Name: Key Period: ____

Gene Mutations Activity

Background: There are two types of mutations, small-scale gene mutations and large-scale chromosomal mutations. In this activity you will be learning about gene mutations. There are two basic types of gene mutations, point (base substitution) and frameshift (insertions and deletions). In frameshift mutations, an insertion or deletion of a base changes the reading frame of the sequence since mRNA is read in groups of three nitrogen bases (codons). This causes several amino acids to be affected unless the deletion or insertion is a group of three. There are very few examples of frameshift mutation diseases in organisms because they are usually fatal to the organism because the proteins do not function. In point mutations, a simple base substitution does not change the reading frame because one nitrogen base is simply substituted with a different nitrogen base, so only one amino acid is affected unless there are several base substitutions.

Part 1: *Frameshift Mutations*

Example 1: Insertion Frameshift

DNA Sequence Sentence: THE BOY CUT HIS LIP AND ATE THE HOT DOG

Affect of Insertion: THE BOY CUT HIS SLI PAN DAT ETH EHO TDO

Insert a nitrogen base

Example 2: Deletion Frameshift

Delete a nitrogen base

DNA Sequence Sentence: THE BOY CUT HIS LIP AND ATE THE HOT DOG

Affect of Deletion: THE BOY CUT HIS LIP ANA TET HEH OTD OG

The insertion shifts the reading frame to the right. The deletion shifts the reading frame to the left. Complete the following lines for frameshift mutations.

Write each codon per line:

DNA Sequence: THE DOG AND FOX DID NOT EAT THE FAT CAT

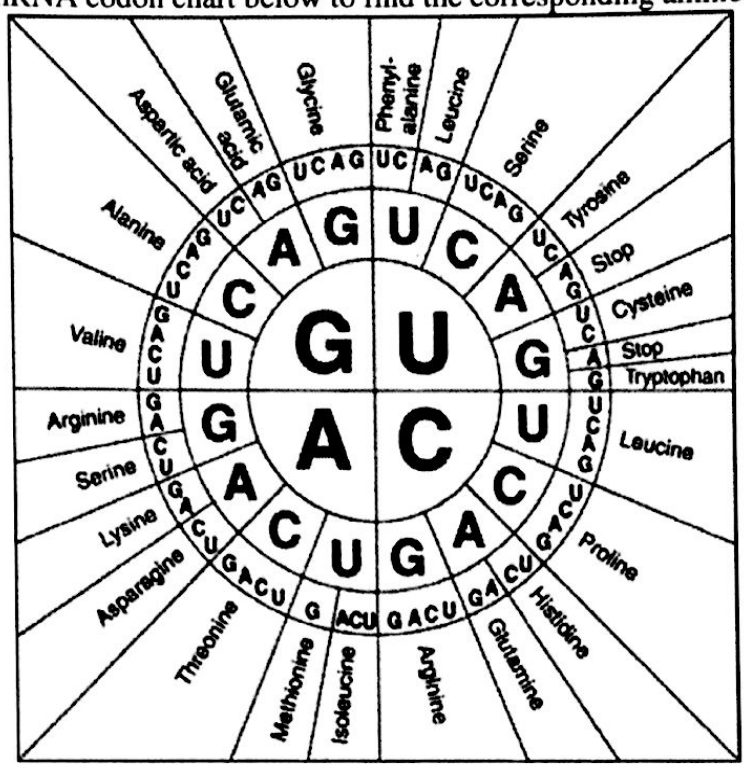
Insertion: THE DOG ANN DFO xOI DNO TEA TTH EFA TCA

Insert a letter

Deletion: THE DOG AND OXO IDN OTE ATT HEF ATC AT

Delete a letter

Part II: Now use a real DNA sequence and transcribe and translate it into the correct amino acids. In the original DNA code put the insertion frameshift mutation in the **FOURTH CODON by inserting a G after the C in TCT**. Please use the mRNA codon chart below to find the corresponding amino acids.



Write each codon per line and **circle** the mutated nitrogen base where the mutation took place and the amino acid.

Original DNA	TAC GGA CGA TCT CAG GAG CCT ATA ATC
Insertion Mutation	TAC GGA CGA TCG TCA GGA GCC TAT AAT
Mutated mRNA	AUG CCU GCU AGC AGU CCU CGG AUA UUA
Mutated Amino Acids	Met Pro Ala Ser Ser Pro Arg Ile Leu
Original Amino Acid Sequence	Met Pro Ala Arg Val Leu Gly Try STOP

In the original DNA code put the deletion frameshift mutation in the **THIRD CODON by deleting the C of CGA**. Please use the mRNA codon chart provided to find the corresponding amino acids. Write each codon per line and **circle** the mutated nitrogen base where the mutation took place and the amino acid(s) affected.

Original DNA	TAC GGA CGA TCT CAG GAG CCT ATA ATC
Deletion Mutation	TAC GGA GAT CTC AGG AGC CTA TAA TC
Mutated mRNA	AUG CCU CUA GAG UCC UCG GAU AUU AG
Mutated Amino Acids	Met Pro Leu Glu Ser Ser Asp Ile
Original Amino Acid Sequence	Met Pro Ala Arg Val Leu Gly Try STOP

Part III: ***Point (Base Substitution) Mutations***

A different type of gene mutation is called a point (base substitution) mutation. It is the simplest type of mutation where a nucleotide pair is replaced with a different nucleotide pair. There are three types of point mutations: missense, silent, and nonsense.

