Name: _____

JUMPSTART: HOW DO WE GET OBSERVABLE TRAITS?

1. Look at the picture of a Siamese cat on the right. What patterns in coat color do you notice?

_____

_____

_____

2. Why do you think Siamese cats are colored the way they are?

_____

_____

_____

_____

Siamese cat,https://www.flickr.com/photos/sonstroem/18314863075/in/photostream/

3. Do you think cells and/or proteins are involved in the coat coloring? Why or why not?

_____

_____

_____

4. A Siamese cat named Boots does not like the snowy cold weather in the winter. His owners decided to put some shoes on his feet so that they would not get cold and wet when he went outside in the snow. One day after Boots had been outside for several hours, he came inside and the owners took off his shoes. They were shocked to see that Boots' feet had turned white! How could this happen?

_____

_____

_____

Name: _____

5. Boots' owners have another Siamese cat named Snowball. Even though they are brothers, Snowball is just the opposite of Boots - he loves cold weather and the snow. Snowball often plays and sleeps outside all winter long. After a few months of being outside during the winter, his owners noticed that Snowball was getting darker. His white body was turning dark like his paws! How could this happen?

_____

_____

_____

6. Create your initial model of how Siamese cats get their coat coloration and pattern.

Name: _____

ACTIVITY 1: WHAT ARE ENZYMES?

PURPOSE

In earlier lessons, we learned that different cells contain different proteins. This activity further investigates proteins and how their structure relates to their function.

PREDICTION

1. In previous lessons, you learned that specialized cells contain different proteins. In what kind of cell do you think you would find a protein or enzyme that breaks down food?

_____

_____

2. Think about enzymes that break down food. What do you think they look like? **Draw a picture** of what your group thinks they look like. **Label important things** you think that it would have. How does the enzyme break down food?

Name: _____

PROCEDURE

3. Get an enzyme packet from your teacher. What observations can you make about the enzymes?

_____

_____

4. What do you think the notches in the enzymes are used for?

_____

_____

5. The notches in the enzymes are called **active sites**. Why do you think the active sites for each enzyme are different shapes?

_____

_____

6. Try to fit the different sugars (S) into the active sites in the enzymes (E). Some active sites may need two sugars together to fill it. Place an "X" in the boxes where the sugars fit the active sites of the enzymes.

	S1	S2	S3	S4	S5	S6	S7	S8	S9
E1									
E2									
E3									
E4									

7. What observations can you make about the sugars and the active sites?

_____

_____

8. Why is it important that the enzyme active sites are different shapes?

_____

_____

Name: _____

MAKING SENSE

9. What is an active site?

_____

10. Why do enzymes have an active site?

_____

_____

11. Why do different enzymes have different active sites?

_____

_____

_____

12. What do you think would happen if the shape of an active site on a protein enzyme changed?

_____

_____

_____

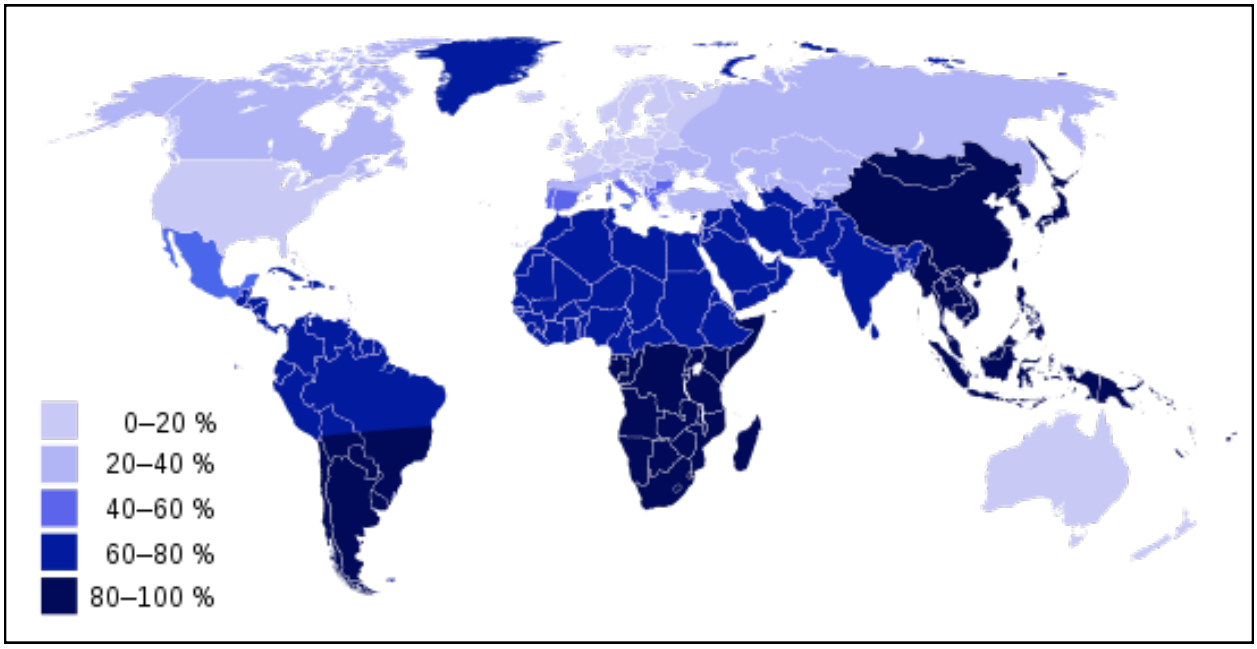
Name: _____

READING 1: HOW DO YOU GET LACTOSE INTOLERANCE?

JUMPSTART

Have you heard of someone having lactose intolerance? Are you or someone you know not able to drink milk or have dairy products? When someone with lactose intolerance ingests dairy, they feel sick and may have nausea, cramping, bloating, and diarrhea. Their body is simply unable to tolerate consumption of dairy products.

Below is a world map showing the percentage of people having lactose intolerance in countries across the world. Light colored nations have a low percentage of lactose intolerance (more people that can ingest dairy) while dark colored nations have a high percentage of lactose intolerance (more people that cannot ingest dairy).



World lactose intolerance, https://commons.wikimedia.org/wiki/File:Laktoseintoleranz-1.svg

1. What observations can you make from the map?

_____

_____

_____

2. What inferences can you make from your observations?

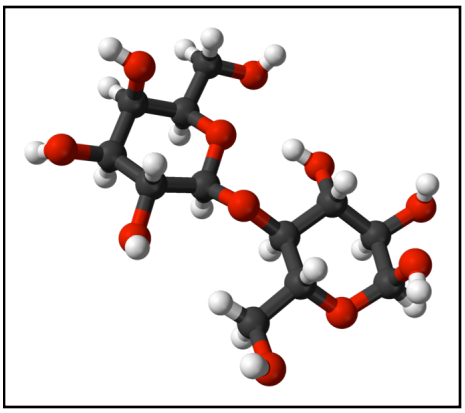
_____

_____

Name: _____

What is Lactose?

Lactose is a sugar found in dairy products. This sugar is named so because "lac" is Latin for milk and the -ose ending is used to name sugars. So lactose is milk sugar. Lactose makes up about 2-8% of milk. Lactose is a complex sugar: a **disaccharide**. This means it is made up of two smaller sugars put together. The picture on the right shows how lactose is made of galactose (one of the rings) and glucose (the other ring) hooked together.



Lactose, http://en.wikipedia.org/wiki/File:Alpha-lactose-from-xtal-3D-balls.png

How Does Our Body Process Lactose?

Humans cannot use complex sugars like lactose for energy until they are broken down. Our bodies produce an enzyme called **lactase** which is able to break down lactose molecules. It is easy to remember that lactase breaks down lactose because enzymes end in -ase, so lactase is the enzyme that breaks down the lactose sugar.

In class, you learned that enzymes have specific **substrates** (or molecules they bind). Therefore, lactose is the substrate for lactase. The cells in your intestines make the protein enzyme lactase and secrete it out into the space in your intestines where the food goes through. When you consume dairy, the lactase enzymes in your intestines bind to lactose molecules and cleave them apart. Now, since lactose is broken up into simple sugars, your cells can take in the galactose and glucose and use them for energy.

