

SECTION III – Post Laboratory Activity

This extension activity allows to students to further explore the molecular basis of sickle cell anemia:

- Have students use the central dogma.
- Have students discuss treatment options and preventive measures such as genetic testing.
- Have students relate sickle cell anemia to evolution

Central dogma

Using the amino acid sequence of the affected and normal hemoglobin, the students can identify the mutation from glutamate to valine that results in the change in net negative charge of the affected hemoglobin. Working back through the central dogma, they can identify the point mutation in the DNA resulting in the amino acid alteration.

Inheritance

Genotypes can be derived from the phenotypic results expressed on the gel and the probability of inheriting sickle cell anemia can be predicted given the genotypes of the parents.

Natural Selection

The sickle cell allele is more prevalent in races whose gene pools originate in tropical areas. People of African, Asian, and Hispanic-Caribbean descent have a higher incidence of sickle cell anemia. Selective pressure for the allele results from its ability to decrease the mortality rate of people infected with malaria. Malaria is caused by a protoctist in the genus plasmodium, which is transmitted to human hosts by mosquitoes. Plasmodia infiltrate red blood cells where they multiply and eventually rupture the cell. Cells with sickle cell hemoglobin are less susceptible to infection by Plasmodia. Therefore, carriers of sickle cell trait (heterozygotes) benefit from the presence of sickle cell hemoglobin while remaining largely asymptomatic (some heterozygous individuals may show mild symptoms) with respect to sickle cell anemia.

Random mutation/Selective Pressure

Plasmodium did not infect humans 10,000 years ago; it was an avian pathogen. However, a mutation in plasmodium enabled it to jump species and infect humans. Ask the students whether they think anyone could have had sickle cell anemia prior to 10,000 years ago. It often leads to a discussion concerning random mutations and the distinction between a Lamarckian and Darwinian perspective on evolution.

Treatments

Ask the students how they would treat sickle cell anemia based on their knowledge of the disease. Bone marrow transplants, blood transfusions, and gene therapy are often mentioned. Recently, attention has been given to turning on the fetal hemoglobin gene, which is turned off shortly after birth. Hydroxyurea, which has been used to treat cancer and blood disorders, has been found to stimulate the production of fetal hemoglobin.

Other Activities

- Have the students write a letter to the fictional patient explaining the results of the test and the precautions the patient may want to consider taking.
- Use the documents at the end of the student section titled A Closer Look at the Cause of Sickle Cell Anemia. This activity shows students how the sickle cell trait is determined at the genetic level.
- Sickle cell anemia is an example of one genetic condition for which there is a test but no cure. Have groups of students research other inherited conditions for which there is a test but no cure, for example; cystic fibrosis, Huntington's disease, muscular dystrophy, and fragile x syndrome. Each group can make an informative display about the disease. The display could be in the form of a poster, mobile, booklet, radio broadcast, interview, role-play etc. After each group has made a presentation about the disease, create a role-play in which a genetic counselor presents a

scenario, for example:

- Both parents are carriers for sickle cell anemia, cystic fibrosis, or any recessive disorder. The couple decides whether or not to try to have children.
- One spouse's parent has been diagnosed with Huntington's disease. The couple has two young children. The counselor asks whether they want to be tested.
- The role-plays can lead to interesting discussions among the students. The teacher can facilitate by writing down ideas and issues on the board as they come up.

Suggested readings:

- Pelehach, Laura. (1995). Understanding Sickle Cell Disease. *Laboratory Medicine* (26), 720-725
- Ogamdi, S. and White, G. (1993). Sickle Cell Disease. *Clinician Reviews* (February), 65-82.
- The Sickle Cell Information Center: www.emory.edu/PED/SICKLE/news.htm