Mutations

TEKS

(6) Science concepts. The student knows the mechanisms of genetics, including the role of nucleic acids and the principles of Mendelian Genetics. The student is expected to:

(E) Identify and Illustrate changes in DNA and evaluate the significance of these changes.

Vocabulary

- Mutation
- Mutagen
- Point Mutation
- Frame shift
- Insertion
- Deletion
- Missense mutation
- Nonsence mutation
- Chromosomal Mutation
- Inversion
- Translocation

Prerequisite Questions

1. How does DNA store our genetic information?

2. What are the processes that create proteins in cells?

Essential Question

- How do mutations affect DNA, RNA and proteins?

What is a gene mutation?

A **mutation** is any change in the Nucleic Acid (DNA/RNA) sequence.

Can be caused by:

1. Errors in replication
2. Errors in transcription
3. Errors in cell division
4. Mutagens

Mutagens

- **Mutagen** - any agent that can cause a mutation

- These are caused by factors in the environment such as:
  1. Radiation (x-rays, UV, nuclear)
  2. Chemicals
  3. Extremely high temperatures
  4. Biological agents such as HPV

Named examples of mutagens:

- Any mutagen that causes cancer is a **carcinogen**
- Any mutagen that causes birth defects is a **teratogen**

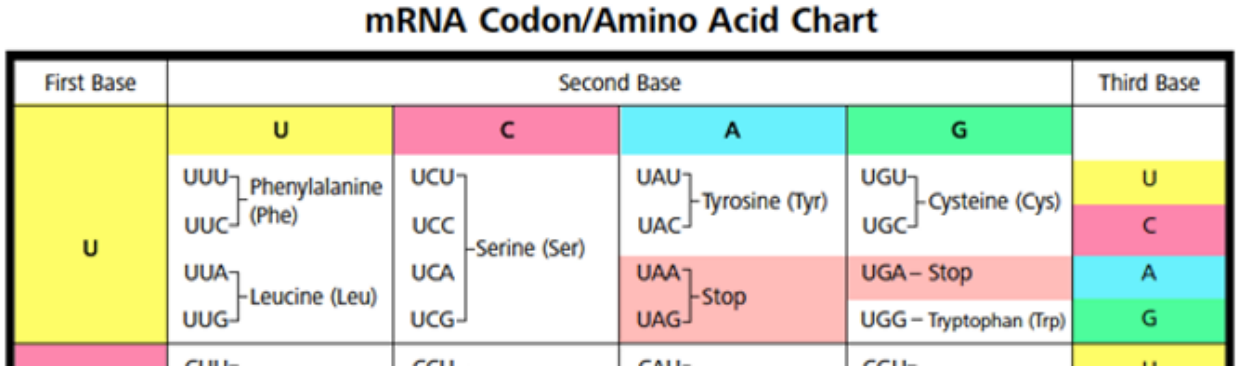
How common are mutations?

- Mutations occurs at a frequency of about 1 in every 1 billion base pairs.
  - That’s about 1 for every 6-7 chromosomes

- Everybody has about 6 mutations in each cell in their body!

Are all Mutations harmful?

- **Silent or missense mutation** – a change in the nucleotide sequence that creates a different codon that still codes for the same amino acid.
  - Remember, some amino acids have multiple codons that code for them:



mRNA Codon/Amino Acid Chart

First Base	Second Base				Third Base
	U	C	A	G	
U	UUU, UUC – Phenylalanine (Phe) UUA, UUG – Leucine (Leu)	UCU, UCC, UCA, UCG – Serine (Ser)	UAU, UAC – Tyrosine (Tyr) UAA, UAG – Stop	UGU, UGC – Cysteine (Cys) UGA – Stop UGG – Tryptophan (Trp)	U C A G

- **Nonsense mutation** – a change in the nucleotide sequence that causes a STOP codon to appear in the middle of a protein sequence.

Types of Mutations

Point Mutations

1. Substitution
2. Insertion w/ frameshift
3. Deletion w/ frameshift

Chromosomal Mutations

1. Duplication (a piece copied)
2. Deletion (a piece missing)
3. Inversion (a piece flipped)
4. Translocation (a piece(s) moved to another location)

Point Mutation: Substitution

1. Substitution mutation – a **different nitrogenous base is substituted** for the original nitrogenous base.

Normal DNA: TAC – TGC – ATC – GGG – CTA

Mutated DNA: TAC – TGC – TTC – GGG – CTA

Where is the mutation and what is happening?

