

Bioinformatics

CS300

Crash course:

Mutations

Week3, Deck 1

Fall 2022

Oliver BONHAM-CARTER



What is Mutation?

- A natural process that changes the DNA sequence
- A common process
 - during replication of the human genome a “typo” occurs every 100,000 or so nucleotides
 - that’s about 120,000 typos each time one of our cells divides
 - most are repaired





What is Mutation?

- Most mutations are neutral – no consequence
- Some mutations are beneficial – provides advantage in particular environment
- Some mutations are harmful





ALLEGHENY
COLLEGE

Chocolate Chip Cookies

Ingredients

2 $\frac{1}{4}$ cups all purpose flour
1 teaspoon baking soda
1 teaspoon salt
1 cup (2 sticks) butter, softened
 $\frac{3}{4}$ cup granulated sugar
 $\frac{3}{4}$ cup packed brown sugar
1 teaspoon vanilla extract
2 large eggs
2 cups chocolate chips

PREHEAT over to 375°F

COMBINE flour, baking soda, and salt in a small bowl. Beat butter, sugars, and vanilla extract in a larger mixer bowl until creamy. Add eggs, one at a time, beating well after each addition. Gradually beat in flower mixture. Stir in chocolate chips. Drop by rounded tablespoons onto ungreased baking sheets.

BAKE for 9 to 11 minutes or until golden brown. Cool on baking sheet for 2 minutes; remove to wire rack to cool completely



Wildtype recipe



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Mutation present!



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Point Mutation



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Inversion

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Substitution



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Types of Mutations

- **Point mutation**
 - A mutation that only affects a single nucleotide of nucleic acid.
- **Inversion mutation**
 - A chromosome rearrangement in which a segment of a chromosome is reversed end to end
- **Substitution mutation**
 - An exchange of one base for another. Such a substitution could: change a codon to one that encodes a different amino acid and cause a small change in the protein produced.



Types of Mutations

- **Insertions**
 - an addition of one or more nucleotide base pairs into a DNA sequence.
- **Deletions**
 - A mutation (a genetic aberration) in which a part of a chromosome or a sequence of DNA is lost during DNA replication
- **Frameshift mutation**
 - Deletion or an insertion that results in the DNA being read from the wrong starting bases during transcription



Codon table

DNA trios to make proteins

Standard genetic code^{[1][10]}

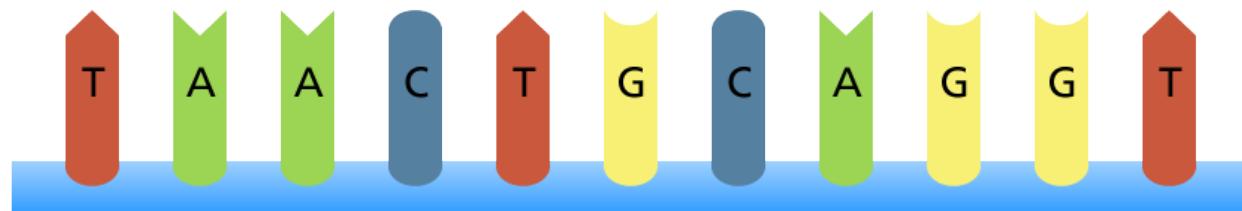
1st base	2nd base								3rd base
	U		C		A		G		
U	UUU	(Phe/F) Phenylalanine ↑		UCU	(Ser/S) Serine ↑	UAU	(Tyr/Y) Tyrosine †		U
	UUC			UCC		UAC	UGU	C	
	UUA			UCA		UAA	Stop (Ochre) *[note 2]	UGC	(Cys/C) Cysteine †
	UUG →			UCG		UAG	Stop (Amber) *[note 2]	UGA	Stop (Opal) *[note 2]
C	CUU	(Leu/L) Leucine ↑		CCU	(Pro/P) Proline ↑	CAU	(His/H) Histidine ‡	CGU	U
	CUC			CCC		CAC		CGC	C
	CUA			CCA		CAA	(Gln/Q) Glutamine †	CGA	(Arg/R) Arginine ‡
	CUG			CCG		CAG		CGG	A
A	AUU	(Ile/I) Isoleucine ↑		ACU	(Thr/T) Threonine ↑	AAU	(Asn/N) Asparagine †	AGU	U
	AUC			ACC		AAC		AGC	C
	AUA			ACA		AAA	(Lys/K) Lysine ‡	AGA	A
	AUG →			ACG		AAG		AGG	G
G	GUU	(Val/V) Valine ↑		GCU	(Ala/A) Alanine ↑	GAU	(Asp/D) Aspartic acid ↓	GGU	U
	GUC			GCC		GAC		GGC	C
	GUA			GCA		GAA	(Glu/E) Glutamic acid ↓	GGA	A
	GUG →			GCG		GAG		GGG	G



