Chapter for today: Chap. 10

Major points for the day:

1. Meiosis allows random segregation of genes to progeny
2. Maternal and paternal chromosomes segregate in Meiosis I
3. Meiosis II is a mitotic division reducing the chromosomes to a haploid number

Reprise

Last Monday Dr. Kloetzel talked about **mitosis**, the process eukaryotic cells use to produce identical copies of cells.

- The essential fact about mitosis is that at metaphase each duplicated chromosome lines up on the metaphase plate and the two sister chromatids separate and move to opposite poles of the cell.
- Since the two sister chromatids are the same this ensures that each of the unique DNA molecules in the cell are transmitted to the next generation.
- Nondisjunction (the name of this event) results in cells with too few or too many chromosomes. Most of the resulting cells would be dead.
  - Down's syndrome is an example of a relatively benign aneuploidy

So clearly, the process of mitosis is essential in the short term to the ability of organisms to survive.

Another process of cell division is essential to the long–term survival of a species—**meiosis**

Down's Syndrome and other aneuploidy diseases really result from nondisjunction during the development of germ cells because of a failure of meiosis

The concept of homologous chromosomes

I have already discussed the idea that each of your cells contains two copies of each unique chromosome

This is easiest to envision when talking about the sex chromosomes:

- In humans, the sex of each individual is determined by the identity of the two sex chromosomes
- There are two types of sex chromosomes, the X and the Y
- A male receives an X chromosome from his mother and a Y from his father
  - This is the clearest example of the idea of there being a "mother's" chromosome and a "father's" chromosome
- A female receives an X chromosome from each parent

However, the existence of a maternal chromosome and a paternal chromosome is not limited to the sex chromosomes

Each of the somatic chromosomes (chromosomes not involved in sex determination, not "chromosomes involved in body formation") also comes as a maternal and a paternal copy

In fact, the two chromosomes in any pair are not identical since the parents are individuals with very different genetic make-ups

- This difference is at the level of genes, as we shall see. Mutations in particular genes cause differences that we can see—we call those **phenotypes**

The two chromosomes that make up a pair are called **homologous**, which literally means that they have a common origin (evolutionarily)

- It does not mean that they are identical

- It means that almost all of their sequences are exactly alike, with only small differences which generate phenotypic differences

Overview of Meiosis

The object of meiosis is to generate a random assortment of chromosome combinations in cells that have half the normal number of chromosomes

- In a diploid organism that means the formation of haploid cells that carry a random collection of chromosomes
- The process is very carefully regulated so that no cell receives less than the full complement of chromosomes
  - All cells have one copy of each chromosome
  - And no cell has more than one of any of those chromosomes

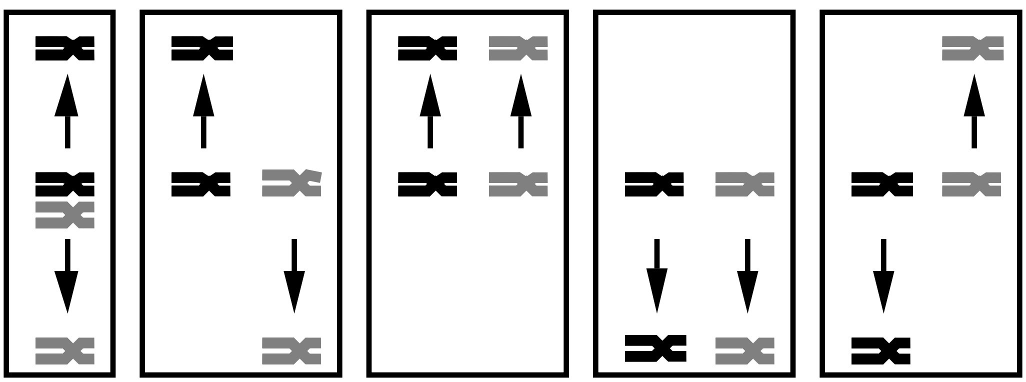
The only way to produce cells with half their normal number of chromosomes is to divide twice without allowing DNA replication

There are certainly many several ways the cell could accomplish this end.

- One necessary part of such a scheme is that chromosomes would have to “pair up” before cell division could occur
- In mitosis each pair of chromosomes is physically connected at the centromere, when the package that we call a chromosome moves to the metaphase plate, the two identical chromosomes are held together.

If chromosomes didn’t pair it wouldn’t be possible to faithfully segregate one copy to each of the daughter cells

- The chromosomes would have no way of knowing which pole of the cell their homologue was going to.
- About half the time they would go to the same pole:



In meiosis pairing occurs between duplicated chromosomes (those involving sister chromatids.

- Pairing of the duplicated chromosomes occurs on a metaphase plate
- The spindle then pulls the pairs apart
- As a result, each cell gets a pair of sister chromatids, not one each of the paternal and maternal chromosomes
- This is the difference between meiosis and mitosis
  - The first division creates a pair of cells which are different
  - Each contains either the paternal or the maternal chromosomes, but not both

<u>However</u>, the direction that each of these chromosomes goes (that is to which cell they segregate) is <u>*random*</u>

- As a result, there is a shuffling of the genes because a random selection of chromosomes is made at each first meiotic metaphase
- In an organism with two chromosomes there are only four possible outcomes for a given cell after this division:

Chromosome I	**Chromosome II**
P	P
P	M
M	P
M	M

- In an organism with three chromosomes there are only eight possible outcomes for a given cell after this division:

Chromosome I	Chromosome II	Chromosome III
P	P	P
M	P	P
P	M	P
P	P	M
M	M	P
M	P	M
P	M	M
M	M	M

- Since humans have 23 chromosomes, the number of possibilities is 2^{23} or 8,388,608 possibilities!

