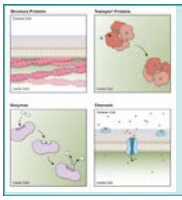


Central Dogma Card-Sorting Activity

hhmi | BioInteractive

Activity
Educator Materials

OVERVIEW

Ever since the discovery of the structure of DNA, scientists have thought that diseases caused by mutations in single genes could someday be treated by intervening in the steps that are carried out from DNA to RNA to protein. This flow of information represents the way most genes are expressed in eukaryotic cells and is also referred to as the central dogma of molecular biology.

In this activity, students will review the steps of eukaryotic gene expression and apply their knowledge of the central dogma to propose new treatment strategies for certain genetic diseases. Next, students will explore a Web-based interactive to learn about the cutting-edge research being done in the field of genetic medicine.

KEY CONCEPTS

- Genes are regions in the DNA that contain the instructions that code for the formation of proteins, which carry out most of the work of cells.
- In most cases, genetic information flows from DNA to mRNA to protein; genetic diseases can be treated at different steps in this pathway.
- The sequence of DNA determines the type and order of amino acids in a protein, which determines the protein's three-dimensional shape and its function.
- Phenotypes, including disease phenotypes, are determined through protein activities.
- New genetic biotechnologies can intervene at various steps from DNA, to RNA, to proteins, ultimately affecting protein structure and function.
- Identifying the mutation that causes a disease can provide a way of treating that disease.

STUDENT LEARNING TARGETS

- Organize the steps of eukaryotic gene expression and identify the primary molecules involved in each step.
- Analyze genetic disease information to predict possible intervention strategies.
- Investigate cutting-edge technologies used in current research to develop intervention strategies for a specific genetic disease.

CURRICULUM CONNECTIONS

Standards	Curriculum Connection
NGSS (2013)	HS-LS1-1, HS-LS3-1, HS-LS3-2
AP Bio (2015)	1.B.1, 3.A.1, 3.A.3, 3.B.1, 3.C.1, 4.A.1, SP1, SP6
IB Bio (2016)	2.4, 2.6, 2.7, 3.1, 3.4, 3.5, 7.2, 7.3, B.4
Common Core (2010)	ELA.RST.9-12.4, WHST.9-12.9
Vision and Change (2009)	CC2, CC3, DP1

KEY TERMS

DNA, exon, gene expression, genetic medicine, genotype, intron, mRNA, mutation, phenotype, protein, RNA splicing, transcription, translation

TIME REQUIREMENTS

- One 50-minute class period is required for the card-sorting activity and items 1-4.
- An additional 50-minute class period is required for item 5 (the computer Click & Learn) and item 6.
- See TEACHING TIPS below for alternative timing strategies.

SUGGESTED AUDIENCE

- High School Biology (General, AP/IB)
- College-level general biology

PRIOR KNOWLEDGE

Students should

- know the steps of eukaryotic gene expression and the main molecules involved at each step.
- understand the flow of information from DNA to RNA to protein and the connection to phenotype.
- know what a genetic mutation is and how it can potentially impact the structure and function of a protein.

MATERIALS

- One set of cut-out cards per group
- One copy of the student handout per student
- Access to the Click & Learn "Central Dogma and Genetic Medicine"
- One copy of the Click & Learn student worksheet per student (optional)
- A computer (with sound/headphones) for the Click & Learn

