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Introduction

The molecule deoxyribonucleic acid (DNA) is the raw material of inheritance and ultimately influences all aspects of the structure and functioning of the human body. A single molecule of DNA, along with associated proteins, comprises a chromosome. Chromosomes are located in the nuclei of all human cells (with the exception of mature red blood cells), and each human cell contains 23 different pairs of chromosomes.

Genes are functional units of genetic information that reside on each of the 23 pairs of chromosomes. These units are linear sequences of nitrogenous bases that code for protein molecules necessary for the proper functioning of the body. The genetic information contained within the chromosomes is copied and distributed to newly created cells during cell division. The structure of DNA provides the answer to how it is precisely copied with each cell division and to how proteins are synthesized.

DNA Structure

James Watson and Francis Crick elucidated the molecular structure of DNA in 1953 using X-ray diffraction data collected by Rosalind Franklin and Maurice Wilkins, and model building techniques advocated by Linus Pauling [1, 2]. Watson and Crick proposed the double helix: a twisted, spiral ladder structure consisting of two long chains wound around each other and held together by hydrogen bonds. DNA is composed of repeating units—the nucleotides. Each nucleotide consists of a deoxyribose sugar, a phosphate group, and one of four nitrogen-containing bases: adenine (A), guanine (G), cytosine (C), or thymine (T). Adenine and

guanine are purines with a double-ring structure, whereas cytosine and thymine are smaller pyrimidine molecules with a single ring structure. Two nitrogenous bases positioned side by side on the inside of the double helix form one rung of the molecular ladder. The sugar and phosphate groups form the backbone or outer structure of the helix. The fifth (5') carbon of one deoxyribose molecule and the third (3') carbon of the next deoxyribose are joined by a covalent phosphate linkage. This gives each strand of the helix a chemical orientation with the two strands running opposite or antiparallel to one another.

Biochemical analyses performed by Erwin Chargaff showed that the nitrogenous bases of DNA were not present in equal proportions and that the proportion of these bases varied from one species to another [3]. Chargaff noted, however, that concentrations of guanine and cytosine were always equal, as were the concentrations of adenine and thymine. This finding became known as Chargaff's rule. Watson and Crick postulated that in order to fulfill Chargaff's rule and to maintain a uniform shape to the DNA molecule, there must be a specific complementary pairing of the bases: adenine must always pair with thymine, and guanine must always pair with cytosine. Each strand of DNA, therefore, contains a nucleotide sequence that is complementary to its partner. The linkage of these complementary nitrogenous base pairs holds the antiparallel strands of DNA together. Two hydrogen bonds link the adenine and thymine pairs, whereas three hydrogen bonds link the guanine and cytosine pairs (Fig. 2.1). The complementarity of DNA strands is what allows the molecule to replicate faithfully. The sequence of bases is critical for DNA function because genetic information is determined by the order of the bases along the DNA molecule.

DNA Synthesis

The synthesis of a new molecule of DNA is called replication. This process requires many enzymes and cofactors. The first step of the process involves breakage of the hydrogen

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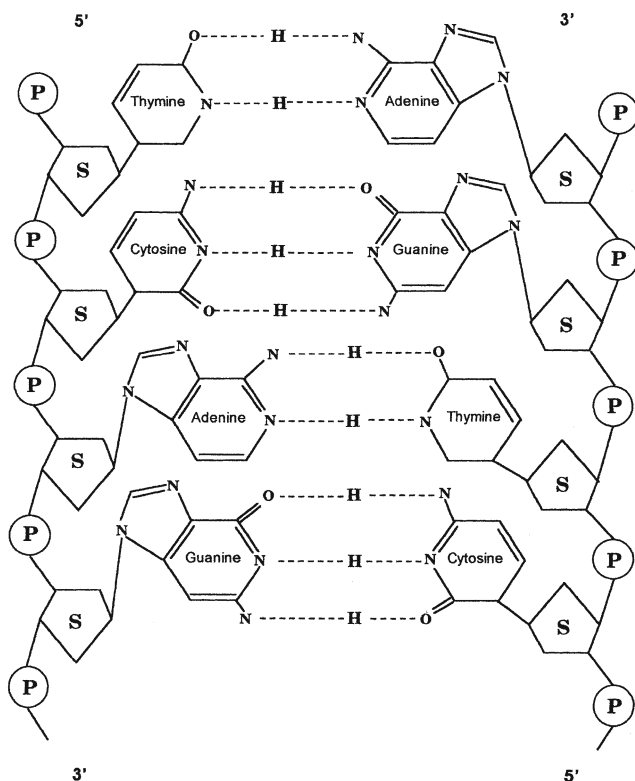


Fig. 2.1 DNA structure. Schematic representation of a DNA double helix unwound to show the complementarity of bases and the antiparallel structure of the phosphate (P) and sugar (S) backbone strands

bonds that hold the DNA strands together. DNA helicases and single-strand binding proteins work to separate the strands and keep the DNA exposed at many points along the length of the helix during replication. The area of DNA at the active region of separation is a Y-shaped structure referred to as a replication fork. These replication forks originate at structures called replication bubbles, which, in turn, are at DNA sequences called replication origins. The molecular sequence of the replication origins has not been completely characterized. Replication takes place on both strands, but nucleotides can only be added to the 3' end of an existing strand. The separated strands of DNA serve as templates for production of complementary strands of DNA following Chargaff's rules of base pairing.

The process of DNA synthesis differs for the two strands of DNA because of its antiparallel structure. Replication is straightforward on the leading strand. The enzyme DNA polymerase I facilitates the addition of complementary nucleotides to the 3' end of a newly forming strand of DNA. In order to add further nucleotides, DNA polymerase I requires the 3'-hydroxyl end of a base-paired strand.

DNA synthesis on the lagging strand is accomplished by the formation of small segments of nucleotides called Okazaki fragments [4]. After separation of the strands, the

enzyme DNA primase uses ribonucleotides to form a ribonucleic acid primer.

The structure of ribonucleic acid (RNA) is similar to that of DNA, except that each nucleotide in RNA has a ribose sugar instead of deoxyribose and the pyrimidine thymine is replaced by another pyrimidine, uracil (U). RNA also differs from DNA in that it is a single-stranded molecule. This RNA primer is at the beginning of each Okazaki segment to be copied, provides a 3'-hydroxyl group, and is important for the efficiency of the replication process. The ribonucleic acid primer then attracts DNA polymerase I. DNA polymerase I brings in the nucleotides and also removes the RNA primer and any mismatches that occur during the process. Okazaki fragments are later joined by the enzyme DNA ligase. The process of replication is semiconservative because the net result is creation of two identical DNA molecules, each consisting of a parent DNA strand and a newly synthesized DNA strand. The new DNA molecule grows as hydrogen bonds form between the complementary bases (Fig. 2.2).

Protein Synthesis

The genetic information of DNA is stored as a code; a linear sequence of nitrogenous bases in triplets. These triplets code for specific amino acids that are subsequently linked together to form protein molecules. The process of protein synthesis involves several types of ribonucleic acid.

