Teacher Background

Meiosis

Note: The Teacher Background Section is meant to provide information for the teacher about the topic and is tied very closely to the PowerPoint slide show. For greater understanding, the teacher may want to play the slide show as he/she reads the background section. For the students, the slide show can be used in its entirety or can be edited as necessary for a given class.

What are the two types of cell division?

There are two types of normal cell division – mitosis and meiosis. Both types of cell division take place in eukaryotic organisms. Mitosis is cell division which begins in the zygote (fertilized oocyte) and continues in somatic cells throughout the life of the organism. Mitosis is important for growth and repair since this type of cell division produces genetically identical diploid copies of the original cell. (See chapter 2 for more details.)

What is meiosis?

Meiosis is cell division that occurs in the ovaries of the female and testes of the male and involves the maturation of primordial ooctyes (eggs) and formation of sperm cells, respectively. Primordial oocytes are present in the ovary at the birth of the female and sperm cells form from spermatogonia (sperm stem cells) in the testes. (See chapter 6 for more details.) Meiosis is a two-phase cell division process that reduces the chromosome number by half (haploid) so when fertilization occurs, the normal chromosome number of the species (diploid) will be maintained. Meiosis ensures genetic diversity by randomly assorting the homologous pairs of chromosomes as oocytes mature and sperm cells are formed.

Much work on cell division was done in Europe during the latter half of the 19th century. Wilhem Hertwig was the first to teach that the chromosome was the physical basis of heredity. One of his greatest achievements was the discovery in 1876 of the process of fertilization and development in sea urchins. (1) His work led Walther Flemming to publish his work on mitotic cell division in 1882 in which

he coined the term 'mitosis' and the idea of chromosomes. (See chapter 2). It also led Edouard van Beneden to describe in 1883 a two-phase cell division process in *Ascaris megalocephala* worm eggs in which he showed fertilization was the union of 2 half nuclei – one from the male and one from the female – producing a cell containing a full number of chromosomes for the species. (2) In 1886, August Weismann published his work stating that the germ cells contain "something essential for the species, something which must be carefully preserved and passed on from one generation to another" which would later be found to be chromosomes, genes, and DNA. He noted that there would have to be a nuclear division to reduce the germ cell chromosome number by half to keep from progressively increasing the chromosome number at fertilization. (3) This nuclear division later became known as meiosis which means "a reduction" in Greek.

What are the phases of meiosis?

As in mitosis, the stages of meiotic cell division are called interphase, prophase, metaphase, anaphase, and telophase. However, in meiosis, there are two phases of cell division including prophase I, metaphase I, anaphase I, telophase I, and prophase II, metaphase II, anaphase II, and telophase II. In both mitosis and meiosis, DNA replication occurs only once in S phase of interphase and sister chromatids line up on the equator at metaphase in mitosis and metaphase II in meiosis. After duplication of the chromosomes in interphase, the chromatids go through cell division only once in mitosis which results in 2 genetically identical diploid cells. In meiosis the chromatids go through cell division twice resulting in 4 haploid cells in which the maternal and paternal homologous pairs of chromosomes are randomly assorted. Mitosis takes place in somatic cells and meiosis takes place only in the testes or ovaries to form gametes - sperm cells and oocytes, respectively. Mitosis and meiosis differ further in that the synapsis (formation of the tetrad) during prophase I of meiosis, crossing over during prophase I of meiosis, and homologous sister chromatid pairs lining up on the equator during metaphase I of meiosis do not occur in mitosis.

Interphase in mitosis and meiosis are very similar proceeding through the G_1, S, and G_2 phases. In G_1, the primary oocyte or primary spermatocyte grows in size and in S phase, the chromosomes replicate exactly; the resulting sister chromatids are held together by a centromere. The chromatin material is not usually visible at this point since the chromosomes must be uncondensed or uncoiled in order to replicate. The cell then proceeds to G_2 phase in which the cell continues to grow by replicating the cytoskeleton, including microtubules, centrosome and spindles, and organelles in preparation for cell division to occur. Single and double membrane-bound organelles must be inherited from parent cells since they cannot be formed *de novo*. After G_2 has occurred, cell begins mitotic or meiotic division depending on where the cell is found in the body.

