Kwame Nkrumah University of
Science & Technology, Kumasi, Ghana

Module 4

DNA Mutations

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Start Module

DNA MUTATION

Module 4

Mutations

Module Dashboard

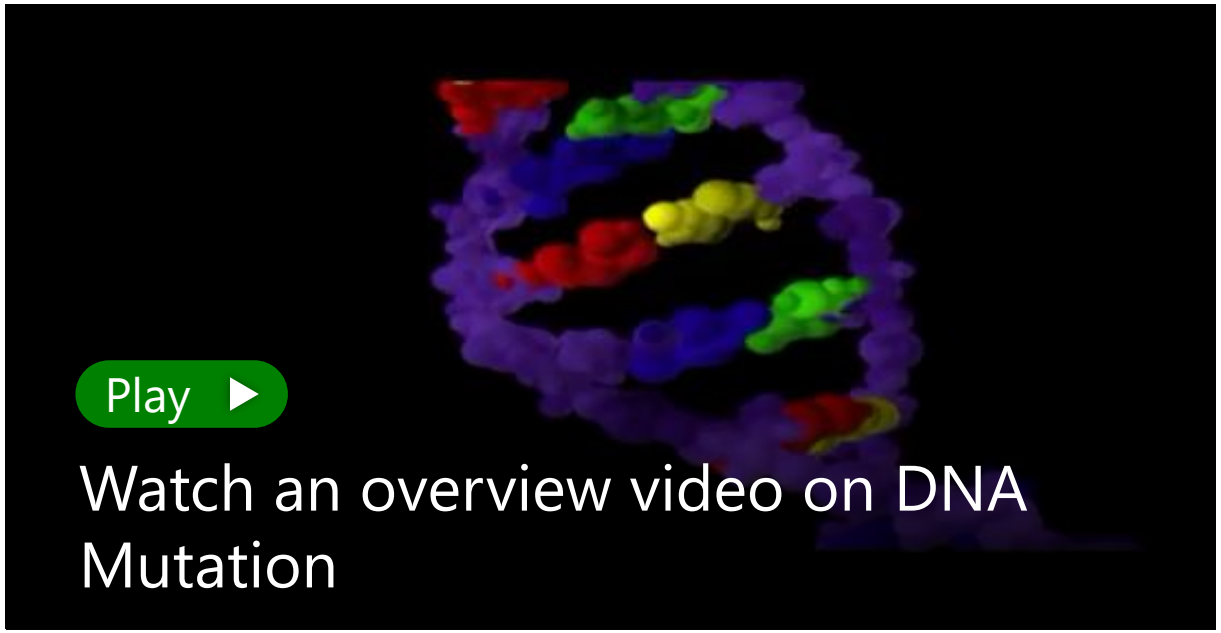
- Dashboard
- Introduction
- Lessons
- Assignments

End of Module

Lessons
3

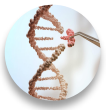
Assignments
1

Start Learning

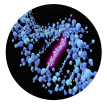


Pick a Lesson

Lesson 1
Mutations



Lesson 2
Generation of Mutations



Lesson 3
Classes of Mutation

2

Module Objectives

Dashboard
Introduction
Lessons
Assignments
End of Module

1. To know how mutations happen and the sequence for reading the Genetic Code
2. To know how mutations are generated
3. To know Classes of mutation

Module 4

Mutations

Module Lessons

- Dashboard
- Introduction
- Lessons
- Assignments

End of Module

Lesson 1

Mutations

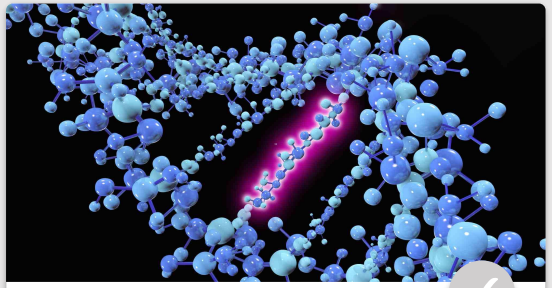
Learn what mutations are, how they happen and the sequence for reading genetic codes

Start

Lesson 2

Generation of Mutations

Start



Lesson 3

Classes of Mutations

Start

Lesson 1

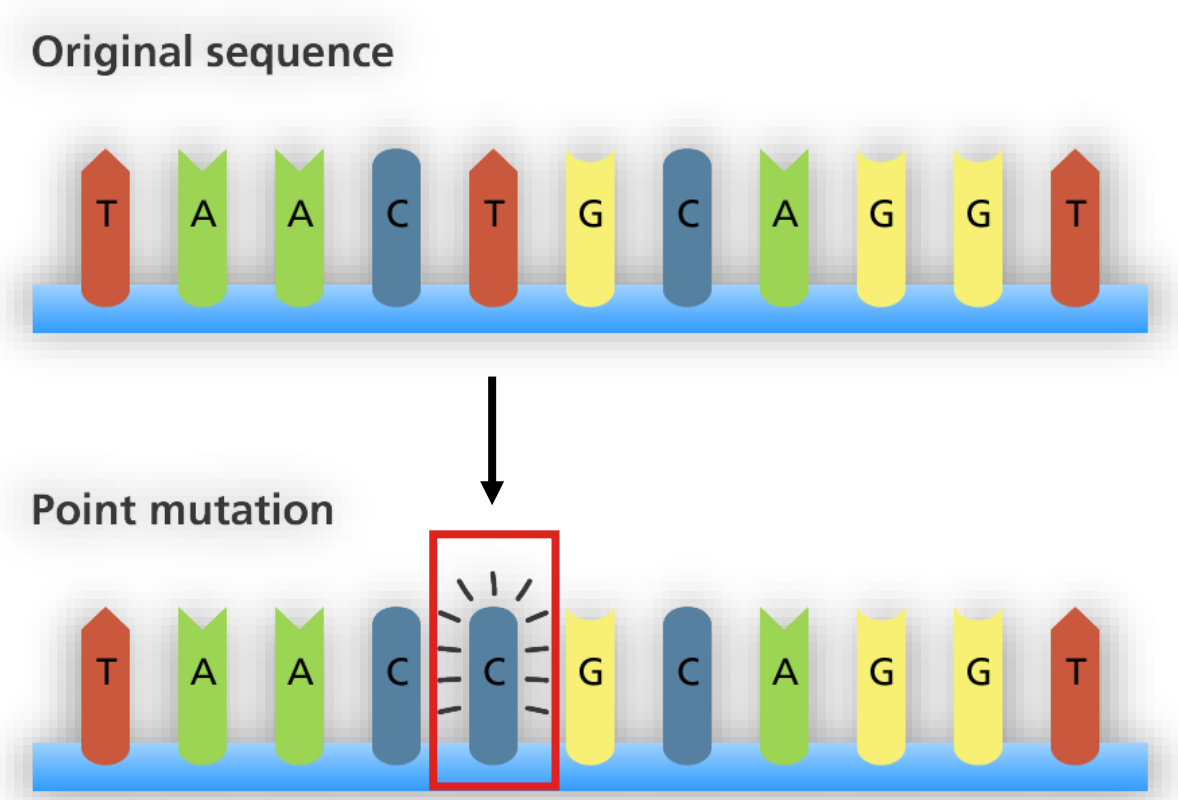
Mutations

Learn what mutations are, how they happen and the sequence for reading genetic codes

Learn Now ▸

Mutations

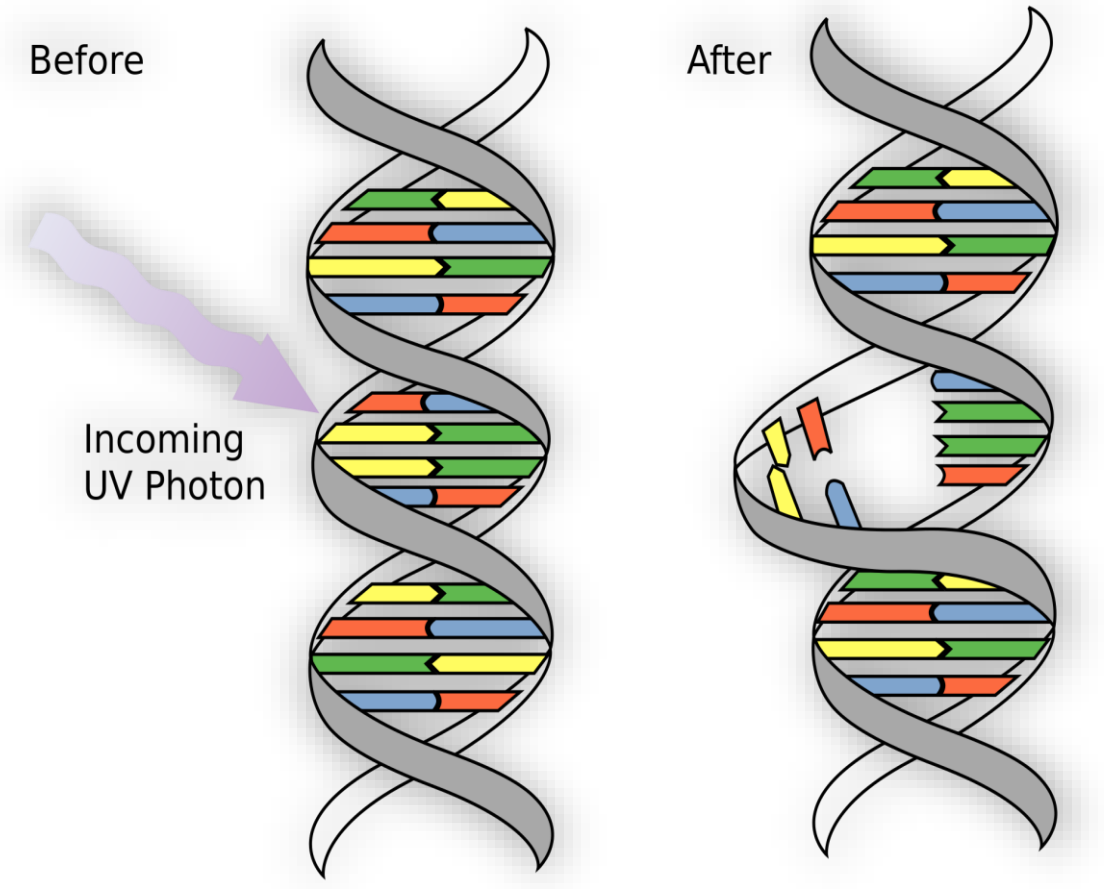
A mutation is any change in the sequence of DNA in a genome



Mutations

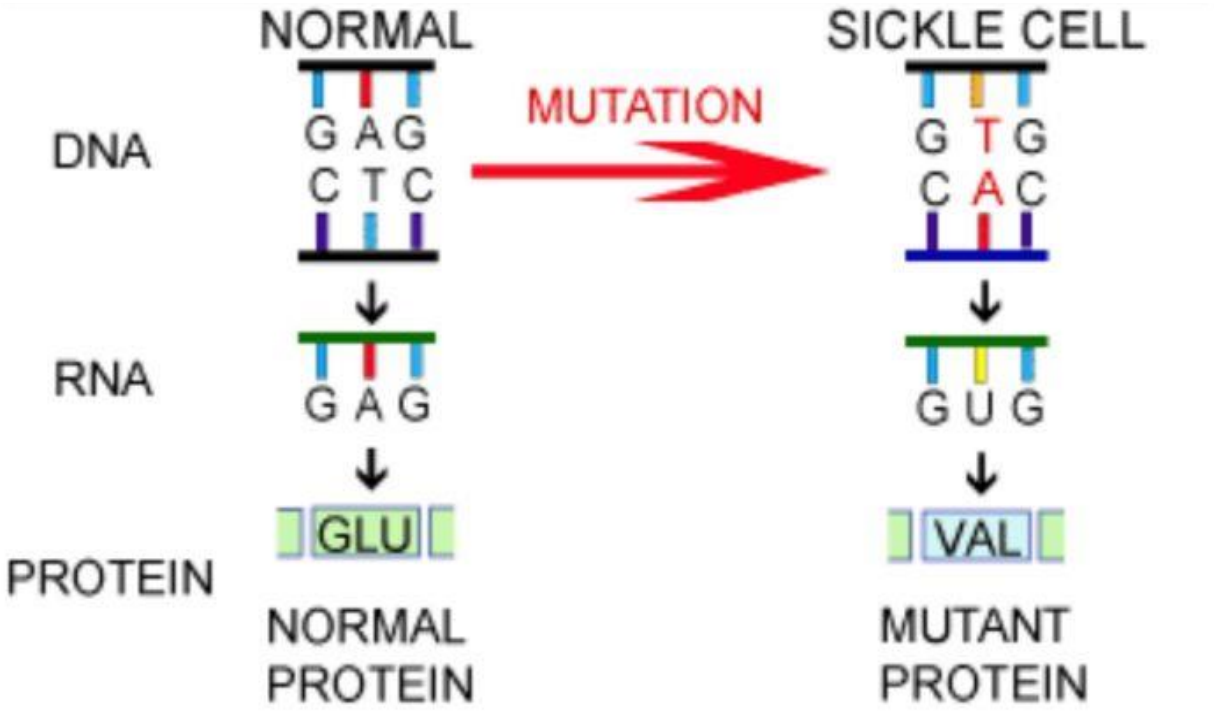
OR

A mutation is a permanent change in the DNA sequence of a gene



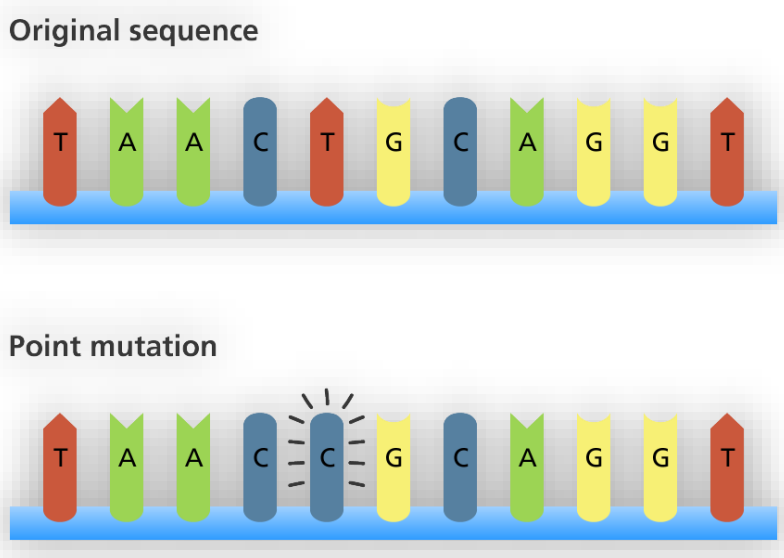
Mutations

Mutations in a gene's DNA sequence can alter the amino acid sequence of the protein encoded by the gene

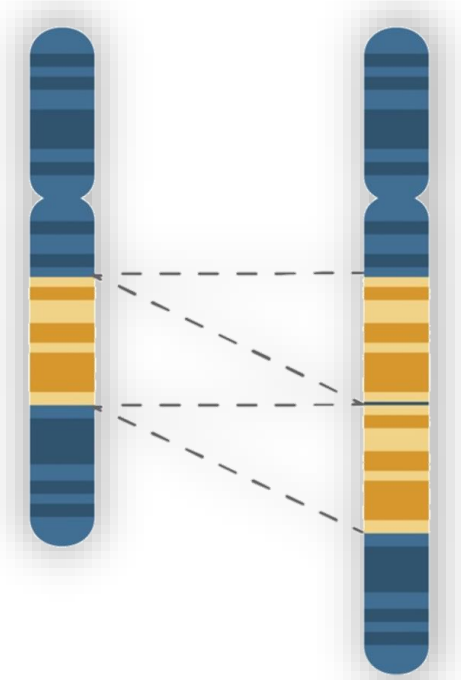


Mutations

Mutations range in size from a single DNA building block (DNA base) to a large segment of a chromosome



DNA Base Mutation



Chromosomal Mutation

Mutations

Mutations can be beneficial, neutral, or harmful for the organism, but mutations do not "try" to supply what the organism "needs"

Beneficial

Neutral

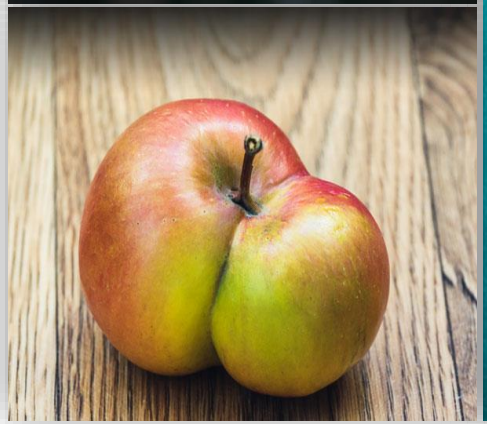
Harmful

Mutations

Mutations are random

whether a particular mutation happens or not is unrelated to how useful that mutation would be

Beneficial



Neutral

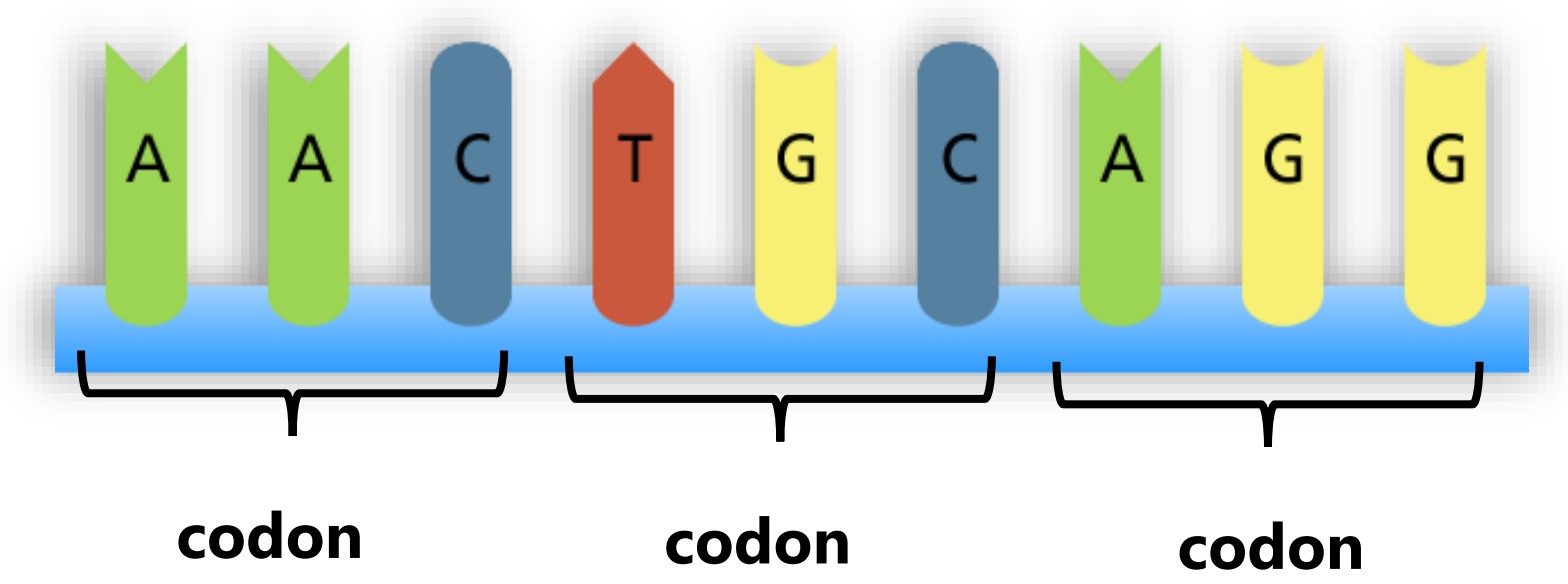
Harmful

How Does Mutation Happen?

Like words in a sentence, the DNA sequence of each gene determines the amino acid sequence for the protein it encodes

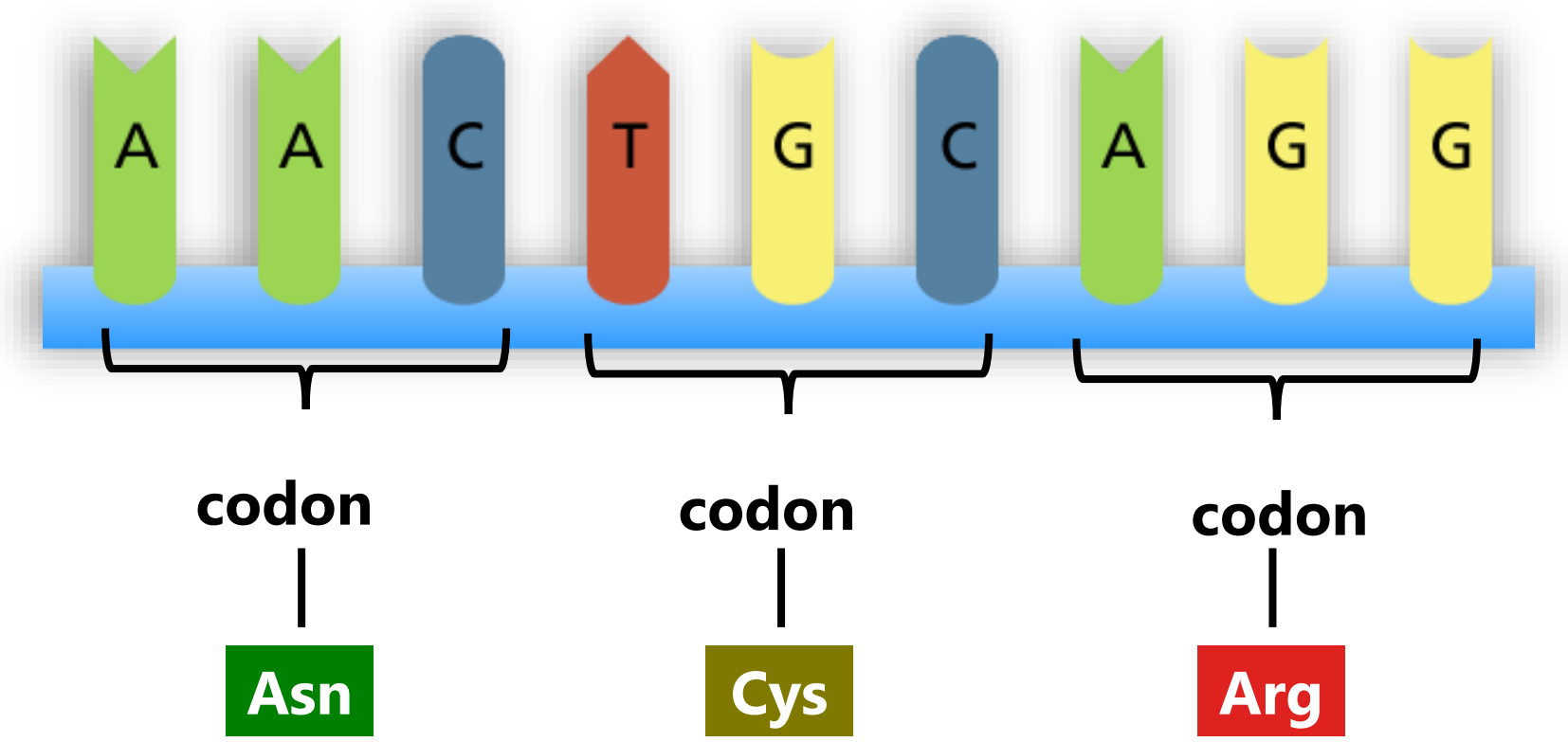
How Does Mutation Happen?

