LECTURE 1: EXTENSIONS TO MENDEL

Reading: Ch. 3, especially p. 45-67

Problems: Ch. 3, Solved problems I, II. Also 2, 3, 5, 10, 11, 15, 17, 20, 23, 25, 29, 32, 36

Announcements:

**Waitlisted students: Unfortunately, we cannot guarantee you a spot in the course and must give first priority to MCB and IB seniors who need this class to graduate. You are welcome to continue on the waiting list, but it may be prudent to investigate other options. If you are a graduating senior in MCB or IB and need this course to graduate, please see the staff advisors in your respective departmental office.

**My policy is to post my lecture notes after class.

**My Office Hours will be Thursdays, 1:30 – 3:30 on 9/4, 9/11, 9/18, and 10/2. There will be no office hours on Sept 25th due to a scheduling conflict.

Have you done the assigned problems from Week 1? Here's a meiosis pop quiz:

1. During meiotic division, what segregates during Meiosis I?
   (A) Sister chromatids
   (B) Homologous chromosomes
2. During meiotic division, what segregates during Meiosis II?
   (A) Sister chromatids
   (B) Homologous chromosomes
3. During which meiotic division do chromosomes behave more like those during anaphase of mitosis?
   (A) Meiosis I
   (B) Meiosis II
4. True or False: The products of meiosis are genetically identical to the original cell, except that they are haploid.
5. True or False: When sister chromatids separate during meiosis, they are genetically identical to each other.
6. What two main features of meiosis contribute to genetic diversity?

EXTENSIONS TO MENDEL

In determining the laws of inheritance, Mendel used a set of guidelines for single gene inheritance: (1) one of the two alleles of a given gene showed complete dominance over the other, (2) there are only two alleles of any given gene, (3) genes determine one specific trait, and (4) all genotypes are equally viable. When these guidelines are not meet, deviations from expected Mendelian ratios can result. In addition, some traits are determined by more than one gene. Let's look at some exceptions to these general "rules" to see how we can identify how these deviations fit Mendel's basic laws.

Single gene inheritance

What if the alleles show **incomplete dominance**? If this is the case, a novel phenotype, unlike that of either parent shows up in the F1. Color in snapdragons is an excellent example.

P: pure-breeding red flowers x pure-breeding white flowers
F1: all pink -- NEW PHENOTYPE (NOT LIKE EITHER PARENT!)
F2: red:pink:white (1:2:1). This ratio is a good indication of the lack of complete dominance. The phenotypic ratios are an exact reflection of the genotypic ratios. Molecularly, one can think of the combinations as follows: C^R C^R gives 2 doses of gene expression and C^W C^W gives no dose. C^R C^W has one dose of gene expression and this intermediate dose gives a novel phenotype.

	C^R	C^W
C^R	$C^R C^R$ (red)	$C^W C^R$ (pink)
C^W	$C^R C^W$ (pink)	$C^W C^W$ (white)

What if the alleles show **co-dominance**? If this is the case, then the F1 progeny display both parental traits. The I^A and I^B blood types in humans are a good example. These two alternative alleles produce a slightly different form of an enzyme that controls the presence of a sugar polymer that sits on the red blood cell membrane. The complex sugar differs depending upon whether the I^A or I^B form of the enzyme is present.

P: $I^A I^A$ x $I^B I^B$
F1: all $I^A I^B$ (and express <u>both</u> kinds of sugars on the RBC membrane)
F2: $I^A I^A$: $I^A I^B$: $I^B I^B$ (1:2:1). Again, this ratio is a good indication of the lack of complete dominance. The phenotypic ratios are an exact reflection of the genotypic ratios.

	I^A	I^B
I^A	$I^A I^A$ ("A"-type sugar)	$I^B I^A$ ("A" and "B" sugars)
I^B	$I^A I^B$ ("A" and "B" sugars)	$I^B I^B$ ("B"-type sugar)

What if there are **multiple alleles** (more than 2) for a given gene? Mutations are the source of new alleles. For human blood type, there is an allele of the I gene (i) that produces a non-functional enzyme. I^A and I^B alleles are co-dominant, but the i allele is recessive to both I^A and I^B alleles. Because each person can only carry two alleles, there are six possible genotypes and 4 possible blood types.

Genotype	Type of sugar (Blood type)	Antibodies in serum
$I^A I^A$ I^A i	A	against B
$I^B I^B$ I^B i	B	against A
$I^A I^B$	AB	none
i i	O	against A and B

Now, we'll consider a situation where a gene contributes to multiple traits (**pleiotropy**), specifically in the case where a particular allele causes **recessive lethality**.