The first step in protein synthesis is transcription. During this process, DNA is copied into a complementary piece of messenger RNA (mRNA). Transcription is controlled by the enzyme RNA polymerase, which functions to link ribonucleotides together in a sequence complementary to the DNA template strand. The attachment of RNA polymerase to a promoter region, a specific sequence of bases that varies from gene to gene, starts transcription. RNA polymerase moves off the template strand at a termination sequence to complete the synthesis of an mRNA molecule (Fig. 2.3).

Messenger RNA is modified at this point by the removal of introns—segments of DNA that do not code for an mRNA product. In addition, some nucleotides are removed from the 3' end of the molecule, and a string of adenine nucleotides are added. This poly(A) tail helps in the transport of mRNA molecules to the cytoplasm. Another modification is the addition of a cap to the 5' end of the mRNA, which serves to aid in attachment of the mRNA to the ribosome during translation. These alterations to mRNA are referred to as mRNA processing (Fig. 2.4). At this point, mRNA, carrying the information necessary to synthesize a specific protein, is transferred from the nucleus into the cytoplasm of the cell, where it then associates with ribosomes. Ribosomes, composed of ribosomal RNA (rRNA) and protein, are the site of

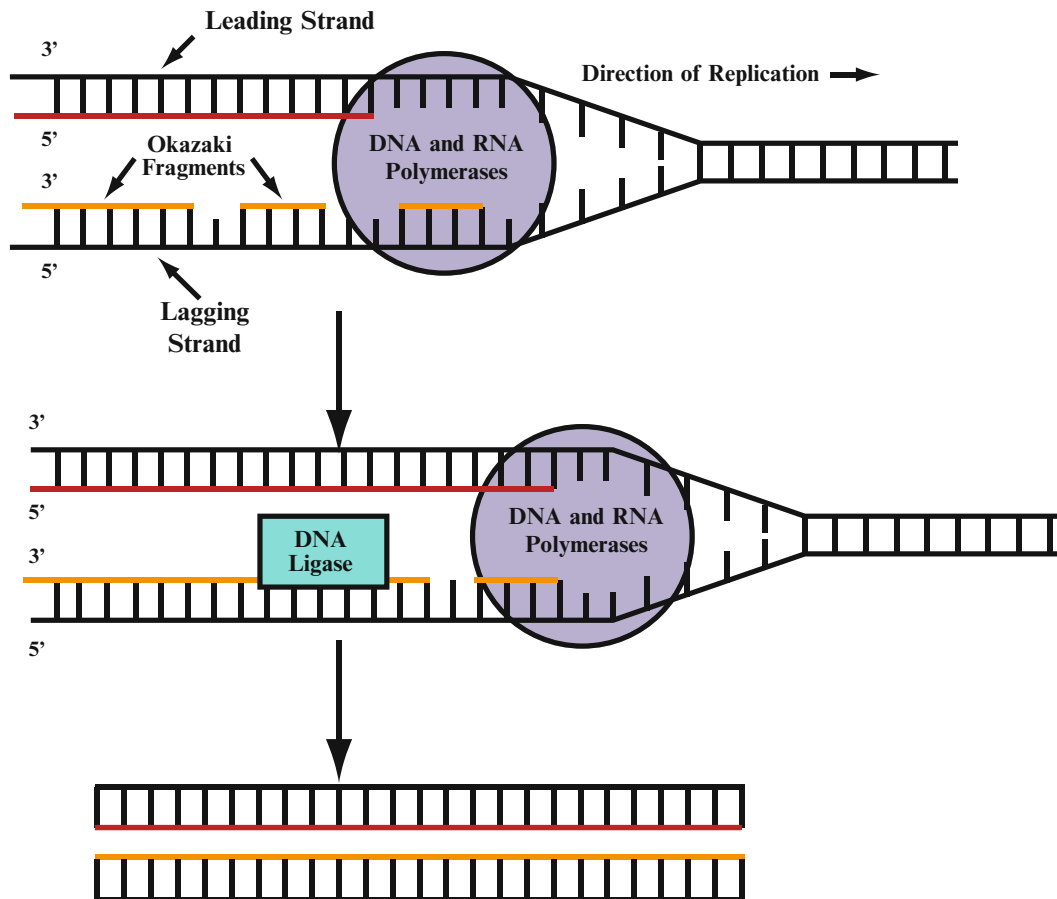


Fig. 2.2 Semiconservative replication. Complementary nucleotides are added directly to the 3' end of the leading strand, whereas the lagging strand is copied by the formation of Okazaki fragments

protein synthesis. Ribosomes consist of two subunits that come together with mRNA to read the coded instructions on the mRNA molecule.

The next step in protein synthesis is translation. A chain of amino acids is synthesized during translation by using the newly transcribed mRNA molecule as a template, with the help of a third ribonucleic acid, transfer RNA (tRNA). Leder and Nirenberg and Khorana determined that three nitrogen bases on an mRNA molecule constitute a codon [5, 6]. With four nitrogenous bases, there are 64 possible three-base codons. Sixty-one of these code for specific amino acids, and the other three are “stop” codons that signal the termination of protein synthesis. There are only 20 amino acids, but 61 codons. Therefore, most amino acids are coded for by more than one mRNA codon. This redundancy in the genetic code is referred to as degeneracy.

Transfer RNA molecules contain “anticodons”—nucleotide triplets that are complementary to the codons on mRNA. Each tRNA molecule has attached to it the specific amino acid for which it codes.

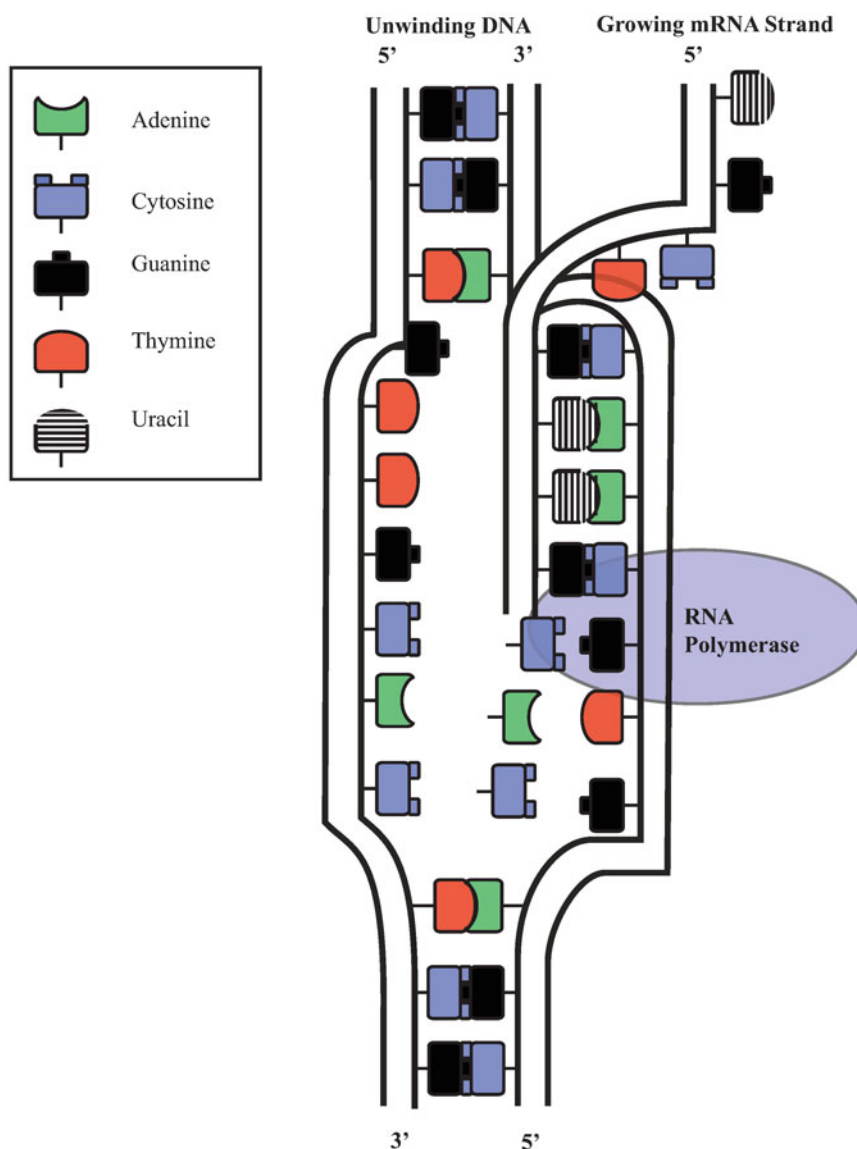
Ribosomes read mRNA one codon at a time. Transfer RNA molecules transfer the specific amino acids to the synthesizing protein chain (Fig. 2.5). The amino acids are joined to this chain by peptide bonds. This process is continued until a stop codon is reached. The new protein molecule is then released into the cell milieu and the ribosomes split apart (Fig. 2.6).