Example 1: ***Missense Point Mutation***

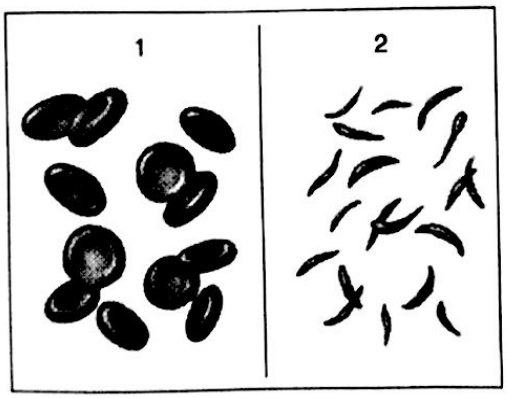
A missense mutation occurs when one nitrogen base is substituted for another nitrogen base causing a different amino acid than previously to occur in the protein sequence.

A. Use the DNA code below to demonstrate a *missense mutation*. All you have to do is change the DNA base in the **SEVENTH CODON from CTC to CAC.** Write each codon per line and **circle** the mutated nitrogen base and affected amino acids. ***This is the mutation that occurs in sickle cell anemia*.**

Original DNA	CAC	GTG	GAC	TGA	GGA	GGA	CTC	CTC	ATC
Transversion Mutation	CAC	GTG	GAC	TGA	GGA	GGA	CAC	CTC	ATC
Mutated mRNA	GUG	CAC	CUG	ACU	CCU	CCU	GUG	GAG	UAG
Mutated Amino Acids	Val	His	Leu	Thr	Leu	Pro	Val	GluA	Stop
Original Amino Acid Sequence	Val	His	Leu	Thr	Pro	Pro	Glu A	GluA	STOP

B. Use the DNA code below to demonstrate another *missense mutation*. All you have to do is change the DNA base in the **SECOND CODON from GCC to ACC.** Write each codon per line and **circle** the mutated nitrogen base and affected amino acids. ***This is one of many "boy in the bubble" syndrome (severe combined immunodeficiency)***

Original DNA	AAT	GCC	AGT	GGT	TCG	CAC	CTG	ACC	ACT
Transition Mutation	AAT	GCC	AGT	GGT	TCG	CAC	CTC	ACC	ACT
Mutated mRNA	UUA	UGG	UCA	CCA	AGC	GUG	GAC	UGG	UGA
Mutated Amino Acids	Leu	Trp	Ser	Pro	Ser	Val	Asp	Trp	Stop
Original Amino Acid Sequence	Leu	Arg	Ser	Pro	Ser	Val	Asp A	Trp	STOP



Example 2: ***Silent Point Mutation* – 40% of all mutations are this type.**
A *silent mutation* happens when one base in a codon is changed but both code for the same amino acid.

DNA Codon CTT → CTC
mRNA codon GAA →GAG
Amino Acid Glu A → Glu A

Use the DNA code below to demonstrate a *silent mutation*. All you have to do is change one DNA base in the **THIRD CODON from TCT to TCC.** Write each codon per line and **circle** the mutated nitrogen base and amino acid.

Original DNA	TAC	CAT	TCT	CGG	TGT	AAA	AGG	GCG	ATT
Silent Mutation	TAC	CAT	TC(C)	CGG	TGT	AAA	AGG	GCG	ATT
Mutated mRNA	AUG	GUA	AGG	GCC	ACA	UUU	UCC	CGG	UAA
Mutated Amino Acids	Met	Val	Arg	Ala	Thr	Phe	Ser	Arg	Stop
Original Amino Acid Sequence	Met	Val	Arg	Ala	Thr	Phe	Ser	Arg	STOP

Example 3: ***Nonsense Point Mutation***
A base mutation that creates a new stop codon in place of an amino acid causing a premature stopping of translation is called a *nonsense mutation*.

DNA codon ATA → ATT
mRNA codon UAU → UAA
Amino Acid Tyr → STOP

Use the DNA code below to demonstrate a nonsense mutation. All you have to do is change one DNA base to create a new amino acid sequence with a premature stop codon in the **FIFTH CODON by changing ATA to ATT**. Write each codon per line and **circle** the mutated nitrogen base and amino acid.

Original DNA	TAC	GGT	AAT	CAA	ATA	GAA	CCT	GAG	ACT
Nonsense Mutation	TAC	GGT	AAT	CAA	A(T)	GAA	CCT	GAG	ACT
Mutated mRNA	AUG	CCA	UUA	GUU	UAA	CUU	GGA	CUC	UGA
Mutated Amino Acids	Met	Pro	Leu	Val	Stop	___	___	___	___
Original Amino Acid Sequence	Met	Pro	Leu	Val	Tyr	Leu	Gly	Leu	STOP

Analysis Questions:

1. How many amino acids were affected in the point mutations?

   one or many depending on the type

2. How many amino acids were affected in the frameshift mutation?

   - All past the frameshift mutation

3. Explain the difference between a frameshift mutation and a point mutation.

   - Both affect only a single nucleotide but point generally only affects one amino acid while frameshift affects many.

4. Which type of mutation, a frameshift or a point mutation, has more effect on the organism? Why?

   - Same as #3.

5. Usually a frameshift mutation results in the synthesis of a nonfunctional protein. Why do you think mutated proteins might not be functional?

   The amino acid sequence determines protein shape while shape gives the protein its function.

6. Which type of point mutation would be insignificant to the organism? Why?

   Silent; does not change the amino acid sequence.

7. Which type of point mutation would have the greatest effect on the organism? Why?

   A nonsense mutation; it stops the protein from being translated.

8. Which type of point mutation would most likely cause major changes to physical structures of the organism?

   Same as #7.