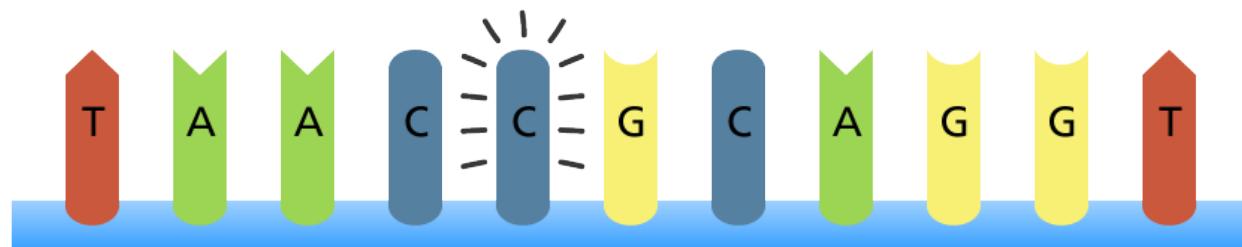
Mutation – Point Mutation

- A point mutation is a mutation that exchanges one base for another

Original sequence



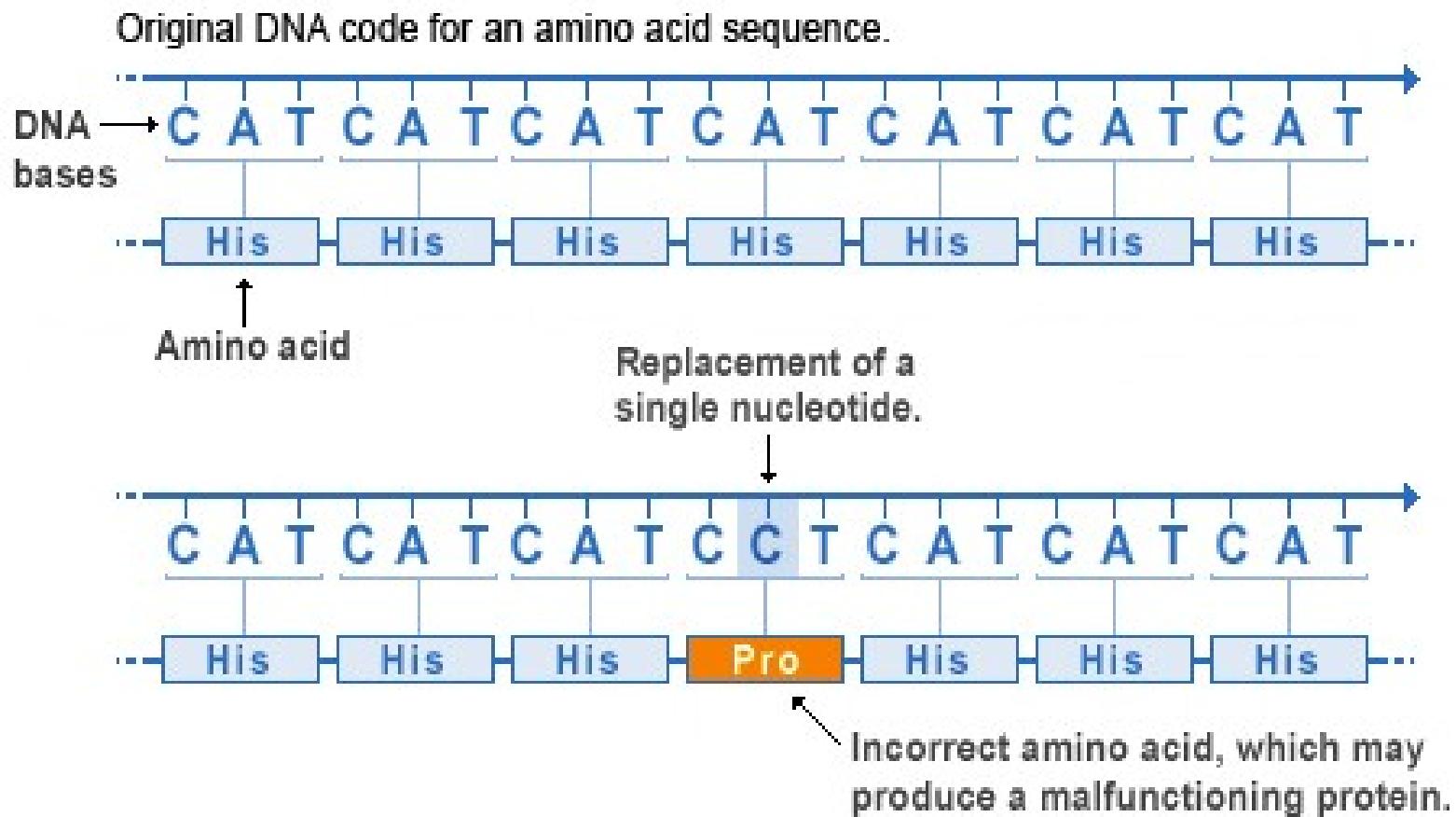
Point mutation





Proteins and Point Mutation

Missense mutation