The DNA sequence is interpreted in groups of 3 nucleotide bases, called **codons**



How Does Mutation Happen?

Each codon specifies a single amino acid in a protein



The Genetic Code

The set of rules that determine how a nucleotide sequence is converted into the amino acid sequence of proteins

First letter	Second letter: U	Second letter: C	Second letter: A	Second letter: 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

The Genetic Code

OR

The rules by which the nucleotide sequence of a gene is translated into the amino acid sequence of a protein

First letter	Second letter: U	Second letter: C	Second letter: A	Second letter: 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

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OR

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Second Letter

First Letter	T	C	A	G	Third Letter
T	TTT, TTC: Phe TTA, TTG: Leu	TCT, TCC, TCA, TCG: Ser	TAT, TAC: Tyr TAA: Stop TAG: Stop	TGT, TGC: Cys TGA: Stop TGG: Trp	T
C	CTT, CTC, CTA, CTG: Leu	CCT, CCC, CCA, CCG: Pro	CAT, CAC: His CAA, CAG: Gln	CGT, CGC, CGA, CGG: Arg	C
A	ATT, ATC, ATA: Ile ATG: Met	ACT, ACC, ACA, ACG: Thr	AAT, AAC: Asn AAA, AAG: Lys	AGT, AGC: Ser AGA, AGG: Arg	A
G	GTT, GTC, GTA, GTG: Val	GCT, GCC, GCA, GCG: Ala	GAT, GAC: Asp GAA, GAG: Glu	GGT, GGC, GGA, GGG: Gly	G

Mutate a Sentence

We can think about the DNA sequence of a gene as a sentence made up of entirely three-letter words

Thesunwashotbuttheoldmandidnotgethishat.

In the sequence, each three-letter word is a codon, specifying a single amino acid in a protein

Thesunwashotbuttheoldmandidnotgethishat.

codon

Mutate a Sentence

If you were to split this sentence into individual three-letter words, you would probably read it like this

The sun was hot but the old man did not get his hat.

This sentence represents a gene

Mutate a Sentence

Each letter corresponds to a nucleotide base, and each word represents a codon

nucleotide base

The sun was hot but the old man did not get his hat.

Codon

Mutate a Sentence

What will happen if you shifted the three-letter "reading frame?"

T hes unw ash otb utt heo ldm and idn otg eth ish at.

Or

Th esu nwa sho tbu tth eol dma ndi dno tge thi sha t.

Mutate a Sentence

From the three “reading frames”, **ONLY ONE** can be translated into an understandable sentence

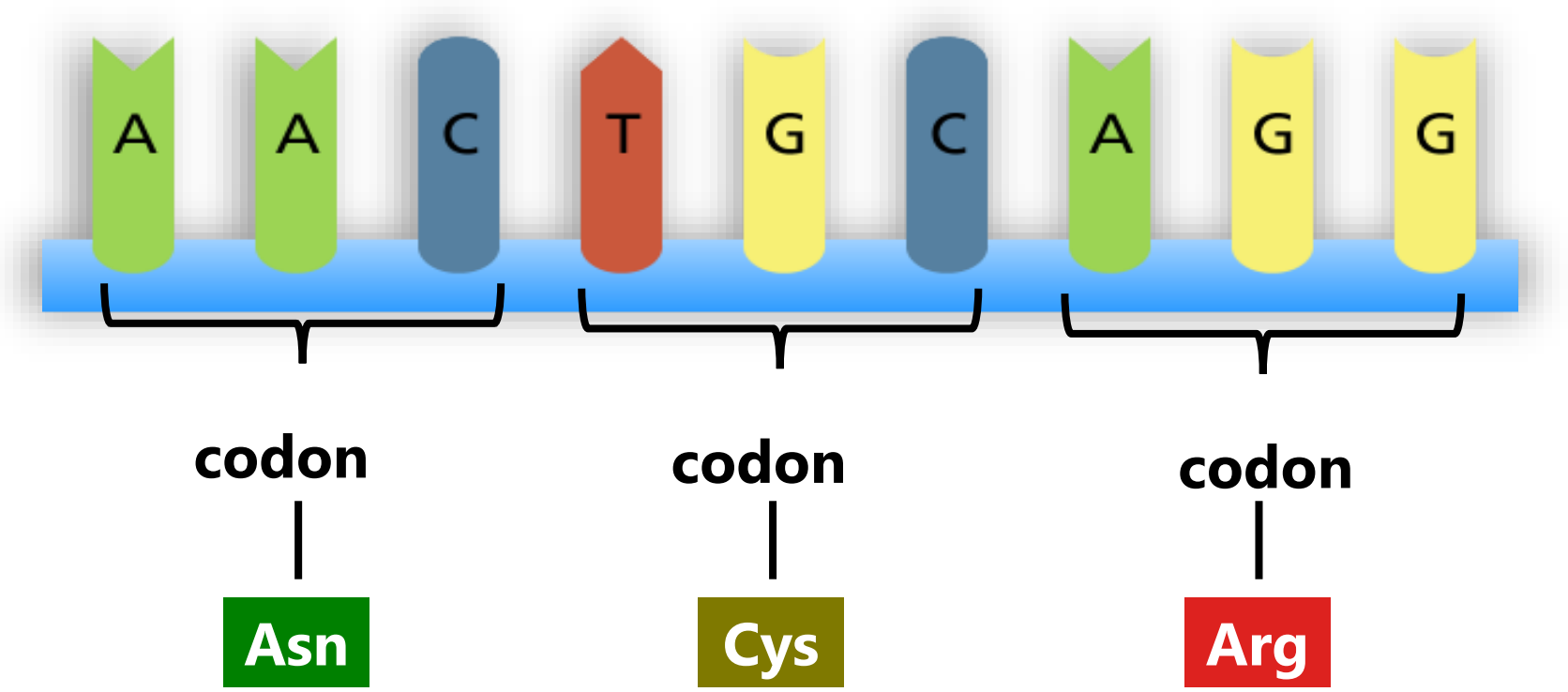
The sun was hot but the old man did not get his hat.

T hes unw ash otb utt heo ldm and idn otg eth ish at.

Th esu nwa sho tbu tth eol dma ndi dno tge thi sha t.

Mutate a Sentence

In the same way, only one three-letter reading frame within a gene code or specify for the correct protein



Mutate a Sentence

Now, back to the original sentence of:

Thesunwashotbuttheoldmandidnotgethishat.

Let us mutate the reading frame of this sentence by inserting or deleting letters within the sentence

What happens?

Module 4

Mutations

Module Lessons

- Dashboard
- Introduction
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- Assignments

Lesson 1

Mutations

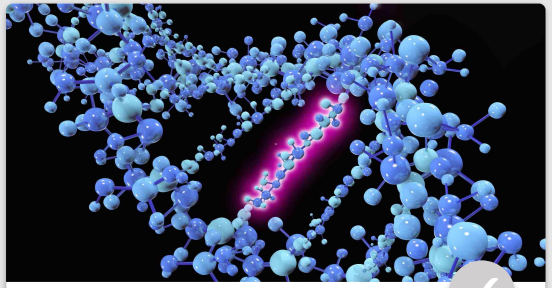
Learn what mutations are, how they happen and the sequence for reading genetic codes

Start ▸

Lesson 2

Generation of Mutations

Start ▸



Lesson 3

Classes of Mutations

Start ▸

End of Module

Lesson 2

Generation of Mutations (Mutagenesis)

Learn more about how mutations come about

Learn Now ▸

Generation of Mutations (Mutagenesis)

In general, the appearance of a new mutation is a rare event

Spontaneous Mutations

Most mutations that were originally studied occurred spontaneously i.e. they are historically recognized in nature from an unknown source

Spontaneous Mutations

This class of mutations are called **Spontaneous mutations** and represent only a small number of all possible mutations

Induced Mutations

To understand biological systems further, geneticists or scientists can create new mutations by treating organisms with a mutagenizing agent or a **mutagen**

These mutations are called Induced Mutations

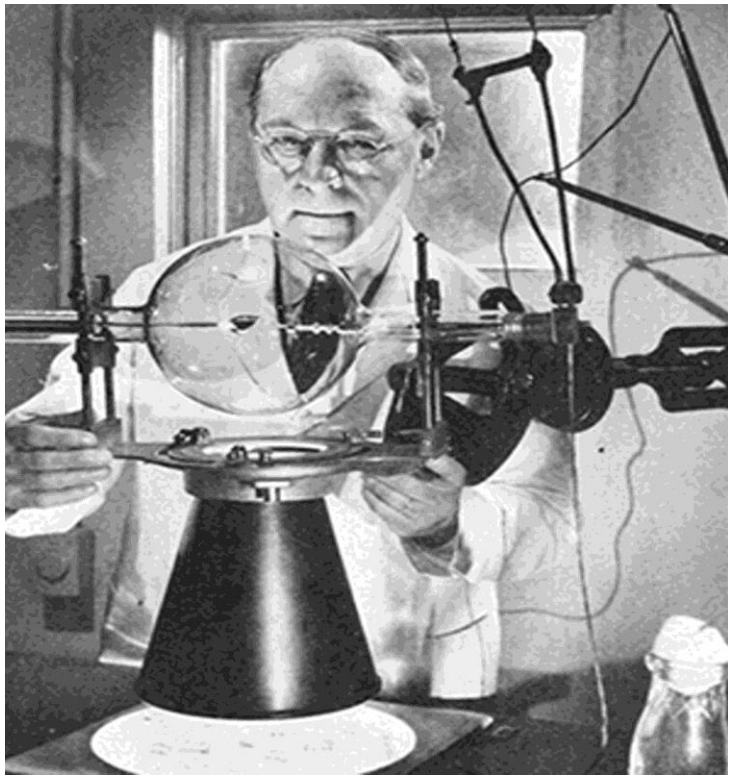
Induced Mutations

Mutations can be induced by several methods

1. **Radiation**
2. **Chemicals**
3. **Transposon Insertion**

Induced Mutations › Radiation

The first induced mutations were created by treating Drosophila with X-rays



Hermann Joseph Muller's Study of X-rays as a Mutagen

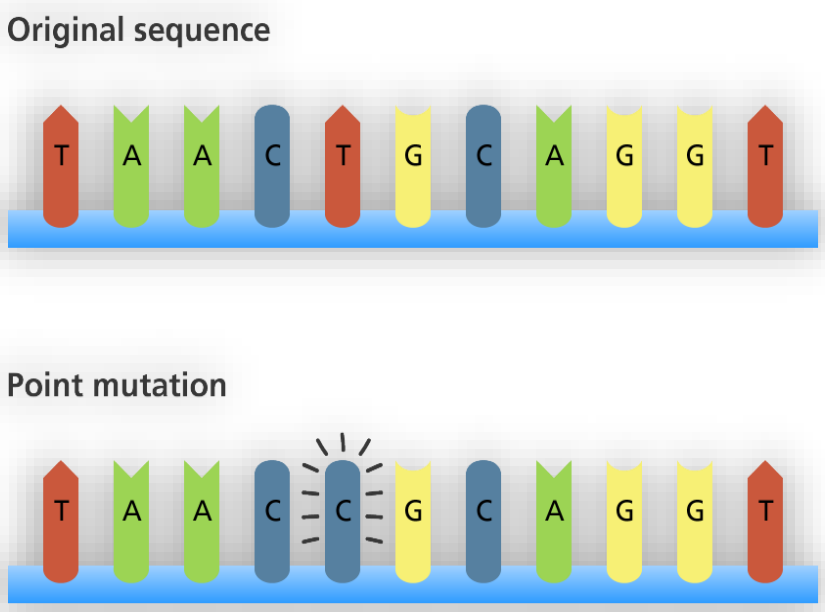
Learn More

Induced Mutations › Radiation

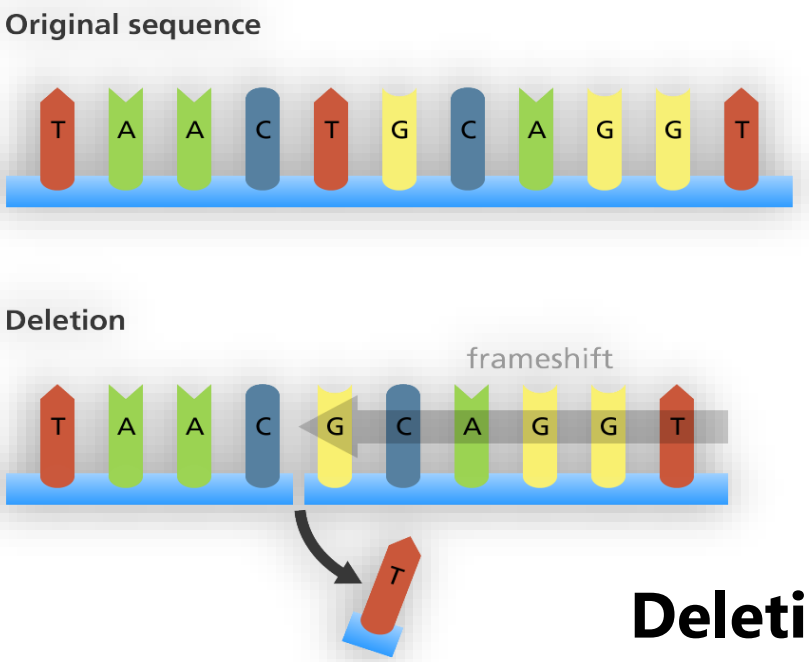
In addition to X-rays, gamma rays and fast neutron bombardment have also been used

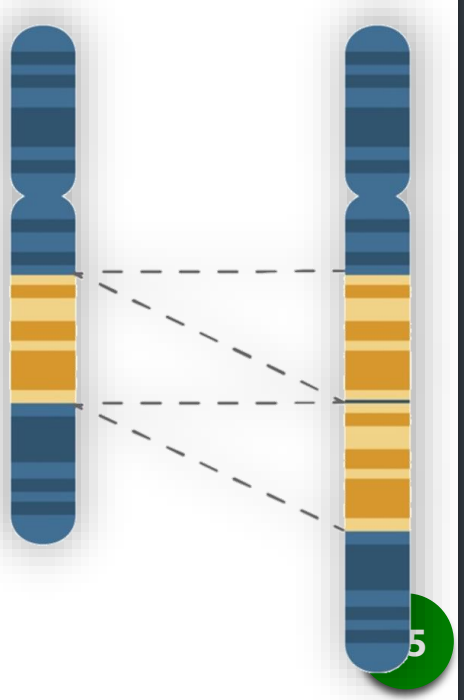
Induced Mutations › Radiation

These treatments can induce **point mutations** (changes in a single nucleotide) or **deletions** (loss of a chromosomal segment)



Point Mutation

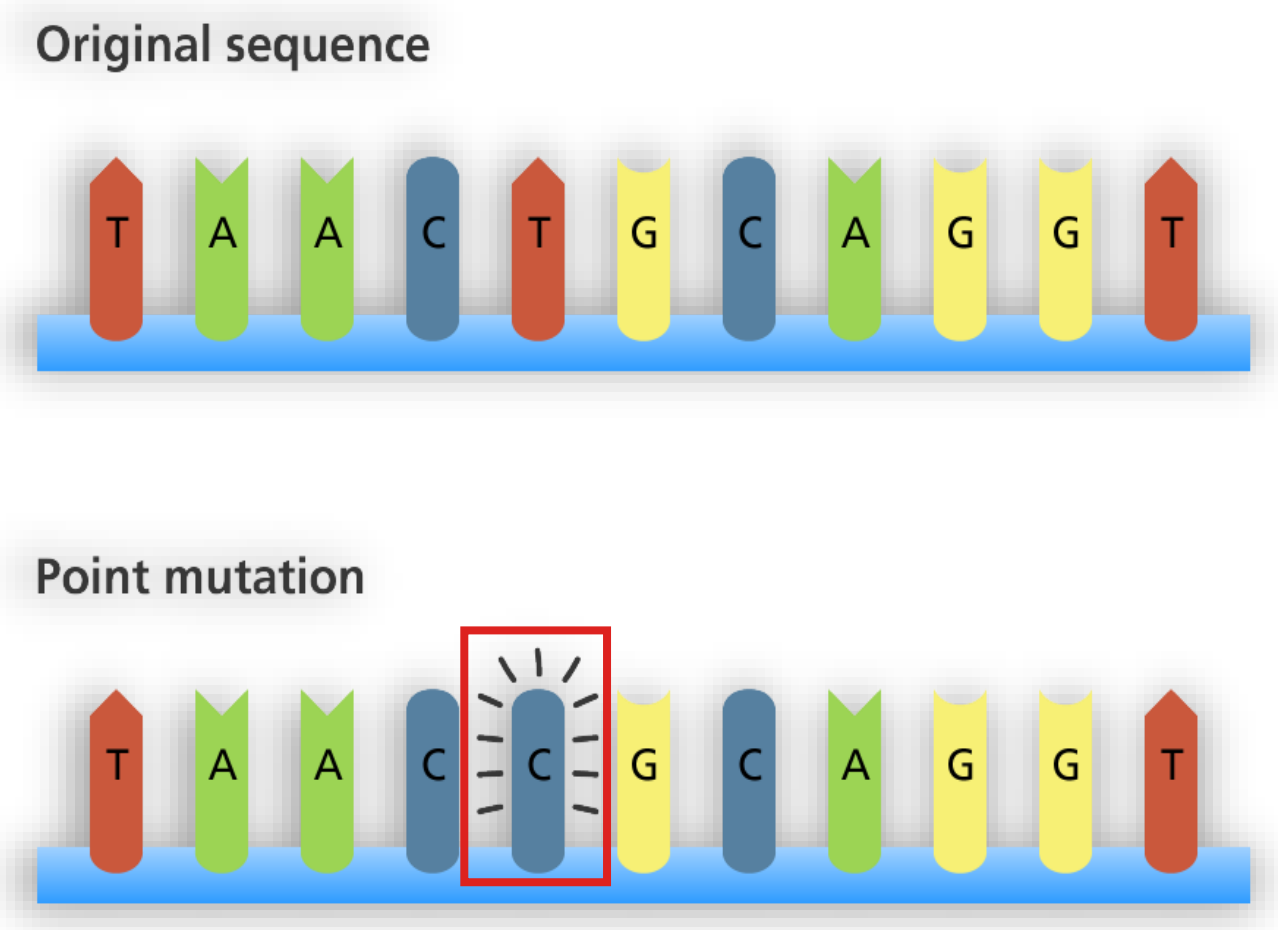




Deletion

Induced Mutations › Chemicals

Chemical mutagens work mostly by inducing point mutations

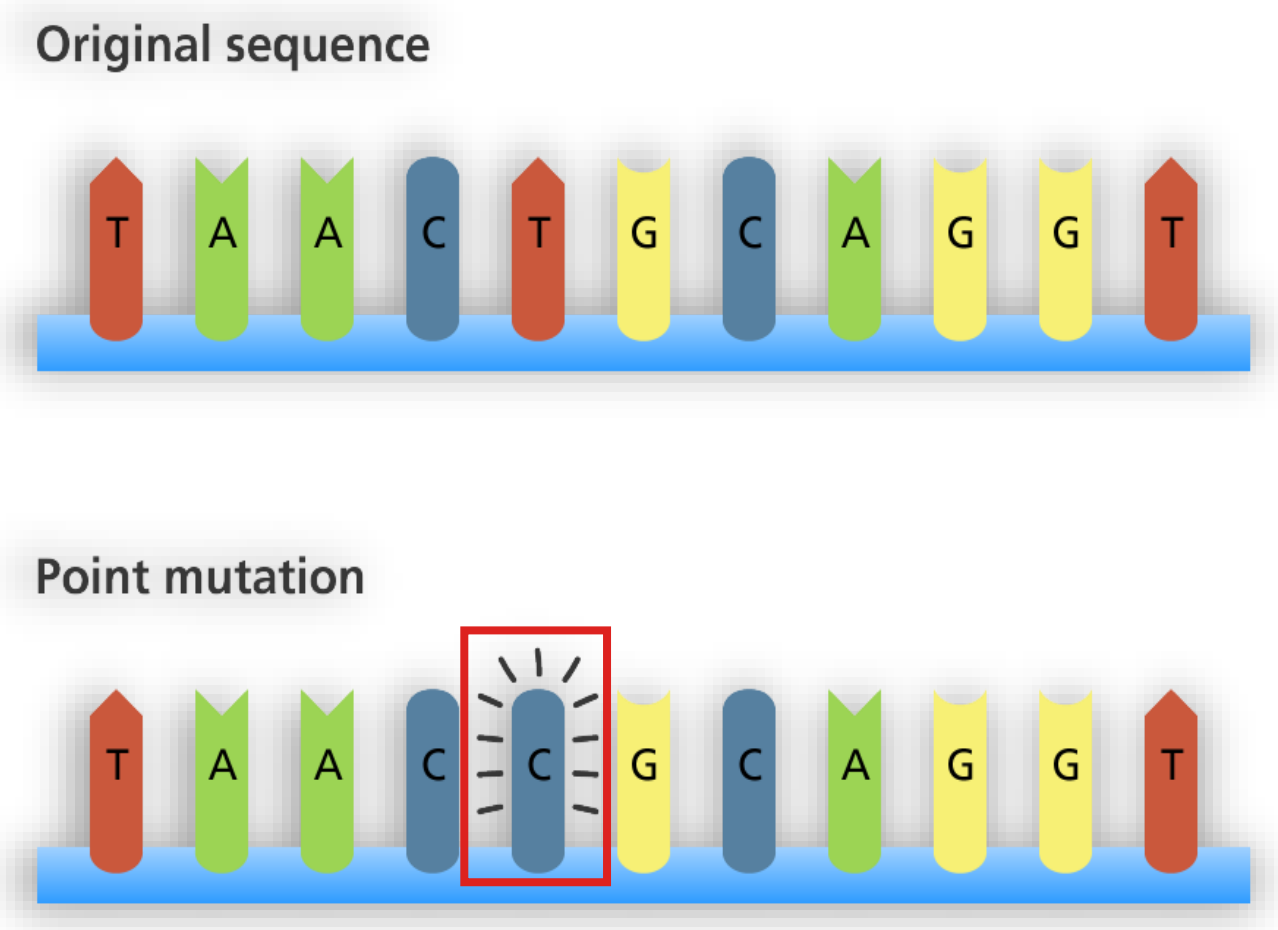


Point Mutation

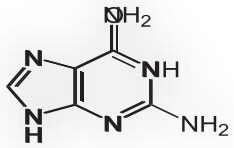
Induced Mutations › Chemicals

Point mutations occur when a single base pair of a gene is changed

These changes are classified as **transitions** or **transversions**



Point Mutation



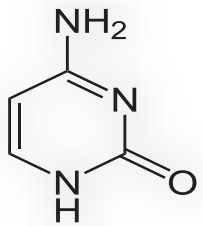
Transitions

Occur when a purine is converted to a purine (**A to G or G to A**) or a pyrimidine is converted to a pyrimidine (**T to C or C to T**)

