

Biochemistry

I. Carbohydrates

Contain the elements C,H,O in 1:2:1 ratio.

Examples include: sugars, starches, glycogen and cellulose.

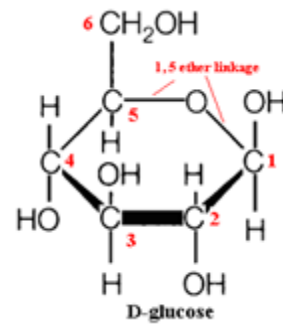
Sugars

Names always end in "ose"

1. Monosaccharides

Single 6 carbon ring (monomer)

Examples Glucose (blood sugar) and Fructose (honey and fruits)



2. Disaccharides

Two 6 carbon rings linked together (2 monomers)

Examples Sucrose, Lactose, Maltose

3. Polysaccharides

A carb formed when 3 or more sugars are linked together.

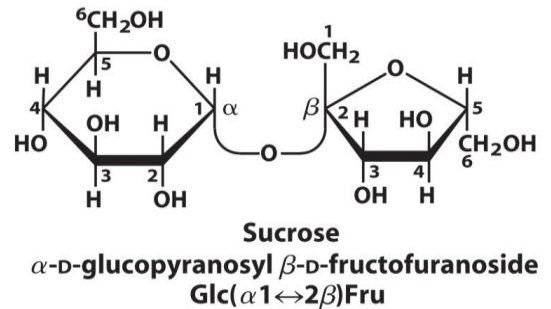
There are 3 main examples of polysaccharides.

- 1) Starch – a sugar storage molecule found only in plants
- 2) Cellulose – a carb based building molecule plants use to construct cell walls.
- 3) Glycogen – a sugar storage molecule found mainly in animal cells (muscle and liver).

A. Starches

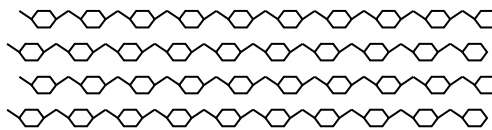
Starch is a sugar storage molecule found only in plants.

Starch can be composed of 1000-6000 sugar units linked together.



B. Cellulose

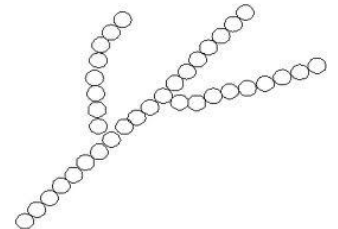
Long chains of sugar that coil when form.



C. Glycogen (AKA animal starch)

The main sugar storing molecule in our bodies.

Glycogen is formed when excess sugars are linked together in our muscle and liver cells forming chains of 16-24 sugars. When sugar levels drop within a muscle cell, the glycogen is broken down and the sugar is released as fuel. When blood sugar levels drop within the body glycogen in the liver is broken down and released into the blood stream.



II. Lipids

Contain the elements C,H,O.

Lipids are the only molecule organisms can use to store vast quantities of energy (calories).

Fat is also important as an insulator, and it protects and cushions internal organs.

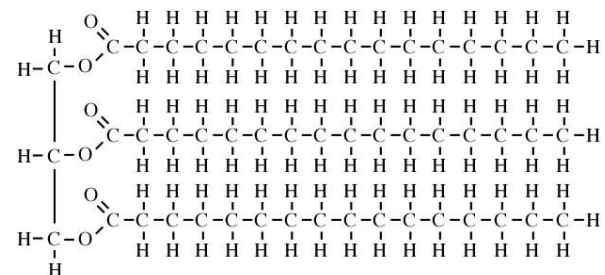
Fat can be modified into hormones, phospholipids (for cell membranes), waxes.

A. Fats

Fat molecules ("triglycerides") are made of 4 parts:

Triglycerides are formed by the union of glycerol (a 3 carbon chain) and three fatty acids (themselves long chains of carbon atoms).

Excess carbs are converted into fatty acids and then into triglycerides before being sent into the blood to a fat cell.



III. Proteins

Contain the elements C,H,O,N.

Proteins are structural molecules that give most cells, and therefore organisms their shape and appearance. Most organelles inside our cells are made of proteins, as well as the cells themselves.

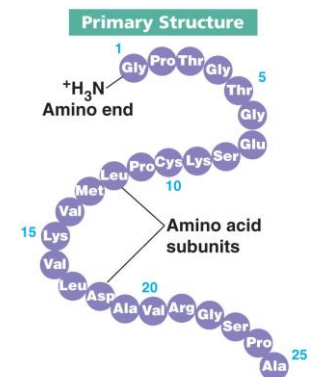
Muscle, nerve, and skin cells are primarily protein. Enzymes are protein molecules that help almost every chemical reaction in the body take place.

Amino Acids

The building blocks (monomers) of proteins.

20 different types are used to make human proteins.

The shape and properties of the protein is dictated by the precise sequence of amino acids and by the length of the amino acid chain. The bond between amino acids is called a peptide bond.

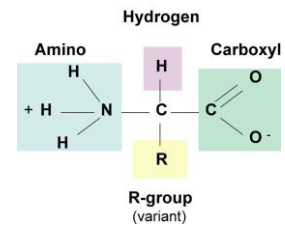


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Each amino acid is constructed of 4 parts.