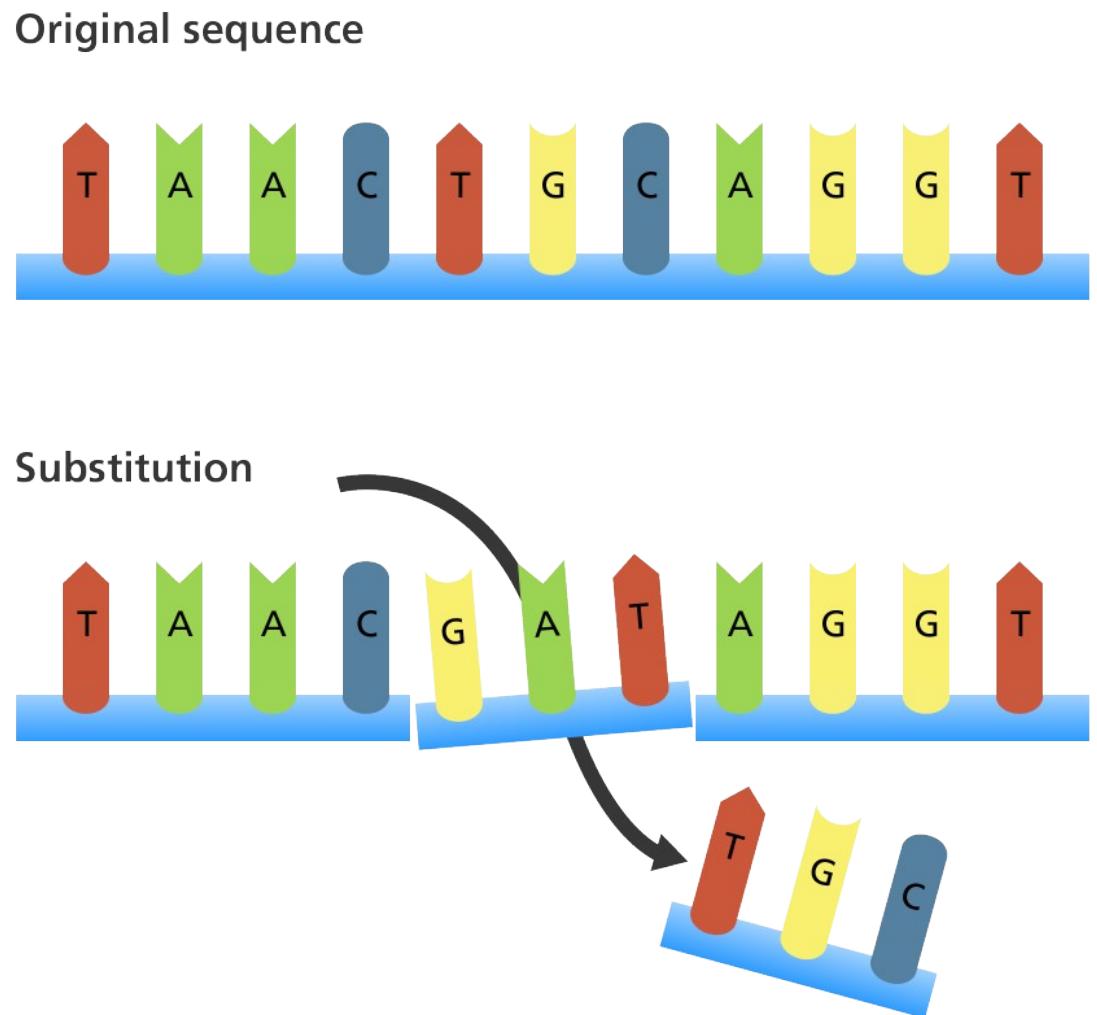


Remember that bases are read in triplets (codons) to make protein.



Mutation - Substitution

- A substitution is a mutation where one or more bases in the sequence is replaced by the same number of bases

