

# C2005/F2401 '10 Lecture 20 -- Meiosis, Life Cycles, & Introduction to Genetics

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**Handouts for today (& last time): 19A = Meiosis/Mitosis**

**19B = Chromosome squashes, karyotypes & chromosome structure**

**20A = Meiotic Chromosome Cycle**

**20B = Super Cycle & Nondisjunction**

## 1. Wrap up of Karyotypes -- Chromosome Banding & Rearrangements

### A. What do you see in a normal squash or karyotype?

- Number of chromosomes
- Size, position of centromere, & banding pattern of each chromosome
- N & ploidy = number of kinds of chromosomes (N) and number of each type (haploid, diploid, etc.)
- Sex chromosomes & autosomes (See details & picture in last lecture).

**To review mitosis and karyotypes, try problem 8-8 parts A-D, & G.**

### B. What can you see in an abnormal karyotype?

1. *'Chromosomal' Mutations* -- changes affecting whole chromosomes and/or large blocks of genes. Bands contain multiple genes and mutations involving single genes or bases are not visible in a karyotype.

**a. Only large changes are visible.** Since you can do banding, you can tell all the chromosomes and chromosome regions apart. Therefore you can detect **large** abnormalities affecting whole chromosomes and/or large blocks of genes from looking at karyotypes. Many of these abnormalities are associated with known genetic conditions -- diseases and/or tendencies thereto.

**b. Rearrangements.** You can pick up extra, missing and rearranged pieces. (If large enough, loss, additions, inversions, or translocations are visible.) Smaller changes must be detected using other methods.

**c. Aneuploidy.** Since you can tell all the individual chromosomes apart, you can see cases of missing or extra chromosomes. Cells are normally haploid (N), diploid (2N) etc. Cells with extra or missing chromosomes (2N + 1, or N - 1, etc.) are called aneuploid. Most aneuploid fetuses abort spontaneously but a few survive to birth. (See handout 19B for examples.) How do aneuploidies occur? See below.

### 2. *'Chromosomal' Mutations vs 'gene' mutations.*

**a. Chromosomal mutations.** Large changes that are visible in a karyotype are known as "**chromosomal mutations.**" Only changes in large sections containing many genes (kilobases not bases) are visible in karyotypes.

**b. Gene mutations.** Changes that are too small to be visible in a karyotype are usually called "**gene mutations.**" Changes of a few bases or even a few genes **cannot** be detected in a karyotype. Remember that each band on a chromosome is a large block containing hundreds of genes.

### 3. *Details of Aneuploidy (See 19B)*

**a. Terminology.** The terms "monosomic" and "trisomic" apply to diploid cells as follows:

**(1). Monosomic or monosomy** = one chromosome missing = one chromosome has no partner (no

homolog), but all other chromosomes still occur in pairs.

(2). **Trisomic or trisomy** = one chromosome has 3 copies (3 homologs) but all other chromosomes still occur in pairs. Note trisomic is different from triploid: trisomic means 3 copies of one type of chromosome, say #2; triploid means three copies of all the chromosomes.



**b. What types of aneuploidy are common?**

(1). **Aneuploidy of the Autosomes.** Most aneuploid fetuses abort spontaneously but a few survive to birth.

(a). **Trisomy 21.** The only autosomal aneuploidy that is not regularly lethal early in life is trisomy 21 or Down syndrome. (Chromosome 22 may look smaller, but 21 is the autosome with the smallest amount of genetic information.)

**(b). Details of Down Syndrome**

- Symptoms: Individuals who are trisomic for chromosome 21 have multiple developmental problems which usually result in significant mental retardation, distinctive facial features and a tendency to develop Alzheimers at a relatively early age. (The gene coding for the protein that clogs the brain in cases of Alzheimers is on chromosome 21.)
- Gene Dosage: All these abnormalities are thought to be due to a "gene dosage" effect. All the gene copies are normal, but trisomics have 3 copies of the genes on chromosome 21 instead of 2.
- Role of Extra (normal) Protein: The extra copies of the genes produce extra protein (for a total of 3 doses instead of 2). The extra amount of protein is what messes up development.