1. amino group (NH_3^+) thus the "amino"
2. carboxyl group (COO^- or COOH) gives up H^+ thus the "acid"
3. alpha carbon
4. "R" group – one of 20 different R groups determines which amino acid is present.

Amino Acid Structure



IV. Nucleic Acids

Contain the elements C,H,O,N,P.

Nucleic acids are biological molecules essential for life.

Examples include DNA and RNA.

They function in encoding, transmitting and expressing genetic information.

The functional units (or building blocks) of nucleic acids are Nucleotides.

Nucleotides consist of three parts:

1. A 5 carbon sugar, either ribose or deoxyribose.
2. A nitrogen base (there are 5 types found here).
3. One or more phosphate groups attached to the 5 carbon sugar.

Base Pairs

Adenine (A) connects to Thymine (T)

Cytosine (C) connects to Guanine (G)

Deoxyribonucleic Acid (DNA)

First described by James Watson and Francis Crick who won the Nobel prize in 1953 (although they stole the work of Rosa Franklin who used X-ray diffraction to work out the exact structure.

The rungs (part you step on) of the ladder are 2 nitrogen bases and the rails are comprised of a sugar-phosphate chain (or backbone). It is the order of the bases along the middle of the DNA molecule that makes up the DNA's "alphabet" that "spells out" code for making life.

RNA

RNA is similar to DNA in that it is a string of nucleotides.

There are however 3 key differences:

- 1) RNA is single stranded. 2) RNA has no Thymine (T). A pairs with U (Uracil). 3) RNA has a ribose sugar.

RNA plays a role in 3 processes we'll examine:

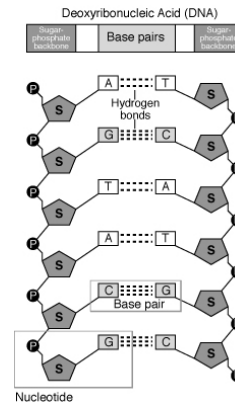
- 1) As RNA primer in DNA replication 2) As mRNA in protein synthesis 3) As tRNA in protein synthesis

DNA Replication

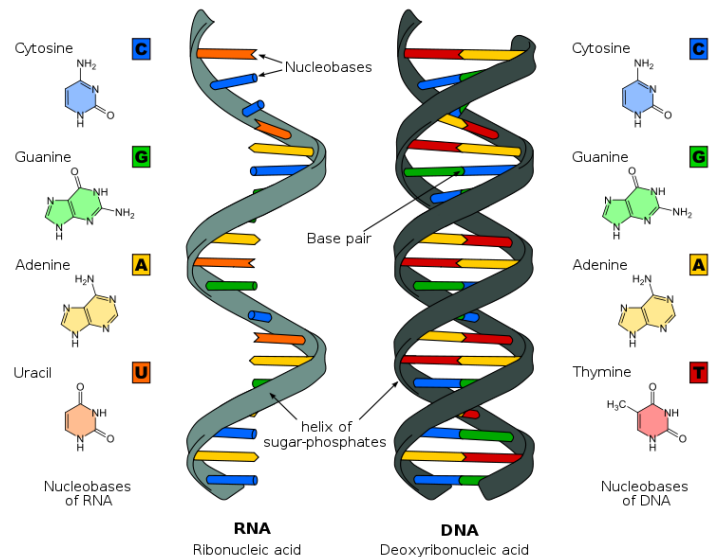
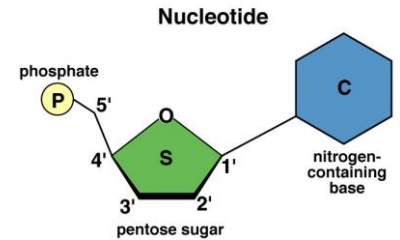
Before a cell can divide the individual strands of DNA (chromosomes) must make copies of themselves.

6 Step Process

1. A portion of the DNA unwinds and opens up (unzips).
2. An RNA primer is added to the parent strand.
3. An enzyme **DNA polymerase** binds to one side of the open DNA (leading strand) and moves **towards the fork** fitting in new complementary nucleotides (A-T and C-G).
4. On the second side of the open DNA. (lagging strand), the RNA primer is again followed by **DNA polymerase** which again binds to the open DNA and moves **away from the fork** fitting in new complementary nucleotides. However in this direction only smaller fragments called "Okazaki fragments" are formed.
5. Next the RNA primers are replaced with DNA nucleotides.
6. Finally the Okazaki fragments are stitched together by the enzyme **DNA ligase**.