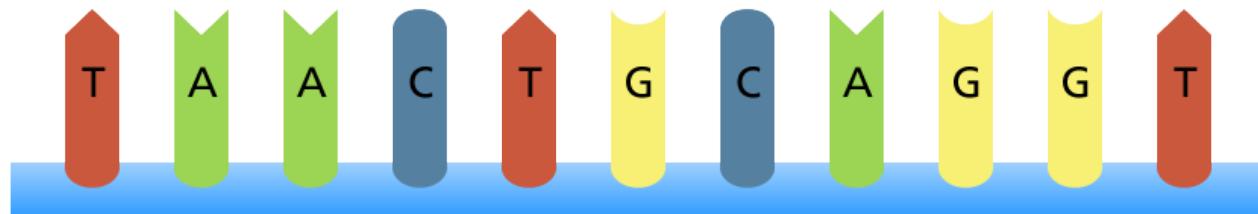




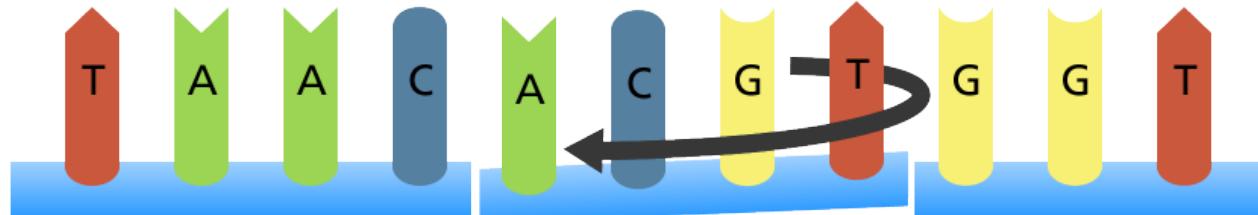
Mutation - Inversion

- An inversion is a mutation where a segment of DNA is reversed

Original sequence



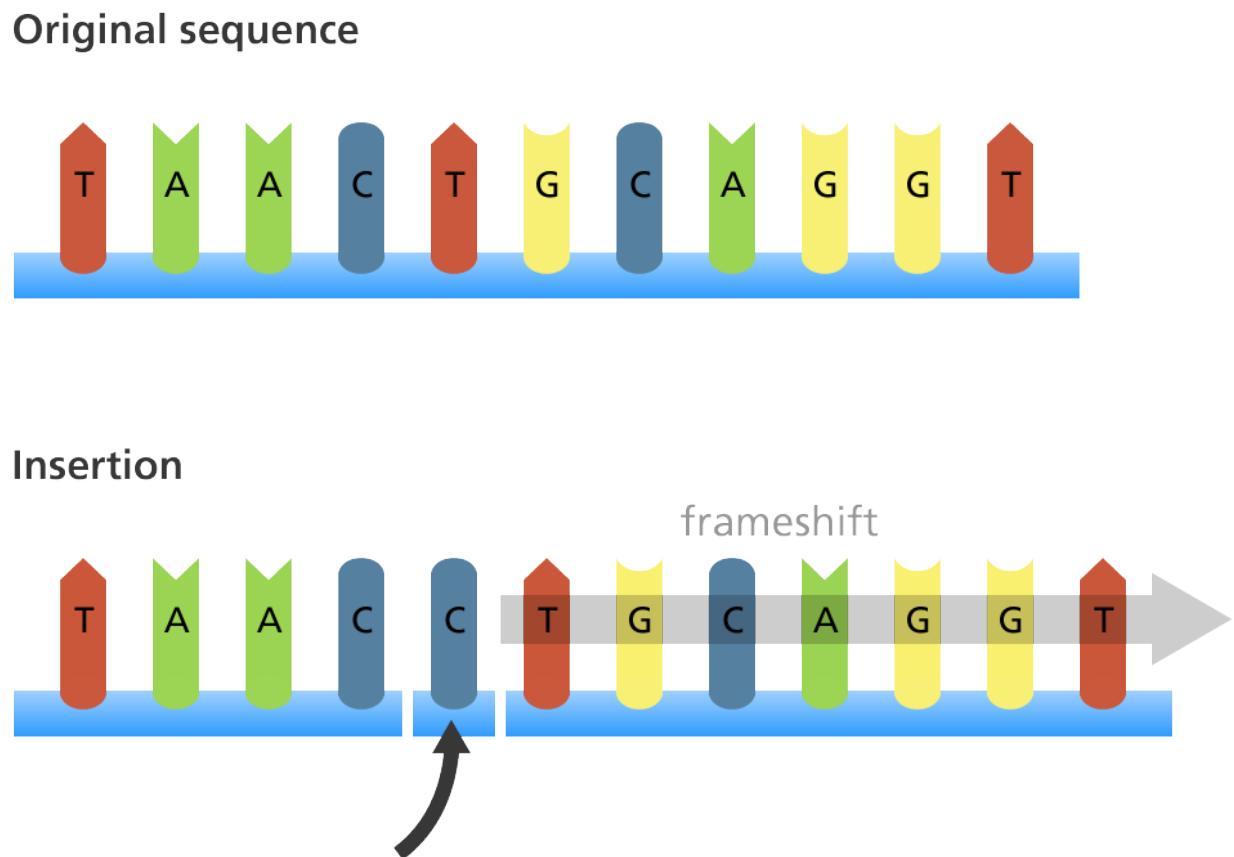
Inversion





Mutation - Insertion

- An insertion is a mutation in which one or more nucleotides are added into the DNA

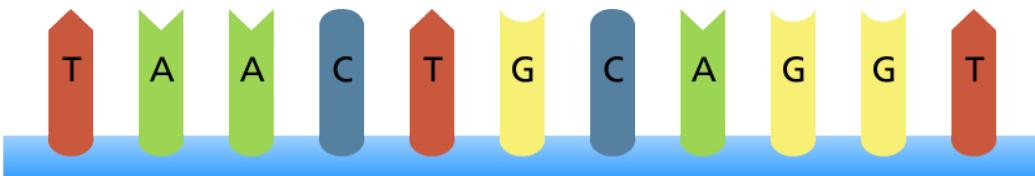




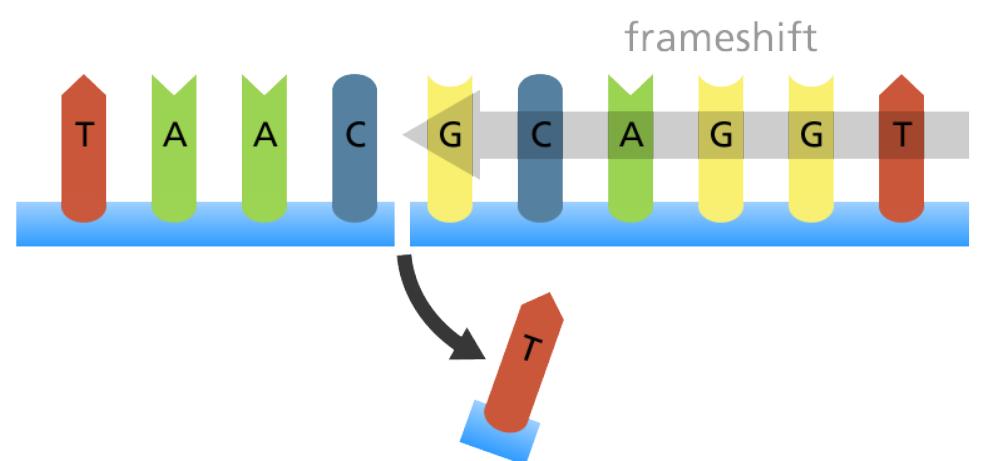
Mutation - Deletion

- A deletion is a mutation in which one or more nucleotides are removed from the DNA sequence

