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miniPCR Sickle Cell LARP (Live Action Role Play)

Summary

In this activity, students will role play to explore how hemoglobin molecules interact in normal, sickle cell disease, and sickle cell trait individuals. Students will represent either alpha-globin or beta-globin and will join together to make hemoglobin tetramers. Students will act out the clumping of hemoglobin molecules in red blood cells depending on the whether the sickle cell mutation is present in beta-globin subunits.

Here we provide materials and list directions to follow, but we encourage teachers to experiment with this activity and to modify it to their needs and class.

Materials

Instructions

Step by step instructions to follow while directing your students.

Teacher Questions

Use these questions throughout the activity to challenge students and assess their understanding. The questions are meant as suggestions to expand upon.

Formative Assessment/Exit Ticket

At the end of the activity or class, use to assess student understanding.

Globin Cards

Printed two per page. Cut pages in half prior to use. Print an equal number of all three types of cards. You should have enough of each type of card for half of your class to use (for a class of 24, you will use 12 of each card).

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Directions

Overview

This activity is designed for 12 or more students in groups of four. The LARP will work better with larger numbers of students. If your class size is not divisible by 4, we recommend having the remaining students act as observers and to switch observers each round. Alternatively, extra students can act as directors and lead the active participants in the activity.

For all three rounds, half of the class will be given an "alpha-globin" card. The other half of students will be given a "beta-globin" card. There are two types of beta-globin cards that will be distributed, "beta-globin 6 Glutamic Acid" or "beta-globin 6 Valine". The "6 Glutamic Acid" and "6 Valine" represent which amino acid is present in the sixth position of the beta-globin amino acid chain. You may decide to have students trade cards each round, so that different students play both the alpha-globin and beta-globin roles, or have students retain the same role through all three rounds.

Round 1: Normal hemoglobin

- Hand out alpha-globin and beta-globin cards. Only hand out "beta-globin 6 Glutamic Acid" cards. Save "beta-globin 6 Valine" for later rounds. Make sure that an equal number of alpha and beta-globin cards are handed out.

- Have students make groups of four. Each group of four must have two alpha-globin members and two beta-globin members.

- Students should lock arms in a square shape facing out with their backs towards the middle of the square. In the square, the alpha-globin participants and the beta-globin should alternate, so that each alpha-globin student is locked arms with two beta-globin students and each beta-globin student is locked arms with two alpha-globin students. Students should hold their card in front of their chests with both hands.

- Inform students that they now represent a molecule of hemoglobin and that they are currently dissolved in the cytoplasm, an aqueous environment.

- Students should be informed that if their card says "6 Glutamic Acid" they have glutamic acid in the sixth position of their bet-globin subunit. If their card says "6 Valine", they have valine in the sixth position of their beta-globin subunit. Glutamic acid is hydrophilic and is not repelled by the surrounding water. Valine is hydrophobic and is repelled by water. To be protected from water they must touch their "6 Valine" card to one other "6 Valine" card.

- At this time no students should have a "6 Valine" card, and so no action is needed.

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Round 2: Sickle Cell Disease

- For this round, again, half the students should be holding alpha-globin cards. The other half of students should be given the "beta-globin 6 Valine" cards.

- Students should again make groups of four and form a square with interlocking arms facing outwards, making sure that alpha-globin and beta-globin students alternate in the square. Again, students should hold their cards in front of their chests with both hands.

- Students should be informed that if their card says "6 Glutamic Acid" they have glutamic acid in the sixth position of their bet-globin subunit. If their card says "6 Valine", they have valine in the sixth position of their beta-globin subunit. Glutamic acid is hydrophilic and is not repelled by the surrounding water. Valine is hydrophobic and is repelled by the surrounding water. To be protected from water they must touch their "6 Valine" card to another "6 Valine" card.

- At this time, every hemoglobin group should have two "beta-globin 6 Valine" subunits. Groups will need to arrange themselves so that the "6 Valine" card from one group is in direct contact with the "6 Valine" card from another group. This should result in all the hemoglobin groups aligning themselves in a single line.

- There will be two students at each end of the line that cannot pair with another "6 Valine" card. In a normal red blood cell, there are hundreds of millions of hemoglobin proteins in a single cell. Therefore, in the cell, there would be plenty of other hemoglobin molecules for these students to pair with. Students may try to turn their line into a circle so that every "6 Valine" cards can pair up. Instruct them that this is unlikely to occur in a cell.

