NOVA

Regulating Genes

Teacher's Guide

OVERVIEW

This is a two-day activity. On Day 1, students use an online gene modeling tool to explore how genes affect the development of an organism, from a fertilized egg to a fully developed creature. On Day 2, students connect what they learned about biological development in individuals to evolution in larger populations.

Day 1 Summary. Devo: Understanding Biological Development

Day 1 focuses on exploring the processes of genetic mutation and development. This activity uses an online tool that models the processes of gene regulation by allowing students to view a DNA mutation and then see how it impacts gene expression during development. By observing how genes are turned on or off, students can make predictions about traits and then see the results in a developed creature.

Day 2 Summary. Connecting the Devo to the Evo

By studying how mutations to DNA can influence the development of individual organisms, students learn about this primary driver of evolutionary change. But to understand how this plays out in evolution, they need to understand how traits that arise through mutation are preserved within groups.

The second day of this activity focuses on how the organisms developed with the gene tool might interact with their environments. Students group the organisms they created by traits and explore their viability in different environmental scenarios. Students discuss which type of organism might be at an advantage or disadvantage in each scenario as a result of its mutation.

In this activity, students will:

- Observe a model that shows the expression of two genes in an imaginary organism to learn how enhancers help regulate gene expression during the organism's development.
- Through a series of tests, students will view mutations in an organism's DNA to learn more about how mutations in different regions of DNA (i.e., coding gene, non-coding enhancer, other non-coding DNA) can differentially affect the development of an organism.
- Students will gather data from the tool and compare organisms in order to predict outcomes and develop theories that explain the processes that af-

fect gene expression.
- Students will group variants in a classroom-created population of creatures by traits and discuss how certain mutations can increase or decrease the chances of survival, based on the environment.
- Students will reflect on why some forms of mutation are more conducive to evolutionary change than others.

Students will be able to:
- Describe how enhancers help regulate gene expression during the organism's development.
- Use the tool to gather data and compare organisms in order to predict outcomes and develop theories that explain the processes that affect gene expression.
- Describe how particular mutations can produce traits that can increase or decrease the chances of survival in a given environment.
- Offer informed opinions on why some forms of mutation are more conducive to evolutionary change than others, based upon examples from this activity.

Grade Level
This activity is recommended for grades 9–12.

The activity involves sophisticated concepts about genes, suited to students with some prior exposure to genes, gene regulation, and DNA mutation. It is ideally suited as part of a genetics unit, or as part of a unit on evolution where students have had prior exposure to genes. Additional teacher guidance may be necessary when doing this activity with less-prepared students.

Suggested Time (including ways to structure for longer or shorter)
Each of the two activities is designed to occupy a single class period, though the activities can easily be expanded into a longer investigation.

***Ways to Shorten*.** If you have limited time, focus on the Day 1 activity, biological development, and either eliminate the Day 2 evolution investigation, or address its key ideas via a "wrap-up discussion."

Ways to Expand. Add the following concepts to your activity:
- Discuss "regulator genes" and how they relate to the model in the gene tool. Regulator genes produce the proteins we see in the tool. Examples of these genes include body plan genes—i.e., hox genes.
- Compare similarities between body plans across species, which exist thanks to the similarities of the "genetic toolkits" between all animals: See NOVA's "Zoo of You" http://www.pbs.org/wgbh/nova/beta/evolution/zoo-you.html and "Genetic Toolkit" on Teachers' Domain http://www.teachersdomain.org/resource/tdc02.sci.life.gen.genetictoolkit/
- Look at actual photos of embryonic development. Compare the development of different species and the appearance of different traits during development. See NOVA's "Guess the Embryo" http://www.pbs.org/wgbh/nova/beta/evolution/zoo-you.html

- The gene model shows only a small part of biological development. Using the list of "areas of conceptual simplification" at the end of this document, expand on the model in order to paint a broader picture of the biological development of embryos.

Before the Activity

Review with students ahead of time some general information about DNA, genes, and gene regulation, such as the processes by which genes code for proteins, the role of proteins in creating body parts, the role of DNA, and the relationship between DNA and individual cells.

Background Essay

You and your students should read and discuss the background essay prior to starting the activity, with the goal of having them understand these key concepts:

1. Humans have roughly the same number of genes as many other species that we typically view as less complex, and far fewer than some plants.
2. This challenges a previously held theory that more genes equals greater complexity.
3. Variations and mutations in the coding genes are insufficient to explain the diversity of species. Scientists had to develop other genetic explanations to explain the diversity of animals with similar sets of genes.

See the recommended discussion questions in the "Setting the Stage" phase of the activity (below and in Appendix) for further guidance.