Original sequence

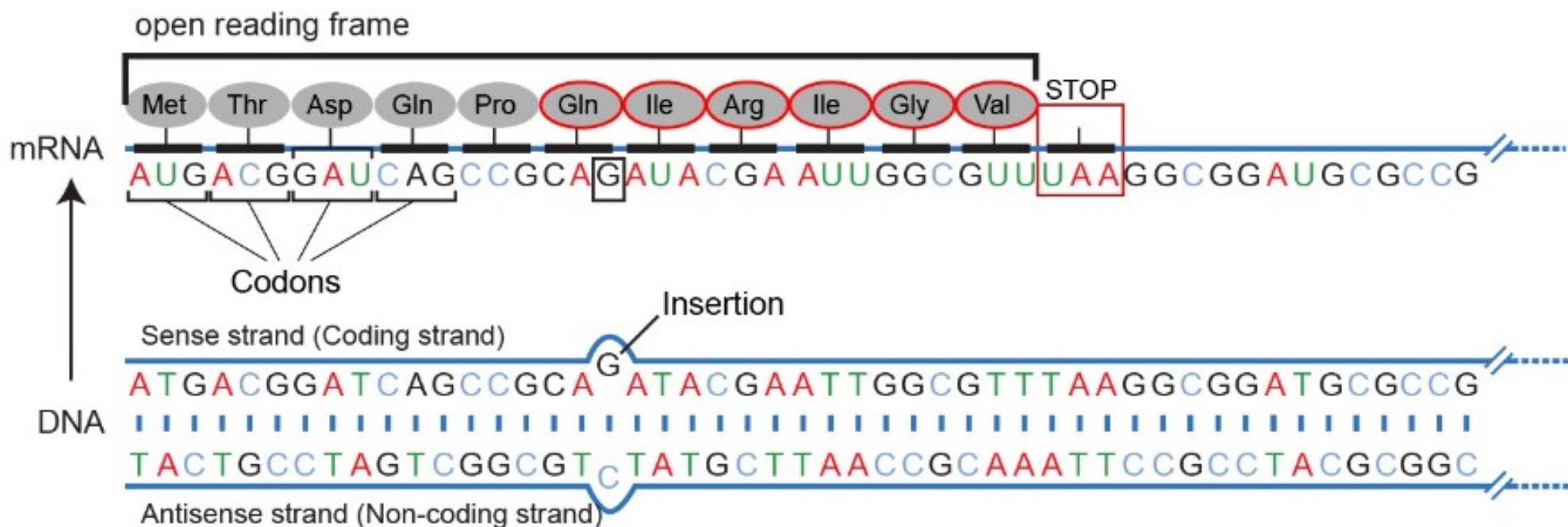


Deletion



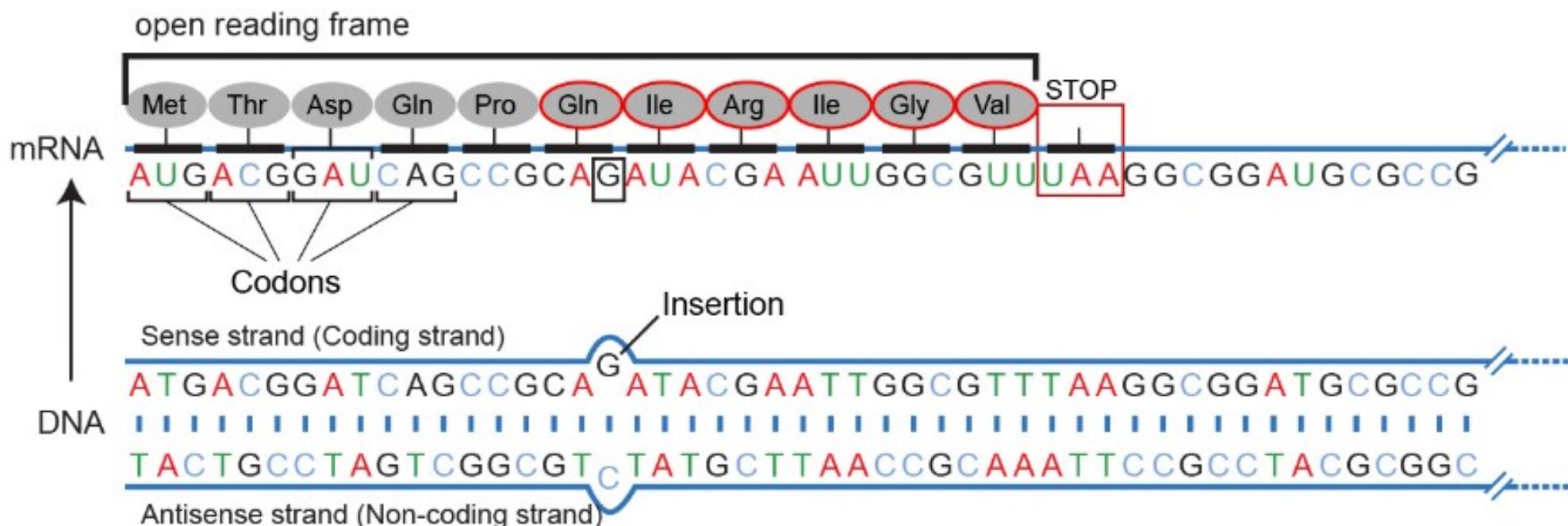
Mutation – Frame Shift

- A frameshift mutation is a type of mutation involving the insertion or deletion of a nucleotide in which the number of deleted base pairs is not divisible by three.



Mutation – Frame Shift

- DNA Codons read in 3's during translation.
- If a mutation disrupts this reading frame, then the entire DNA sequence following the mutation will be read incorrectly.

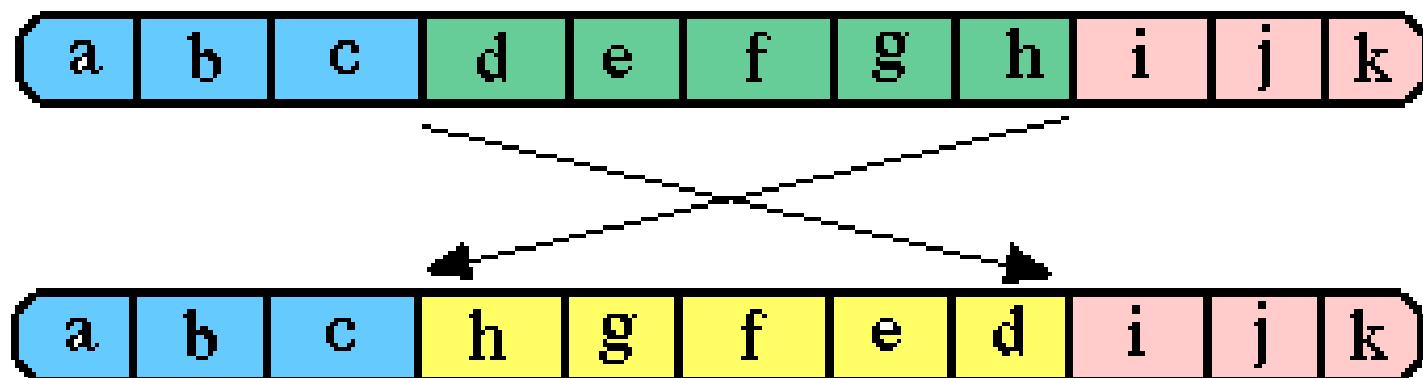


Changing the reading frame changes the protein codon sequence almost entirely.



Where Do Mutations Come From?

- During Cell division (meiosis), errors can occur as DNA is copied. These errors can often be “corrected” by bio-machinery.