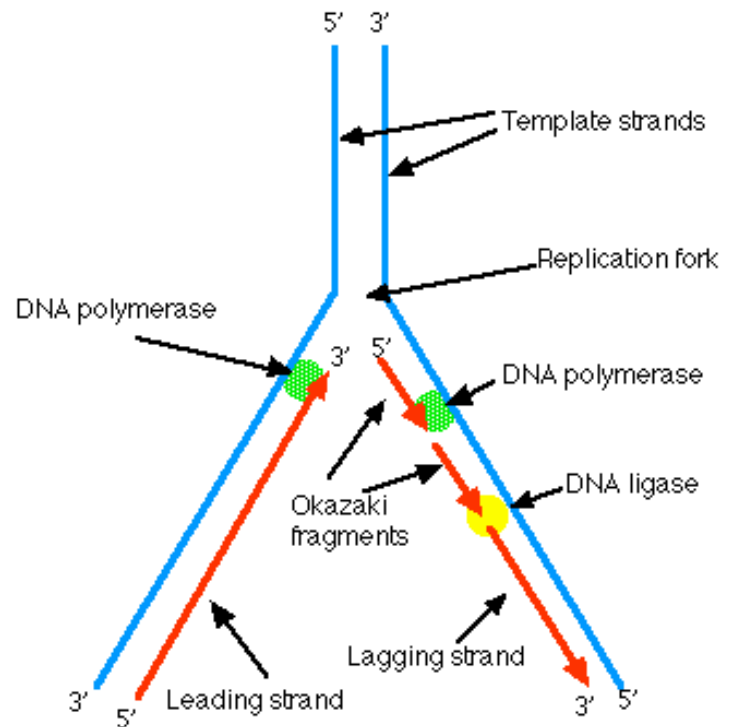
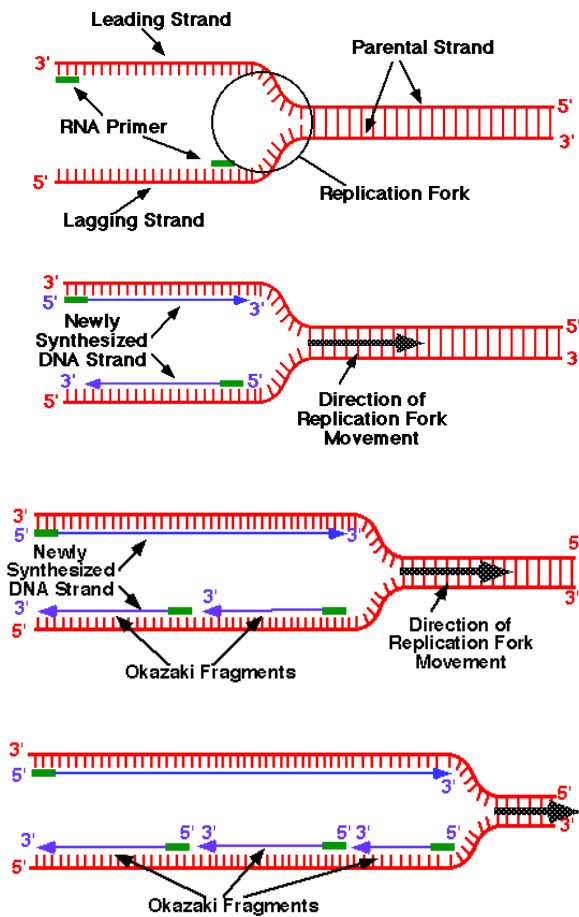


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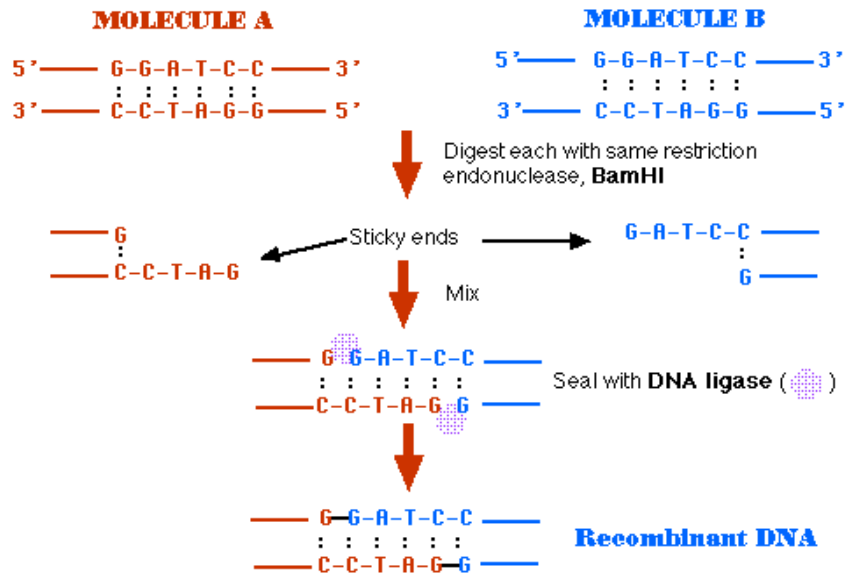
The end result is 2 **identical** strands of DNA.

The average human chromosome contains 150 000 000 nucleotide pairs and can replicate (including proof reading for errors) in less than 1 hour.



Recombinant DNA

DNA that is created artificially or "genetically engineered". Two or more sources of DNA are spliced together by special enzymes. (DNA restrictase cuts the DNA and DNA ligase links the new sections together) The result is a new segment of DNA inserted into an existing strand. For example: Inserting a segment of DNA that codes for the production of a protein that would make a plant resistant to roundup. ie. Round-Up Resistant Canola.



CRISPR Cas9

Clusters of Regularly Interspaced Short Palindromic Repeats

Discovered in 2012 by Emmanuelle Charpentier and Jennifer Doudna while studying bacterial defense mechanisms.

