ehp

LESSON:

Protein Puzzles

Summary: Students read the *EHP Student Edition* article "The Shape of Food Allergenicity" and then learn about primary, secondary, and tertiary protein structure. Students then construct a 3-D model of an insulin protein and investigate how protein structure relates to allergens, insulin resistance, and mad cow disease. 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: "The Shape of Food Allergenicity"
EHP Student Edition, October 2005, p. A448
http://ehp.niehs.nih.gov/docs/2005/113-7/forum.html

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

1. identify the basic building blocks of proteins;
2. differentiate between primary, secondary, and tertiary structures of proteins; and
3. list examples of how protein structure relates to its functionality.

Class Time: 2 hours for Steps 1 and 2
4 hours for Steps 1, 2, and 3

Grade Level: 9–12

Subjects Addressed: Biology, Biochemistry, Molecular Biology, Environmental Health, Health

Prepping the Lesson (20–25 minutes)

INSTRUCTIONS:

1. Obtain a class set of *EHP Student Edition*, October 2005, or download the article "The Shape of Food Allergenicity" at http://ehp.niehs.nih.gov/docs/2005/113-7/forum.html.
2. Make copies of the Student Instructions, including the page titled "The Insulin Protein Puzzle."
3. Reserve computer lab space and gather the materials. If students do not have Internet access, then print and copy the webpages for students to be able to complete Step 3.
4. Review the article and Student Instructions.

MATERIALS:

- 1 copy of *EHP Student Edition*, October 2005, or 1 copy of "The Shape of Food Allergenicity" per student
- 1 copy of Student Instructions, including the page titled "The Insulin Protein Puzzle" per student
- 1 set of coloring markers per group
- Scissors, per student or group as available
- Clear tape, per group
- Computers with Internet access, or copies of the webpages listed in Step 3.

VOCABULARY:

- allergen
- alpha (α)-helix
- amino acids
- atom
- beta (β)-sheet
- carbohydrate
- element
- enzymes

- genes
- insulin
- molecule
- peptide
- polypeptide
- primary structure
- protein
- secondary structure
- tertiary structure

BACKGROUND INFORMATION:
The article, assessment section, and student handouts provide sufficient information.

RESOURCES:
Environmental Health Perspectives, Environews by Topic page. Choose Molecular Biology, Proteomics, http://ehp.niehs.nih.gov/topic

Entrez Protein databases, NCBI, http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Protein

Insulin: Monomers, Dimers, and Hexamers, University of London, http://www.med.unibs.it/~marchesi/pps97/course/section11/insulin.html

Insulin Resistance and Pre-diabetes, National Diabetes Information Clearinghouse, http://diabetes.niddk.nih.gov/dm/pubs/insulinresistance/

Principles of Protein Structure, Birbeck College, http://www.cryst.bbk.ac.uk/PPS2/top.html

Proteins, Virtual Chembook, http://www.elmhurst.edu/~chm/vchembook/565proteins.html

Protein Structure, http://web.indstate.edu/thcme/mwking/protein-structure.html

Protein Structure and Function, http://medweb.bham.ac.uk/bmedsci/bms2/chime/structure/structure.html

Implementing the Lesson

INSTRUCTIONS:
1. Have students read the article "The Shape of Food Allergenicity."
2. Review amino acids, proteins, and protein structure as needed.
3. Hand out the Student Instructions, including the page titled "The Insulin Protein Puzzle."
4. Review the instructions on constructing a model of the insulin protein under Step 2. Students will build their insulin protein individually but will share scissors, tape, and markers as needed. Some tips to help the students build their model: a) Cut the strips by rows (not columns) since they are already sequentially numbered. b) Point out that there will be two separate strips labeled "a" and "b." c) When the students make their spiral (secondary structure) they can wrap the strip around their finger loosely and then tape.
5. In order to complete Step 3, students will need either Internet access or printouts of the webpages listed under Step 3 in the Student Instructions.

NOTES & HELPFUL HINTS:
- Depending on how advanced your students are, you may consider having the class investigate the types of bonds in the primary, secondary, and tertiary protein structures. Students could even draw the chemical structure on each amino acid and properly align the areas of the amino acid that bond in each structural level.

