HOW TO USE THIS RESOURCE

The images for this resource compare wild-type animal models to mutants that lack a protein involved in coloration. These images can serve as phenomena to explore the key concepts described below.

The pedagogical practice of using phenomena to provide a context for understanding science concepts and topics is an implementation practice supported by the Next Generation Science Standards (NGSS). Phenomena are observable occurrences that students can use to generate science questions for further investigation or to design solutions to problems that drive learning. In this way, phenomena connect learning with what is happening in the world while providing students with the opportunity to apply knowledge while they are building it.

The "Implementation Suggestions" and "Teaching Tips" sections provide options for incorporating the images into a curriculum or unit of study and can be modified to use as a standalone activity or to supplement an existing lesson. The student handout includes reproductions of the images and the "Background Information" section.

KEY CONCEPTS

A. Studies of model organisms can provide valuable information about gene function.

B. Coloration in vertebrates can be studied through molecular, cellular, and genetic analyses in diverse organisms and helps shed light on the evolution of human skin color.

NGSS PERFORMANCE EXPECTATIONS

HS-LS1-1. Construct an explanation based on evidence for how the structure of DNA determines the structure of proteins, which carry out the essential functions of life through systems of specialized cells.

HS-LS4-4. Construct an explanation based on evidence for how natural selection leads to adaptation of populations.

BACKGROUND INFORMATION

Many animals have colors that serve a variety of important functions. These colors may help the animals communicate, blend in with their environments (camouflage), recognize family members, or choose mates. Therefore, an animal's set and arrangement of colors, or coloration, can have important evolutionary effects.

How colorations, including skin color, are formed is not well understood in vertebrates. Researchers use model organisms, including zebrafish and mice, to investigate the genes behind coloration. One gene that scientists are investigating is *MFSD12*, which plays a role in human skin color. Scientists have used a technique called CRISPR-Cas9 to knock out the *MFSD12* gene in zebrafish and mice. "Knocking out" a gene stops the expression of its protein.

Images A through D (Zebrafish)

These four images are close-ups of six-day-old zebrafish embryos. Images A and C show wild-type zebrafish. Images B and D show mutants that had the *MFSD12* gene knocked out.

Most zebrafish have horizontal stripes, which are formed by pigment-containing cells called chromatophores. A xanthophore is a type of chromatophore that typically contains yellow pigments.

For Images A (wild type) and B (mutant), scientists stained the xanthophores' pigments with a dark-colored dye. For Images C (wild type) and D (mutant), scientists used a technique that allowed them to visualize the locations of the xanthophores. The xanthophores appear as light-colored areas.

Images E and F (Mice)

Image E shows two mice from the same litter. The brown mouse on the left is a wild-type mouse, and the gray mouse on the right is a mutant that had the *MFSD12* gene knocked out.

Image F shows close-ups of hairs from each mouse. The hair on the left was taken from the wild-type mouse, and the hair on the right was taken from the mutant.

IMPLEMENTATION SUGGESTIONS

The following suggestions outline several options for incorporating the images into a unit of study as phenomena:

Engagement, establishing prior knowledge, and providing context:

- Divide students into groups of two or three and provide each group with a copy of the images. Explain that Images A through D are of six-day-old zebrafish embryos. Images E and F are of mouse littermates and their hair.
- Ask each group of students to examine the images and to make a list of observations, first of the zebrafish and then of the mice. Encourage them to use the sentence stems "I notice …", "It reminds me of …", and "I wonder …"'
- Have students share their observations with the class. Record class observations, noting when groups make similar observations. Also, be sure to record and discuss questions the students have about these images. These observations and questions can be referred back to later in the activity.
    - Students may wonder what part of the zebrafish they are seeing in Images A through D.
    - Students may wonder why Image A seems to have spiderweb-like structures, but Image B does not.
    - Students may question what techniques were used to visualize the structures in Images A and B versus Images C and D.
    - Students may wonder why the two mice in Image E have different colors of fur.
    - Students could mention that the hair on the left in Image F is yellow or brown at the tip, but the hair on the right is not.
    - Students might observe that the bases of each hair in Image F are similarly dark in color.
- Tell students that the images are comparing wild-type (normal) zebrafish and mice with individuals that have a mutation. This mutation affects a gene related to coloration in both zebrafish and mice. Ask students why scientists might be interested in investigating this gene.
    - Students might state that the gene could also be present in other animals, such as humans.
    - Students may suggest that the gene could be linked to the ability of the zebrafish and mice to survive under different environmental conditions.
    - Students may suggest that the gene could be linked to one or more health problems.
- At this point, have students read the "Background Information" for the images.
    - As a note, this background reading discusses *MFSD12*, a gene in humans that affects skin color. This gene has differently named orthologs in different organisms. In zebrafish, the corresponding gene is named *mfsd12a*. In mice, the corresponding gene is named *Mfsd12*. This activity uses the name *MFSD12* throughout for the sake of simplicity.
- Ask students to reread the section labeled "Images A through D (Zebrafish)" and discuss the following questions:
    - Do the amounts of pigmentation in the wild-type and mutant embryos appear to differ? (Students should use Images A and B to answer this question.)
    - Do the numbers of xanthophores in the wild-type and mutant embryos appear to differ? (Students should use Images C and D to answer this question.)