They won the Nobel Prize for their work with CRISPR Cas9 in 2020. It's an extremely precise, technique for GENE EDITING.

CRISPR as a Bacterial Defense

CRISPR systems were discovered in bacteria as an acquired means to help defend against viral attacks.

Bacterial CRISPR systems are like a vault that stores pieces of viral DNA as a means to help identify future invading viruses (similar to our ANTIGEN-ANTIBODY response).

If the same virus enters the bacteria again a Cas9 protein would quickly identify it and destroy it by cutting it up.

CRISPR System is a section of DNA that holds sections of CRISPR spacers (viral DNA) and short palindromic repeats that store segments of virus DNA that have been captured.

Guide RNA (gRNA) is a section of RNA synthesized by the CRISPR spacers that are used to identify future invading viruses.

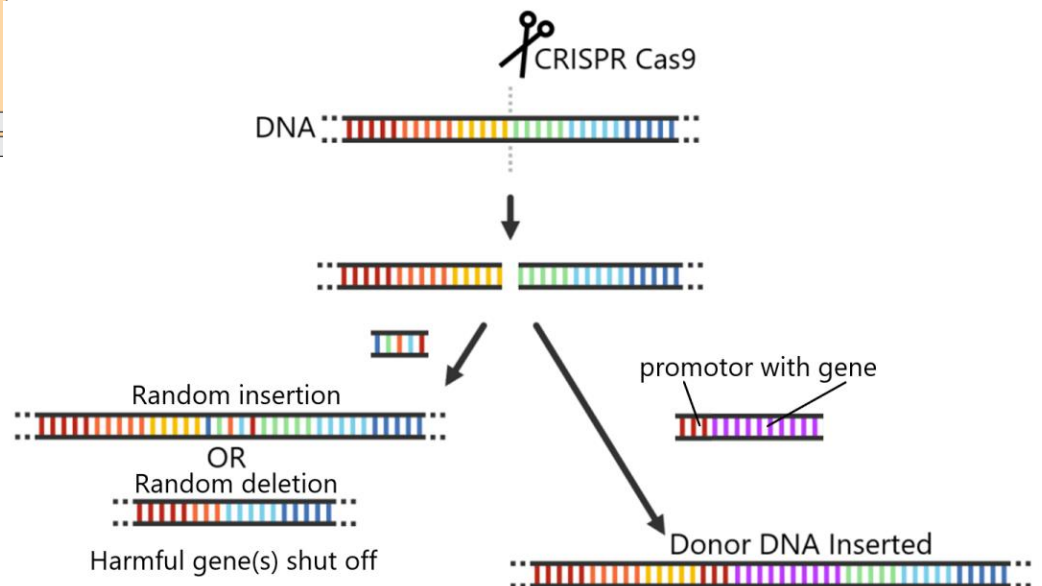
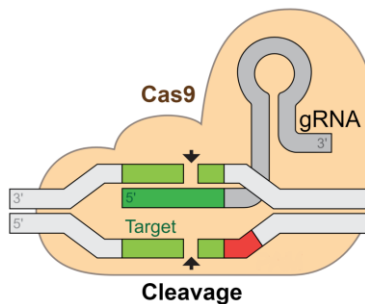
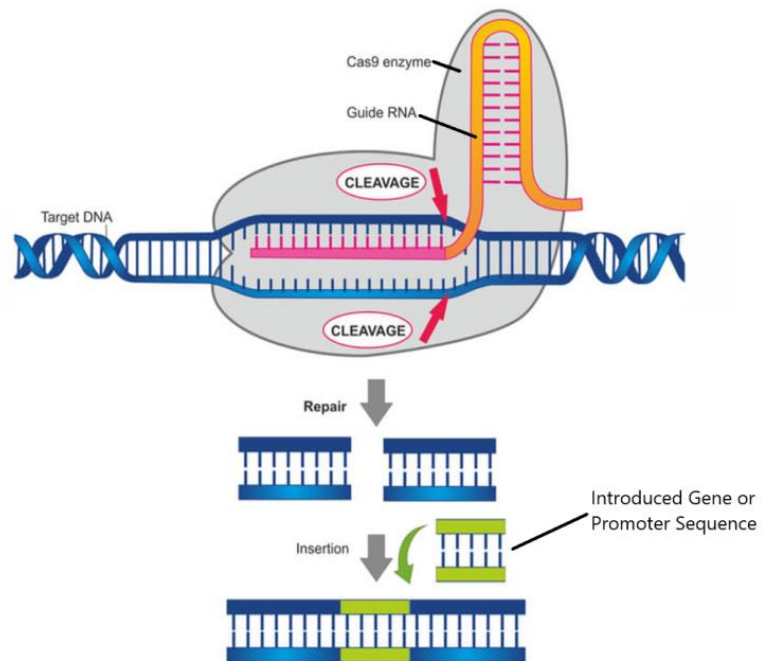
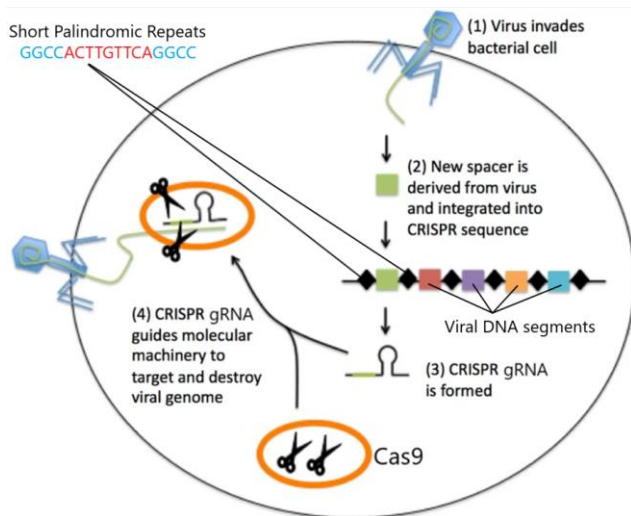
Cas9 is a protein that is guided by the gRNA to seek out and cut the specific viral DNA if it enters the cell again.