DNA Organization

Human chromatin consists of a single continuous molecule of DNA complexed with histone and nonhistone proteins. The DNA in a single human diploid cell, if stretched out, would be approximately 2 m in length and therefore must be condensed considerably to fit within the cell nucleus [7]. There are several levels of DNA organization that allow for this.

The DNA helix itself is the first level of condensation. Next, two molecules of each of the histones H2A, H2B, H3, and H4 form a protein core: the octamer. The DNA double

Fig. 2.3 Transcription. A DNA molecule is copied into mRNA with the help of RNA polymerase



helix winds twice around the octamer to form a 10-nm nucleosome, the basic structural unit of chromatin. Adjacent nucleosomes are pulled together by a linker segment of the histone H1. Repeated, this gives the chromatin the appearance of “beads on a string.” Nucleosomes are further coiled into a 30-nm solenoid, with each turn of the solenoid containing about six nucleosomes. The solenoids are packed into DNA looped domains attached to a nonhistone protein matrix. Attachment points of each loop are fixed along the DNA. The looped domains coil further to give rise to highly compacted units, the chromosomes, which are visible with the light microscope only during cell division. Chromosomes reach their greatest extent of condensation during mitotic metaphase (Fig. 2.7).

Chromosome Structure

A chromosome consists of two sister chromatids, each of which is comprised of a contracted and compacted double helix of DNA. The centromere, telomere, and nucleolar organizer regions are functionally differentiated areas of the chromosomes (Fig. 2.8).

The Centromere

The centromere is a constriction visible on metaphase chromosomes where the two sister chromatids are joined together. The centromere is essential to the survival of a chromosome

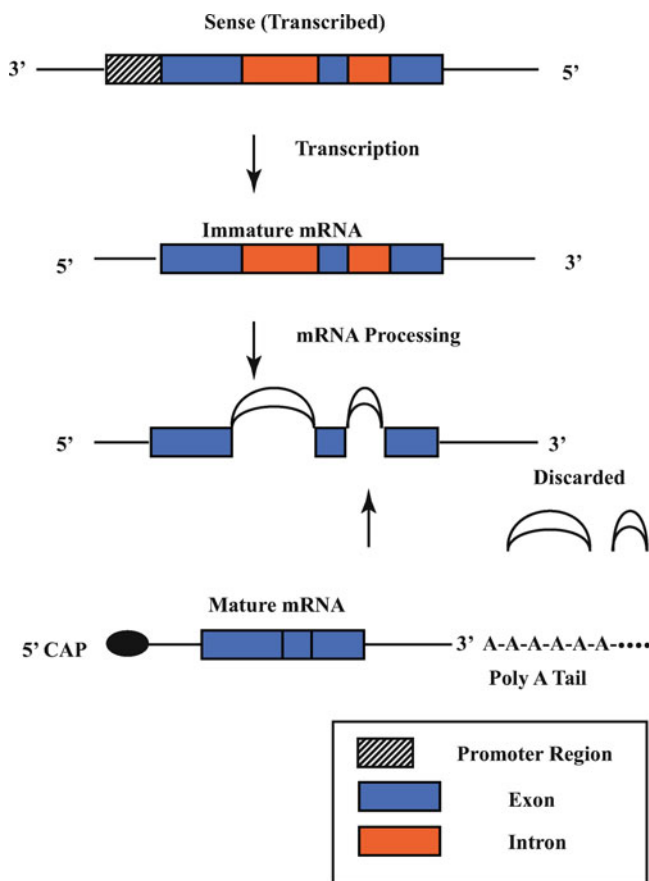


Fig. 2.4 Messenger RNA processing. The transcribed strand of DNA is modified to produce a mature mRNA transcript

during cell division. Interaction with the mitotic spindle during cell division occurs at the centromeric region. Mitotic spindle fibers are the functional elements that separate the sister chromatids during cell division.

Human chromosomes are classified based on the position of the centromere on the chromosome. The centromere is located near the middle in metacentric chromosomes, near one end in acrocentric chromosomes, and between the middle and end in submetacentric chromosomes. The kinetochore apparatus is a complex structure consisting of proteins that function at the molecular level to attach the chromosomes to the spindle fibers during cell division. Although the kinetochore is located in the region of the centromere, it should not be confused with the centromere. The latter is the DNA at the site of the spindle-fiber attachment.

The Nucleolar Organizer Regions

The satellite stalks of human acrocentric chromosomes contain the nucleolar organizer regions (NORs), so-called because this is where nucleoli form in interphase cells. NORs are also the site of ribosomal RNA genes and production of

rRNA. In humans, there are theoretically ten nucleolar organizer regions, although all may not be active during any given cell cycle.

The Telomeres

The telomeres are the physical ends of chromosomes. Telomeres act as protective caps to chromosome ends, preventing end-to-end fusion of chromosomes and DNA degradation resulting after chromosome breakage. Nonhistone proteins complex with telomeric DNA to protect the ends of chromosomes from nucleases located within the cell [9]. The telomeric region also plays a role in synapsis during meiosis. Chromosome pairing appears to be initiated in the subtelomeric regions [10].

Telomeres contain tandem repeats of the nitrogenous base sequence TTAGGG over 3–20 kb at the chromosome ends [11]. At the very tip of the chromosome, the two strands do not end at the same point, resulting in a short G-rich tail that is single stranded. Because of this, DNA synthesis breaks down at the telomeres and telomeres replicate differently than other types of linear DNA. The enzyme telomerase synthesizes new copies of the telomere TTAGGG repeat using an RNA template that is a component of the telomerase enzyme. Telomerase also counteracts the progressive shortening of chromosomes that results from many cycles of normal DNA replication. Telomere length gradually decreases with the aging process and with increased numbers of cell divisions in culture. The progressive shortening of human telomeres appears to be a tumor-suppressor mechanism [12]. The maintenance of telomeric DNA permits the binding of telomeric proteins that form the protective cap at chromosome ends and regulate telomere length [12]. Cells that have defective or unstable telomerase will exhibit shortening of chromosomes, leading to chromosome instability and cell death.