Remember that this is the number of alternative outcomes for a single individual—meiosis could occur in over 8 million ways. If you consider the genetic variability in a population, it is clear that it is extremely unlikely that any two gametes would be the same

The mechanics of meiosis

Meiosis consists of two successive divisions without an intervening DNA replication

Each of the divisions looks similar to a mitotic division, though the first involves a separation of chromosomes which is unlike mitosis (the second is simply a mitotic division)

The two divisions are called **Meiosis I** and **Meiosis II**. In each of these divisions the intervals within are designated with a I or II (e.g, **Prophase I** and **Prophase II**)

Meiosis I

- Meiosis I begins as Mitosis, with the disassembly of the nuclear membrane and condensation of the chromosomes (<u>Prophase I</u>)
  - We will not be concerned right now with the process of recombination which occurs during Prophase I, but return to it in a minute.
- The duplicated chromosomes (each with two sister chromatids) attach to the spindle and move to the metaphase plate (<u>Metaphase I</u>)
  - Note that each pair of duplicated chromosomes is still paired
  - They therefore align with each other at the metaphase plate
  - The centromeric regions of each duplicated chromosome is fused into one structure which is attached to one of the spindle poles by microtubules
- The spindle pulls the duplicated chromosomes to the poles (<u>Anaphase I</u>)

  - At this stage the maternal and paternal chromosomes are separated from each other
  - This is the separation which is random, giving rise to the large number of possible segregation patterns
- The chromosomes dissociate from the spindle (Telophase I)

Meiosis II (which occurs after cell division—two cells are now involved)

- The two resulting cells then proceed directly to the next division with the assembly of new spindles in each cell, and attachment of the still condensed chromosomes to it (Prophase II)
  - Note that each sister chromatid must attach to a different spindle in preparation for division of the sister chromatids from each other
- The chromosomes line up on the metaphase plate (Metaphase II)
  - Since each of the duplicated chromosomes in these cells are unique they can not pair
  - Each chromosome lines up by itself on the plate
  - This is a mitotic division, but unlike normal mitosis the cells are diploid and will give haploid progeny (mitosis in diploid somatic tissue occurs by a tetraploid producing two diploid cells)
- Each pair of sister chromatids then separates and moves to opposite poles of the cell (Anaphase II)
- The chromosomes decondense and the nuclear membrane reforms (Telophase II)

The result is the production of four haploid cells each containing a single copy of each chromosome.

The second meiotic division resembles a mitotic division

During the second meiotic division duplicated chromosomes align on the metaphase plate and then separate to the opposite poles.

This results in each of the cells having one copy of each of the chromosomes.

The division resembles a mitotic division but the number of unique chromosomes is different

- Mitosis occurs immediately after a round of DNA duplication, so the cells have four copies of each DNA molecule, 2 in each of the pairs of duplicated chromosomes.
- The cell is technically diploid because there are only two types of chromosomes present, though each chromosome is duplicated
- After division the cell is still diploid, but there is only one copy of each chromosome in the cell.
- In Meiosis II the cells begin as haploids because each cell has only one copy of each unique chromosome, though it is duplicated (two sister chromatids)
- At metaphase the two sister chromatids separate to the two poles, as in mitosis, resulting in two haploid cells, each with one copy of each chromosome.

DNA recombination and meiosis

There is another level at which the collection of genes in the genome are randomized—DNA recombination

- During prophase I the chromosomes pair with each other so that the maternal and paternal chromosomes are in close contact.
- This pairing is how the cell determines which chromosomes are homologues

- Enzymes in the cell recognize regions of identical sequence in the chromosomes leading to formation physical linkage between the chromosomes
- Other enzymes catalyze the breakage and rejoining of DNA strands to exchange sequences between non–sister chromatids
- This changes the **linkage** of genes on the chromosome

Remember that the two homologous chromosomes are not identical in every way.

- They carry sequence differences between the genome of the mother and the father
- These differences are called alleles
- The father's chromosome will have a set of alleles on each chromosome many of which will be different from those on the mother's chromosome
- Recombination puts some of the mother's alleles and some of the father's alleles on the same DNA molecule

The take–home–lesson for meiosis is that random segregation of chromosomes at Anaphase I and the shuffling of sequences by recombination during Prophase I provides an immense variability in the products of meiosis.

- The segregation provides over 8 million possible ways chromosomes can segregate into the gametes
- Recombination greatly increases this number since each chromosome probably undergoes at least one recombination per chromosome arm per meiotic prophase
- In combination with the great diversity of alleles present in a population, this random assortment of alleles provides for an immense number of possible gametes
- Fusion of two such gametes creates a new individual who is almost certainly unique genetically