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LESSON:

Mutations, Proteins, and Autism: Modeling a Pathway

Summary: Students make a model of cell parts including the endoplasmic reticulum, ribosomes, proteins, and the golgi apparatus and learn about the creation and distribution of proteins in cells. Then they show how a mutation can affect the formation, distribution, and function of two proteins that may be linked to autistic spectrum disorders.

Lesson Type: Graphic Organization and Modeling—This lesson has students organize information graphically (e.g. using figures, graphs, and/or webs) or by creating a model.

***EHP* Article:** "Misfolded Protein Presents Potential Molecular Explanation for Autism Spectrum Disorders"
EHP Student Edition, October 2006, p. A409
http://www.ehponline.org/docs/2006/114-7/niehsnews.html#syne

Objectives: By the end of this lesson, students should be able to

1. create a model of the endoplasmic reticulum and golgi apparatus of the cell, and describe their functions; and
2. describe how a mutation can impact the function of certain proteins, including how the malfunction can result in specific diseases.

Class Time: 1 hour

Grade Level: 9–12

Subjects Addressed: Biology, Biochemistry, Anatomy/Physiology

Prepping the Lesson

INSTRUCTIONS:

1. Download the entire October 2006 *EHP Student Edition* at http://www.ehponline.org/science-ed/, or download just the article "Misfolded Protein Presents Potential Molecular Explanation for Autism Spectrum Disorders" at http://www.ehponline.org/docs/2006/114-7/niehsnews.html#syne.
2. Review the Background, Instructions, and Student Instructions.
3. Make copies of the Student Instructions and gather the materials needed for each pair of students.

MATERIALS

per student:

- 1 copy of *EHP Student Edition*, October 2006, or 1 copy of "Misfolded Protein Presents Potential Molecular Explanation for Autism Spectrum Disorders"
- 1 copy of the Student Instructions

per pair of students:

- 2 pieces of paper
- Scissors
- Tape
- 2 small blank label stickers
- 1 pen or pencil
- 1 marker
- 1 paperclip

VOCABULARY:
- autism
- eukaryotic
- endoplasmic reticulum
- enzyme
- etiology
- genes
- golgi apparatus
- homologous
- mutation
- neurotransmitter
- protein

BACKGROUND INFORMATION:
The article and Student Instructions provide sufficient background information for the lesson. The Resources section provides links for more detailed information about the endoplasmic reticulum and the golgi apparatus. The October 2005 *EHP Student Edition* lesson "Protein Puzzles" may complement this lesson by providing more information on protein structure and other potential impacts of mis-folded proteins (such as mad cow disease and diabetes).

RESOURCES:
Environmental Health Perspectives, Environews by Topic page, http://ehp.niehs.nih.gov. Choose Genetic Research, Neurology

Cellupedia, Golgi apparatus, http://library.thinkquest.org/C004535/golgi_apparatus.html

De Jaco A, Comoletti D, Kovarik Z, Gaietta G, Radić Z, Lockridge O, et al. 2006. A mutation linked with autism reveals a common mechanism of endoplasmic reticulum retention for the α,β-hydrolase fold protein family. J Biol Chem 281:9667–9676, http://www.jbc.org/cgi/content/full/281/14/9667.

EHP Student Edition, "Protein Puzzles" lesson, October 2005, http://www.ehponline.org/science-ed/lessons2005.html

University of Texas Medical Branch, Endoplasmic reticulum: structure and function, http://cellbio.utmb.edu/cellbio/rer1.htm

Wikipedia, Endoplasmic reticulum, http://en.wikipedia.org/wiki/Endoplasmic_reticulum

Wikipedia, Golgi apparatus, http://en.wikipedia.org/wiki/Golgi_apparatus

Implementing the Lesson

INSTRUCTIONS:
1. Divide the students into pairs and hand out the supplies and instructions for the activity.
2. Review the instructions with your students as needed.
3. After the students have completed Steps 4 and 5 you can have them turn in their work to you or share their models with each other in class and discuss their responses to the questions. Sharing and discussion is encouraged to advance their understanding.

NOTES & HELPFUL HINTS:
- Although it is helpful for students to be familiar with eukaryotic cells as they begin this lesson, it is not a prerequisite for completing the lesson successfully.
- An extension of this lesson could involve having students create scaled models of the cell parts and proteins. This would involve math skills using a scaling factor, and can help students conceptualize size and proportion.
- Students could investigate in more depth any of the cell parts and processes discussed in this lesson.
- This lesson would pair nicely with other *EHP Student Edition* lessons that discuss autism, including "Tracing the Origins of Autism: A Spectrum of New Studies" (October 2006) and "Three Is a Toxic Number" (September 2005).