Types of DNA

DNA is classified into three general categories: unique sequence, highly repetitive sequence DNA (>105 copies), and middle repetitive sequence DNA (102–104 copies). Unique sequence or single-copy DNA is the most common class of DNA, comprising about 75% of the human genome [13]. This DNA consists of nucleotide sequences that are represented only once in a haploid set. Genes that code for proteins are single-copy DNA. Repetitive or repeated sequence DNA makes up the remaining 25% of the genome and is classified according to the number of repeats and whether the repeats are tandem or interspersed among unique sequence DNA [13].

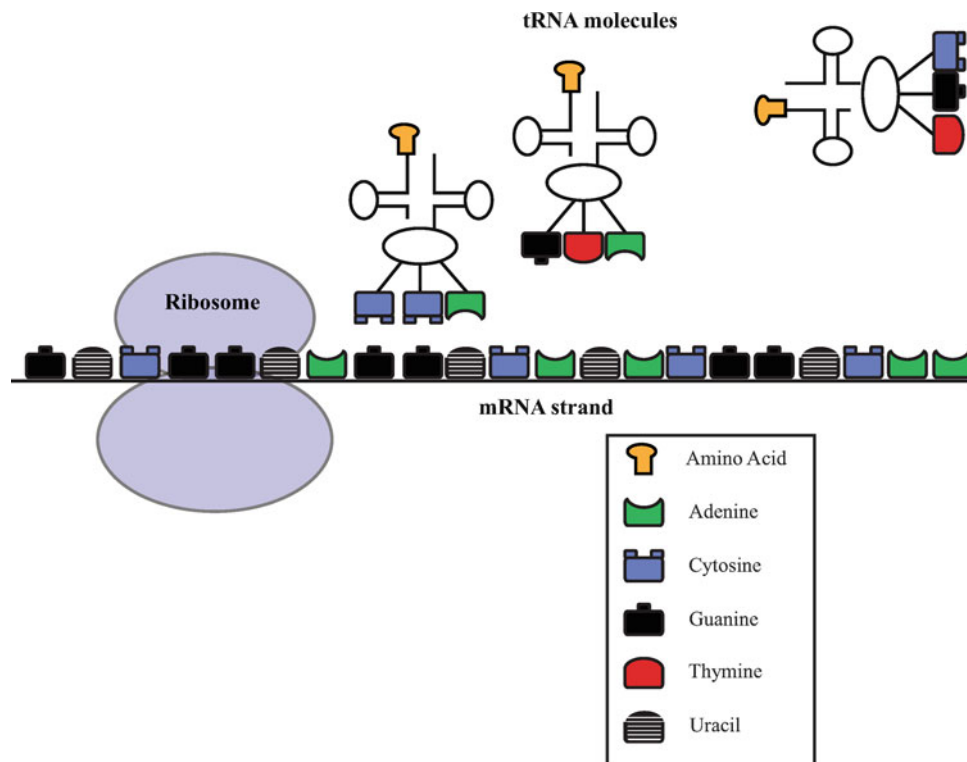


Fig. 2.5 Translation. Transfer RNA molecules bring in specific amino acids according to the triplet codon instructions of mRNA that are read at the ribosomes

Repetitive, tandemly arranged DNA was first discovered with a cesium chloride density gradient. Repetitive, tandem sequences were visualized as separate bands in the gradient. This DNA was termed satellite DNA [14]. Satellite DNA is categorized, based on the length of sequences that make up the tandem array and the total length of the array, as α (alpha)-satellite, minisatellite, and microsatellite DNA.

Alpha-satellite DNA is a repeat of a 171-base pair sequence organized in a tandem array of up to a million base pairs or more in total length. Alpha-satellite DNA is generally not transcribed and is located in the heterochromatin associated with the centromeres of chromosomes (see later). The size and number of repeats of satellite DNA is chromosome specific [15]. Although α -satellite DNA is associated with centromeres, its role in centromere function has not been determined. A centromeric protein, CENP-B, has been shown to bind to a 17-base pair portion of some α -satellite DNA, but the functional significance of this has not been determined [16].

Minisatellites have repeats that are 20–70 base pairs in length, with a total length of a few thousand base pairs. Microsatellites have repeat units of two, three, or four base pairs, and the total length is usually less than a few hundred base pairs. Minisatellites and microsatellites vary in length among individuals and, as such, are useful markers for gene mapping and identity testing.

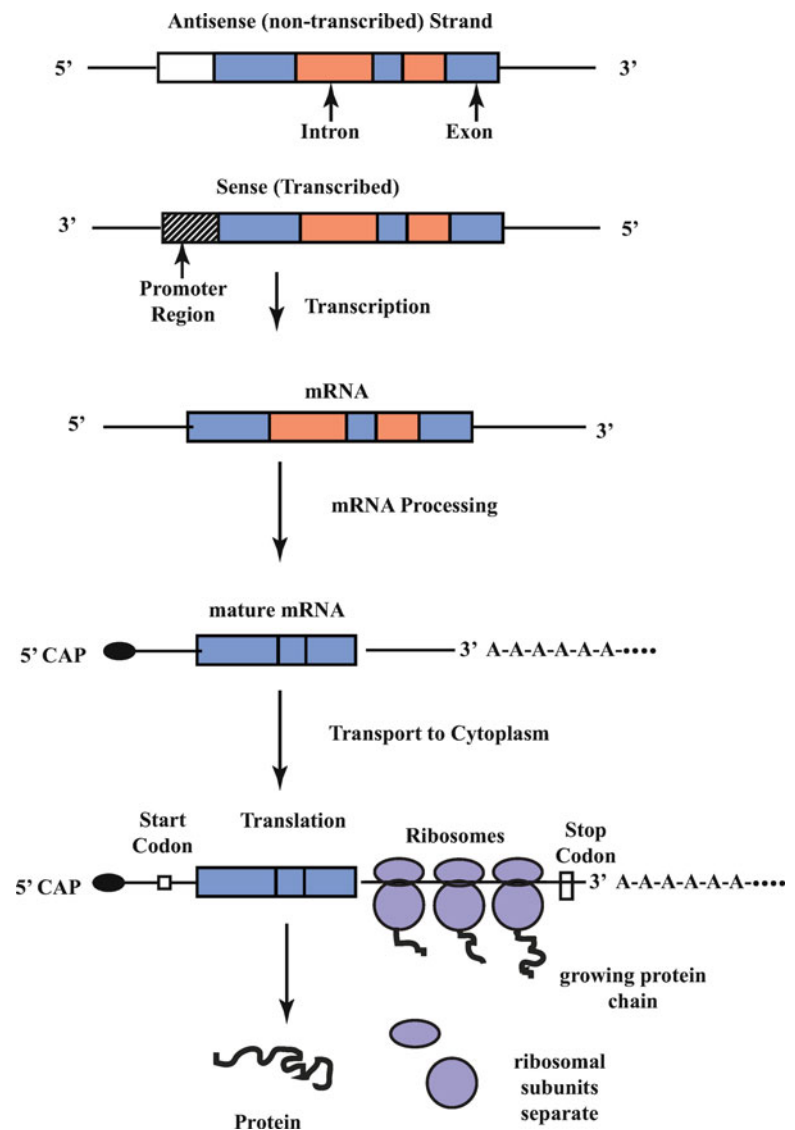
The genes for 18S and 28S ribosomal RNAs are middle repetitive sequences. Several hundred copies of these genes are tandemly arranged on the short arms of the acrocentric chromosomes.