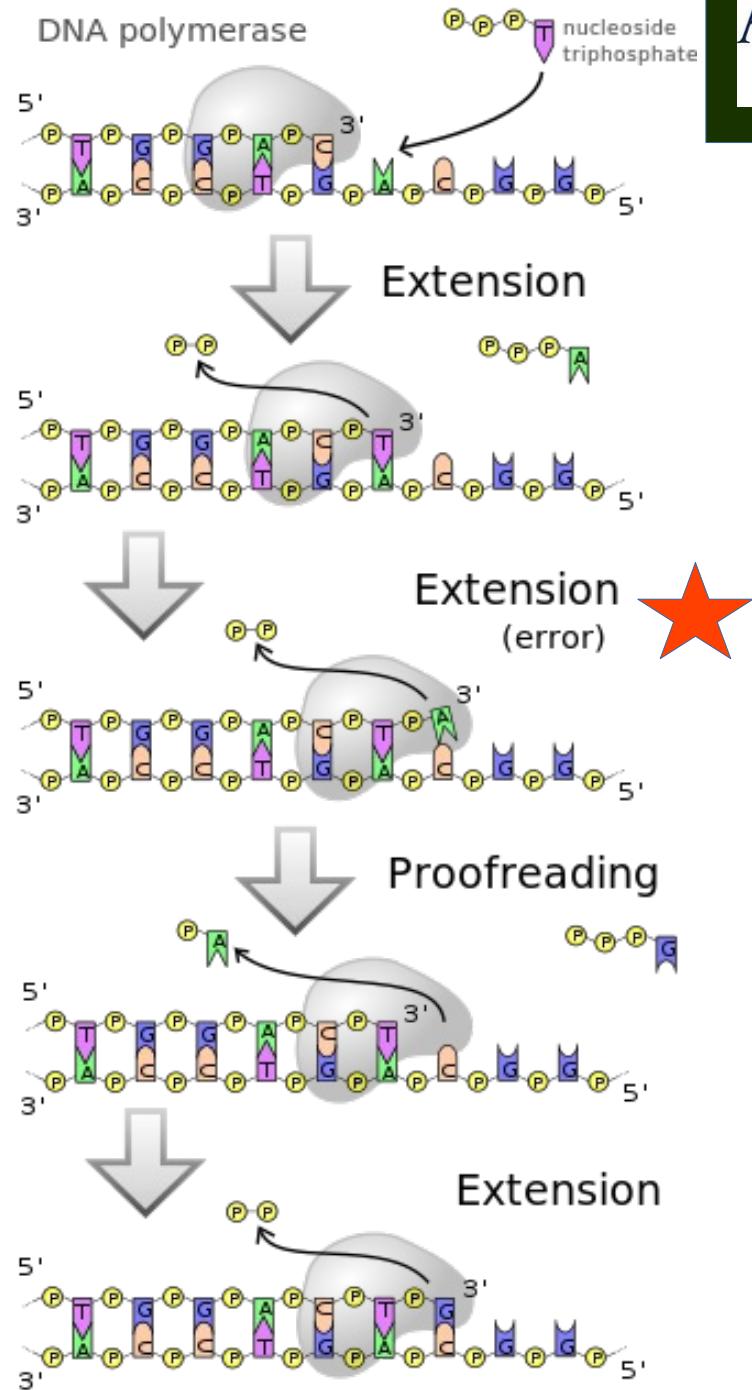




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Mutations From DNA Polymerase

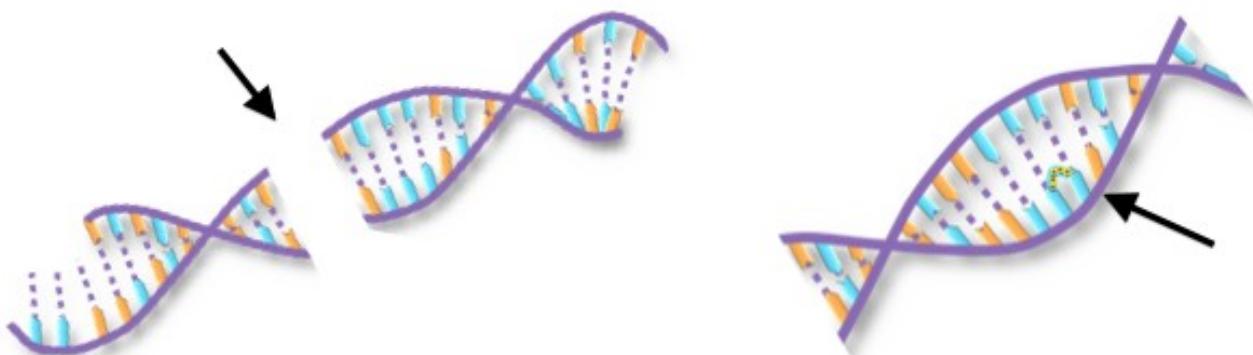
- DNA Polymerase are enzymes that catalyze the synthesis of DNA molecules
- The function of DNA polymerase can make mistakes; the enzyme could make one error for every billion base pairs copied.





Damage to DNA

- Damage and imperfect repair
 - Cell can still divide but DNA sequence has changed



Type of Damage: Double-strand break

Chemical bond between neighboring nucleotides

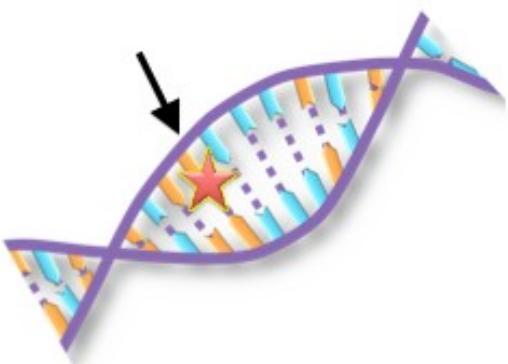
Common Causes:

- Normal cellular activity
- Ionizing radiation (including X-rays)
- Chemotherapeutic drugs
- DNA repair of other types of damage

- Ultraviolet (UV) light

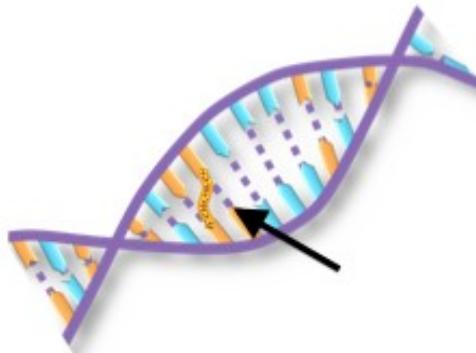
Damage to DNA

- Damage and imperfect repair
 - Cell can still divide but DNA sequence has changed



Chemical modification
of a nucleotide

- Reactive oxygen species (ROS)
- Chemotherapeutic drugs
- Other cellular and environmental chemicals
- Normal modifications that regulate what genes are active



