

Sickle Cell at the Molecular Level

In sickle cell anemia, there is a mutation in the gene that encodes the chain of hemoglobin. Within this gene (located on Chromosome 11), ONE BASE in the DNA is replaced with another base, and this mutation causes the normal amino acid #6 to be replaced by another amino acid.

1. Making a Normal Beta Chain of Hemoglobin

The sequence below is the first part of the DNA sequence for the chain of normal hemoglobin. Fill in the complementary DNA strand using the base-pairing rules for making DNA (A pairs with T, C pairs with G).

DNA: GTG CAC CTG ACT CCT GAG GAG

DNA:

Now make the messenger RNA from the new, complementary strand of DNA that you just wrote down. Use the RNA base-pairing rules (same as DNA but use U instead of T).

mRNA:

Now, using the Genetic Code chart in your textbook, translate this mRNA into a sequence of amino acids.

Amino Acids:

2. Making Sickle Cell Hemoglobin

In sickle cell anemia, there is a mutation at the seventeenth nucleotide of DNA in this gene; the nucleotide is changed from A to T. Fill in the complementary DNA strand, mRNA, and amino acid sequence in the hemoglobin protein.

DNA: GTG CAC CTG ACT CCT GTG GAG

DNA:

mRNA:

Amino Acids:

3. The Effect of Changing One Amino Acid

You can see that in normal hemoglobin, amino acid #6 is glutamic acid (Glu) and in sickle cell hemoglobin, amino acid #6 is valine (Val). Observe the two structural

formulas for these amino acids (find pictures of these in your books and draw each of them):

This altered hemoglobin deforms the normally rounded cell into the sickle shape. These red blood cells are destroyed at an increased rate, causing anemia. They are also prone to becoming stuck in capillaries, causing pain, organ damage, and often premature death.

Summary

1. How does sickle cell hemoglobin differ from normal hemoglobin?
2. What is the effect on the red cell containing this altered hemoglobin?
3. Write a possible DNA sequence that includes a non harmful mutation from the normal hemoglobin sequence. This mutation should not change the final amino acid sequence.
4. Imagine the nucleotide “A” was added to the sequence:

GTGACACCTGACTCCTGAGGAG

How would that affect the final protein?

5. Which kind of mutations should have a larger affect on the expressed protein, a mutation that switches one nucleotide, or one that inserts a nucleotide? Explain how some mutations are more harmful than others (please be specific).

Modified from the following website:

<http://chroma.gs.washington.edu/outreach/genetics/sickle/worksheet.html>

Protein Synthesis Resources:

1. Allows you to build a protein from a DNA strand online:
<http://gslc.genetics.utah.edu/units/basics/transcribe/>
2. List of useful sites that are genetics related:
<http://www.kumc.edu/gec/lessons.html>