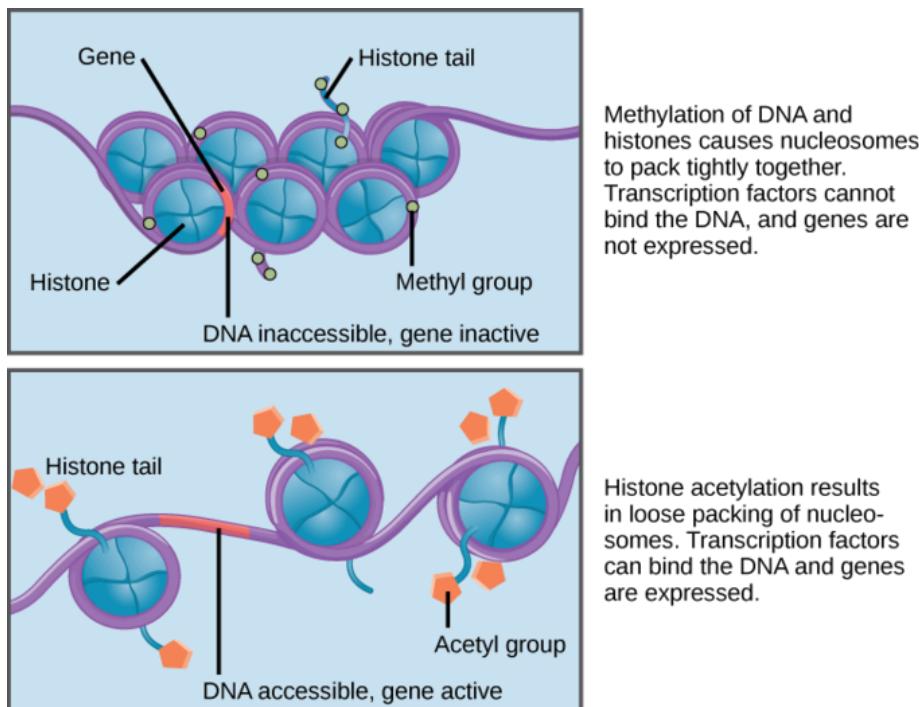


To transcribe a gene into RNA, the **nucleosomes** around that part of the DNA can move, opening up the region for **RNA polymerase** to **start transcription**. The **movement of these nucleosomes is controlled by signals on the histones and DNA itself**. These signals are chemical tags (like acetyl, methyl, or phosphate groups) added to the histones or DNA. These tags don't change the DNA sequence but affect how tightly the DNA is wrapped around

the histones. For example, adding acetyl groups to histones makes them less positive, loosening the DNA.

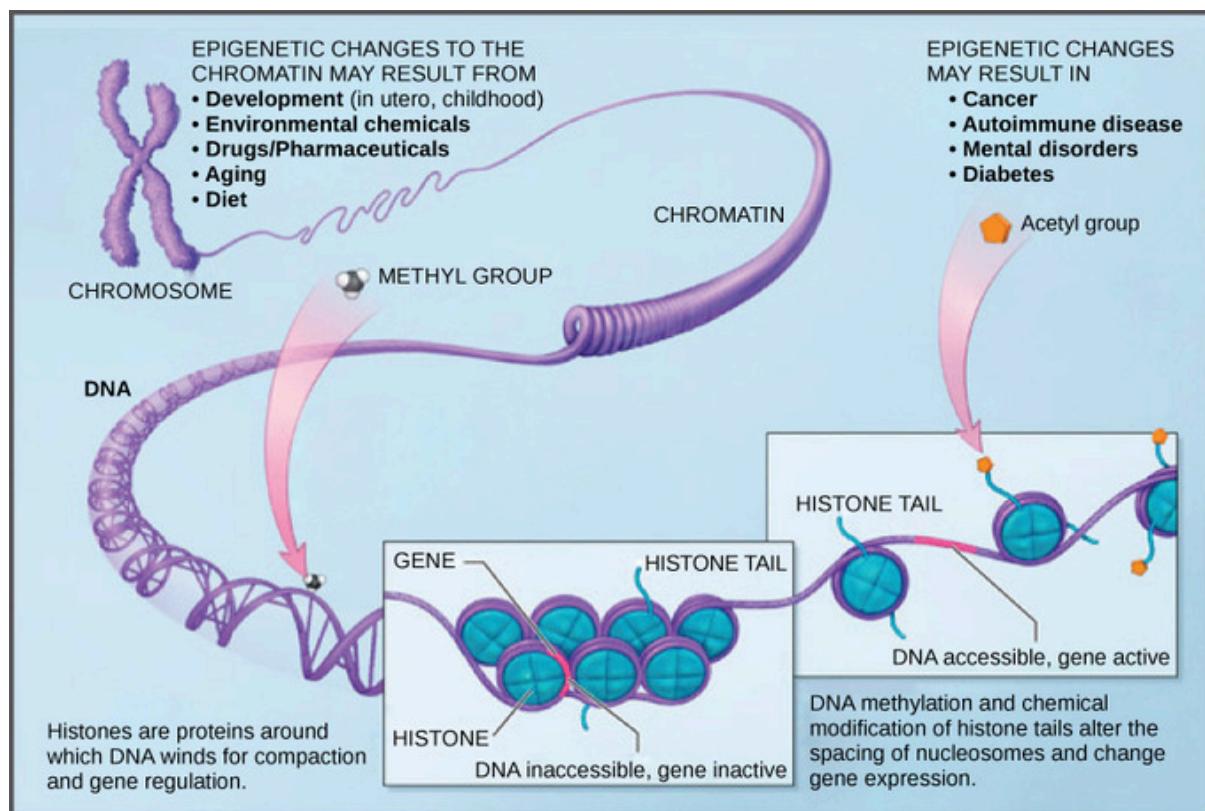


DNA itself can also be modified, especially in **CpG islands** (regions rich in cytosine and guanine). Adding a **methyl group** to the cytosine can affect how DNA interacts with proteins, including histones. Highly methylated DNA is tightly coiled and inactive, preventing transcription.