3. What is lactose and where is it found?

_____

_____

4. How does your body digest lactose?

_____

_____

What is Lactose Intolerance?

People who are lactose intolerant do not make the enzyme lactase. If they do not have that enzyme, any lactose they consume is unable to be taken up by their cells to use as energy. Remember, the cells can only take up simple sugars and lactose is a complex sugar until it is broken down by lactase.

So what happens when someone who is lactose intolerant consumes dairy? If the person's cells do not make any lactase enzyme, the lactose cannot be broken down. If

the lactose is not broken down, then the person's cells can't absorb the sugars to use as energy. The lactose then becomes food for something else: your gut bacteria! Your body contains trillions of bacteria in your intestines to help you digest food. If your body does not break down lactose, your gut bacteria will!

If someone has the lactase enzyme, lactose is broken down in the small intestine. However, most of your gut bacteria live in your large intestine. Therefore, if someone does not make the lactase enzyme, lactose passes through the small intestine and into the large intestine. When the lactose makes it into the large intestine, the gut bacteria break it down and use it for food, releasing gases in the process. This is what produces the nausea, cramping, bloating, and diarrhea after a person who is lactose intolerant consumes dairy.

5. What does "lactose intolerance" mean?

_____

_____

6. What happens to lactose when a lactose intolerant person consumes dairy products?

_____

_____

_____

Can Someone Who is Lactose Intolerant Ever Have Ice Cream?

Fortunately, someone who is lactose intolerant does not have to live their life without ice cream! Scientists can insert the gene that codes for the lactase protein inside of bacteria, yeast, or fungi. When they do this, they turn that organism into a "lactase factory" - these organisms produce large amounts of the lactase enzyme. They can then lyse the single celled organisms and purify out all the lactase protein enzymes, giving them large amounts of purified lactase. This is also how insulin for diabetics is made - bacteria are turned into insulin factories.

Purified lactase enzymes can then be added to milk and other dairy products to break down the lactose for people who are lactose intolerant. These products would no longer contain the complex sugar lactose but the simple sugars galactose and glucose instead. Dairy products treated with purified lactase enzymes are then safe for lactose intolerant people to consume without the worries of intestinal issues. Additionally, some pharmaceutical companies have made capsules containing the purified lactase protein enzyme (such as LACTAID®) for people to eat prior to consuming normal untreated dairy products. So

even though people who are lactose intolerant don't produce the lactase enzyme in their bodies, when they eat a LACTAID® capsule, they are eating the purified protein enzyme which can then function to break down the lactose they are about to consume.

7. What is LACTAID® and how does it work?

_____

_____

How Do You Become Lactose Intolerant?

It is actually normal for mammals (including humans) to develop lactose intolerance as you age. When you were a baby, you drank a lot of milk. But then as you grew up, you relied on other foods to get your nutrients such as bread, meat, fruits, and vegetables. You have probably heard the expression "if you don't use it, you lose it." Your body is programmed to stop the production of the protein enzyme lactase at the end of the weaning period (or length of time you drink your mother's milk) because it is no longer necessary - you can eat many other things for your nutrients when you are older, but must rely only on milk when you are a baby. This is another example of how cells produce only the specialized proteins they need for their function.

8. How does a person become lactose intolerant?

_____

_____

Why Isn't Everyone Lactose Intolerant?

You may have noticed that South America and parts of Africa and Asia show large percentages of the population with lactose intolerance while the United States, Europe, Russia, and Australia show large percentages of the population without lactose intolerance. Why is this?

The ability to continue producing the lactase enzyme appears to be a recent adaptation to dairy consumption. People who acquired a mutation that stopped lactase from being turned off (thus, lactase production never stopped) are able to continue to consume dairy products without intestinal difficulties. In countries such as the US, animals are domesticated and their milk is often consumed by humans. Because dairy has been widely available in countries that have domesticated animals, people who are able to keep producing the lactase enzyme in these countries are able to keep getting nutrients from dairy sources as well. Over time, this trait was selected for and thus, a large population in the country was able to continue consuming dairy products. In countries that do not consume dairy in adulthood, this trait was not selected for, so many people develop lactose intolerance.

Name: _____

9. What would you expect to happen if people in the US stopped drinking milk?

_____

_____

10. Do you think more or less people in the world will be lactose intolerant 100 years from now? Why?

_____

_____

_____

Questions to Consider

11. Why is lactase important in the body?

_____

12. Why doesn't the enzyme that breaks down sucrose (another disaccharide) just break down lactose in people who are lactose intolerant?

_____

_____

Name: _____

ACTIVITY 2: WHY ARE ENZYMES IMPORTANT?

PURPOSE

This activity further investigates enzymes and how their structure relates to their function.

PROCEDURE

Go to the following website and start the animation All About Enzymes:

- http://www.learnerstv.com/animation/animation.php?ani=324&cat=Biology

1. Why is it important that enzymes are not changed after they help a reaction?

_____

_____

2. What are some things that can affect the shape and function of an enzyme?

_____

3. How do you think these things change the shape of an enzyme?

_____

_____

4. Click on "Why Enzymes?" and view the reaction **without** the enzyme. What happens?

_____

4. View the reaction again, this time **with** the enzyme. What happens this time?

_____

5. Why do you think the reaction was different with and without the enzyme?

_____

_____

6. Return to the Enzyme Menu and view **Specificness**. What happens when the green enzyme tries to break apart the double sugar molecule? What about the yellow enzyme? Why is there a difference?

Name: _____

_____

_____

_____

7. Return to the Enzyme Menu and view **Reusing Enzymes**. Why is it helpful that enzymes can be reused?

_____

_____

8. Return to the Enzyme Menu and view **Denaturing**. How does heat make the enzyme not work anymore?

_____

_____

Making Sense

9. What would happen to a reaction if you added more enzymes to it?

_____

_____

10. Diabetic patients can be given purified insulin (a protein) to help them regulate their blood sugar. One patient reads that his insulin must be kept in the refrigerator. Why is this?

_____

_____

11. What do you think would happen to the insulin if it were left out on a table for a few hours?

_____

_____

_____

Name: _____

12. Look again at the picture of the Siamese cat on the right. Do you think an enzyme could be responsible for the coat color of the cat? Why or why not?

_____

_____

_____

Siamese cat,https://www.flickr.com/photos/sonstroem/18314863075/in/photostream/

13. What did you learn from this lesson that you may be able to apply to your model of how the Siamese cat gets its coloration?

_____

_____

_____

_____

Name: _____

READING 2: WHY CAN'T A WOODCHUCK EAT WOOD?

JUMPSTART

Woodchucks have it rough. Not only do they have a tongue twister saying that they can't chuck wood, but they also are unable to eat wood. You have probably heard of termites. Termites are a common pest that can destroy houses by eating the wood. Look at the following pictures of a woodchuck (left) and a termite (right).

Woodchuck, https://commons.wikimedia.org/wiki/File:Woodchuck_offspring_in_our_yard_%285825855337%29.jpg

Termite, https://commons.wikimedia.org/wiki/File:Workertermite1.jpg

1. Why do you think a woodchuck can't eat wood but a termite can?

_____

_____

_____

WHAT IS WOOD MADE OF?

You know that wood comes from trees. But what exactly is wood? Wood is **xylem** in the stems or trunks of trees. Xylem transports water and minerals from the soil up the tree and to the leaves and other growing areas. It is the part of the tree inside the bark. If you have ever taken the bark off a tree, cut down a tree, or looked at a slice of a tree (right) you can see that the majority of a tree's stem or trunk is made of xylem.

Tree cross section, https://commons.wikimedia.org/wiki/File:Taxus_wood.jpg

WHAT IS XYLEM MADE OF?

Xylem is actually just a fancy name for the plant cells that transport water and minerals up from the roots to the leaves. You learned before that plants are made up of

Name: _____

cells just like we are. However, plants contain some special things like chloroplasts to make sugar from sunlight, water, and carbon dioxide and cell walls to support and protect the plant's cells. Because plants don't have a skeleton, they need strong cell walls to hold the plant up. Think about trees compared to other plants. Are trees stronger and harder than other green plants? Which do you think contains thicker cell walls?