Aligning with Standards

SKILLS USED OR DEVELOPED:
- classification
- comprehension
- critical thinking and response
- manipulation
- research

SPECIFIC CONTENT ADDRESSED:
- amino acids
- proteins

- protein structure
- allergens
- insulin
- mad cow disease

NATIONAL SCIENCE EDUCATION STANDARDS MET:

Unifying Concepts and Processes Standard
- Systems, order, and organization
- Evidence, models, and explanation
- Form and function

Science As Inquiry
- Abilities necessary to do scientific inquiry
- Understanding about scientific inquiry

Physical Science Standards
- Structure and properties of matter

Life Science Standards
- The cell
- Matter, energy, and organization in living systems

Science and Technology Standards
- Abilities of technical design
- Understanding about science and technology

Science in Personal and Social Perspectives Standard
- Personal and community health
- Environmental quality
- Natural and human-induced hazards

Assessing the Lesson

Step 2: Students color, cut out, and assemble the insulin model. Make sure the amino acids are colored and are in the proper primary sequence (following the sequential numbering for each a and b strand). Check that the proper sections of the protein are spiraled in an α-helix (amino acids are labeled with H). Check that the tertiary structure is properly "bonded" (S1, S2, and S3 labels are matched).

1.a. Which two amino acids occur the most in insulin? Spell out the full amino acid name instead of the abbreviation.

Cystine (there are 6) and Leucine (there are 6)

1.b. Which two amino acids occur only once in insulin? Spell out the full amino acid name instead of the abbreviation.

Lysine and Proline

3.a. Which protein structural level does taping the amino acids together in a linear fashion represent?

Primary

4.a. Which protein structural level does wrapping the protein around your finger represent?

Secondary

4.b. Does insulin have an α-helix, β-sheet structure, or both?

Both

5.a. Which protein structural level does taping the S's (sulfide bonds) together represent?

Tertiary

Step 3: Describe how the 3-D shape of a protein may be related to the following. Students will need to do research on the Internet to answer questions 2 and 3.

1. Proteins that cause allergic responses.

This answer is found in the article "The Shape of Food Allergenicity." The scientists hypothesize that the tertiary structure of the protein generates strong bonds, making the protein stable and resistant to digestion.

2. Insulin resistance is the cause of type 2 diabetes, the most common form of diabetes.

Insulin works by fitting into a special insulin receptor on cells. When the insulin is on the receptor, the cell is "unlocked," and glucose can go from the blood into the cell. Insulin resistance appears to have both a genetic component and a physical component (being overweight). In both circumstances it is believed that the shape of the receptor is altered. This relates to the 3-D structure of the protein because the protein will not fit properly into the receptor in order to give the signal to allow glucose into the cell from the blood.

3. Prions are proteins located on a cell's plasma membrane. The highest concentration of prions are on cells in the central nervous system. The function of a normal prion is unknown. Mad cow disease is caused by a "rogue" prion.

The secondary and tertiary structures of a rogue prion are altered (the primary structure or amino acid sequence remains the same). The secondary structure of a normal prion is an α-helix, whereas the secondary structure of a rogue prion is the β-sheet. Alterations in the secondary structure also affect the shape of the tertiary structure because bonding occurs in different places.

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Images: courtesy of Tudor I. Oprea, University of New Mexico

ehp Student Instructions: Protein Puzzles

Step 1: Read the article "The Shape of Food Allergenicity," *EHP Student Edition*, October 2005, p. A448.

Step 2: Read the information below and follow the instructions to build an insulin protein model.

You probably already know that atoms, the smallest representative sample of an element, bond together to form molecules. Different atoms of elements (like carbon, oxygen, and nitrogen) bond together in different amounts and different ways to form the billions of chemicals that make up everything in our universe. Living things tend to create complex molecules in order to do specific jobs to maintain life.

Some of the complex molecules that help life function are carbohydrates, fats, steroids, and proteins. Some of these molecules are used in cell structure, others are "active" compounds that move or change chemicals. Proteins are a class of chemicals that participate in every function of the living cell, including structural support for the cell, muscle movement, breaking down chemicals (these proteins are called enzymes), turning genes off or on, or cell signaling.

Proteins play a very important role in biology and biochemistry. You can differentiate proteins from other chemicals in a living thing because proteins are made up of amino acids. Proteins also often have complex multidimensional structures. There are 22 amino acids. The human body uses 20 of these amino acids and can make 10 of them on its own. The other 10 we have to get through eating.