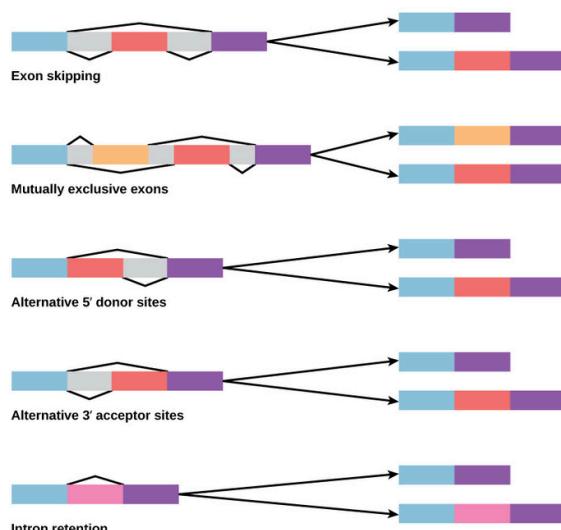
These modifications to histones and DNA are part of **epigenetic regulation**, which doesn't change the DNA sequence but instead **temporarily controls gene activity**. Changes in histone and DNA modifications can turn genes on or off as needed. If a gene needs to be transcribed, the DNA and histones are modified to open the chromosomal region and allow transcription to occur. If a gene should remain off, the region is closed, blocking access for transcription.

- DNA is wrapped around histones to form **nucleosomes**, which control DNA access.
- When a gene is to be transcribed, nucleosomes move to open the region for transcription.
- Chemical modifications to histones and DNA control whether a gene is "open" or "closed" to transcription.
- **Epigenetic regulation** involves temporary changes that don't affect the DNA sequence but control gene expression.
- **Nucleosome**: DNA wrapped around histone proteins.
- **Epigenetics**: Changes in gene activity without changing the DNA sequence.
- **Histone**: Proteins that help package DNA into nucleosomes.



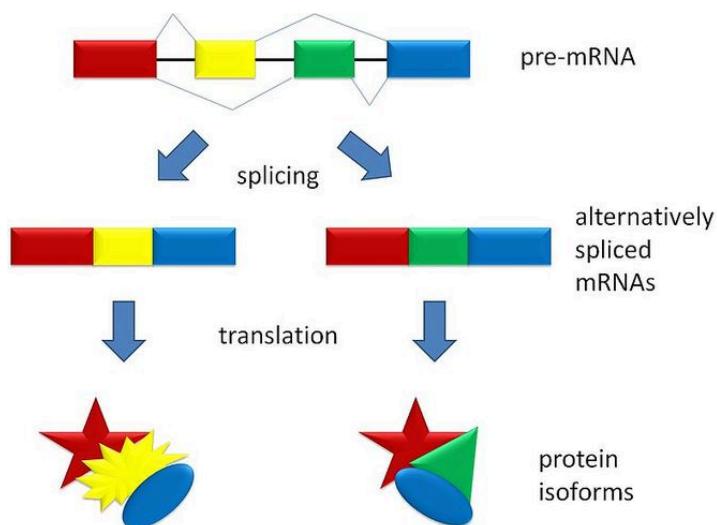
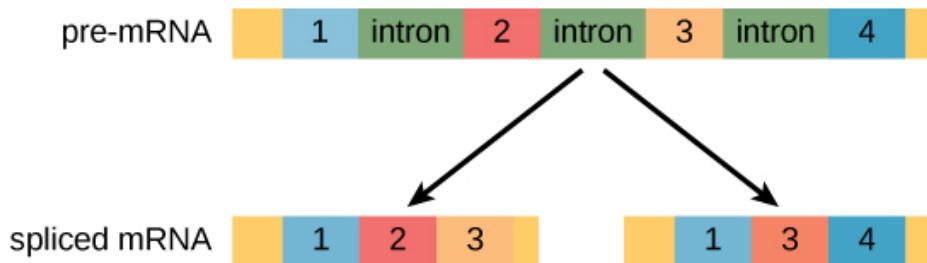
Gene expression is the process where information from a gene (DNA) is used to create RNA or protein. After transcription, in eukaryotes, the **RNA produced (pre-mRNA) contains both coding and non-coding regions. The non-coding regions, called introns, must be removed, and the coding regions, called exons, are joined together to form mature mRNA. This process is called splicing.**

Alternative splicing is a process that allows a single gene to produce multiple proteins by combining exons in different ways. For example, if a pre-mRNA has four exons (A, B, C, and D), it can be spliced in many combinations, like A, B, C, or A, C, D. This creates different proteins from the same gene. The pattern of splicing is controlled by regulatory proteins, which can either promote or block certain splicing events.

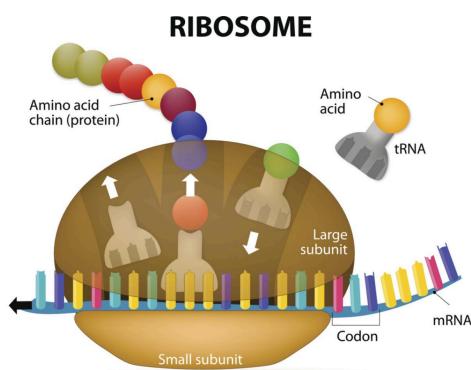


The **spliceosome** is a complex of proteins and RNA that carries out splicing by cutting out introns and joining exons together.

- **Introns** are non-coding regions in pre-mRNA that are removed during splicing.
- **Exons** are the coding regions that are joined together to form the final mRNA.
- **Alternative splicing** allows a single gene to produce multiple proteins.
- The **spliceosome** is a protein-RNA complex that performs splicing.