Videos

Review this vocabulary list with your students

coding gene: The region of DNA containing code that can be translated into proteins.

promoter: The non-coding region of a gene that is responsible for regulating a gene's expression. Promoters are located next to the gene they regulate.

enhancer: The mechanism within a gene's promoter region that, in conjunction with transcription factors (see below), is responsible for activating or repressing the gene's expression at a specific time and place during development.

transcription factors: Proteins that bind to a gene's enhancer to determine when, where, and to what degree that gene is expressed at different stages of development. They are themselves the product of other genes known as "regulator" genes.

For additional background, see these related NOVA Resources

Cell Transcription and Translation, Interactive Slide Show
http://www.teachersdomain.org/resource/lsps07.sci.life.stru.celltrans/

How DNA Replicates, Movie clip
http://www.teachersdomain.org/resource/tdc02.sci.life.gen.dnaanimation/

Body Plan (Homeobox) Genes, Article
(this activity does not discuss body plan genes, but it does illustrate the tran-

scription factors they create)
http://www.teachersdomain.org/resource/tdc02.sci.life.gen.homeobox/

Gene Switches, Slide Show
http://www.pbs.org/wgbh/nova/beta/evolution/gene-switches.html

What is Evo Devo, Interview with Cliff Tabin
http://www.pbs.org/wgbh/nova/beta/evolution/what-evo-devo.html

The Genetic Factor, Interview with Sean Carroll
http://www.pbs.org/wgbh/nova/beta/evolution/genetic-factor.html

THE ACTIVITY, DAY 1: EXPLORING GENETIC DEVELOPMENT

Setting the Stage (10 min)
The goal of the introduction is to "set the stage" for the investigation and provide students with a set of driving questions for the activity. Facilitate a discussion, using questions such as these (see Appendix for answer key):

- What do you think has more genes, a chicken, a worm, an ear of corn, a chimp or a human?
- Would you expect a large or small amount of diversity in the genes of different animals?
- Optional Follow-up: It might seem like humans should have more genes than other animals, but really humans, chickens, chimps, and worms all have about the same number of genes. Corn has more than any of those animals. In light of the new information, does that help make sense of any of the theories or questions you had?
- What do you think controls the diversity we see within vertebrates? What about between vertebrates and invertebrates? What about between plants and animals? Biologically, what makes these differences?
- How can we evaluate the theories you propose?

Now view the video segment, "Switching Genes On and Off." This will familiarize students with the concept that two species can have different traits (such as spotted or non-spotted wings) despite the fact that they possess identical genes that code for such traits. Developmental biologists have discovered that enhancer segments in DNA act as "switches" that turn these gene segments on or off at various stages of an organism's development, and differences in these enhancers determine whether or not a gene is expressed at a particular time and location in the body. Students can also read the background essay that accompanies this activity, in class or as a homework assignment. (See "Background Essay" section above for details.) Ask students whether and how this additional information alters the theories they have proposed.

Set up the Task (5 min)
Students should work in pairs or in groups of three. If you have enough computers, students may work individually. Students in groups may take on the following

roles:

- Controlling the software
- Recording results in the "Data Log"
- Drawing creatures in the "Creature Recording Template" (not necessary if you allow printing)
- Each student should record their own answers to the "Analysis Questions"

Use or adapt the following text to set up the task:

"Your challenge is to understand and explain the genetic mechanisms that lead to variation in the traits of organisms.

We are going to do an investigation of how genes manifest as traits in an imaginary organism. We will look deep into DNA by exploring a model that illustrates the factors that influence how the organism's genes are expressed during development. Development happens in a continuous process from conception through adulthood. We will look at just a few stages of development in the organism—a fertilized egg, a four-cell embryo, and a developed creature— and observe how mutations might influence the organism's traits."

Direct students through the following activity steps. The tasks are supported by instructions in a student worksheet and data journal where students record their findings. Students should respond to the analysis questions on separate sheets of paper.

Step 1: First Run: Use the model to develop an organism (5 min)
In the first run of the model, students develop an un-mutated organism as a way to establish a baseline for comparison: they need to see what the organism looks like with no mutations so that when it changes later they can recognize the differences.

Teacher Tips:

- **In this initial run, the "View Mutation" button is disabled.**
- **Note that the activity always begins with the same gene set.**
- Students examine a portion of the organism's DNA via the "close-up" view of each cell's nucleus.
- **IMPORTANT**! In the developing embryo, each cell produces its own proteins. This model highlights just one of many types proteins in each cell. The protein "shapes" shown are called transcription factors. In reality, each cell contains many different types of proteins.