2. What is wood made of?

_____

_____

_____

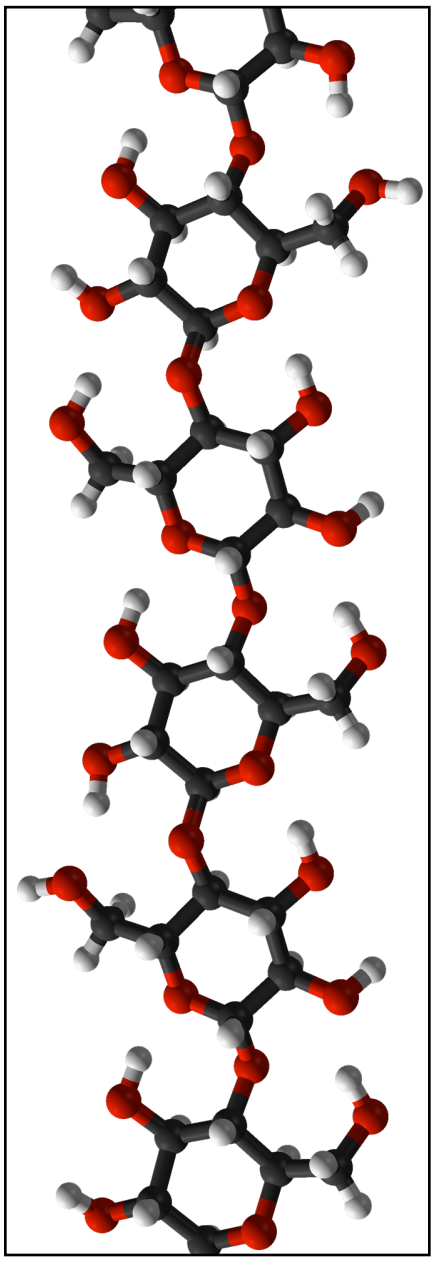
3. Why are cell walls important?

_____

_____

What are Cell Walls Made Of?

Cell walls in plants are composed mainly of **cellulose**. The last reading you did was about lactose. Do you remember that the -ose in lactose meant sugar? What do you think cellulose is? Like its name suggests, cellulose is a sugar found in cells! Cellulose is similar to lactose because it is another complex sugar. But it is a lot more complex than lactose! Cellulose is actually made of several hundred to over ten thousand glucose molecules hooked together (above). Cellulose forms long chains and these long strong chains make up the strong cell wall to hold a plant up. With the world having so many plants, cellulose is the most common organic compound found on Earth! Just cellulose by itself makes up almost half (40-50%) of wood.



Cellulose, https://commons.wikimedia.org/wiki/File:Cellulose-Ibeta-from-xtal-2002-3D-balls.png

4. What is cellulose and where is it found in plant cells?

_____

_____

Name: _____

How Can Termites Eat Wood?

Like humans and lactose, termites must first break down the complex sugars to be able to use them for energy. If lactase was the enzyme that breaks down lactose, what do you think the enzyme that breaks down cellulose would be? Termites produce **cellulase** enzymes in their digestive system to break down the wood that they eat. Cellulase breaks down the long chains of cellulose (a complex sugar) into simple sugar molecules of glucose. Once the cellulose is broken down into glucose, the termite's cells can absorb the simple sugar to use it for energy.

5. How do termites digest cellulose?

_____

_____

Why Can't Woodchucks Eat Wood?

Most mammals (including humans and woodchucks) do not produce the cellulase enzyme. This is very similar to the previous reading about lactose intolerance where a person who does not make the enzyme lactase cannot break down the complex lactase sugar. Since mammals do not make the enzyme cellulase, they are unable to break the complex sugar cellulose down into simple sugar molecules of glucose to use as energy.

What Happens If You Eat Cellulose?

You don't sit down with a pile of sticks to eat for lunch. First of all, wood is hard to chew and it doesn't really taste good. But most importantly you can't digest the cellulose in wood. Plants are a part of a healthy diet though (broccoli, asparagus, lettuce, etc.) and do contain a lot of cellulose. So what happens when you eat broccoli? You may have heard of **dietary fiber** (or roughage). Dietary fiber is the part of plants that your body cannot break down, such as cellulose. Dietary fiber is an important part of your diet and helps to keep your digestive system healthy by softening stool and shortening the amount of time it takes for digested food to move through your system. So although you cannot break down cellulose, it is an important part of a healthy diet.

6. Why can't humans digest cellulose?

_____

_____

7. What happens when humans ingest cellulose?

_____

_____

Name: _____

ACTIVITY 3: CAN I SEE ENZYMES IN ACTI0N?

PURPOSE

This experiment tests for the presence and specificity of enzymes in fruits.

PREDICTION

1. What is Jell-O made of?

_____

2. Why do you think there is a warning in the directions not to add fresh pineapple to Jell-O?

_____

3. What do you think is different about pineapple compared to other fruit?

_____

_____

4. List the different liquids you will add to the Jello in the chart below. Then predict what will happen to the Jell-O when you add each different liquid.

Liquid Added	Prediction for Jello

Name: _____

PROCEDURE

PART I

5. Number your test tubes from 1-10.

6. Add 10 mL of the Jell-O mixture to each test tube. Be careful - it will be HOT!

7. Place 3 mL of each test liquid into each tube. Use one pipette for each liquid and **do not mix pipettes between liquids!** Record which liquid went in which test tube in the following table.

Test Tube Number	Test Liquid Added
1	
2	
3	
4	
5	
6	
7	
8	
9	
10	

8. Cover the tube with your thumb and shake well to mix the test liquid and Jello.

9. Refrigerate test tubes overnight.

10. Why was it important to use one pipette for each liquid and not to mix pipettes?

_____

11. Do you expect to see any differences between the fresh juice and juice from concentrate? Why or why not?

_____

_____

Name: _____

Part II

12. On day 2, check the contents of each test tube. Record your observations on the table below.

Test Tube Number	Observations
1	
2	
3	
4	
5	
6	
7	
8	
9	
10	

Making Sense

13. Which tube was your control and why?

_____

_____

14. Which liquids gave you positive results (Jell-O still liquid)?

_____

15. Which liquids gave you negative results (Jell-O solid)?

_____

16. Were there any differences between the fresh juice and juice from concentrate?

_____

_____

Name: _____

17. Why do you think there were these differences?

_____

_____

18. What enzymes do the meat tenderizers contain?

_____

19. Why are these used to tenderize meat?

_____

_____

20. Imagine that you ran out of meat tenderizer at home. What else could you use for meat tenderizer? Why would you add this?

_____

_____

21. Other than good hygiene, can you think of a reason why pineapple processors are required to wear gloves and surgical masks when they process pineapple?

_____

_____

_____

22. What do you think would happen if you heated the pineapple juice before adding it to the Jell-O mixture? Why?

_____

_____

_____

Name: _____

READING 3: HOW DO WE KNOW WHAT PROTEINS LOOK LIKE?

JUMPSTART

You know that cells are so small that they cannot be seen with the naked eye. In class, you observed different types of cells using light microscopes. There are several different types of microscopes. Three types of microscopes are listed below along with their **resolution** (size of smallest thing they can image) and sample preparation guides.

Microscope	Resolution	Sample Preparation
Light	200 nm	may need to stain sample to view it
Scanning Electron	1-5 nm	must be electrically conductive or coated with a metal
Transmission Electron	0.05 nm	must be able to withstand a vacuum so need to be "fixed" by plastic embedding

1. What is the smallest thing you could see with a light microscope?

_____

2. If proteins are 1-100 nm large, which microscope(s) would you use to view proteins?

_____

WHY ARE PROTEINS SO HARD TO VIEW?

Have you seen the head of a pin? It is very tiny - about 2 mm large. The cells in your body are about 10 μm large, or 200 times smaller than the head of a pin. Proteins are even smaller. They are 1-100 nm large, or at least 20,000 times smaller than the head of a pin. That's tiny!