Point Mutation: Substitution

1. Substitution mutation – a different nitrogenous base is substituted for the original nitrogenous base.

Normal DNA: TAC – TGC – ATC – GGG – CTA

Mutated DNA: TAC – TGC – **T**TC – GGG – CTA

In the 3rd codon set, adenine is replaced with thymine.

How many amino acids will be affected?

Point Mutation: Substitution

1. Substitution mutation – a different nitrogenous base is substituted for the original nitrogenous base.

Normal DNA: TAC – TGC – ATC – GGG – CTA

Mutated DNA: TAC – TGC – **T**TC – GGG – CTA

Only the 3rd amino acid will be changed

Point Mutation: Substitution

1. Substitution mutation – a different nitrogenous base is substituted for the original nitrogenous base.

- Original protein from DNA: Met – Thr – (STOP)

  ATC would code for : STOP

- Mutated protein: Met – Thr – Lys – Pro – Asp.A.

  TTC would code for: Lysine

Substitution Mutation Analogy 1

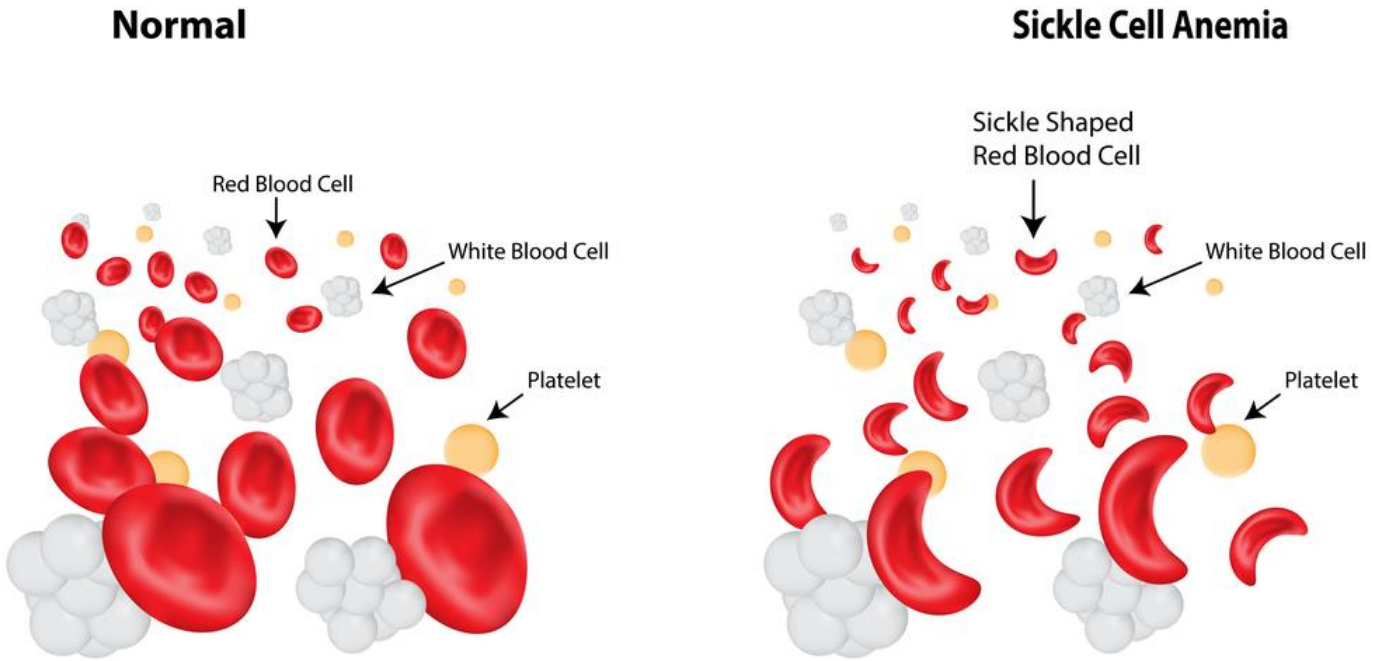
- Compare the sentences below. All the words have 3 letter words to simulate a codon in mRNA.