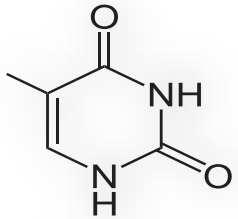
adenine — guanine

A ⟷ **Transitions** ⟷ **G**

C ⟷ **Transitions** ⟷ **T**



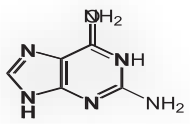
cytosine

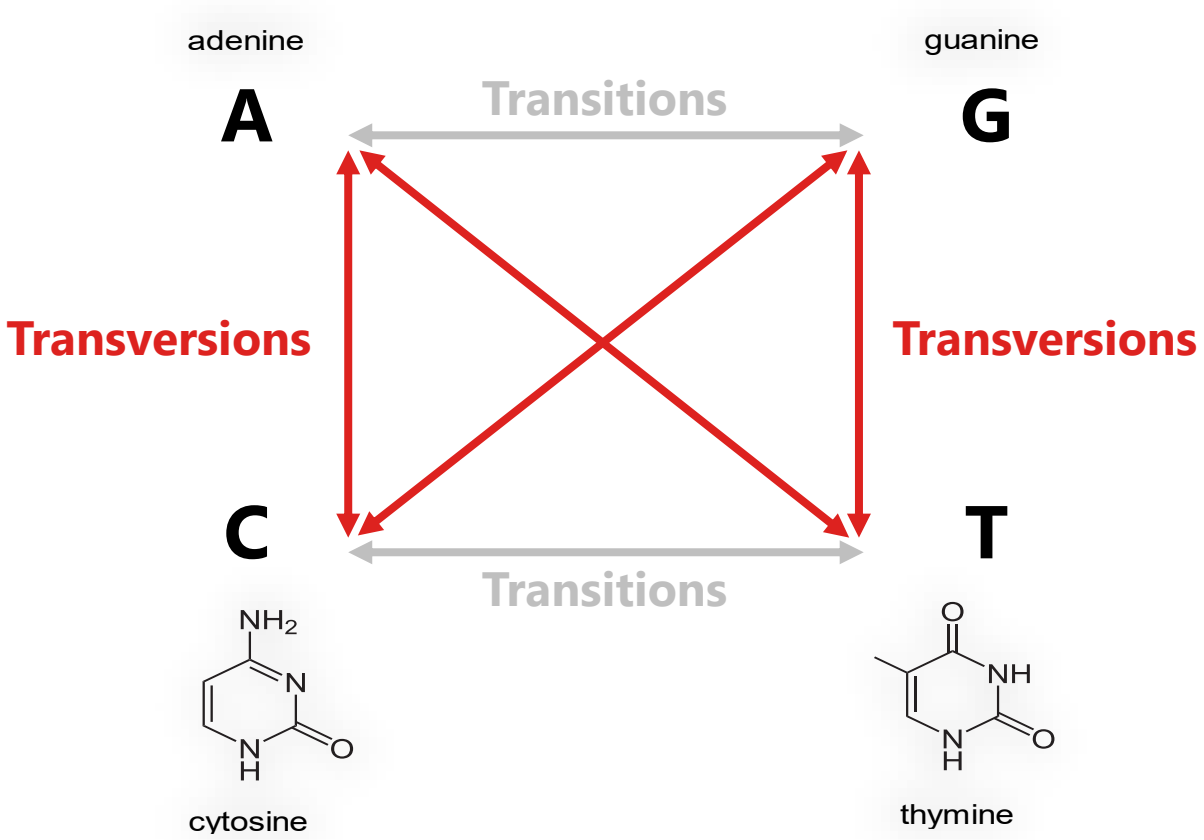


thymine

Transversion

Results when a purine is converted to a pyrimidine or a pyrimidine is converted to a purine





Induced Mutations › Chemicals

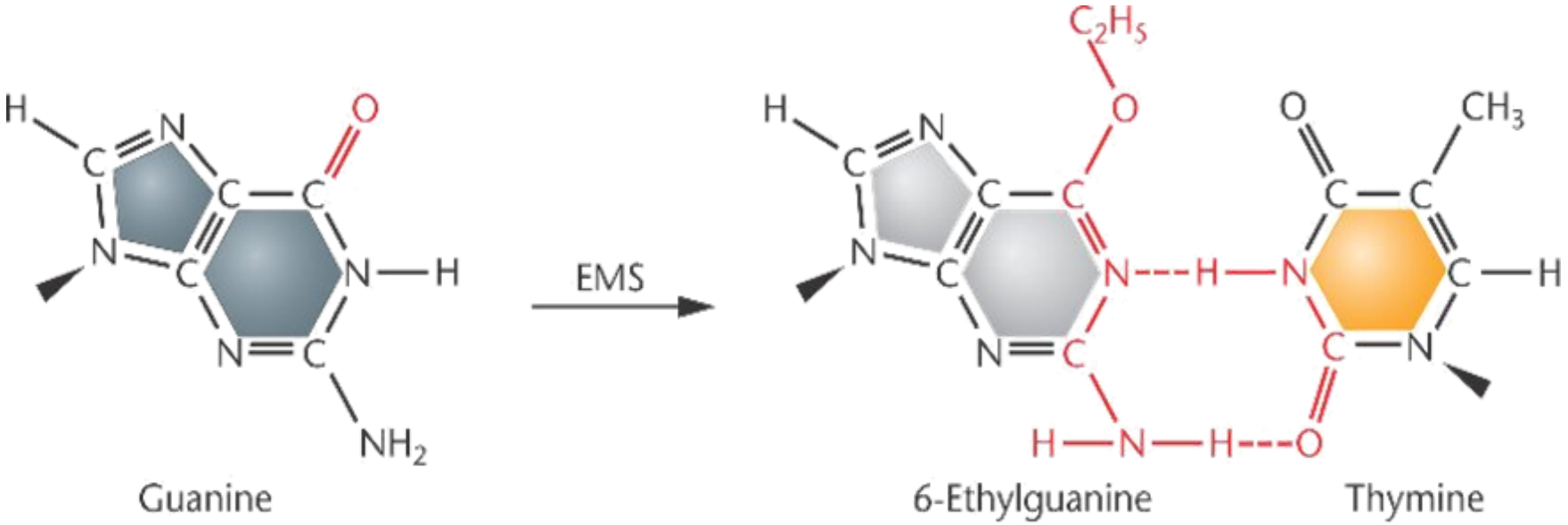
Two major classes of chemical mutagens which are routinely used are

1. **Alkylating Agents**
2. **Base Analogs**

Each has a specific effect on DNA

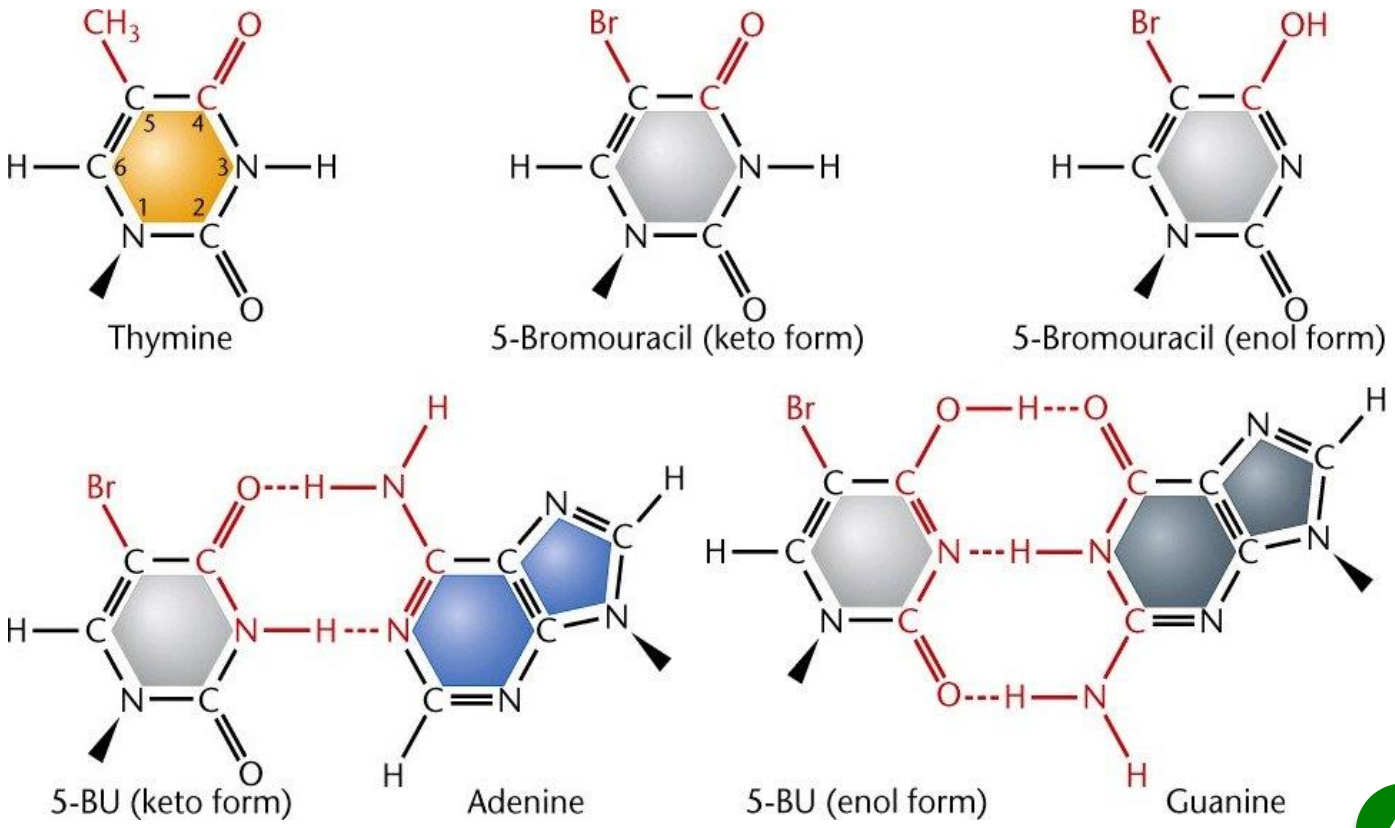
1 Alkylating Agents

Agents such as **Ethyl Methane Sulphonate (EMS)** and **Ethyl Ethane Sulphonate (EES)** can mutate both replicating and non-replicating DNA



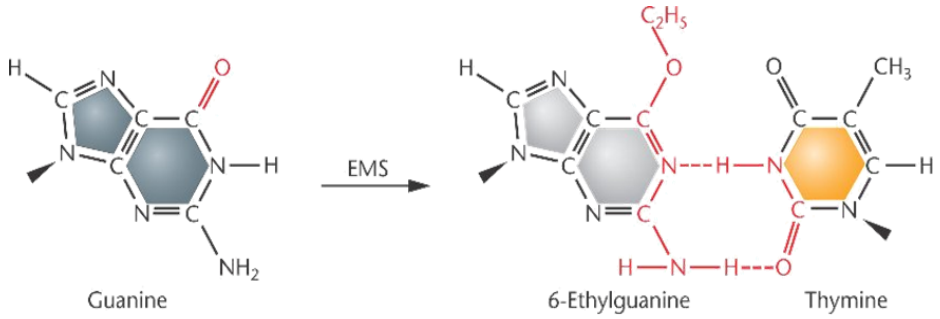
2 Base Analogs

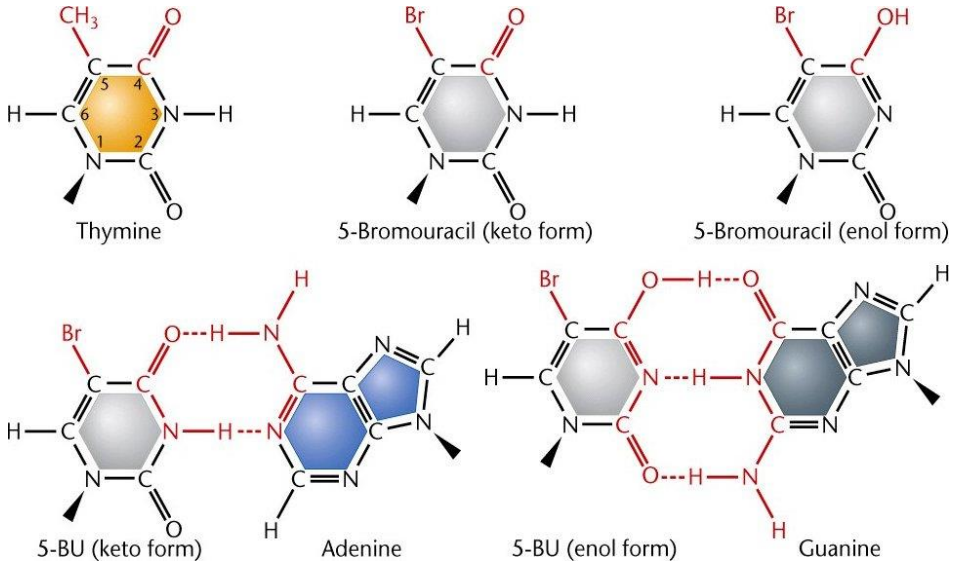
A base analog (e.g.,5-bromouracil) only mutate DNA when the analog is incorporated into replicating DNA



Induced Mutations › Chemicals

Each class of chemical mutagen has specific effects that can lead to transitions, transversions or deletions





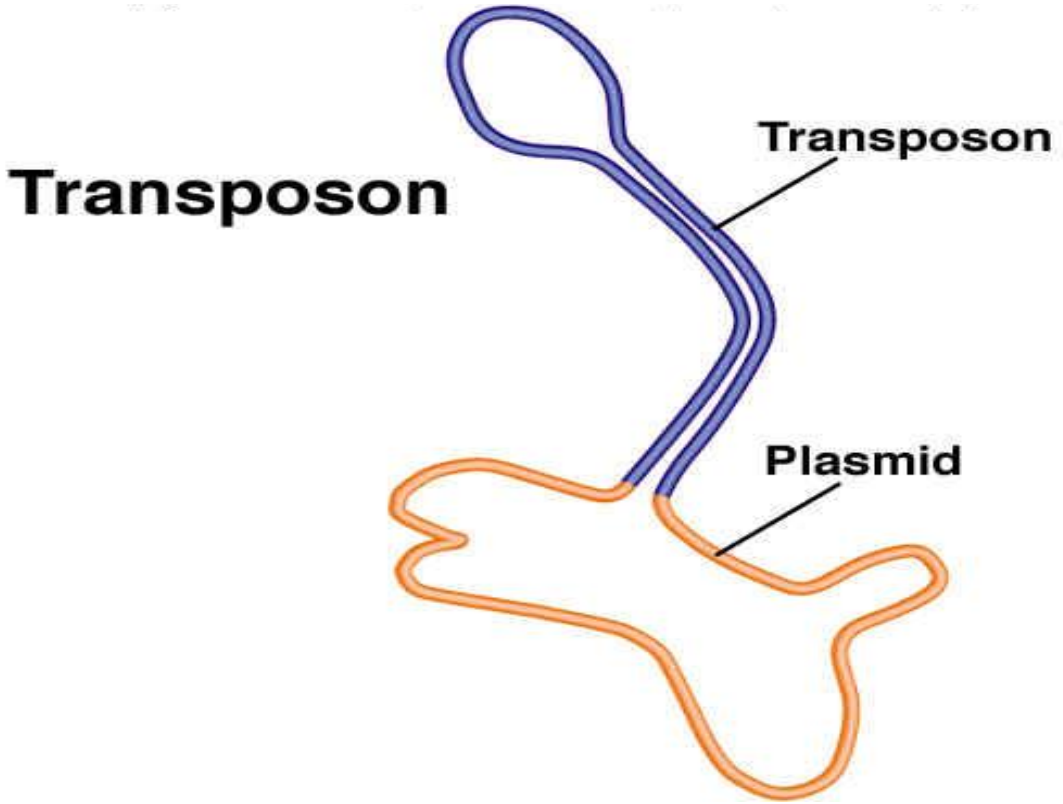
Induced Mutations › Transposon Insertion

Scientists are now using the power of transposable elements to create new mutations

Transposase

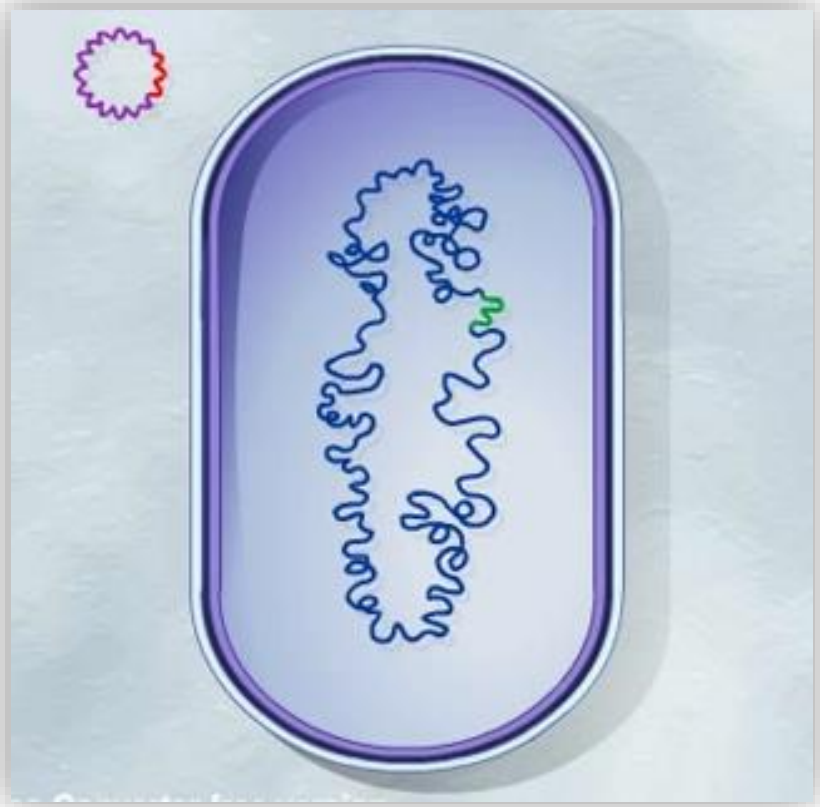
Induced Mutations › Transposon Insertion

Transposable elements are mobile pieces of DNA that can move from one location in a genome to another



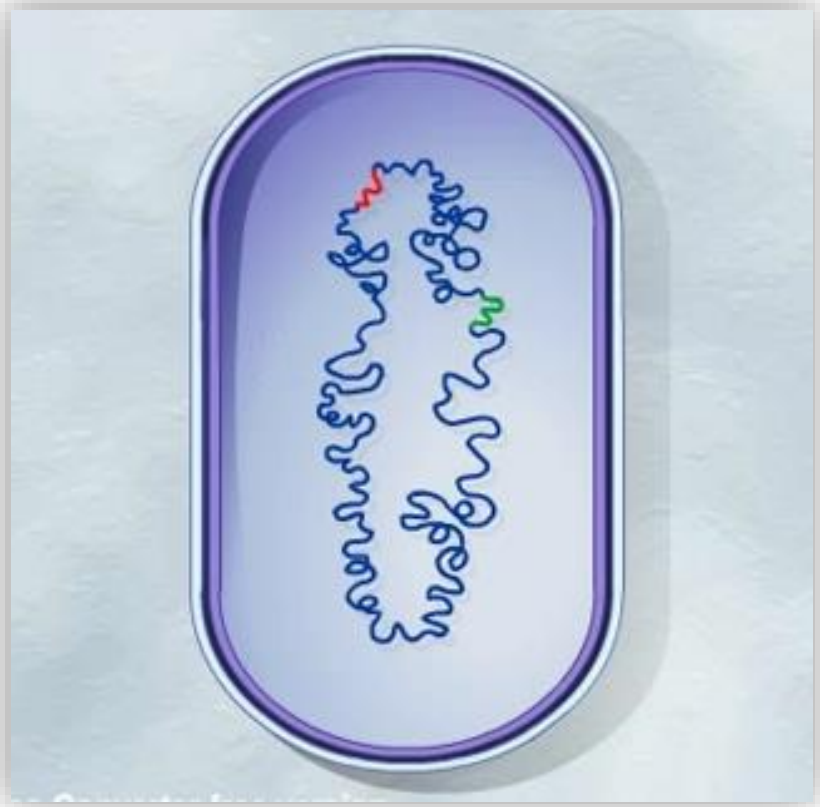
Induced Mutations › Transposon Insertion

Often when they move to a new location, the result is a new mutant



Induced Mutations › Transposon Insertion

The mutant arises because the presence of a piece of DNA in a wild type gene disrupts the normal function of that gene

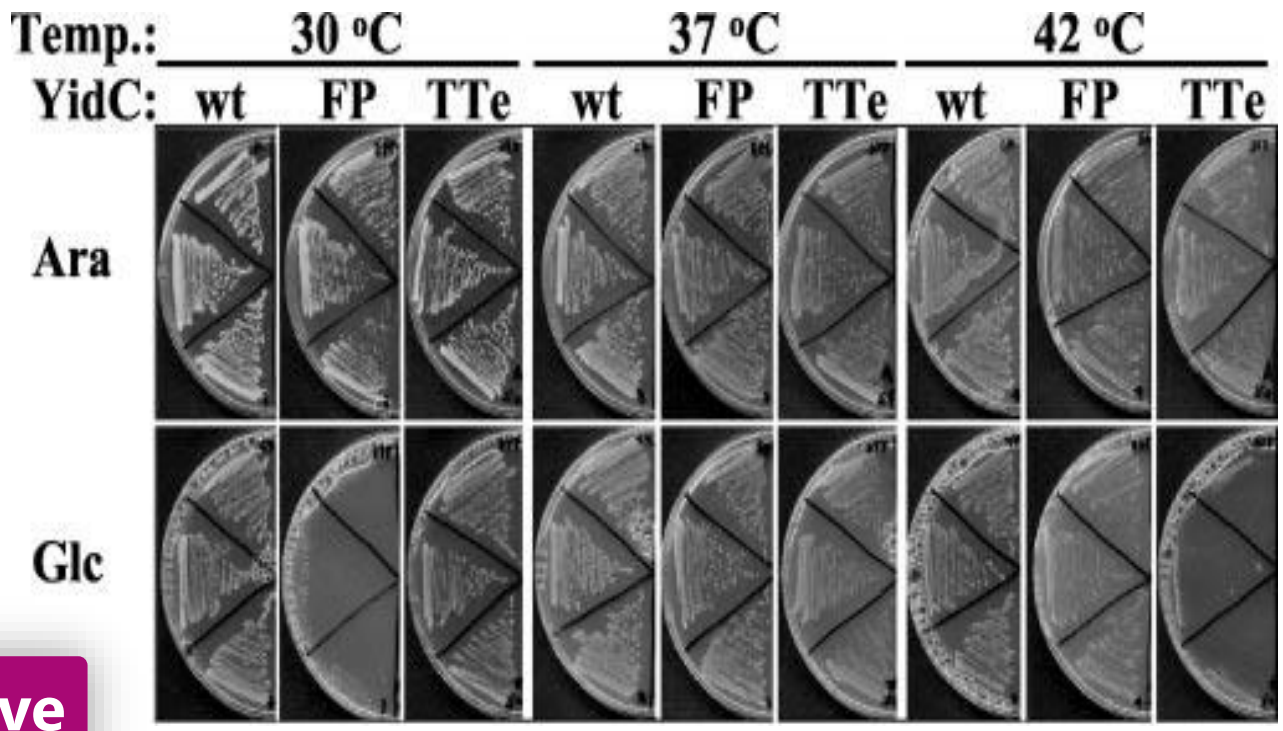


Heat/Cold-sensitive Mutations

Among the mutations that affect the function of a protein (gene), some allow the protein to be **active** at the s **normal** **ure** but t either **higher** or **lower** temperatures

