A LESSON ON THE NATURE OF SCIENCE

INTRODUCTION

Dr. Tony Allison is credited with demonstrating the link between the inherited blood disorder sickle cell disease (also called sickle cell anemia) and malaria. His work showed that an infectious disease could act as a selective force to drive human evolution. What inspired him to do this research?

While growing up on a chrysanthemum farm in Kenya, Dr. Allison became interested in natural history, anthropology, human diversity, and medicine. Dr. Louis Leakey's excavations of fossils in East Africa and Charles Darwin's work on evolution and natural selection had a strong influence on the budding scientist. Later, while a student at Oxford University in England, he learned about the connection between evolution and population genetics and how evolution results from changes in the frequencies of alleles in populations.

Dr. Allison's work built on the contributions of many other scientists. It reminds us that science is a human endeavor.

TIMELINE

1910 Dr. James Herrick observed sickled red blood cells (RBCs) in the blood of a dental student with anemia. This condition was later called sickle cell anemia by Dr. Verne R. Mason. (Today the condition is called sickle cell disease.)

1917 Dr. Victor Emmel discovered that when blood from people with sickle cell disease is sealed under glass and allowed to sit at room temperature for 24 hours, the RBCs become sickle shaped. Using the same technique, Dr. Emmel also found that the parents of individuals with sickle cell disease had RBCs that became sickle shaped, even though they had no noticeable symptoms of the disease. (We now know that Dr. Emmel's assay can identify people who have sickle cell trait—that is, they are heterozygous—as well as those who have sickle cell disease.)

1923 Using the technique developed by Dr. Emmel, Dr. William Taliaferro and Dr. John Huck analyzed several pedigrees of families with sickle cell disease. They determined that sickle cell disease is inherited.

1927 Dr. E. Vernon Hahn and Dr. Elizabeth Gillespie demonstrated that the sickling of RBCs is linked to deoxygenation.

1940 Dr. Irving Sherman conducted an experiment that showed a clear distinction in the behavior of RBCs in individuals who were homozygous for the sickle cell allele (they had sickle cell disease) and individuals who were heterozygous for the sickle cell allele (they were carriers). He sampled blood from the venous system of both groups. For those with sickle cell disease, he found that 20–60 percent of the RBCs were sickled, but for carriers, less than 1 percent of RBCs were sickled in vivo.

1948 Dr. Geneva Daland and Dr. William Castle developed a simple and rapid method for detecting sickled RBCs by using a chemical agent to deoxygenate blood.

1949 Dr. James Neel used the mathematical analysis of allele frequencies and pedigree analysis to show that sickle cell disease is autosomal recessive.

1949 Dr. Linus Pauling knew that RBCs contain hemoglobin, a protein responsible for carrying oxygen. He also knew that the sickling behavior depends on oxygen. Dr. Pauling investigated the hemoglobin of people with sickle cell disease and discovered that it was abnormal. He also found that those with sickle cell trait had both the abnormal and normal forms of hemoglobin.

Researchers later discovered that a point mutation on one of the hemoglobin genes is responsible for the abnormal form of hemoglobin. The mutant hemoglobin is called HbS, and the normal hemoglobin is called HbA. Individuals who carry one mutant hemoglobin allele (*S*) and one normal hemoglobin allele (*A*) are heterozygous (*AS*) and have sickle cell trait. Those who are homozygous for the mutant hemoglobin allele (*SS*) have sickle cell disease, and those with both copies of the normal hemoglobin allele (*AA*) have neither sickle cell disease nor sickle cell trait.

SUMMARY

The work of these scientists established the following:

- Scientists can identify those who have the sickle cell allele by deoxygenating their blood, which causes the sickling of RBCs.
- Sickle cell disease is inherited.
- Sickle cell disease is autosomal recessive.
- Sickle cell disease is caused by a mutation in the hemoglobin gene.

QUESTIONS

PART 1: Before you watch the short film, answer these questions by using the information provided in the introduction.

1. Explain how analyzing the inheritance patterns of sickle cell disease through pedigrees allowed scientists to determine that the disease is autosomal recessive.

_____

_____

_____

_____

_____

_____

2. Discuss how the timeline demonstrates that science is a social process done by people working together and sharing information with the scientific community and the public.

_____

_____

_____

_____

PART 2: Read the following passage and then watch the short film *The Making of the Fittest: Natural Selection in Humans*. Answer the questions that follow.

DR. ALLISON'S WORK

Early in his scientific career, while waiting to start medical school, Dr. Allison participated in a University of Kenya expedition. It was his task to investigate the distribution of ABO blood types and other inherited characteristics in people of the East African tribes. One of the characteristics he assayed for was the sickling of the RBCs in deoxygenated conditions. Using this assay, he could identify people who had sickle cell trait and sickle cell disease.

- High frequencies (20–30 percent) of individuals living close to the coast of East Africa and near Lake Victoria carried the sickle cell allele.
- Low frequencies (<1 percent) of individuals living in the highland regions carried the sickle cell allele.

He knew that the survival of people with sickle cell disease (*SS*) was extremely rare in places where health care was limited, such as rural Africa. Therefore, selection against the *SS* genotype should be very strong.

Why, then, had the sickle cell allele become so common in some parts of East Africa and not in others?

In addition to knowing the past research on sickle cell disease, Dr. Allison had studied malaria. He knew the following:

- The malaria parasite (*Plasmodium falciparum*) is transmitted by the *Anopheles* mosquito and other related mosquito species.
- These mosquitoes flourish in hot, humid environments (such as the coast of East Africa and near Lake Victoria), but they cannot survive in the highlands and other arid regions of Africa.
- From the age of five through adulthood, individuals living in areas with a high incidence of malaria have a high level of acquired immunity to malaria.

Dr. Allison had a flash of inspiration! He predicted that the high frequency of the sickle cell allele and the presence of malaria were somehow related, and he hypothesized that people with the sickle cell allele had a selective advantage against malaria.

Dr. Allison collected blood samples from children between the ages of four months and four years and tested for the presence of the malaria parasite and the sickle cell allele. If his malaria–sickle cell hypothesis was correct, he would find high sickle cell allele frequencies in areas where there was a high incidence of malaria.

3. Provide two examples of how Dr. Allison used the work and observations of other scientists to complete his own research.

a. _____

_____

b. _____

_____

4. List at least two pieces of data supporting the hypothesis that there is a link between the sickle cell allele and malaria.

a. _____

_____

b. _____

_____

_____

5. Both environmental factors and genetics can account for an individual's susceptibility to infectious disease. For the sickle cell–malaria example, explain how genetics accounts for an individual's susceptibility to infectious disease.

_____

_____

_____

_____

_____

_____

6. Describe how the relationship between sickle cell disease and malaria is an example of natural selection in humans.

_____

_____

_____

_____

_____

7. In science, discoveries often lead to new questions for future investigation. With the knowledge that you have gained about malaria and sickle cell disease through this worksheet, propose two questions that scientists could ask about either of these diseases or the link between them.

_____

_____

_____

_____

_____

_____

AUTHOR

Mary Colvard, Cobleskill-Richmondville High School (retired), New York