THE DOG BIT THE CAR
THE DOG BIT THE CAT
THE DOG HIT THE CAR
THE HOG BIT THE CAR
THE LOG BIT THE CAR
THE DOG FIT THE CAR

The message (protein) is still mostly understandable.

Example of Substitution mutations

- Sickle Cell – abnormal red blood cells cause by a Thymine to Adenine substitution in the 6th codon.
  - Sickle Red blood cells can not carry oxygen as well



Point Mutation: Insertion w/ Frameshift

2. Insertion mutation – a **new nitrogenous base is added** to the original nitrogenous base sequence shifting all the following bases to the right.

Normal DNA: TAC – TGC – ATC – GGG – CTA

Mutated DNA: TAC – TAG – CAT – CGG – GCT – A

Where is the mutation and what is happening?

Point Mutation: Insertion w/ Frameshift

2. Insertion mutation – a new nitrogenous base is added to the original nitrogenous base sequence shifting all the following bases to the right.

Normal DNA: TAC – TGC – ATC – GGG – CTA

Mutated DNA: TAC – T**A**G – CAT – CGG – GCT – A

In the 2nd codon set, adenine is added causing a shift to the right.

How many amino acids will be affected?

Point Mutation: Insertion w/ Frameshift

2. Insertion mutation – a new nitrogenous base is added to the original nitrogenous base sequence shifting all the following bases to the right.

Normal DNA: TAC – TGC – ATC – GGG – CTA

Mutated DNA: TAC – T**A**G – CAT – CGG – GCT – A

The 2nd, 3rd, 4th and 5th codons (basically anything that comes after)

Point Mutation: Insertion w/ Frameshift

2. Insertion mutation – a new nitrogenous base is added to the original nitrogenous base sequence shifting all the following bases to the right.

- Original protein from DNA: Met – Thr – (STOP)

- Mutated protein: Met – Iso – Val – Ala – Arg

  2^{nd}, 3^{rd}, 4^{th} and 5^{th} codon reading frames have shifted changing the STOP codon.

Point Mutation: Deletion w/ Frameshift

3. Deletion mutation – a **new nitrogenous base is deleted** from the original nitrogenous base sequence shifting all the following bases to the left.

Normal DNA: TAC – TGC – ATC – GGG – CTA

Mutated DNA: TAC – TGC – TCG – GGC – TA

Where is the mutation and what is happening?

Point Mutation: Deletion w/ Frameshift

3. Deletion mutation – a new nitrogenous base is deleted from the original nitrogenous base sequence shifting all the following bases to the left.

Normal DNA: TAC – TGC – **A**TC – GGG – CTA

Mutated DNA: TAC – TGC – TCG – GGC – TA

In the 3rd codon set, adenine is removed causing a shift to the left.

How many amino acids will be affected?

Point Mutation: Deletion w/ Frameshift

3. Deletion mutation – a new nitrogenous base is deleted from the original nitrogenous base sequence shifting all the following bases to the left.

Normal DNA: TAC – TGC – **A**TC – GGG – CTA

Mutated DNA: TAC – TGC – TCG – GGC – TA

The 3rd, 4th and 5th codons (basically anything that comes after)

Point Mutation: Deletion w/ Frameshift

3. Deletion mutation – a new nitrogenous base is deleted from the original nitrogenous base sequence shifting all the following bases to the left.

- Original protein from DNA: Met – Thr – (STOP)