Dispersed repetitive DNA is classified as either short or long. The terms SINEs (short interspersed elements) and LINEs (long interspersed elements) were introduced by Singer [17]. SINEs range in size from 90 to 500 base pairs. One class of SINEs is the Alu sequence. Many Alu sequences are transcribed and are present in nuclear pre-mRNA and in some noncoding regions of mRNA. Alu sequences have high G-C content and are found predominantly in the Giemsa-light bands of chromosomes [18]. LINEs can be as large as 7,000 bases. The predominant member of the LINE family is a sequence called L1. L1 sequences have high A-T content and are predominantly found in the Giemsa-dark bands of chromosomes [17]. See Chaps. 3 and 4.

Chromatin

There are two fundamental types of chromatin in eukaryotic cells: euchromatin and heterochromatin. Euchromatin is loosely organized, extended, and uncoiled. This chromatin contains active, early replicating genes, and stains lightly with GTG-banding techniques (see Chap. 4).

Fig. 2.6 Overview of protein synthesis. DNA is transcribed to mRNA, which is modified to mature transcript and then transferred to the cytoplasm of the cell. The codons are read at the ribosomes and translated with the help of tRNA. The chain of amino acids produced during translation is joined by peptide bonds to form a protein molecule



There are two special types of heterochromatin that warrant special mention: facultative heterochromatin and constitutive heterochromatin. Both are genetically inactive, late replicating during the synthesis (S) phase of mitosis, and are highly contracted.

Constitutive Heterochromatin

Constitutive heterochromatin consists of simple repeats of nitrogenous bases that are generally located around the centromeres of all chromosomes and at the distal end of the Y chromosome. There are no transcribed genes located in constitutive heterochromatin, which explains the fact that variations in constitutive heterochromatic chromosome regions apparently have no effect on the phenotype. Chromosomes 1, 9, 16, and Y have variably sized constitutive heterochromatic regions.

The heterochromatic regions of these chromosomes stain differentially with various special staining techniques, revealing that the DNA structure of these regions is not the same as the structure of the euchromatic regions on the same chromosomes. The only established function of constitutive heterochromatin is the regulation of crossing-over—the exchange of genes from one sister chromatid to the other during cell division [19].

Facultative Heterochromatin

One X chromosome of every female cell is randomly inactivated. The inactivated X is condensed during interphase and replicates late during the synthesis stage of the cell cycle. It is termed facultative heterochromatin. Because these regions are inactivated, it has been proposed that facultative heterochromatin regulates gene function [20].

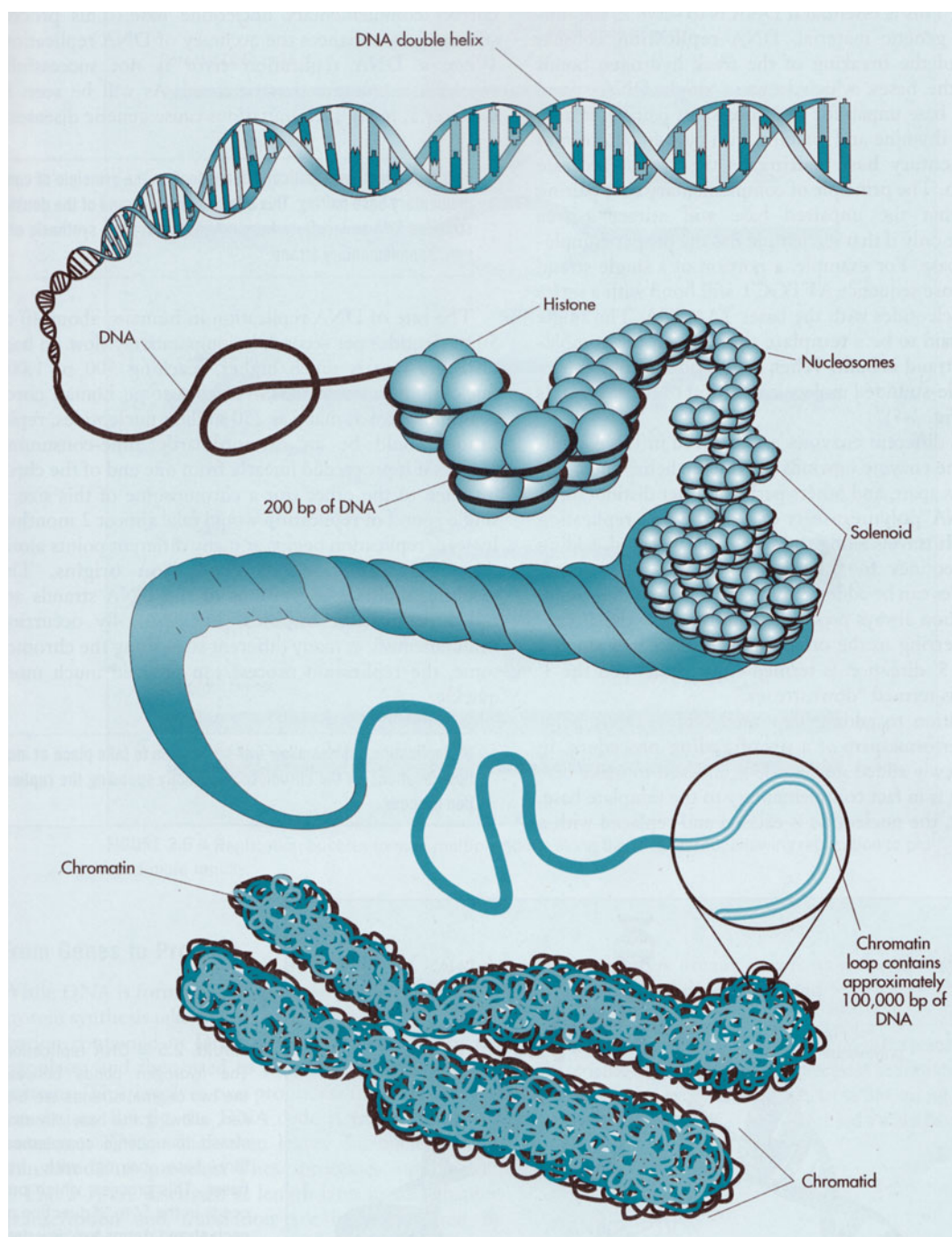


Fig. 2.7 The levels of DNA organization (Reprinted with permission from Jorde et al. [8])

Cell Division

An understanding of cell division is basic to an understanding of cytogenetics. Dividing cells are needed in order to study chromosomes using traditional cytogenetic techniques, and many cytogenetic abnormalities result from errors in cell division.