Student Tasks:
The primary tasks in step 1 are to *observe* the processes that impact gene expression and to predict trait outcomes. The learning goal is to become familiar with the mechanisms and processes involved in gene expression. Students will not be expected to fully comprehend these mechanisms and processes yet, and their predictions may be off.

1. On a separate sheet of paper students should record notes on the following:

a. *Observe* what happens to the genes in the four-cell embryo. Which genes are active and inactive, and how does this differ in each cell? Why?
b. *Predict* what will happen in the developed creature.
c. *Analyze* the outcomes in the developed creature.

2. In the *Data Log* (see Student Guide), students will find a sample response for this run.
3. Students complete this step by answering the analysis questions (see Appendix).

Step 2: Second Run: Click the "View Mutation" button, then develop an organism with a mutation in either the appendage gene or the spot gene (5 min)
In this second run of the model, students develop an organism with a mutation in the coding gene in order to learn about the consequences of such mutation. (Before scientists fully understood the role of gene regulation in evolution, the default explanation was that species diversity and evolution was driven by mutations in the coding portion of genes.)

After the initial run (step 1), the "View Mutation" button is partially enabled, but at this stage the only mutations will be to one of the two coding genes (and not mutations in enhancers or other non-coding areas of the chromosome).

Teacher Tips:

- At this stage, the goal is (a) to demonstrate that mutations to coding genes can have unpredictable consequences for an organism's development, (b) to challenge students' prior conceptions that gene mutations are primarily responsible for the evolution of new traits, and (c) to leave them wondering "if not gene mutations, what else could contribute to the evolution of new traits?"
- In subsequent runs, students will discover that mutations to enhancers can alter how a coding gene is expressed in a particular body region. In this way, a coding gene can be turned on or off in a body region without being effected in other regions. This process is called "gene regulation." As we shall see, this concept is very important in describing evolutionary change.
- Mutations have already taken place (in the sperm or egg) and have been inherited by the fertilized egg that students see here.
- Mutations are random (though for the purposes of this tool, the enhancers have a slightly higher probability of being mutated).
- In this run, mutations will only appear in the coding gene. This is intended to ensure that students first recognize the far-reaching consequences of mutations in coding genes.
- In this tool, students will discover that mutations to coding genes usually result in the gene's dysfunction. For clarity, this tool limits the results of mutations to coding genes as follows: A mutation to the gene that codes for "appendage" will always result in no appendages developing. A mutation to the gene that codes for "spot" will either result in either no spots developing or in an alteration of all spots from black to red.
- By demonstrating mutations in coding genes in this way, the goal is to con-

front the preconceived notion—likely held by many students and also shared by scientists until recent decades— that gene mutations are the primary driver of evolutionary change.
- Since a specific coding gene can be expressed at many times and in many places throughout an organism's development, changes in the coding portion of the gene can have unpredictable consequences throughout the organism.
- In future runs, students will observe mutations to other parts of DNA—namely enhancers and other non-coding regions of DNA that do not affect the gene.

Student Tasks:

1. On a separate sheet of paper students should record notes on the following:
    a. *Notice* where the mutation occurred.
    b. *Observe* what happens to the genes in the four-cell embryo. What is different as a result of the mutation?
    c. *Predict* what will happen in the developed creature.
    d. *Analyze* the outcomes of the mutation in the developed creature.
2. They will also record the results of their run in their Data Log. (See Student Guide.)
3. Students complete this step by answering the analysis questions. (See Appendix.)

Step 3: Develop organisms with random mutations (15 min)

In the third and subsequent rounds of the model, students develop organisms with random mutations. After the second run (step 2), the "View Mutation" button is completely enabled. Depending on the area of DNA that is mutated, the mutation can result in new traits forming in or disappearing from the developed creature, the alteration of the spot trait (changes color), or no visible changes at all.

At this stage, we expect students to develop numerous organisms in order to explore the various possible outcomes of random mutation.

Teacher Tips:

- The goal of these runs is for students to figure out how the mutation they identify in the initial stage affects gene expression in the developed creature.
- Students are now more familiar with the basic processes of the gene model, but they need to figure out how these processes can affect development. The key to figuring this out is to compare the differences across each run.
- So the primary task at this stage is to continue the process of observation-prediction, but rely on the controlled conditions of each run to isolate the function of each mechanism to learn it's impact on development.
- There are three different types of mutation that can occur: mutations in the coding gene (discussed in step 2), mutations in the non-coding enhancer that regulates the gene's expression, or mutations on "other" non-coding DNA which has no visible impact on development.
- *Note that it is possible to view more than one mutation per run, but students may not notice this until later. That's fine; it's best to start with one muta-*

tion per run in order to create a controlled experiment. Later, students can experiment with several mutations at once.

