

LECTURE 2: Chromosomes and Inheritance

Reading: Ch. 4, p. 81-88; 105-110

Many of the classic papers mentioned in this and previous lectures are available at

<http://www.esp.org/foundations/genetics/classical/>

Problems: Ch. 4, solved probs I, II; also 12, 24, 27, 33, 34, 38, 39

Announcements:

**The first quiz will be given next week in section that will cover material through today's lecture. The GSIs have agreed that students with legitimate, excused absences can take the quiz in a different section during the week of the quiz as long as you arrange it with your GSI ahead of time.

**No calculators are allowed on quizzes or exams.

**We will cover pedigree analysis on Monday. If you are having difficulties with the assigned pedigree problems, please re-attempt them after Monday's lecture.

**See 9/3 Lecture notes for correction to parentl genotype/phenotype in the sweet pea example.

**DSP students should contact the DSP office as soon as possible.

**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.

Today, we'll finish discussing epistasis (see notes from 9/3/08), as well as discuss the evidence that confirms that genes reside on chromosomes.

THE CHROMOSOMAL THEORY OF INHERITANCE

Evidence that genes reside in the nucleus

About the time Mendel began his experiments, cytologists were using microscopy to follow the union of paternal and maternal gametes during fertilization in sea urchins and in frogs. Because the nuclei are the only elements that are contributed equally from the male and female gametes, it was hypothesized that the nucleus contained the genetic material.

Evidence that genes reside in chromosomes

In the 1880s, technological advances allowed microscopists to follow chromosomes in the nucleus during mitosis and meiosis. During mitosis, each daughter cell inherited the same number and type of chromosomes as the parent cell. During meiosis, each of the gametes receives only one chromosome of each chromosome pair and the chromosomes assort independently as predicted by Mendel. Furthermore, the union of maternal and paternal gametes during fertilization yields a zygote with two complete chromosomal sets, and the maternally- and paternally-derived chromosomes are alike in size and shape (with the exception of the **sex chromosomes** in most species.) This suggested that chromosomes carry the hereditary information.

Sexual identity is correlated in many organisms with the inheritance of particular chromosomes. Several cytologists (McClung, Sutton, Boveri, Wilson) at the beginning of the 1900s suggested that in insects, there was a relationship between specific chromosomes and the determination of sex. For example, Sutton showed that in the great lubber grasshopper, there were 11 pairs of **autosomes** in both females and males, but females carried an additional matched set (XX) of chromosomes and males carried only one X. Sutton missed the Y chromosome in males, but others to follow showed that in many sexually reproducing species, not just insects, that two distinct chromosomes (**sex chromosomes**) are the basis for sex determination.

Sexual identity in other organisms:

In humans, females carry 23 pairs of chromosomes, 22 autosomal pairs and two X chromosomes, whereas males carry 22 autosomal pairs and one X and one Y chromosome. The fruit fly *Drosophila* also uses an XX=female, XY=male strategy, although in flies it is the ratio of X to autosomes that ultimately determines sex, not the presence or absence of the Y. In birds, it is the female that has the unmatched set, designated WZ, and males are ZZ. In some insect species, the female is XX, but the male is XO, having only one sex chromosome. Wilson pointed out this difference in the early 1900's, and used this to suggest that the "accessory chromosomes" (sex chromosomes) probably themselves weren't the actual sex determinants, but that they acted in a quantitative manner to determine sex.

Based upon his observations, Sutton proposed that the chromosomes carried Mendel's units of heredity. But confirmation depended upon showing that specific traits were inherited with specific chromosomes.

Validation of the Chromosome Theory of Inheritance**Thomas Hunt Morgan describes an X-linked gene for eye color in *Drosophila***

In 1910, a white-eyed male fly arose in a stock of red-eyed flies in Morgan's laboratory. Morgan called the gene responsible for eye color the *white* gene, because a mutation destroying its function gives white eyes. The wild-type allele is designated w^+ (red eyes) and the mutant allele is designated w . (This is different symbolism than what we used for Mendel's peas).