In mice, coat color is determined by the *agouti* gene. Unlike the traits that Mendel described in peas, the *agouti* gene has multiple alleles. Multiple alleles arise by mutation (a change in genetic sequence). Mice homozygous for the wild-type *agouti* allele (AA) have a dark grey coat color. One of the mutant alleles of *agouti* gives rise to mice that have a yellow coat. When pure-breeding wild-type agouti mice (AA) are mated with yellow mice, one observes dark grey and yellow progeny in equal numbers (1:1). This suggests that (1) a single gene with 2 alleles determines the two phenotypes, (2) yellow mice must carry the *agouti* gene (heterozygous A^yA), and (3) yellow must be dominant to agouti. The Punnett Square looks like this:

	A^y	A
A	A^yA (yellow)	AA (dark grey)

When two yellow mice are bred together one observes yellow and grey progeny in a ratio of **2:1**. Yellow mice must indeed then be heterozygotes (A^yA). But why the 2:1 ratio, not 3:1, as we've come to expect from cross between heterozygotes? The Punnett Square looks like this:

	A^y	A
A^y	$A^y\ A^y$ (lethal)	A^yA (yellow)
A	A^yA (yellow)	AA (dark grey)

The A^yA^y homozygous combination is lethal and A^yA^y mice die in utero. Thus even though the A^y allele is dominant to the wild-type allele for coat color, the same A^y allele is **recessive** to the wild-type allele for survival. This explains why pure-breeding yellow mice can never be obtained.

Because of the dominant effect of the A^y allele on coat color, it is easy to detect carriers of the recessive lethal A^y allele because of this visible phenotype. Many recessive lethal alleles do not have heterozygous phenotypes.

What about **multifactorial inheritance** – when a trait is determined by the action of two or more genes? We will consider several examples.

Consider a simple case - color in lentils – where the combined action of alleles of two genes gives new phenotypes.

P: Pure-breeding tan lentils (AA bb) x pure-breeding gray lentils (aa BB)
F1: All brown (Aa Bb) – both dominant alleles are needed to produce brown!
F2: 9 brown (A- B-): 3 tan (Aa bb): 3 gray (aa Bb): 1 green (aa bb)

RATIO of 9:3:3:1 (remember Mendel's independent assortment of 2 separate genes determining different traits!) In this example, each genotypic class gives a specific phenotype.

For some two-gene interactions, the four F2 phenotypic classes give rise to fewer than 4 phenotypes. This can occur when the two genes are required together to produce a phenotype – like pigment in sweet peas. In this case of complementary gene action, a dominant allele of both traits is required for pigment formation. Think of pigment synthesis as a multi-step enzymatic reaction, with wildtype versions of Enzymes A and B required for pigment synthesis.

P: **White (AA bb) x White (aa BB)** (correction from lecture in bold – there are two ways to make pure-breeding white flowers!)
F1: All purple (Aa Bb)
F2: 9 purple (A- B-): 7 white (3 A- bb: 3 aa B-: 1 aa bb)
RATIO: 9:7

What if a particular allele at one gene masks the effects on another gene determining a particular trait? This is called **epistasis**, and the masking allele is epistatic to the other and can be recessive or dominant.

----------*We will continue with material below this line on Friday!*----------

Recessive epistasis – Coat color in Labradors
The dominant B allele determines black coat color, and bb dogs are brown. However, a second gene is also involved – in this case, the dominant E allele has no effect on black or brown coat color, but dogs carrying ee are yellow, regardless of the genotype at the B gene.

P: Black (BB EE) x purebreeding Yellow (bb ee)
F1: All Black (Bb Ee)
F2: 9 Gray (B- E-): 3 brown (bb E-), 4 yellow (-- ee)
RATIO: 9:3:4

Dominant Epistasis I – Color in summer squash
A dominant allele of one gene hide the phenotypic effects predicted by genotype at another gene. In summer squash, the dominant A allele determines yellow, and aa fruits are green. If the fruit carries a dominant B allele (a different locus), the fruit is white, regardless of the genotype at A. A bb fruit does not mask the genotype. That is, the presence of B masks the effects of any combination of A and a alleles. In genetic terminology, we say that B is epistatic to both A and a.

P: White (AA BB) x green (aa bb)
F1: All white (A-B-)
F2: 12 White (9 A- B-; 3 aa B-): 3 yellow (A- bb): 1 green (aa bb)
RATIO: 12:3:1

Dominant Epistasis II – Feather color in chickens
The dominant effects of one gene hide the effects of alleles of the dominant allele of another gene. In this case, B is epistatic to A, and at least one copy of A (in the absence of B) is required to give color, but a, B, and b alleles give no color.

P: White leghorn (AA BB) x White wyanadotte (aa bb)
F1: All white (A-B-)
F2: 13 White (9 A- B-; 3 aa B-; 1 aa bb): 3 colored (A/- bb)
RATIO: 13:3

To confirm for sure that a trait is determined by two alleles (instead of by one allele), breeding experiments of the F2s will determine whether gene interactions are occurring (p 63-64, especially Fig. 3.18). Look at this and convince yourself that you understand the concepts.

Lastly, the same genotype does not always produce the same phenotype. We saw this in the examples of epistasis above, e.g. that the phenotype determined by one gene/locus could be affected by the genotype at another locus. In other cases, phenotype depends upon **penetrance** (how many members of a population with a particular genotype show the expected phenotype) and **expressivity** (the degree or intensity with which a particular genotype is expressed in a phenotype). Phenotypes can be modified by the presence of modifier genes that can alter the phenotype in a more subtle way than genes that have major contributions to the phenotype, or by the environment. You will learn more about these types of influences later in the course.

POP QUIZ ANSWERS:
1. B (Homologous chromosomes)
2. A (Sister chromatids)
3. B (Meiosis II)
4. False
5. False
6. Independent assortment of non-homologous chromosomes and crossing over between homologous chromosomes