In both mitosis and meiosis during prophase, the nuclear membrane and nucleolus appear to disappear, the chromatid pairs become more pronounced as they condense in preparation for division, each of the

two centrosomes containing a pair of centrioles migrate to opposite poles, and spindle fibers made of microtubules begin to appear and attach to each of the sister chromatid pairs at the kinetochore found on the centromere of each chromatid. However, prophase I in meiosis is much longer than prophase in mitosis and is much more complicated. It is divided into five sequential stages – leptotene, zygotene, pachytene, diplotene, and diakinesis which describe the assembly (synapsis-where homologous chromatid pairs fuse along their lengths and possibly exchange DNA) and disassembly (desynapsis) of the complex. (4, 5)

a) Leptotene - The already replicated chromosomes in the leptotene stage appear within the nuclear envelope as sister chromatids but are not fully condensed. The chromatids appear like beads on a thin string and are called chromomeres. *Lepto-* in Greek means thin and *–tene* in Greek means ribbon or band. This is a very short stage of prophase I. (5, 6)

b) Zygotene - In the zygotene stage, synapsis begins to form. *Zygo-* in Greek means union, fusing, or yoking. Each autosomal sister chromatid pair associates with the sister chromatid pair of the homologous or same original chromosome pair forming a synapsis or fusion of the homologous chromatids up and down the chromatids allowing numerous points of contact called a synaptonemal complex. This synaptonemal complex facilitates synapsis by holding the aligned chromosomes together. After synapsis of homologous chromatids occurs, it is called a tetrad (4 homologous chromatids) or a bivalent (2 homologs or a chromosome pair). Bivalent is the preferred term since an unfused single homolog is called a univalent and three fused homologs (as seen in plants) are called a trivalent. (5, 6, 7)

   Autosomal chromatids pair and form a synaptonemal complex. However, in the case of meiosis in the testes, the male Y chromosome is much shorter than the X chromosome so homologous pairing occurs differently. On each end of the Y chromosome are short lengths of DNA called pseudoautosomal regions (PAR) and there are corresponding regions on the X chromosome. In late zygotene-early pachytene stage of prophase I of meiosis, the X and Y chromosome synapse at the PAR segment located on the p arm forming a fused X and Y tetrad which is known as the sex body. The PAR segment which forms the sex body is near the location of the SRY (Sex-determining Region Y) gene (also known as TDF or Testis-Determining Factor gene) which is responsible for beginning male sex determination in the fetus. (11) The sex body is often found on the edge of the nuclear area. Within the sex body, unsynapsed

regions are transcriptionally inactivated (silenced). While this inactivation is transient, it isn't fully activated until after meiosis is completed and often not until late spermatogenesis. (12, 13) The PAR segments at each end of the X chromosome escape X-chromosome inactivation when Barr Bodies form. In this way, the X chromosomes in the ovaries can synapse at each end of the X chromatids forming a tetrad or bivalent much like those formed by autosomal homologous pairs.

c) Pachytene - The third stage, pachytene, occurs once the synapse is completely formed and crossing over can now possibly occur. *Pachy*- in Greek means thick and the chromosomes are about ¼ their leptotene length. The pachytene stage can persist for days and during that time, localized breakages of the non-sister chromatids DNA can occur followed by exchanges of DNA between those homologs. Crossing over produces "cross-over chromatids" which are different from the original chromatid and contains segments of DNA from the mother and other segments from the father. In addition to crossing over occurring in autosomal tetrads, crossing over can take place in the PAR regions when XX are synapsed and when XY are synapsed.

   The process of crossing over was discovered and described by Frans Janssens in 1909 in the process he described as 'chiasmatypie'. (8) Thomas Hunt Morgan continued Janssens' work on crossing over and provided a first true genetic interpretation of meiosis. He also discovered sex-linked genes in *Drosophila melanogaster* (fruit flies). Because of his work, he won the Nobel Prize in Physiology or Medicine in 1933 "for his discoveries concerning the role played by the chromosome in heredity". (9, 10)

d) Diplotene - During the diplotene stage, the sister chromatids repel each other and move away but remain attached at places where the exchange of DNA took place in crossing over. Since the two strands form an X-shaped structure, it is called a chiasma (sing.) or chiasmata (pl.) The term chiasma means a crossing and is taken from the Greek letter X (Chi), (pronounced ki, rhyming with why). The chiasmata then begin to move or slide toward the ends of the chromatids in a process called terminalization.

e) Diakenesis - As terminalization is completed, diakenesis is the last stage of prophase I and involves the disassembly (desynapsis) of the synaptonemal complex. The chromatids tightly coil becoming shorter and thicker. The nucleolus and the nuclear envelope begin to disappear and the centrosomes reach the poles at opposite ends of the cell. (6)

In metaphase I of meiosis, each tetrad lines up on the equator to prepare for the first cell division. Spindle fibers made of microtubules begin to appear and attach to each of the sister chromatid pairs at the kinetochore found on the centromere of each chromatid. (In metaphase in mitosis, the homologous chromatid pairs line up randomly along the equator by being pulled at the centromere (kinetochore) by the attached spindle fibers.)

In anaphase I of meiosis, the tetrad is pulled apart with the sister chromatids still attached to each other. One set of sister chromatids from the homologous pair goes to one end of the cell and the other set goes to the opposite end. (In anaphase of mitosis, the sister chromatids are pulled apart by the spindle fibers toward opposite poles becoming distinct sister chromosomes.)