Round 3: Sickle Cell Trait

- For this round, again, half the students should be holding "alpha-globin" cards. The other half of students should be given "beta-globin" cards. An equal number of "beta-globin 6 Valine" and "beta-globin 6 Glutamic Acid" should be distributed.

- Students should again make groups of four and form a square with interlocking arms facing outwards. Students should disregard whether their card says "6 Valine" or "6 Glutamic Acid" while forming groups. Ideally, at least one group will have both a "6 Glutamic Acid" and "6 Valine" member. Again, make sure that alpha-globin and beta-globin students alternate in the square. Again, students should hold their cards in front of their chests with both hands.
  *Note: The most realistic portrayal of this situation will have some groups with two "beta-globin 6 Valine" cards, some with one "6 Valine" and one "6 Glutamic Acid" cards and some with two "6 Glutamic Acid" cards.

- Students should be informed that if their card says "6 Glutamic Acid" they have glutamic acid in the sixth position of their bet-globin subunit. If their card says "6 Valine", they have valine in the sixth position of their beta-globin subunit. Glutamic acid is hydrophilic and is not repelled by the surrounding water. Valine is

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hydrophobic and is repelled by the surrounding water. To be protected from water they must touch their "6 Valine" card to another "6 Valine" card.

– At this time, different groups will need to respond differently. You should observe some joining of groups either in pairs or a short line, but a single long line should not form.

Notes on implementing

– While hemoglobin tetramers are clumping, students will be trying to move, sometimes backwards or sideways, in a crowded environment while linked to other students in groups. Make sure that you have a large space free of obstacles while performing this LARP.

– We recommend completing all three rounds of this activity to ensure a fuller student understanding of how sickle cell genotypes affect hemoglobin thin the cell. If time is a constraint, however, demonstrating just the sickle cell disease portion of the activity is an option.

– Fun Fact: There are roughly 300 million hemoglobin proteins in a red blood cell. To do this LARP more realistically, you would need four times that many students to create the number of tetramers in a living cell. That would require about 1.2 billion people (about the population of India) performing this LARP together in a single very large room.

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Example Questions

Round 1

Hemoglobin is a tetramer. Can anyone explain what it means to be a tetramer?

- *Tetra is a prefix derived from the Greek work for four. There are four protein subunits that come together to make one hemoglobin molecules. That is why there are four students in each hemoglobin molecule.*

Beta-globin, what amino acid do you have at position six? How does that amino acid react to being exposed to water?

- *Beta-globin has glutamic acid at position six. Glutamic acid is hydrophilic and is attracted to the surrounding water.*

As you are currently configured, are any hemoglobin molecules interacting with other hemoglobin molecules?

- *Currently all hemoglobin molecules have hydrophilic amino acids covering the outside of the protein and so no hemoglobin molecules are interacting with each other.*

What genotype would produce a cell like this?

- *This represents an individual who has normal hemoglobin. They are homozygous for the normal beta-globin allele (HbA).*

Round 2

Beta-globin, what amino acid do you have at position six? How does that amino acid react to being exposed to water?

- *All of the beta-globin subunits will have valine at position six. Valine is hydrophobic and is repelled by the surrounding water.*

As you are currently configured, are any hemoglobin molecules interacting with other hemoglobin molecules?

- *All beta-globin subunits have a hydrophobic valine on the exposed surface of the protein. These valine amino acids should be interacting with each other. This means that all hemoglobin proteins should be interacting with other hemoglobin proteins. Because each hemoglobin molecule has a beta-globin subunit on either side of the protein, the class should be aligned in a single line.*

What genotype would produce a cell like this?

- *This represents an individual who has sickle cell disease. They are homozygous for the sickle cell version of the beta-globin allele (HbS).*

What is the biggest group of Hemoglobin molecules that we made? Do you think that it is likely that we would make very large groups of hemoglobin molecules in the cell?

- *The class should have aligned in a single large group. In the cell there can be 200-300 million hemoglobin proteins. This will create many very long chains of hemoglobin proteins.*

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How could this lead to damage in the cell?

- *The many long filaments of hemoglobin proteins will distort and damage the cell membrane leading to the sickle shaped cell for which the disease is named.*

Alpha-globins, how have you been affected by this?

- *Alpha-globins are not affected.*

Round 3

Beta-globin, what amino acid do you have at position six? How does that amino acid react to being exposed to water?

- *Half of the beta-globin subunits will have glutamic acid at position six. Glutamic acid is hydrophilic and is attracted to the surrounding water. Half of the beta-globin subunits will have valine at position six. Valine is hydrophobic and is repelled by the surrounding water.*

As you are currently configured, are any hemoglobin molecules interacting with other hemoglobin molecules?