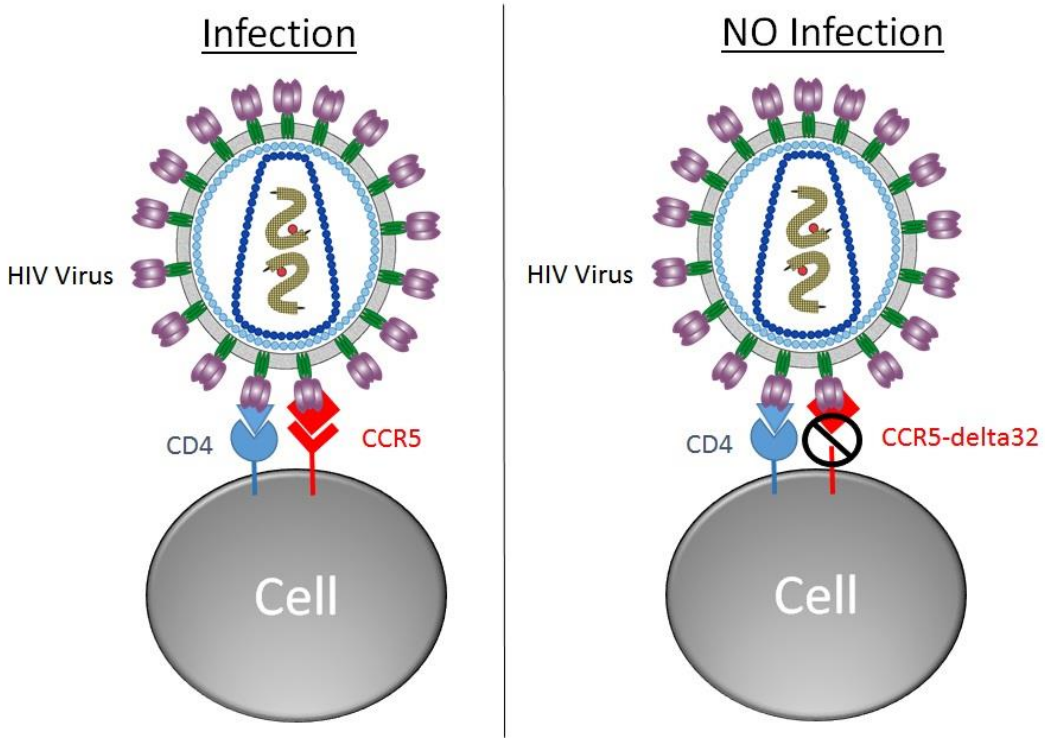
- Mutated protein: Met – Thr – Ser – Pro

  3rd, 4th and 5th codon reading frames have shifted changing the STOP codon

Example of Frameshift mutation

- HIV susceptibility – a frameshift in the CCR5 gene which codes for the receptor protein the virus uses to enter the cell. An early stop codon (nonsense) cuts the protein short.

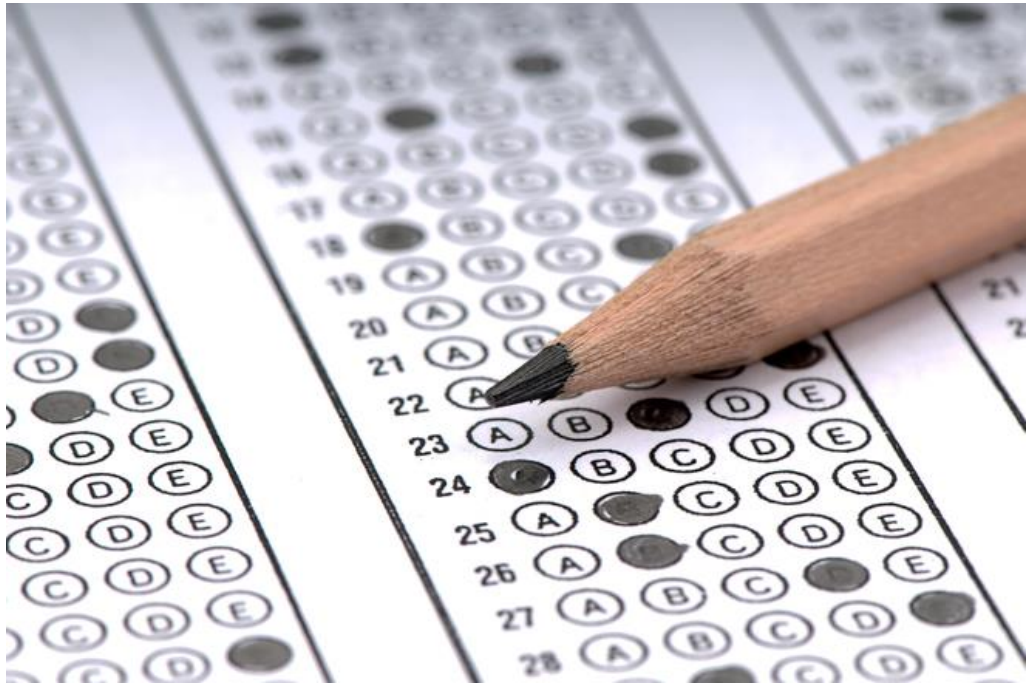
- Individuals with this mutation are more resistant to HIV attacks, and do not contract HIV which leads to AIDS.