Temperature-sensitive (Ts) Mutations

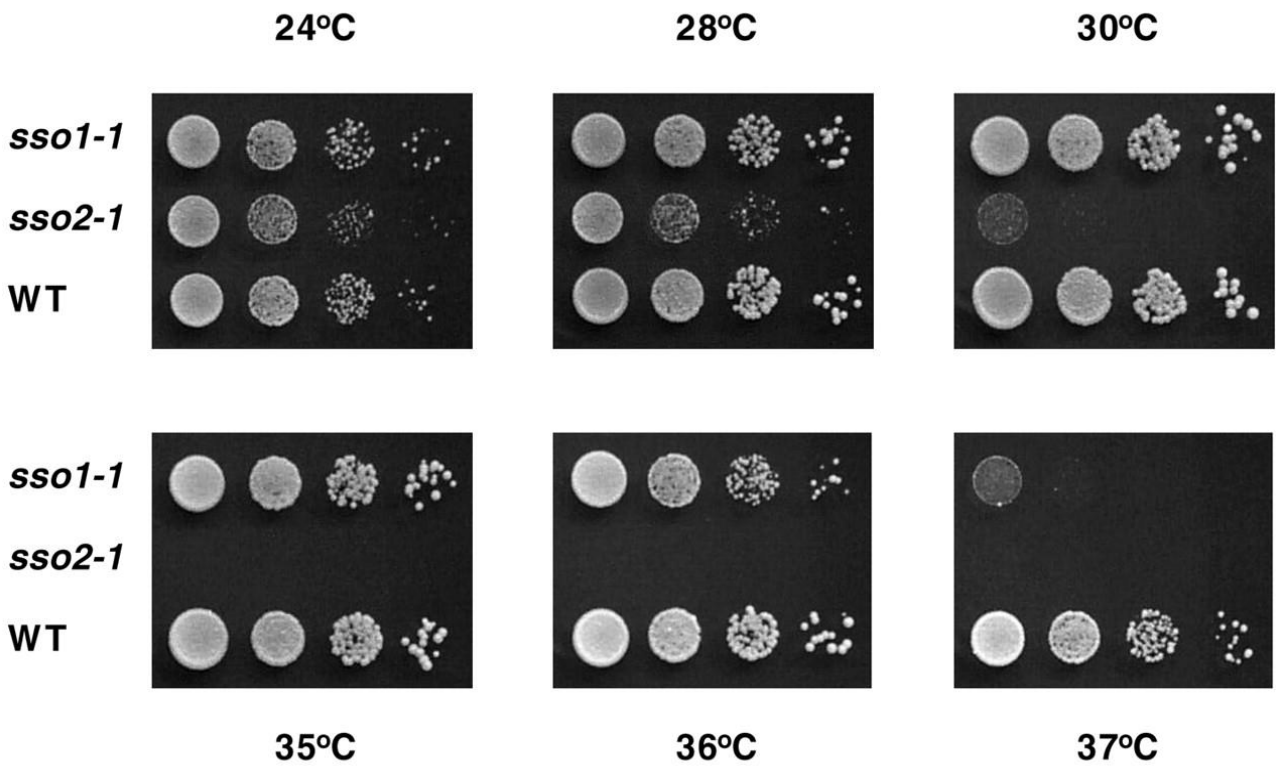
Cold-sensitive Mutations



Heat/Cold-sensitive Mutations

Temperature-sensitive (Heat-sensitive) Mutations

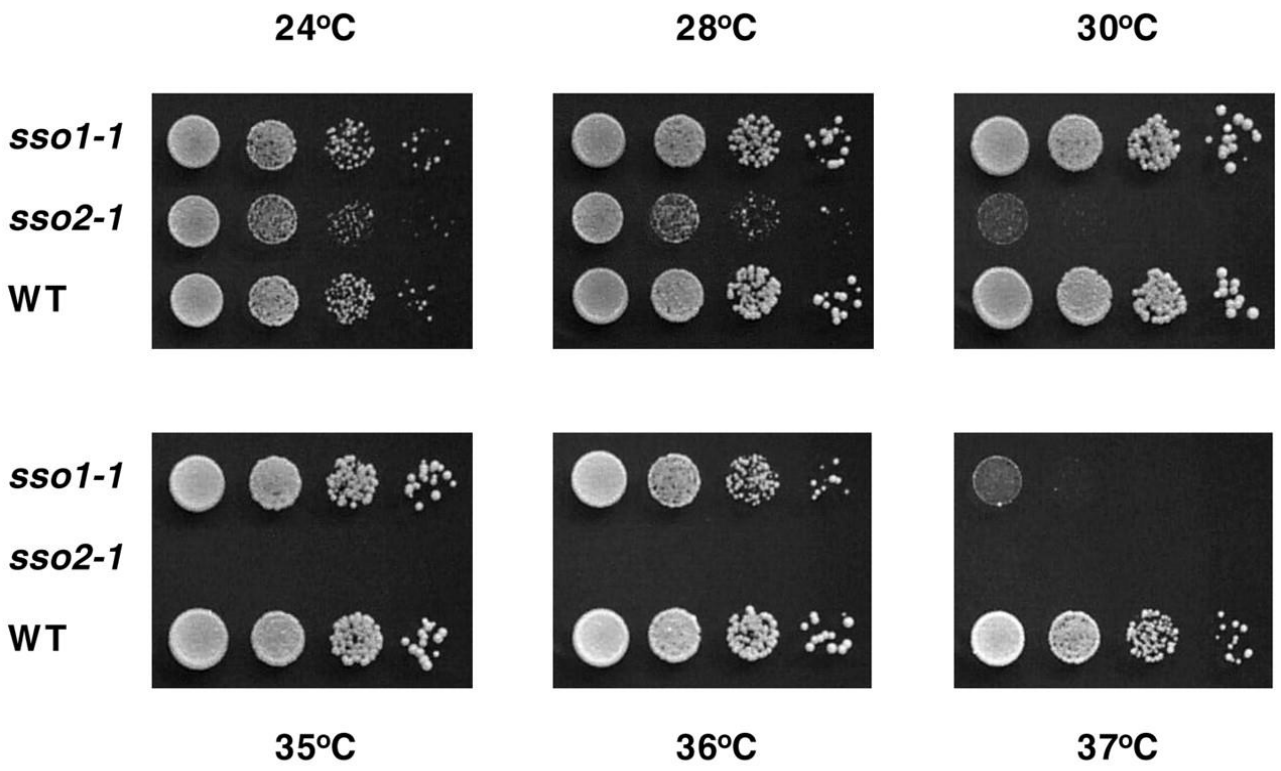
A gene fails to function at a higher temperature, but functions normally at a low temperature



Heat/Cold-sensitive Mutations

Cold-sensitive Mutations

Function normally at higher temperatures, but fail to function at a reduced temperature



Module 4

Mutations

Module Lessons

- Dashboard
- Introduction
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- Assignments

End of Module

Lesson 1

Mutations

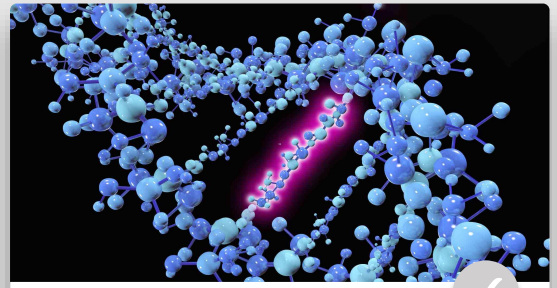
Learn what mutations are, how they happen and the sequence for reading genetic codes

Start

Lesson 2

Generation of Mutations

Start



Lesson 3

Classes of Mutations

Start

Lesson 3

Classes of Mutations

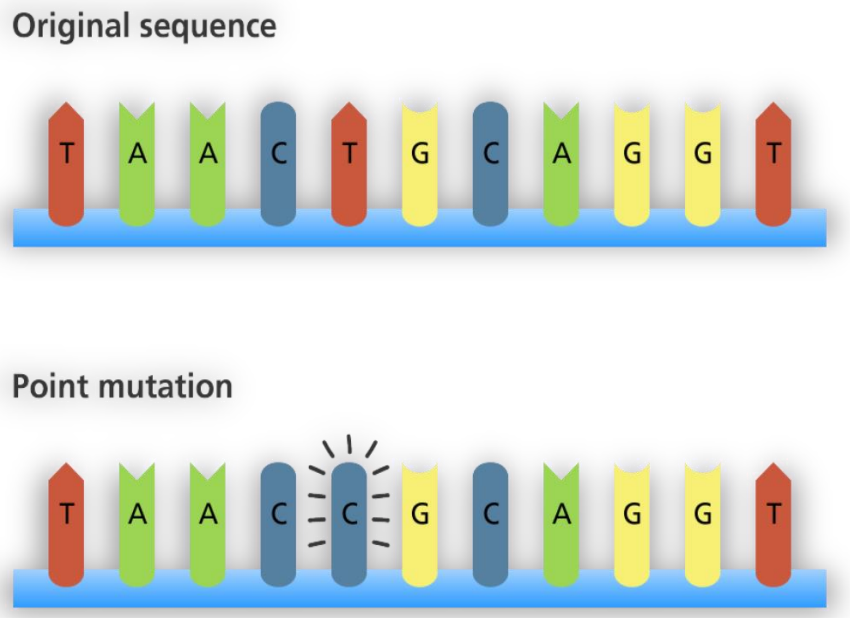
Learn more about the two general classes of mutations

Learn Now ▸

Classes of Mutations

Two general classes of mutations

1. **Point Mutations**



2. **Rearrangement or Chromosomal Mutations or Frameshift Mutations**

Classes of Mutations

Point Mutations

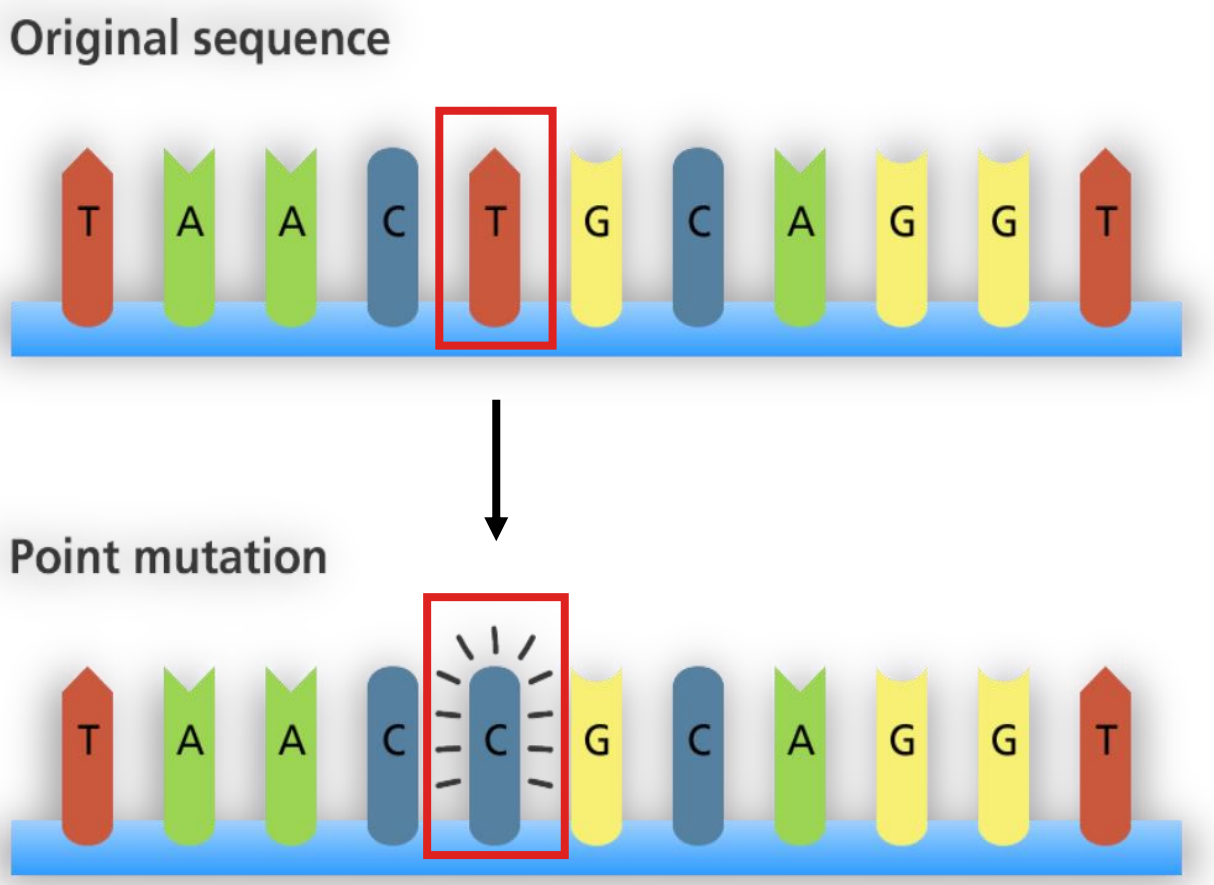
Cause a corresponding change in the protein that the gene produces

Rearrangement or Chromosomal Mutations

- Affects a large region
- The simplest type of rearrangements are **insertions** of additional material or **deletions** of a stretch of the gene

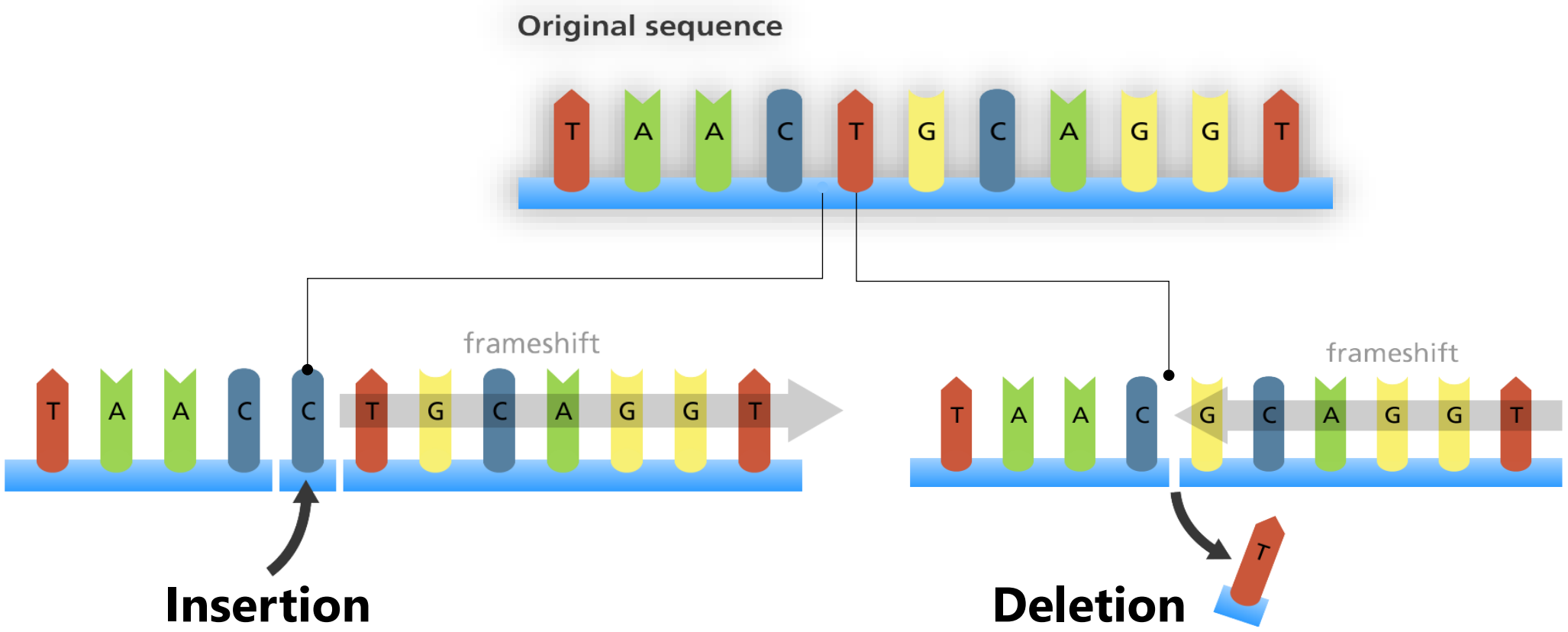
Point Mutation

This is when a single base in the nucleotide sequence is replaced by another



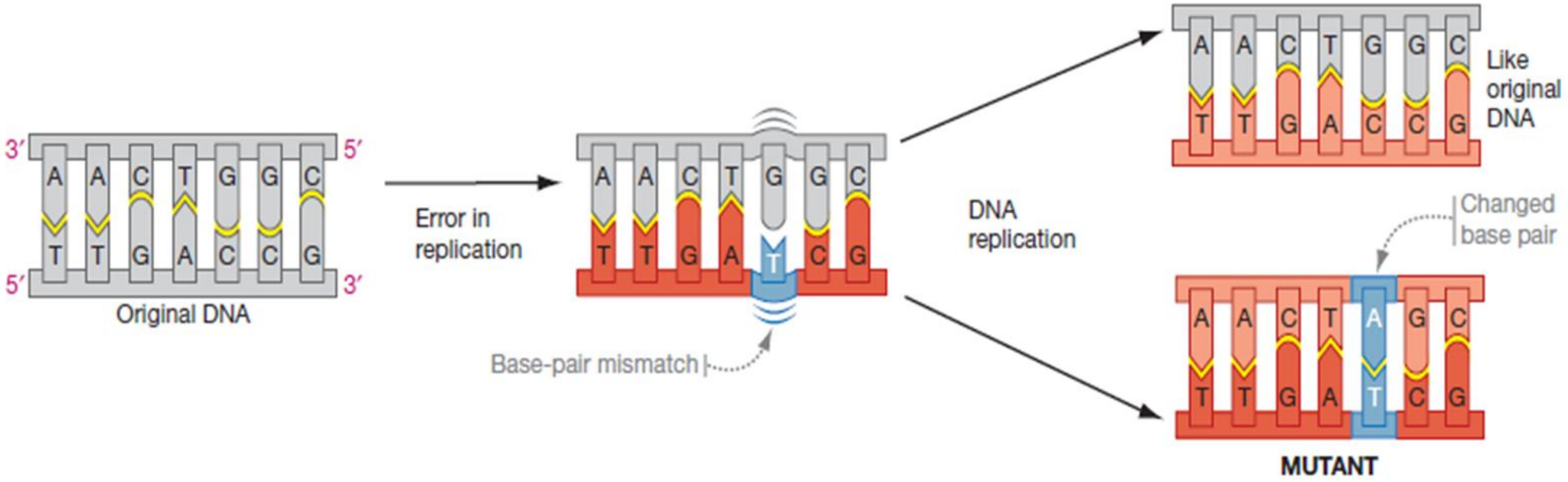
Point Mutation

Point mutations also include insertion and/or deletion of a single base in the DNA strand



