



MOLECULAR GENETICS OF THE COLOR MUTATIONS IN ROCK POCKET MICE

INTRODUCTION

THE ROCK POCKET MOUSE

The rock pocket mouse, *Chaetodipus intermedius*, is a small, nocturnal animal found in the deserts of the southwestern United States. Most rock pocket mice have a sandy, light-colored coat that enables them to blend in with the light color of the desert rocks and sand on which they live. However, populations of primarily dark-colored rock pocket mice have been found living in areas where the ground is covered in a dark rock called basalt caused by geologic lava flows thousands of years ago. Scientists have collected data from a population of primarily dark-colored mice living in an area of basalt called the Pinacate lava flow in Arizona, as well as from a nearby light-colored population. Researchers analyzed the data from these two populations in search of the genetic mutation responsible for the dark coat color. Their analyses led to the discovery of a mutation in the *Mc1r* gene that is involved in coat-color determination.

THE *MC1R* GENE

Two pigments primarily determine the coat color of rock pocket mice: eumelanin, which is dark-colored, and pheomelanin, which is light-colored. The products of several genes, including the *Mc1r* gene, control the synthesis of these pigments. This gene encodes a protein called the melanocortin 1 receptor (MC1R) and is found embedded in the cell membranes of melanocytes, specialized pigment-producing skin cells. The melanocytes of wild-type (nonmutant) mice produce more pheomelanin than eumelanin. The result is a sandy-colored mouse. The mutated version of the *Mc1r* gene, however, triggers melanocytes to increase the production of eumelanin, resulting in the dark coat-color phenotype.

GENE MUTATION

A gene mutation is any change in the DNA sequence of a gene. Gene mutations can change the structure of the resulting protein. A change in protein structure can change, negate, or have no effect on function. There are several types of mutations, and they affect the amino acid sequences of proteins in different ways.

Types of mutations:

- Substitution mutation: the replacement of one nucleotide of DNA for another. Mutations that affect a single nucleotide are called “point mutations.”
- Insertion mutation: the addition of one or more nucleotide(s) to the DNA gene sequence. The insertion of nucleotide(s) can result in “frame-shift” mutations.
- Deletion mutation: the loss of one or more nucleotide(s) from the DNA gene sequence. The deletion of nucleotide(s) can result in “frame-shift” mutations.



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Potential effects a gene mutation has on a protein:

- Silent mutation: This mutation does not cause a change in the amino acid sequence of the protein; therefore, there is NO change in the resulting protein.
- Missense mutation: This mutation causes an amino acid in the sequence to be changed to another amino acid. This type of mutation causes a change in the primary structure of the protein (the linear sequence of amino acids), which can result in a change in the three-dimensional conformation of the protein.
- Nonsense mutation: This mutation causes the protein to be truncated (cut short) due to the incorporation of a “stop” signal into the DNA sequence. This results in translation being stopped before the amino acid sequence of the protein is completed.

MATERIALS

- genetic code chart (see page 6 of this handout or a biology textbook)
- blue, red, and green colored pencils

PROCEDURE

1. Watch the Howard Hughes Medical Institute’s 10-minute film [*The Making of the Fittest: Natural Selection and Adaptation*](#).
2. Using the DNA nucleotide sequences for the wild-type and mutant genes in the following tables (page 3), determine the complementary mRNA sequence for the five portions of the *Mc1r* gene provided. (Note: You are only transcribing short portions of the DNA sequence for this protein. The actual gene contains 954 base pairs.)
3. Using the mRNA sequence completed in Step 2, determine the resulting amino acid sequence of the MC1R protein. (Note: You are translating only a portion of protein. The full protein is 317 amino acids long. The numbers above the columns in the tables indicate amino acid positions in the protein sequence.) You may use the genetic code chart provided in your textbook or the one on page 6 of this handout.
4. There are five substitution mutations in the dark-colored mutant *Mc1r* gene. Compare the DNA sequence of the light-colored wild-type *Mc1r* gene with the DNA sequence of the dark-colored mutant *Mc1r* gene. Indicate the locations of the five mutations by circling the five single DNA nucleotides that are mutated in the mutant *Mc1r* gene table.
5. Using the information in the introduction, determine whether each of these mutations is a silent, missense, or nonsense mutation.
 - a. Using the mutant *Mc1r* gene data, shade in the columns (including DNA, mRNA, and amino acid) in **gene table 2** that contain a silent mutation using a **BLUE** colored pencil.
 - b. Likewise, shade in the columns that contain a missense mutation using a **RED** colored pencil.
 - c. Shade any columns that contain nonsense mutations using a **GREEN** colored pencil.
6. Answer the questions following the gene tables.