Morgan's crosses:

<u>Generation</u>	<u>Genotypes:</u>
P: red-eyed female x white-eyed male	X^{w+}/X^{w+} x X^w/Y
F1: all red-eyed	X^{w+}/X^w and X^{w+}/Y
F1: red-eyed female x red-eyed male	X^{w+}/X^w x X^{w+}/Y
F2: 3:1 red eyes:white eyes (all white-eyed flies are male!)	X^{w+}/X^{w+} ; X^{w+}/X^w ; X^{w+}/Y ; X^w/Y

[If the two traits (eye color and sex) assorted independently, then one would expect that half the white-eyed flies would be female and half would be male.]

Reciprocal cross:

Cross: white-eyed female x red-eyed male	X^w/X^w x X^{w+}/Y
Progeny: red-eyed daughters and white-eyed sons	X^{w+}/X^w and X^w/Y

Note also that this cross gives a different result than the parental cross above; Mendel never observed differences in his reciprocal crosses.

The *white* gene is X-linked and the Y chromosome does not carry an allele of this gene for eye color. Thus, male flies are **hemizygous** for the *white* gene.

Nondisjunction (Rare meiotic mistakes)

Calvin Bridges, one of Morgan's students, repeated Morgan's crosses on a larger scale. When he crossed white-eyed females (X^w/X^w) to red-eyed males (X^{w+}/Y), he observed that the

progeny was almost always red-eyed daughters and white-eyed sons, except about 1 in 2000 males had red eyes and about the same proportion of females had white eyes. He hypothesized that these exceptions were caused by a failure of the X chromosomes to separate during meiosis (**nondisjunction**) in the mothers. This leads to gametes carrying 2 X chromosomes or no X chromosomes.

The cross is: X^w/X^w (white-eyed female) \times X^{w+}/Y (red-eyed male)

The Punnett square for the exceptional cases looks like this:

	X^{w+}	Y
$X^w X^w$	$X^w X^w / X^{w+}$ (lethal)	$X^w X^w / Y$ (white female)
O	X^{w+} / O (red male, sterile)	Y / O (lethal)

Cytologically, Bridges showed that the white-eyed exceptional females had XXY chromosomal content and that the red-eyed exceptional males were XO. Furthermore, he predicted that the exceptional $X^w X^w / Y$ females could make 4 kinds of gametes depending on how the 3 sex chromosomes segregated after pairing during meiosis. Most commonly, the X chromosomes paired and separated, resulting in $X^w Y$ and X^w gametes, and less frequently, the X chromosomes went to one gamete and the Y to the other, generating $X^w X^w$ and Y gametes. Bridges correctly predicted the results of such a cross and confirmed his predictions of genotype by examining the chromosomes of the progeny.

-----We will finish what is below the line next lecture-----

The cross is: $X^w X^w / Y$ (exceptional white-eyed female) \times X^{w+}/Y (red-eyed male)

The Punnett Square looks like this (but think about the chromosomes as well!):

	X^{w+}	Y
$X^w Y$	$X^{w+} / X^w Y$ (red female)	$X^w Y / Y$ (white male)
X^w	X^w / X^{w+} (red female)	X^w / Y (white male)
$X^w X^w$ (rarer)	$X^w X^w / X^{w+}$ (lethal)	$X^w X^w / Y$ (white female)
Y (rarer)	X^{w+} / Y (red male)	Y / Y (lethal)

The X chromosomes of the exceptional females are exact duplicates of mom (having inherited both X's from her and the Y from dad) and these exceptional females can produce exceptional progeny when crossed to any male. The exceptional males inherit their X from their dad. This was compelling evidence that genes are located on chromosomes.

In Bridges' own words:

“There can be no doubt that the complete parallelism between the unique behavior of the chromosomes and the behavior of sex-linked genes and sex in this case means that the sex-linked genes are located in and borne by the X-chromosomes”. –Bridges, 1914.

Non-disjunction also occurs in humans, as Professor Dernburg mentioned last week. Here's an example of a problem (Ch 4 Solved Problem I) that you can use to figure out whether the non-disjunction event occurred in mom or dad, and whether it occurred in meiosis I or II.

Sample problem

A trisomy 16 fetus was miscarried. A karyotype of the fetus showed that two of the three chromosomes 16 had a heterochromeric knob (“blob”). Both chromosome 16 homologs in the mother lacked blobs, but the father was heterozygous for blobs. Which parent experienced nondisjunction and in which meiotic division did it occur?

(Answer: Nondisjunction occurred in meiosis II of the father.)

Next time, we'll talk about how geneticists study inheritance in human populations.