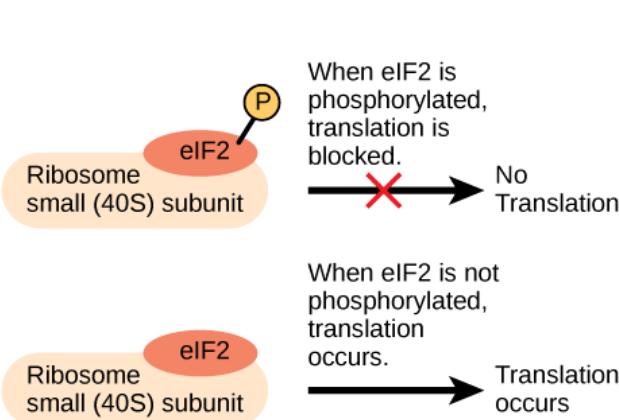
Before protein synthesis (translation) can start, the ribosome needs to be assembled. This is a multi-step process.



begins. The anticodon of the tRNA_i binds to this codon, and the large ribosomal

1. Ribosome Assembly: The small and large ribosomal subunits, along with an initiator tRNA (**tRNA_i**) **carrying the first amino acid**, come together at the **start codon (AUG)** of the mRNA to begin translation. The **small ribosomal subunit binds to the tRNA_i, which is charged with methionine** in eukaryotes. The small subunit then moves along the mRNA until it finds the start codon (AUG), where translation

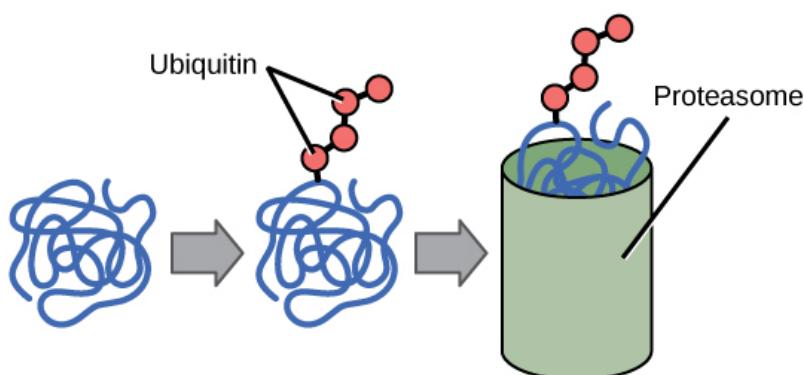
subunit attaches to complete the ribosome. This process is aided by proteins called initiation factors and energy from GTP.



In Eukaryotes: Several initiation factors (eIFs) assist in ribosome assembly. eIF-2 binds to GTP and helps the small ribosomal subunit attach to the mRNA's 5' cap. The complex then scans the mRNA until it reaches the start codon. The tRNA_i-Met binds to the start codon, and the GTP is hydrolyzed to provide energy for the ribosome to assemble and begin translation.

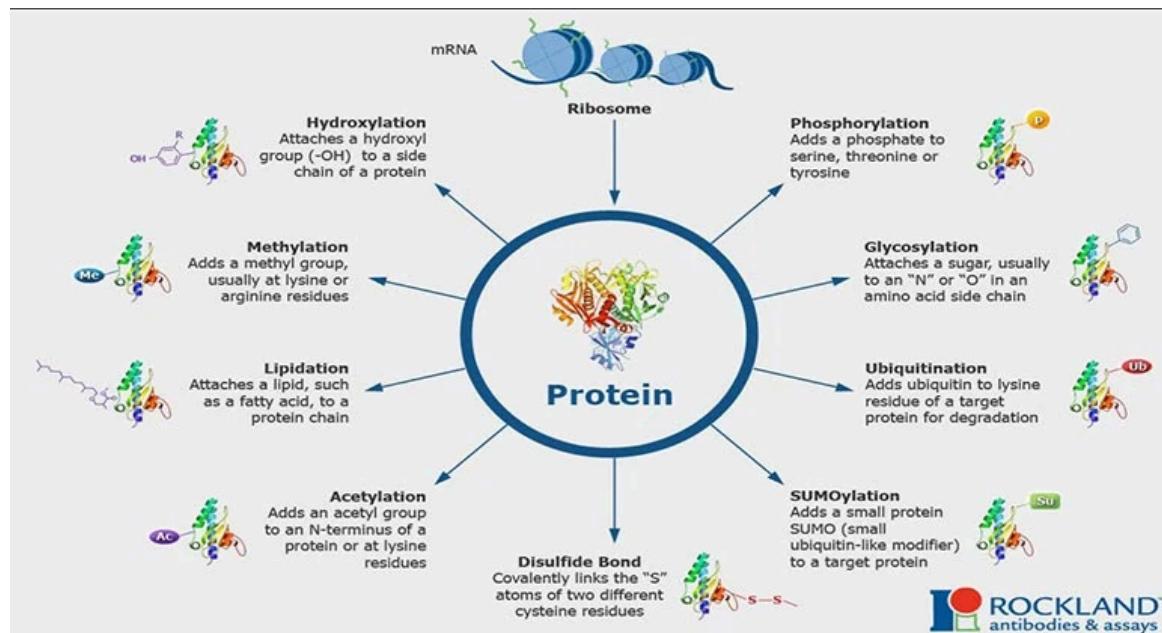
2. **Translation Control:** The rate of translation is influenced by the assembly of the ribosome. If key components like eIF-2 are phosphorylated, translation may be slowed or stopped. The overall rate of protein synthesis is also influenced by factors like mRNA, tRNA, and ribosomal RNA synthesis.

- Ribosome assembly is essential for translation to start.
- In eukaryotes, initiation factors help form the translation initiation complex.
- The rate of translation can be controlled by various factors, including the phosphorylation of proteins like eIF-2.
- The components involved in ribosome assembly are brought together by the help of proteins called initiation factors which bind to the small ribosomal subunit.
- Initiator tRNA is used to locate the start codon AUG (the amino acid methionine) which establishes the reading frame for the mRNA strand.
- GTP carried by eIF2 is the energy source used for loading the initiator tRNA carried by the small ribosomal subunit on the correct start codon in the mRNA.
- GTP carried by eIF5 is the energy source for assembling the large and small ribosomal subunits together.



Ubiquitin is a very small protein (~76aa) that functions as a highly conserved regulator of protein homeostasis. It is ubiquitously expressed in all eukaryotic cells and is part of a larger family of ubiquitin-like proteins and modifiers including SUMO, NEDD8, and ISG15. While ubiquitin plays many

roles within the context of autophagy, cell signaling, and endocytosis, its primary function is to serve as an intracellular label for targeted protein degradation. Ubiquitination involves adding a ubiquitin tag to a protein, marking it for degradation. This helps control how long a protein lasts in the cell, as ubiquitination signals that the protein should be broken down by the proteasome.



