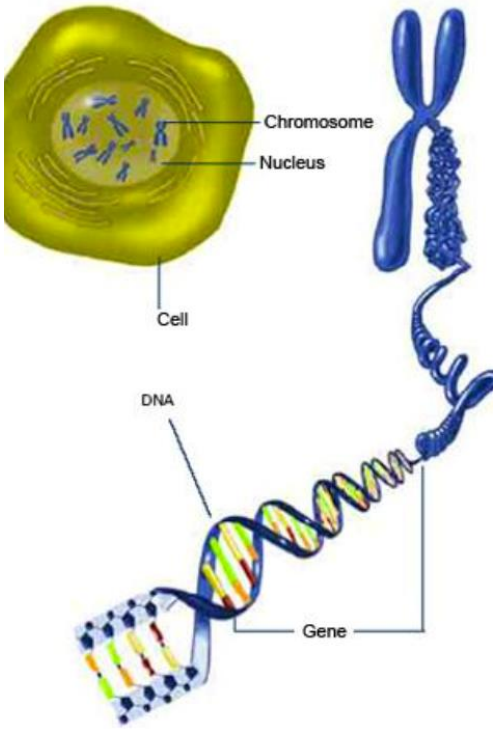
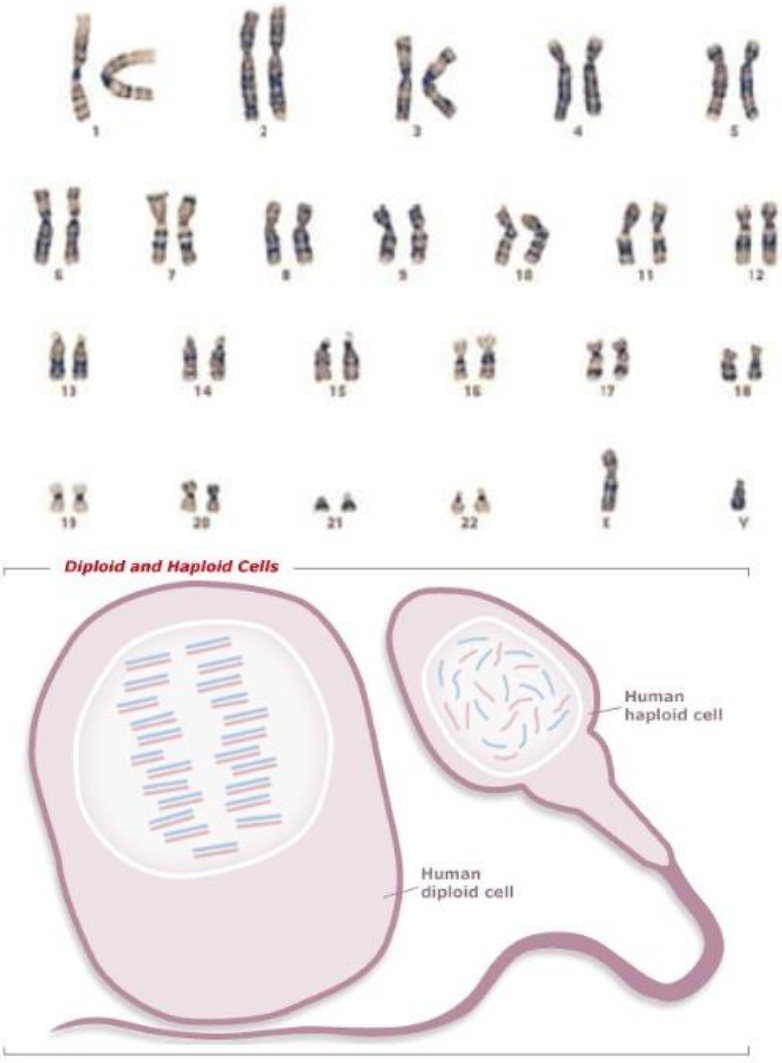
Biology 30
DNA