(2). **Aneuploidy of the sex chromosomes.** This is usually not lethal as long as there is at least one X.

**(a). Examples.**

- Individuals are known who are XXY, XO (O stands for no 2nd sex chromosome), XYY, XXX etc.
- Humans who are XO are female, but have certain abnormalities called Turner's syndrome.
- Humans who are XXY are male, and have Klinefelter's syndrome.

**(b). What determines maleness?**

- The Q: Is it the presence of Y or the absence of a second X?
- The data: The sex of the aneuploid individuals described above indicates that it is the presence of the Y that is the male-determining factor in humans, not the absence of the second X.
- Role of Y: The human Y chromosome has relatively few genes, but it has one critical gene (Sry) that triggers a sequence of events leading to male development; the default is female.
- Flies vs. Humans: The case in fruit flies is different: XO flies are male, and XXY flies are female. In flies it is the ratio of X's to autosomes that determines sex.

(c). **Why do XO and XXY survive?** Why is an extra and/or missing X compatible with a more or less normal existence while a missing or extra autosome is almost always deadly? Because variation in the number of X's is "normal" -- females have twice as many as males, yet both males and females are "normal." So there must be a mechanism to cope with "extra" X's (or missing X's, depending on your point of view). See below.

**(d). FYI: Secondary Sex Characteristics.** Most genes on X and Y have nothing to do with secondary sex characteristics (beard growth, breast development); most genes for secondary sex characteristics are autosomal (although some are on the X). Presence of Y determines which hormones are made and therefore which autosomal (and X linked) genes are turned on. If you add hormones externally, either sex can develop secondary sex characteristics of the other. Also note there is **no** correlation between unusual combinations of sex chromosomes and sexual preferences.

**(e). The birds & the bees.** The mechanism of sex determination is similar in many other organisms, in that one sex has a matching pair of chromosomes (the homogametic sex) and the other has a non-matching pair (the heterogametic sex). Which is which, and the fine points of how the balance determines sex, varies. The sex ratio (males/females) is about 1:1 in all these cases because the heterogametic sex produces male-determining and female-determining gametes in equal proportions.

In birds, the female, not the male, is the heterogametic sex. In bees, one sex is diploid and one is haploid -- an extension of the sex-is-determined-by-chromosome-balance principle to the whole set of chromosomes. So when they say they are going to 'tell you about the birds and the bees', it's not a good way to explain human sex!

*How do aneuploidies occur? Through mistakes in meiosis. Need to look at normal meiosis first.*

**II. Overview of Meiosis** -- See handout 20A; See last lecture for a complete version of this section. Only topic headings are given here.

**A. What is meiosis for? (See last lecture for details)**

1. *Need for meiosis/reduction division -- to keep karyotype & ploidy constant from generation to generation.*

2. *Why bother with all this? Why sex?*

3. *How reshuffling works*

a. **Reshuffling Chromosomes.**

b. **Reshuffling genes.**

**B. How many chromosomes, chromatids & cells during meiosis?** What happens if there is one pair of homologs? See picture on 20A, bottom.

1. *DNA synthesis occurs first -- before division.*

2. *Products:* There are 4 products, each haploid (from meiosis), instead of 2 products, each diploid (from mitosis).

3. *Number of Divisions* : Meiosis consists of two divisions. (Mitosis has only one.)

4. *What happens to N, c (DNA content -- see below) and # of chromatids/chromosome in meiosis?*

**C. What happens to chromosomes per cell during meiosis?** See pictures on 20A top.

Picture on bottom of Handout 20A shows what happens to **one pair** of chromosomes. It shows **all cells** at each stage of meiosis -- before DNA synthesis, after S, after 1st div, and after 2nd div. See Becker fig. 20-3 for a similar diagram of meiosis in a cell with **2 pairs** of chromosomes.