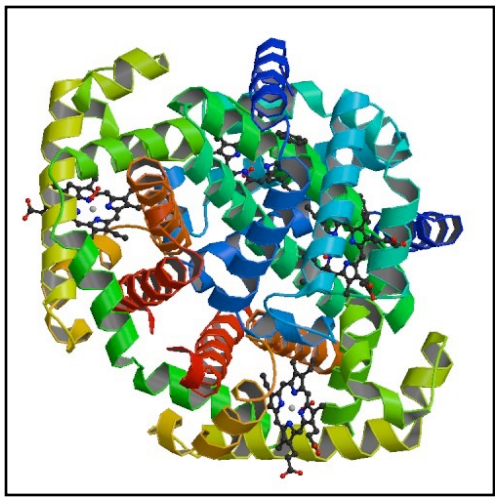
Not only are proteins super small, but they are also extremely active. You learned before that proteins zip around your cells doing chemistry, performing structural functions, helping them move, helping them keep their shape, receiving signals, and lots of other things. Have you ever tried to take a picture of a child or animal moving around? It's very difficult to get a clear picture. Now imagine you were trying to take a picture of something moving around, only that thing is 20,000 times smaller than the head of a pin. It's almost impossible! This is why it has taken scientists years to get pictures of proteins and why we still don't know what many proteins look like.

3. How big are proteins?

_____

Name: _____

What Do Proteins Look Like?



Hemoglobin, http://www.rcsb.org/pdb/explore/images.do?structureId=2DN1

Proteins come in all sorts of shapes and sizes. In class, you learned that certain types of cells had certain shapes because that helped with their function. The structure and function of proteins go hand-in-hand as well. The majority of proteins are **globular** in shape. Like the name suggests, the protein is a big glob or ball. Other proteins have different shapes because they perform specific functions. Look at the structure of hemoglobin on the right. In a previous lesson, you learned that proteins are made up of amino acids. These amino acids are attached together to make a long chain of amino acids. This is called the primary structure of the protein. The chains then fold into a secondary structure of **α-helices** or **β-sheets** to make a unique shape for the protein. In the hemoglobin shown on the right, the chain is folded into many α-helices that look like springs. The α-helices are then further folded into a globular shape to make the shape of the protein. β-sheets happen when parts of the amino acid chain run parallel to each other.

4. Describe the two different types of secondary structures in proteins.

_____

_____

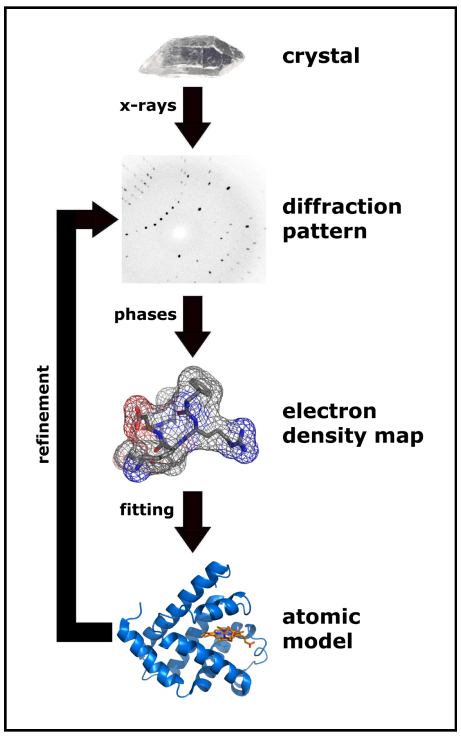
How Do You Image Proteins?

Which kind of microscope did you think would be best to use to image proteins in the Jumpstart? Actually, none of these options for microscopes are very good for imaging proteins, so scientists use instruments other than microscopes to image proteins. The main way scientists image proteins is by using **X-ray crystallography**. Like the name sounds, scientists make protein crystals and shoot x-rays through the crystals. X-ray crystallography is an extremely time consuming and complicated technique. It often takes years for scientists to make the proper protein crystals and then to interpret the data to get the structure of the protein.

How Does X-Ray Crystallography Work?

If scientists want to get the structure of a certain protein, they must first purify it. Protein purification can be complex and time consuming. Some proteins are easy to purify while scientists have not yet been able to purify others despite years of trying. Once you have pure protein, you must then **crystallize** it. Protein crystallization is when you make a solid out of the protein with the proteins arranged in an orderly repeating pattern. You are already familiar with one type of crystal - table salt. Have you ever

Name: _____



X-ray crystallography, https://en.wikipedia.org/wiki/File:X_ray_diffraction.png

looked closely at table salt? Did you notice that the grains were little cubes? When you crystallize table salt, the atoms arrange themselves in an orderly repeating cubic pattern. Protein crystallization is another time consuming process that can take scientists years.

Once you finally have your protein in a crystal in an orderly repeating pattern, you can then shoot x-rays through the crystal (see diagram on left). The x-rays go through the crystal and scatter, producing a **diffraction pattern**. This pattern is a series of dots produces by the light scattering through the protein crystal. Interpreting the pattern of dots can also take years! Eventually though, scientists end up with a model of what the protein looks like. As you can tell, it takes a very long time to be able to get a good image or structure of a protein.

5. How do scientists know what proteins look like?

_____

_____

What Can You Use the Structures For?

So after you spent all that time finding the structure of a protein, what do you do with it? Protein structures are extremely useful for scientists. As you read previously, the structure and function of proteins go hand-in-hand: a piece that sticks off a protein may attach to something else. Scientists can also use the protein structures to see how proteins bind to each other. They can use computer programs that try to fit the proteins together to see what parts of the proteins touch each other. A lot of diseases are caused by changes in the proteins that make them not able to bind to other proteins correctly. Scientists can use the protein structures to better understand these diseases.

Another neat application of protein structures is drug design. Drug companies use the structures of enzymes to figure out the shape of their active sites, or where the substrates or targets bind. When they know what shape the active site is, they can design small molecules (or drug targets) to fit inside of that active site to **inhibit** its activity. If you had an enzyme that made cholesterol, you could design a drug target to fit inside the active site and stop it from making cholesterol. This drug could then be useful for patients with high cholesterol. So even though it may take many years to get the structure or image of a protein, the structures are extremely useful!

Name: _____

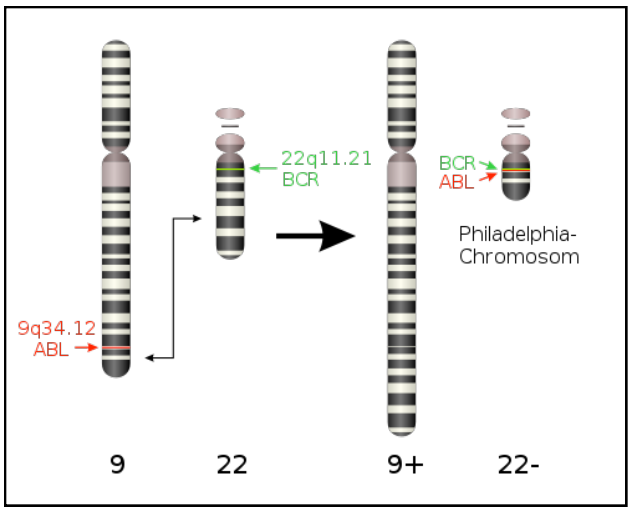
6. What can you do knowing the structure of proteins?

_____

_____

How Have Scientists Used Protein Structures?

One of the biggest success stories that involves protein structures is the development of the drug Gleevec to treat chronic myelogenous leukemia (CML). One of the mutations that causes CML is a chromosome translocation. Chromosomes 9 and 22 both break and swap their pieces. This is a particularly nasty mutation because the breaks on both chromosomes occur right in the middle of genes. So when the new chromosomes are formed, the one dubbed the "Philadelphia chromosome" contains a new mutant gene that contains half of the gene *ABL1* from chromosome 9 and *BCR* from chromosome 22. And, since genes code for proteins, this new mutant gene codes for a new mutant protein.



CML chromosome translocation, http://en.wikipedia.org/wiki/File:Philadelphia_Chromosom.svg

ABL1 is another example of an enzyme. It doesn't break down sugars like the other enzymes you have studied; it signals cells to divide. Normally, this enzyme has another section attached (the silencing portion) that keeps it turned off until it is needed. But in CML, the chromosome break divides the active portion of the gene from the silencing portion. The active portion of the gene is then attached to the *BCR* gene. Scientists don't know the exact function of the normal BCR protein, but when a section of it is attached to the ABL1 enzyme, it forms the mutant BCR-ABL protein enzyme. This enzyme is always active (because the silencing portion was removed and replaced) and is always signaling the cells to grow and divide. You learned in a previous unit that cancer cells express more proteins telling them to grow and divide, so this is another example of how pro-growth proteins can lead to cancer.

