CONCEPT: EPISTASIS AND COMPLEMENTATION

Complementation

● A **complementation test** is performed to determine if two mutants have mutations in the same gene

□ A complementation test is performed by mating two recessive mutants with the same phenotype together

- If offspring are WT: The two mutations are in different genes

- If offspring are mutant: The two mutations are in different genes

EXAMPLE:

You have three white mutants (1,2,3) and want to know if the mutation causing them each to be white is in the same gene for each mutant. WT color is blue. Which mutations complement (meaning the two mutations are in different genes)?

White 1	x	White 2	→	F_1 all white
White 1	x	White 3	→	F_1 all blue
White 2	x	White 3	→	F_1 all blue

Non-Epistatic Genes

□ **Epistasis** is the interaction of two different genes

- Generally, the presence of one gene's allele will ____________ the phenotype of the second gene's allele
- Two non-epistatic genes will show the expected 9:3:3:1 dihybrid ratio
    - Genes under epistasis will show an altered ratio

EXAMPLE:

Corn snakes come in four color patterns: orange, black, camouflaged, and albino.

- The color pattern is determined by two different genes (O,o or B, b).

Genotype	**Phenotype**
$O^+/-$; b/b	Orange
o/o ; $B^+/-$	Black
$O^+/-$; $B^+/-$	Camouflaged
o/o ; b/b	Albino

What is the offspring's genotype and phenotype derived from the mating of two heterozygous camouflaged corn snakes?

O^+/o ; B^+/b x O^+/o ; B^+/b

_______ Orange ⇒ _______ Black ⇒ ________ Camouflaged

_______ Not black ⇒ ________ Orange

_______ Not Orange ⇒ ________ Black ⇒ ________ Black

________ Not Black ⇒ ________ Albino

Epistatic Genes

□ **Dominant epistasis** occurs when a dominant allele of one gene masks the effects of either allele of the 2nd gene

- The dominant allele is epistatic
- The offspring phenotypic ratio of a heterozygous cross is **12:3:1**

EXAMPLE:

A certain breed of squash comes in three colors; white, dark red, and light red. Coloration is determined by two genes, D and W.

Genotype	**Phenotype**	**Genotypic Ratio**	**Phenotypic Ratio**
D/- ; W/-	White	9	12
d/d ; W/-	White	3	
D/- ; w/w	Dark red	3	3
d/d ; w/w	Light red	1	1

Phenotypic ratio is 12:3:1 because the dominant W allele is epistatic.

- This means that when there is a dominant W present in the offspring, it will mask the phenotype of the D allele

□ **Recessive epistasis** occurs when a recessive allele of a gene masks the effects of either allele of the 2nd gene

- The offspring phenotypic ratio of a heterozygous cross is **9:3:4**

EXAMPLE:

A certain breed of flower comes in three colors: blue, magenta, and white. Coloration is determined by two genes, w^+ and m^+.

Genotype	**Phenotype**	**Genotypic Ratio**	**Phenotypic Ratio**
w^+/- ; m^+/-	Blue	9	9
w^+/ ; m/m	Magenta	3	3
w/w ; m^+/-	White	3	4
w/w ; m/m	White	1	

Phenotypic ratio is 9:3:4 because the mutant w allele is epistatic

- This means that when an organism has w/w it will mask the phenotype of the m^+ or m alleles.