- What do your previous observations seem to suggest?

- Have students reexamine Image F and discuss the following question:
  - What are some similarities and differences between the hairs in Image F? (Students should observe that both hairs have a dark pigment at the bottom. However, the hair from the wild-type mouse has a light-yellow pigment at the top, which is missing in the hair from the mutant mouse.)
- Have students consider the following questions, either as a formative assessment or as a transition to one of the activities suggested in the following section:
  - Based on your observations of all the images, what does the *MFSD12* gene appear to regulate in both the zebrafish and mice? How might the presence or absence of this gene be beneficial or harmful? What questions does this raise regarding the role of *MFSD12* in human skin color?

Exploration, assessment, and extension:

- Exploration/Investigation:
  - Students can further investigate the relationship between zebrafish coloration and human skin color through the "Zebrafish and Skin Color" activity. This activity focuses on a different gene, *SLC24A5*, that is also involved in zebrafish coloration. Variations in this gene play an important role in the expression of lighter skin tones in people of European descent.
    - In this activity, students explore data generated from genetic studies in zebrafish to help them understand the function and evolution of *SLC24A5*. They use real data to construct explanations, make predictions, propose hypotheses, and make evidence-based claims.
    - As part of this activity, students watch the short film *The Biology of Skin Color*. This film proposes an explanation for the evolution of different skin tones among human populations living in different parts of the world.
  - Alternatively, students can learn directly about the evolution of human skin color though the following activities and films:
    - Students could start with the activity "Human Skin Color: Evidence for Selection." During this activity, they watch the short film *The Biology of Skin Color*. After watching a particular segment of the film, they analyze data presented in a scientific figure and make evidence-based claims using the data and information from the film.
    - Students could then work through the *How We Get Our Skin Color* interactive video. This video shows an animation that describes how and where melanin is produced in our cells and what factors affect our skin color. Students can pause the animation at five points to learn more information and further engage with the material.
- Assessment:
  - Provide each student with a sheet of paper. Ask them to write their name at the top and to list three factors that have influenced the evolution of human skin color. Next, have students pass their lists to another person. Establish a system so that the passing will progress in an organized way.
  - The next person should examine the new list and add any ideas from their original list that are missing on the new one. Signal when it is time to pass the lists. Based on your class size, determine how many responses each student should review. Continue the process until that number has been reached. At that point, the lists should be returned to their original authors.
  - Ask students to share one of the factors from their list and explain how that factor influenced the evolution of human skin color.
  - Also ask students to share any additions made to their lists that they have questions about. Have the class discuss whether these factors may have influenced skin color and what they would need to know in order to make that decision.

- Extension:
  - Have students complete the activity "Developing an Explanation for Mouse Fur Color." This activity is based on the classic study of the evolution of fur color in rock pocket mouse populations. It supports the short film *The Making of the Fittest: Natural Selection and Adaptation*. Students are asked to summarize the evidence for evolution by natural selection presented in the film and in figures from a scientific paper.
    - Ask students to apply what they have learned through this activity to the evolution of human skin color. Are there commonalities?
    - Divide students into groups of two or three and ask them to discuss how variation, inheritance, and differential survival and reproduction have played a role in the evolution of mouse fur color and human skin color.
    - Have each group share their ideas with the class. Students should conclude that skin color is regulated by a number of different genes. There are variants of these genes in all vertebrate populations. In many instances, environmental factors select for or against skin color variants, leading to differential survival and reproduction, and therefore change, in mouse populations over time.
  - Have students complete the Data Point "Skin Color and Human Evolution," which explores a figure from the same scientific paper as the images used in this activity.
    - Advanced students can read the original scientific paper, listed in the "Source" section below, to learn more about the images used in this activity and in the Data Point.
  - Have students work through the Click & Learn *CRISPR-Cas 9 Mechanism and Applications*, which explores CRISPR-Cas9 as a biotechnology tool. CRISPR-Cas9 was used to generate the mutant zebrafish and mouse in the images. The Click & Learn includes videos of researchers using CRISPR-Cas9 for basic research, as well as for medical and agricultural applications.

TEACHING TIPS

- Present students with the image first, before they read the background information.
- Background information may be edited to support student proficiency, course sequence, etc.
- The image may be projected in lieu of handouts.
- Printed images can be laminated for use in multiple classes.

RESOURCE-PAIRING SUGGESTIONS

Use these images to introduce a lesson on:

- Model organisms
- CRISPR-Cas9
- Inheritance and variation of traits
- Natural selection and adaptation

SOURCE

Figure 7 from:

Nicholas G. Crawford, Derek E. Kelly, Matthew E. B. Hansen, Marcia H. Beltrame, Shaohua Fan, Shanna L. Bowman, Ethan Jewett, et al. "Loci associated with skin pigmentation identified in African populations." *Science* 358, 6365 (2017). https://doi.org/10.1126/science.aan8433.

An annotated version of the article is also available from Science in the Classroom.

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