**STORYBOARDING the EPISTSIS of EYE COLOR: Conceptual Biology-Art Frameworks for Exploring Complex Topics in Biology**

**Objectives of Lesson Plan:** This innovative lesson plan encourages the use of storyboarding techniques or comic book layout to sequentially present a multilayered topic of Epistasis. Relying on the current model for human eye color genetics, Drawing-for-Biology techniques, genetic, genomic, and evolutionary consequences of the topic are experienced through the storyboard enabling students to engage individually, in groups, and creativity in a paper lab exercise. The gene and its broader cellular, individual, population, and evolutionary consequences are considered.

**Age/Grade:** 7-12

**Duration of lesson**: approximately two hours

**Topics considered**: cells, chromosomes, genes, DNA, proteins, eye color, eye structure, Mendelian genetics, Non-Mendelian genetics, variation, and evolution

**Activity**: Both teachers and students will storyboard the current narrative (model) of eye color and epistatic activity by creating a layout, comic strip, or storyboard for the concept of epistasis. The storyboard itself is simply an interesting, individual choice of a blueprint or page design for flowing ideas from one concept to another and is ideal for dynamic biological activity. Sample storyboards are provided along with how to create one by hand. It is preferred that students and teachers not print storyboards but make their own with paper, rulers, templates, and drawing materials. Students are expected to take the role of a graphic designer for a short comic strip and translate a biological problem into that comic strip. After a penciled rough draft of the storyboard is completed, students are asked to read about epistasis and the epistasis of eye color. Students then highlight what they believe are the important concepts or terms and with a group or in pairs, decide how they want to present this storyboard. At this point students can alter the rough draft to best support the visual concepts. It is strongly suggested that the teacher do the same and create a representative of their own storyboard of epistasis for students to observe. Once the storyboard is created, students are then asked to perform an epistasis cross of eye color genes, followed by a short quiz.

**Background:** Eye color has in the past often been presented as a Mendelian Dominant and Recessive trait, with Brown eyes dominant to blue eyes. Clearly this could not be the reality. By simply observing the variation of human eye color, it is readily apparent to almost everyone that more than blue and brown eyes exist. Even among only blue and brown eye color there is tremendous variation along with many variations of green, hazel, and even violet colored eyes. In standard textbooks eye color is presented as a polygenic trait, which, to a degree represents a range of pigment deposition, however, even this range of pigment concentration does not explain why two blue eyed people can have a brown eyed child or how a person’s eyes can have green, brown, and red pigment. It seems that almost any variation of eye color is possible, even diet, age, and disease can cause changes in eye color. This suggests that while there is a general dominance in Nature towards pigmentation, there are far more than two genes switching “on” and “off” to produce that variation. Every facet of a trait has multiple possibilities and gradients of expression and these are the result of genes interacting with each other at the cellular level. This gene-gene interaction is known as Epistasis.

Epistasis essentially represents a network of genes affecting each other or other gene’s behavior. The gene (DNA) is essentially a recipe or instruction to assemble or construct a protein that will be involved in a complex metabolic grid. Gene variants, known as alleles, at multiple locations, and often on different chromosomes communicate or express the necessary protein and the amounts of it based on what the cell and its local environment biochemically request. Epistasis genotypes suggest how those interactions might occur and the probability of their occurrence. Since many underlying processes of gene-gene interactions of various phenotypic traits are unknown, models of those interactions are created.

Eye color is a very observable phenotype in which the genes for eye color at one location are dependent upon genes in another location on another chromosome. If the effects of the genes are added up separately does not produce or predict the effect of those two genes then another gene is most likely involved with the third, fourth, or fifth gene modifying the first two. This would be an example of epistasis. A gene may be amplified by another gene, or it may be dampened or suppressed by the modifier gene(s). If these pathways raise the fitness or survivability or lower the fitness of a certain species or population, they may become conserved in time or lost. So, Epistasis is an important part of evolutionary processes and patterns.

The Mendelian model of dominant/recessive designates two alternate forms of the gene for eye color (B or b) or a single gene pair. In polygenic inheritance it is the additive affects of the genes that determine the melanin deposition. So, BBBBB would be the darkest brown eyes, bbbbb would be the lightest blue. This suggest five genes for eye color, with more dominants meaning darker eyes, more recessives creating lighter eyes but it does not explain gene-gene influences, modifications, and interactions. The polygenic model does not consider green eyes. The genes for brown and blue color are found on chromosome 15, another gene for green was later found on chromosome 19. The genes have named and renamed since then. Currently the gene for brown and blue on chromosome 15 is called the OCA2 gene. This gene accounts for the amount of melanin deposited. To appreciate the importance of epistasis within cellular environments, we should look at the complex environment of the iris. The iris essentially is a delicate network of connective tissue fibers that are under sympathetic and parasympathetic control and it constricts or dilates like the diaphragm of a camera to regulate the amount of light entering the eye. The iris is multilayered with crypts, depressions, and blood vessels. These layers have variable cell types such as melanocytes and fibroblasts, the layer with these cell types is called the stroma and it is where the action of the OCA2 gene takes place. This layer is relatively thin in blue eyed people and contains very few melanocytes, similar to the layers of the skin, alternatively, in brown eyed people this layer is thick and has many melanocytes, so both the fibroblasts and the melanocytes are greater. The stroma and the layer above it are interfaced and also contain a network of collagen with macrophages, mast cells, lymphocytes and nerves. Other cells related to these and the metabolism of the iris stroma include myofilaments. Melanin is produced in two types of colors, black and yellow. It is a mixture of these pigments that can give rise to browns, greens, hazels, and blue variations, exact mechanisms of this is accomplished are not well understood. This physiological elaborate setting or scene is important as it helps visualize the complexity of genetic networks that function within it and create it.