7. How does a chromosome translocation help cause CML?

_____

_____

_____

Name: _____

Because this mutant enzyme causes such devastating effects to cells, scientists have studied the structure of the mutant BCR-ABL protein to see if they could design a drug target to inhibit this enzyme. If they were able to inhibit this mutant enzyme (and not other normal ABL1 enzymes), they would be able to essentially "correct" these mutated cells and potentially stop them from turning into cancerous cells.

BCR-ABL enzyme with Gleevec, http://en.wikipedia.org/wiki/File:Bcr_abl_STI_1IEP.png

The drug Gleevec was the first drug to actually alter the progression of CML cancers. The picture on the right shows Gleevec binding to the BCR-ABL active site. The binding of Gleevec prevents the enzyme from being able to signal cells to divide. Because of the initial success of Gleevec, TIME Magazine actually called this drug "the magic bullet" to cure cancer. Indeed, Gleevec has been successful in helping treat CML, however some people have developed Gleevec resistance. Scientists have since made other drugs that fit the active site of the mutant BCR-ABL protein using the protein structure to try to inhibit it to stop the progression of CML cancers.

Want To Learn More About Gleevec & CML?

Visit www.insidecancer.org, diagnosis & treatment, targeted activators, Gleevec & Chronic Myeloid Leukemia to view short videos about CML and Gleevec

Questions to Consider

8. Why is it important to find structures of proteins?

_____

_____

_____

9. If scientists discovered a protein looked similar to another protein, do you think they would have a similar function? _____ Why or why not?

_____

_____

_____

Name: _____

ACTIVITY 4: ARE SOME PROTEINS MICRO-MACHINES?

PURPOSE

This activity further investigates proteins and how their structure relates to their function.

PREDICTION

Your teacher is going to show you a video called "The Inner Life of the Cell." Pay special attention to the motor protein called kinesin that is carrying a vesicle.

http://www.studiodaily.com/2006/07/cellular-visions-the-inner-life-of-a-cell (music only)
http://multimedia.mcb.harvard.edu/anim_innerlife.html (narrated)

1. How do you think kinesin is able to move like that?

_____

_____

PROCEDURE

PART I (http://www.molecularmovies.com/showcase/#Cytoskeleton%20/%20Molecular%20Motors), scroll down to Kinesin Mechanism

2. Watch the short video on kinesin. What is kinesin?

_____

_____

3. What happens to kinesin when ADP is released and ATP binds?

_____

_____

4. What happens to kinesin when ATP is broken down to ADP plus phosphate?

_____

_____

5. How does the structure of kinesin relate to its function?

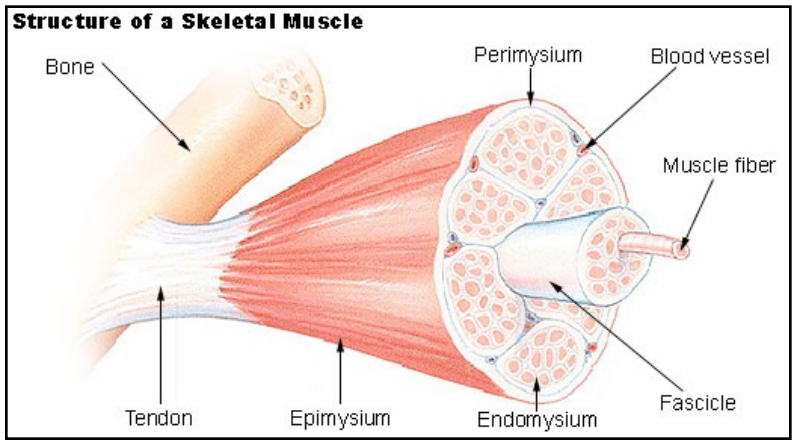
_____

_____

Name: _____

PART II

We are now going to be looking at proteins involved in muscle contraction. Look at the picture on the right of the structure of muscles. Muscle cells are combined into bundles. Inside the cells, they contain the proteins actin and myosin.



Muscle diagram, https://commons.wikimedia.org/wiki/File:Illu_muscle_structure.jpg

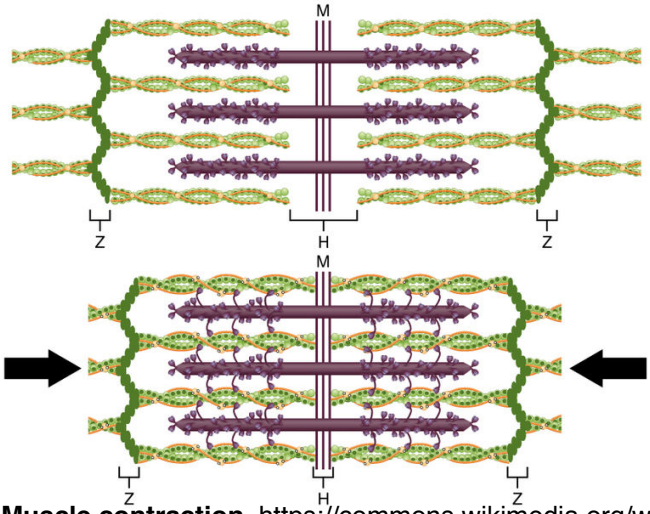
6. Look at the picture of muscle contraction. Actin and myosin are both very long, but the myosin has bulbs on each end of the protein. According to the picture, what happens when muscles contract?

_____

_____

_____

_____



Muscle contraction, https://commons.wikimedia.org/wiki/File:1006_Sliding_Filament_Model_of_Muscle_Contraction.jpg

7. How do you think the bulbs on myosin help muscles contract?

_____

_____

8. Watch the short video on myosin (http://www.molecularmovies.com/showcase/#Cytoskeleton%20/%20Molecular%20Motors), scroll down to Myosin Mechanism.

What is myosin? Where is it found in the body?

_____

9. What happens when myosin releases phosphate and ADP?

_____

_____

Name: _____

10. What happens when ATP binds to myosin?

_____

_____

11. How does myosin contract your muscles?

_____

_____

_____

Making Sense

12. The proteins you studied are sometimes called “molecular motors.” Why do you think they are called this?

_____

_____

13. Why are these motor proteins important?

_____

_____

_____

14. Familial Hypertrophic Cardiomyopathy (FHC) is a disease caused by a mutation to the cardiac myosin protein. The symptoms are an enlarged heart and sudden death. How could a mutation to cardiac myosin cause sudden death?

_____

_____

_____

15. Can proteins lead to visible traits? _____ Why or why not?

_____

_____

Name: _____

16. Was there anything you learned from this lesson that you may be able to apply to your model of how the Siamese cat gets its coloration?

_____

_____

_____

_____

Siamese cat,https://www.flickr.com/photos/sonstroem/18314863075/in/photostream/

17. Create a revised model of how Siamese cats get their coat coloration and pattern. Be sure to include anything helpful you have learned so far in this unit.

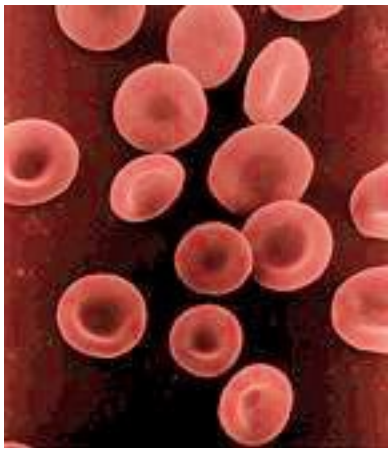
Name: _____

READING 4: WHY DO WE HAVE DIFFERENT BLOOD TYPES?

JUMPSTART

You have probably heard of people having different blood types. Can you name the different blood types? Do you know your own blood type?

There are four main blood types: A, B, AB, and O. There is also an additional factor that gives you a positive or negative. Have you seen hospital shows on TV where trauma doctors yell for "O neg." blood for patients? O negative blood is the "universal donor."



