LECTURE 6

Epistasis

A form of gene interaction where the effects of a single gene or genes are masked or "suppressed" by a non-allelic gene or genes

A. Early experiments were Mendelian crosses involving coat color in rats

P_1	yellow x black
F_1	all gray
F_2	9/16 gray
	3/16 yellow
	3/16 black
	1/16 cream

1. 9:3:3:1 ratio indicated two genes, a dihybrid F_1, *but* that only one trait (coat color) was involved

   a) inferred genotypes were:

9/16	Y-; B-	(gray)
3/16	Y-; bb	(yellow)
3/16	yy; B-	(black)
1/16	yy; bb	(cream)

   b) referred to as *simple gene interaction*

B. Like all types of gene interaction, epistasis effects in nature occur between numerous genes and undoubtedly is the rule rather than the exception; this, however, becomes tedious (if not impossible) to study, largely because of the large number of genes that likely are involved for any given trait

   1. We will consider examples involving only two genes because genetic models are straightforward and the interactions can be understood at the biochemical level

C. *Model System* Eye-pigment pathway in *Drosophila* [OVERHEAD]

Precursor → → → → → → brown pigment
+ → wild-type eye color
→ → → red pigment

1. Define four loci:

w locus:	three alleles,	W, w^+, w
b locus:	three alleles,	B, b^+, b
cn locus:	two alleles,	cn^+, cn
bw locus:	two alleles,	bw^+, bw

2. Epistatic interaction — Modified F_2 ratio

Simple gene interaction	9:3:3:1
Recessive epistasis	9:3:4
Duplicate recessive epistasis	9:7
Dominant epistasis	12:3:1
Duplicate dominant epistasis	15:1
Dominant and recessive epistasis	13:3
Interaction/duplicate dominant epistasis	9:6:1

3. Examine series of dihybrid crosses, following general rule…

P_1 AA;BB x aa;bb F_1 Aa;Bb

F_2
9/16 A-; B-
3/16 A-; bb
3/16 aa; B-
1/16 aa; bb

a) Cross #1: F_1, cn^+/cn; bw^+bw — Simple gene interaction

b) Cross #2: F_1, w^+w; cn^+cn — Recessive epistasis

c) Cross #3: F_1, w^+w; b^+b — Duplicate recessive epistasis

d) Cross #4: F_1, Ww^+; cn^+cn — Dominant epistasis

e) Cross #5: F_1, Ww^+; Bb^+ — Duplicate dominant epistasis

f) Cross #6: F_1, Ww^+; b^+b — Dominant and recessive epistasis

g) 9:6:1 ratio: exists but with no simple explanation

D. Final comments:

1. One "white" eye gene codes for a transporter molecule (i.e., a protein that transports pigment to the eye); this gene is not in the above pigment pathway, yet individuals that are homozygous for a recessive (defective) allele have "white eyes" and are indistinguishable from individuals homozygous *w/w* or *b/b* – this is an example of the same phenotype coming not only from two different genes but from two different pathways

2. One gene obviously does not necessarily engender a single trait

3. Epistasis is the rule rather than the exception; epistatic interactions often may involve >100 genes

4. Eye-color pathway: noteworthy because of absence of linkage of coordinately expressed genes (e.g., "red" mutants)