

Unit V Activity 4



Protein Malfunction and Disease: Making a Sickle Cell Mutation

(Student version)

Scientists know that Sickle Cell Disease is an example of a disorder caused by mutation in the DNA. The result of the mutation is a misshaped protein that includes a replacement of a hydrophilic glutamic acid (E) for hydrophobic valine (V). In this activity you will look at the amino acid change and determine the molecular basis for the disease that lies in the DNA. You will then be asked to relate the change in the protein to the implications for the health of the individual that has the mutation.

The molecular defect that causes Sickle Cell Anemia can be only ONE amino acid, although the full hemoglobin complex is over 574 amino acids long! You can model the effect of one amino acid change by making the critical piece of hemoglobin.

A model of the critical hemoglobin fragment in the red blood cell of a normal person.

1. Open the [Molecular Workbench:Hemoglobin](#)

The model can be opened in one of two ways:

1. From your browser. Click the link below.:

* [Molecular Workbench: Hemoglobin](#)

[\[http://xeon.concord.org:8080/modeler/webstart/protein/hemoglobin.jnlp\]](http://xeon.concord.org:8080/modeler/webstart/protein/hemoglobin.jnlp)

2. By going through the Molecular Workbench application on your computer (workbench.jar). Then you should click the following links: Student Pages, Protein Folding, Mutations or Hemoglobin.

It may take a short while to launch the Molecular Workbench the first time.

2. Build a string, modeling the hemoglobin fragment of a **normal** person with the following amino acids: (remember to change amino acids and you are using a **windows** machine you do control +right click on an amino acid or on a **Macintosh** control+apple+click on the amino acid to change it)

The amino acid list is: Valine-Histadine-Leucine-Threonine-Proline-Glutamic Acid-Glutamic Acid-Lysine-Serine-Alanine-Valine-Threonine-Alanine-Leucine-Tryptophan-Glycine-Lysine-Valine-Asparagine-

This is part of the code that is usually in every hemoglobin in our body. You might want to work with another student to make sure you get the right sequence.

Write down the DNA codon for the sixth amino acid., Glutamic Acid.

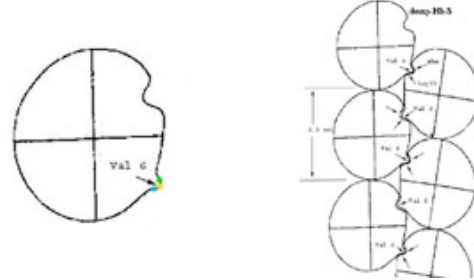
3. Run the model and draw and describe the shape.

4.. Build a model of the critical hemoglobin fragment from **someone with Sickle Cell Anemia** by clicking on the sixth amino acid from the left, the *Glutamic Acid*, and replacing it with *Valine*.

Write down the DNA codon for the sixth amino acid., *Glutamic Acid*.

5. Draw a picture of the shape of the chain in the space below. There should be a more pronounced "bump" in the shape, though this might be hard to see, as computers sometimes vary.

When the codon for the wrong amino acid makes a section of protein shape more like a "bump", the whole hemoglobin gets distorted. The "bump" fits into other hemoglobins and they get held together in



long strings that stretch the cells into a sickle shape.

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