Student Tasks:

1. On a separate sheet of paper students should record notes on the following:
   a. *Notice* where the mutation occurred.
   b. *Observe* what happens to the genes in the four-cell embryo. What is different as a result of the mutation?
   c. *Predict* what will happen in the developed creature.
   d. *Analyze* the outcomes of the mutation in the developed creature.
2. They will also record their results of each run in their Data Log. (See Student Guide.)
   Note: The gene tool will not save students' work. To preserve the data for the next class period, you may wish to have students preserve a record of each creature they develop as they go, either by printing the developed creature or by using the "Creature Recording Template." If you are certain that you will have enough class time, you can save the recording until the end.
3. Students complete this step by answering the analysis questions. (See Appendix.)

Step 4: Refine your argument (10 min)

In the final stage of the investigation, students analyze the data they recorded in their Data Logs about the organisms they created and answered the analysis questions. You may ask them to share their results with another group or the entire class during this step.

Teacher Tips:

- The primary goal of this section is for students to compare the creatures they developed and explain how different types of mutations—i.e., to the coding gene, the enhancer, or the other "non-coding" DNA—affects the outcomes of the organism's development.
- On their own, students should begin to realize that mutations to coding genes have much more drastic (and, potentially, more detrimental) outcomes. For instance, a mutation to the gene that codes for "appendage" results in no arms or legs anywhere in the creature.
- By comparison, students should discover that mutations to enhancers can have much more localized effects on the creature's outcomes.
- They should begin to formulate theories, supported by evidence, on which type of mutation is more likely to contribute to the creature's viability, and thus its ability to survive and reproduce.
- Ultimately, survival is linked to environment, so at this point students may be limited by the claims they can make about viability. We will explore how mutations relate to evolution in Day 2.

Student Tasks:

1. Students analyze the creatures they created in their Data Logs, using the analysis questions.

2. You may ask students to discuss/compare their findings with the entire the class or with another group.
3. Students complete this step by answering the analysis questions. (See Appendix.)

Step 5: Preserving your data for the next phase
In order to use their results in the next class period, students should either create printouts of each of their developed creatures in their creature gallery or draw each organism and its mutation(s), using the "Creature Recording Template (provided in the Student Guide). Consider requiring students record each developed creature as they go.

IMPORTANT! Students' work cannot be saved in the gene tool. Closing the browser or clicking "reload" will erase all data.

Step 6: Taking it Further: You control the mutations
If students finish early, they can do this **optional step** while they wait for their peers to finish. Provide students with a picture of a sample creature, which is a variation on the organism they have been studying in the software application. Using the picture of the default section of DNA, have students draw (or conceal) the receptacles on all the enhancers that would be necessary to create the creature shown in the image and note the specific mutations that would have to take place. This can also be used as an assessment task.

THE ACTIVITY, DAY 2: CONNECTING THE "DEVO" AND THE "EVO"

Setting the Stage: Analyzing the population of creatures
The gene tool investigation of Day 1 provides the foundational understanding of how genetic mutations can lead to changes in animals.

The goal for the Day 2 activity is to connect what students learned about genetic development to our understanding of the factors that drive evolutionary change. Day 2 may be omitted if the lesson is focused only on genetic mechanisms, or it can be reintroduced during an evolution lesson later in the year.

In this stage of the activity, students can use data collected from Day 1 (via their data logs and printouts or drawings) to connect the variation that they found across each student's creatures to a discussion of species change and evolution.

Key Concepts:
The key challenge in connecting these two days is that mutation happens in individual organisms, whereas evolution happens in populations.

The basic point of the gene investigation is that mutations to mechanisms that regulate gene expression—namely enhancers—provide a stronger explanation of evolutionary change than do mutations to coding genes. A mutation to an enhancer affects how a gene expresses during a specific time and place of development, leading to development of new traits. A mutation to a coding gene, however, might impact many stages of development, and is therefore more likely to have detrimental consequences for the developed creature (making it less likely to survive).

This understanding of enhancers underscores a key principle of the "modularity" of gene regulation—that mutations in regulation can happen without impacting the genes themselves. This form of mutation, therefore, happens much more frequently. It also explains how two species can have very similar coding genes yet look very different.

Data Sharing:
Depending on the size of your class and whether students worked individually, or in groups of two or three, your class should have cumulatively developed anywhere from 100-300 creatures—a population.

Step 1: Sorting by traits
The first step is for students to "sort" their population according traits.

- Lead a discussion in which students decide how to group their creatures. You might consider grouping creatures by matching spots, according to many vs. few appendages, or perhaps whether they developed specialized traits, such as "pincer" appendages in their heads. See if there are three or four groups of similar features.
- Using a wall or empty tables, have students place their creature printouts or drawings into similar groups. Be sure they put their names on their papers.