When amino acids bond together they are called peptides. "Polypeptide" is simply another name for a protein, where many amino acids are joined together (poly = many). There are proteins that are very short, such as the artificial sweetener aspartame, which is a dipeptide (two amino acids bonded). And there are proteins that contain several thousand amino acids.

When many amino acids bond together, the molecules can get quite large compared to the rest of its microscopic cellular surroundings. Imagine trying to stretch out a 50-foot rope in a 10 x 10 foot room. You would not be able to fully extend the rope into a straight position. You would need to bend or curve the rope, or pile it upon itself. Large proteins face a similar challenge, so they fold in upon themselves to generate a three-dimensional (3-D) structure.

There are three parts to this 3-D structure. The primary structure is the amino acid "chain" bonded together (Figure 1), much like the "straight" rope in our analogy. The order and type of amino acids in this primary structure are what define a specific protein. The amino acid type, order, and number are different for the hemoglobin protein (which carries oxygen in the blood) compared to the insulin protein (which manages sugar in the blood).

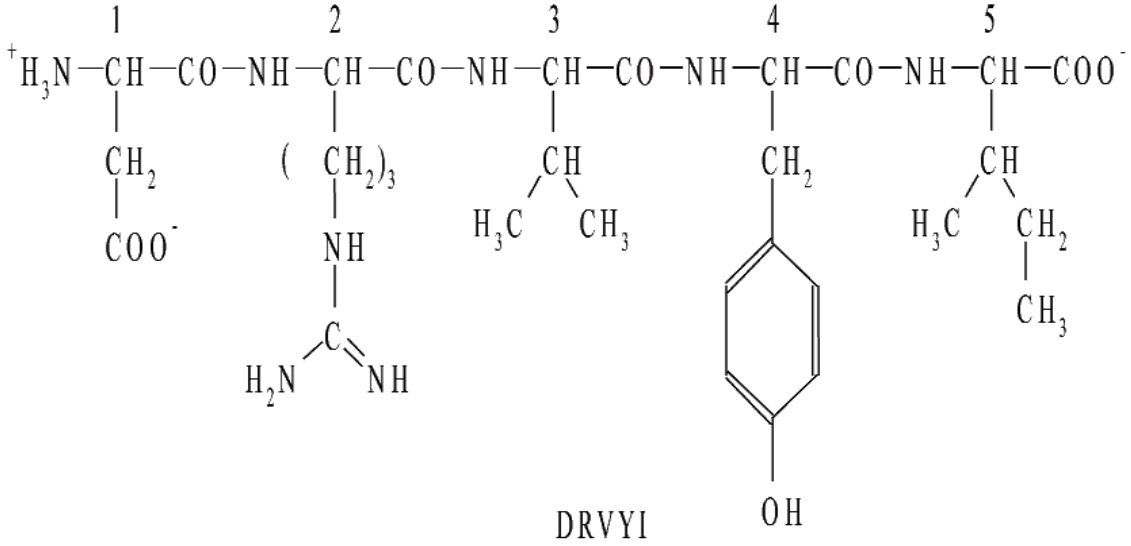

Figure 1: Portion of a peptide chain, the primary protein structure.

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The secondary structure of a protein is the first step of a protein "folding in" on itself. The secondary structure folding is typically in a regular, repetitive pattern, like an alpha (α)-helix, or spiral, or a beta (β)-sheet (Figure 2). For an α-helix structure, imagine taking your rope and swirling it into a circular pile. Then imagine that where each part of the rope touches the rope above and below, they stick together or bond. For a β-sheet you would fold the rope so there are many parallel strands, like making compressed S's or zigzags. The pieces of rope (or protein) that are parallel or next to each other would bond. The bonds are what stabilize the secondary structure.