Red Blood Cells, https://commons.wikimedia.org/wiki/File:RBC_micrograph.jpg

1. Why do you think O negative is called the "universal donor"?

_____

2. Why do you think this type of blood could be given to anyone?

_____

_____

WHAT IS THE DIFFERENCE BETWEEN A, B, AND O BLOOD?

Your blood is made up of all kinds of different cells such as platelets, white blood cells, macrophages, red blood cells, and much more. Red blood cells are the cells that carry oxygen throughout your body. Everyone has red blood cells filled with hemoglobin proteins to carry oxygen, but there are also proteins on the surface of red blood cells. The different surface proteins on the red blood cells make up the different blood types.

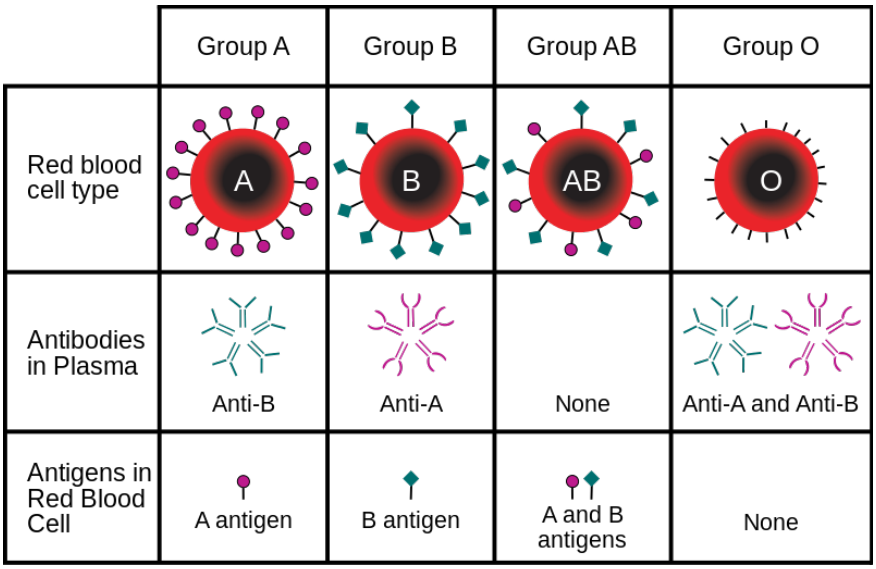
Do you remember that cells can have different proteins sticking out of the cells to contact other cells or bind to other things? Some of these proteins are **antigens**. Antigens are so named because they are antibody generators. Therefore, antibodies bind to antigens, or proteins sticking out of the cells. Red blood cells can have two different protein antigens on their surface: A and B. This is where the A and B blood types come from.

A person whose red blood cells express the protein antigen A on the surface of their red blood cells would have blood type A. A person whose red blood cells express the protein antigen B on the surface of their red blood cells would have the blood type B.

Name: _____

These protein antigens are different in shape (see diagram on right) so that only antibodies specific to that antigen may bind to it.

People can also express <u>both</u> protein antigens A and B! These people have the fairly rare blood type AB because their red blood cells express both the A and B protein antigens on the surface of their red blood cells.



Antigens, https://commons.wikimedia.org/wiki/File:ABO_blood_type.svg

If people can express one or both of the protein antigens A and B, do you think someone can express <u>neither</u> of the protein antigens? Certainly! These people whose red blood cells do not produce either of the A or B protein antigens have the blood type O.

3. What are antigens?

_____

_____

4. What is the difference between Type A and Type B blood?

_____

_____

5. What is the difference between Type AB and Type O blood?

_____

_____

What Happens When a Person with Type A Blood Gets Type B Blood?

To make things a little more complicated, people with different blood types also have different antibodies. The bottom part of the picture on this page shows the A antibody binding to the A surface molecules, or antigen. A antibodies bind to A antigens and B antibodies bind to B antigens.

Name: _____

You may have heard that antibodies bind to pathogens or bad things in your body. When antibodies bind to these pathogens, they are signaling that the pathogen needs to be destroyed by the body's immune system. If antibodies bind to antigens to signal for their destruction, do you think someone with Type A blood would have Type A antibodies?

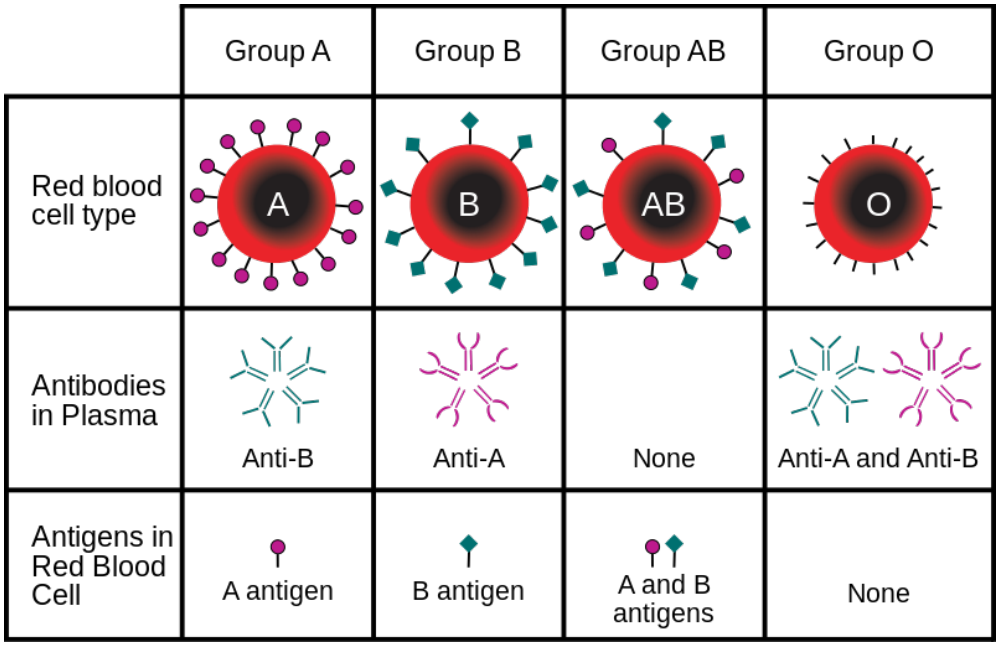
If a person has Type A blood, his or her red blood cells express the antigen A on the surface of the cell. If they had Type A antibodies, these antibodies would be able to bind to their red blood cells and would signal for their destruction. This would not be good! The person's body would be attacking itself and killing all its red blood cells! What do you think would happen if all the person's red blood cells were killed off?

6. What antibodies do you think a person with Type A blood would have?

_____

Because you wouldn't be able to transport oxygen throughout your body without your red blood cells, a person with Type A blood does not have Type A antibodies. However, that person does have Type B antibodies (see diagram on right). These Type B antibodies would be able to bind any red blood cells that express the Type B antigen. This makes sense because if you were Type A, you would want your body to get rid of any blood cells that were Type B because they would not be yours! All of your red blood cells are Type A, so any Type B ones would be foreign to your body and would not be good for you!

Similarly, someone with Type B blood would not have Type B antibodies (these antibodies would attack the body's own red blood cells). They would have Type A antibodies to mark any Type A red blood cells as foreign. What kind of antibodies do you think a person would have if they



Antigens, https://commons.wikimedia.org/wiki/File:ABO_blood_type.svg

contained both A and B antigens and were Type AB? Since these people have both antigens on their red blood cells, they would have neither antibody because both antibodies would mark their red blood cells as foreign. What about people with Type O blood? They have neither antigen on their red blood cells, so they have both antibodies.

So what would happen if you gave someone who has Type A blood Type B blood instead? If you remember from earlier, someone who has Type A blood has Type B antibodies. These antibodies would then bind to the Type B red blood cells and signal the person's immune system that they are foreign and need to be destroyed. This is called **immune rejection**. You have probably heard of this before but didn't know quite what it is. Your body rejects, or signals that the blood cells are foreign by tagging the foreign red blood cells with antibodies. The immune system then destroys the foreign red blood cells. This can also happen when a patient is transplanted with a new organ such as a liver. If the blood and tissue types do not match, the body will have antibodies against the foreign cells and will attack and reject the organ.