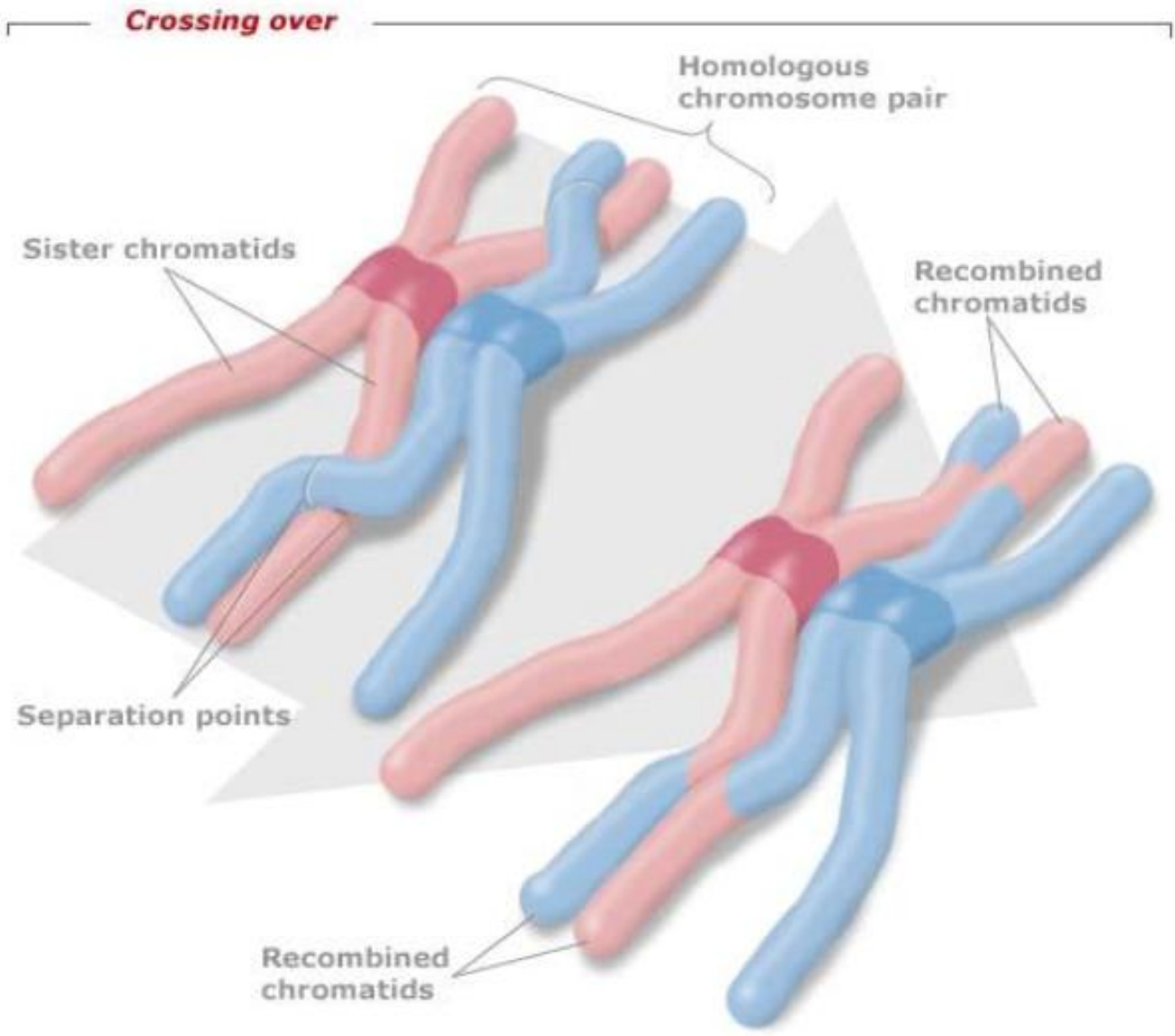


Review: Importance of Meiosis

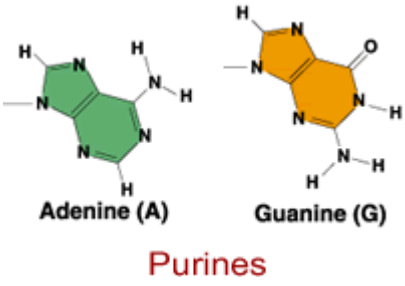
- Every cell has a **nucleus** and every nucleus has **chromosomes**.
- The number of chromosomes depends on the species.
    - Examples:
        - Chicken – 78
        - Chimpanzee – 48
        - Potato – 48
        - Human – 46
        - Frog – 26
        - Pea – 14
- **Genes** are located on chromosomes. Genes control the traits of an individual.
- Genes are made up of **DNA** molecules.
- Chromosomes come in matching sets. These are called homologous pairs (see right).
- The cells in your body have a complete set of chromosomes (46 in total). These are called diploid cells.
- Sex cells (sperm and egg) only have half the number of chromosomes (23). These are called haploid cells.
- Sex cells are also known as gametes.
- When the gametes combine, they form a zygote (offspring). The zygote gets half its chromosomes from mom (23) and half from its dad (23).
- Zygotes are diploid (46).
- When the sperm and egg meet they must match up for the zygote to develop properly.
- The process of creating a gamete (sex cell) is called meiosis.
- Meiosis is similar to mitosis (making a copy of the cell), but meiosis will produce 4 daughter cells, each of which are haploid.
- There are many steps to meiosis, but the first is called Prophase I.



- During Prophase I, the important thing that happens is that homologous pairs **cross over and chromosomes trade genes with each other.**

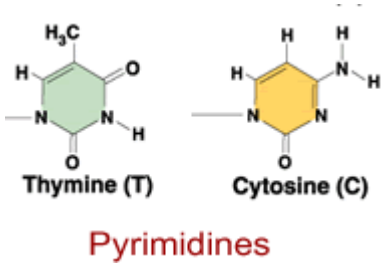


- Crossing over increases the number of possible gene combinations. This is one of the reasons that sexual reproduction has so much variation in traits from one generation to the next.
- Evolutionarily, this is an advantage for the species because a wide variety of traits means that if the environment changes, the species will have a better chance of adapting to the new stresses.