CRISPR used for Gene Editing

For use in GENE EDITING scientists engineer a specific gRNA segment that will target a precise section of DNA like a laser guided scope. These engineered gRNA segments are then mounted into a Cas9 protein capable of cutting DNA.

The Cas9 (along with its gRNA guidance system) called the Cas9-gRNA complex, are introduced into the cell of interest where the gRNA leads the Cas9 to the DNA section of interest (typically a promoter or gene).

The Cas9 then surgically cuts the DNA in the precise location allowing the gene to be deleted, replaced, repaired etc.



Gene Drives

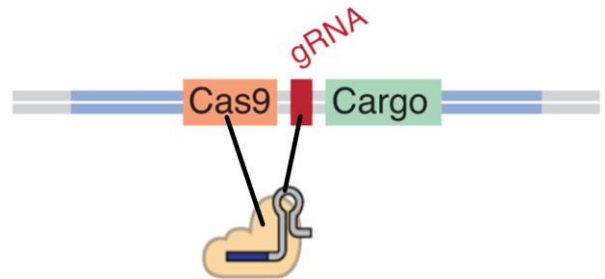
A gene drive is a type of genetic engineering technique that modifies genes so that they don't follow the typical rules of heredity. Gene drives dramatically increase the likelihood that a particular gene will be passed onto the next generation, allowing the gene to rapidly spread through a population and override natural selection.

CRISPR-Cas9 gene editing technology allows gene drives to be researched and built much easier.

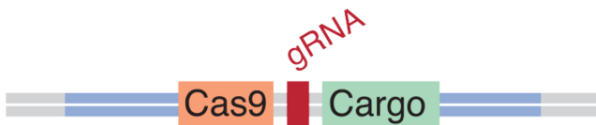
Cargo = gene(s) of Interest



Cargo + CRISPR System



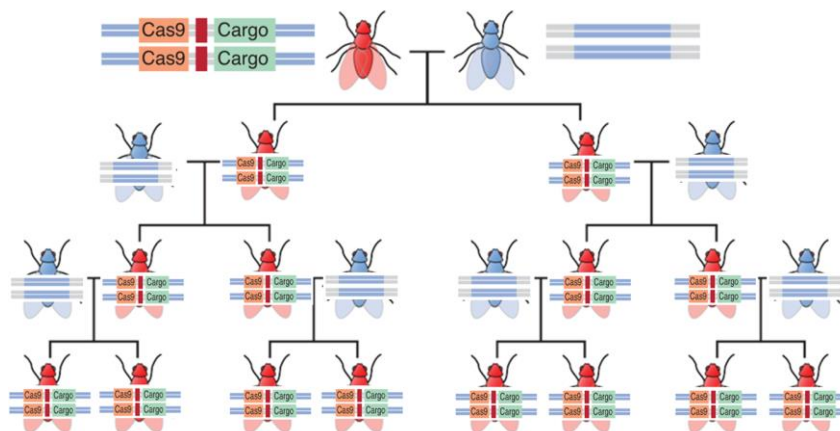
Cargo + CRISPR System



AFTER Gene Drive Editing



Gene drive inheritance



Altered gene is always inherited

DNA Typing

Analysis of DNA (similar to fingerprint analysis) is widely used in law enforcement to identify rapists, murderers, and determine paternity (who is the father).

Rooted in the fact that each person's DNA is unique.

A restriction enzyme (molecular scissors) is added to the sample of DNA.

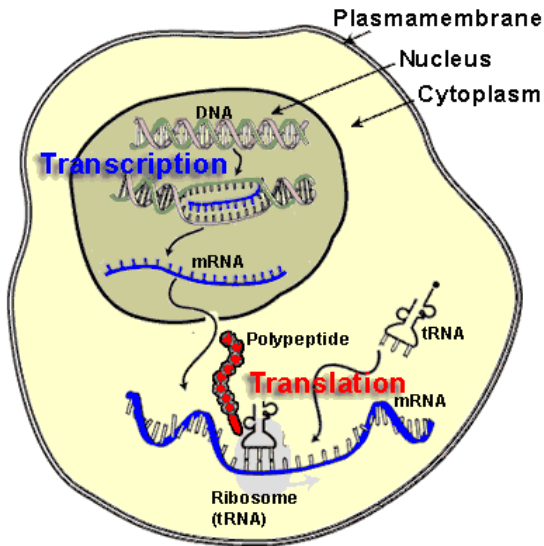
The DNA is cut into various fragments.

