THE MOLECULAR EVOLUTION OF GENE BIRTH AND DEATH

INTRODUCTION

Natural selection acts on phenotypes, which are largely shaped by genotypes. Because of this relationship, gene frequencies change as phenotypes are selected for or against within a population. Genes that code for beneficial traits tend to accumulate in populations. Similarly, genes that code for traits that reduce an individual's fitness tend to decrease in frequency. But how do new genes arise? And once they arise, do they ever change? Can once-functional genes become useless and "die"? And can "extra" genes take on new functions? This lesson explores the mechanisms of gene birth and death and provides several examples of the role these processes play in evolution.

MATERIALS

- student presentation slides
- Internet connection for hyperlinks
- genetic code chart on page 8 of this handout

PROCEDURE

1. In order to complete this lesson, you will need to access the accompanying presentation slides titled "Mutations and the Birth and Death of Genes."

2. As you proceed through the slides, they will prompt you to answer the questions in this handout. Some answers will require you to apply what you learn from watching the animations, lecture clips, and short films embedded in the slides. (Note: Be sure to have your computer's speakers turned on or wear headphones before clicking on the video links.)

QUESTIONS

1. What drives the evolution of new genes? Define "mutation." Are mutations random?

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2. Which of the following has the greater potential effect on the evolution of a population: mutations in somatic (body) cells or mutations in gametes (egg and sperm)? Explain.

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3. What is a point mutation?

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4. When can an insertion or deletion be something other than a point mutation?

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5. DNA is transcribed to messenger RNA (mRNA), which is translated into a sequence of amino acids that fold to form a protein.

a. Complete the tables below by first transcribing the DNA triplets to mRNA codons and then translating them to amino acids by using a genetic code chart on page 8 of this handout.

Wild-Type DNA Sequence

DNA	GAC	TCT	GGA	CAC	CTC
mRNA					
Amino Acid					

Mutant DNA Sequence 1

DNA	GAC	TCT	GGA	CGC	CTC
mRNA					
Amino Acid					

Mutant DNA Sequence 2

DNA	GAC	ACT	GGA	CAC	CTC
mRNA					
Amino Acid					

b. Which mutant sequence contains a missense mutation? Explain your answer.

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c. Which mutant sequence contains a nonsense mutation? Explain your answer.

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6. Which type of substitution mutation has the greatest chance of leading to a nonfunctional protein? Explain your answer.

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7. Describe the cause of sickle cell anemia.

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8. Rett syndrome occurs almost exclusively in girls, but there are a few male patients. The right side of **slide 10** depicts the normal protein (A) and the proteins produced by three different *MECP2* mutations, (B,C, and D) along with the resulting phenotypes of the male Rett syndrome patients. The top illustration (A) shows the healthy protein with the most important domains highlighted in light blue and pink. The orange band in the bottom illustration (D) indicates the presence of a different amino acid in the protein sequence compared to the normal protein.

a. What type of substitution mutation would result in the protein structures shown in B and C?

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b. Even though the proteins depicted in B and C are caused by the same type of mutation, patients with the mutation depicted in the third illustration have less-severe symptoms. Develop a hypothesis to explain why.

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c. What type of substitution mutation causes the protein depicted in D?

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d. Form a hypothesis to explain why patients with the mutation depicted in D have less-severe symptoms than patients with the other type of mutation.

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e. There are many more female patients with Rett syndrome than males; furthermore, female patients exhibit a much wider range of symptoms than males do. Explain both observations. (Hint: Think about what you know about the X chromosome; you may also watch the *X Inactivation* animation at http://www.hhmi.org/biointeractive/x-inactivation.)

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9. The following sequence contains an insertion mutation, shown in the larger, red font.

a. Use the genetic code chart to complete the table below.

Mutant DNA Sequence 3

DNA	GAC	**C**TC	TGG	ACA	CCT
mRNA					
Amino Acid					

b. Compare this amino acid sequence to the wild-type sequence in Question 5. Explain why frameshift mutations can have such major consequences on a protein's function.

10. What is a trinucleotide repeat?

11. After watching the 14-minute lecture clip regarding spinocerebellar ataxia type 1 (SCA1) on **slide 13**, answer the following questions.

a. What type of mutation causes SCA1, and how does the mutation occur?

b. Explain how the number of CAG repeats relates to the severity of the disease.

c. What is another human disease caused by a trinucleotide repeat expansion?

12. Many people mistakenly think that "all mutations are bad."

a. Explain how it is possible for a mutation to have no effect on an organism.

b. Use the example of rock pocket mice to explain how a mutation can have a positive effect on an organism.

13. When in the cell cycle do most chromosomal alterations that affect chromosome structure occur?

14. List and describe the four types of alterations that affect chromosome structure.

15. How might these chromosomal alterations affect gene expression? (Hint: Watch the *Gene Switch* animation at http://www.hhmi.org/biointeractive/gene-switch.)

16. What type of chromosomal alteration causes cri-du-chat syndrome? How do you know?

17. View the four-minute lecture clip and animation on **slide 18**. (Note: Gleevec is a pharmaceutical drug developed to help treat chronic myelogenous leukemia, or CML.)

a. What type of chromosomal alteration causes CML?

b. Which chromosomes are affected by this meiotic error?

c. What is the "Philadelphia chromosome"?

d. Explain the mechanism by which Gleevec works to treat CML.