Chemical Linkage of
Two Strands

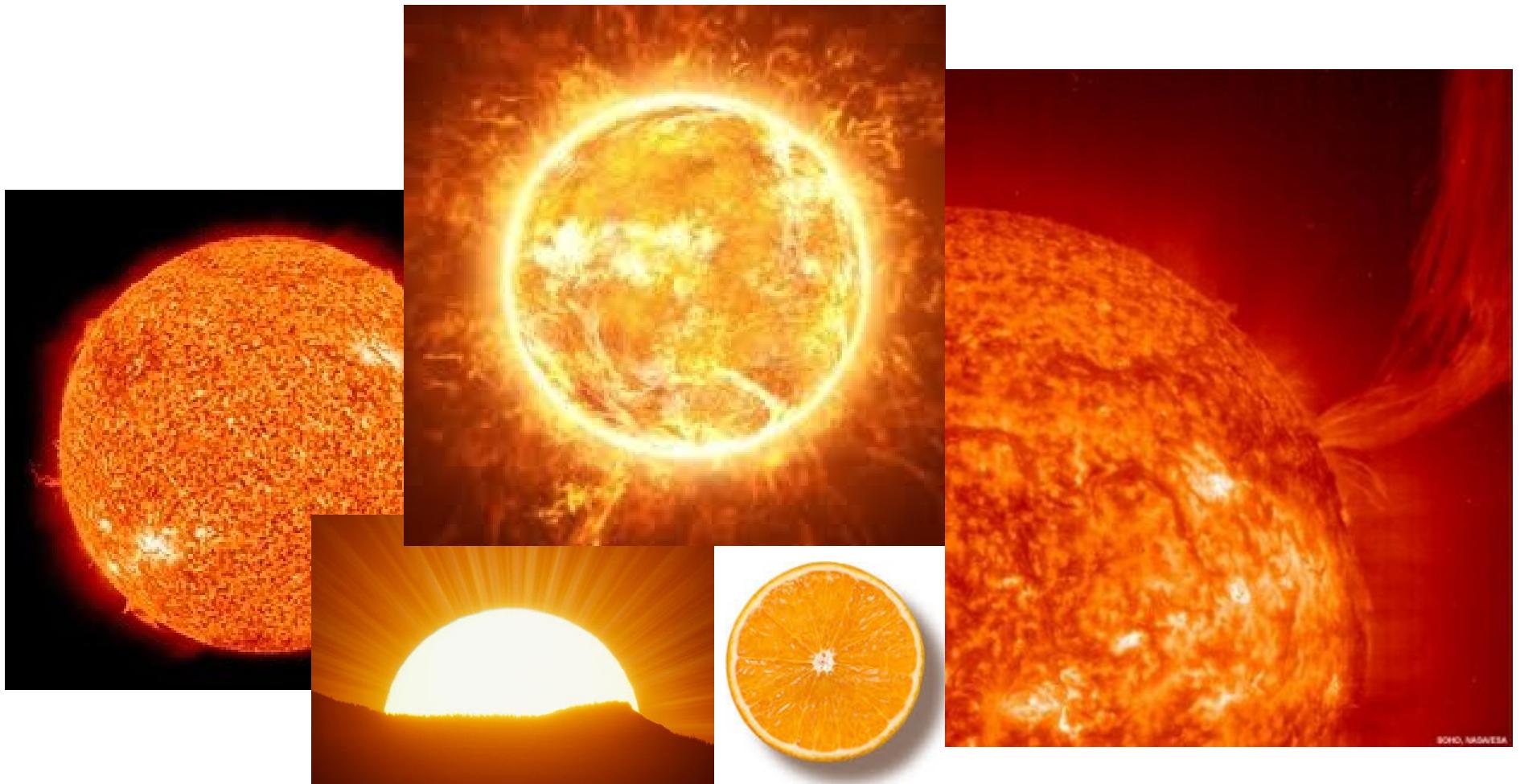
- Reactive oxygen species (ROS)
- Chemotherapeutic drugs
- Other cellular and environmental chemicals



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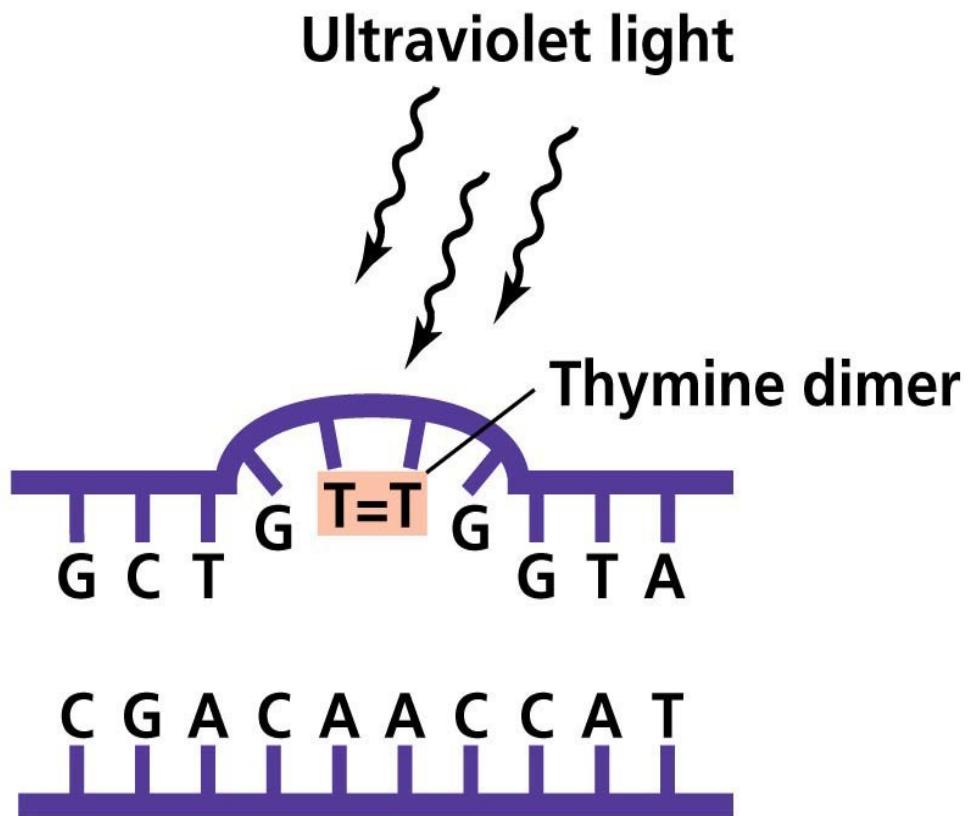
Mutations from Environment

- Ultraviolet radiation from the sun





Mutations from Environment



UV light causes bond to form between adjacent Ts

If left unrepaired, polymerase “guesses”

- 25% chance per site
- cell can still divide
- hopefully not in a gene

Chance of mistakes during repair process

- polymerase isn't perfect when correcting errors



Consequences of Mutation?