TEACHING TIPS

- Consider having students work in pairs or small groups of up to 4 students to complete the card-sorting activity, labeling, and analysis questions.
- Two different classroom implementation strategies are outlined below in the "Implementation Suggestions" section, which also use the student worksheet that accompanies the Click & Learn.
- Your students may have difficulty coming up with ways to treat the different diseases. If they are struggling, offer them some feedback as you walk around the class. For question 3, you might suggest finding a way to turn on fetal hemoglobin transcription and to think of the molecules involved in regulating transcription. For question 4, offer the hint that you might want to block production of the abnormal protein and to think of the molecules involved in translation and how you could prevent translation of that protein.
- To use less class time, consider having students complete the Central Dogma and Genetic Medicine Click & Learn as homework after completing the card-sorting activity and questions 1-4 on day 1. On day 2, the student groups can reconvene to answer question 6 together, which should take approximately 10 minutes.
- Consider laminating the central dogma card sets to use from class to class and year to year. The students could also label them using Expo markers that can be erased easily.
- The last question in the student worksheet that accompanies the Click & Learn is about a disease called progeria. You may be familiar with a film about progeria called "Life according to Sam"; the main protagonist, who unfortunately has since passed away, gave a Ted Talk.
- After completing the activity and Click & Learn, if you'd like to learn more about Genetic Medicine, watch the HHMI BioInteractive short film *Genes as Medicine*.

PROCEDURE

The table below provides two strategies for implementing the Central Dogma card-sorting activity, the Central Dogma and Genetic Medicine Click & Learn, and associated worksheets in the classroom.

Implementation Suggestions

- Strategy A: more appropriate for students who recently learned about the steps and molecules of gene expression
- Strategy B: more appropriate for students who are reviewing the steps and molecules of gene expression from previous years

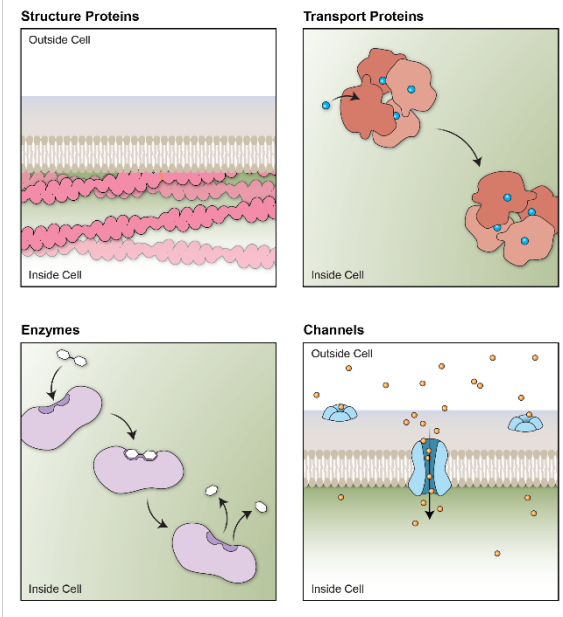
Timing	Strategy A	Strategy B
Day 1 (50-min class period)	• Complete the card sorting and labeling. • Confirm card sorting and labeling with instructor. • Complete the card-sorting activity questions 1-4.	• Complete the card sorting (without labeling) • Start the Click & Learn. Review only the Central Dogma tab to review the steps and molecules of gene expression. • Complete the Click & Learn student worksheet, questions 1-3.
Day 2 (50-min class period)	• Start the Click & Learn and complete the card-sorting activity question 5. • Complete the Click & Learn student worksheet, questions 1, 3, and 4 (omit 2). ***Note**: Consider jig-sawing items 3 and 4 within each student group, having each student report out to the others.* • Return to the card-sorting activity questions and complete question 6.	• Revisit the card-sorting activity, labeling the steps and molecules on each card, and share out with the group. • Complete card-sorting activity questions 2-4. • Return to the Click & Learn student worksheet and complete question 4. • Reconvene groups, discuss answers to questions 2-4 of the card-sorting activity, and revise if necessary.
Future day (assessment)	Instructor uses Click & Learn student worksheet question 5 as a follow-up assessment question.	Instructor uses Click & Learn student worksheet question 5 as a follow-up assessment question.

ANSWER KEY

1. A genotype is the complete genetic makeup of an individual, whereas a phenotype is all observable characteristics of the individual. Because genes direct the production of proteins and proteins are responsible for an individual's observable characteristics, genotypes control phenotypes. The final card in the series shows a mature protein. Proteins can play several different cellular functions, as shown in the figure below.