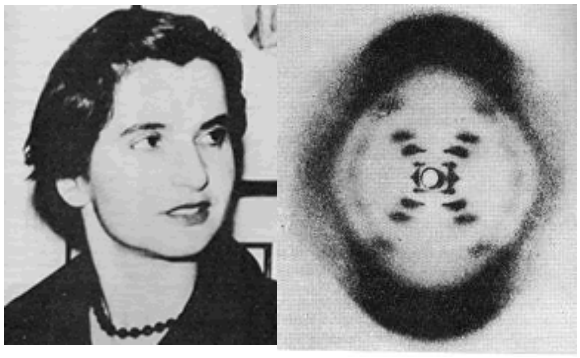


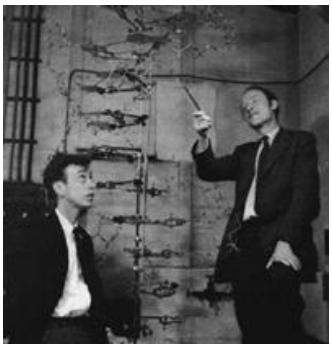
<u>DNA History and Basics</u>

- **Erwin Chargaff** analyzed the amounts of the four nucleotides found in DNA (Adenine, Thymine, Guanine, Cytosine) and noticed a pattern.
    - The amount of A, T, G, C varies from species to species.
    - In each species, the amount of A = T, and the amount of G = C (Base Pair Rule).
    - Bases come in two types: **pyrimidines** (cytosine and thymine) and **purines** (guanine and adenine).



- **Rosalind Franklin and Maurice Wilkins** spent time taking **X-ray diffraction** pictures of the DNA molecule in an attempt to determine the shape of the DNA molecule.

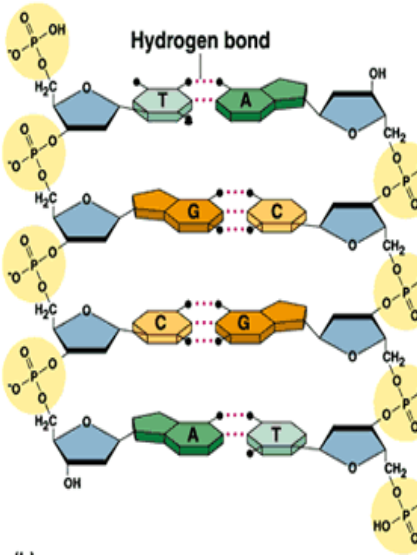


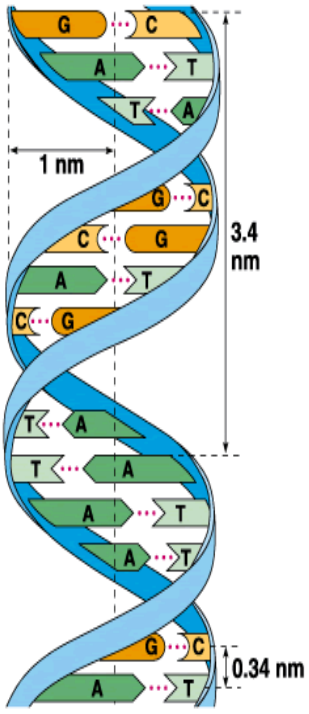


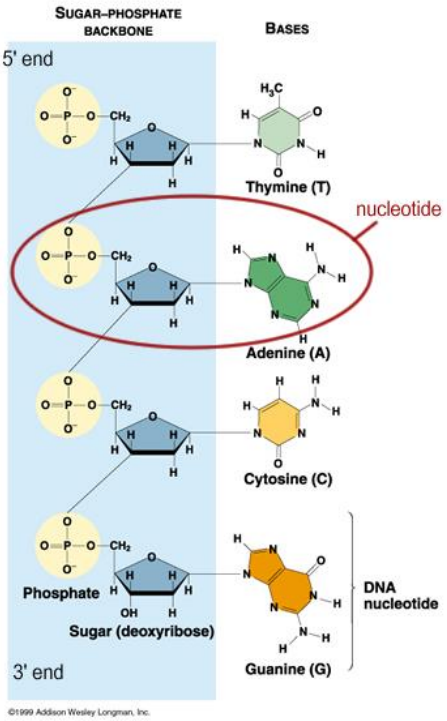
- **James Watson and Francis Crick** are credited with finally piecing together all the information previously gathered on the molecule of DNA. They established the structure as a **double helix** - like a ladder that is twisted. The two sides of the ladder are held together by hydrogen bonds.

Watson & Crick Model of DNA

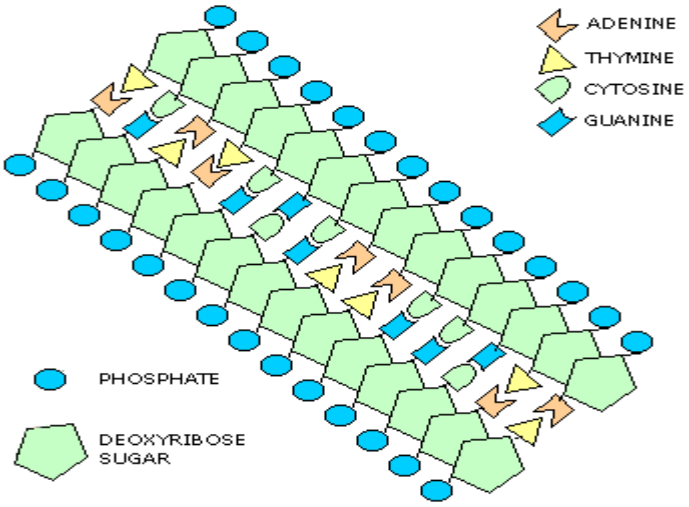
- The sugar (deoxyribose) and phosphates make up the "backbone" of the DNA molecule. The phosphate is attached to the 5’ carbon (the 5 is a number given to sugar molecules). The DNA strand has a free phosphate on the 5' end, and a free sugar on the 3' end - these numbers will become important later.
- **Adenine always pairs with Thymine | Guanine always pairs with Cytosine**
  Side1:: A A T T G G C C A G A T A C
  Side2:: T T A A C C G G T C T A T G
- DNA is composed of subunits called **nucleotides**, strung together in a long chain -- Each nucleotide consists of: a phosphate, a sugar (deoxyribose), and a base.