- *Currently half of all beta-globin subunits have a hydrophobic valine on the exposed surface of the protein. These valine amino acids should be interacting with each other. The beta-globin subunits that have glutamic acid at position six will not be interacting with other beta-globin subunits.*

What genotype would produce a cell like this?

- *This represents an individual who has the sickle cell trait. They are heterozygous for the beta-globin allele.*

What is the biggest group of hemoglobin molecules that we made? Do you think that it is likely that we would make very large groups of hemoglobin molecules in the cell?

- *Typically, hemoglobin molecules will make groups of two or chains of three. This will vary by class size and how "6 Valine" and "6 Glutamic Acid" cards are distributed. It is unlikely that large chains will form. This is especially true because some hemoglobin proteins have only one "6 Valine" beta-globin card, and can therefore group with only one other hemoglobin protein.*

Alpha-globins, how have you been affected by this?

- *Alpha-globins are not affected.*

Would you expect the groups that you made by 6 Valine coming together to damage the cell membrane?

- *It is unlikely that this would cause damage to the cell as the clumping of hemoglobin is limited. This clumping is why in extreme circumstances individuals with sickle cell trait may experience some symptoms of sickle cell disease, however.*

Exit Ticket Name:_____

In your own words, explain a basic difference between valine and glutamic acid and how that difference affects the hemoglobin molecules in a red blood cell.

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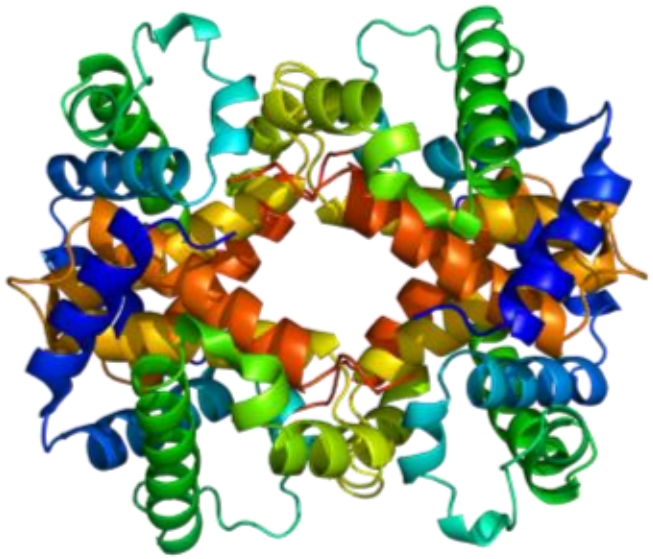
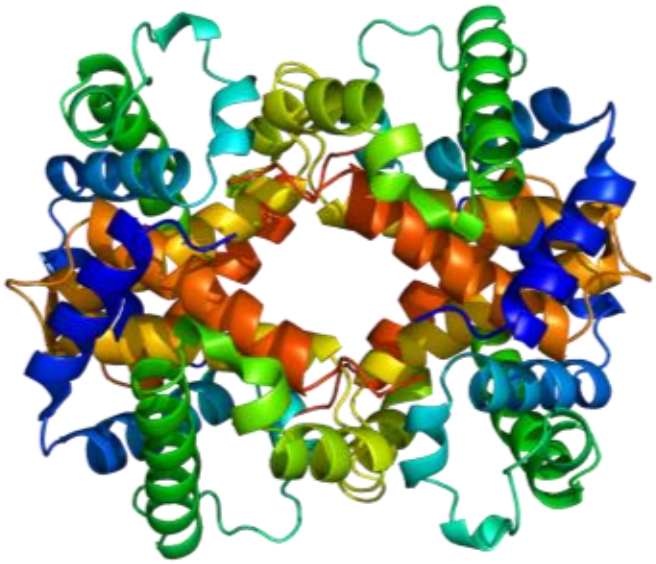


alpha-globin

minipcr



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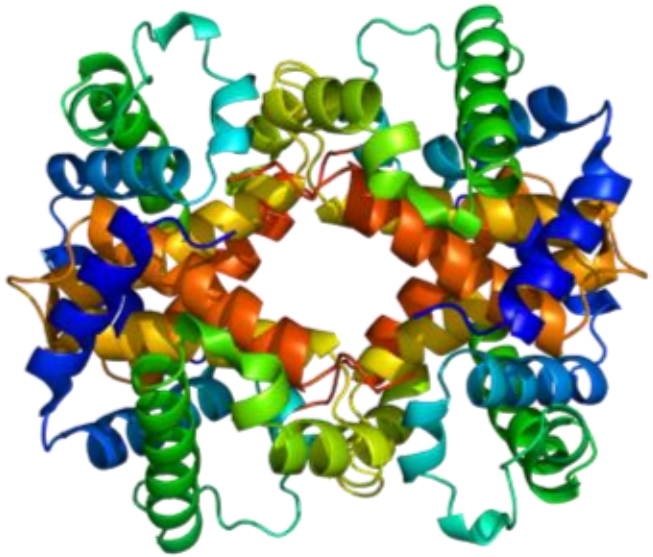