There are two types of cell division: mitosis and meiosis. Mitosis is the division of somatic cells, whereas meiosis is a special type of division that occurs only in gametic cells.

The Cell Cycle

The average mammalian cell cycle lasts about 17–18 h and is the transition of a cell from one interphase through cell division and back to interphase [21]. The cell cycle is divided into four major stages. The first three stages, gap 1 (G1), synthesis (S), and gap 2 (G2), comprise interphase. The fourth and final stage of the cell cycle is mitosis (M) (Fig. 2.9).

The first stage, G1, is the longest and typically lasts about 9 h [21]. Chromosomes exist as single chromatids during this

Fig. 2.8 The functional and structural components of metaphase chromosomes

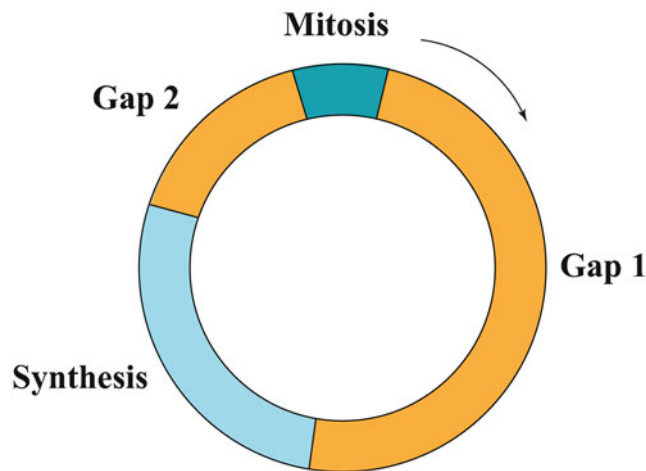
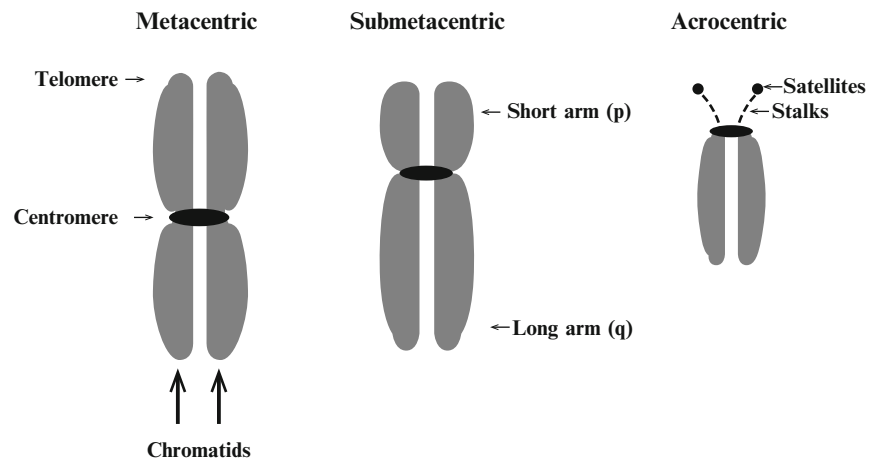


Fig. 2.9 The cell cycle: gap 1, synthesis, gap 2, and mitosis

stage. Cells are metabolically active during G1, and this is when protein synthesis takes place. A cell might be permanently arrested at this stage if it does not undergo further division. This arrested phase is referred to as gap zero (G0).

Gap 1 is followed by the synthesis phase, which lasts about 5 h in mammalian cells [21]. This is when DNA synthesis occurs. The DNA replicates itself, and the chromosomes then consist of two identical sister chromatids.

Some DNA replicates early in S phase, and some replicates later. Early replicating DNA contains a higher portion of active genes than late-replicating DNA. By standard G-banding techniques, the light-staining bands usually replicate early, whereas the dark-staining bands and the inactive X chromosome in females replicate late in the S phase.

Gap 2 lasts about 3 h [21]. During this phase, the cell prepares to undergo cell division. The completion of G2 represents the end of interphase.

The final step in the cell cycle is mitosis. This stage lasts only 1–2 h in most mammalian cells. Mitosis is the process by which cells reproduce themselves, creating two daughter cells that are genetically identical to one another and to the original parent cell. Mitosis is itself divided into stages (Fig. 2.10).

Mitosis

Prophase

Chromosomes are at their greatest elongation and are not visible as discrete structures under the light microscope during interphase. During prophase, chromosomes begin to coil, become more condensed, and begin to become visible as discrete structures. Nucleoli are visible early in prophase but disappear as the stage progresses.

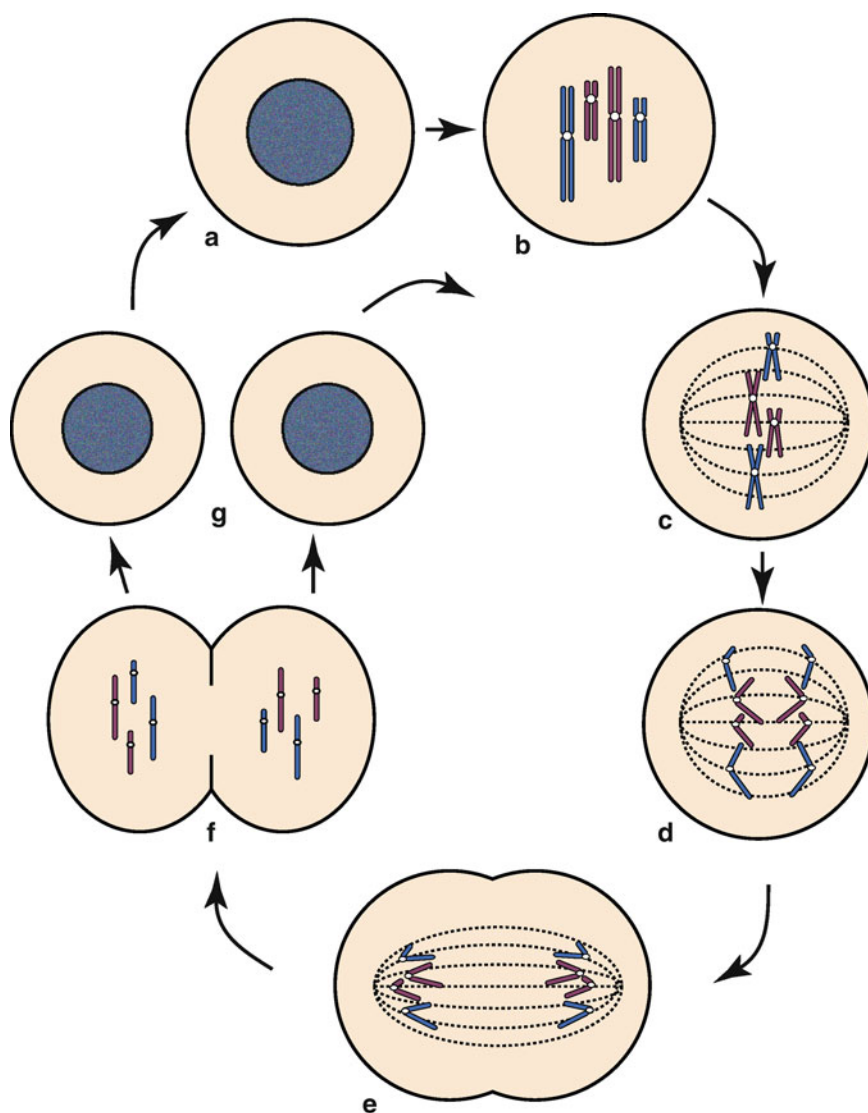
Prometaphase

Prometaphase is a short period between prophase and metaphase during which the nuclear membrane disappears and the spindle fibers begin to appear. Chromosomes attach to the spindle fibers at their kinetochores.

