Differential Gene Expression:
Enhancers and Transcription Factors

Why?

The trillions of cells in the human body can be categorized into hundreds of specialized cell types. Examples of specialized cells include skeletal muscle cells that contract and relax, red blood cells that carry oxygen from the lungs to tissues, and photoreceptors in the retina that detect light and send an electrical signal to the brain in response. All of these cells arise from the original fertilized egg. How does one cell give rise to hundreds of different specialized cell types that all contain the same DNA? The answer lies in how the genetic information in each cell is used, leading to the production of different collections of proteins in each different cell type. In this activity, you will explore how cells utilize different genes to become specialized in their structure and function.

Learning Goals

When you have successfully completed this activity, you will be able to:

1. Explain and illustrate how cells that contain the same DNA can produce different proteins.
2. Predict the activity of genes based on the presence of relevant transcription factors and enhancer regions.
3. Form an argument and reach a conclusion supported with evidence from the Models and from your knowledge of molecular biology. [Process skill goal: *critical thinking*]

Pre-requisite knowledge

- Cell structure and mitotic division
- The Central Dogma of Biology (DNA is transcribed into mRNA which is translated into protein)
- General molecular characteristics of nucleic acids and proteins

Notes

- The models are found at the end of the activity and can be detached for ease of use.
- [RQ] signifies that the question is a review question. All other questions can be answered by analyzing the models, but review questions require you to remember information from previous lessons or courses.
- [RQ+] signifies that the question connects review material to new content from the activity.

Team Roles

- Manager: keeps track of time and ensures that the team progresses together through the activity.
- Spokesperson: speaks for the team and is the only team member who can ask questions of the instructor.
- Consensus Builder: ensures that all members of the team are contributing ideas to discussions and that each member has agreed upon and recorded an answer before the team moves to the next question.
- Model Wrangler: focuses the team's attention to relevant parts of the models and makes sure that all parts of the models are considered when coming up with an answer to a question.

Megan Morgan Hoffman, Berea College

POGIL APPROVED ACTIVITY

https://doi.org/10.62629/EBMK7491

Model 1: DNA, RNA, and Protein in Different Cell Types

See page 14.

Model Wrangler: Place Model 1 where all team members can see it clearly. As the team examines the model and answers questions, point to the areas that you and other team members are discussing.

Manager: consider having team members take turns reading a question and providing a tentative answer prior to team discussion.

1. List the four cell types illustrated in Model 1.

2. Label the cytoplasmic region in the hair cell.

3. [RQ+] List the **six** proteins found in the cells.

4. What molecule does the black, wavy ribbon represent? 

5. According to the figure legend for Model 1,
   a. What type of molecule is designated by the italicized label, *protX*? (choose one)
      i. DNA
      ii. RNA
      iii. Protein
      iv. More than one of these molecules

   b. What type of molecule is designated by the non-italic, capitalized label, ProtX? (choose one)
      i. DNA
      ii. RNA
      iii. Protein
      iv. More than one of these molecules

6. Answer the questions below about the *protX* gene in the hair cell.
   a. List the five labeled regions of the gene.

   b. Which cell type(s) contain DNA for *protX*?
      i. Liver cell
      ii. Brain cell
      iii. Hair cell
      iv. Muscle cell
      v. All of the above

   c. Explain the details of Model 1 that led to your team's answer to the previous question.

   d. [RQ+] Use your knowledge of mitosis to explain why you would expect *all cells*[1] in the body to contain identical DNA.

Consensus Builder: Once your team members have agreed on an answer to Question 6d, check with another team to see if they agree with your answer. If not, bring the two teams together to talk through their reasoning and try to come to a consensus.

Spokesperson: If the two teams cannot come to consensus, ask your instructor to clarify the issue.

[1] A very few cells in the body contain different DNA combinations in their mature state. Mature sperm and egg cells that contain only half of the chromosomes of other cells, and mature red blood cells and lymphocytes are exceptions. As a rule, however, all cells contain the same DNA as they move along their developmental paths.