Proteins can be chemically modified by adding groups like methyl, phosphate, acetyl, and ubiquitin. These modifications control a protein's activity, location, and lifespan within the cell. For example, they can determine whether a protein is in the nucleus, cytoplasm, or on the cell membrane.

These chemical changes happen in response to external factors like stress, lack of nutrients, or exposure to heat or UV light. They can affect various processes, such as protein function, gene expression, and how the cell reacts to its environment. One common modification is phosphorylation, where a phosphate group is added to a protein by enzymes called protein kinases. This can either activate or deactivate a protein, affecting its function, stability, or location within the cell.

Another modification is methylation, where methyl groups are added to proteins. This can affect how proteins interact with each other, regulate gene expression, and respond to stress or other signals. **Methylation is mostly irreversible and changes the protein's charge and hydrophobicity, influencing its activity.**

In summary, these chemical modifications allow the cell to rapidly adjust protein functions and gene expression in response to changing conditions.

Cell Differentiation and Specialization

To form a multicellular organism, cells must differentiate into specialized types to perform different functions. There are three main types of cells in mammals: **germ cells, somatic cells, and stem cells.**

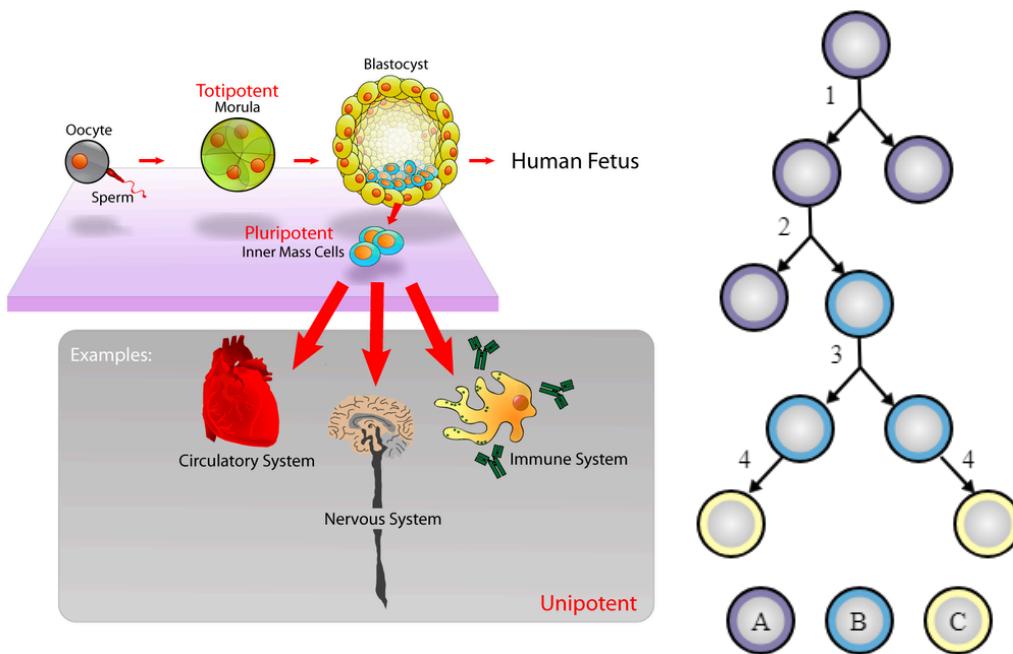
- **Germ cells** are responsible for producing eggs and sperm.
- **Somatic cells** make up most of the body (e.g., skin and muscle cells) and are diploid, meaning they have two copies of each chromosome.
- **Stem cells** can divide for long periods and give rise to specialized cells.

Each of the approximately 100 trillion cells in the human body carries its own copy of the genome, except for certain cells like red blood cells that lose their nuclei when fully mature. Cells differentiate through the actions of **transcription factors** (proteins that control gene expression) and **growth factors** (which help in cell division). The differences in the proteins produced by these cells, known as their **proteomes**, lead to their specialization.

Stem Cells and Their Role in Cell Division

Stem cells are undifferentiated cells that can either divide to create more stem cells (symmetric division) or differentiate into specialized cells (asymmetric division). There are two main types of stem cells in mammals: **embryonic stem cells** (from early-stage embryos) and **adult stem cells** (found in various tissues). Stem cells in adults help repair tissues by replenishing cells like skin, blood, or gut cells. **In embryos, stem cells can develop into all types of cells in the body.**

Stem cells go through a process where they first start as **totipotent** (able to form any cell) and then become **pluripotent** (able to form many but not all types of cells). The key to maintaining healthy tissues is having a pool of stem cells that can self-renew.



This diagram illustrates stem cell division and differentiation, through the processes of (1) symmetric stem cell division, (2) asymmetric stem cell division, (3) progenitor division, and (4) terminal differentiation. Stem cells are indicated by (A), progenitor cells by (B), and differentiated cells by (C).

Sources of Stem Cells:

1. **Bone marrow** (extracted by drilling into the bone)
2. **Adipose tissue** (fat cells, extracted by liposuction)
3. **Blood** (extracted through a process called apheresis)
4. **Umbilical cord blood** (collected right after birth)

Adult stem cells, particularly from bone marrow, are often used in medical treatments like bone marrow transplants. They can also be cultured in the lab to become specialized cells like muscle or nerve cells.

Symmetric and Asymmetric Cell Division: Stem cells divide in two ways:

1. **Symmetric division:** Produces two identical stem cells, maintaining the stem cell pool.
2. **Asymmetric division:** Produces one stem cell and one **progenitor cell** (a cell with limited self-renewal ability) that will eventually differentiate into a specialized cell.

In asymmetric division, two daughter cells end up with different fates—one remains a stem cell, while the other becomes a progenitor cell that will specialize.

Controlling Asymmetric Division:

- **Intrinsic factors:** Differences in proteins or other molecules in the cells cause them to behave differently.
- **Extrinsic factors:** Signals from neighboring cells or the environment influence the fate of the daughter cells.