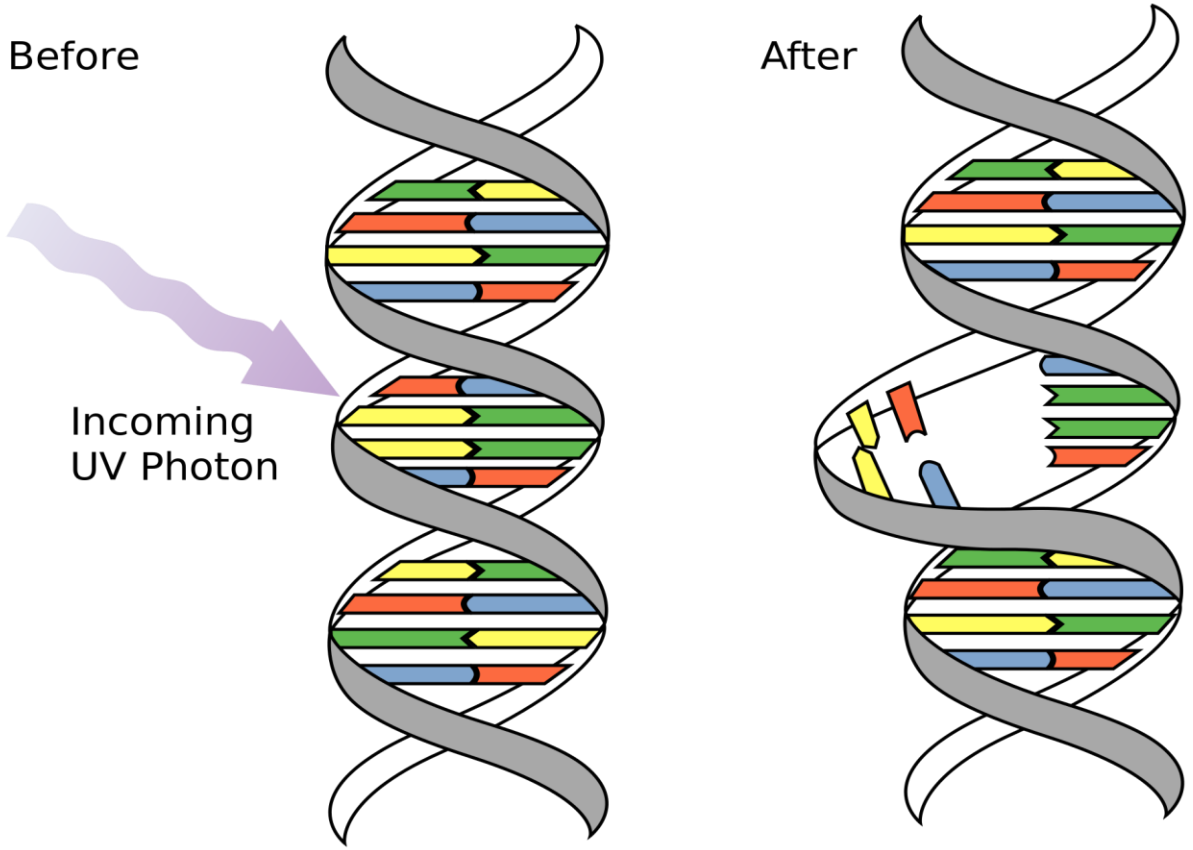
Point Mutation

Usually, they are caused due to error in DNA replication



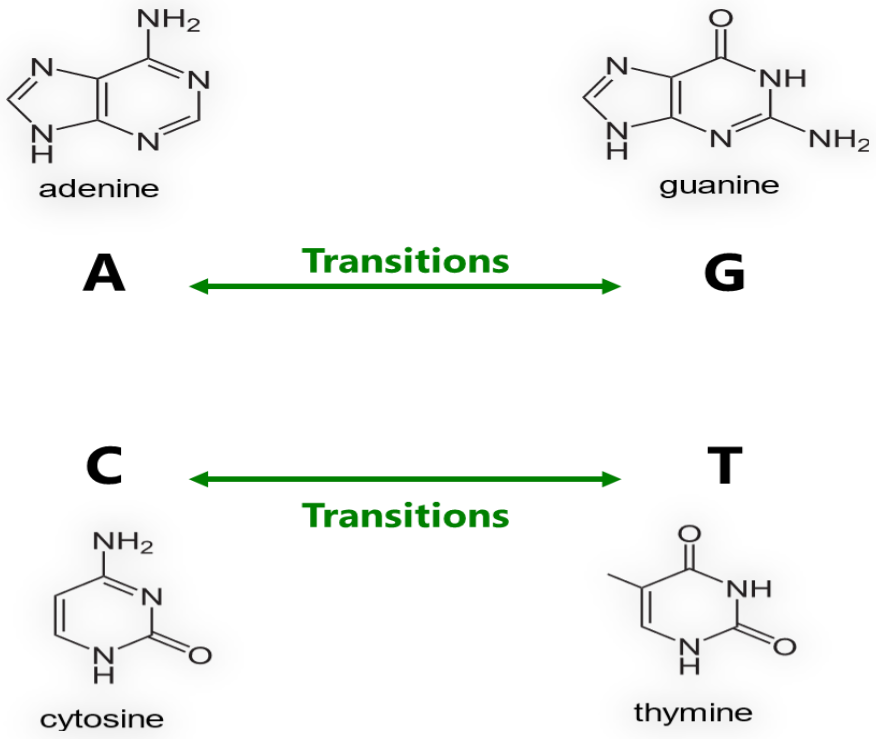
Point Mutation

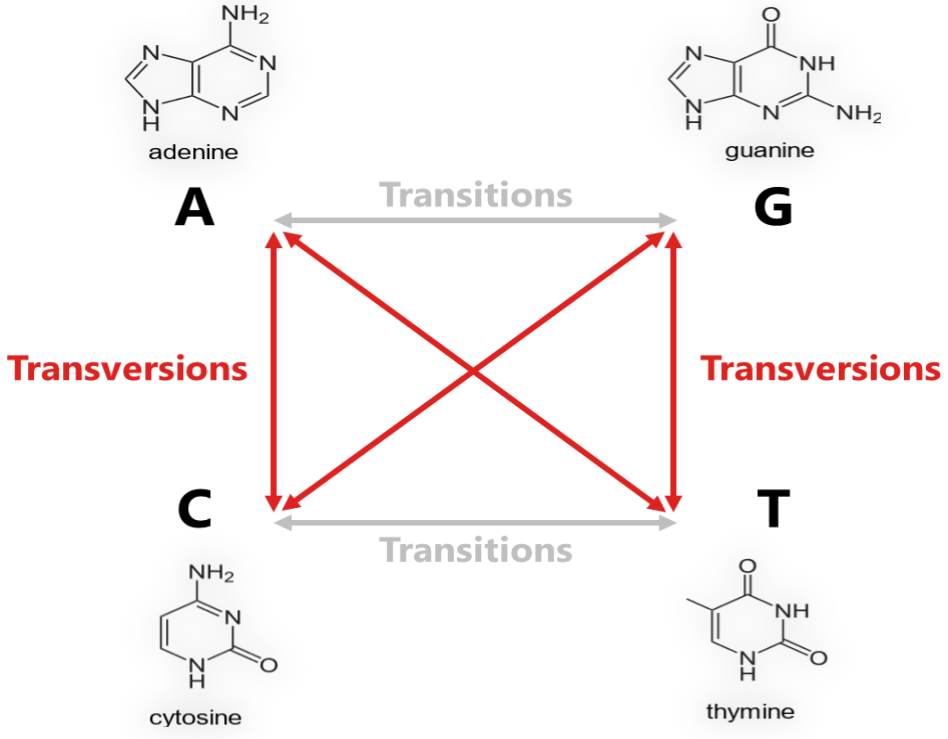
At times, it occurs after exposure to mutagens like heat and radiation



Point Mutation

Point mutations can be either:

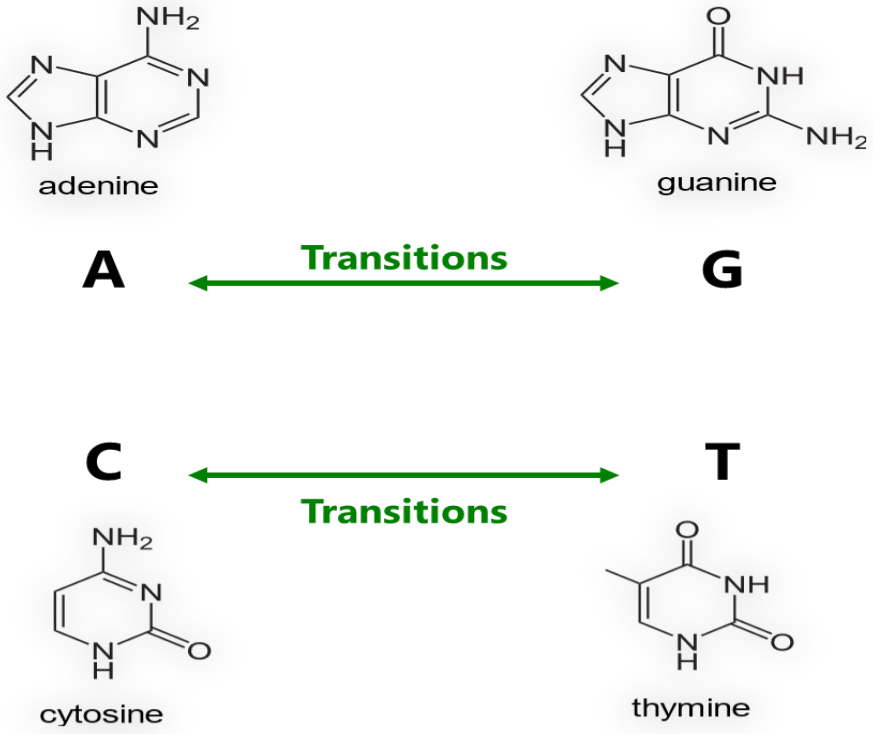


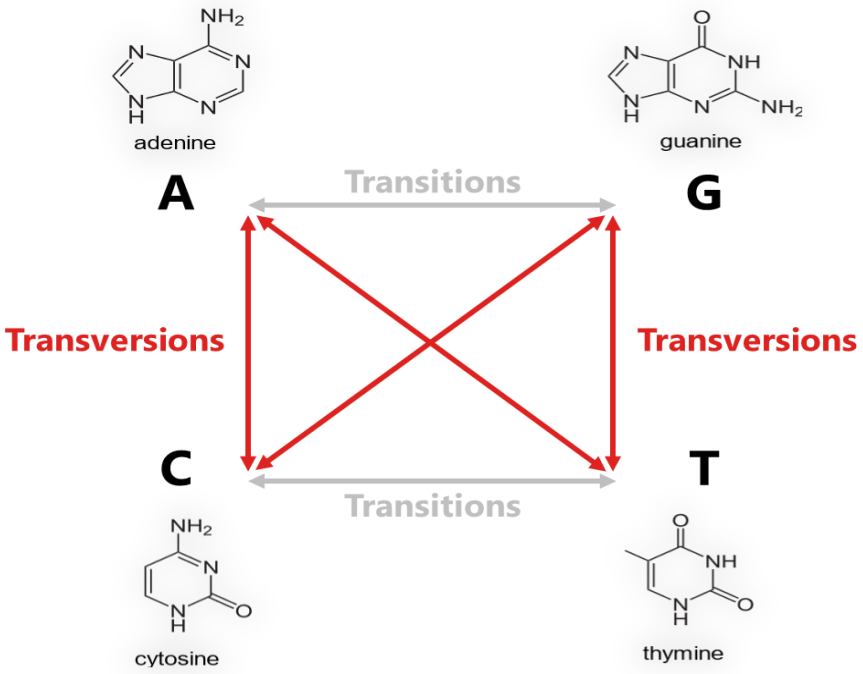


Transitions or **Transversions**

Point Mutation

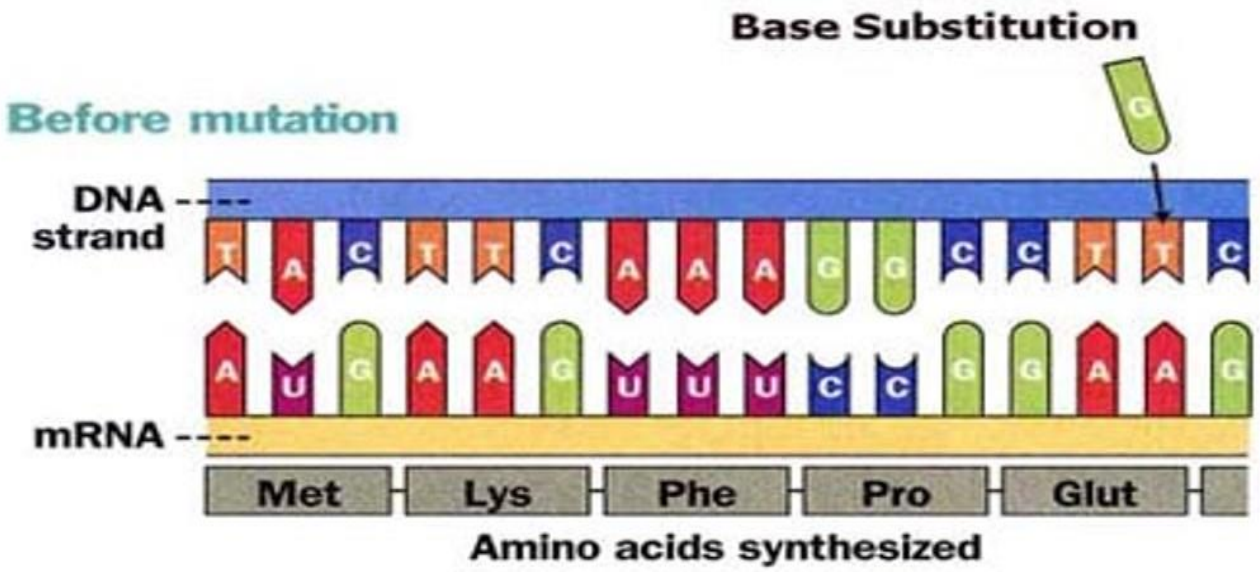
Transition point mutation is more common than transversion type





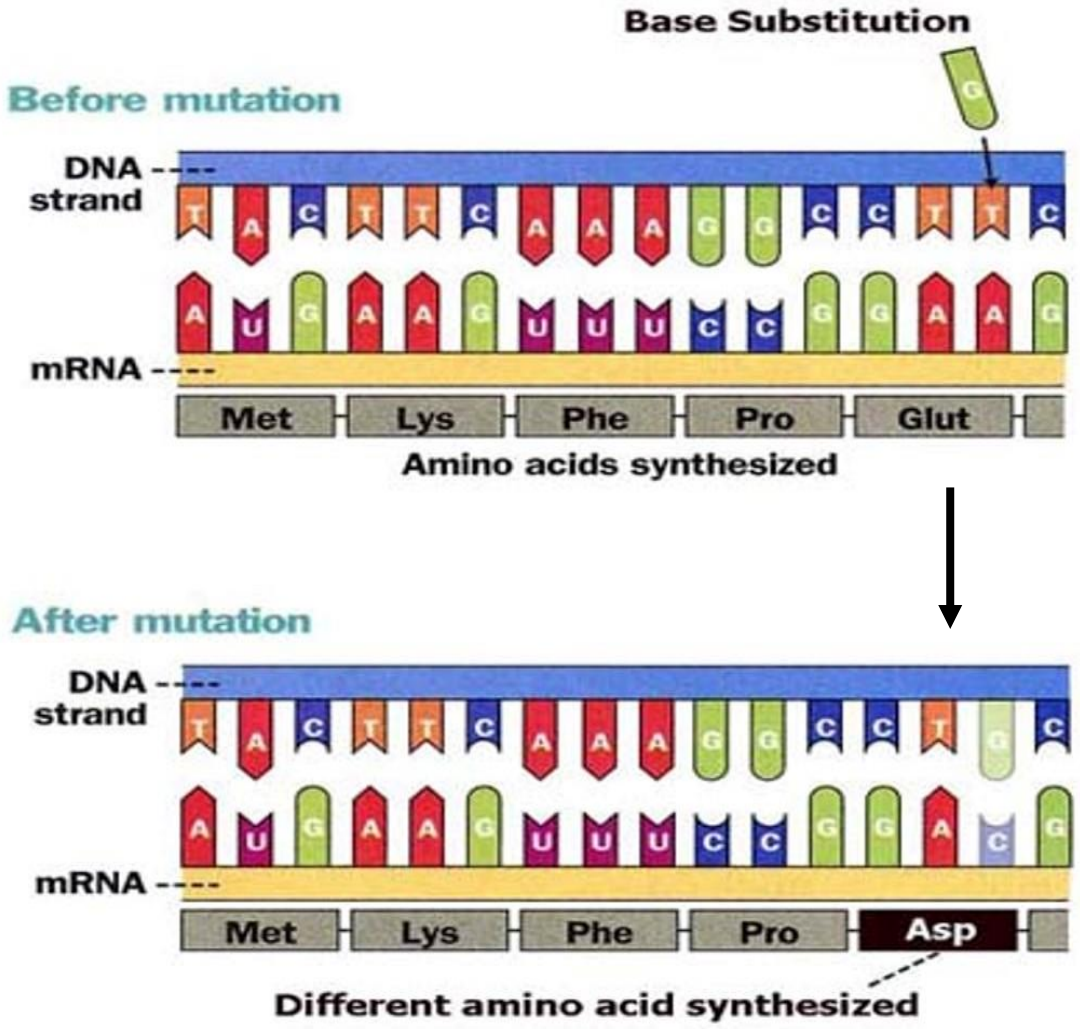
Point Mutation

The effects of point mutation can vary depending upon the site of mutation on the gene



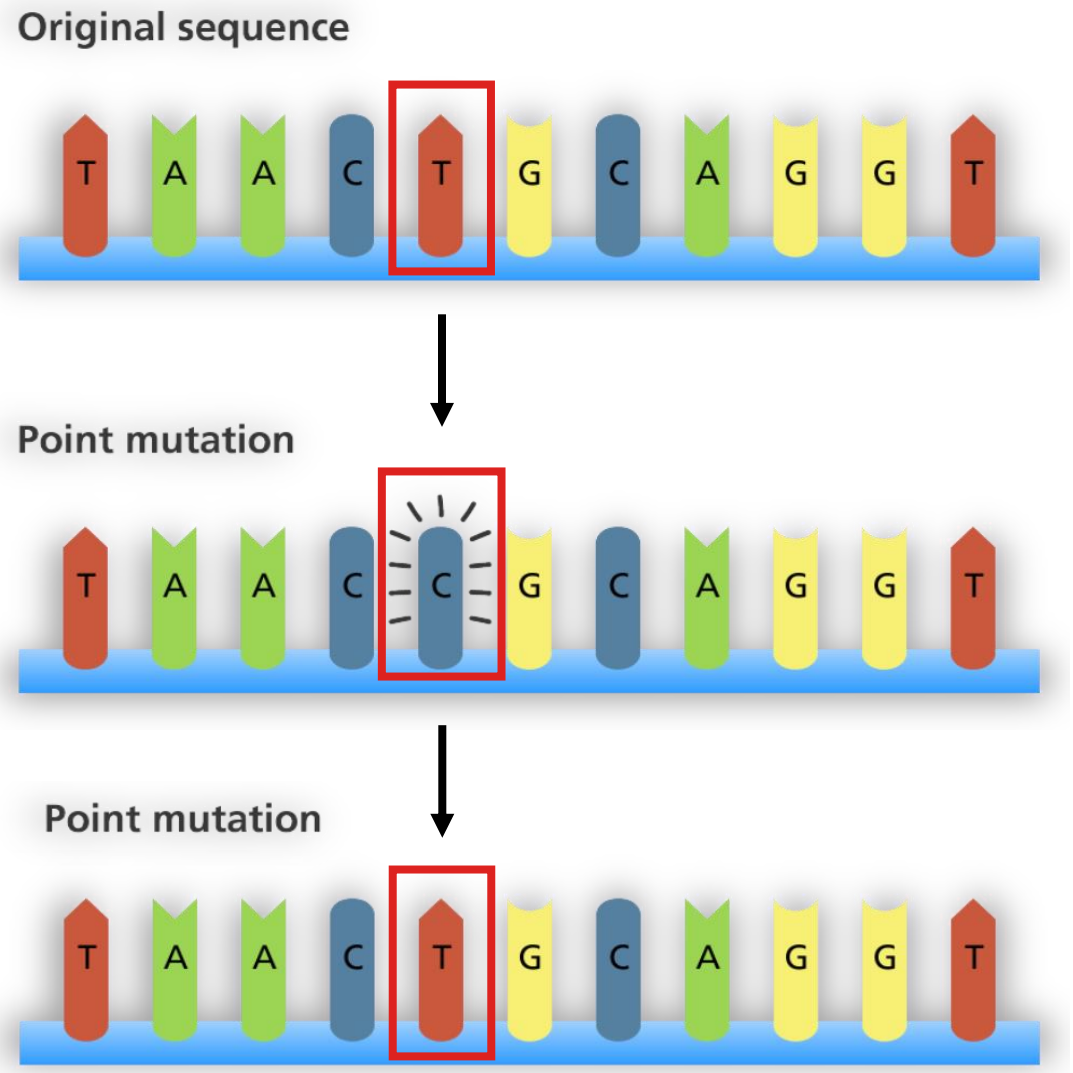
Point Mutation

If point mutation occurs in the coding sequence of DNA or exon, then the protein coded by the altered gene is changed



Point Mutation

A point mutation can be reversed by another point mutation, in which the nucleotide is changed back to its original state



Point Mutation Classifications

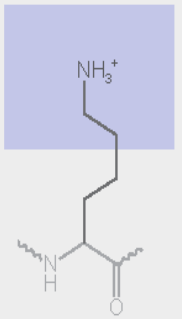
1. **Silent Mutations**

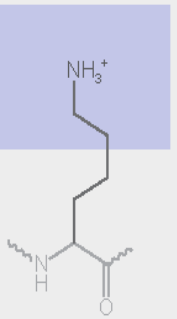
   which code for the same (or a sufficiently similar) **amino acid**

2. Nonsense Mutations

3. Missense Mutations

	No mutation	Silent
DNA level	TTC	TTT
mRNA level	AAG	AAA
protein level	Lys	Lys

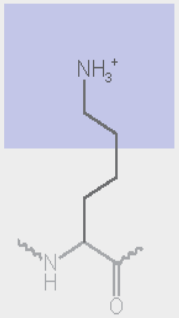




Point Mutation Classifications

1. Silent Mutations
2. **Nonsense Mutations** which code for a stop and can truncate the protein
3. Missense Mutations

	No mutation	Nonsense
DNA level	TTC	ATC
mRNA level	AAG	UAG
protein level	Lys	STOP

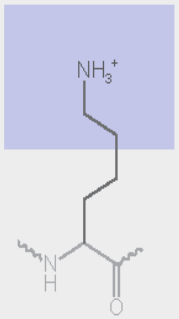


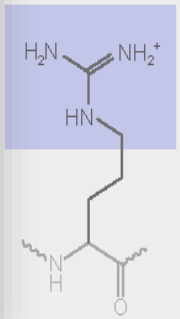
Point Mutation Classifications

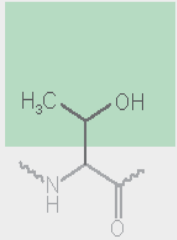
1. Silent Mutations
2. Nonsense Mutations
3. **Missense Mutations**

   which code for a different amino acid

	No mutation	Missense	
		conservative	non-conservative
DNA level	TTC	TCC	TGC
mRNA level	AAG	AGG	ACG
protein level	Lys	Arg	Thr







Point Mutation Classifications › Silent Mutations

Wild Type DNA	TAC	GGG	AAA	GTC	CGT	GGC
Wild Type mRNA	AUG	CCC	UUU	CAG	GCA	CCG
Amino Acids	Met	-Pro-	-Phe-	-Gln-	Ala-	Pro

↓

Mutated DNA	TAC	GGG	AA<u>G</u>	GTC	CGT	GGC
Mutated mRNA	AUG	CCC	UU<u>C</u>	CAG	GCA	CCG
Amino Acids	Met	-Pro-	-Phe-	-Gln-	Ala-	Pro

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

Silent Mutations

Such mutations are said to be silent because they cause no change in their product and cannot be detected without sequencing the gene (or its mRNA)

Wild Type DNA	TAC	GGG	AAA	GTC	CGT	GGC
Wild Type mRNA	AUG	CCC	UUU	CAG	GCA	CCG
Amino Acids	Met	-Pro-	-Phe-	-Gln-	Ala-	Pro

↓

Mutated DNA	TAC	GGG	AAG	GTC	CGT	GGC
Mutated mRNA	AUG	CCC	UUC	CAG	GCA	CCG
Amino Acids	Met	-Pro-	-Phe-	-Gln-	Ala-	Pro

Missense Mutations

Missense mutation is a genetic change that results in the substitution of one amino acid in protein for another

ATG	GAA	GCA	CGT
Met	Glu	Ala	Gly

↓

ATG	GAC	GCA	CGT
Met	Asp	Ala	Gly

Missense Mutations

OR

It is a mutation in which a codon specifying one amino acid is altered so as to specify a different amino acid

ATG	GAA	GCA	CGT
Met	Glu	Ala	Gly

↓

ATG	GAC	GCA	CGT
Met	Asp	Ala	Gly

Missense Mutations

ATG	GAA	GCA	CGT
Met	Glu	Ala	Gly

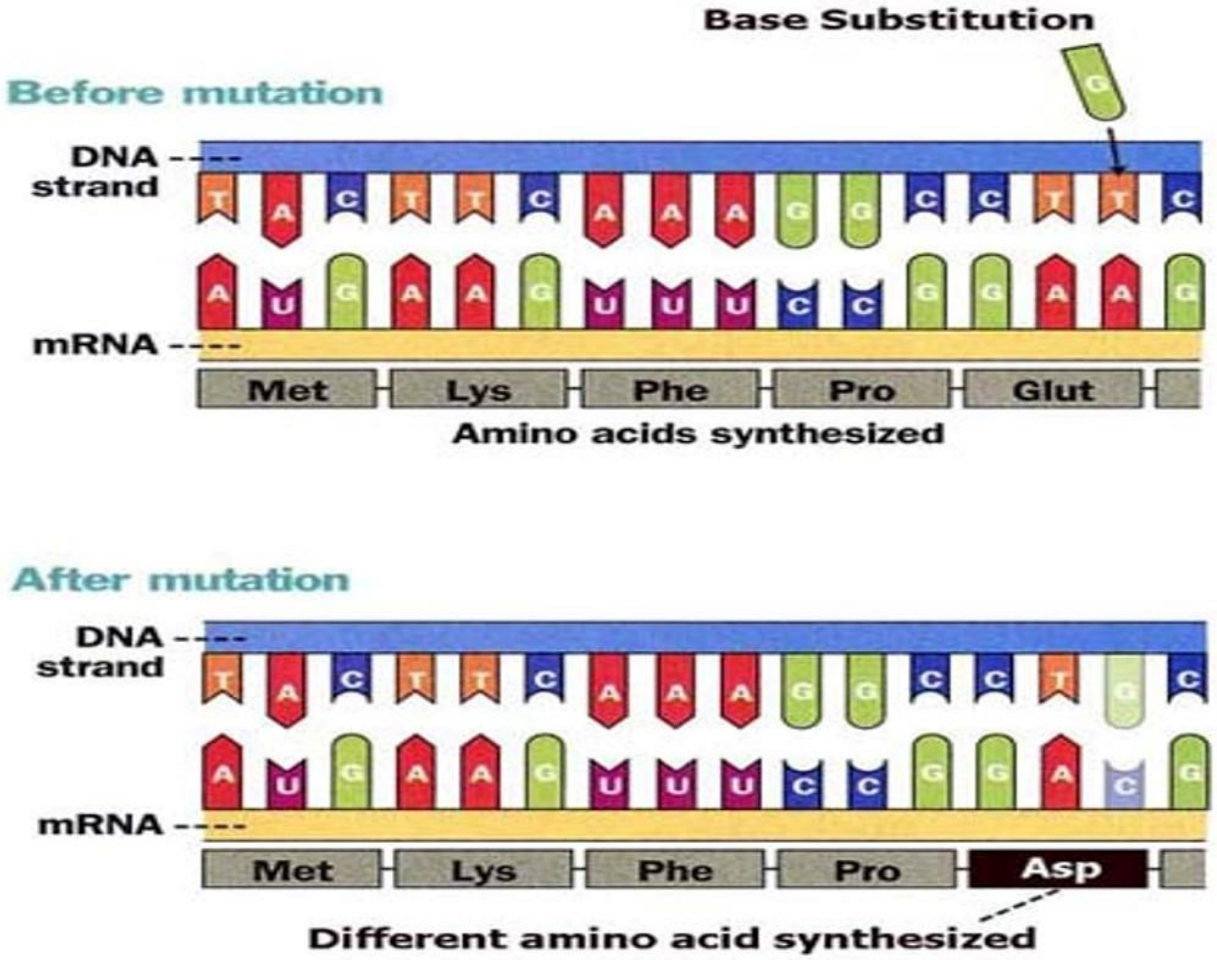
↓

ATG	GAC	GCA	CGT
Met	Asp	Ala	Gly

It is missense because the resulting codon has the "wrong sense" for an amino acid

