MCB C142/ IB C163 Review of Amacher Lectures

Today, we will review the early lectures of the course (not the rearrangements or ploidy lectures, since those were so recent). But first, we will cover aneuploidy from the last lecture. This provides us an opportunity to review allele segregation during meiosis. (see notes from last lecture).

In the beginning lectures, we discussed how alleles segregate from one another in a cross, whether they are unlinked or linked.

If two alleles of one gene are segregating in a monohybrid cross, and they have a straightforward dominance relationship, one expects a 3:1 ratio of dominant:recessive phenotypes among the progeny of F1 heterozygotes.

We talked about cases where one might see deviations from a 3:1 monohybrid ratio.

If the alleles show incomplete dominance or co-dominance, the heterozygote will have a phenotype different for either homozygous parent and the ratio will be 1:2:1.

If there are multiple alleles for a certain gene, there may be multiple phenotypes possible and one will see a series of 3:1 ratios.

If a particular allele is recessive lethal, you will see a 2:1 ratio because homozygous recessive individuals will die. Pure-breeding lines for the recessive lethal allele cannot be established.

Lastly, if a particular gene contributes to more than one trait, one might see different ratios, depending upon the dominance relationship of the alleles.

If two genes are segregating in a dihybrid cross, and they have a straightforward dominance relationship and no gene interaction, one expects a 9:3:3:1 ratio of dominant:recessive phenotypes among the progeny of F1 heterozygotes.
9 A-B-
3 A-bb
3 aaB-
1aabb

We talked about the importance of the TESTCROSS to determine genotype. The individual bearing the dominant phenotype is cross to a homozygous recessive individual. If the het is AA, no recessive phenotypes will be observed in the cross, if the het is Aa, then half the progeny will display the recessive phenotype.

We talked about cases where two genes determine one trait, and how these ratios are affected with different relationships. In some of these cases, new phenotypes arise among the progeny.

If the two genes don't genetically interact, you get the same 9:3:3:1 ratio, but you do get four distinct F2 phenotypes. (Lentil seed color)

If the two genes show complementary gene action (that is you need dominant alleles of both genes to get the dominant trait, then you observe a 9:7 ratio. (Sweet pea flower color)
9 A-B- (Dominant trait)
3 A-bb (Recessive trait)
3 aaB- (Recessive trait)
1aabb (Recessive trait)

If the genes interact showing recessive epistasis, then homozygosity at one allele will mask the phenotype of both alleles at another locus and you will observe a 9:3:4 ratio. (Retriever coat color)
9 A-B- Dominant A- phenotype
3 A-bb Masked phenotype
3 aaB- Recessive aa phenotype
1aabb Masked phenotype

There are two flavors of dominant epistasis.

In one case, the dominant allele of one gene masks the effects of both alleles of the other gene (Summer squash color). The masked phenotype is distinct form either the dominant or recessive phenotypes at the first locus. You see 12:3:1 ratio.
9 A-B- Masked phenotype (distinct from the A phenotype)
3 A-bb Dominant A phenotype
3 aaB- Masked phenotype (distinct from the A phenotype)
1aabb Recessive aa phenotype

In other cases, the dominant allele of one gene masks the effect of the dominant allele at the other gene (Chicken feather color). You see a 13:3 ratio. The dominant phenotype at A is expressed only in the absence of B.
9 A-B- Recessive aa phenotype
3 A-bb Dominant A phenotype
3 aaB- Recessive aa phenotype
1aabb Recessive aa phenotype

We briefly covered pedigree analysis in humans and talked about how one uses pedigrees to recognize inheritance patterns.

Autosomal Dominant Traits:

1. Affected children always have one affected parent
2. Dominant traits show a vertical pattern of inheritance
3. Two affected parents can produce unaffected childen, if both parents are hets.