   Using prior knowledge, describe a specific role each type of protein performs for the cell and provide an example. (Write your answer next to each picture.)

   - *Structure: proteins that perform a structural role in a cell or tissue by giving the cell its shape or support. Examples: microfilaments, keratin, actin, collagen, and dystrophin.*
   - *Transport: proteins that move materials into, out of, or throughout a cell, tissue, or organism. Examples: hemoglobin, sodium-glucose co-transporter, ATP synthase, and the sodium-potassium pump.*
   - *Enzymes: catalytic proteins that speed up chemical reactions by lowering the activation energy required for the reaction. Examples: pepsin, amylase, lactase, DNA polymerase, and RNA polymerase.*
   - *Channels: proteins that allow the transport of specific substances across a cell membrane. Examples: sodium channels, calcium channels, and aquaporins.*



2. Cystic fibrosis is a devastating illness that affects the lungs, pancreas, and intestines. In 1989, researchers discovered that the disease is caused by a mutation in a gene that produces a protein that channels chloride across cellular membranes. People with two copies (or alleles) of the mutated gene have a buildup of mucus in the airways, intestines, and other organs due to nonfunctioning or absent channel proteins. Suggest two ways you could intervene to treat the disease by targeting the DNA molecule and justify why each approach could be effective.

Student answers will vary, but answers should be scientifically sound. One possible student answer is "fix the gene by changing the DNA sequence." If students have greater prior knowledge in this area, they might say "use CRISPR-Cas9 technology to edit the DNA sequence." Another possibility is "introduce a nonmutated gene into the appropriate cells." Again, students might refer to this approach as gene therapy.

3. Like cystic fibrosis, sickle cell anemia is an autosomal recessive condition. It can be caused by mutations in the gene for β-globin (HBB). HBB is one of the two subunits of adult hemoglobin, the protein that carries oxygen in red blood cells. People who inherit two copies of the mutation produce abnormal hemoglobin, and their tissues are starved of oxygen. One interesting finding is that some individuals with HBB mutations do not have sickle cell anemia because they have another mutation that allows them to produce fetal hemoglobin throughout their lives. Fetal hemoglobin production is normally turned off after birth. Based on this knowledge, suggest two ways you could treat sickle cell anemia by targeting the transcription step of the fetal hemoglobin gene and justify why each approach might be effective.

Student answers will vary, but answers should be scientifically sound. Depending on a student's prior knowledge, he/she might suggest introducing the necessary activators and transcription factors to begin transcription or a way to remove any repressors that might be present keeping the transcription of the fetal hemoglobin gene off.

4. Another disease caused by a mutation in a single gene is Huntington's disease (HD), an autosomal dominant condition. It is caused by mutations in a gene required for normal nerve cell function. The mutations cause abnormal proteins to be produced which "stick" together and accumulate in nerve cells, eventually interfering with normal cell operations. Suggest two ways you could treat the disease by targeting the translation step for the HD protein and justify why each approach might be effective.

Student answers will vary, but answers should be scientifically sound. A student might suggest blocking the mRNA from being translated by the ribosome or destroying the mRNA so that it cannot be translated.

5. (Optional) For any genetic disease, several approaches for treating it at different steps of gene expression could work. Complete the Click & Learn "Central Dogma and Genetic Medicine," paying particular attention to the genetic medicines that have been developed or are in development for the diseases above. Were the approaches you identified in this activity like the ones in the interactive? If so, how were they similar? If not, how did they differ? *Student responses will vary.*

6. Consider hemophilia again. Identify two ways the researcher could design an intervention to treat hemophilia, provide a brief explanation of each, and justify why each approach might be effective.

Student answers will vary, but answers should be scientifically sound. Possible answers include: gene therapy introducing a healthy gene into the proper blood cells that secrete the specific clotting factors; CRISPR-Cas9 to edit the gene in the proper blood cells that secrete the specific clotting factors; or develop a small-molecule oral drug that increases the concentration of clotting factors similar to the current infusions.

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