LECTURE 7

Sex chromosomes

A. Distinguish sex chromosomes vs. autosomes and homogamety vs. heterogamety

B. Types of sex chromosome mechanisms:

XX:XY mechanism (male heterogamety)	all mammals, other organisms (e.g., *Drosophila*)
ZZ:ZW mechanism (female heterogamety)	all birds, other organisms
XX:XO mechanism (male heterogamety)	several insects, some lower vertebrates

Multiple sex chromosomes (generally sex chromosome-autosome translocations)

C. Sex linkage and sex-linked genes:

1. Genes on X but not on Y -- leads to a "criss-cross" pattern of inheritance where sons receive their X chromosome from the maternal parent and daughters receive an X from both parents

2. Historically, sex chromosomes were the basis for the chromosomal theory of heredity

3. There are several, well-known sex-linked traits in humans: examples include hemophilia, color blindness, and the fragile X syndrome

   a) "fragile X" is characterized by a "constriction" at the tip of the long arm of the X chromosome

   b) the syndrome includes mental impairment, with varying physical and behavioral abnormalities; it is inherited (formally) as an X-linked dominant with incomplete penetrance

   c) the molecular basis involves what are called "trinucleotide repeats" where an increase in the number of repeats increases the severity of the phenotype (this will be discussed later in the course); the incidence of fragile-X syndrome is about 1/2000 births

4. Remember that the pattern of "criss-cross" inheritance reversed in ZZ:ZW organisms

D. Incomplete sex linkage:

1. Genes on both the X and Y (called pseudoautosomal)

   a) in humans, pseudoautosomal regions are at the distal ends (tips) of both X and Y

   b) in *Drosophila*, genes for the ribosomal RNAs are pseudoautosomal (near the centromeres)

E. Holandric inheritance:

1. Genes on the Y but not the X

Nondisjunction

A. Misdivision of chromosomes at meiosis (or mitosis), generally leading to daughter cells that possess an extra or are missing a single chromosome

1. In humans, nondisjunction of sex chromosomes can generate Turners (XO) and Klinefelters (XXY) individuals

2. Additional proof of the chromosomal theory of inheritance

B. In mammals, incidence of nondisjunction, as measured by the incidence of Turners and Klinefelters individuals, increases dramatically at some point beyond "normal" reproductive age, but *only in females*; inflection point in human females is around 40 years of age

1. Essentially a "storage effect -- sperm are turned over every 20 or so days, whereas eggs are generated, held at meiosis I, and stored

2. Because the increase is in nondisjunction, there also is an increased incidence of miscarriages and stillborns, the majority of which stem from aneuploidy for an autosome (generally lethal)

Sex effects

A. Sex-influenced dominance

1. Interaction between alleles in heterozygote differs between the sexes

a) examples include horns in sheep, pattern baldness in humans

B. Sex-limited inheritance

1. Where trait exists in only on one of the two sexes

a) can occur at single-locus level (long feathers in chickens)

example: feather length in chickens

females all have short feathers

in males, s^+s^+ and s^+s = short feathers
ss = long feathers

b) more common at the multiple-gene level involving complex traits (e.g., egg laying, milk production)

C. Maternal effects

1. Where the phenotype of an individual is a function of the genotype(s) of the maternal parent

2. Single-locus examples include dextral vs sinestral coiling in land snails, phenylkeonuria in humans

3. Multiple-locus examples include many developmental and other embryonic traits that can presumably be under the influence of natural selection

D. Genomic imprinting

1. Phenomenon where regulatory or other genes silence (perhaps by direct modification) an allele at a gene such that one copy of the gene (either maternal or paternal) is not expressed during development and/or thereafter

E. Sex chromatin, gene expression, and dosage compensation

1. M. L. Barr and the discovery of "X-chromatin (Barr) bodies" in somatic cells of mammals

2. Barr bodies are facultatively heterochromatic X chromosomes, and are found according to the following:

X chromosomes – 1 = # Barr bodies per cell

a) normal XX females have a single Barr body, whereas normal XY males do not have a Barr body

b) however, Turners (XO) females do not have a Barr body, whereas Klinefelters (XXY) males do have a Barr body, i.e., possession of a Barr body is not related strictly to the sex of an individual

c) purpose of the body is to compensate dosage for sex-linked genes so that the quantity of gene product is the same in both sexes

d) X-inactivation (the Mary Lyon Effect) is the mechanism of dosage compensation in mammals

(i) note that which of the X chromosomes is inactivated is random, but that once inactivation occurs it is a "permanent" state

(ii) note also that inactivation of an X chromosome occurs subsequent to the initial cell divisions of a zygote (between the 16- and 64-cell stage)

(iii) this can produce "mottled" (sometimes called calico) phenotypes; note that mammalian females heterozygous for sex-linked genes are phenotypic "mosaics"

3. Mechanisms of dosage compensation (where known) differ among organisms