Missense Mutations

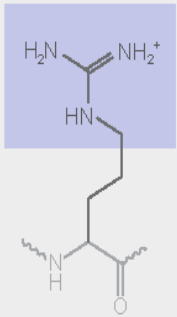
A missense mutation is a "readable" genetic message although its "sense" (its meaning) is changed

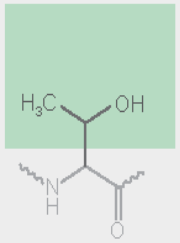


Missense Mutations

This is in contrast to a nonsense mutation which has no meaning except to halt the reading of the genetic message

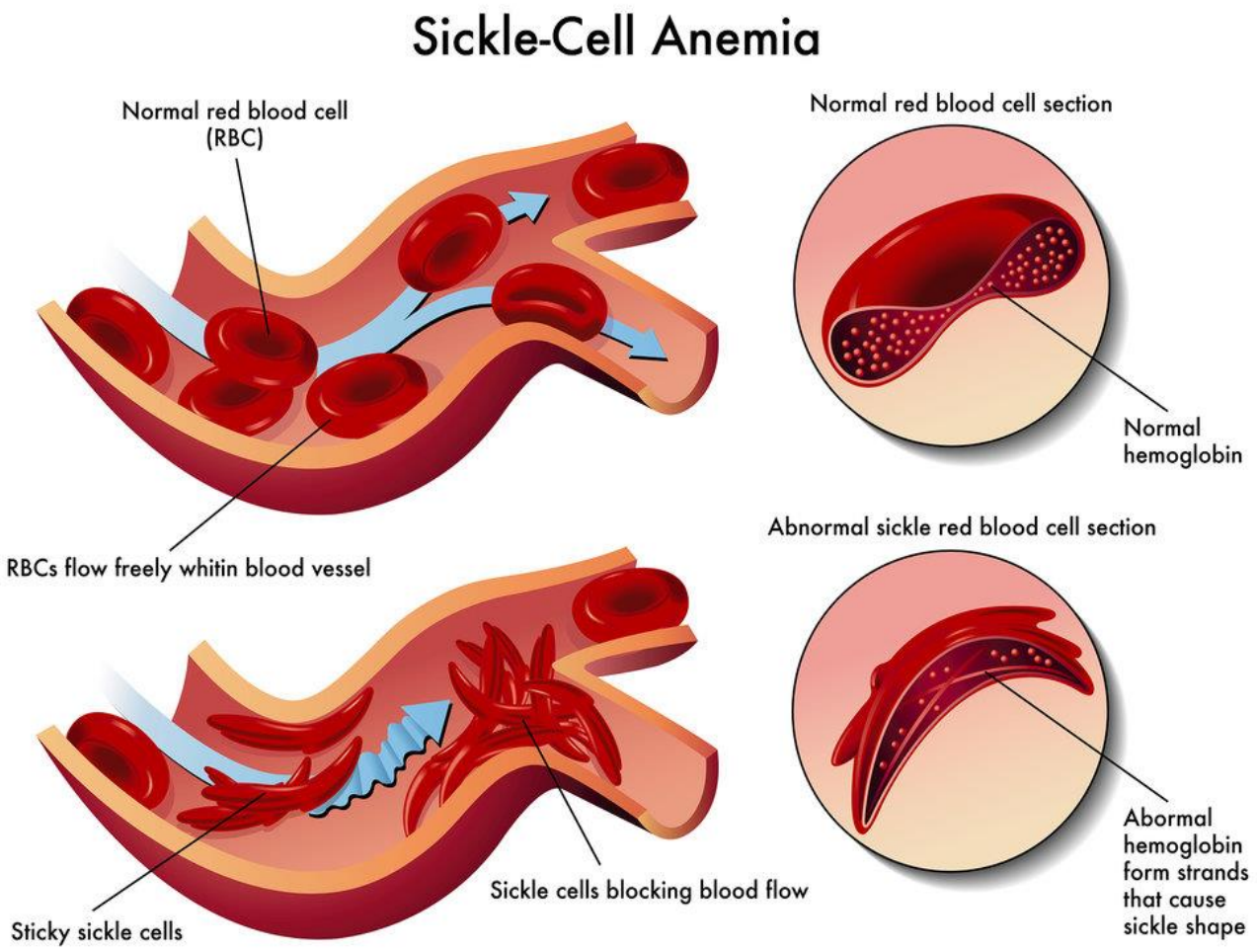
Missense		Nonsense
conservative	non-conservative	
TCC	TGC	ATC
AGG	ACG	UAG
Arg	Thr	STOP





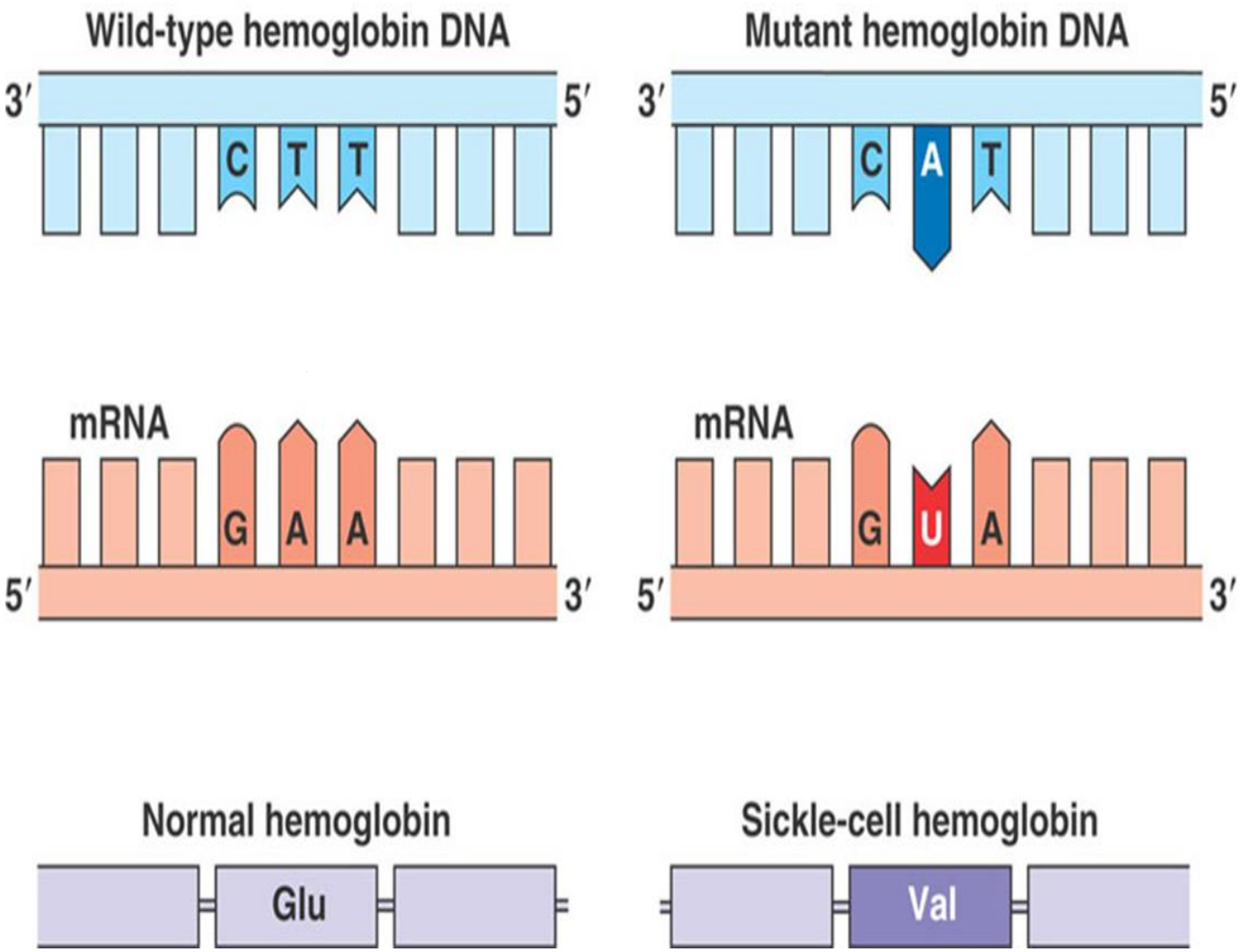
Missense Mutations

The first missense mutation discovered in humans was found to be responsible for sickle hemoglobin, the molecular basis of sickle cell trait and sickle cell anemia



Missense Mutations

The mutation causes an amino acid change from glutamic acid to valine, converting normal adult hemoglobin (hemoglobin A) to sickle hemoglobin (hemoglobin S)



Point ... ons

The n... cause... acid ... glutam... valine... norm... hemo... (hem... sickle... (hem...

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

Nonsense Mutations

A change in a base in the DNA that prematurely stops the translation of messenger RNA (mRNA) resulting in a polypeptide (protein) chain that ends prematurely

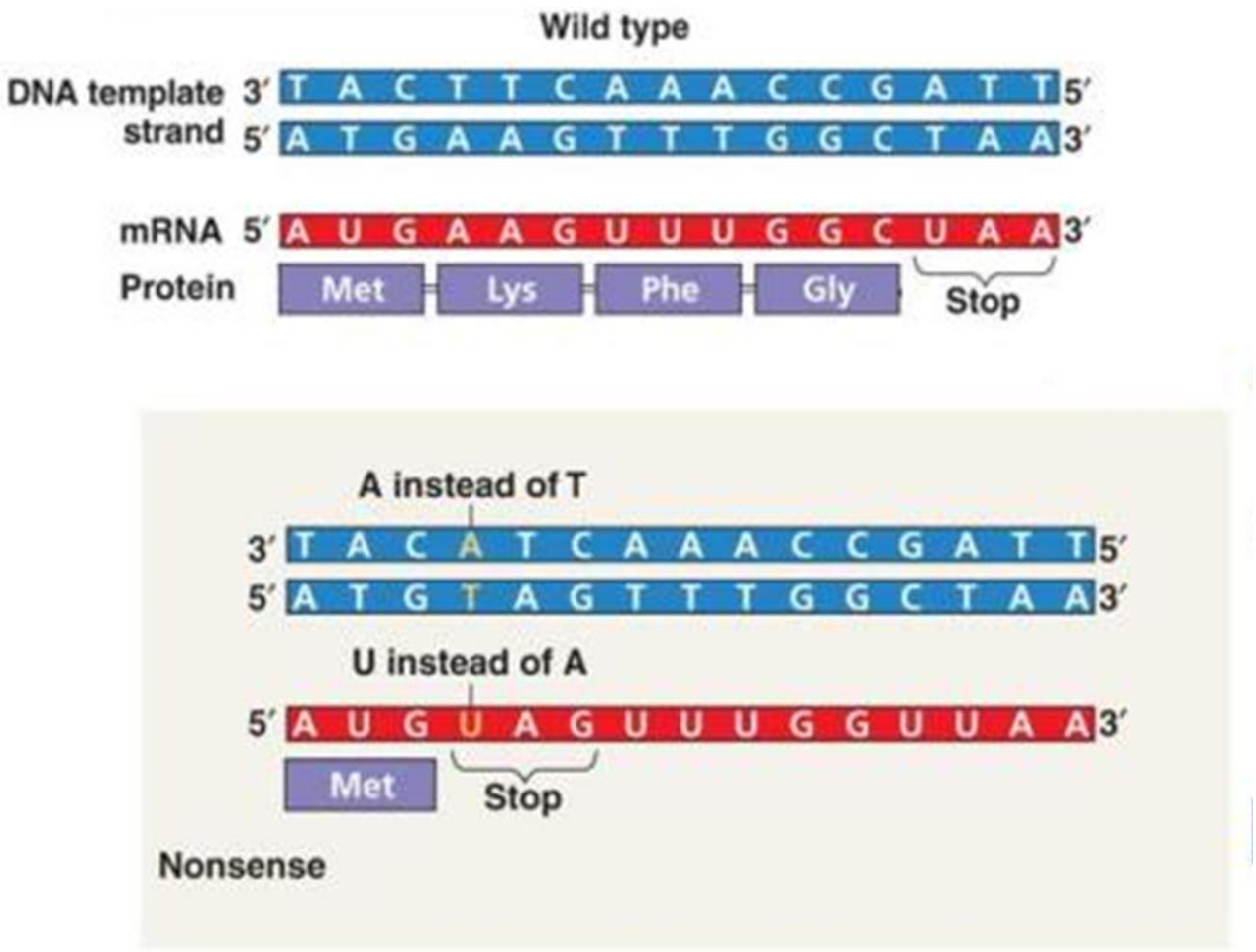
ATG	GAA	GCA	CGT
Met	Glu	Ala	Gly

↓

ATG	TAA	GCA	CGT
Met	STOP		

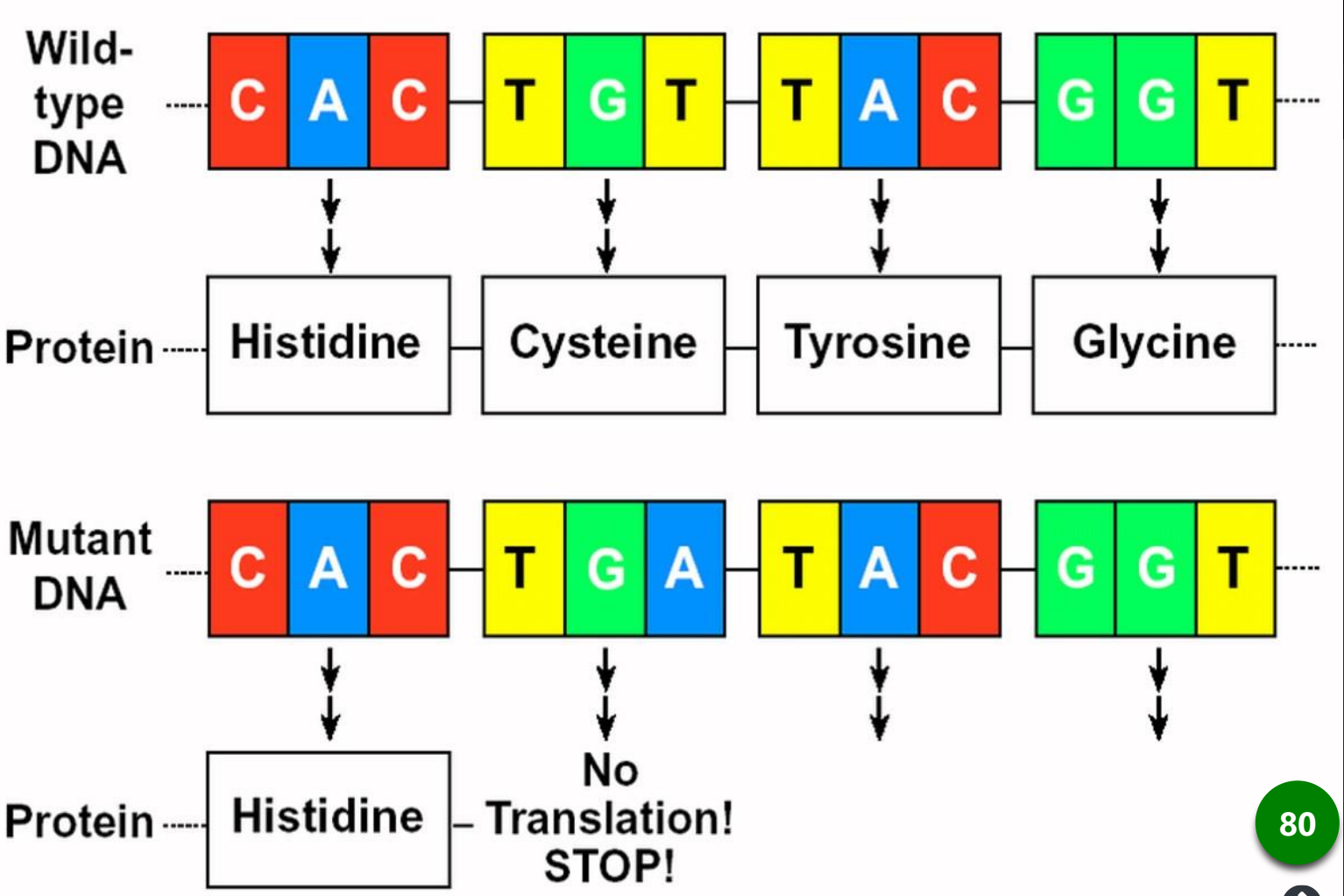
Nonsense Mutations

This results in a protein product that is truncated and incomplete and usually nonfunctional



Nonsense Mutations

The nonsense mutation converts a codon that encodes an amino acid into a **stop codon**, i.e., a code that specifies the termination of translation



Nonsense Mutations

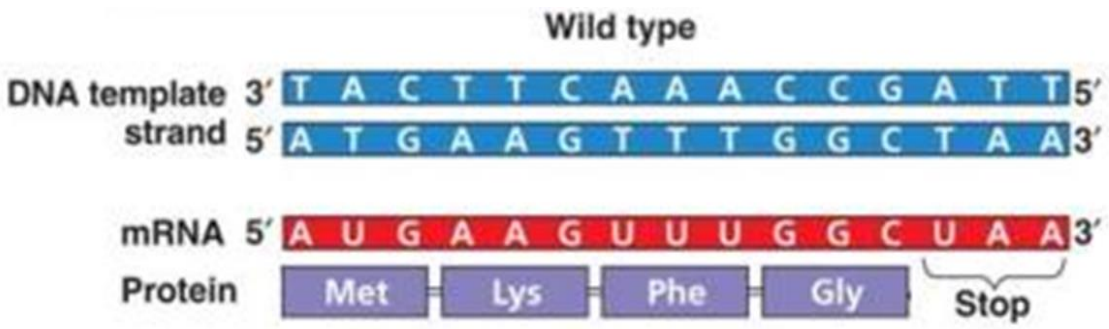
There are three nonsense codons (**UAG**, **UAA**, and **UGA**) in mRNA.