7. What antibodies does someone who is Type B have?

_____

8. What types of blood can someone who has Type A blood receive without rejecting it?

_____

Where Does the Positive and Negative Come From?

Remember the Jumpstart asking you about hospital shows on TV where trauma doctors yell for "O neg." blood for patients? You just learned that Type O red blood cells do not contain A or B antigens on their surface. But what does the "neg." or negative mean?

Red blood cells also contain another type of protein on their surface - the **Rh factor**. The Rh blood group system is so named because the early experiments describing it were done with Rhesus monkey blood. The Rh blood group system actually consists of 50 different types of antigens, but the commonly used term "Rh factor" just refers to the presence or absence of the D antigen. Like Type A and Type B blood, if a person is Rh positive (Rh+), the person contains the Rh blood group system D antigen. Conversely, if a person is Rh negative (Rh-), the person does not contain the D antigen on red blood cells.

9. Why are some blood types positive and some types negative?

_____

_____

Name: _____

The Rh factor can cause problems during pregnancy, leading to **Rh disease**. In mild cases, the fetus can have **anemia**. You have probably heard of anemia, but may not know that it is simply a lower than normal amount of red blood cells or not enough hemoglobin protein in the red blood cells. In severe cases of Rh disease, the baby may be stillborn. Rh disease typically occurs in second or subsequent pregnancies in an Rh- woman. If the father is Rh+, the baby has a chance of also being Rh+. During pregnancy, a small amount of the baby's blood can enter the mother's circulation. If the baby is Rh+ and the mother is Rh-, the mother will begin to produce antibodies against the D antigen. These antibodies are able to travel through the mother's bloodstream into the baby. If the antibody levels are high enough, they can then begin to attack the baby's red blood cells and cause the fetus to develop anemia or even worse. The main time that the baby's blood enters the mother's circulation is during birth. So, generally, the first Rh-incompatible pregnancy is not a problem because the mother begins to produce the antibodies after the birth of the baby. However, after the Rh+ baby's blood enters the mother's system during birth, any subsequent Rh+ children are at risk for developing Rh disease. Because of this, Rh disease becomes more severe with each additional Rh-incompatible pregnancy.

Rh disease used to kill 10,000 babies each year in the United States alone. However, most Rh disease can now be prevented. Now, nearly all Rh- mothers are given an injection of antibodies against the D antigen at 28 weeks gestation. These antibodies are injected into the mother so that they are able to find and destroy any of the baby's Rh+ red blood cells that entered the mother's blood before the mother's immune system can discover them and begin making her own antibodies. The injected antibodies only last about 4-6 weeks in the mother's blood, so the immunity typically wears off shortly after the baby is born.

10. How does Rh disease occur?

_____

_____

11. How do doctors prevent Rh disease?

_____

_____

Why is O- the "Universal Donor"?

Let's put together what we have just learned about blood types and the Rh factors. What different antigens does Type O blood have on its red blood cells? They have none. What about red blood cells that are Rh-? They have no Rh antigen as well. Can antibodies bind to red blood cells with no antigens? No - you need antigens for antibodies to bind.

Name: _____

So what happens when someone with Type A blood gets Type O blood? That person has type A antigens on his or her red blood cells, so what antibodies does that person have? That person would have type B antibodies to attack any red blood cells that have antigen B. What antigens does Type O red blood cells have? They have none! So do the antibodies in the person attack the Type O blood? No, because Type O red blood cells do not contain any antigens for the Type B antibodies to bind. The same is true for the Rh factor. O- red blood cells do not contain any Rh factor antigens, so the antibodies cannot bind to them.

Type O- blood has red blood cells with no antigens for the A, B, or Rh antibodies to bind. Because none of the antibodies can bind to the red blood cells, this blood may be given to anyone because it cannot be attacked by antibodies. This is why Type O- blood is called the universal donor.

12. What blood types can someone who is type B positive receive?

_____

13. What blood types can someone who is type O positive receive?

_____

14. Why is Type O negative the universal donor?

_____

_____

Is There a "Universal Acceptor"?

If Type O- is the universal donor, what would the universal acceptor be? The universal acceptor means that someone with that blood type can accept any type of blood.

15. What blood type is the universal acceptor and why?

_____

_____

The universal acceptor would probably have the exact opposite blood type as the universal donor. That person would be able to accept any type of blood, so would the person have any A, B, or Rh antibodies? What blood type has no A or B antibodies? Someone with both A and B antigens, or someone with the blood type AB. What about the blood type that has no Rh antibodies? Someone with the Rh antigen (or Rh+) would have no Rh antibodies. So someone with the blood type AB+ would be able to accept any type of blood because they do not have the antibodies to attack the red blood cells. Someone with type AB+ blood is the universal acceptor.

Name: _____

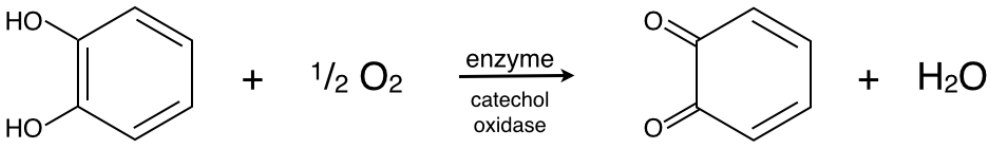
ACTIVITY 5: CAN PROTEINS MAKE TRAITS THAT WE CAN SEE?

PURPOSE

This activity shows how proteins can lead to observable traits.

PRE-LAB

In a previous lesson, you did experiments with enzymes and Jell-O and you also read about different enzymes. Enzymes are special proteins that catalyze chemical reactions such as breaking down sugars, breaking down collagen, and signaling cells to grow, among many other activities. In this lab, we will be doing another experiment with an enzyme. The enzyme you will be using is called catechol oxidase. Let's look at the name "catechol oxidase" to give us clues to what this enzyme does. If the -ase tells you that it is an enzyme, what do you think the oxid- tells you? Like the name suggests, "oxidase" means an enzyme that **oxidizes** (or removes hydrogens from) a molecule. What about the "catechol" in its name? Could it be the **substrate**? Catechol is indeed the substrate, so the name "catechol oxidase" tells you that it is an enzyme that oxidizes catechol. The reaction is shown below:



catechol (light) benzoquinone (dark)

You have probably seen this reaction take place, but just didn't know it. What happens when you take a few bites out of an apple and let it sit on the table? Does the apple turn brown where it was exposed to the air? When you see this, you just saw catechol oxidase in action. Catechol is a compound found in plant cells. The enzyme catechol oxidase is also found in plant cells. The left side of the equation shows the **reactants**: catechol and oxygen. When you bite into an apple and break the skin, you expose the catechol to air. Since both products are now present, the enzyme can now function and the reaction takes place. It makes the **products** (right side of the arrow): benzoquinone and water. If the apple turns brown, what do you think benzoquinone is? Benzoquinone is a **pigment**, or molecule that has coloring. This is why your apple turns brown - a pigment is formed as a product from the reaction. Your apple was light colored before the catechol was oxidized, but then turns dark after the reaction when benzoquinone is formed.

In organisms, after benzoquinone is formed, it is then converted to **melanin**. Melanin is another type of pigment. You should be familiar with melanin as well because this is the pigment that gives our skin color. Someone with a lot of melanin has darker skin while someone with less melanin has lighter skin.

Name: _____

1. What is catechol oxidase and what does it do?

_____

_____

2. Where is catechol found?

_____

3. What would happen to a pear if you cut it up and let it sit in a bowl on the table? Describe it at a molecular level.

_____

_____

_____

_____

PREDICTION

4. Look at the picture of a Siamese cat on the right. Do you think an enzyme could be responsible for the coat color of the cat? Why or why not?

_____

_____

_____

Siamese cat,https://www.flickr.com/photos/sonstroem/18314863075/in/photostream/

5. What could you take from this pre-lab and apply to your model of how the Siamese cat gets its coloration?

_____

_____

_____

_____

Name: _____

READING 5: WHAT MAKES A SQUIRREL ALBINO?

JUMPSTART

Have you seen an albino squirrel before? There are many different kinds of squirrels at the University of Texas at Austin and there is a long standing legend that seeing an albino squirrel before a test is good luck!