beta-globin

6 Glutamic Acid

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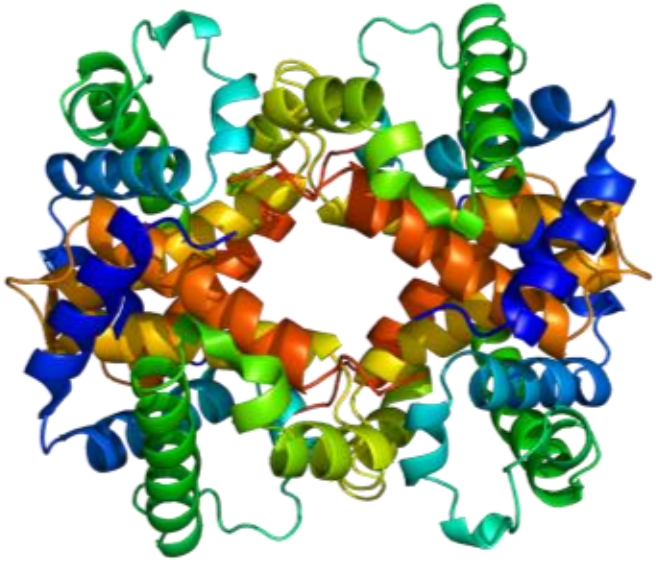

beta-globin

6 Glutamic Acid

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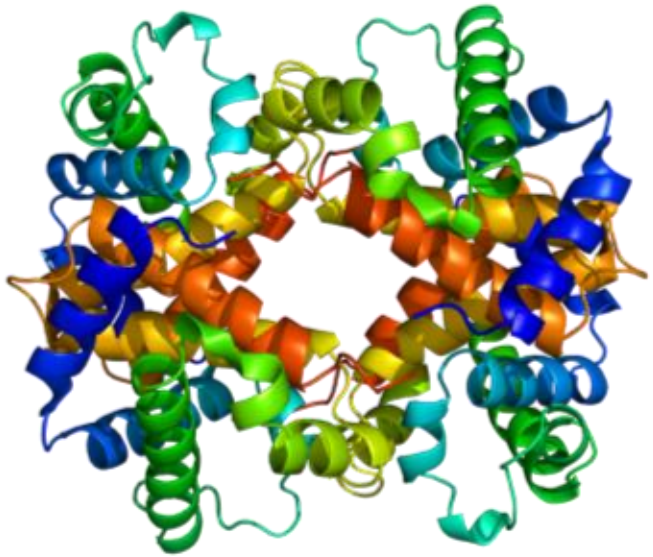

beta-globin

6 Valine

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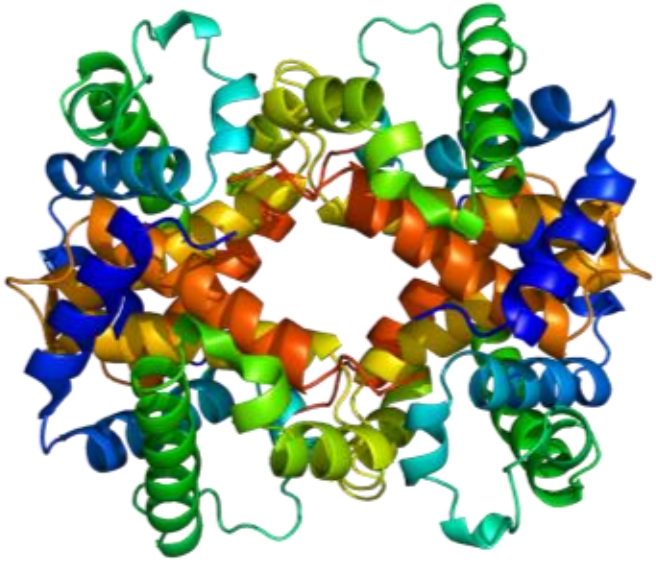

beta-globin

6 Valine

minipcr