- Review the kinds of mutation that produced each creature and group.

Complete this step with a brief discussion using the discussion questions provided. (See Appendix.)

Step 2: Environment and Time

During this stage, discuss specific environmental scenarios and have a discussion on how each trait group might fare under those conditions. Examples to discuss:

- What if the population moves near to water or into a wet, marshy area?
- What if the population exists in trees?
- What if they move to an area with little light?
- What if there is a drought?

Answers vary based on example, but the goal here is to connect specific traits to evolutionary fitness. For example, more legs might make it easier to cling to branches, enabling living in trees. No appendages might helpswimming or burrowing under ground. Red color might help if the animal lives on red clay.

Complete this step with a brief discussion using the discussion questions provided. (See Appendix.)

Step 3: Journal Writing

Have students write a response to the following questions, using their best ideas:

Based on what you have observed in the mutations of the organisms, what kinds of mutations are most likely to impact an organism's evolution? What evidence do you have to support this claim?

ASSESSMENT

Assessment strategies

Evaluate Analysis Questions

Each of the activity's main steps ends with several analysis questions. Have students record their answers on a separate sheet of paper. Use the answers and notes supplied in this document to evaluate student responses.

Evaluate Data Logs

Students log information about the developed creatures in their data logs. Examine these logs to assess the quality of student observations.

Ask students to identify the mutations necessary to produce a specific creature

At the end of Day 1, there is an optional task that asks students to draw in the enhancer mutations necessary to produce the sample organism given. You can use this example or reproduce additional examples to "test" students grasp of gene regulation.

Evaluate Understanding of Key Vocabulary Terms

Use the Key Vocabulary list in this document to evaluate students' grasp of the key terms related to classification, the hominid family tree, and fossil features.

KEY CONCEPTS AND STANDARDS

Key Curriculum Concepts

Prerequisite Concepts:

- Know that genes encode proteins, which are the building blocks of visible traits.
- Know what DNA is, its role, and that it is found in the nuclei of cells.

Focus Concepts:

- Species can have very similar genes, even if they look different.
- Enhancers are non-coding regions of DNA that control the expression of genes.
- Transcription factors in a cell's nucleus regulate gene expression by binding to a gene's enhancers.
- Gene expression is a key part of the process that leads to the development of traits.
- Mutations can happen anywhere along a DNA strand, including the coding region of genes, the non-coding region (enhancers), and other less understood parts of non-coding DNA.
- Mutations in genes can result in different traits. Most likely, these mutations will result in organism failure.
- Mutations to enhancers can alter traits by changing how and when a gene expresses.

Follow-up Concepts:

- Organisms cannot tolerate much gene mutation, thus all species have had similar genes for eons.

- Organisms can tolerate mutation in enhancers, and this is what more often drives adaptation and evolution.

Key Areas of Conceptual Simplification

- The model is represented as a deliberate abstraction. We are accentuating key relationships and aiming for instructional and conceptual clarity, not "actual" biological depictions. The system is intended to describe relationships between factors and not illustrate them in a lifelike manner.
- When we illustrate gene regulation, we are only showing variation in where genes express. In this model, enhancers only turn a gene on and off. We are not representing the different timing of gene expression (since we are only showing one "moment" of expression in a four-cell embryo), nor are we showing modulated degrees of gene expression.
- We have simplified the role of the regulator proteins. Transcription factors are expressed only as activators and not as repressors. Transcription of the regulator gene is not described.
- We are emphasizing only one type of protein (transcription factor) in each cell at the four-cell stage. In fact, each cell contains many different types of proteins, some of which they share in common. The goal here is to isolate proteins responsible for regulation of the two genes being observed.
- We are only showing one layer of regulation, and we are making it fairly one-dimensional, whereas in fact gene regulation is a complex, nested process.
- We are not showing the regulator genes that produce the transcription factors we see in the four-cell embryo. We are only illustrating regulation at a "frozen moment" of the embryo's ongoing evolution. The implication of the model is that gene regulation happens both upstream and downstream from the visible instance (a four-cell stage). This decision was made in order to make the model graspable. Embryo development over time involves so many layers of nested interaction between thousands of genes and proteins. Instead, we are relying on animated "passages of time" between stages of development to imply other events happening at other stages of development.
- We are using a simplified fictional creature. And we are making a significant jump from two genes at one moment of development to fully developed traits in that creature. The connection between the four-cell stage and the developed creature is one of implied connection and inference. Many other stages of development are necessary to achieve the outcomes we observe.
- Mutations are not occurring in the fertilized egg, but rather are inherited from the sperm and egg. For simplicity we are showing mutations at the one-cell stage, but it is important to understand that we are "viewing" mutations that have already occurred, not "triggering" mutations at that moment.
- We are showing only two of many genes in the developing organism, and these genes have been fictionalized to describe their functionality. In reality, many genes can contribute to the formation of an appendage, for instance.
- We are not showing gene transcription or translation at all.