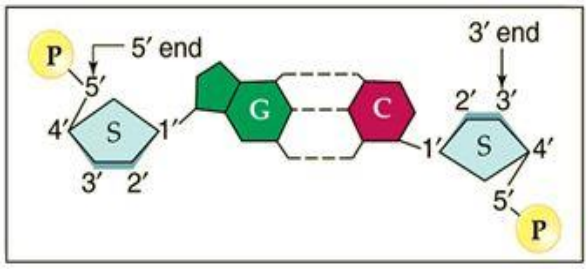


- This DNA molecule is not represented well. What is wrong with it?

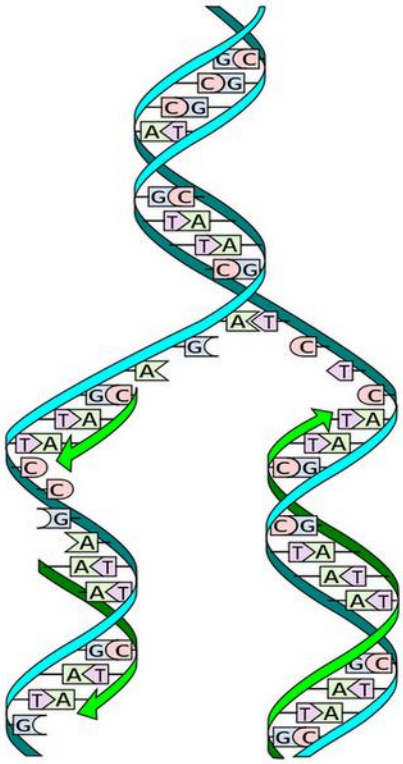


(Answer: the sugar molecules are not antiparallel ^)

- Here the 5' end and the 3' end are seen again: each side of the ladder has an opposite orientation. One side of the ladder as a free sugar (the 3'end) the other side has a free phosphate (the 5'end). This arrangement is called: **ANTI-PARALLEL.**