Asymmetric division plays a critical role in development, allowing some cells to specialize while maintaining a pool of stem cells for future growth and repair.

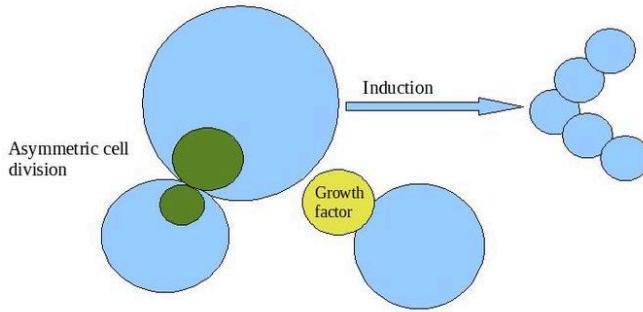
- Symmetric division ensures a constant supply of stem cells.
- Asymmetric division produces one stem cell and one progenitor cell.
- Progenitor cells eventually specialize into mature, differentiated cells.
- Both intrinsic and extrinsic factors control the fate of daughter cells during division.

Embryonic Development:

- After fertilization, a single cell begins to divide into identical cells. These cells eventually form a hollow sphere called a **blastocyst**.
- The blastocyst has an outer layer of cells and an inner mass of cells. These inner cells are called **pluripotent** because they can form almost any cell type in the body, though they can't form a whole organism.
- These pluripotent stem cells then specialize into **multipotent progenitor cells** that become more specific cell types.

Examples of Stem and Progenitor Cells:

- **Hematopoietic stem cells** (from bone marrow) produce red and white blood cells, and platelets.
- **Mesenchymal stem cells** (from bone marrow) form fat cells, bone cells, and others.
- **Epithelial stem cells** form skin cells.
- **Muscle satellite cells** help form muscle tissue.



During development, cells move through three layers: **ectoderm**, **mesoderm**, and **endoderm**. These layers will form the skin and nervous system (ectoderm), bones and muscles (mesoderm), and internal organs (endoderm).

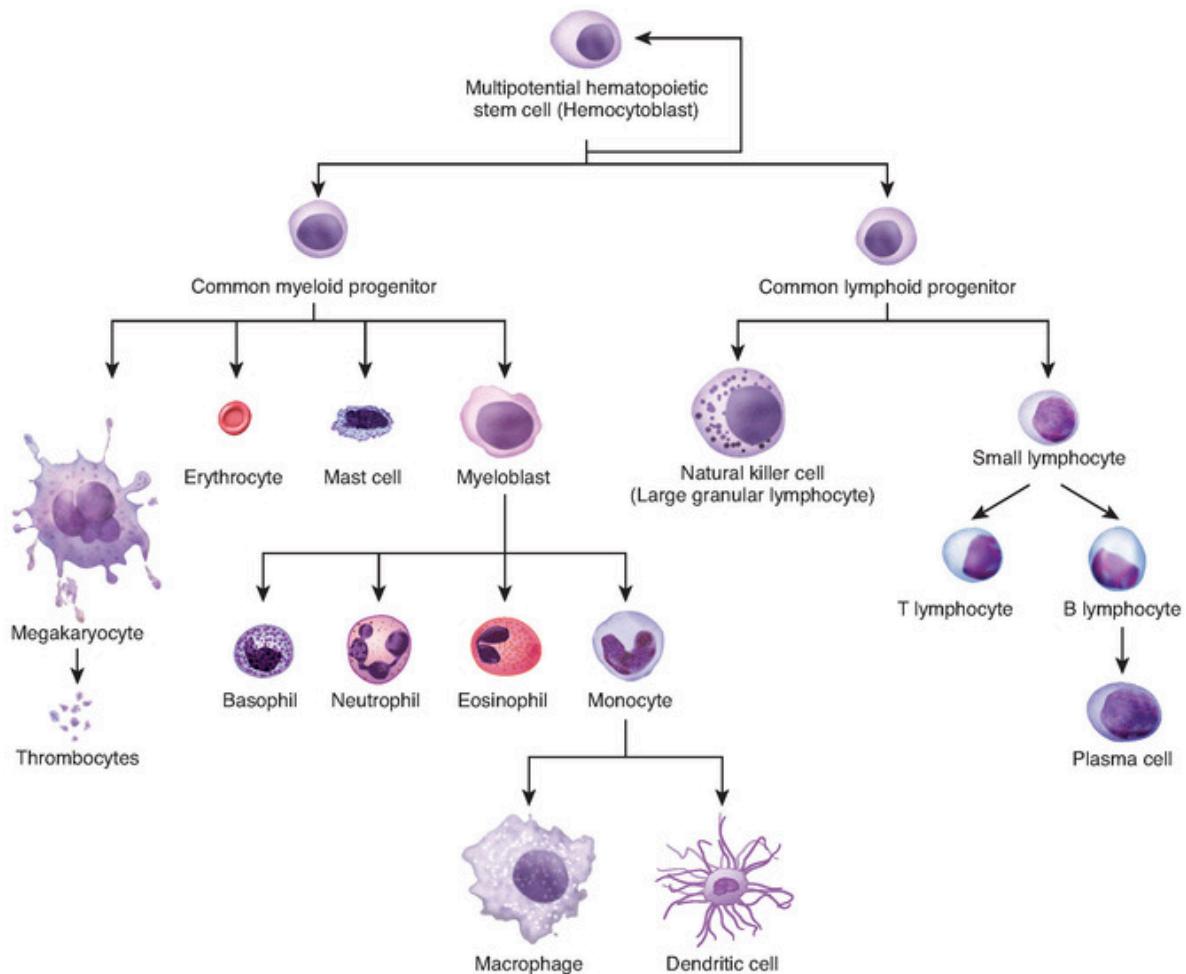
- Germ cells create eggs and sperm, somatic cells make up most of the body, and stem cells can divide indefinitely.
- The inner cell mass in early development can form all body tissues but not a whole organism.
- Stem and progenitor cells specialize into specific cell types like blood, bone, muscle, and skin cells.
- Differentiation allows cells to specialize for specific functions in the body.