Aligning with Standards

SKILLS USED OR DEVELOPED:
- Classification
- Communication (note-taking, oral, written—including summarization)
- Comprehension (listening, reading)

- Critical thinking and response
- Manipulation
- Observation

SPECIFIC CONTENT ADDRESSED:

- Eukaryotic cells
- Protein formation
- Mutation
- Neurotransmitters
- Autism spectrum disorders

NATIONAL SCIENCE EDUCATION STANDARDS MET:

Science Content Standards

Unifying Concepts and Processes Standard

- Systems, order, and organization
- Evidence, models, and explanation
- Change, constancy, and measurement
- Evolution and equilibrium
- Form and function

Life Science Standard

- The cell
- Molecular basis of heredity
- Matter, energy, and organization in living systems
- Behavior of organisms

Science in Personal and Social Perspectives Standard

- Personal and community health

Assessing the Lesson

Step 2: Instructions to create the model are on the Student Instructions. Check to see that the students created and labeled all of the cell parts (endoplasmic reticulum, ribosomes, AChE and BChE proteins, golgi apparatus) per the instructions.

Step 3: Observe the students completing the steps.

Step 4: Read the article "Misfolded Protein Presents Potential Molecular Explanation for Autism Spectrum Disorders" and answer the following questions.

a. What do the mutations in the two genes (*neuroligin 3* and *neuroligin 4*) appear to do to the proteins AChE and BChE?

The mutation appears to make the proteins fold incorrectly, which makes them stick to the endoplasmic reticulum and bond incorrectly with its partner β-neurexin.

b. Using your cell parts model, create a visual model of your answer to question 4a (showing how the mutation appears to affect AChE and BChE). Discuss your ideas with your partner as needed, and then give the new "mutated" model to your teacher.

The most obvious adaptation to the model would be to take the backing off the stickers that represent the proteins AChE and BChE and stick them to the endoplasmic reticulum. There may be some different approaches; just be sure they are accurate and that the students can justify why they created their model that way. The lesson does not discuss the bonding changes with β-neurexin, so students are not expected to show this aspect.

Step 5: Answer the following question using complete sentences. Although you can discuss the answer with your partner to help your understanding of the information in the article, write your answers individually in your own words (do not have the same wording as your partner or classmates).

a. Why are the mutations of the genes *neuroligin 3* and *neuroligin 4* important? Be sure to consider the roles of the AChE and BChE proteins as described in Step 2e and the potential "real-life" impacts as described in the article.

The mutations cause the proteins AChE and BChE to form incorrectly, which affects their ability to do their job of facilitating the action of specific neurotransmitters. This change may be linked to autism.

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Give us your feedback! Send comments about this lesson to ehpscienceed@niehs.nih.gov.

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STUDENT INSTRUCTIONS:

Mutations, Proteins, and Autism: Modeling a Pathway

Step 1: Divide into teams of two and make sure you have the following materials:

- 2 pieces of plain or construction paper
- Scissors
- Tape
- 2 small blank label stickers
- 1 pen
- 1 marker
- 1 paperclip

Step 2: For the first part of this lesson you are going learn about and construct some parts of a eukaryotic cell. Eukaryotic cells are those found in animals and people. These cells have a nucleus surrounded by a membrane.

One part of a cell is the endoplasmic reticulum (ER). The ER is a membrane consisting of tubes and folds. One of the main jobs of the ER is to make and deliver proteins.

With your partner, complete the following steps to create a model of an ER:

a. Cut a piece of paper in half and fold it in a zig-zag fashion like a fan or accordion.

b. Write the words "rough ER" on one end of the fan.

c. Use your marker to make round dots all over this "rough ER."

d. Use your pen to label one of the dots "ribosome." The ribosome assembles amino acids to make proteins.

e. On one small blank label sticker write the letters "BChE." On the other sticker write "AchE." Leave the backing on these stickers and set them aside for now.

You need to know that BChE (butyrylcholinesterase) and AChE (acetylcholinesterase) are both a type of protein called an enzyme. These enzymes help facilitate the action of specific neurotransmitters, which communicate signals to and from our brain to the rest of our body. Different neurotransmitters have different jobs, such as muscle movement, keeping us awake or asleep, causing our emotions, and transmission of sensations like pain. You will use these proteins later as part of the activity.

f. Cut 2–3 strips of paper about 2 inches wide and 3 inches long.

g. Roll each strip lengthwise into a tube and tape to hold the tube shape in place.

h. Tape the tubes together side-by-side and label them "smooth ER." The smooth ER does not have any ribosomes, which is why it is called "smooth."

i. Take one final strip of paper about 3 inches by 6 inches in size and fold it into another fan. Label this "golgi apparatus."