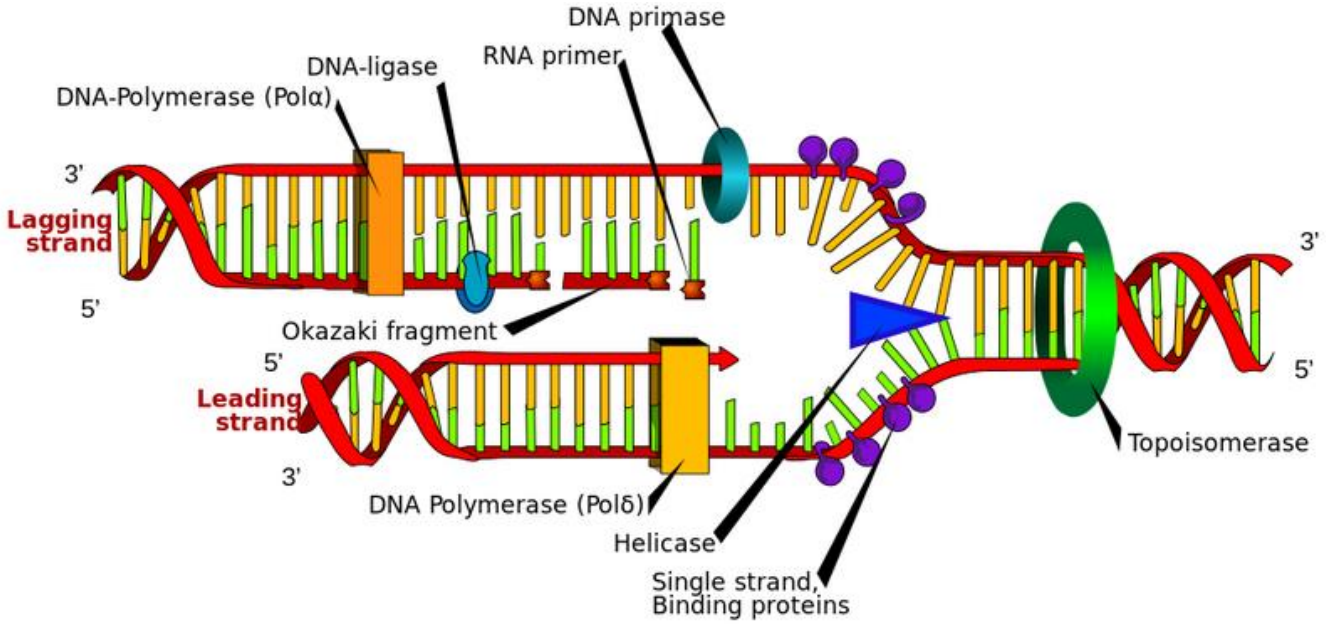
<u>DNA Replication</u>



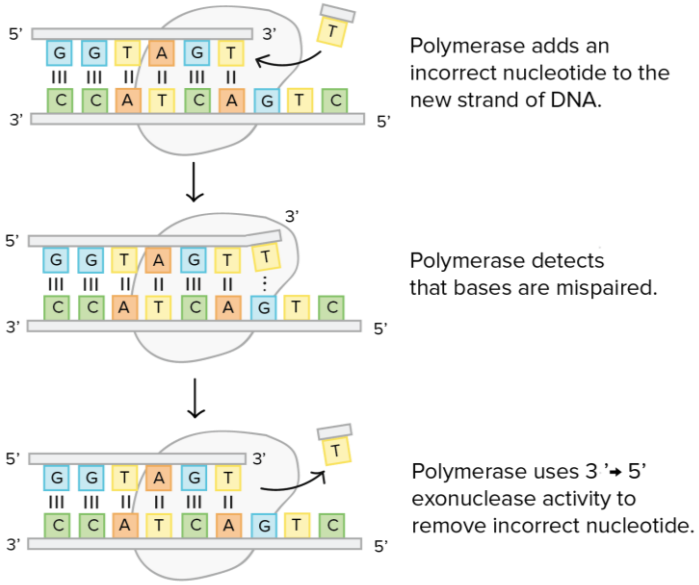
- This is the process by which DNA makes a copy of itself. It occurs during interphase, prior to cell division.
- There are three phrases of DNA replication.
    1. Phase 1: Initiation
        - An initiator protein unwinds a short stretch of DNA double helix.
        - **DNA helicase** (enzyme) breaks apart the hydrogen bonds in the DNA. The junction is called a **replication fork**.
    2. Phase 2: Priming
        - At the same time, an enzyme called primase briefly attaches to each strand and lays a foundation for replication to begin.
    3. Phase 3: Matching
        - **DNA polymerase** wraps itself around the strand and adds the complementary nucleotides and binds the sugars and phosphates. DNA polymerase travels from the 3' to the 5' end. The DNA is called the **template** strand.
        - DNA polymerase also adds **complementary** nucleotides on the other side of the ladder, traveling in the opposite direction.
        - One side is the **leading strand** - it follows the helicase as it unwinds.
        - The other side is the **lagging strand** - it's moving away from the helicase (in the 5' to 3' direction).

- *Replication is called **semi-conservative**, because one half of the original strand is always saved, or "conserved."*
- Problem: it reaches the replication fork, but the helicase is moving in the opposite direction. It stops, and another polymerase binds farther down the chain. This process creates several fragments, called **Okazaki Fragments**, that are bound together by **DNA ligase**.

- Note: During replication, there are many points along the DNA that are synthesized at the same time (multiple replication forks). It would take forever to go from one end to the other, it is more efficient to open up several points at one time.