Picture on top of Handout 20A shows a different view of the stages of meiosis. It emphasizes the 'chromosome cycle' -- the number of chromosomes, the number of chromatids, and the DNA content **per cell** at each stage. It summarizes the chromosome cycle for cells with one chromosome pair (N = 1), for 3 pairs (N = 3), and for any

general value of N.

**D. Definition of c** -- Important: "c" is a measure of DNA content per cell, not the number of chromosomes or chromatids.

**To review Meiosis (so far), and compare to Mitosis, do (or finish) problems 8-1, 8-2 (parts A to E), 8-3, & 8-8 (parts A-D & G).**

### III. The Mechanism of Meiosis -- see handout 19A.

**A. Steps:** These are diagrammed in detail on handout 19A, and comparisons to mitosis are summarized there. For similar diagrams of mitosis vs. meiosis see Sadava fig. 11.20 (9.19) or Becker fig. 20-8 (20-9). For nicer pictures of meiosis see Sadava 11.17(9.16) or Becker 20-5 & 20-6.

**B. What if  $N > 1$ ?** Handout 19A shows what will happen to a cell with 1 pair of chromosomes. ( $2N$  cell,  $N = 1$ .) If there are additional chromosome pairs ( $N > 1$ ), each pair will line up independently at metaphase I. This has important genetic implications, as will be discussed later.

#### **C. Prophase I -- Some Differences from Mitosis**

**1. Crossing over.** This is the time when recombination occurs by a "cut & rejoin" mechanism, which switches equivalent sections of chromosomes between 2 members of a pair. Recombination requires pairing, so homologous chromosomes are paired in pro. I of meiosis but not mitosis. More details to follow. (Pictures of pairing are shown in the texts.)

Note: Crossing over (recombination) involves cutting and rejoining of double stranded DNA molecules; production of mRNA (splicing) involves cutting and rejoining of single stranded RNA molecules. Restriction enzymes cut double stranded DNA. Three **different** sets of enzymes are involved in these processes -- splicing, crossing over, and restriction.

**2. Duration.** Prophase I in meiosis is generally much longer and more complex than prophase in mitosis. (Both texts divide prophase into early, mid and late substages; Becker 20-6 (20-6 & 20-7) has even more details if you are curious.) Pro. I can be very prolonged -- in human females, it lasts from before birth to the time the egg is shed. Consequences of this very long pro. I are discussed below.

#### **D. Products of human meiosis** (see Sadava fig. 43.3 (42.3) or Becker fig. 20-9 [20-10])

**1. In Females:** When female germ cells go through meiosis, the equivalent of 4 haploid nuclei are formed, but only one ends up in an egg. The genetic material that would end up in the "other 3" nuclei is shunted aside -- it forms small structures called polar bodies. The egg contains (at least) the amount of cytoplasm that would be sufficient for 4 meiotic products and the genetic information of only one.

**2. In males:** When male germ cells go through meiosis, 4 sperm are formed.

**IV. Life Cycles** -- How do meiosis and mitosis fit together? Or how does 1 multicellular organism give 2? Or better, for organisms engaging in sexual reproduction, how do 2 (parents) give 1 (offspring)?

#### **A. Supercycle -- Handout 20B (top).**

##### **1. General idea** -- Overview

Many different life cycles are possible, depending on the number of mitotic divisions that follow meiosis and/or fusion. The diagram on the top of handout 20 labeled "Supercycle" shows a generalized life cycle and explains the terminology. (Sadava fig. 11.15 (9.14) or 28.4 (29.2) is equivalent; Becker fig. 20-4 is similar.) If an organism goes through all the stages shown, then it has both haploid and diploid phases.

## 2. Haploid vs Diploid Life Cycles

**a. Diploid Life Cycle.** What you get if meiosis → gametes. An organism can skip most of the stages on the left half of the supercycle diagram and go directly from germ cells to gametes. Such an organism has a basically diploid life cycle, as humans do. See Becker, fig. 20-4 (d) [18-4 (d)].