Cellular Differentiation

Cellular differentiation is the process by which unspecialized cells become specialized to perform specific functions in the body. This process is essential for the development of a complex organism, such as a human, from a single fertilized egg into many different types of cells, such as nerve cells, muscle cells, and skin cells.

Stem Cells:

- **Stem cells** are unspecialized cells that can divide indefinitely and, under certain conditions, differentiate into specialized cells.
- **Totipotent stem cells** (the first cells after fertilization) can develop into any type of cell needed for the entire organism.
- **Pluripotent stem cells** can form any type of tissue in the body but cannot develop into a whole organism.
- **Multipotent stem cells** can develop into a limited number of cell types, such as blood cells (e.g., red or white blood cells).
- **Oligopotent cells** can develop into only a few specific types of cells.
- **Unipotent cells** are fully specialized and can only produce more of their own cell type.

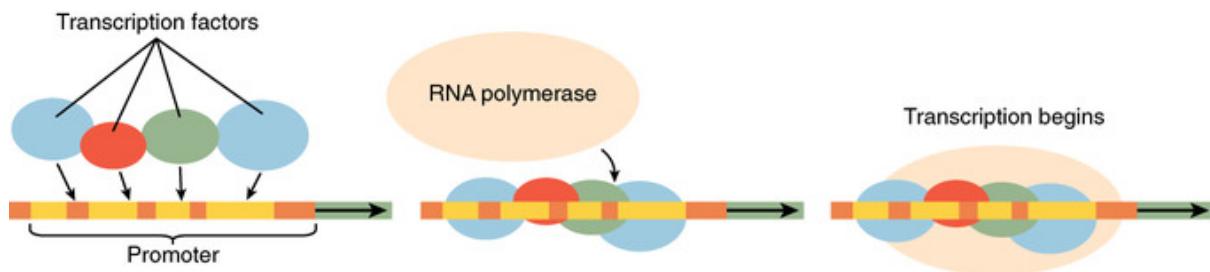


There are different types of stem cells at various stages of life:

- **Embryonic stem cells** in early development,
- **Fetal stem cells** in the fetus,
- **Adult stem cells**, such as **epithelial stem cells** (in skin) and **hematopoietic stem cells** (in bone marrow), which give rise to blood cells.

Mechanism:

- **Transcription factors** bind to specific genes on the DNA and either promote or inhibit their expression.
- These factors control which genes are turned on or off, helping cells differentiate into their specialized forms.
- Stem cells range in their ability to differentiate, from **totipotent** (all cells) to **unipotent** (one specific type of cell).
- **Totipotent** cells can become any cell necessary for an organism's development, while **pluripotent** cells can become any tissue but not a whole organism.
- **Multipotent** and **oligopotent** cells can form specific groups of related cells.
- The differentiation process is regulated by transcription factors, which affect gene expression and the cell's proteome (the proteins it produces), ultimately leading to cell specialization.

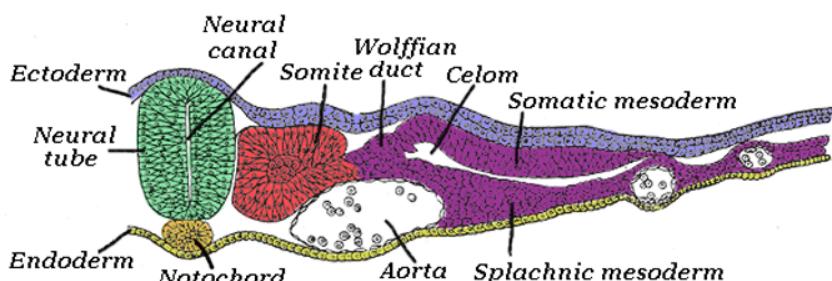


Differentiation Process:

- As cells differentiate, they undergo changes in size, shape, activity, and function.
- Although all cells in the body have the same DNA, different cell types "read" different parts of the DNA based on their function. This is called **genetic expression**.
- Transcription factors (proteins) play a key role in turning genes "on" or "off" to regulate which genes are expressed in each cell, guiding it to become specialized.

Vertebrate Axis Formation

During development, animal bodies develop three main axes: **lateral-medial** (left-right), **dorsal-ventral** (back-belly), and **anterior-posterior** (head-feet). These axes are established through the action of specific genes. In a famous experiment, Spemann and Mangold showed that dorsal cells (from the back of an embryo) can form a new notochord when transplanted to the belly region, suggesting these cells are programmed to define the axis. Mutations in genes involved in axis formation can cause asymmetry, which is crucial for proper organ placement, such as the heart on the left and liver on the right.



Neural Tube Formation

The **neural tube** is the precursor to the brain and spinal cord in chordates (vertebrates). It forms from the **neural groove** which deepens as the neural folds rise and fuse in the middle, creating the tube. This process is called **neurulation**. There are two types of neurulation:

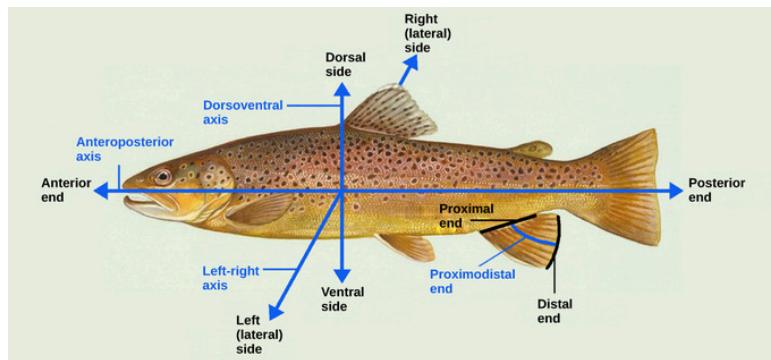
1. **Primary neurulation:** The ectoderm forms the neural tube, epidermis, and neural crest cells.
2. **Secondary neurulation:** A cord-like structure forms and hollows out to become the neural tube.

Different animals use these processes to varying degrees. For example, fish use secondary neurulation, while birds and mammals use both.