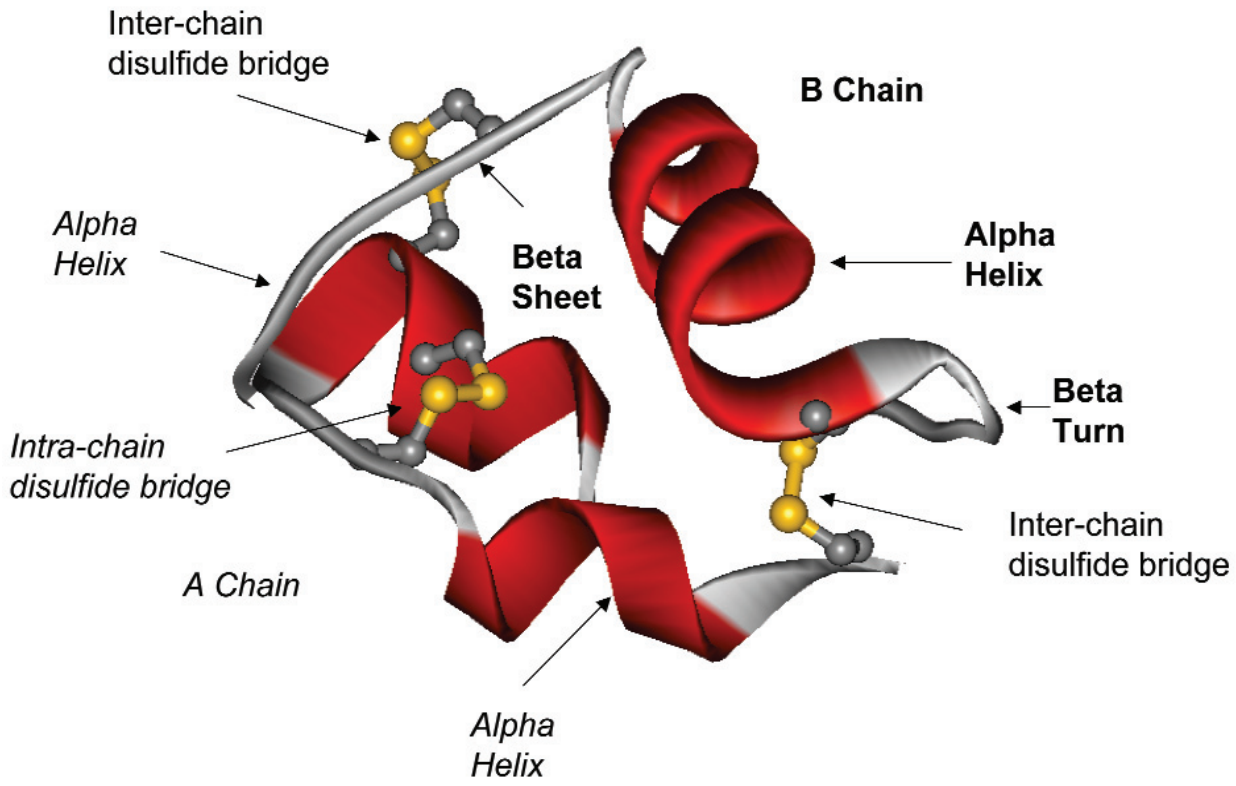

Figure 2: Three-dimensional model of the insulin protein.

The third part of the protein structure is called the tertiary structure (Figure 2). This is additional bending and kinking of the secondary structure to compress the protein even more. Like the primary and secondary structures, the tertiary structure is formed and held by bonds. The really interesting feature of the protein's tertiary structure is its function beyond saving space. The hills and valleys of the outside of the protein act like a key that fits to a specific lock or a puzzle piece. When the key or puzzle piece fits with its intended counterpart, the protein is doing its job—like carrying oxygen, stimulating the release of hormones, or fighting off infection.

Now you are going to build a model of a protein called insulin. Insulin helps regulate the amount of sugar in our blood. People who do not release enough insulin or whose insulin becomes less effective get a disease called diabetes. If diabetes is left untreated, the excess sugar in the body can cause blindness, kidney damage, artery damage, or death. Diabetes can be prevented or managed through a healthy diet of fruit, vegetables, "good" fats (like the fat in nuts, olives, and fish), plenty of water, and exercise. Extreme cases of diabetes require that a person inject insulin into their bodies near meal time.

Follow the steps to build a model of the protein insulin and answer the questions.

1. Refer to the handout titled "The Insulin Protein Puzzle." Color each amino acid rectangle in Table 2 with the assigned color found in the parenthesis next to the amino acid name and abbreviation in Table 1.

1.a. Which two amino acids occur the most in insulin? Using Table 1 on the "Insulin Protein Puzzle" handout, spell out the full amino acid name instead of the abbreviation.

1.b. Which two amino acids occur only once in insulin? Spell out the full amino acid name instead of the abbreviation.