Standards

National Science Education Standards (1996)

- The Cell: http://www.nap.edu/openbook.php?record_id=4962&page=184
- The Molecular Basis for Heredity: http://www.nap.edu/openbook.php?record_id=4962&page=185
- Science as Inquiry: http://www.nap.edu/openbook.php?isbn=0309053269&page=105>

AAAS content benchmarks (2007)

- Human Development: http://www.project2061.org/publications/bsl/online/index.php?chapter=6#B4
- Evolution of Life: http://www.project2061.org/publications/bsl/online/index.php?chapter=5#F4
- Nature of Science: http://www.project2061.org/publications/bsl/online/index.php?chapter=1#B4

APPENDIX: DISCUSSION QUESTIONS AND ANSWERS

Day 1 Discussion Questions and Answers

"Setting the Stage" Discussion Questions:

(these questions are not in the student guide and are intended to support teacher facilitation.)

- **What do you think has more genes, a chicken, a worm, an ear of corn, a chimp or a human?**
  If students do not recall the film, likely responses are that humans have the most and chimps have the next most. As students discuss their ideas, try to identify any differing viewpoints. For example, if someone suggests that humans have more genes than another species, and someone else suggests that maybe something else controls the diversity between species, highlight this distinction and help students think about how they might determine which theory actually fits best with the information we have about the genomes of various species.
- **Would you expect a large or small amount of diversity in the genes of different animals?**
- **Optional Follow-up: It might seem like humans should have more genes than other animals, but really humans, chickens, chimps, and worms all have about the same number of genes. Corn has more than any of those animals. In light of the new information, does that help make sense of any of the theories or questions you had?**
  Students may express surprise that our genes are so similar in number to those of other animals. It is worth pointing out that many scientists working on the genome project also were very surprised by this finding and that it led them to do a lot more work about what causes the differences we observe if it's not the number of genes. Help students to evaluate other theories they developed in light of the new evidence that the number of genes is very similar from species to species among animals.
- **What do you think controls the diversity we see within vertebrates? What about between vertebrates and invertebrates? What about between plants and animals? Biologically, what makes these differences?**
  If your class has studied genetics, you may have students who can describe the transcription and translation process and describe some differences in the number of chromosomes. Some students may respond with simplistic answers such as "DNA" or "genes," which will give you valuable information about their understanding. At this point in the lesson, help students focus on genetics as the difference between species and encourage them to begin to ask their own questions about what controls genetic information in a living organism.
- **How can we evaluate the theories you propose?**
  This can lead to a conversation about studying genes. Students might suggest comparing the genes between different species to learn about their differences (which is what many scientists used to think). If so, point out that we already have learned that there is a great deal of gene similarities across species. What else?

Encourage students to identify other factors that might play a role in how the genes cause observable traits. Some students may suggest environmental factors such as food supply, shelter options in native habitats, and availability of fresh water. These factors do cause differences in the lifestyles and ability to thrive among individuals. However, humans survive with very similar genetic information in a wide variety of environments, so it is unlikely that gene expression is controlled in large part by the environment.

Someone might suggest that the genes can mutate to change from species to species. It is true that gene mutation does cause diversity among living organisms. However, since there are very similar genes in chimps and humans who have different traits, it is unlikely that the traits that are consistent in all chimps are caused by mutations.

Still other students may suggest that there are still unanswered questions or undiscovered parts of the genome. It is undoubtedly true that humans have much to learn about gene expression, but we do have some information that will help us to understand why almost the same genes in two different species can result in such different traits.

It is okay to leave this unresolved with students for now, though the teacher should realize that the activity will focus on what we have learned about **how genes are used** during development.

Step 1 Analysis Questions:

1. **After the fertilized egg develops into the four-cell embryo, what happens to the DNA that you observed in the initial stage?**
   Through cell division, the same DNA carries over to each cell. The DNA in each cell is identical.

2. **What does each of the four cells in the developing embryo represent?**
   In this model and at this stage of development, each cell represents a body section of the developing organism: the head, tail, middle section 1 and middle section 2.

