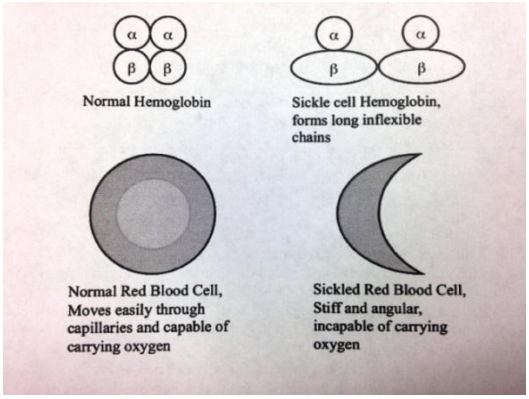
Name _____

Population Genetics Lab using Sickle Cell Anemia

Introduction: Sickle cell anemia was first described in 1910 by James Herrick who observed crescent shaped red blood cells in an anemic patient. The disease was linked to alternative forms of hemoglobin (the substance in red blood cells that carries oxygen) in 1949 when Linus Pauling identified a single amino acid substitution mutation. Symptoms of sickle cell anemia include increased blood clotting due to the stickiness and shape of the cells, severe pain and tissue damage. More severe effects include stroke, heart problems and death, often at a very young age. From a genetic and evolutionary standpoint, one would expect the trait to eventually die out along with the people who carry the trait due to selective pressure. However, around the time of Pauling's discovery, researchers began to notice that the prevalence of the sickle cell trait was conspicuously high in certain regions, particularly Africa, India and Greece. Interestingly, these regions also happened to have a high incidence of malaria, a deadly blood disease caused by the Plasmodium parasite. In 1954, a group of scientist conducted a study comparing malarial infection of 15 adults with sickle cells to 15 adults without sickle cells and concluded that the presence of sickle cells inhibits malarial infection. The base substitution/mutation that causes the sickle cell allele is typically denoted as the "S" allele, and a normal allele without this base substitution is typically denoted as the "A" allele. A person with the SS genotype will have sickle cell anemia and generally not live long enough to reproduce. An individual with the AS genotype, however, is usually healthy AND they have a natural immunity to a malarial infection. An individual with the AA genotype will not have sickle cell anemia, but they have a higher chance of getting malaria (which often leads to death) when compared to an AS individual. In terms of population genetics, the heterozygote has a selective advantage over either homozygote and therefore the trait can be maintained at a high frequency in a given population.



Problem: Why is the allele frequency for sickle cell anemia higher in certain areas like Africa, India and Greece?

Hypothesis: If the sickle cell allele _____ malarial infection, then the sickle cell allele frequency ("S" allele) will _____.

Materials: red beans, white beans, 3 empty cups, a cup marked "gene pool", and a coin

Experimental Procedure: In order to demonstrate the selective advantage of individuals heterozygous for sickle cell anemia, you will examine a gene pool (beans) in a region of Africa that is infested with malaria. The red beans represent gametes carrying the β globin "A" allele, or the non-sickle allele. The white beans represent gametes carrying the β globin "S" allele, or the sickled allele.

1. Working in groups of 2-3, obtain 3 empty cups and a cup marked "Gene Pool". The "Gene Pool" cup has 75 red beans ("A" alleles) and 25 white beans ("S" alleles) in it.

2. The cups should have the following labels:
    a. AA
    b. AS
    c. Non-surviving
    d. Gene Pool

3. Make sure the "Gene Pool" beans are well mixed

4. Without looking at the beans in the "Gene Pool" cup, one partner will pick out 2 beans/alleles.

5. At the same time, the other partner will flip a coin to determine whether that individual is infected with malaria (really only needs to be done if two red beans "AA" are picked).

