Epistasis:

Epistasis is a type of gene interaction where genes code for enzymes in a pathway. Each enzyme must function correctly to produce a wildtype phenotype. Not having a functional gene to produce a wildtype enzyme means an individual cannot move past that step in the pathway. This results in them "getting stuck" in a phenotypic class because they cannot proceed forward and cannot make the next protein product in the pathway.

In dominant and recessive epistasis, three distinct phenotypic classes exist. The first phenotypic class is for double mutant individuals. These individuals cannot make the first enzyme in the pathway and thus cannot proceed forward. Only individuals who can make the first enzyme can move forward. This enzyme produces an intermediate protein. This intermediate protein can be transformed into another protein with the help of the second enzyme. To proceed forward at this step, an individual who has made the intermediate protein must then also make a functional (wildtype) version of the second enzyme. These individuals who make both enzymes express a wildtype phenotype. If an individual made the first enzyme but cannot make the second enzyme, they get stuck in the intermediate phenotypic class.

While this general information is true of both dominant and recessive epistasis, these two types of epistasis differ in haplosufficiency. Dominant epistasis has dominant mutant alleles and the wildtype alleles are recessive. This means an individual must have two recessive wildtype alleles to make the corresponding wildtype enzyme or they do not proceed forward through the pathway. Recessive epistasis has a dominant wildtype allele and the mutant alleles are recessive. This means that an individual must have at least one dominant wildtype allele to make the corresponding wildtype enzyme or they do not proceed forward in the pathway. Only having recessive (mutant) alleles for a gene means that the individual cannot make a functional enzyme that that gene codes for.

It is important to memorize the difference between the two types of epistasis. One way of remembering which type of epistasis is which is by saying "dominant to stay" for dominant epistasis and "recessive to stay" for recessive epistasis. This works because a single dominant allele for that step in the pathway means an individual cannot proceed forward in dominant epistasis and two recessive alleles for that step in the pathway means an individual cannot proceed forward in recessive epistasis. From this information, you can figure out if the mutant allele is dominant, what the ratio is based on the dihybrid cross ratio for unlinked genes, and determine which genotypes fall in each phenotypic class.

Learning Objectives:

- Remember that each enzyme in an epistasis pathway is separate but because epistasis is a pathway, each step must be completed in order or else an individual ends up "stuck" in a phenotypic class when the enzyme cannot be made.
- Be able to compare and contrast dominant and recessive epistasis.
- Be able to identify if an example is dominant or recessive epistasis.
- Memorize and be able to apply expected ratios for types of epistasis.
- Understand which genotypes fall into each phenotypic class and why.

Order of Activities:

1. Read the summary of epistasis on the following website. https://www.britannica.com/science/heredity-genetics/Epistatic-genes
2. Read the following article about epistasis. Pay attention to the analogies to understand how an individual can get "stuck" in a phenotypic class. https://learn.genetics.utah.edu/content/pigeons/epistasis/
3. Test yourself by completing the corresponding worksheet for this material. Attempt to first complete this on your own, then pair up with a partner or group to discuss when possible. There is an answer key provided so you can check your work and read through all explanations for the questions. Any questions you get wrong or confused about you should attempt to explain why the answer is correct and then complete again after you finish the activities in this guide.
4. After reviewing any topic, it is a good idea to have a metacognition check. Ask yourself the following questions:

    - What are my emotional responses to learning this material? Which material am I frustrated with and need aid in understanding?
    - What difficulties have I had with the learning tasks? What specific tasks will I do to master this content?
    - Do I understand all of the learning goals? Can I explain each of them out loud to someone clearly and concisely?
    - How is what I learned related to other things I have learned in this class? How is it related to other classes, my career, and my life?

5. If you would like to have more aid in learning this material, please reach out. There are numerous individuals who want to help you feel confident in your understanding. If your course has learning assistants or teaching assistant(s), you should reach out to them to review concepts you want to learn more about. Your professor is also a great resource to go to when you do not understand a topic. You can study with your peers or receive academic support through the LRC as well. If you would like help identifying how to receive the support you need, do not hesitate to contact the CU Denver Learning Resources Center at LRC@ucdenver.edu or stop by our front desk in the learning commons building.
6. Challenge: Think about how dominant and recessive epistasis compare to other ratios you have learned about. Complete the chart found here to organize your notes and have a deeper understanding of how the ratios compare to each other. Reminder, you may see problems where the type of gene interaction is not explicitly stated. For such problems, you will have to determine the gene interaction type to fully and correctly answer the question. If you need help, view table 4 of this website. https://www.nature.com/scitable/topicpage/epistasis-gene-interaction-and-phenotype-effects-460/# This features more types of ratios than you may need for your course.