EXAMPLE: Rare example of recessive epistasis in humans: **The Bombay Phenotype**

□ There are two genes responsible for blood type – those in the I family, and those in the H family

- The I family determines what protein will be on the blood cells (A, B, both, or none)

- The dominant H allele makes a protein that adds the proteins onto the blood cell

Genotype	Blood Type	Protein
I^A/I^A or I^A/i	A	A
I^B/I^B or I^B/i	B	B
I^A/I^B	AB	AB
i/i	O	none

□ There is a rare mutation, represented by h, which doesn't create the protein needed to attach the enzyme

- The h/h genotype is epistatic, meaning that it masks the phenotype of any I allele

Genotype	Blood Type
I^A/I^A or I^A/I and hh	O
I^B/I^B or I^B/I and hh	O
I^A/I^B and hh	O
i/i and hh	O

Other Gene Interactions

□ **Complementary gene action** occurs when the two genes interact because they'r ein the same pathway

- The offspring phenotypic ratio of a heterozygous cross is **9:7**

EXAMPLE:

A breed of flower comes in two colors; purple and white. Coloration is determined by two genes, C and P

Genotype	Phenotype	Genotypic Ratio	Phenotypic Ratio
C/- ; P/-	Purple	9	9
C/- ; p/p	White	3	7
c/c ; P/p	White	3	
c/c ; p/p	White	1	

- The genes are complementary, because both genes need to have a dominant allele in order to be purple.

□ **Suppressors** are mutant alleles of one gene that reverses the effect of a mutation in a second gene

- When the suppressor causes the phenotype to be like WT, then the F_2 ratio is **13:3**

- When the suppressor causes the phenotype to be mutant, then the F_2 ratio is **14:2**

EXAMPLE:

A breed of flower comes in two colors; The WT red and the mutant purple color. Coloration is determined by two genes p^+ and R.

Genotype	Phenotype	Genotypic Ratio	Phenotypic Ratio
p^+/- ; R/-	Red	9	12
p^+/- ; r/r	Red	3	
p/p ; R/-	Purple	3	3
p/p ; r/r	Red	1	1 (total 13)

- The p^+ allele and the R allele both cause the plant to be red.
- The mutant p allele causes the plant to be purple, UNLESS the recessive suppressor (r/r) is present, which cancels or reverses the purple phenotype and turns the plant red.

□ **Modifiers** occur when a mutation at one gene changes the degree of expression of a mutated second gene

EXAMPLE:

Genotype	Protein phenotype
a^+/- ; b^+/-	WT
a^+/ ; b/b	Defective (low transcription)
a/a ; b^+/-	Defective (mutated protein A)
a/a ; b/b	Extremely defected

□ **Synthetic lethal alleles** occur when two viable single mutations result in death when found as double mutants

- F_2 generation is 9:3:3

EXAMPLE:

Genotype	Phenotype	Genotypic Ratio	Genotypic Ratio
C/- ; P/-	Purple	9	9
C/- ; p/p	Cyan	3	3
c/c ; P/p	White	3	3
c/c ; p/p	Dead	1	Dead

PRACTICE:

1) When performing a complementation test, how do you know if two mutations complement?
    a) The offspring will have a wild-type phenotype
    b) The offspring will have the mutant phenotype
    c) The offspring will have an intermediate phenotype between wild-type and mutant
    d) The offspring will not look like either wild-type or mutant

2) How can you tell if two genes are epistatic?
    a) The F_2 offspring from a cross show a 9:3:3:1 phenotypic ratio
    b) The F_2 offspring all show a mutant phenotype
    c) The F_2 offspring show a phenotypic ratio that is NOT 9:3:3:1
    d) The F_2 offspring all show a wild-type phenotype

3) Two heterozygous organisms are crossed, and the F_2 phenotypic ratio is 12:3:1. What form of epistasis do these two genes exhibit?
   a) Dominant Epistasis
   b) Recessive Epistasis
   c) Suppressors
   d) Complementary Gene Action

4) A cross of white plants and red plants was performed. Using the F_2 phenotypic ratio data below, determine what form of gene interaction is taking place.

Phenotype	# of offspring
Red	1125
White	875

   a) Dominant Epistasis
   b) Recessive Epistasis
   c) Suppressors
   d) Complementary Gene Action

5) In the rare Bombay phenotype, a mutation in a second gene can control an individual's what?
   a) Hair color
   b) Height
   c) Blood type
   d) Skin color