**b. Haploid Life Cycle.** What you get if the zygote divides immediately by meiosis, not mitosis. An organism can skip most of the right half of the diagram if the zygote divides immediately by meiosis, not mitosis. Such an organism has a basically haploid life cycle. Some simple algae are like this. See Becker fig. 20-4 (b).

**3. Alternation of Generations** What you get if you don't skip any stages; common in plants. See Sadava fig. 28.3 (28.4)

- Most plants go through both haploid and diploid phases, with mitotic divisions of both haploids and diploids. However the haploid phase is so short (involves so few mitotic divisions) that the haploid form of the organism is usually not visible to the naked eye.
- Both phases may be visible. A few of the simpler plants, such as moss, produce both haploid and diploid forms that are visible to the naked eye. See Sadava fig. 28.4 (28.3 & 28.5) and/or Becker fig. 20-4 (c). You can see both the sporophyte (spore bearing form of plant) and the gametophyte (gamete bearing form of plant).
- For moss, the green fuzzy stuff is haploid and produces gametes, so it is called the gametophyte = gamete-bearing plant. Two gametes fuse to form a zygote, which divides by mitosis to produce the brown stalks (diploid) on top of the green mat. Some cells of the stalk go through meiosis to produce spores (inside the capsule at the end of the stalk), so the stalk is called a sporophyte = spore-bearing plant.

## 4. Gametes and Spores -- Terminology

- Two ways to get gametes -- by meiosis of 2N or specialization of N cells. Moss produces gametes by specialization of haploid cells; humans produce gametes by meiosis of diploids.
- Products of meiosis can be spores or gametes. In moss, the products of meiosis are called spores, not gametes, because the meiotic products are going to divide by mitosis (before specializing to make gametes). In humans, the products of meiosis are called gametes.
- Gametes vs spores: If meiotic products will never divide by mitosis, but simply fuse to form a zygote, then they are called gametes. If the meiotic products are going to divide by mitosis, then they are called spores. [{Q&A}](#)

## 5. Super cycle can reduce to haploid or diploid life cycle

**a. Diploid Life Cycle.** If meiosis → gametes. No mitotic division of haploids. No spores.

**b. Haploid Life Cycle.** If zygote → immediate meiosis. (Meiosis → spores, not gametes.) No mitotic division of diploids. No germ cells.

## B. Some implications of this cycle:

**1. The Problem of Development.** If zygote → us by mitosis; how does development work? If all cells have the same DNA, why do cells make different proteins? In other words, why are the genes 'expressed' differently in different cell types? What sets and maintains the switches? How differential gene expression is set up and maintained is not entirely understood, but will be discussed some more next term.

**2. Forensics.** Virtually all the cells of the adult have the same DNA. Therefore you can compare DNA from a suspect to DNA found at the scene of the crime. It doesn't matter what types of cells the DNA comes

from -- hair, saliva, blood, sperm, etc.

**3. PGD & Amniocentesis.** If all cells of embryo & fetus have same genes/DNA/chromosomes, you can test the DNA or chromosomes of any cell to look for abnormalities, even if the gene involved only affects (makes proteins in) certain specialized tissues.

**a. Testing embryonic cells (PGD)** -- one cell can be removed from an 8 cell embryo without damaging the ability of the remaining cells to develop into a normal individual. Therefore one cell can be removed from an embryo (fertilized *in vitro*) and the DNA of the cell can be tested. If the embryo does not have a disease genotype, the remaining 7 cells can be implanted in the womb and development can proceed normally. This is called pre-implantation genetic diagnosis (PGD).

**b. Testing fetal cells (Amniocentesis, etc.)** If you identify a fetus that will have sufficiently serious disabilities, you have the option to consider a therapeutic abortion. There are several current ways to test fetal cells, and more ways are under development. The most common current method is amniocentesis (testing fetal cells from amniotic fluid).

