Unit 4.3 Learning Targets

Preface

In this lesson students will begin to explore what happens inside the body when the heart is unable to function properly. Now that they understand basic structure and function of the heart, students will dive deeper into Anna's Garcia medical history and assess her cardiac function.

Students will investigate the function of cholesterol in the body and research how this lipid can impact health. They will design and create a brochure, poster, newsletter, or webpage that accurately informs high school and college students about cholesterol, LDL, and HDL. They will then analyze Anna Garcia's cholesterol test results and make recommendations about her cardiac care.

Students will notice that Anna's cholesterol is incredibly high. They will further investigate genetics and molecular biology laboratory techniques as they learn about the disease, *familial hypercholesterolemia*. LDL transports cholesterol to the cells. In some families, the risk of heart disease is increased due to a genetic mutation that leads to very elevated levels of LDL in the blood. The genetic defect causes the LDL receptor on cells to be deformed and inefficient at binding LDL. The inefficient uptake or binding of LDL by the receptor results in elevated LDL in the bloodstream. This is turn leads to the accumulation of a fatty substance called plaque in the blood vessels. The plaque accumulation in the arteries can cause blockages in the blood flow which results in heart attacks or strokes. In many cases this defect is due to a single mutation in the receptor gene and is inherited as an autosomal dominant trait. Often this mutation is referred to as the FH mutation, because it is the mutation that is most closely associated with familial hypercholesterolemia. Whereas diet and exercise play a huge role in regulating cholesterol levels, more invasive interventions such as medications may be needed to keep this genetic disorder under control.

To detect the FH mutation, DNA is obtained from the patient's blood or saliva; the section of DNA containing the LDL receptor gene is then amplified by the polymerase chain reaction (PCR). The amplified DNA is analyzed to see if there is a mutation. To analyze the DNA, investigators use restriction enzymes to cut the DNA in specific places. By examining the sizes of the DNA fragments obtained after exposing the DNA to the restriction enzymes, it is possible to detect mutations or changes in the DNA. This detection is possible because of Restriction Fragment Length Polymorphorism or RFLP. RFLP simply means that when different DNA samples are exposed to the same restriction enzyme, the DNA fragments produced by the enzyme may be different lengths. The different lengths are due to differences in the DNA sequences of the two samples; the DNA sequence differences are a polymorphism. A mutation or change in the DNA sequence can change where the enzyme cuts the DNA, so the DNA fragments are different sizes, or are greater or

lesser in number, than in the normal DNA. The resulting DNA fragments can be visualized and analyzed through gel electrophoresis.

In past activities students analyzed the results of gel electrophoresis experiments. In this lesson they will actually use DNA electrophoresis to separate and analyze DNA fragments. They will use their final gel to determine if Anna and members of her family have familial hypercholesterolemia.

In the final problem of the lesson, students will explore the human heart as a pump and investigate what happens to overall health when factors such as cholesterol plaque impede flow. Students will design and build a simple pump to simulate the heart on the most basic level. They will then design an experiment to simulate the effects of decreased vessel diameter on blood flow rate. In the next lesson, students will dig deeper into the diagnosis of heart disease and begin to think about interventions that may help individuals save a failing cardiovascular system.

Understandings

1. Cholesterol is a lipid that is necessary for the proper functioning of cells and for maintaining a healthy body.
2. The measurement of the HDL and LDL complexes may indicate a person's risk for heart disease.
3. Restriction Fragment Length Polymorphism (RFLP) analysis can be used to diagnose genetic disease and disorders.
4. The human heart pumps blood around the body, and the efficiency of this pump is affected by the rate at which blood can move through the vessels.
5. Experiments are designed to find answers to testable questions.

Knowledge and Skills

It is expected that students will:

- Recognize that cholesterol is transported in the blood by protein complexes called high density lipoprotein (HDL) and low density lipoprotein (LDL).
- Describe how restriction enzymes and gel electrophoresis can be used to analyze genetic information.
- Describe how cholesterol buildup can impact blood flow through arteries.
- Compare and contrast the role of HDL and LDL in the body and how each relates to health.

- Use proper laboratory techniques to separate DNA fragments by gel electrophoresis.
- Analyze the results of the gel electrophoresis to correctly diagnose the presence of the familial hypercholesterolemia mutation.
- Generate ideas as a team to solve a problem.
- Design a controlled experiment to demonstrate how cholesterol plaques impact flow rate in blood vessels.

Essential Questions

1. What is cholesterol?
2. What roles does cholesterol play in our cells and in the body?
3. What are LDL and HDL?
4. How are LDL, HDL, and cholesterol related to heart disease?
5. How do doctors interpret the results of a cholesterol test?
6. What is familial hypercholesterolemia and how is it inherited?
7. How can techniques of molecular biology be used to analyze DNA for the presence of the FH mutation?
8. What lifestyle changes may help a patient obtain healthy cholesterol levels?
9. What are the pros and cons of using cholesterol lowering medications?
10. How does the heart work as a pump?
11. What is atherosclerosis?
12. How can cholesterol plaques affect the overall function of the heart?