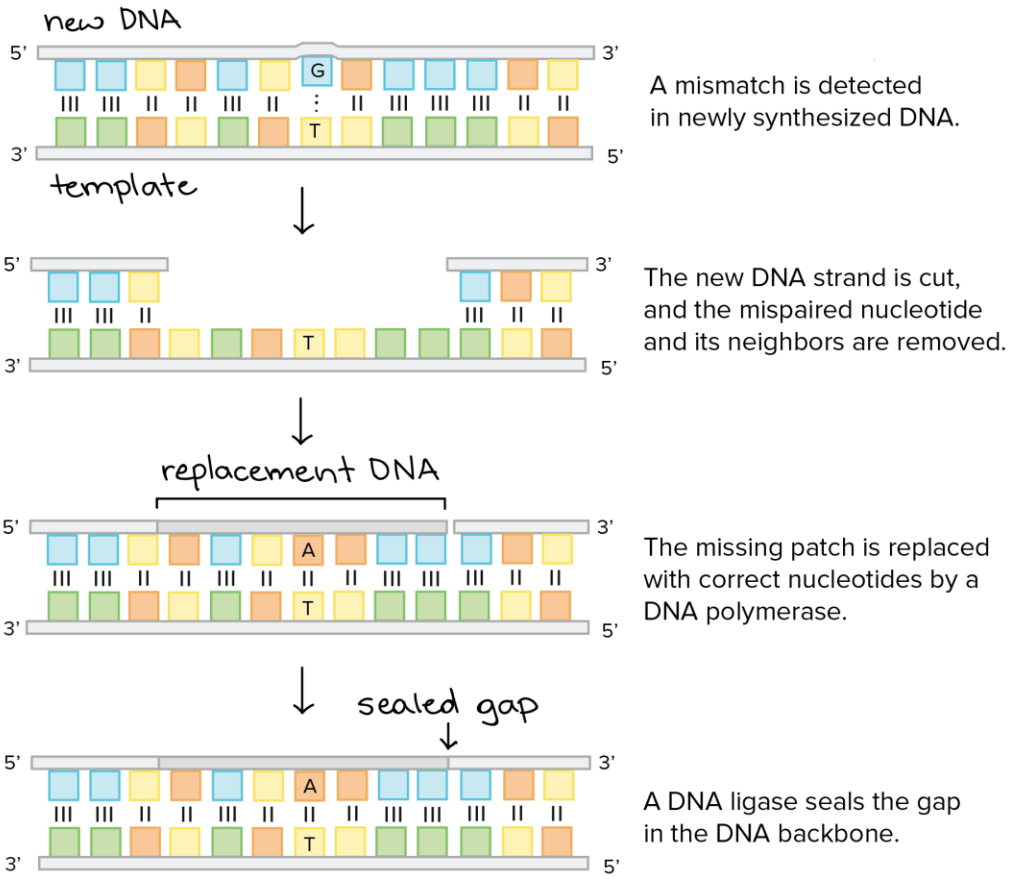


- Sometimes there are **replication errors** – these can cause a genetic mutation.
- Replication errors and DNA damage are actually happening in the cells of our bodies all the time. In most cases, however, they don't cause cancer, or even mutations. That's because they are usually detected and fixed by DNA proofreading and repair mechanisms. Or, if the damage cannot be fixed, the cell will undergo programmed cell death (apoptosis) to avoid passing on the faulty DNA. Mutations happen, and get passed on to daughter cells, only when these mechanisms fail. Cancer, in turn, develops only when multiple mutations in division-related genes accumulate in the same cell.
- There are ways to try to prevent these mutations: *(From Khan Academy…)*
  - **<u>PROOFREADING</u>** by the polymerase prevents mismatches.
    - **DNA polymerases** are the enzymes that build DNA in cells. During DNA replication (copying), most DNA polymerases can "check their work" with each base that they add. This process is called **proofreading**. If the polymerase detects that a wrong (incorrectly paired)



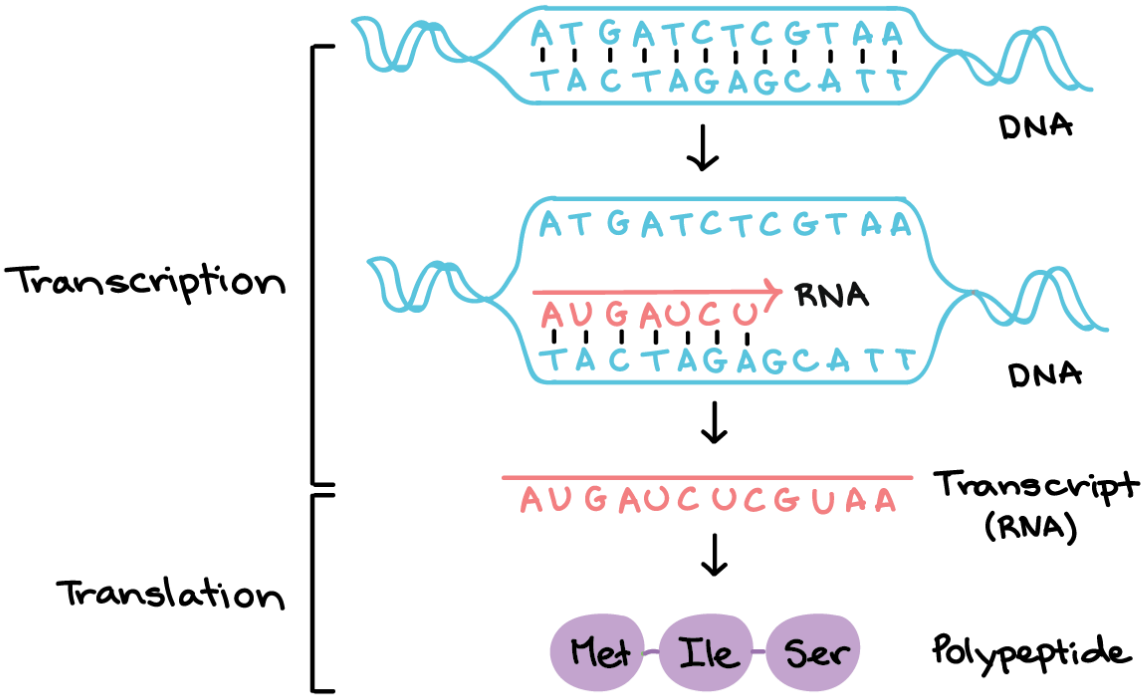
nucleotide has been added, it will remove and replace the nucleotide right away, before continuing with DNA synthesis.

- **<u>DNA REPAIR ENZYMES</u>** can repair damaged DNA also. *(From Khan Academy…)*
  - Many errors are corrected by proofreading, but a few slip through. **Mismatch repair** happens right after new DNA has been made, and its job is to remove and replace mis-paired bases (ones that were not fixed during proofreading). Mismatch repair can also detect and correct small insertions and deletions that happen when the polymerases "slips," losing its footing on the template.
  - How does mismatch repair work? First, a protein complex (group of proteins) recognizes and binds to the mispaired base. A second complex cuts the DNA near the mismatch, and more enzymes chop out the incorrect nucleotide and a surrounding patch of DNA. A DNA polymerase then replaces the missing section with correct nucleotides, and an enzyme called a DNA ligase seals the gap.



<u>Protein Synthesis: Transcription</u> *(From Khan Academy…)*

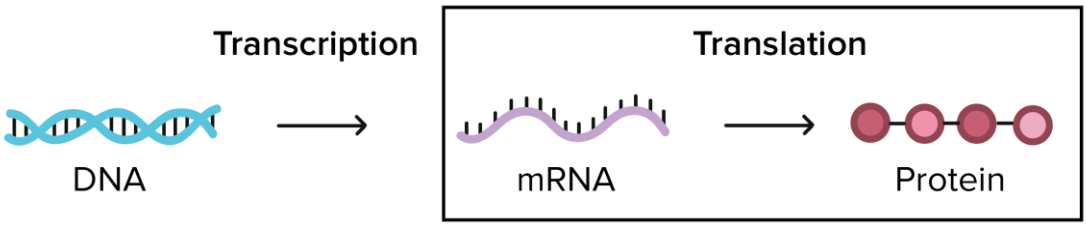
- Transcription is a process where information is rewritten. In biology, **transcription** is the process of copying out the DNA sequence of a gene in the similar alphabet of RNA.
- Transcription is the first step in gene expression, in which information from a gene is used to construct a protein. The goal of transcription is to make an RNA copy of a gene's DNA sequence. For a protein-coding gene, the RNA copy, or **transcript**, carries the information needed to build a polypeptide (protein or protein subunit).