- Sometimes nothing happens
 - “**Silent mutations**”
 - Mutation does not occur in a gene
 - Protein-coding regions make up only approximately 1 percent of the human genome
 - Silent changes
 - Occurs in gene, but does not change message
 - Genetic code is redundant

TAT

Tyr

TAC

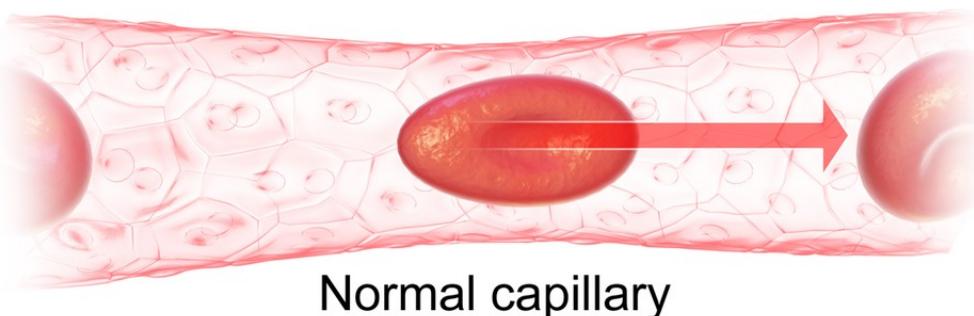
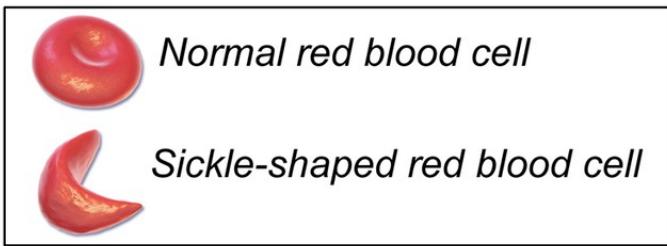
Tyr

After error,
same protein
still emerges

You notice mutations when they interfere with some product production.



Sickle Cell Anemia: A Missense Mutation



Normal capillary



Sickle Cell Anemia

- Sickle cells are in the shape of sickles.
- An inherited form of anemia — a condition in which there are not enough healthy red blood cells to carry adequate oxygen throughout your body.
- There's no cure for most people with sickle cell anemia.
- Treatments can relieve pain and help prevent problems associated with the disease.

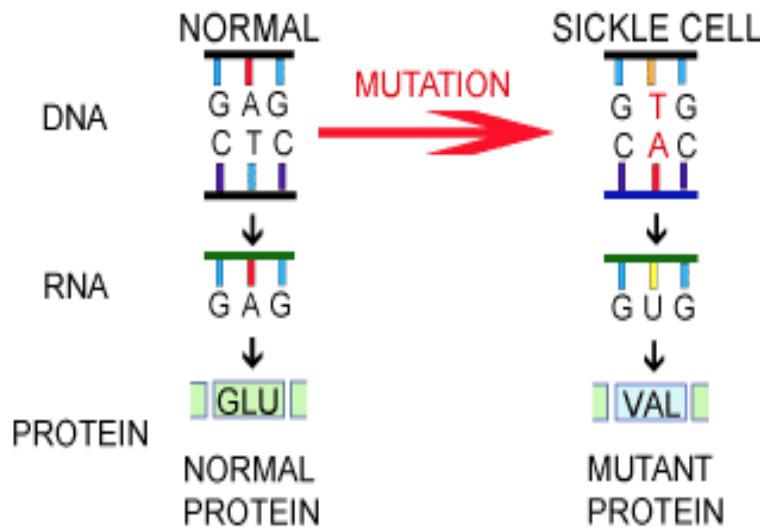
For more information:

<https://www.mayoclinic.org/diseases-conditions/sickle-cell-anemia/symptoms-causes/syc-20355876>

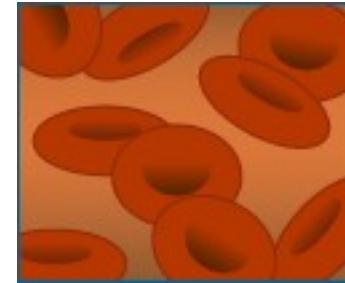


A Mutation Did This?

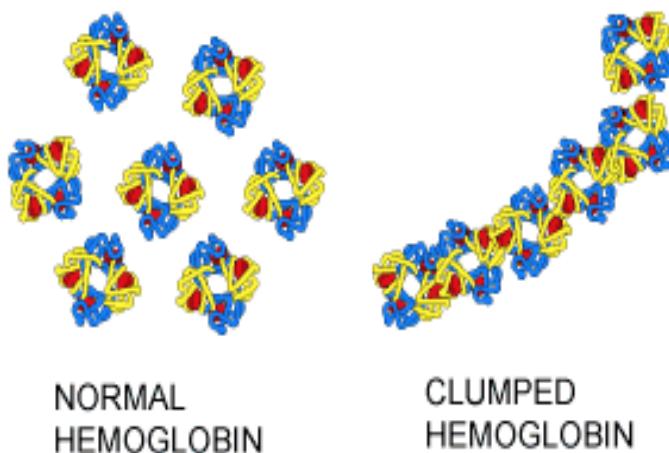
HBB gene - Sickle cell anemia - missense mutation



Normal RBC



Sickle RBC



- A group of disorders that cause red blood cells to become misshapen and to break down.
- Sickled red blood cells are abnormally shaped and rigid
- Sickle shape can interrupt blood flow