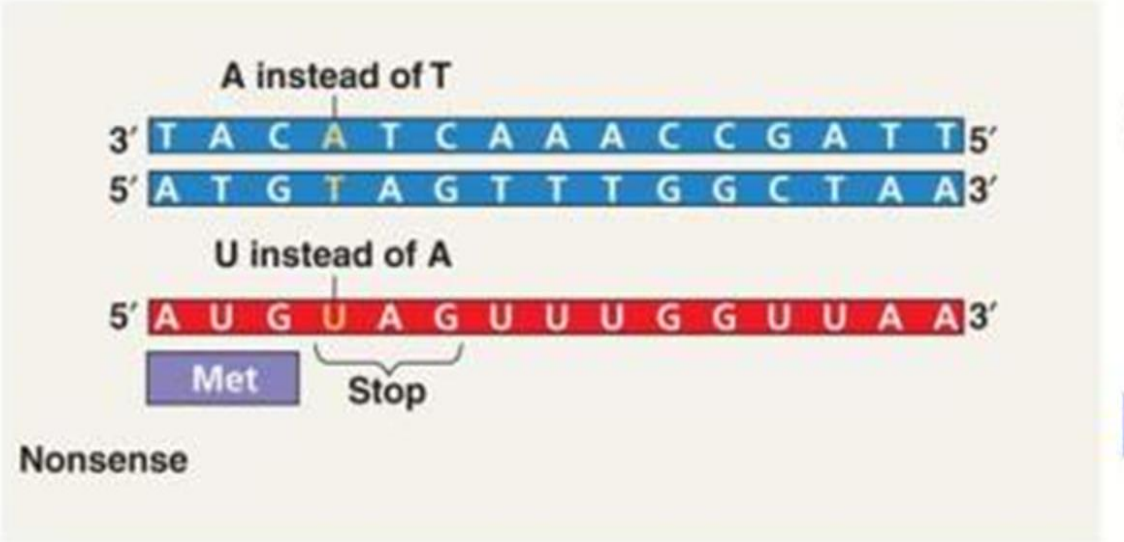
Look for the names of these codons

1st letter	Second Letter: U		Second Letter: C		Second Letter: A		Second Letter: G		3rd letter
U	UUU	Phe	UCU	Ser	UAU	Tyr	UGU	Cys	U
	UUC		UCC		UAC		UGC		C
	UUA	Leu	UCA		UAA	Stop	UGA	Stop	A
	UUG		UCG		UAG	Stop	UGG	Trp	G
C	CUU	Leu	CCU	Pro	CAU	His	CGU	Arg	U
	CUC		CCC		CAC		CGC		C
	CUA		CCA		CAA	Gln	CGA		A
	CUG		CCG		CAG		CGG		G
A	AUU	Ile	ACU	Thr	AAU	Asn	AGU	Ser	U
	AUC		ACC		AAC		AGC		C
	AUA		ACA		AAA	Lys	AGA	Arg	A
	AUG	Met	ACG		AAG		AGG		G
G	GUU	Val	GCU	Ala	GAU	Asp	GGU	Gly	U
	GUC		GCC		GAC		GGC		C
	GUA		GCA		GAA	Glu	GGA		A
	GUG		GCG		GAG		GGG		G

Nonsense Mutations

One of them comes normally at the end of each polypeptide





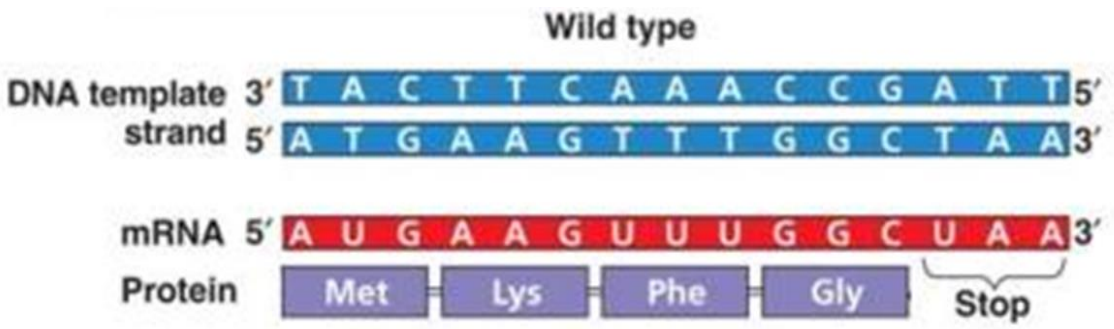
Nonsense Mutations

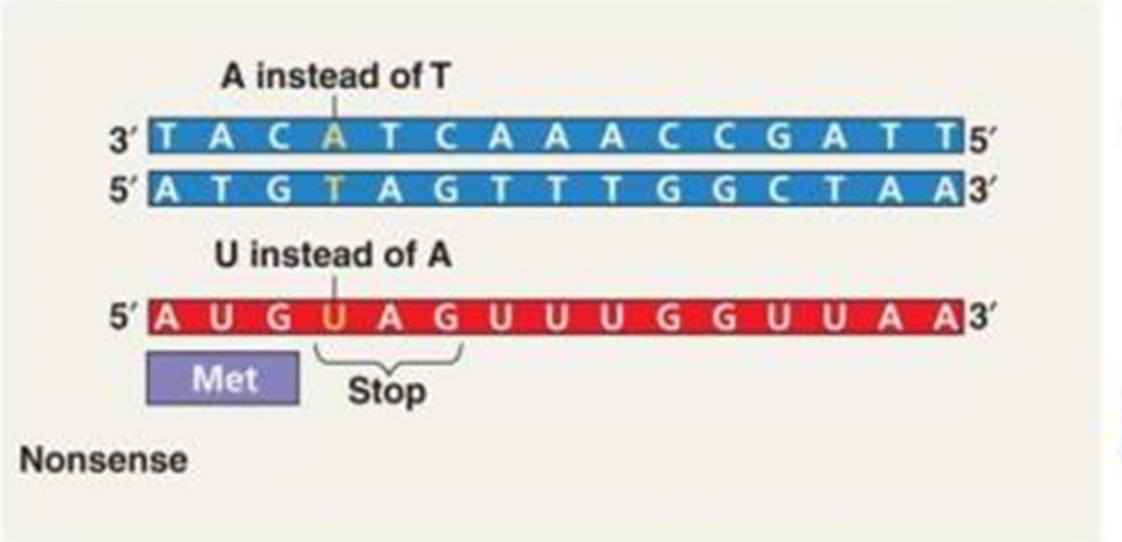
Three codons in the genetic code tell the cell to stop adding amino acids to a protein because the end of the gene has been reached

1st letter	Second Letter: U		Second Letter: C		Second Letter: A		Second Letter: G		3rd letter
U	UUU	Phe	UCU	Ser	UAU	Tyr	UGU	Cys	U
	UUC		UCC		UAC		UGC		C
	UUA	Leu	UCA		UAA	Stop	UGA	Stop	A
	UUG		UCG		UAG	Stop	UGG	Trp	G
C	CUU	Leu	CCU	Pro	CAU	His	CGU	Arg	U
	CUC		CCC		CAC		CGC		C
	CUA		CCA		CAA	Gln	CGA		A
	CUG		CCG		CAG		CGG		G
A	AUU	Ile	ACU	Thr	AAU	Asn	AGU	Ser	U
	AUC		ACC		AAC		AGC		C
	AUA		ACA		AAA	Lys	AGA	Arg	A
	AUG	Met	ACG		AAG		AGG		G
G	GUU	Val	GCU	Ala	GAU	Asp	GGU	Gly	U
	GUC		GCC		GAC		GGC		C
	GUA		GCA		GAA	Glu	GGA		A
	GUG		GCG		GAG		GGG		G

Nonsense Mutations

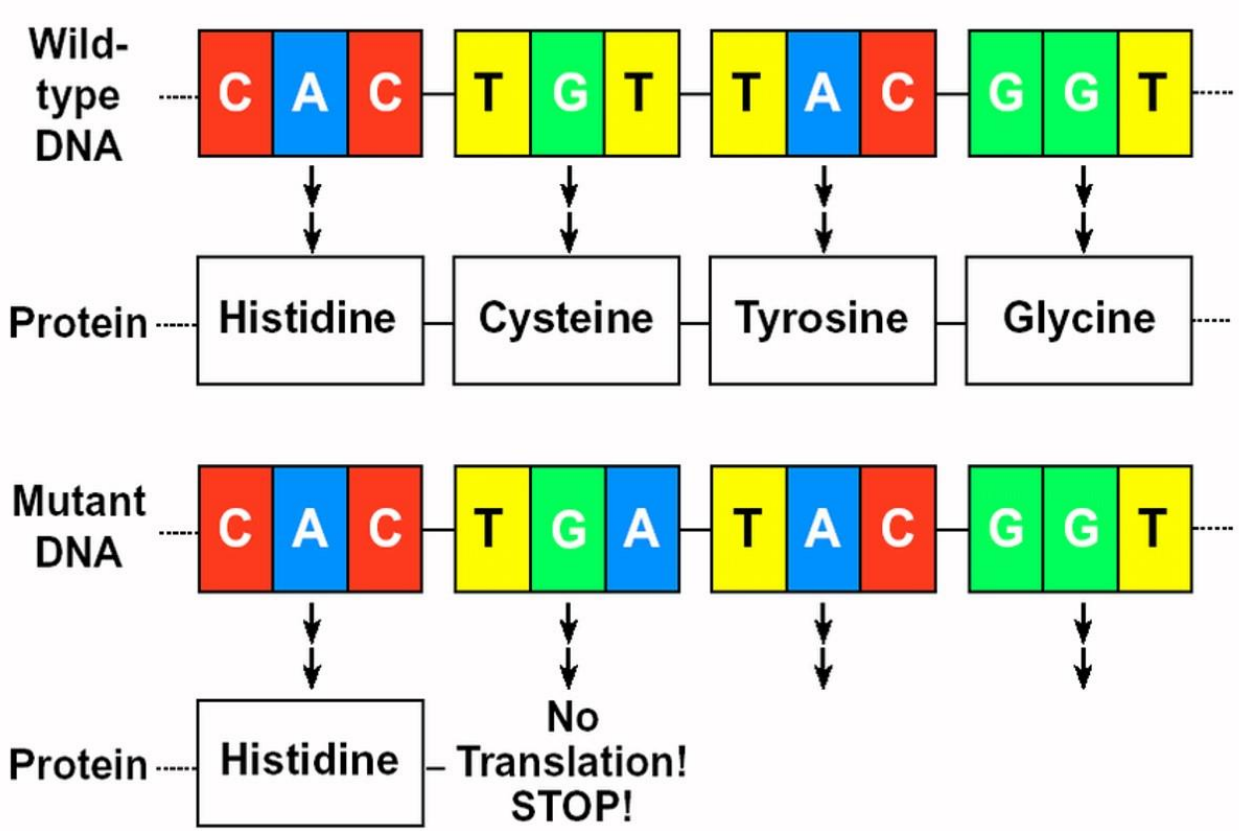
In a nonsense mutation, a codon that stands for an amino acid mutates to one of these three stop codons





Nonsense Mutations

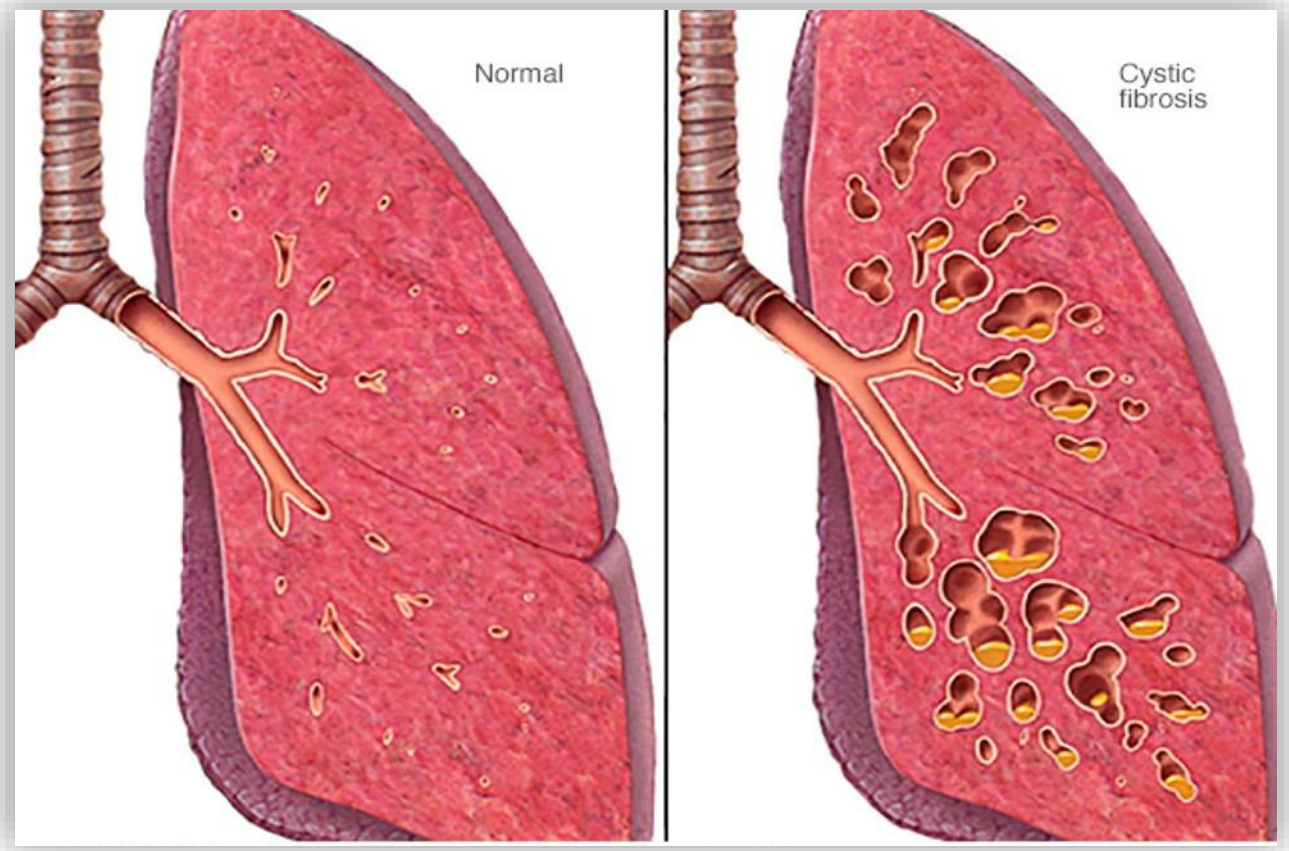
The term "nonsense mutation" is used because the stop codon has "no sense" for an amino



Nonsense Mutations

Cystic fibrosis

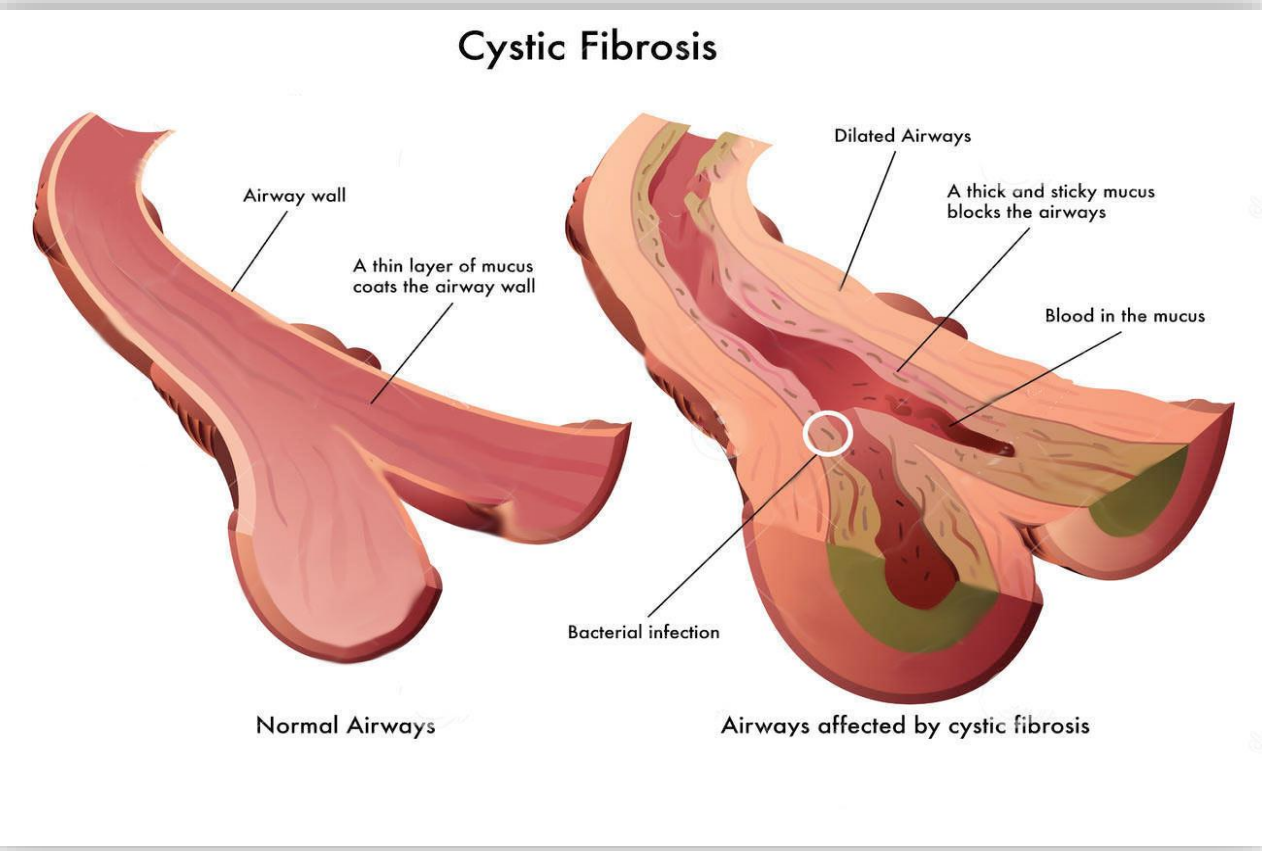
A disease caused by a nonsense mutation



Cystic fibrosis in lungs

Cystic fibrosis

It is a genetic disorder that affects most critically the lungs, and also the pancreas, liver, and intestine



Cystic fibrosis in liver

Nonsense Mutations

Cystic fibrosis

The signs and symptoms are poor growth and poor weight gain despite a normal food intake, frequent chest infections, and coughing

Frameshift Mutation

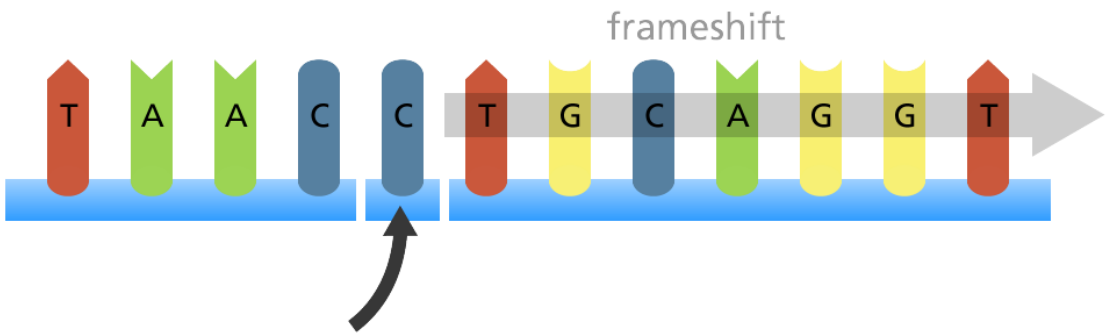
A mutation in a DNA chain that occurs when the number of nucleotides inserted or deleted is not a multiple of three

ACG	AGG	ACU	GCA	UAC	CA...	Normal Translation
Thr	Arg	Thr	Ala	Tyr		
A	CGA	GGA	CUG	CAU	ACC	A...
	Arg	Gly	Leu	His	Thr	+1 Frameshifted Translation
AC	GAG	GAC	UGC	AUA	CCA...	
	Glu	Asp	Cys	Ile	Pro	-1 Frameshifted Translation

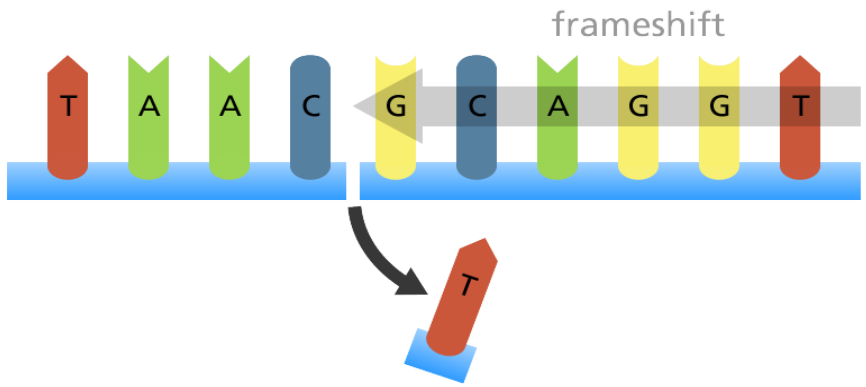
Frameshift Mutation

OR

It is a type of mutation in which a number of nucleotides not divisible by three is inserted into or deleted from a coding sequence



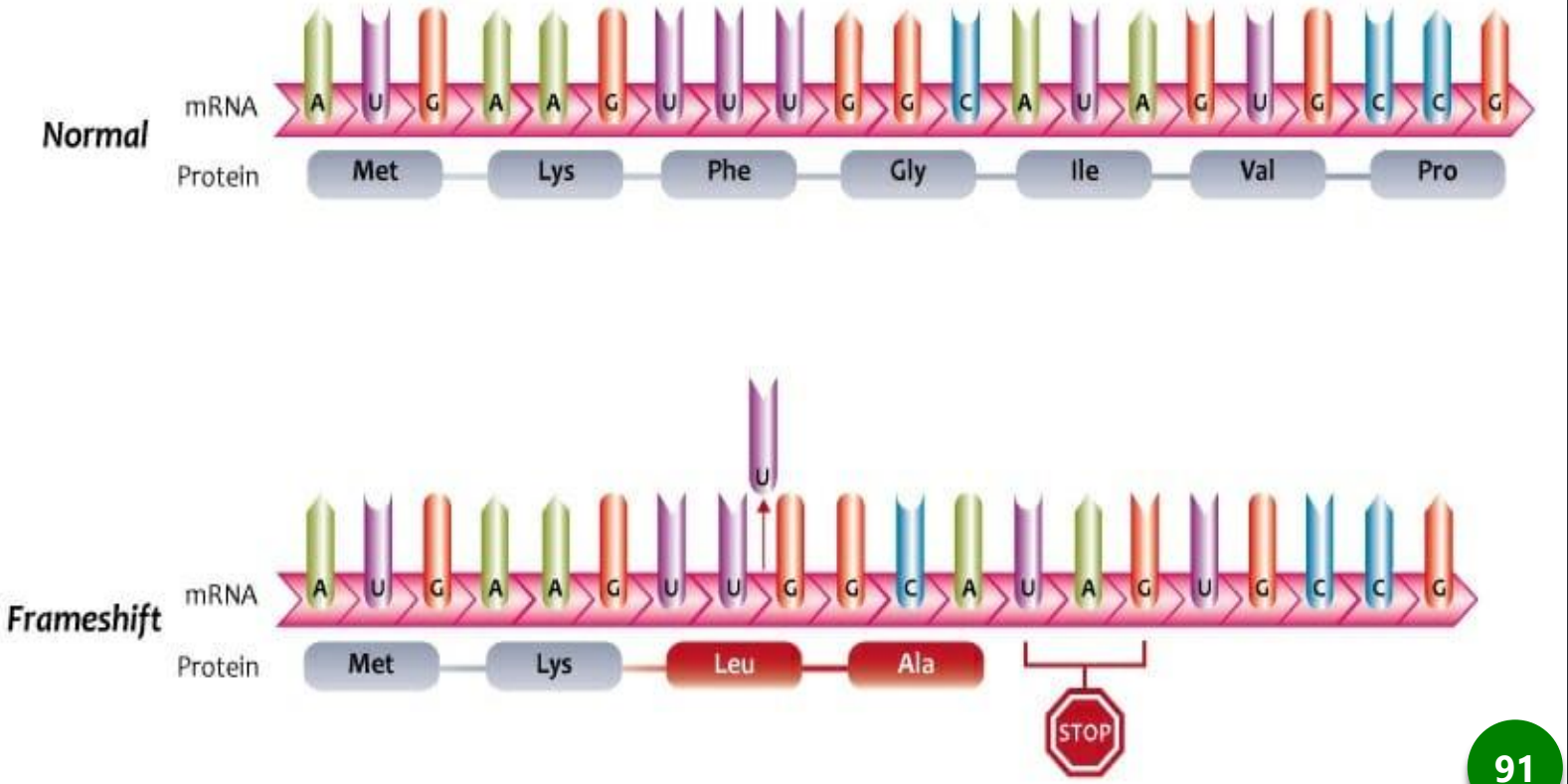
Insertion



Deletion

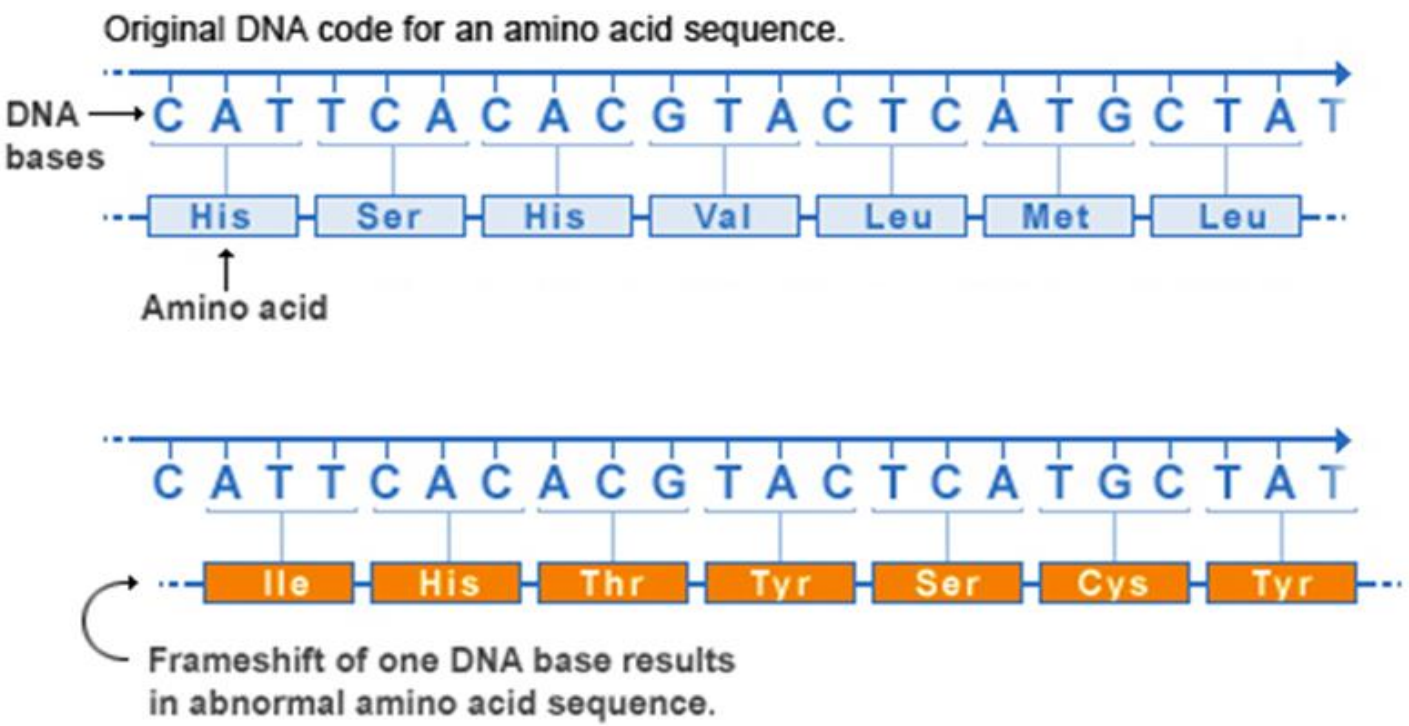
Frameshift Mutation

This therefore will make every codon beyond the point of insertion or deletion (downstream) read incorrectly during translation