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GENE TABLE 1: WILD-TYPE *MC1R* GENE (LIGHT COAT-COLOR PHENOTYPE)

015								022
DNA	TTG	AGG	TGG	GCG	TGT	CCG	CAA	GGA
mRNA								
Amino Acid								

105								112
DNA	CGG	GAC	CGG	TGG	GCC	CAC	TGA	CAC
mRNA								
Amino Acid								

154								161
DNA	TCA	TAA	CAC	TGT	GAC	GGG	GCC	CGA
mRNA								
Amino Acid								

209				212			
DNA	GTG	TAC	GAA	CGT			
mRNA							
Amino Acid							

230								237
DNA	GAA	CAG	GTG	GTT	CCA	AAG	GCT	GAG
mRNA								
Amino Acid								

GENE TABLE 2: MUTANT *MC1R* GENE (DARK COAT-COLOR PHENOTYPE)

015								022
DNA	TTG	AGG	TGG	ACG	TGT	CCG	CAA	GGA
mRNA								
Amino Acid								

105								112
DNA	CGG	GAC	CGG	TGG	ACC	CAC	TGA	CAC
mRNA								
Amino Acid								

154								161
DNA	TCA	TAA	CAC	TGT	GAC	GGG	ACC	CGA
mRNA								
Amino Acid								

209				212			
DNA	GTG	TAC	GAG	CGT			
mRNA							
Amino Acid							

230								237
DNA	GAA	CAG	GTG	GTG	CCA	AAG	GCT	GAG
mRNA								
Amino Acid								



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QUESTIONS

1. In gene expression, which enzyme is responsible for transcribing the DNA sequence into mRNA by adding complementary RNA nucleotides? _____
2. In a eukaryotic cell, where does transcription occur? _____
3. Describe the process of translation.
4. In a eukaryotic cell, which main organelle is involved in translation? _____
5. Explain the relationship between DNA sequence, amino acid sequence, and protein structure and function.
6. The *Mc1r* gene codes for the _____ protein.
7. If the MC1R protein is 317 amino acids long, why are there 954 base pairs in the coding region of the gene?
8. Of the five mutations you identified in the mutant *Mc1r* gene, how many are:
_____ substitutions _____ insertions _____ deletions (Enter a number on each line.)
9. Of the five mutations you identified in the *Mc1r* gene, how many are:
_____ silent _____ missense _____ nonsense (Enter a number on each line.)
10. Mice with the wild-type (nonmutant) *Mc1r* gene have light-colored fur. Which pigment is responsible for this coloration? _____
11. Using the information in the introduction on mutations and your knowledge of proteins, develop a hypothesis to explain how the changes in the MC1R protein's amino acid sequence might affect its function.



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12. Explain how silent mutations affect the structure and function of the protein

13. Using the information provided in the introduction, explain how the mutant MC1R protein directly affects a rock pocket mouse's coat color.

14. Mutations are a source of genetic variation. In the film, Dr. Carroll says that mutations occur randomly. What does that mean?

15. It is a common misconception that "all mutations are bad." Use the example of rock pocket mice to explain why this is not true. In your answer, explain how the dark coat color mutation can be an advantage to some mice and a disadvantage to others.

16. Use your understanding of evolution and the information in the film to explain how the dark-colored mutation came to be so common in some populations of rock pocket mice. Be specific.



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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 followed by the second and third ring. Find the corresponding amino acid in the outer circle.