18. Define "paralogous genes" and explain the evolutionary significance of gene duplication.

19. Describe the possible outcomes of gene duplication.

20. Explain how gene duplication led to the evolution of a key mammalian trait.

21. What is a pseudogene?

22. Explain how the accumulation of mutations could lead to gene death.

23. Develop hypotheses to explain the evolutionary significance of the gene death events for the examples listed below.

a. Olfactory receptor genes in humans and mice

b. Myoglobin gene in some icefish species

24. Explain the evolutionary significance of icefish "antifreeze" proteins. What types of chromosomal rearrangements and gene mutations led to the development of the antifreeze protein? (Hint: Watch the animation about the ancestral and antifreeze gene in the film very closely. Three mutation events follow the initial gene duplication.)

25. What "gene death" event occurred in icefish? How did it affect their ability to survive and reproduce?

26. Explain how icefish serve as an example of both the birth and death of genes.

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27. Using what you know about the icefish genome, explain this statement: "Genes tell the story of evolution."

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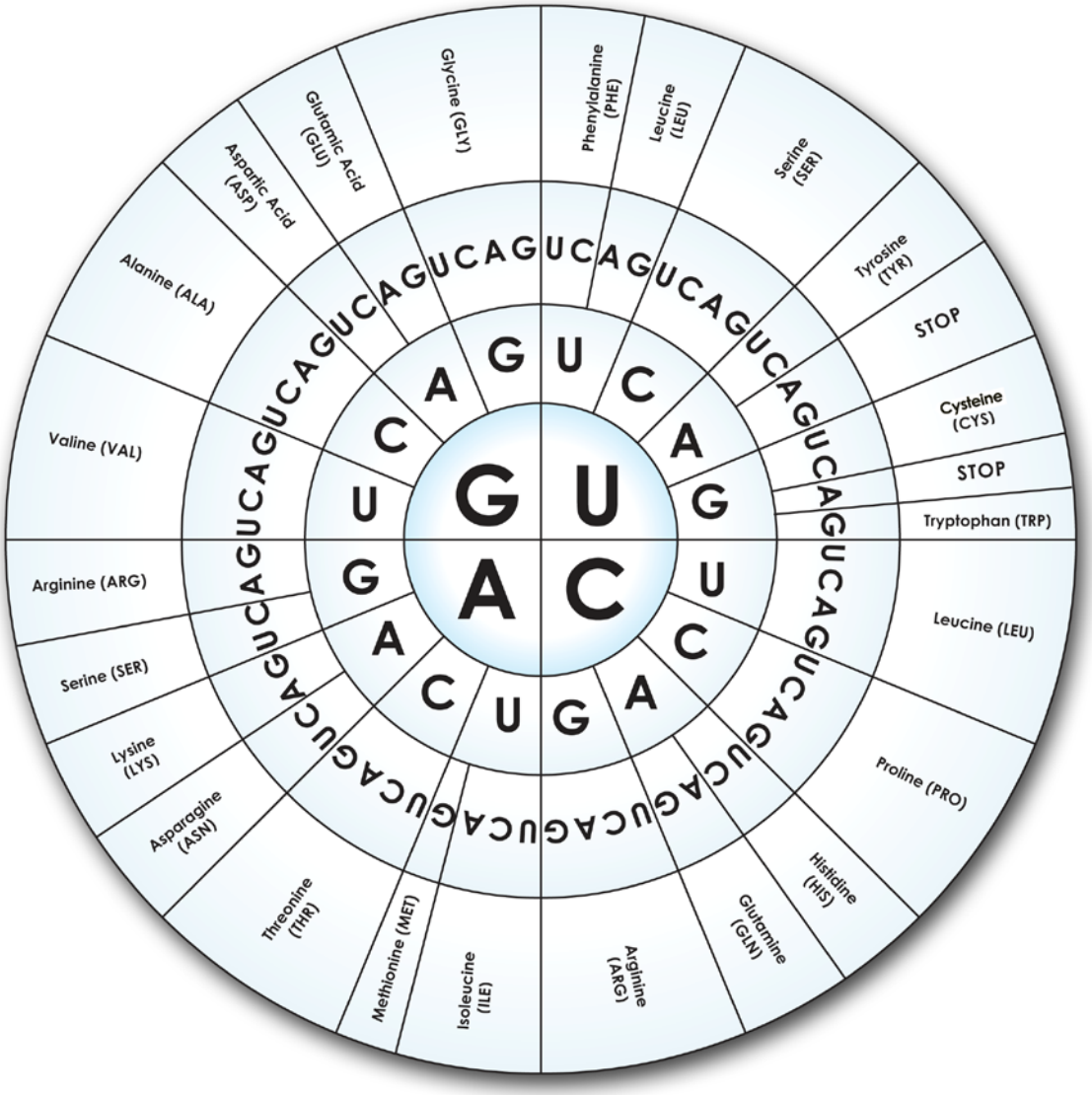
GENETIC CODE CHART

Below is the standard genetic code: mRNA → amino acid. The inner circle represents the first letter of the codon, and the remaining letters follow in the second and third rings. Find the corresponding amino acid in the outer circle.