3. **During the four-cell embryo stage, describe what happens to the proteins in each cell.**
   Each cell has a unique protein. Depending on the type of protein and the nature of the enhancer in the visible section of DNA, the proteins may "bind" to the enhancer, activating the corresponding gene. Only certain proteins will bind with certain enhancers.

   [Teacher note: These proteins are called "transcription factors," and are created by regulator genes to control the expression of other genes. Also note that in reality these are but one of many proteins in each cell.]

   This model uses shapes to signify the real-life "match" between certain proteins and enhancers. However, in real life proteins are not shaped like this,

nor do enhancers have like-shaped receptacles. Note that each cell produces many other proteins as well, but here only enhancer proteins are shown.

4. **During the four-cell embryo stage, what happens to the appendage gene in the "middle 1" and "head" cells? What causes the gene to turn on or off? How about the spot gene in the same two cells?**
   In "middle 1," the appendage gene is activated because the square-shaped proteins in that cell bound to the square-shaped enhancer associated with the appendage gene.

   In "head" the appendage gene is inactive because there is no place for its circle-shaped proteins to bind.

   The same pattern is found in the spot gene of the same cells.

5. **Based on your observations of each gene in the four-cell embryo, could you predict the traits that the creature developed? If so, what traits did you expect? Why did you predict this?**
   During the first run, students might have had difficulty predicting what traits might develop from the visible set of genes. At this stage, teacher emphasis should be placed on the process of using evidence to make a prediction, not on "right" answers.

   In middle 1, Students might predict that the activation of the spot and appendage genes will lead to the development of spots and appendages in that body section.

   Likewise, because those genes were not activated, there will be no spots or appendages in the head.

   In middle 2, they should predict the development of an appendage, but no spot.

   In tail, they should predict no appendages or spots because no genes were activated (no proteins bound to the enhancers).

   In middle 2, they should predict appendages but no spots, for the same reasons.

6. **How could the genes that are turned on and off in the four-cell embryo have affected the traits of the developed creature?**
   Here students should confirm or refute their predictions and, if they were wrong, they should click "back" and try to understand why they were wrong.

7. **What do you think might happen to the organism if one of the coding genes were mutated?**
   This is a "setup" question for the next run. Valid student predictions might include "the trait will change somehow" to "the trait won't function." Don't

give anything away yet!

Step 2 Analysis Questions:

1. **Where did your mutation occur?**
   In their first mutation, only mutations to the appendage or spot coding genes are possible.

2. **After the fertilized egg develops into a four-cell embryo, what happens to the mutation you saw in the initial stage?**
   The key point here is that each time a cell divides the mutation carries over to each cell. In other words, the DNA in each cell is identical.

3. **How did the mutation impact what happened in the four-cell embryo?**
   If their gene mutated in a way that made it dysfunctional (a red zigzag shape), students should note that the gene did not activate, even if a protein bound to its enhancer.

   If their gene mutated in a way that altered its function (this can only happen with the spot gene), they should note that the gene turned into a red curvy line, and that it became active in any cell that had a protein that matched its enhancer.

   During this first mutation, students might not yet know the meaning of each gene mutation symbol (red zigzag, red curvy line), though they will learn soon enough, once they develop the organism.

4. **How did the mutation affect what happened in the developed creature? Is this what you expected would happen?**
   If the gene had a dysfunctional mutation (red zigzag), the gene that carried the mutation (spot or appendage) did not become active, regardless of whether proteins bound to its enhancer.

   If the spot gene had a mutation that altered its function (red curvy line), it will behave as a gene normally would, but the spots may look different (in this case, the spots will be red instead of black). The gene will become active in any cell/body section that contains a protein that matches a receptacle in its enhancer.

5. **Does mutation increase the chances of survival for a given individual? Explain your answer.**
   There is no right answer here. It depends on the environment. Students' explanations may imply certain environmental conditions.

   The purpose of this question is to get students thinking about the relationships between an organism's traits and its environment. Ultimately, whether a mutation is advantageous depends on the conditions in which the organism lives.

Step 3 Analysis Questions:

1. **Where did your mutation occur?**
   Unlike earlier runs, mutations can now happen in any of three regions of the two chromosomes: in the gene that codes for proteins, in a non-coding region containing an enhancer, and in other non-coding DNA that does not immediately impact the gene.

2. **How did the mutation affect what happened in the four-cell embryo?**
   Answers will vary depending on where the mutation happened. Students should describe specifically how the mutation is influencing gene expression. Mutations to enhancers may activate or deactivate the gene in different cells. Mutations to coding genes may prevent the gene from being activated (even if proteins bind to its enhancer). Mutations to other regions of DNA have no visible impact.

3. **How did the mutation affect what happened in the developed creature? Is this what you expected would happen?**
   Answers will vary. Students should observe the new traits and explain how they resulted from the observed mutation(s).