In telophase I of meiosis, the attached sister chromatids of the homologous pair are gathered at opposite end of the cell. (In telophase of mitosis, the sister chromosomes begin to form at the opposite poles into 2 new distinct nuclei in cells which are genetically identical to the nucleus of the parent cell.)

In meiosis, cytokinesis occurs and now there are two cells, each with attached sister chromatids from one of the original pair of homologous chromosomes. (In mitosis, the cytoplasm begins to furrow or pinch in the middle from all sides in a process called cytokinesis. While the genetic material is exactly replicated and divided, the organelles, cytoplasm containing the cytoskeleton and cell membrane are roughly divided evenly between the two identical new daughter cells (diploid) during cytokinesis.)

Now begins the 2^{nd} set of phases of cell division in meiosis. There is no further duplication of chromosomes. As prophase II begins, new spindle fibers form and attach at the centromere of the sister chromatids in preparation for further division. The sister chromatid pairs are lined up on the equator in metaphase II and begin to be pulled apart in anaphase II. As telophase II and cytokinesis begins, the sister chromatids are pulled apart into two cells. Since there were four chromatids/pair of homologous chromosomes, four cells result, each with half the number of chromosomes (haploid) as the original cell.

<u>What occurs in oogenesis?</u>

The ovary contains a large number of small primordial oocytes in primordial follicles. They are present at birth and will be all of the primordial oocytes the female will ever have. A small number of these primordial oocytes will develop into primary oocytes which are arrested in prophase I of meiosis I. Beginning at puberty in response to specific levels of estrogen and progesterone achieved during a monthly cycle, one primary oocyte will complete its first meiotic division to form two unequal cells; one is the secondary oocyte and the other is the 1^{st} polar body, each containing 23 chromatid pairs (or 46 chromatids). At the end of the meiosis I, the follicle containing the secondary oocyte with its polar body will be stimulated to burst open and release the secondary oocyte and its polar body – a process called ovulation. The ovulated secondary oocyte in the female reproductive tract can survive for about 24 hours. Meiosis II division is triggered by the entry of a sperm into the secondary oocyte as it is fertilized. The secondary oocyte divides during meiosis II to form two unequal cells: the haploid (monoploid) oocyte (sometimes called an ovum) and a haploid 2^{nd} polar body. The haploid oocyte pronucleus fuses with the haploid sperm pronucleus to form the zygote (fertilized oocyte). The zygote has 46 chromosomes – 23 from the oocyte after meiosis II and 23 from the mature sperm cell. The 1^{st} and 2^{nd} polar bodies will eventually go through apoptosis. If there is no fertilization of the secondary oocyte, it will be sloughed from the body, usually undetected. A primary oocyte will mature and be ovulated once

a month, in response to changing levels of estrogen and progestin, until the female reaches menopause when she is 40-50 years old and the hormone levels begin to substantially decrease.

What occurs in spermatogenesis?

Spermatogenesis begins at puberty in response to testosterone and continues the entire lifetime of the male. Millions of sperm at made at a time. Spermatogonia (plural for spermatogium) are undifferentiated Type A (d) stem cells in the testes which divide by mitosis to produce Type A (p) cells and more Type A (d) cells. Type A (p) cells divide by mitosis to produce Type B cells which divide by mitosis to produce primary spermatocytes. The primary spermatocytes undergo meiosis I to form two equally sized secondary spermatocytes. The secondary spermatocytes each undergo meiosis II to form four equally sized haploid (monoploid) spermatids. The spermatids continue to develop through cell differentiation into four mature haploid sperm cells flagellated for motility. The mature sperm is one of the smallest human cells - Its head measures 0.005 mm by 0.003 mm; with the tail included, the sperm is 0.05 mm in length. A sperm has the ability to swim the entire length of the female reproductive tract. Sperm can live is a female's cervical mucus and upper genital tract for about 72 hours (about 3 days). Sperm ejaculated outside the female body might survive in the semen for only up to a few hours.

What is nondisjunction?

Nondisjunction is a condition that can occur when the sister chromatids in meiosis do not separate, either in metaphase I or in metaphase II. The result is either a gamete with no chromosome or a gamete with two copies of the chromosome when it should have one. Turner's syndrome, 45XO, is a case in which nondisjunction results in one gamete without an X chromosome. Down's syndrome, 47Trisomy21, is a case where one gamete has the normal one copy of chromosome 21 and the other gamete has two copies as a result of nondisjunction. The chromosome number is critical and, other than Turner's syndrome, there are no other cases of live births in which a full chromosome is missing. A live Turner's birth is possible because in a normal XX female, one of the X chromosomes in each cell will be inactivated forming a Barr body. There are only a few types of incidences of live births of trisomy individuals, but only the Down's syndrome children survive childhood. Usually, the embryo will be miscarried (spontaneously aborted) long before birth if the chromosome number is other than the norm.

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