7. Answer the following questions about ProtM.
   a. What cell(s) contain(s) ProtM?

   b. Where in the cell(s) is ProtM located? Circle the correct answer.
      i. In the nucleus
      ii. In the cytoplasm
      iii. In both regions
      iv. In neither region

   c. To what molecule does ProtM bind **and** where on that molecule does it bind?

8. Identify the RNA polymerase II molecule in Model 1.
   a. What is the abbreviation used for RNA polymerase II?

   b. Is RNApol-II found in all four cell types?

   c. In what region of the cell is the RNApol-II found? Circle the correct answer.
      i. In the nucleus
      ii. In the cytoplasm
      iii. In both regions
      iv. In neither region

   d. In some of the cells, the RNApol-II binds to another molecule. What molecule is this **and** where on that molecule does the RNApol-II bind?

   e. [RQ] What cellular process begins with the binding of RNApol-II to DNA?

   f. [RQ] What molecule is made by this process?

g. Is the RNApol-II bound to the promoter region of the *protX* gene in all of the cell types in Model 1?

h. Using the table below, compare the presence or absence of RNApol-II binding to other characteristics of the four cell types.

	Muscle cell	Hair cell	Liver cell	Brain cell
Is RNApol-II bound to the promoter region?				
What protein(s) is/are bound to an enhancer region?				
What protein(s) is/are present in the cytoplasm?				
What mRNAs are present?				
Add other observations, if any				

i. [RQ+] Which of the factors in the table *lead to* RNApol-II binding and which are the *results* of RNApol-II binding?

9. Messenger RNA from the *protX* gene (mRNA-X) is produced in the nucleus and moves to the cytoplasm.

a. [RQ] What process is performed *in the cytoplasm* using this mRNA?

b. [RQ] What organelle is necessary for this process but is not illustrated in Model 1?

c. What protein will be produced from this messenger RNA by this cytoplasmic process?

10. Which cell type(s) does/do not produce ProtX?
    a. Does this cell type contain the *protX* gene?

    b. Does this cell type contain RNApol-II?

    c. Propose a hypothesis to explain why the muscle cell produces ProtX but this cell does not.

11. Using your analysis of Model 1, describe the sequence of events leading to ProtX production in liver cells.

12. Proteins M, L, B, and H are called **transcription factors**.
    a. Given the apparent function of proteins M, B, and L in Model 1, define *transcription factor*.

    b. What is the general name of the gene region to which a transcription factor binds?

    c. ProtH is also a transcription factor. If the hair cell has a transcription factor, an RNA polymerase II molecule, and the *protX* gene, why doesn't the hair cell produce mRNA-X or Protein X?

13. As a team, write a statement about how transcription factors and enhancer regions work together to control the transcription of a gene.

14. Consider these hypothetical situations:

    a. If the muscle cell in Model 1 contained a normal *protX* gene and RNApol-II, but lacked ProtM, would you expect the cell to produce Protein X? Explain your reasoning.

    b. If ProtL were injected into the nucleus of the hair cell in Model 1, would you expect the hair cell to produce ProtX? Explain your reasoning.

    c. What would you expect to happen if ProtM were injected into the nucleus of the brain cell in Model 1? Explain your reasoning.

Spokesperson: Be prepared to share your team's answers to Question 14 with the rest of the class. Include the reasoning your team used to come to agreement on the answers.

Manager: Lead a brief discussion with your team on how well you are pulling information out of the Model and building your understanding of the material.

What is one strength of your team's work in this area?

What is one way your team could improve?

……

Human cells contain at least 20,000 different genes and hundreds of transcription factors, so the situation is more complicated than is illustrated in Model 1. Although still simplified, Model 2 illustrates the increased complexity that results from adding additional genes and transcription factors. (Note: Refer back to Model 1 for symbols not explained in Model 2's figure legend.)