**4. What you can detect by amniocentesis, PGD, etc.** These examples will not be discussed in class but are included FYI.

**a. Chromosome Mutations.** Since you can do banding, you can tell all the chromosomes and chromosome regions apart. Therefore you can detect large abnormalities affecting whole chromosomes and/or large blocks of genes (so called "chromosomal" mutations) from looking at karyotypes as discussed previously.

**b. Gene Mutations.** You can look at DNA sequence (by PCR, use of probes, etc) for smaller changes affecting one or a few genes and/or nucleotides (so called "gene" mutations). Sometimes you can look at the protein the gene makes as in amniocentesis for case (1) below, but sometimes you have to look at the DNA instead as in case (2). Some examples:

**(1). Tay-Sachs disease.** The gene that causes Tay-Sachs disease (when mutant) codes for an enzyme. The enzyme is made in many cell types, including the cells in the amniotic fluid. Using amniotic fluid cells, you can look at the DNA or measure the enzymatic activity of the protein made from the gene. In embryonic cells, you have to look at the DNA.

**(2). PKU.** The gene that causes phenylketonuria or PKU (when mutant) codes for an enzyme (PAH) that is made only in liver cells. So using amniotic fluid cells, you can't measure the activity of the enzyme. But you can test the state of the gene itself (in embryonic or amniotic fluid cells) to see if the gene is normal or mutant.

**To review life cycles, cell cycle, etc. and how they all fit together, try 8-11 and/or 8-14.**

## V. Non disjunction -- see handout 20B bottom.

### A. Where do individuals with missing and extra chromosomes come from?

Answer: Mistakes in Meiosis. Two types of mistakes:

- Homologs can fail to separate (fail to "disjoin") properly at first division (= 1st div. nondisjunction), or
- Sister chromatids can fail to separate properly at second division (= 2nd div. ND).

Either way, nondisjunction gives gametes with extra and/or missing chromosomes (aneuploidy). See handout 20B, bottom half of page. When an aneuploid gamete (= gamete with missing or extra chromosomes) from one parent meets a normal gamete from another parent, then a monosomic or trisomic zygote is formed. The zygote can divide by mitosis to produce an aneuploid individual. Aneuploid zygotes containing missing or extra autosomes usually do not develop into viable individuals, but aneuploid zygotes containing missing or extra sex chromosomes (XO, XXY, XXX etc.) are usually viable as long as there is at least one X. (Why is this? See below.)

On handout 20B: Note that the "empty" cells are not really empty -- they are only missing a chromosome from the pair involved in ND. They have all the other chromosomes, but the others are not shown to keep the picture as simple as possible. ND is a **rare** error that generally affects only one event at a time -- one pair of chromatids or one pair of homologs fails to separate at one stage of meiosis. **Two or more mistakes in a single meiosis are extremely unlikely. In the rare event of a ND there is usually only one event (separation) that fails to occur** -- usually all other separations of chromosomes and chromatids proceed normally. See Sadava fig. 11.21 (9.20 (9.18)).

**B. What types of aneuploidy are common?** See above for details.

1. *Trisomy 21.*
2. *Aneuploidy of the sex chromosomes.*

**To review Nondisjunction, try 8-8E & 8-9.**

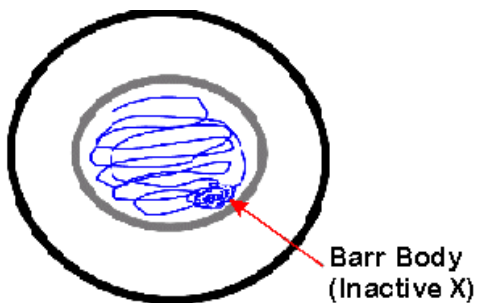
## **VI. Inactive X's and Barr bodies -- Why are extra or missing X's usually tolerated, while extra or missing autosomes are not?**

**A. Lyon Hypothesis = inactive X Hypothesis**

The idea that extra X's are genetically inert is called the Lyon hypothesis (or the inactive X hypothesis). According to the Lyon hypothesis, every female is a mosaic, since some of her cells use her maternal X to make proteins and some use her paternal X.