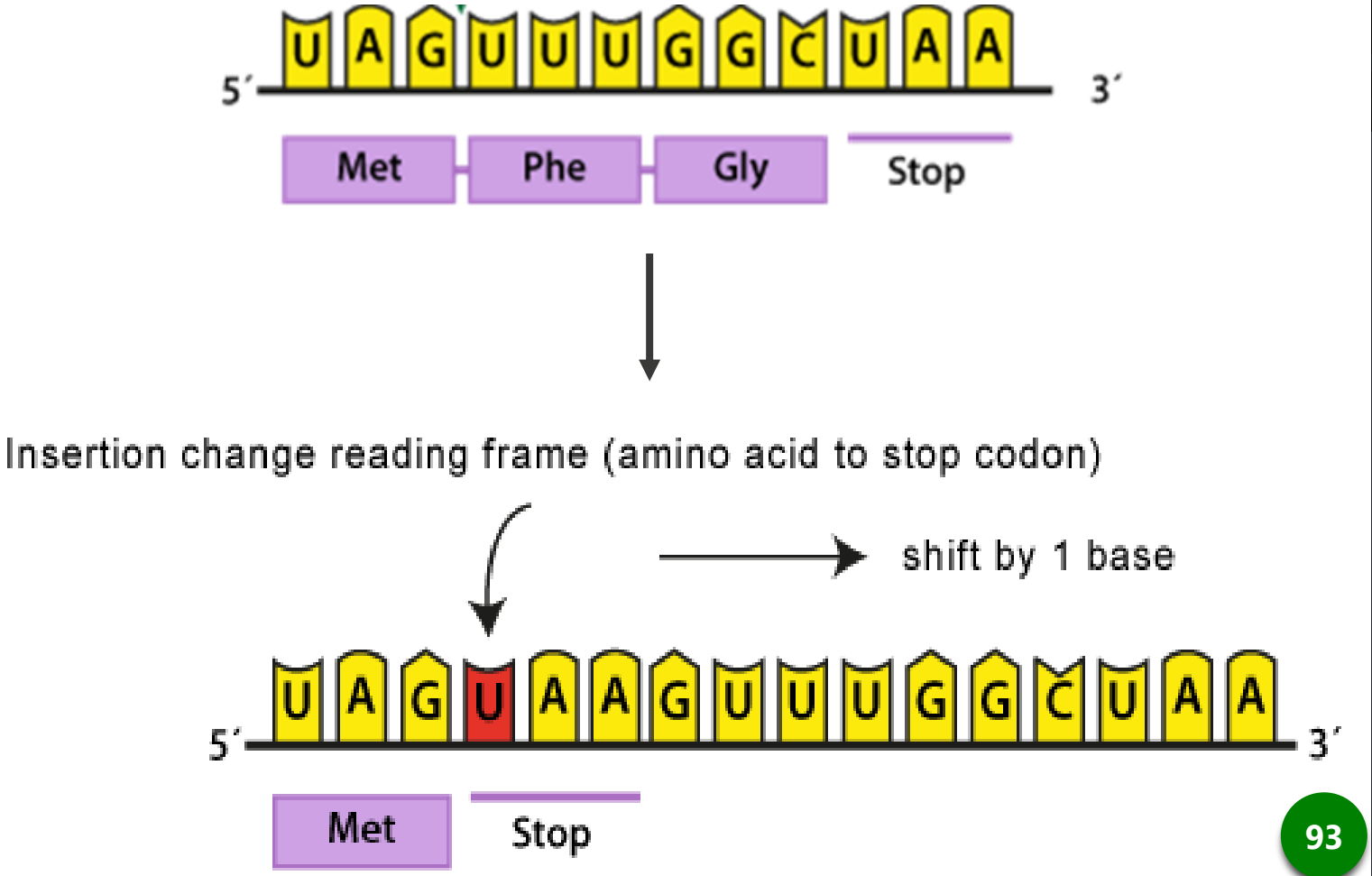
Frameshift Mutation

A frameshift mutation will in general cause the reading frame of the codons after the mutation to code for different amino acids



Frameshift Mutation

The frameshift mutation will also alter the first stop codon ("UAA", "UGA" or "UAG") encountered in the sequence

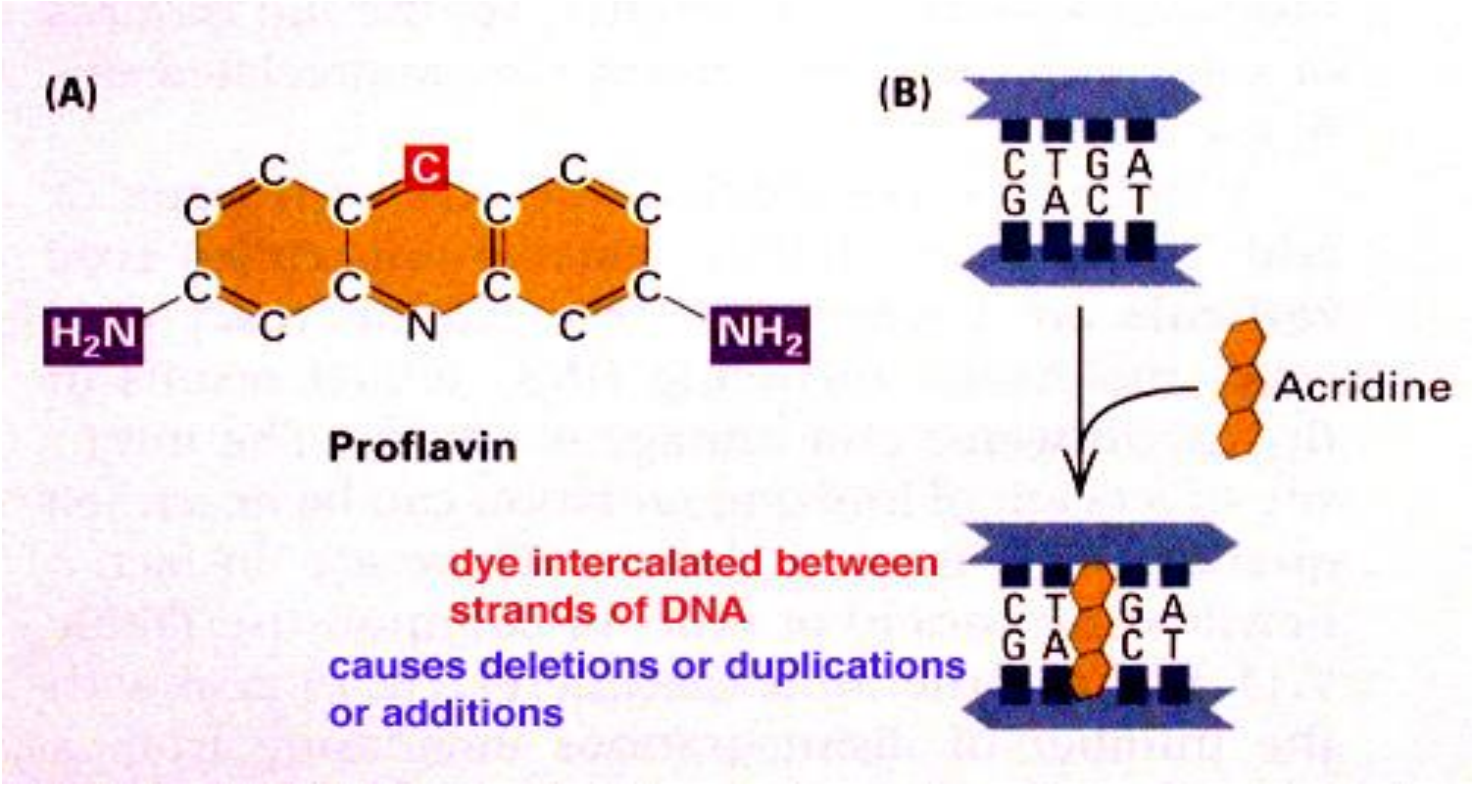


Frameshift Mutation

The polypeptide which is being created could be abnormally short or abnormally long, and will most likely not be functional

Frameshift Mutation

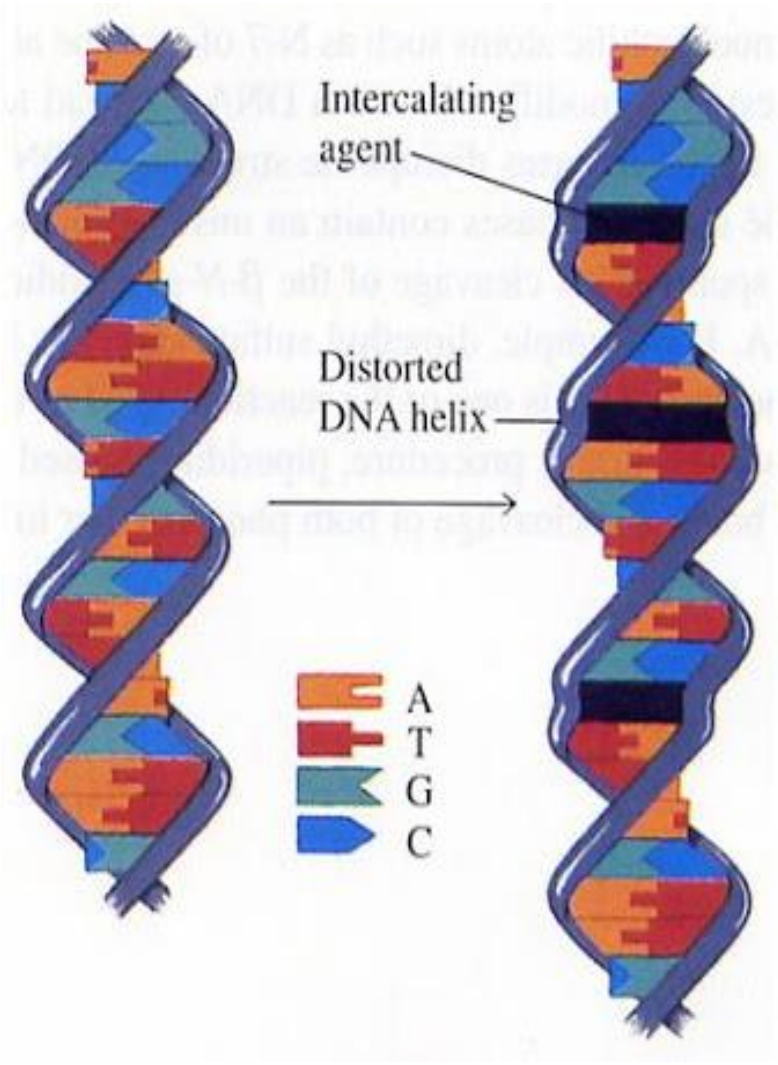
Frameshift mutations can be caused by **Intercalating Agents**



Frameshift Mutation

Intercalating Agents

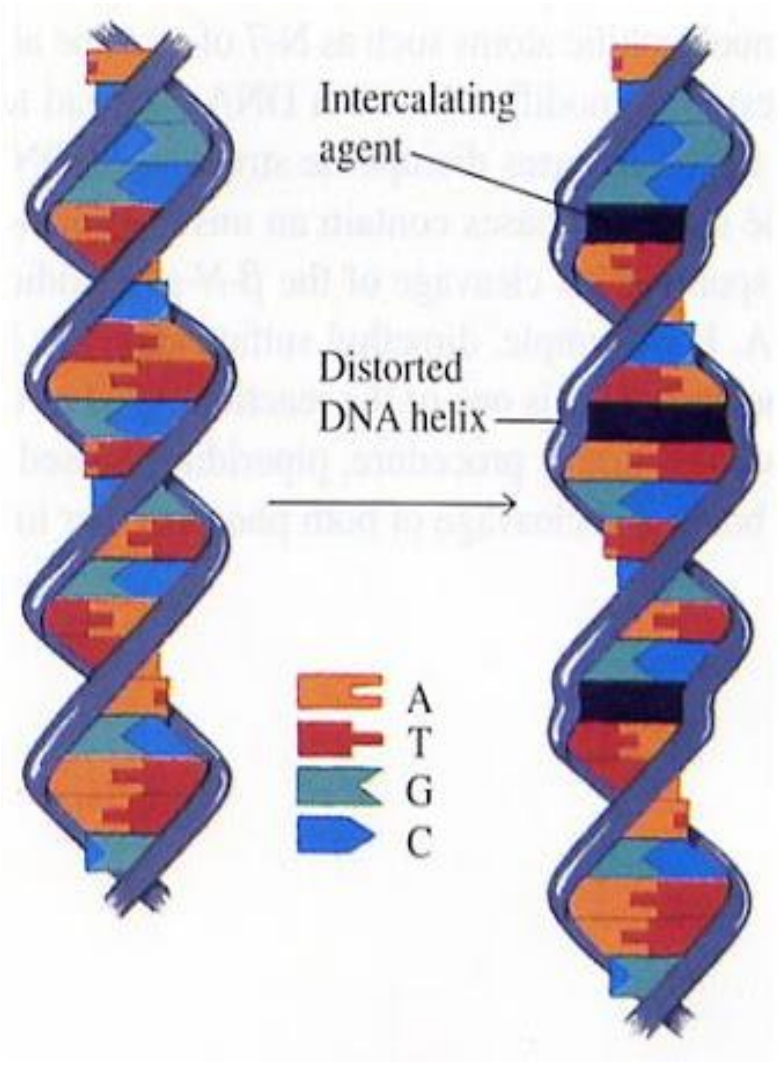
These are chemical agents that insert between adjacent base pairs (like inserting between the rungs of a ladder)



Frameshift Mutation

Intercalating Agents

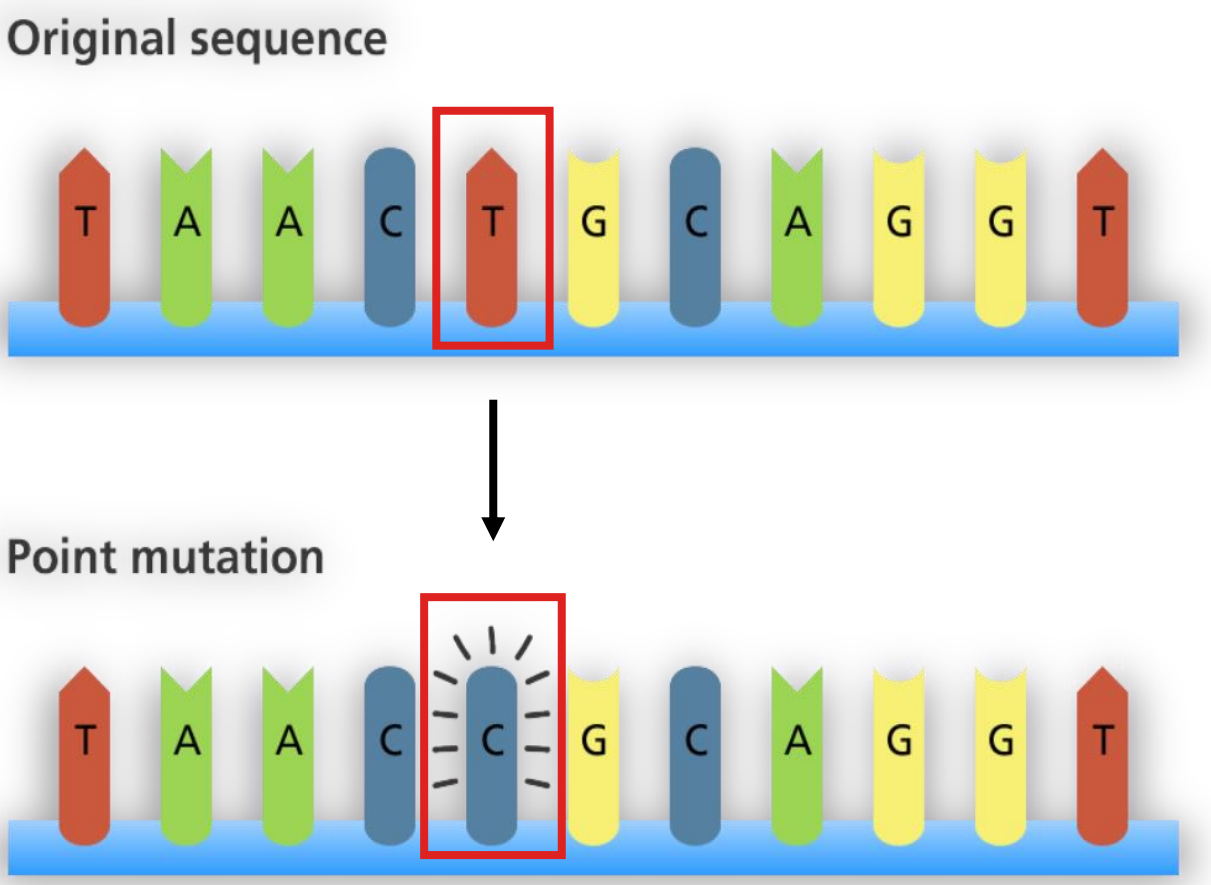
The intercalation causes a conformational change in the double helix, so that when replication occurs, the aberrant conformation causes small deletions or insertions to occur in the newly synthesized DNA



Difference between Point and Frameshift Mutations

Point Mutation

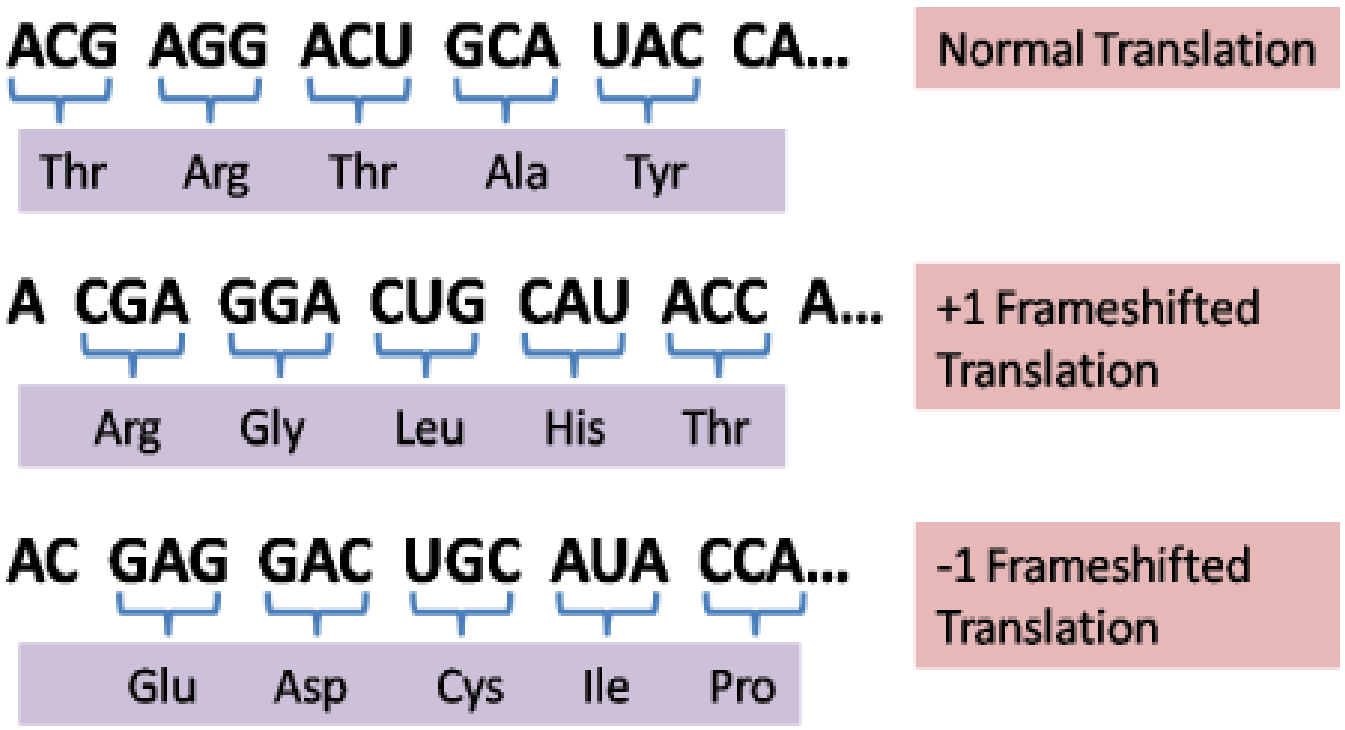
A single letter is the only thing changed in the DNA sequence



Difference between Point and Frameshift Mutations

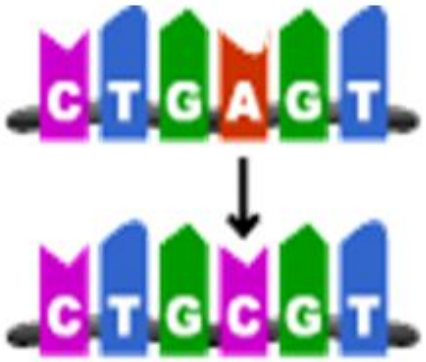
Frameshift Mutation

Generally much more serious and will cause a change all the way down (downstream) a DNA sequence, making each codon a different sequence, not just in one point or base like a point mutation



Difference between Point and Frameshift Mutations

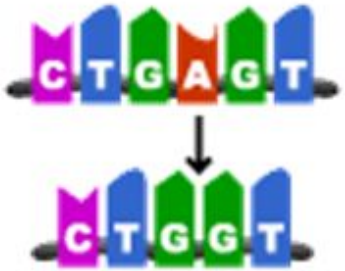
Point Mutation



Point mutation

Frameshift Mutation

Insertion



Deletion

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