4. **Does mutation increase the chances of survival for a given individual? Explain your answer.**
   There is no right answer here. It depends on the environment. Students' explanations may imply certain environmental conditions.

   The purpose of this question is to get students thinking about the relationships between an organism's traits and its environment. Ultimately, whether a mutation is advantageous depends on the conditions in which the organism lives.

Step 4 Analysis Questions:

1. **If a mutation occurs in the coding part of the gene (labeled "Coding Gene" in the close-up view), what happens to the organism?**
   Mutations to coding genes often lead to changes throughout the organism—if a coding gene mutates, its impact can be seen throughout all the body parts. For instance, if "spot" becomes dysfunctional, it fails to appear anywhere in the body regardless of whether proteins bind to its enhancer. Likewise, if "spot" is altered, red spots (rather than black) appear anywhere that gene is expressed.

2. **If a mutation occurs in the non-coding/regulatory part of the DNA (labeled "enhancers" in the close-up view), what happens to the organism?**
   Mutations to enhancers can have small but helpful impacts—for instance added spots on the tail might increase the chance of mating, added arms might improve locomotion. These changes don't necessarily reverberate throughout the entire organism.

3. **If a mutation occurs in other parts of the DNA (labeled "Other DNA" in the**

close-up view), what happens to the organism?
Mutations to other regions of DNA have no visible impact.

4. **What types of mutations tend to have consequences that increase the chances of survival for an individual?**
   While survival is tied to the conditions in which the species lives, we could speculate that mutations to coding genes, because they affect the entire organism, are more likely to have a negative impact on the organism.

   By contrast, mutations to enhancers can have small but helpful impacts—for instance, added spots on the tail might increase mating, added arms might increase locomotion. These changes don't necessarily reverberate throughout the entire organism.

5. **How do you think these mutations might be related to the differences between the traits expressed in different species?**
   Two different species might have the same gene, but due to mutations in that gene's enhancers at different stages of development, the gene results in different traits.

   This can explain how different species have the same or similar sets of genes.

Day 2 Discussion Questions and Answers
Step 1 Discussion Questions:

The goal of this discussion is to begin to think about how certain mutations in individuals might begin to play out in groups. The questions are largely speculative and are intended to trigger an open-ended discussion.

1. **Is there reason to believe that some groups you have created might be better suited to survival?**
   Focus on the functional aspects of the traits. Start by ruling out groups that seem highly unviable, such as ones for which certain genes failed to function entirely. Then discuss the role of appendages and the potential advantages and disadvantages of having them in different body sections. Then discuss spots and their potential evolutionary role (see next question).

   Note that nature is full of surprises, so there's no telling what features (or lack thereof) could prove advantageous given certain circumstances. Snakes, for instance, are known to have evolved from ancestors with appendages.

2. **Is one group more or less likely to reproduce?**
   Spots are often noted as a feature that attracts mates.

Step 2 Discussion Questions:

1. **How do the mutations in the creatures relate to their ability to survive?**

Survival is highly dependent on context, but we can generalize that certain mutations produce traits that can, in certain circumstances, be either advantageous or not. You can use this as a transition to the next step.

2. **Is one group more or less likely to survive a natural disaster like an earthquake, fire, or flood?**
   Example: Creatures with more appendages might be more mobile over land, whereas ones with fewer appendages might have an easier time moving through soil.

Next, explore what might happen over time if one of the groups that you established in Step 1 were to be cut off from the rest of the larger population—such as move over a mountain range to find food, or be cut off from the rest of the population due to a fire.

3. **If all three groups in different locations survive, will they specialize to the point of becoming different species over many generations?**
   If a mutation contributes to the survival of organisms that carry that mutation, it is more likely to reproduce and thus pass that mutation on to future generations. Thus the genetic mutation will be preserved across generations.

4. **Which types of mutations are most likely to result in evolutionary change (the formation of a new species): mutation to the coding part of a gene, mutation to the non-coding regulatory part of the gene (the enhancer) part of the gene, or mutation to other non-coding parts of the DNA?**
   Mutations in enhancers provide the best explanation of evolutionary change. Since they regulate gene expression at specific times and in specific locations, they lead to new traits without affecting the entire organism.

   Mutations to coding genes also are significant, but given that a single gene may affect many areas of an organism's development, such changes are more likely to adversely impact the organism's survival. This doesn't mean that mutations to coding genes don't happen in evolution, but that they are less common.

   Furthermore, evidence of the similarities of genes across the animal kingdom illustrates the diminished role of mutations in coding genes in favor of mutations in the regulatory mechanisms that govern how they are used.

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