2. Cut out the colored amino acid rectangles. You will save time and effort if you cut in rows (rather than cutting out individual squares) keeping the sequential numbering.

3. Tape the amino acids in the numbered sequence for each strand (a and b). You will end up with two straight strands (1a–21a and 1b–30b).

3.a. Which protein structural level does taping the amino acids together in a linear fashion represent?

4. Spiral the paper sections that are labeled with sequential H's (e.g., 1a–8a). Tape the helix so that it is stable. You may find it helpful to loosely wrap the paper around your finger, then tape the paper.

4.a. Which protein structural level does spiraling represent?

4.b. Does insulin have an α-helix structure, β-sheet structure, or both?

5. Next, tape together the corresponding "disulfide bonds" labeled with S in the upper right-hand corner of some of the amino acids rectangles (pair S1 with S1, S2 with S2, etc.).

5.a. Which protein structural level does taping the S's (sulfide bonds) together represent?

Step 3: Refer to the article "The Shape of Food Allergenicity" to answer question 1 below. You will need to do research on the Internet to answer questions 2 and 3, unless your teacher made copies of the webpages. The website addresses are provided for each corresponding question. Describe how the 3-D shape of a protein may be related to the following:

1. Proteins can cause allergic responses.

2. Insulin resistance in the cell is one mechanism for diabetes. Insulin resistance can be caused by genetics, obesity, or a combination of the two.

   Clinical course of genetic diseases of the insulin receptor (type A and Rabson-Mendenhall syndromes): a 30-year prospective. (Abstract)
   http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Abstract&list_uids=15232309

   Fat Cell Hormone Promotes Type 2 Diabetes, National Institute of Diabetes and Digestive and Kidney Diseases, http://www.niddk.nih.gov/welcome/releases/1-01.htm

3. Prions are proteins located on a cell's plasma membrane. The highest concentration of prions are on cells in the central nervous system. The function of a normal prion is unknown. Mad cow disease is caused by "rogue" prions.

   Prions: Infectious Proteins Responsible for Mad Cow Disease, http://www.bioteach.ubc.ca/Biomedicine/Prions/

The Insulin Protein Puzzle

Table 1: The Amino Acids and Their Abbreviations	
Essential Amino Acids (those the human body cannot generate on its own)	Nonessential Amino Acids (those the human body can generate on its own)
Tryptophan—Trp *(not found in the insulin protein)* Lysine—Lys—(blue stripes) Methionine—Met *(not found in the insulin protein)* Phenylalanine—Phe—(orange dots) Threonine—Thr—(black dots)) Valine—Val—(orange) Leucine—Leu—(green dots) Isoleucine—Ile—(yellow) Histidine—His—(brown dots) (essential in children) Arginine—Arg—(orange stripes) (essential in children)	Tyrosine—Tyr—(red dots) Glycine—Gly—(red) Serine—Ser—(green dots) Glutamic acid—Glu—(blue) Aspartic acid—Asp *(not found in the insulin protein)* Cystine—Cys—(purple) Proline—Pro—(purple stripes) Alanine—Ala—(green stripes) Aspargine—Asn—(purple dots) Glutamine—Gln—(green)

Table 2: Insulin Amino Acids to Cut Out														
1a	H Gly		2a	H Ile		3a	H Val		4a	H Glu	S1	5a	H Gln	
6a	H Cys		7a	H Cys	S2	8a	H Thr		9a	 Ser		10a	 Ile	
11a	 Cys	S1	12a	 Ser		13a	 Leu		14a	 Tyr		15a	H Gln	
16a	H Leu		17a	H Glu		18a	H Asn		19a	H Tyr		20a	 Cys	S3
21a	 Asn					1b	 Phe		2b	 Val		3b	 Asn	
4b	 Gln		5b	 His		6b	 Leu		7b	 Cys	S2	8b	 Gly	
9b	H Ser		10b	H His		11b	H Leu		12b	H Val		13b	H Glu	
14b	H Ala		15b	H Leu		16b	H Tyr		17b	H Leu		18b	H Val	
19b	H Cys	S3	20b	 Gly		21b	 Glu		22b	 Arg		23b	 Gly	
24b	 Phe		25b	 Phe		26b	 Tyr		27b	 Thr		28b	 Pro	
29b	 Lys		30b	 Ala										