The OCA2 gene has two versions or variations, Brown and Blue. The Brown version of OCA2 works in the stroma of the iris, the blue version of the OCA2 gene does not work in the stroma as pigment is very sparse and so it may deposit much in this layer or other pigmented layers. Damage to this gene can cause a particular type of Albinism called oculocutaneous albinism. If a mutation occurs in the OCA2 gene, Africans more than other ethnicities will be affected. This demonstrates that the DNA of this gene functions in other locations throughout the body depending upon the tissue and cell types that contain the damaged gene. This is a good place to appreciate that the genes are functioning according to their cellular environments, not just because of the mutation. But let’s get back to the other eye color variations. We have a blue-brown gene. The gey gene on chromosome 19 is believed to result in green eyes. The gey gene suppresses the function of the OCA2 gene in its blue version. Brown eyes are still dominant in their expression (BB, Bb), while blue eyes are still recessive (bb), however when the gey gene is present and active with blue (bb) it generates green eyes (bbGg). Even if you have brown eyes (BB or Bb with Gg) you will still have brown eyes. A blue (bb) mutant with a recessive gey gene (gg) still, however results in blue because there are two alleles for this gene as well. The blue in this case appears dominant, but it is not, the gg condition does not appear to exert any influence or modify the OCA2 gene still resulting in green eyes. This implies a dominance among the thee genes. Brown eyes dominant to green and blue, and green eyes dominant to blue. There are estimated to be about 16 genes involved in eye color to date but there are probably many more. The color is dependent on the amount of melanin and the type of melanin being deposited in melanosomes of the stroma. One SNP in the OCA gene results in a switch from Cytosine to Thymine and a result in glutamine replacing arginine. This then gives less pigment and blue eyes. There appears to be another gene on chromosome 15 that determine the deposition of melanin accounting for the concentration of pigment. This gene has been called HERC2 which contains the promotor (start) region for the OCA2 gene. So, if this start signal never happens, the protein won’t be made (transcription) and blue eyes will result. The HERC2 gene then can modify the OCA2 gene. This is also an epistatic relationship. Clearly there are many levels and degrees of expression as well as genes at work in human eye color and so we can generally call human eye color epistatic in its behavior.

From an evolutionary perspective we can ask where did these variations in eye color genes come from and when? Why did they evolve. There is some speculation that the blue-eyed mutation of the OCA2 gene originated in Northern Europe. Some studies show that many more genes affect brown eyes than blue eyes (White 2011). Why there are so many eye colors in humans is an interesting question and one that may be too premature to attempt answering but it is a good question to present to students (suggested questions will be provided in this lesson plan).

References

White, Désirée, and Montserrat Rabago-Smith. "Genotype–phenotype associations and human eye color." *Journal of human genetics* 56.1 (2011): 5-7.

Eiberg, Hans, et al. "Blue eye color in humans may be caused by a perfectly associated founder mutation in a regulatory element located within the HERC2 gene inhibiting OCA2 expression." *Human genetics* 123.2 (2008): 177-187.

Sturm, Richard A., et al. "A single SNP in an evolutionary conserved region within intron 86 of the HERC2 gene determines human blue-brown eye color." *The American Journal of Human Genetics* 82.2 (2008): 424-431.

ASSESMENT MATERIAL

The following material can be used to assess students.

Short Quiz Questions:

1. Describe epistasis:
2. Why is eye color epistatic?
3. It is a simple Mendelian trait
4. b. It involves multiple genes and gene interactions
5. It can modify genes
6. Both a and c
7. What chromosome is the OCA2 gene found on?
8. Chromosome 3
9. Chromosome 19
10. Chromosome 22
11. Chromosome 15
12. If you have BbGg, what color eyes will you have?
13. Hazel
14. Green
15. Brown
16. Blue

Open ended Questions for Students:

1. Why are there so many variations of human eye color from an evolutionary point of view?
2. Why do you think most humans have brown eyes?
3. Why does it take more than a few genes to create a complex trait?
4. What is the advantage of variation in traits such as eye color?
5. What is the advantage of having multiple gene interactions over simply dominant and recessive?

SUGGESTED PRESENTATION SEQUENCE FOR EDUCATORS

1. Start with the open-ended questions
2. Draw an eye on the board and show lots of pictures of different eye colors in humans or teach students to draw the eye
3. Talk about the current background information for eye color
4. Talk about storyboarding a little and tell students they will be creating a graphic presentation or comic book on eye color and will work in pairs to do this
5. Give them the background information (make a simpler version if necessary)
6. Create your storyboard for them to see
7. Hand out materials (large paper, rulers, templates, art supplies)
8. Ask students to layout the storyboard roughly
9. Have students decide and highlight the most important concepts
10. Give students about 1 hour to create a storyboard (this is the shortest amount of time; this can be done in a 2-hour lab or carried over to the following week)
11. Go back and discuss the idea of “fitness” and DNA changes creating variation in genes, connecting DNA changes to protein variation and resulting in variation of traits. The complex webs of gene interactions (epistasis, incomplete dominance, pleiotropy, and polygenic inheritance, along with environment create most phenotypes.
12. Give students short quiz

STORYBOARD SAMPLE TEMPLATES:

(These were generated by Word, however, drawing your own is much better. Please see further examples)

Hand Drawn Storyboard Outlines like this can be more original