- Transcription of a gene takes place in three stages: initiation, elongation, and termination.
    1. **Initiation.** RNA polymerase binds to a sequence of DNA called the **promoter**, found near the beginning of a gene. Each gene (or group of co-transcribed genes, in bacteria) has its own promoter. Once bound, RNA polymerase separates the DNA strands, providing the single-stranded template needed for transcription.
    2. **Elongation.** One strand of DNA, the **template strand**, acts as a template for RNA polymerase. As it "reads" this template one base at a time, the polymerase builds an RNA molecule out of complementary nucleotides, making a chain that grows from 5' to 3'. The RNA transcript carries the same information as the non-template (coding) strand of DNA, but it contains the base uracil (U) instead of thymine (T).
    3. **Termination.** Sequences called **terminators** signal that the RNA transcript is complete. Once they are transcribed, they cause the transcript to be released from the RNA polymerase.
- After this, the strand of RNA that is produced is called a **messenger RNA** (mRNA), which starts the process of translation.

Protein Synthesis: Translation *(From Khan Academy…)*

- In this stage, the mRNA is "decoded" to build a protein (or a chunk/subunit of a protein) that contains a specific series of amino acids.



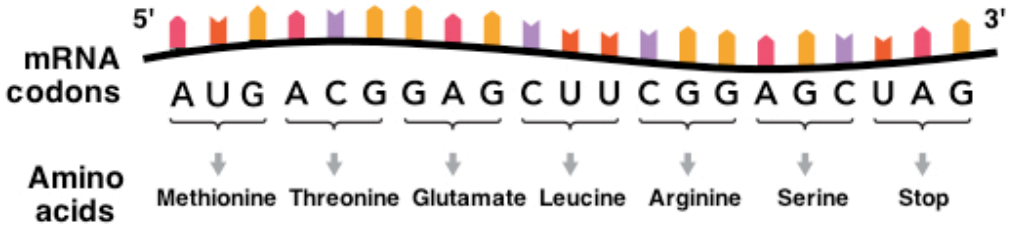
- During translation, a cell “reads” the information in an mRNA and uses it to build a protein. Actually, an mRNA doesn’t always encode—provide instructions for—a whole protein. Instead, what we can confidently say is that it always encodes a **polypeptide**, or chain of amino acids.
- In an mRNA, the instructions for building a polypeptide are RNA nucleotides (As, Us, Cs, and Gs) read in groups of three. These groups of three are called **codons**.

- There are 61 codons for amino acids, and each of them is "read" to specify a certain amino acid out of the 20 commonly found in proteins. One codon, AUG, specifies the amino acid methionine and also acts as a **start codon** to signal the start of protein construction.

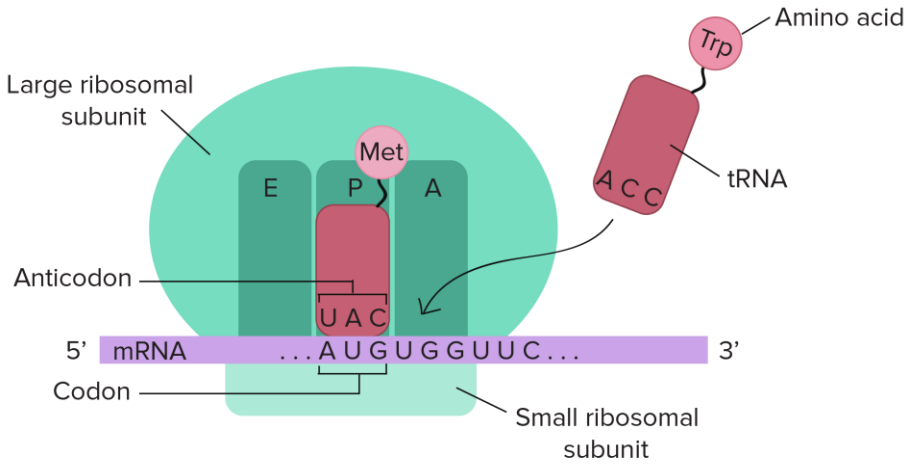
Second letter

First letter	U	C	A	G	Third letter
U	UUU, UUC: Phe UUA, UUG: Leu	UCU, UCC, UCA, UCG: Ser	UAU, UAC: Tyr **UAA Stop** **UAG Stop**	UGU, UGC: Cys **UGA Stop** UGG Trp	U C A G
C	CUU, CUC, CUA, CUG: Leu	CCU, CCC, CCA, CCG: Pro	CAU, CAC: His CAA, CAG: Gln	CGU, CGC, CGA, CGG: Arg	U C A G
A	AUU, AUC, AUA: Ile AUG: Met	ACU, ACC, ACA, ACG: Thr	AAU, AAC: Asn AAA, AAG: Lys	AGU, AGC: Ser AGA, AGG: Arg	U C A G
G	GUU, GUC, GUA, GUG: Val	GCU, GCC, GCA, GCG: Ala	GAU, GAC: Asp GAA, GAG: Glu	GGU, GGC, GGA, GGG: Gly	U C A G

- There are three more codons that do *not* specify amino acids. These **stop codons**, UAA, UAG, and UGA, tell the cell when a polypeptide is complete. All together, this collection of codon-amino acid relationships is called the **genetic code**, because it lets cells "decode" an mRNA into a chain of amino acids.