Metaphase

During metaphase, the mitotic spindle is completed, the centrioles divide and move to opposite poles, and the chromosomes line up on the equatorial plate. Chromosomes reach their maximum state of contraction during this phase. It is metaphase chromosomes that are traditionally studied in cytogenetics.

Fig. 2.10 Mitosis. Schematic representation of two pairs of chromosomes undergoing cell division: (a) interphase, (b) prophase, (c) metaphase, (d) anaphase, (e) telophase, (f) cytokinesis, and (g) interphase of the next cell cycle



Anaphase

Centromeres divide longitudinally and the chromatids separate during this stage. Sister chromatids migrate to opposite poles as anaphase progresses.

Telophase

The final stage of mitosis is telophase. The chromosomes uncoil and become indistinguishable again, the nucleoli reform, and the nuclear membrane is reconstructed. Telophase is usually followed by cytokinesis, or cytoplasmic division. Barring errors in DNA synthesis or cell division, the products

of mitosis are two genetically identical daughter cells, each of which contains the complete set of genetic material that was present in the parent cell. The two daughter cells enter interphase, and the cycle is repeated.

Meiosis

Meiosis takes place only in the ovaries and testes. A process involving one duplication of the DNA and two cell divisions (meiosis I and meiosis II) reduces the number of chromosomes from the diploid number ($2n=46$) to the haploid number ($n=23$). Each gamete produced contains only one copy of each chromosome. Fertilization restores the diploid number in the zygote.

Meiosis I

Meiosis I is comprised of several substages: prophase I, metaphase I, anaphase I, and telophase I (Fig. 2.11).

Prophase I

Prophase I is a complex stage that is further subdivided as follows.

Leptotene

In leptotene, there are 46 chromosomes, each comprised of two chromatids. The chromosomes begin to condense but are not yet visible by light microscopy. Once leptotene takes place, the cell is committed to meiosis.

Zygotene

Zygotene follows leptotene. Homologous chromosomes, which in zygotene appear as long thread-like structures, pair locus for locus. This pairing is called synapsis. A tripartite structure, the synaptonemal complex, can be seen with electron microscopy. The synaptonemal complex is necessary for the phenomenon of crossing-over that will take place later in prophase I.

Synapsis of the X and Y chromosomes in males occurs only at the pseudoautosomal regions. These regions are located at the distal short arms and are the only segments of the X and Y chromosomes containing homologous loci. The nonhomologous portions of these chromosomes condense to form the sex vesicle.

Pachytene

Synapsis is complete during pachytene. Chromosomes continue to condense and now appear as thicker threads. The paired homologs form structures called bivalents, sometimes referred to as tetrads because they are composed of four chromatids.

The phenomenon of crossing over takes place during pachytene. Homologous or like segments of DNA are exchanged between nonsister chromatids of the bivalents. The result of crossing over is a reshuffling or recombination of genetic material between homologs, creating new combinations of genes in the daughter cells.

Diplotene

In diplotene, chromosomes continue to shorten and thicken, and the homologous chromosomes begin to repel each other. This repulsion continues until the homologous chromosomes are held together only at points where crossing-over took place. These points are referred to as chiasmata. In males, the sex vesicle disappears, and the X and Y chromosomes associate end to end.

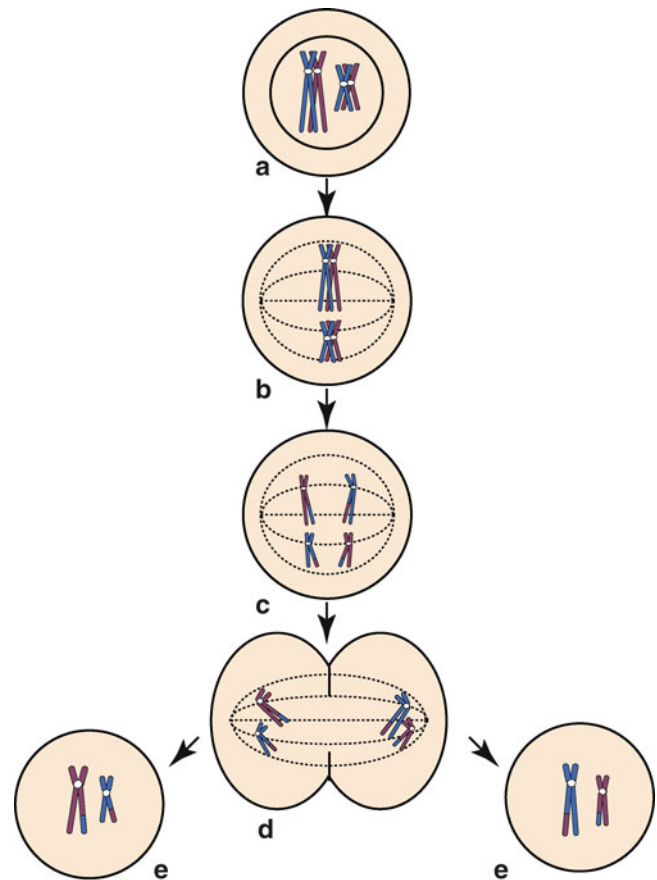


Fig. 2.11 Schematic representation of two chromosome pairs undergoing meiosis I: (a) prophase I, (b) metaphase I, (c) anaphase I, (d) telophase I, and (e) products of meiosis I

Diakinesis

Chromosomes reach their greatest contraction during this last stage of prophase.

Metaphase I

Metaphase I is characterized by disappearance of the nuclear membrane and formation of the meiotic spindle. The bivalents line up on the equatorial plate with their centromeres randomly oriented toward opposite poles.

Anaphase I

During anaphase I, the centromeres of each bivalent separate and migrate to opposite poles.

Telophase I

In telophase, the two haploid sets of chromosomes reach opposite poles, and the cytoplasm divides. The result is two cells containing 23 chromosomes, each comprised of two chromatids.

Meiosis II

The cells move directly from telophase I to metaphase II with no intervening interphase or prophase. Meiosis II proceeds much like mitotic cell division except that each cell contains only 23 chromosomes (Fig. 2.12).

The 23 chromosomes line up on the equatorial plate in metaphase II, the chromatids separate and move to opposite poles in anaphase II, and cytokinesis occurs in telophase II. The net result is four cells, each of which contains 23 chromosomes, each consisting of a single chromatid. Owing to the effects crossing-over and random assortment of homologs, each of the new cells differs genetically from one another and from the original cell.

Spermatogenesis and Oögenesis

The steps of spermatogenesis and oögenesis are the same in human males and females; however, the timing is very different (Fig. 2.13).