Step 3: You are now ready to see how these parts of the cell work together. Refer to the image showing protein synthesis and delivery in the cell.

a. Working with your partner, one of you should hold the "rough ER."

b. Get the BChE and AChE stickers. Leaving the backs on the stickers, place them inside the folds of the "rough ER." This indicates that the ribosomes are making BChE and AChE (genes provide the instructions to the cell for how to make the BChE and AChE proteins).

c. The assembled proteins are then moved to the "smooth ER" for further processing. So, slide the loose BChE and AChE from the "rough ER" to the "smooth ER" tubes.

d. Now the proteins (enzymes) are ready to be transferred to the "golgi apparatus." Slide the BChE and AChE proteins onto the paperclip for transport over to the "golgi apparatus," where they will be removed from the paperclips, dropped off, and sorted for delivery (like a post office) to other places in the cell.

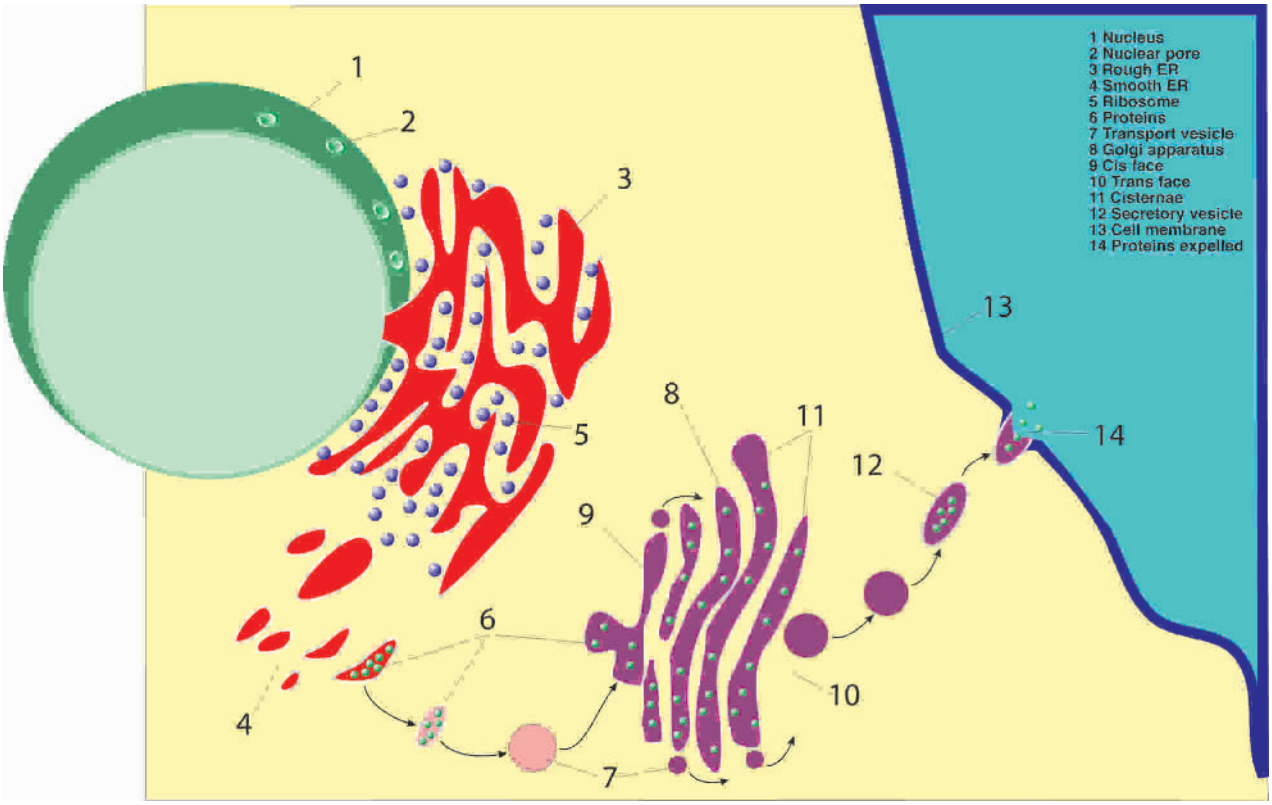

image credit: Magnus Manske

Step 4: Read the article "Misfolded Protein Presents Potential Molecular Explanation for Autism Spectrum Disorders" and answer the following questions.

a. What do the mutations in the two genes (*neuroligin 3* and *neuroligin 4*) appear to do to the proteins AChE and BChE?

b. Using your cell parts model, create a visual model of your answer to question 4a (showing how the mutation appears to affect AChE and BChE). Discuss your ideas with your partner as needed, and then give the new "mutated" model to your teacher.

Step 5: Answer the following question using complete sentences. Although you can discuss the answer with your partner to help your understanding of the information in the article, write your answers individually in your own words (do not have the same wording as your partner or classmates).

a. Why are the mutations of the genes *neuroligin 3* and *neuroligin 4* important? Be sure to consider the roles of the AChE and BChE proteins as described in Step 2e and the potential "real-life" impacts as described in the article.