The cut up DNA is separated using a technique called gel electrophoresis.

Protein Synthesis

Literally "making protein". The process is divided into two parts:

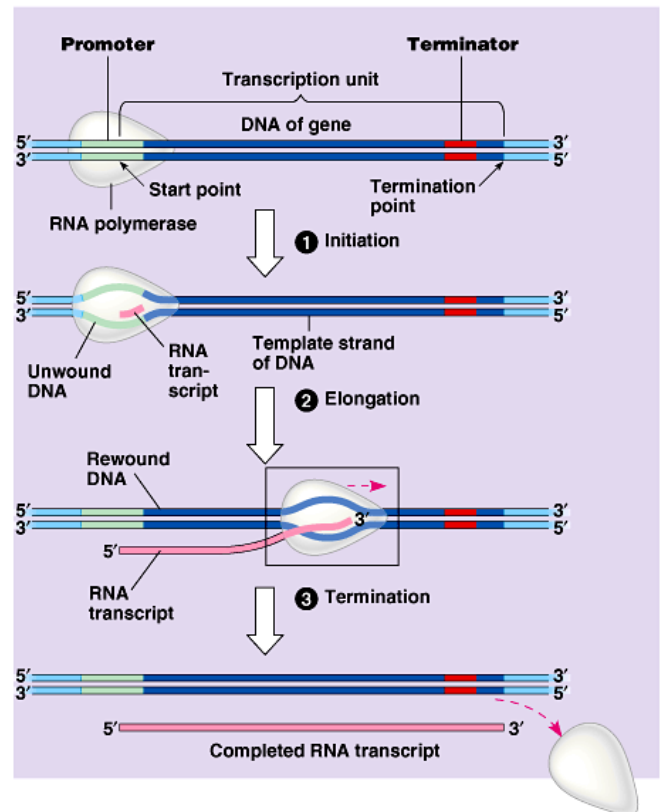
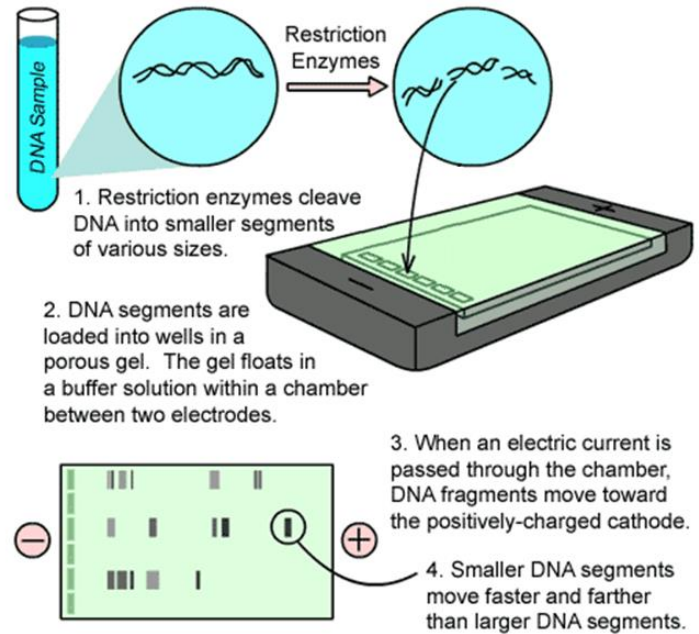
1. Transcription
2. Translation



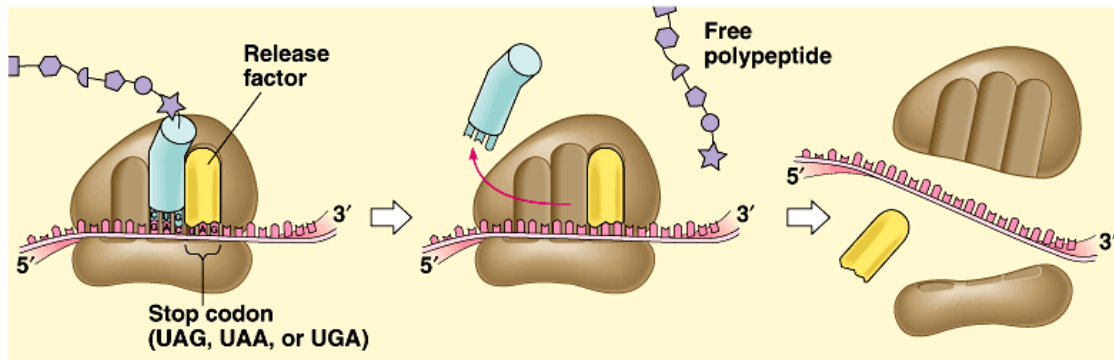
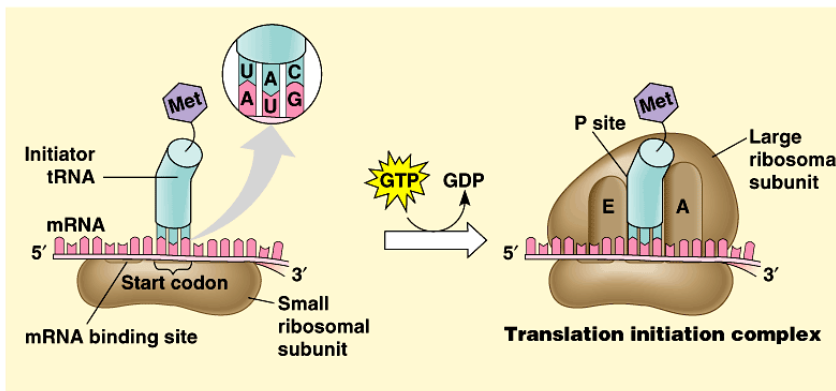
1. Transcription