6. Using the chart below, place the beans in the appropriate cup:

Genotype	**Phenotype**	**Malaria (heads)**	**Not Infected (tails)**
AA (red-red)	No sickle cell disease. Malaria susceptibility.	Die: **Place in non-survivor cup.**	Live: **Place in AA cup**
AS (red-white)	No sickle cell disease. Malaria resistance.	Live: **Place in AS cup**	Live: **Place in AS cup**
SS (white-white)	Sickle cell disease. Malaria resistance.	Live only for a brief time: **Place in non-survivor cup**	Live only for a brief time: **Place in non-survivor cup**

7. Repeat steps 3-6 until the "Gene Pool" cup is empty.

8. Record the number of beans placed in each cup on your data sheet for "Cup Tally" under the F1 column.

9. From the AA and AS containers count and record the number of red beans ("A" alleles) and white beans ("S" alleles) and record these numbers on your data sheet for "Number of alleles surviving" for the F1 generation. The easiest way to do this is to add up the red beans in your AA and AS column from your "Cup Tally" data table for each generation; then, do the same with the white beans.

10. Place the surviving alleles (from the AA and AS cups) back into the "Gene Pool" cup.

11. Empty the beans from the 'non-surviving' cup and place them off to the side (DO NOT place these beans back into the gene pool cup!!).

12. Repeat the whole procedure for the F2 generation using **ONLY** the survivors from the F1 generation. Record the results in your data tables under the F2 generation.

13. Once you've finished return ALL beans to the "Gene Pool" cup, and clean up your area. Do NOT lose any beans!

14. Calculate the allele frequency of each generation for the "Number of alleles surviving" data table.

Example: Your P (parent) generation had 100 total beans, 75 red and 25 white. 75 out of (divide) 100 is 0.75 (or 75%) and 25 out of (divide) 100 is 0.25 (or 25%). This is the allele frequency for the parent generation. You will do the same for the F1 and F2 generations; however, *your total number of beans can be different (not out of 100)*. You need to know the # of red beans out of the total number of surviving beans in order to calculate the allele frequency. The same goes for the white beans.

15. Plot your allele frequency data on the line graph provided. Each graph should have **two lines**; one for the frequency of the "A" allele and one for the frequency of the "S" allele.

Name _____ Period _____

Hypothesis: If the sickle cell allele _____ malarial infection, then the sickle cell allele frequency ("S" allele) will _____.

Data:

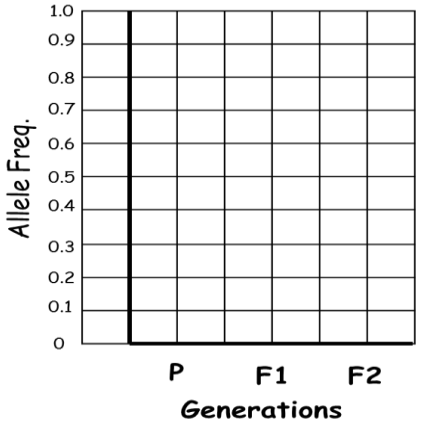
Cup Tally

	F1		F2	
	Red	**White**	**Red**	**White**
AA				
AS				
Non-survivors				

Number of alleles surviving:

		Total Surviving Alleles	Allele Frequency
Parent (P) generation	**Number of A (red) alleles**	**75**	**0.75**
	Number of S (white) alleles	**25**	**0.25**
F1	**Number of A (red) alleles surviving.** (Count out of AA and AS cups)		
	Number of S (white) alleles surviving. (Count out of AS cup)		
F2	**Number of A (red) alleles surviving.** (Count out of AA and AS cups)		
	Number of S (white) alleles surviving. (Count out of AS cup)		

Line graph of "A" and "S" allele frequencies:



Results/Conclusion:

1. Based on your graph, what is the general trend for the A allele over 3 generations (does it go up, down, or stay the same)? Is this what you expected?

_____
_____

2. Based on your graph, what is the general trend for the S allele over 3 generations (does it go up, down, or stay the same)? Is this what you expected?

_____
_____

3. What do you think will happen to the allele frequencies after 10 generations? Why?

_____
_____

4. Since few people with sickle cell anemia (SS) are likely to survive to have children of their own, why hasn't the S allele been eliminated from the population in Africa?

_____
_____
_____

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

_____
_____

6. Scientists are working on a vaccine against malaria. What impact might the vaccine have on the frequency of the sickle cell allele after many generations in Africa? Why?

_____
_____
_____
_____

7. What is allele frequency and how does it relate to evolution?

_____
_____
_____

8. According to your data, do you accept or reject your hypothesis? _____