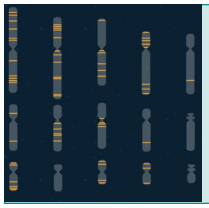

The Search for a Mutated Gene

hhmi | BioInteractive

Interactive Video
Educator Materials

OVERVIEW

This case study is based on a short video that presents the approaches scientists used to identify a mutation that causes retinitis pigmentosa (RP) in a patient. RP is a progressive visual disease that results in the deterioration of the retina and loss of vision. As students watch the video, they are prompted to answer a number of embedded questions at selected time points.

Videos can be used for teaching by stopping at appropriate time points and asking questions to cue student attention, encourage critical thinking, and make the students part of the story. This interactive video, which was created using BioInteractive's *Interactive Video Builder* tool, incorporates embedded questions at automatic pause points. Students can answer the questions directly in the interactive video or in the "Student Worksheet."

After finishing the video, students can review their answers and add to their explanations if their thinking has changed.

Additional information related to pedagogy and implementation can be found on this resource's webpage, including suggested audience, estimated time, and curriculum connections.

STUDENT LEARNING TARGETS

- Formulate a hypothesis to explain how a mutation in a gene would affect the function of a cell and an organism.
- Describe the possible steps involved in identifying a disease-causing gene mutation in a patient.
- Predict how replacing a mutated gene with a functioning copy of that gene will affect the phenotype of a cell and/or organism.
- Explain how the identification of disease-causing mutations can be used to develop medical treatments.

PRIOR KNOWLEDGE

Students should be familiar with:

- the definition of mutation and how genetic mutations can be inherited
- the process of gene expression

BACKGROUND

Most human traits, including diseases, are influenced by multiple genes. It is difficult to develop genetic therapies for diseases caused by variations or mutations in many genes (**multigene diseases**). However, a relatively small number of genetic diseases are caused by mutations in single genes (**single-gene diseases**). It's more feasible to identify mutations for single-gene diseases and develop effective therapies.

Retinitis pigmentosa (RP) is a progressive visual disease that causes photoreceptor cells in the retina to die. It is caused by mutations in any one of several different genes. Mutations in any one of these genes are sufficient to cause RP. Many mutations that cause RP have been identified. When scientists tested the DNA of the patient featured in this video, Sam, they did not find any of these known mutations.

Scientists determined that Sam's DNA contains a previously unknown mutation that affects tRNA structure and function. They then discovered that two other patients with RP have mutations in the same gene. Scientists were able to confirm that the mutation affects photoreceptor cells through experiments in zebrafish, a model research organism.

TEACHING TIPS

- Students can work on the questions individually or in small groups.
- Students should type responses into the answer boxes that appear during the interactive video.
  - If students are not using the interactive video individually (e.g., you are projecting the video to the entire class), they can write their responses in the "Student Worksheet" instead.
- **The interactive video will not proceed until an answer is submitted.** You must type at least one letter into the answer box to continue.
  - If some questions do not fit the context of your course, you can direct students to skip those questions by typing "I am skipping this question." in the answer box.
- If students are answering questions within the interactive video, they will be prompted to submit their answers at the end of the video. They will have the opportunity to review and add further explanation to each answer if their thinking has changed.
  - Once they are done, they can download a report of their answers. The report can be saved as a PDF or printed. You can have students submit the PDF or screenshots/photos of the report.
- The original video without embedded questions is available under *The Search for a Mutated Gene*.

SUMMARIES AND QUESTIONS

The interactive video has multiple sections. After each section, the video automatically pauses and prompts students to answer an **embedded question**. This document provides additional **extension questions** that do not appear in the video, which can be used for discussion prompts and written assessments.

Below are summaries of the sections and their associated embedded/extension questions.

Introduction (0:00–0:10)

Summary

Before the main video, students answer a question that assesses their preexisting knowledge on gene therapy.

Embedded Question

In a few words, describe what you know about gene therapy.

Section 1 (0:11–1:27)

Summary

This section establishes the genetic basis of retinitis pigmentosa (RP) and describes other features of the disease.

Embedded Question

Sam's parents don't have RP. How can it be an inherited condition?

Extension Questions

- How do our brains convert information from light entering our eyes into an image?

- What is disease? How do organisms get diseases?

Section 2 (1:28–2:57)

Summary

This section discusses identifying mutations linked to inherited diseases, which can be used to design gene therapies.

Embedded Question

You collect blood samples, which contain DNA, from a patient with RP and their relatives. Some of the relatives have RP and some do not. Outline a strategy for using these samples to identify the disease-causing mutation in the patient.

Extension Questions

- What is a genetic mutation and what are its effects?
- How is searching for a treatment for a genetic disease different from that for a disease caused by something else, such as bacteria or viruses?

Section 3 (2:58–3:21)

Summary

This section explains how comparing the DNA of relatives can identify a mutation that causes disease and how this approach has been used to identify many different mutations that cause RP.

Embedded Question

How can mutations in different genes be associated with a single disease?

Extension Questions

- Why would a researcher use a pedigree to study a disease?
- Many characteristics of an organism are controlled by more than one gene. Likewise, many biochemical processes and pathways involve proteins produced by different genes. Explain how this relates to the existence of many different mutations that cause RP.
- Can you think of any other diseases or conditions that are caused by mutations in different genes?

Section 4 (3:22–4:03)

Summary

This section explains how a scan of Sam's genome did not find any of the known common or rare mutations that cause RP.

Embedded Question

A scan of Sam's genome for the 100 most common mutations known to cause RP didn't find anything. How can you explain this result?

Section 5 (4:04–5:16)

Summary

This section reveals that Sam's DNA has a mutation that had never been identified as a possible cause of RP.

Embedded Question

Sam has a mutation in a gene that affects the function of a transfer RNA (tRNA). Human cells have 20 different types of tRNAs, and each adds a different amino acid to growing peptide chains, which form proteins.

Based on what you know so far, would you expect this mutation to affect all proteins produced in Sam's cells? Explain your reasoning.

Section 6 (5:17–6:30)

Summary

This section reveals how a mutation that affects tRNA function is not necessarily lethal. The mutation in Sam's DNA reduces tRNA function but does not completely stop protein synthesis.

Embedded Question

What evidence could you collect to confirm that the mutation identified in Sam's DNA causes symptoms of RP?

Extension Question

Some mutations are lethal and others are not. Explain the difference between these two types of mutations in terms of cellular function.

Section 7 (6:31–7:57)

Summary

This section demonstrates the experimental procedure used to confirm that the mutation in Sam's DNA causes RP. By genetically engineering zebrafish, a model organism, to have a mutation in the same gene, scientists demonstrated that the mutation impacts how zebrafish respond to light.

Embedded Question

Doctors may be able to inject a functioning copy of the gene mutated in Sam's DNA into the cells of his eyes. If the procedure were successful, would you expect Sam to regain his vision? Why or why not?

Extension Question

In your own words, explain why researchers use model organisms such as zebrafish. Can you name any other model organisms?

Section 8 (7:58–8:30)

Summary

This section concludes the case study and mentions applications to gene therapy.

Embedded Question

Other than identifying a target for gene therapy, how does identifying a disease-causing mutation help a patient and their family?

Extension Questions

- Genetic medicine is an emerging technology that holds great promise for many diseases. Are there any ethical concerns with genetic medicine as described in this case study? Explain your perspective.
- Are there any other diseases you know of that currently are or could potentially be treated or cured through genetic medicine?
- Search newspapers, magazines, or the scientific literature for diseases being treated through genetic medicine. Have there been successes? Failures?

CREDITS

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