**B. Barr bodies**

You can actually see the inactive X during interphase because it forms a Barr body. There are 2 X chromosomes in every female cell, but (according to the inactive X hypothesis) only 1 of them works (is transcribed) most of the time. In general, if there are extra X chromosomes, all the extras are inactive, whether the cell is male or female. The inactive X's remain tightly coiled during interphase and are called Barr bodies. (So you can tell the sex of the cell without doing a karyotype.) Note that inactive X chromosomes are replicated, but not transcribed.



**C. How is mosaic detected? Summary of Basic Genetic Terminology**

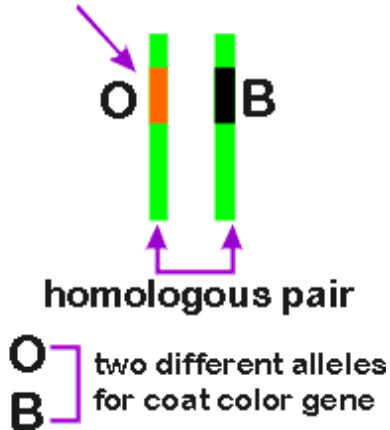
Consider coat color in cats. This is how Lyon actually figured out the inactive X existed. In cats, a gene controlling coat color is on the X. The position of the gene is known as the **locus** of the gene. This gene has two **alleles** (alternate forms); one → black coat color and the other → orange. One of the alleles is present at the coat color locus on every X. The Y chromosome does not carry an allele of the coat color gene. What genotype and phenotype are cats?

1. **Males.** Males have only one X, which carries either the black or the orange allele, so normal male cats are all black or all orange. (They may have regular stripes, superimposed on the black or orange, but the background color is either all black or all orange -- they don't have areas of orange and areas of black).

2. **Females.** Females have two X's, so they carry two alleles of the coat color gene -- one on each X. The **genotype** of a female can be

- a. **homozygous** black (have 2 black alleles)
- b. **homozygous** orange (have 2 orange alleles) or
- c. **heterozygous** (have one allele of each color), as shown in figure.

### locus for coat color



The **phenotype** of a female can be orange, black or patchy (with areas of each color). Only heterozygous females are patchy.

All this makes sense if only one copy of the X works in each patch so only one copy of the coat color gene works per cell (and per patch). Rare patchy males are XXY (Klinefelter's Kats).

Note "Patchy" is called tortoise shell, not tabby; calico = patchy plus white. (Tabby = regular pattern of stripes that occurs in both males and females.)

### D. When do Barr bodies form? How do you get the mosaic?

Fertilized egg (zygote) → ball of cells → each cell inactivates one X at random → each cell divides by mitosis → descendants with same X on/off. Once an X is inactivated, it generally remains inactivated through succeeding mitoses, so all mitotic descendants of a single cell have the same X on and the same X off → all cells in one area (or with same lineage) have same X on/off.

Germ line cells (which will go through meiosis) turn both X's back on before gametes are made, before meiosis occurs. So either one of the two X chromosomes can be used or inactivated in the next generation.

To review Genetic Terminology so far, try 8R-1. (Also see Becker fig. 20-2.)

## VII. Patterns of Inheritance

### A. What are the Big Issues to consider?

1. How are genes/genotypes (such as the ones for coat color) inherited, and
2. How does a particular **genotype** (state of the genetic information) **determine phenotype** (appearance, function, etc)? How do genes specify 'orange' or black?

**B. How do you figure out the pattern of inheritance?** Next time we'll start by looking more closely at the example of orange/black coat color in cats and then go on to other examples and the general case.

**Next time: How does inheritance work for genes on the X? Genes on the autosomes?**