Frameshift Mutation Analogy 1

- What happens to an answer document if you leave out an answer and slide all of the other answer up one number?

- If you shift the answer reading frame, everything that comes after the shift (insertion/deletion) could potentially be wrong (mutation)



Frameshift Mutation Analogy 2

- Compare the sentences below. All the words have 3 letter words to simulate a codon in mRNA.

THE DOG BIT THE CAR	(Original, unmutated)
THH EDO GBI TTH ECA R	(Insertion – H, 1ST Codon)
THE DOB ITT HEC AR	(Deletion – G, 2nd Codon)

Chromosomal Mutation: Duplication

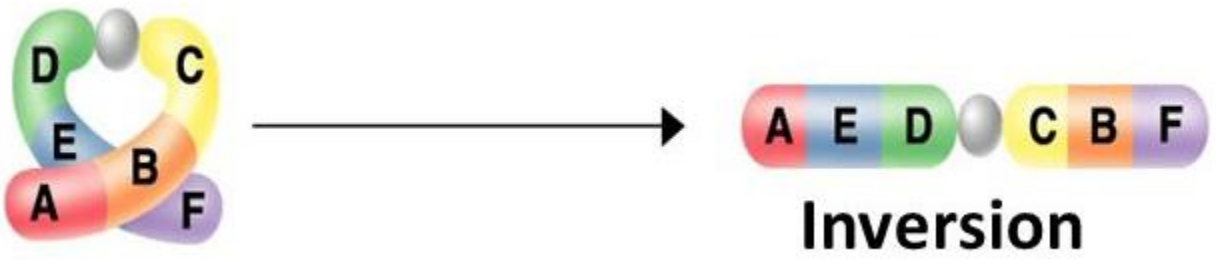
1. Large sections of genetic material (multiple genes) are copied and inserted into the same DNA sequence.

Chromosomal Mutation: Deletion

2. Large sections of genetic material (multiple genes) are removed from a DNA sequence.

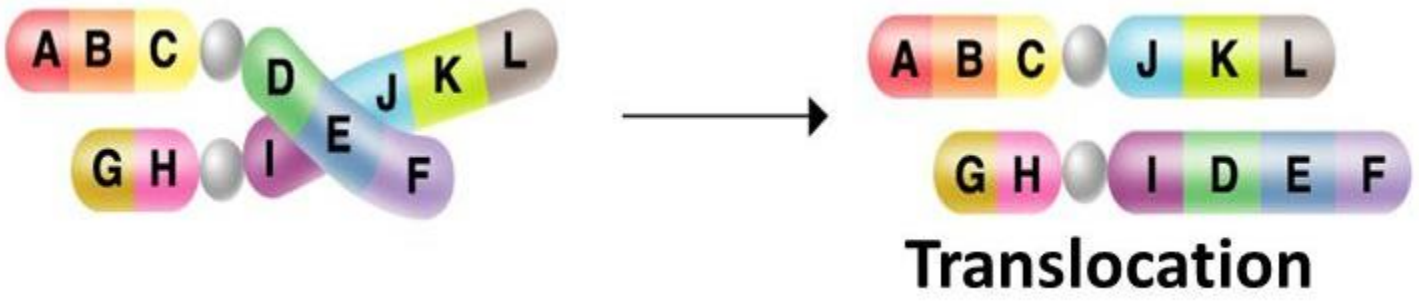
Chromosomal Mutation: Inversion

3. Large sections of genetic material (multiple genes) are moved out of order in a DNA sequence.



Chromosomal Mutation: Translocation

4. Large sections of genetic material (multiple genes) are swapped between two different chromosomes.



We will see this in meiosis during Prophase 1. (Crossing Over)

Are all Mutations harmful?

- A change in the genetic code can be beneficial or harmful (even lethal)

Advantages

New genes created by mutations can add new adaptations to an organism making it able to outcompete a neighbor

Disadvantages

New genes created by mutations can reduce efficiency of a protein, or even remove a necessary protein making it deadly for the organism or its offspring

Are all Mutations harmful?