- the process wherein a molecule of mRNA (messenger RNA) is made using a template strand of DNA.
- occurs inside nucleus in the nucleolus.
- **Step 1 Initiation**
a section of DNA (called a gene) opens up and a promoter sequence allows an enzyme **RNA Polymerase II** to attach to 1/2 the parent DNA.
- **Step 2 Elongation**
pre-mRNA forms using open DNA as template
RNA Polymerase II assembles the RNA nucleotides complementary to the DNA template strand.
- **Step 3 Termination**
when **RNA Polymerase II** reaches a terminator sequence of base pairs along the DNA template, transcription halts.
- before it leaves the nucleus, the pre-mRNA is processed by:
 - 1) having its ends capped to protect it.
 - 2) having introns (non coding sections) removed while leaving exons (coding sections) in place.
- mRNA moves to cytoplasm to find a ribosome

Gel Electrophoresis



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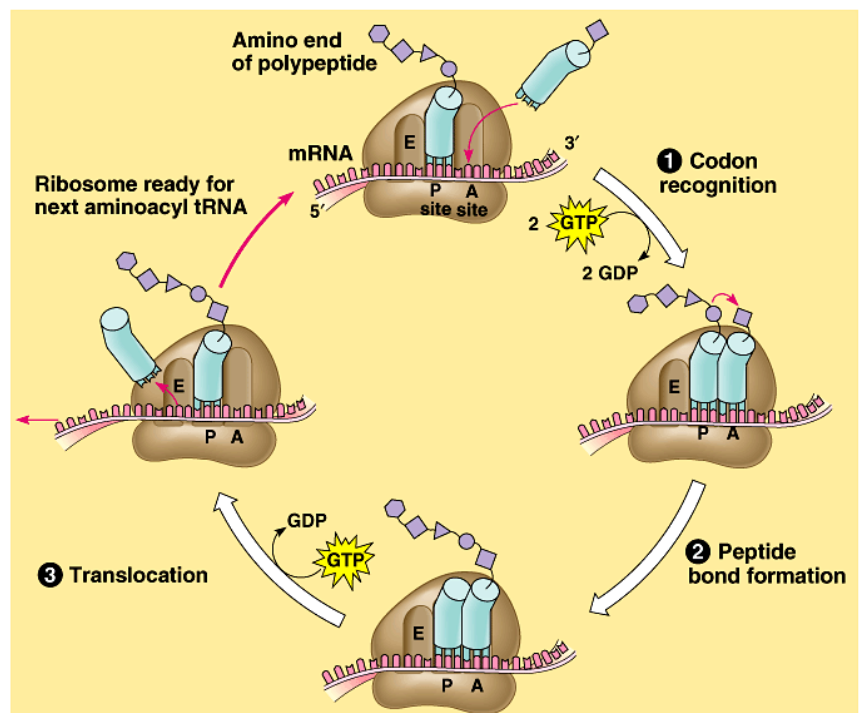
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2. Translation

- the process of creating a polypeptide (protein) using the genetic information present in the mRNA molecule.
- occurs in cytoplasm at a ribosome.
- Step 1 Initiation**
when the mRNA attaches itself to both the ribosome and the tRNA at the “AUG” initiator sequence.
- Step 2 Elongation**
Every 3 nucleotides of mRNA called a "**codon**" codes for a particular amino acid.
Transfer RNA (tRNA) carrying an amino acid, binds its "**anticodon**" to the complementary mRNA codon.
A peptide bond forms between adjacent amino acids and the “empty” tRNA is released to find another amino acid.
This continues as the mRNA slides along the ribosome.
- Step 3 Termination**
Translation is terminated when a “stop codon” is reached in the mRNA strand.
The completed polypeptide (now called a protein) is released.

Note:

- there are 20 different types of amino acids
- links between amino acids are called peptide bonds



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Mutations and Cancer

A mutation is a failure of DNA repair.
There are 3 general types of mutations.

1. Single Base Substitutions
2. Insertions and Deletions
3. Translocations

1. Single Base Substitutions

Example: Adenine (A) replaced with Guanine (G)

- a. Missense Mutation - alters the codon to produce different protein.
- b. Nonsense Mutation - alters codon to one of the STOP codons resulting in a shortened protein.
- c. Silent Mutation - the altered codon happens to code for the same amino acid as the original therefore no change in the protein produced.