……

Model 1: DNA, RNA, and Protein in Different Cell Types

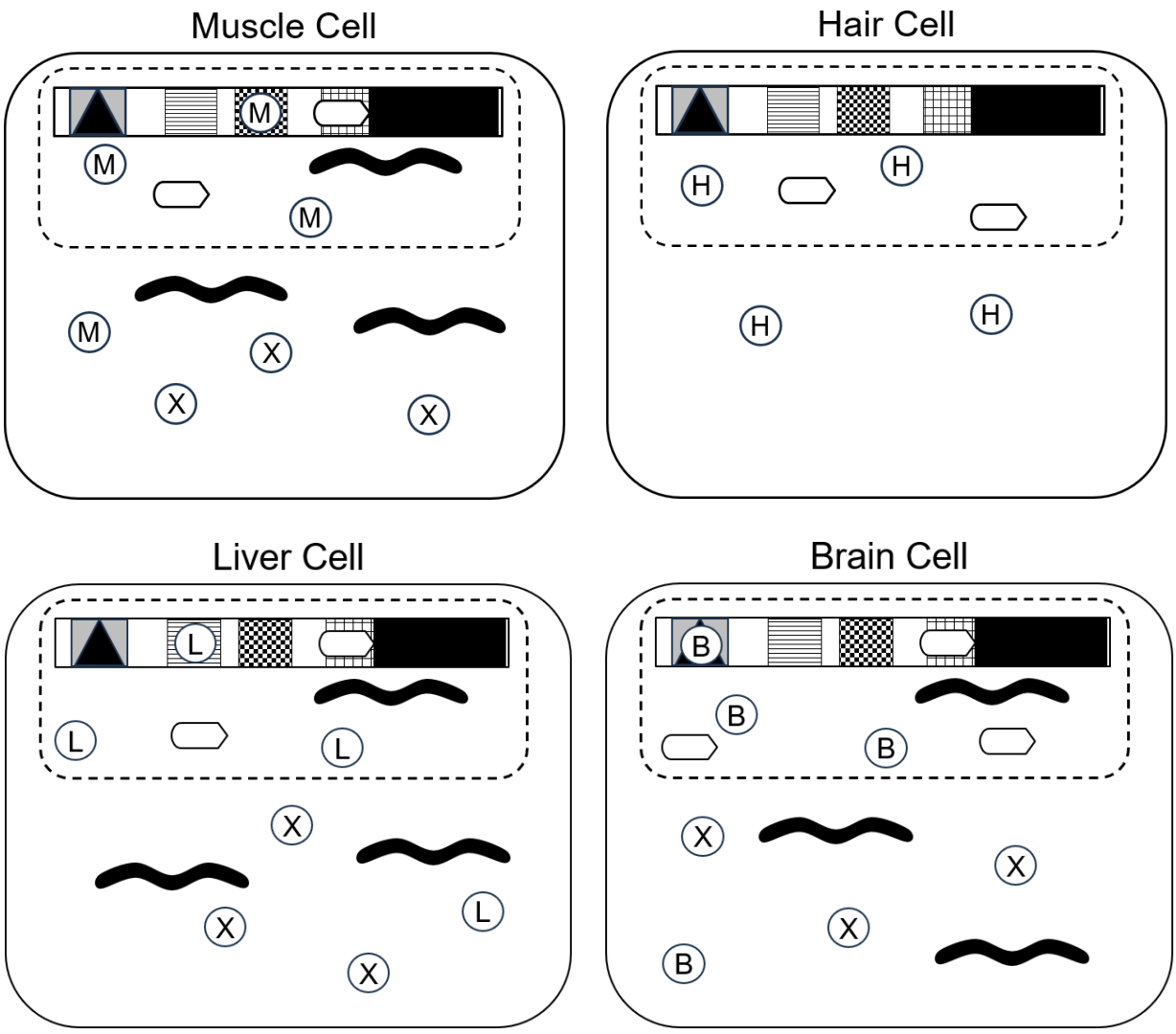

Figure Legend for Model 1			
DNA for the Protein X gene (*protX*)		Protein B (ProtB)	B
ProtB-specific enhancer region			
ProtL-specific enhancer region		Protein H (ProtH)	H
ProtM-specific enhancer region			
Promoter region		Protein L (ProtL)	L
Coding region for *protX*			
RNA polymerase II (RNApol-II)		Protein M (ProtM)	M
Messenger RNA for Protein X (mRNA-X)			
Nuclear membrane		Protein X (ProtX)	X
Cell membrane			