Neural Tube Subdivisions

The neural tube divides into:

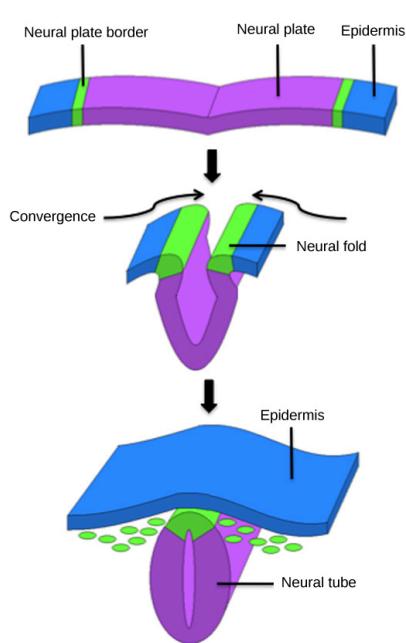
- **Prosencephalon** (forebrain, later becoming the cerebrum and hypothalamus)
- **Mesencephalon** (midbrain)
- **Rhombencephalon** (hindbrain, becoming the pons and cerebellum)
- **Spinal cord**



Neural tube openings, called **neuropores**, close in humans around the fourth week of development. If they don't close properly, conditions like **anencephaly** (absence of the brain) or **spina bifida** (spinal defects) can occur.

Patterning and Signaling Molecules

The neural tube's development is influenced by signaling molecules:



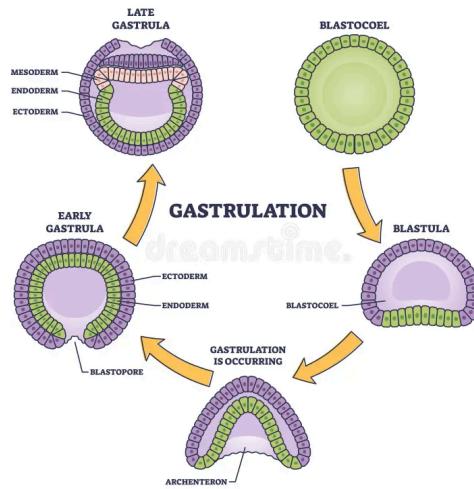
- **Sonic hedgehog (Shh)** patterns the **ventral** (bottom) side.
- **Bone morphogenetic proteins (Bmp)** and **Wnt** pattern the **dorsal** (top) side. Other molecules like **fibroblast growth factors (FGF)** and **retinoic acid** help further guide development.

Shh, released from the notochord and floor plate, helps form motor neurons and other cell types in the neural tube. The concentration of Shh defines cell types along the ventral axis.

- The body's three axes (left-right, back-belly, head-feet) are set during development by specific genes.
 - **Neural tube** development is vital for the central nervous system and occurs through primary and secondary neurulation.
 - Signaling molecules like Shh, Bmp, Wnt, and FGF help shape the neural tube and the axes of the body.
- Proper closure of the neural tube is critical for brain and spinal cord development.

Genes Provide Positional Information

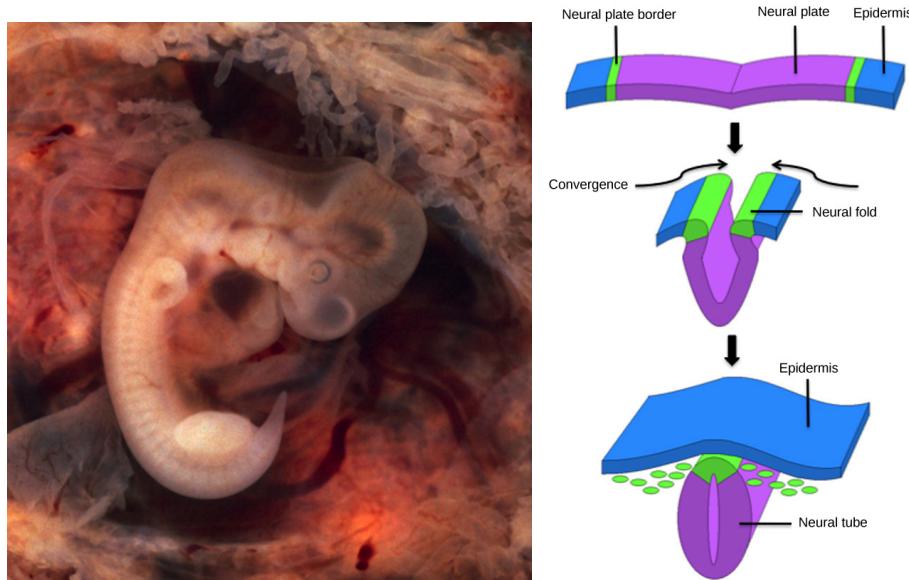
During **gastrulation**, the embryo forms three germ layers, which later develop into different organs. This process is called **organogenesis**, and it involves rapid and precise cell movements to form organs.

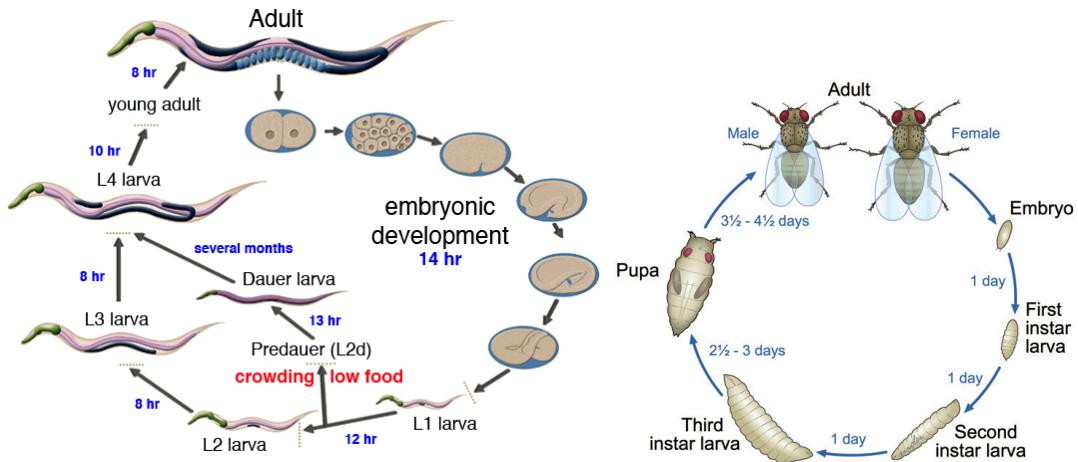


Organogenesis and Differentiation

Organ formation occurs when stem cells in the embryo express specific genes, causing them to become specialized cells. For example, some ectoderm cells (the outer layer) express genes for skin, so they become epidermal cells. **Differentiation** is controlled by signals that guide the development of these cells.