Spermatogenesis

Spermatogenesis takes place in the seminiferous tubules of the male testes. The process is continuous and each meiotic cycle of a primary spermatocyte results in the formation of four nonidentical spermatozoa. Spermatogenesis begins with sexual maturity and occurs throughout the postpubertal life of a man.

The spermatogonia contain 46 chromosomes. Through mitotic cell division, they give rise to primary spermatocytes. The primary spermatocytes enter meiosis I and give rise to the secondary spermatocytes, which contain 23 chromosomes, each consisting of two chromatids. The secondary spermatocytes undergo meiosis II and give rise to spermatids. Spermatids contain 23 chromosomes, each consisting of a single chromatid. The spermatids differentiate to become spermatozoa, or mature sperm.

Oögenesis

Oögenesis in human females begins in prenatal life. Ova develop from oögonia within the follicles in the ovarian cortex. At about the third month of fetal development, the oögonia, through mitotic cell division, begin to develop into diploid primary oöcytes. Meiosis I continues to diplotene, where it is arrested until sometime in the postpubertal reproductive life of a woman. This suspended diplotene is referred to as dictyotene.

Subsequent to puberty, several follicles begin to mature with each menstrual cycle. Meiosis I rapidly proceeds with an uneven distribution of the cytoplasm in cytokinesis of meiosis I, resulting in a secondary oöcyte containing most of the cytoplasm, and a first polar body. The secondary oöcyte,

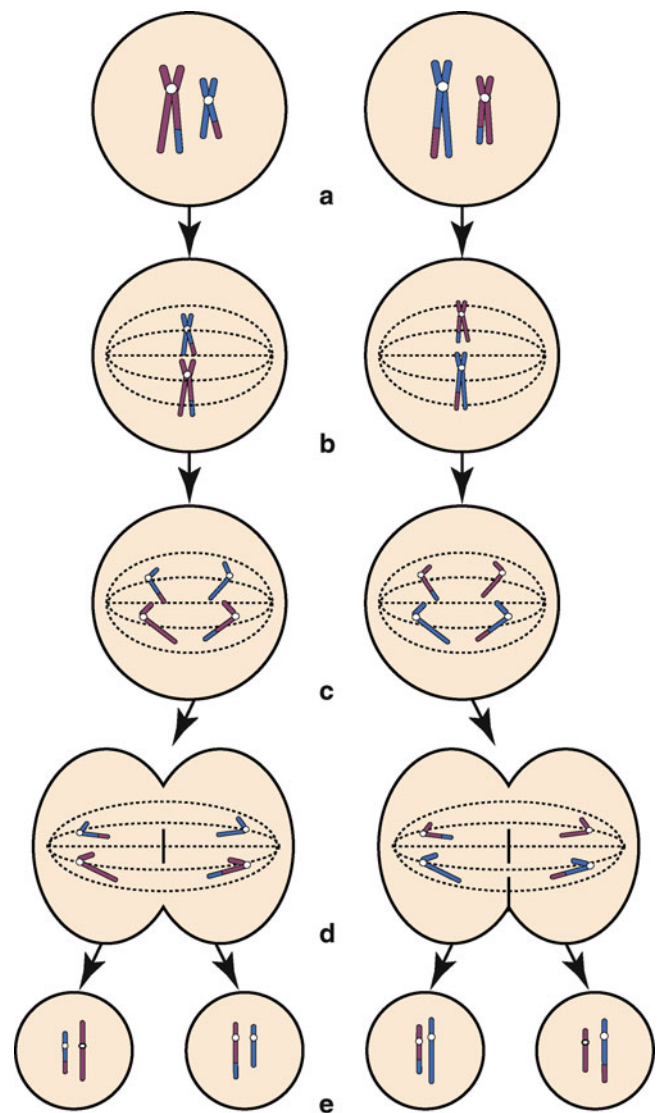


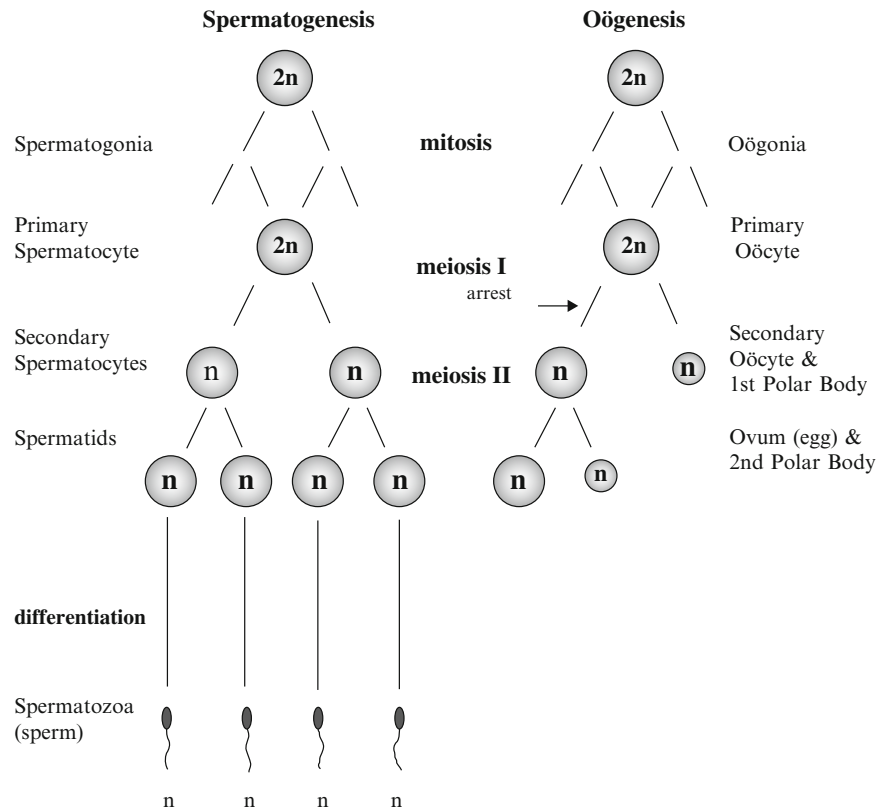
Fig. 2.12 Schematic representation of two chromosome pairs undergoing meiosis II: (a) products of meiosis I, (b) metaphase II, (c) anaphase II, (d) telophase II, and (e) products of meiosis

which has been ovulated, begins meiosis II. Meiosis II continues only if fertilization takes place. The completion of meiosis II results in a haploid ovum and a second polar body. The first polar body might undergo meiosis II, or it might degenerate. Only one of the potential four gametes produced each menstrual cycle is theoretically viable.

Fertilization

The chromosomes of the egg and sperm produced in meiosis II are each surrounded by a nuclear membrane within the cytoplasm of the ovum and are referred to as pronuclei. The male and female pronuclei fuse to form the diploid nucleus of the zygote, and the first mitotic division begins.

Fig. 2.13 Spermatogenesis and oögenesis. The events of spermatogenesis and oögenesis are the same, but the timing and net results are different. Oögenesis begins prenatally and is arrested in meiosis I until the postpubertal life of a woman; spermatogenesis begins with the sexual maturity of the male and is continuous. Each cycle of spermatogenesis results in four functional gametes, while each cycle of oögenesis results in a single egg



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