In 2001, students even created the Albino Squirrel Preservation Society to celebrate this legend and to foster compassion and goodwill towards albino squirrels.

1. What do you think makes a squirrel albino?

Albino squirrel, https://commons.wikimedia.org/wiki/File:Rare_White_Albino_Squirrel.jpg

_____

_____

HOW DO WE GET OUR COLORING?

You have probably heard of pigments or pigmentation as things that give certain colors. Plants and animals have **pigments**, or molecules, that give coloration to leaves, fur, hair, and skin. Trees express certain red, orange, and yellow pigments in their leaves in the fall to turn them bright colors. Red foxes have red pigments in their fur to make it red. Humans also have pigments in their hair, skin, and eyes to give them coloration. The main pigment found in most organisms is **melanin**. Melanin is responsible for making our skin and hair dark. There are different forms of melanin which give slightly different colors. The most common melanin is brownish-black and is responsible for dark skin color and dark hair. Another form is a redish-brown color and is responsible for red hair and freckles.

2. What are pigments and where are they found?

_____

_____

HOW DO WE TAN?

In a previous unit, you learned that specialized cells become specialized by expressing certain proteins specific to their function. Melanin is made by protein enzymes from the amino acid tyrosine. These enzymes that produce melanin are proteins, so they are

expressed by only certain types of cells. Your muscles don't need to be colored, so the enzymes to produce melanin are not expressed in your muscles. However, your skin helps protect you from damaging sun rays, so being a darker color helps protect your body.

You should also remember that the amounts or levels of proteins can vary inside of cells. Someone who has dark skin has more protein enzymes to produce melanin inside of their skin cells than someone who has light skin. When we go outside, we are exposed to UV radiation from the sun. This radiation causes skin cells to start producing more enzymes that make melanin. The more melanin the skin cells produce, the darker the skin cells become. This is how we are able to tan.

3. How do we tan?

_____

_____

4. What do you think albinism is caused by?

_____

What Causes Albinism?

If tanning is caused by producing more enzymes that make melanin, you probably said that albinism is caused by producing less or no enzymes to make melanin or having no melanin. This is indeed correct. Organisms that have a complete absence of melanin are called an **albino** while organisms with a lesser amount of melanin than normal are described as an **albinoid**.

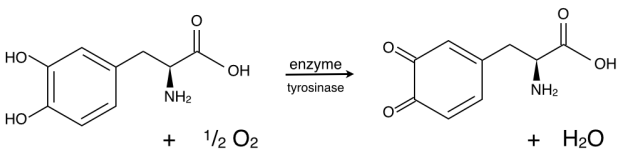
So how do organisms have a complete absence of melanin? You learned earlier that melanin is made by enzymes from the amino acid tyrosine. The first step to synthesize melanin is done by the enzyme tyrosinase. Tyrosinase oxidizes tyrosine to convert it to a dopaquinone. Dopaquinone can then combine with other molecules to make the different forms of melanin.

5. Draw how melanin is synthesized, starting with tyrosine:

Look at your drawing of how melanin is synthesized. If albinos have no melanin, something must be going wrong in the pathway to synthesize melanin. Most albinism is caused by the absence or a defect in one of the enzymes that synthesize melanin. One of the most common causes of albinism is caused by a mutation to the tyrosinase gene

Name: _____

which results in a non-functional tyrosinase protein. Put your finger over the arrow between tyrosine and dopaquinone in your drawing. If the tyrosinase enzyme is not functional, this reaction cannot occur. Everything to the right of your finger will not be able to be made. Dopaquinone cannot be made, and if it cannot be made, then the product of melanin further down the pathway cannot be made either either.



tyrosine (light)

dopaquinone (dark)

6. How does a mutation to the tyrosinase gene cause albinism?

_____

_____

_____

_____

Are All Albinos White?

There are varying levels of albinism in organisms. The albino squirrel on the first page had white fur and red eyes. The albino freshwater snail on this page is very red all over its entire body. This is because these freshwater snails contain hemoglobin to carry oxygen throughout its body. When hemoglobin has oxygen bound, it is bright red. Since the snail is an albino and does not have any melanin, the bright red hemoglobin shows through the body and is easy to see.

Albino freshwater snail, http://en.wikipedia.org/wiki/File:Biomphalaria_glabrata.jpg

There are two main categories of albinism in humans: oculocutaneous albinism and ocular albinism. The word “ocular” means eyes and “cutaneous” means skin. Someone with ocular albinism, therefore, is lacking pigment only in their eyes. Someone with oculocutaneous albinism is lacking pigment in their eyes, skin, and hair. In non-humans oculocutaneous albinism results in lack of melanin in the fur, scales, or feathers. Animals that are albino lack the normal coloration of their species. Although it is not so much a worry in humans, many animals use their coloration to hide from predators. Albino animals in nature are unable to camouflage or hide from predators, so they generally have a shorter life span than other non-albino animals. In humans, lack of skin pigmentation makes a person more susceptible to sunburn and skin cancers.

7. What are some problems with being an albino (human and non-human)?

_____

_____

Name: _____

ACTIVITY 5: PROCEDURE

PART I

6. In this lab, you will be converting catechol to benzoquinone. You will mix catechol with potato extract. What does the potato extract supply to the reaction?

_____

7. What happens to enzymes when they are heated?

_____

_____

8. What do you think will happen if you heat the potato extract?

_____

_____

_____

9. The following table is the layout of your experiment:

Tube	Distilled Water	Catechol	Distilled Water	Potato Extract	Heated Potato Extract	Chilled Potato Extract
1	5 mL	10 drops	10 drops	-	-	-
2	5 mL	10 drops	-	10 drops	-	-
3	5 mL	-	10 drops	10 drops	-	-
4	5 mL	10 drops	-	-	10 drops	-
5	5 mL	-	10 drops	-	10 drops	-
6	5 mL	10 drops	-	-	-	10 drops
7	5 mL	-	10 drops	-	-	10 drops

In which tubes do you think benzoquinone will form (indicated by a dark color)? Why?

_____

_____

_____

Name: _____

PART II

10. Label your test tubes 1-7.

11. Add 5 mL of distilled water to each test tube.

12. Carefully add 10 drops of catechol in tubes 1, 2, 4, and 6.
    (!!!) Catechol is a poison! Avoid contact with all solutions and wear gloves. Wash your hands thoroughly after the experiment.

13. Add 10 drops of distilled water in tubes 1, 3, 5, and 7.

14. Add 10 drops of room temperature potato extract into tubes 2 and 3.

15. Add 10 drops of heated potato extract into tubes 4 and 5.

16. Add 10 drops of chilled potato extract into tubes 6 and 7.

17. Record your observations in the table. Include rough time it took for color change.

Tube	Observations
1	
2	
3	
4	
5	
6	
7	

18. In which tubes did benzoquinone form?

_____

Name: _____

19. How did your results compare to your predictions in Part I?

_____

_____

_____

Making Sense

20. Which tube(s) was/were your control tube(s)? Why?

_____

_____

_____

21. What happened when you heated the potato extract? Why?

_____

_____

_____

22. What happened when you chilled the potato extract? Why?

_____

_____

_____

Explaining the Driving Question

23. Look back at the picture of the Siamese cat in the Prediction section. What parts of the cat's body would be the warmest? What parts would be the coolest?

_____

_____

24. Do you notice a pattern between the cat's coat color and the temperature of the body areas?

_____

_____

Name: _____

25. Siamese cats have tyrosinase enzymes to make dopaquinone, and then melanin. However, their enzymes have a mutation that causes them to denature more easily in lower temperatures than the non-mutated enzymes normally would. What does this mean for the enzyme?

_____

_____

_____

26. If Siamese cats have tyrosinase and the ears of the cat are cooler, why are they dark colored?

_____

_____

_____

27. Why are Siamese cats light colored on their warmer body?

_____

_____

_____

28. What would happen if you left a Siamese cat outside all winter? Why?

_____

_____

29. What would happen if you put boots on the feet of a Siamese cat? Why?

_____

_____

30. Can proteins lead to visible traits? _____ Why or why not?

_____

_____

Name: _____

31. Create your final model of how Siamese cats get their coat coloration and pattern. Be sure to include anything helpful you have learned in this unit.