Scientists study organogenesis in model organisms like fruit flies (**Drosophila**) and nematodes (**Caenorhabditis elegans**). Drosophila has body segments that help researchers understand gene patterns in organ development. In *C. elegans*, which has about 1000 cells, scientists track the development of each cell, which is less variable compared to mammals.





1. Differentiation:

Think of all your body's cells like students in a school. They all have the **same syllabus** (DNA), but not everyone studies every subject — some become artists, others scientists.

- All cells **have the same DNA**, but only **some genes are turned "on"** in each cell type.
This selective gene usage is called **gene expression**.
Transcription factors are like teachers who decide which part of the syllabus (DNA) the student (cell) studies — they help cells become muscle, nerve, skin, etc.

2. Vertebrate Axis Formation:

Animals' bodies are built around **three directions or axes**:

- **Anterior-Posterior** = head to tail (front to back)
Dorsal-Ventral = back to belly
Left-Right = symmetry (e.g., heart on left, liver on right)

Certain **genes act like GPS** during early development to set these directions.

The **Spemann and Mangold experiment** showed that **cells on the embryo's back (dorsal)** can control body layout — like a blueprint for the body's structure.

Spemann and Mangold Experiment (1924) — A Milestone in Developmental Biology

What they did:

- They took a group of **dorsal cells** (from the back side of a frog embryo), specifically from an area called the **dorsal lip of the blastopore**.

Then they **transplanted** these cells into the **ventral (belly) side** of another embryo.

What happened:

- The transplanted dorsal cells **induced the surrounding belly cells to form an entirely new body axis**, including a **second notochord**, spinal cord, and other structures.

Why it's important:

- It proved that **certain cells (dorsal cells)** have special instructions or "**organizer properties**" — they can **instruct** other cells to become part of the nervous system and define the body's layout.

This organizer region is now called "**Spemann's Organizer**."

In the real embryo, the original spot (where the dorsal cells normally go) would still try to follow its programmed instructions and might form part of the natural body axis — but the newly placed dorsal cells (in the wrong spot) would dominate and induce a second axis. The natural pattern could still develop, but the induced second axis could lead to symmetry issues or extra structures (like a second notochord), which is why this experiment is fascinating and shows the power of cellular induction. In Hans Spemann and Hilde Mangold's 1924 experiment, they showed that a specific part of an embryo, called the **dorsal lip** (a tissue at the back of the embryo), is very important for organizing the body and guiding how different parts of the embryo develop. They discovered that when this tissue was moved to a different part of another embryo, it didn't just keep growing as usual—it also started to create a new set of structures, like a second neural tube (which becomes the brain and spinal cord) and a new body axis. This tissue helped build a second embryo attached to the first one. Because of this, Spemann called the dorsal lip the "**organizer**", as it has the power to control how the embryo develops. In simpler terms, the dorsal lip is like the "**master controller**" of the embryo's development, and when it's transplanted to a different place, it can create a whole new body!

Relevance to Axis Formation:

- **Axis formation** = deciding which side is **left/right, front/back, top/bottom**. Genes in the organizer region help establish these directions. If these genes **mutate**, you can get **asymmetry disorders**, like:

Heart on the right side instead of the left (**situs inversus**)
Organs in wrong positions (**heterotaxy syndrome**)

Simple Analogy:

Imagine you have blueprints for building a house. Spemann's Organizer is like the **head architect** — even if you move the architect to a different location, he can still **recreate the plan** and build a second house there. That's what those dorsal cells did!

3. Neural Tube Formation (Neurulation): The neural tube becomes the brain and spinal cord.

Two ways it forms:

- **Primary neurulation:** Folding and fusing of ectoderm layer — like rolling a paper into a tube.
Secondary neurulation: A solid rod forms and hollows out — more common in lower animals like fish.
In humans: both types are used depending on location.
-

4. Neural Tube Subdivisions:

As the neural tube forms, it's divided into regions:

- **Forebrain (prosencephalon)** → thinking, senses (cerebrum, hypothalamus)
Midbrain (mesencephalon) → motor control
Hindbrain (rhombencephalon) → balance, breathing (pons, cerebellum)
Spinal cord → movement and reflexes
If the **neuropores** (ends of the tube) don't close → serious conditions like:
 - **Anencephaly** (brain missing)
Spina bifida (spinal opening)
-

5. Patterning & Signaling Molecules:

These are **chemical messengers** that help different parts of the neural tube become the correct types of cells.

- **Shh (Sonic hedgehog)** → patterns the **bottom** side → motor neurons
BMP, Wnt → pattern the **top** side → sensory neurons
FGF, retinoic acid → support development
 **Concentration of signals** tells a cell what it should become (like ingredients in a recipe).

6. Organogenesis & Gene Control:

During **gastrulation**, the embryo forms **three layers**:

- **Ectoderm** → skin, nervous system
 - Mesoderm** → muscles, bones
 - Endoderm** → lungs, liver, gut
- Cells get **positional signals** that tell them:
- “Hey! You’re ectoderm. Become skin!”
“Hey! You’re mesoderm. Become heart!”

Scientists study this in **fruit flies** (segments help show gene roles) and **C. elegans** (transparent body, fixed cell number).

Summary in Simple Words:

- All your cells have the **same DNA**, but **different genes get turned on** in each one. **Special proteins (transcription factors)** guide cells to become what they need to be.
The **body's direction map** (front-back, top-bottom, left-right) is set early using specific genes.
The **neural tube** becomes the brain/spinal cord. Errors here cause major problems.
Chemical signals guide how each part forms — like a cooking recipe with different ingredients in different spots.
Organogenesis turns early stem cells into full organs.