# Allele Frequencies and Sickle Cell Anemia Lab

**Background: Genetics of Sickle Cell Anemia**

Sickle cell anemia was the first genetic disease to be characterized at the molecular level. The mutation responsible for sickle cell anemia is small just ONE nucleotide of DNA out of the three billion in each human cell. Yet it is enough to change the chemical properties of hemoglobin, the iron and protein complex that carries oxygen within red blood cells.

Sickle cell anemia, also known as sickle cell disease, is caused by a point mutation. As a result of this mutation, valine is inserted into the amino acid chain instead of glutamic acid. The mutation causes the RBCs to become stiff and sometimes sickle-shaped when they release their load of oxygen. The sickle cell mutation produces a "sticky" patch on the surface of the cell and they adhere to each other. The sickled cells tend to get stuck in narrow blood vessels, blocking the flow of blood. They may also suffer strokes, blindness, or damage to the lungs, kidneys, or heart. Although many sufferers of sickle cell disease die before the age of 20, modern medical treatments can sometimes prolong these individuals lives into their 40s and 50s. About 2.5 million African-Americans (1 in 12) are carriers (AS) of the sickle cell trait.

**Sickle Cell Anemia and Malaria**

In the United States, about 1 in 500 African-Americans develops sickle cell anemia. In Africa, about 1 in 100 individuals develops the disease. The answer is related to another potentially fatal disease, malaria. Malaria is characterized by chills and fever, vomiting, and severe headaches. Malaria is caused by a parasite that is transmitted to humans by a mosquito. When malarial parasites invade the bloodstream, the red cells that contain defective hemoglobin become sickled and die, trapping the parasites inside them and reducing infection, thus individuals with sickle cell anemia have less chance of contracting malaria.

**Introduction:**

Allele frequency refers to how often an allele occurs in a population. Allele frequencies can change in a population over time, depending on the **selective forces** shaping that population. Predation, food availability, and disease are all examples of selective forces. **Evolution occurs when allele frequencies change in a population!**

In this activity, red and white beans are used to represent the two alleles. The **RED** beans represent gametes carrying the **A** allele, and the **WHITE** beans represent gametes carrying the **S** allele. The Gene Pool exists in a region of Africa that is infested with malaria. You are simulating the effects of a high frequency of malaria on the allele frequencies of a population.

**Materials:** 75 red beans, 25 white beans, 1 coin, 5 containers

**Hypothesis/Prediction:** What do you think will happen to the frequencies of the A and S alleles as a result of the presence of malaria? (Will the frequency of A increase or decrease? What about S?) Formulate a hypothesis and corresponding prediction. Be sure to explain your reasoning.

______________________________________________________________________________

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**Procedure:**

1. Together with your lab partner, obtain five containers and label them as follows:
    a. 1) AA 2) AS 3) SS 4) Non-surviving alleles 5) Gene Pool
2. Place the 75 red and 25 white beans in the Gene Pool container and mix the beans up.
3. Simulate fertilization by PICKING OUT two alleles (beans) WITHOUT LOOKING.
4. For every two beans that are chosen from the gene pool, another person will FLIP A COIN to determine whether that individual is infected with malaria.
5. Using the table below, the coin flipper tells the bean picker in which containers to put the beans.
6. Repeat steps 3-5 until all the beans in the Gene Pool are used up.
7. Record the results in the F1 CUP TALLY table on the data sheet.

8. At the end of the round, COUNT the number of individual red beans (A alleles) and white beans (S alleles) in the containers labeled AA and AS. These individuals survive to reproduce. RECORD those numbers in the F1 TOTAL SURVIVING ALLELES table. Put them in the gene pool afterwards.
9. Because SS individuals do not survive to reproduce, move all beans from the SS alleles container into the Non-surviving alleles container. STOP AFTER ONE GENERATION.
10. CHECK WITH YOUR TEACHER BEFORE GOING ON!
11. Repeat the procedure for the F2 generation. Record your results in the F2 CUP TALLY table and F2 TOTAL SURVIVING ALLELES table.

| Genotype | Phenotype | Malaria | Not infected |
|---|---|---|---|
| **AA (red/red)** | No sickle cell (malaria susceptibility) | Die: Place in non-surviving | Live: Place in AA |
| **AS (red/white)** | No sickle cell (malaria resistance) | Live: place in AS | Live: place in AS |
| **SS (white/white)** | Sickle cell disease | Die: Place in non-surviving | Live for a brief time: place in SS |

**Data Sheet for Allele Frequencies and Sickle Cell Anemia Lab**

**F1 CUP TALLY:** Put a mark for each bean next to the appropriate cup.

| Cup | Tally |
|---|---|
| **AA** | |
| **AS** | |
| **SS** | |
| **Non-surviving** | |

**F1 TOTAL SURVIVING ALLELES:** (very important to record – add to board)

| | |
|---|---|
| Number of A (RED) alleles surviving (Count out of AA and AS containers) | |
| Number of S (WHITE) allele surviving (Count out of AS container) | |

**Put the survivors in the gene pool and create the next generation.**

**F2 CUP TALLY:** Put a mark for each bean next to the appropriate cup.

| Cup | Tally |
|---|---|
| **AA** | |
| **AS** | |
| **SS** | |
| **Non-surviving** | |

**F2 TOTAL SURVIVING ALLELES:** (very important to record- add to board)

| | |
|---|---|
| Number of A (RED) alleles surviving (Count out of AA and AS containers) | |
| Number of S (WHITE) allele surviving (Count out of AS container) | |

**Class Results**

On the board, record your number of A alleles surviving for the next generation and number of S alleles surviving from both the F1 TOTAL SURVIVING ALLELES and F2 TOTAL SURVIVING ALLELES tables. Then record the class totals below and calculate the frequencies using the formula below.

Using the formulas below, calculate the % allele frequency for each allele in each generation:

<u>Total A</u> x 100 = % Allele A <u>Total S</u> x 100 = % Allele S

**Class Results Table**

| | **Parent** | | **F1** | | **F2** | |
|---|---|---|---|---|---|---|
| | **A** | **S** | **A** | **S** | **A** | **S** |
| **Class Total** | **75** | **25** | | | | |
| **Allele Frequency** | **75%** | **25%** | | | | |

**Analysis Questions: Answer in complete sentences!**

1. What do the red and white beans represent in this simulation? What does the coin represent?

2. What do you think "allele frequency" means? How are allele frequencies related to evolution?

3. What are the "selective forces" in this simulation (the forces changing the allele frequencies)?

4. What was the general trend you observed for Allele A over the three generations (did it increase or decrease)? What was the general trend for Allele S over time? Was your hypothesis supported?

5. Do you anticipate that the trends in question 4 will continue for many generations? Why or why not?

6. Since few people with sickle cell anemia (SS) are likely to survive to have children of their own, why hasn't the mutant allele (S) been eliminated? (Hint: what is the benefit of keeping it in the population?)

7. Why is the frequency of the sickle cell allele so much lower in the United States than in Africa?

8. Scientists are working on a vaccine against malaria. What impact might the vaccine have in the long run on the frequency of the sickle cell allele in Africa? (Would it increase or decrease? Why?)

Class Totals

| NAMES | Parent | | F1 | | F2 | |
|---|---|---|---|---|---|---|
| | A | S | A | S | A | S |
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| Class Total | | | | | | |
| Allele Frequency | | | | | | |