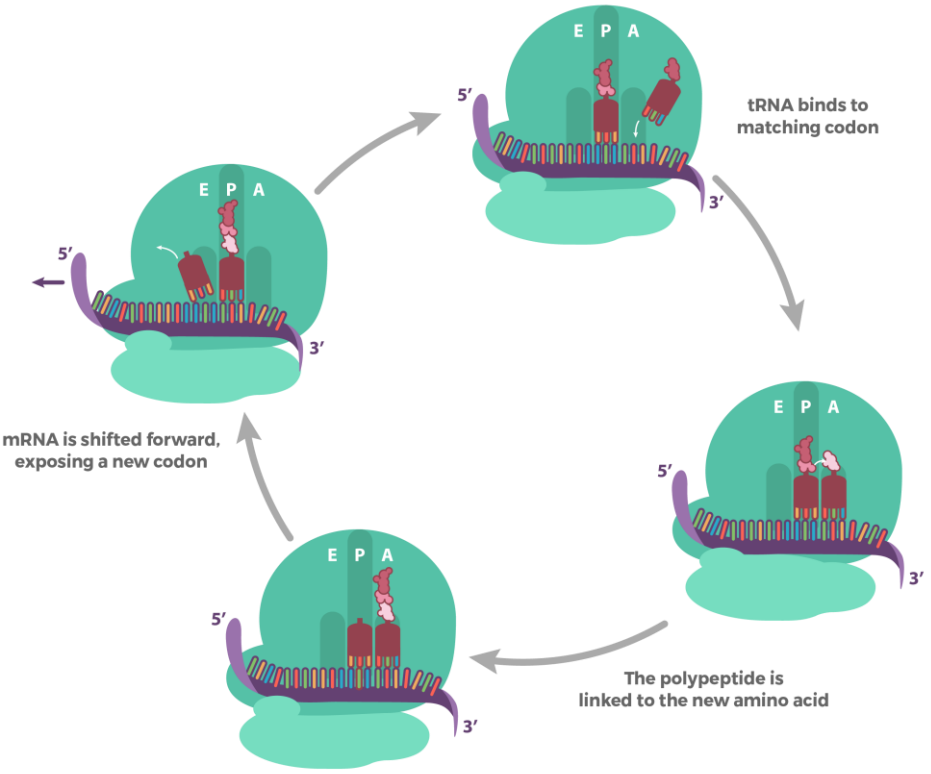


- When building polypeptides mRNA is "read" make a polypeptide by two types of molecules: tRNAs and ribosomes.
    - **Transfer RNAs**, or **tRNAs**, are molecular "bridges" that connect mRNA codons to the amino amino acids they encode. One end of each tRNA has a sequence of three nucleotides called an **anticodon**, which can bind to specific mRNA codons. The other end of the tRNA carries the amino acid specified by the codons.
    - There are many different types of tRNAs. Each type reads one or a few codons and brings the right amino acid matching those codons.



- **Ribosomes** are the structures where polypeptides (proteins) are built. They are made up of protein and RNA (**ribosomal RNA**, or **rRNA**). Each ribosome has two subunits, a large one and a small one, which come together around an mRNA—kind of like the two halves of a hamburger bun coming together around the patty. The ribosome provides a set of handy slots where tRNAs can find their matching codons on the mRNA template and deliver their amino acids. These slots are called the A, P, and E sites. Not only that, but the ribosome also acts as an enzyme, catalyzing the chemical reaction that links amino acids together to make a chain.

- There are three steps in translation:
  - **Initiation**: the ribosome assembles around the mRNA to be read and the first tRNA (carrying the amino acid methionine, which matches the start codon, AUG). This setup, called the initiation complex, is needed in order for translation to get started.
  - **Elongation:** is the stage where the amino acid chain gets longer. In elongation, the mRNA is read one codon at a time, and the amino acid matching each codon is added to a growing protein chain.
    - Each time a new codon is exposed:
      - A matching tRNA binds to the codon.
      - The existing amino acid chain (polypeptide) is linked onto the amino acid of the tRNA via a chemical reaction.
      - The mRNA is shifted one codon over in the ribosome, exposing a new codon for reading.



  - **Termination** is the stage in which the finished polypeptide chain is released. It begins when a stop codon (UAG, UAA, or UGA) enters the ribosome, triggering a series of events that separate the chain from its tRNA and allow it to drift out of the ribosome. After termination, the polypeptide may still need to fold into the right 3D shape, undergo processing (such as the removal of amino acids), get shipped to the right place in the cell, or combine with other polypeptides before it can do its job as a functional protein.

Gene Mutations

- **Point Mutation**: substitute one base for another.
  Original: A T A C A C
  Mutant : **T** T A C A C

- **Frameshift Mutation**: a base is either added or removed which causes a shift in the reading frame. Many genes affects.
  Original: A T A C A C A A G C C A
  Mutant: A T **T** A C A C A A G C C A

- **Silent Mutation**: a base is changed but the resulting amino acid is the same as in the non-mutant DNA. No outward changes.
  Original: A A A C A G
  Mutant: A A **G** C A G

- **Nonsense Mutation**: a codon is changed to a STOP codon
  Original: A T A C C C A A A
  Mutant: **A T T** C C C A A A ***ATT – translates to UAA in mRNA = STOP***

- **Nondisjunction**: when homologous chromosomes fail to separate as they should.