Autotosomal Recessive Traits:

1. Affected individuals can have two unaffected parents. Matings between relatives can reveal the recessive trait as related individuals may more likely be carriers of the rare allele.
2. All the children of two affected parents should be affected
3. Rare recessive traits show a horizontal pattern of inheritance (can look vertical if the trait is common in the population).

X-linked recessive

1. Trait appears in more males than females
2. Mutation will never pass from father to son
3. An affected male passes on the X-linked mutation to all his daughters (who are carriers). One-half of the carrier's sons will inherit the X-linked mutation and have the trait. Half her daughters will be carriers.
4. The trait often skips a generation (except in cases where the sister of an affected male is a carrier)
5. A rare affected female will pass the X-linked mutation to all her children: all sons will be affected, all daughters will be carriers.

X-linked dominant

1. More females than males show the trait.
2. The inheritance pattern is vertical
3. All daughters but no sons of affected males will be affected, whereas half the sons and daughters of affected females will be affected.

Y-linked inheritance

1. The trait is seen only in males
2. All male descendents of an affected male will display the trait
3. Females cannot exhibit or transmit the trait.

This leads us nicely into a discussion of LINKAGE! We spend a long time discussing the inheritance patterns of linked genes, which are inherited together more often than not. That is the parental chromosomes and recombinant chromosomes are not inherited in a 1:1:1:1 ratio, but instead we see more parental chromosomes. In the case of X-linked traits, one can examine the sons of doubly heterozygous mothers to determine the linkage relationships between the genes segregating in the cross. For autosomal traits, one must perform a test cross to reveal the genotypes of the gametes that are produced from a doubly heterozygous individual. Remember that in *Drosophila*, the male must be the test cross parent because recombination does not occur in *Drosophila* males.

$$RF = \#recombinants/total \times 100$$

Chi-Square Test: review this probability test that determines the goodness of fit between experimental and predicted results.

MAPPING: review how one uses 3-point crosses to estimate map distance. For each segregating gene, two phenotypes appear in the progeny, thus for 3 segregating genes, one expects 2^3 (=8) phenotypic classes. The 8 classes represent the reciprocal pairs of recombinants: for linked genes, the largest pair represents the parental genotypes, the two middle pairs represent single crossovers, and the smallest pair represent the double crossovers. This information tells you which gene is in the middle!

We talked about INTERFERENCE, which is a measure of the independence of crossovers from each other. When interference is high, there are no DCOs, when it is zero, one observes the expected number of DCOs based upon the distance between the two genes.

TETRADS! Allows one to observe the products of a single meiosis! And ordered tetrads let you estimate the distance between each gene segregating in the cross and it's respective centromere.
PD tetrad = all spores have parental genotype (2:2)
NPD tetrad = all spores have nonparental genotype (2:2)
T tetrad = tetrad contains all 4 possible combinations (2 non-recombinant, 2 recombinant)

RF = (1/2T + NPD)/100 * 100

And we derived in class another equation that gives a more accurate estimation of map distance in yeast, especially if two genes are less closely linked. In our derivation, we consider all the chromatids that were involved in crossover events (because crossovers reflect the distance between two genes), even if they are not recombinant in terms of phenotype.

Advice for the Exam:

The exam covers material through Friday, October 3rd.

To study, do the PRACTICE PROBLEMS! One, twice, three times…

Draw out the information from the problem in terms of genotype and/or phenotype before you jump into the problem. How many segregating genes? How many phenotypes? Is there a clear dominance relationship? Unlinked or linked? Sex-linked? Take the extra time to set up the problem as it could save valuable time later.

Logic out the problem before crunching numbers. What are your expectations? This is a good way to get an idea of the expected results – if your actual numbers end up different from your expectations, you will know to double-check your answer for sloppy math mistakes.

Stay calm. Look over the entire exam first. Do the problems that look easy first, then attempt the ones that appear more challenging. If you get stuck on a problem, move on. If you can't work out an entire problem (or you run out of time), then write out what your expectations are. You could get partial credit if we are able to see that you were on track.