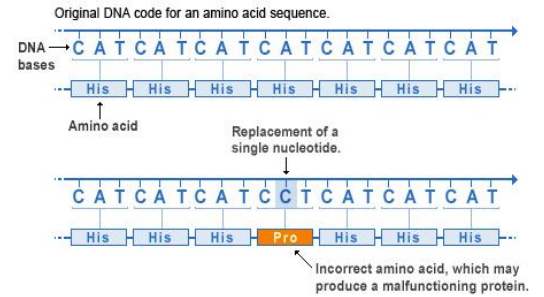
2. Insertions and Deletions

Extra base pairs are added or deleted from the DNA of a gene. Insertions and deletions of 1 or 2 base pairs result in a "frameshift" and are particularly devastating.

3. Translocations

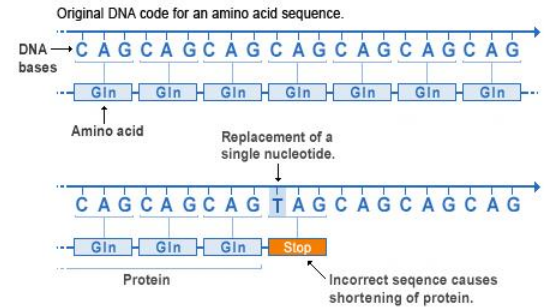
Transfers of an entire piece of one chromosome to a nonhomologous chromosome.

Missense mutation



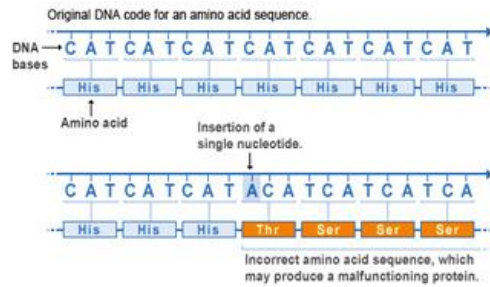
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Nonsense mutation



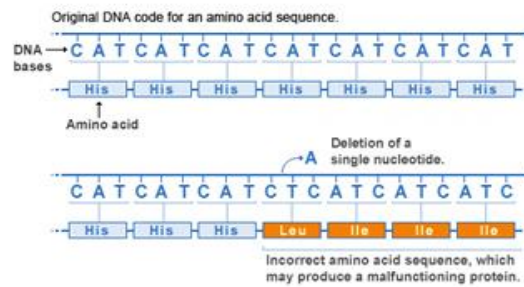
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Insertion mutation

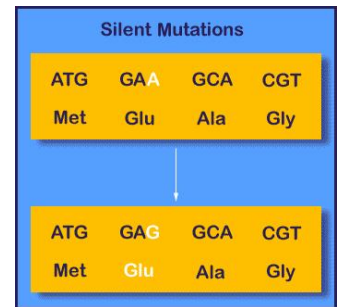


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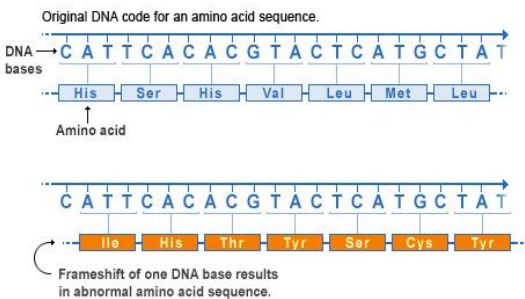
Deletion mutation



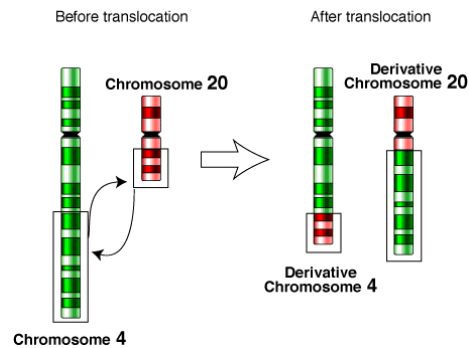
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Frameshift mutation



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Cancer

Cancer is an uncontrolled growth of cells. The cell division can be fast or slow but the cells never stop dividing.

Malign tumors are cancerous, **benign** are not.

Cancers begin as a primary tumor and often establish metastases (moves through blood stream or lymph) in other body locations. These regions of secondary growth usually end up being fatal.

Causes of Cancer

Anything that damages the DNA and causes a mutation can cause cancer. If the mutation is such that it "codes" for the cell to divide uncontrollably, then cancer has begun.

Chemicals that damage the DNA increasing the risk of cancer are called carcinogens.

Other factors such as exposure to radiation can also damage the DNA and lead to cancer causing mutations.

An **Ames Test** can be used to determine if a chemical is carcinogenic or not. The test uses a mutant strain of bacteria which lacks the ability to produce a certain amino acid. If, after exposure to the "test chemical", colonies of bacteria begin to grow again, it is assumed that the "test chemical" caused a high number of mutations in the bacteria allowing it to again produce the amino acid it was lacking. Thus the "test chemical" is deemed a mutagen and classified as "carcinogenic".

A and B are the control plates.

C and D are the experimental chemicals.

Does C pass the Ames test?

Is C a carcinogen?

Does D pass the Ames test?

Is D a carcinogen?

