DNA & Chromosome

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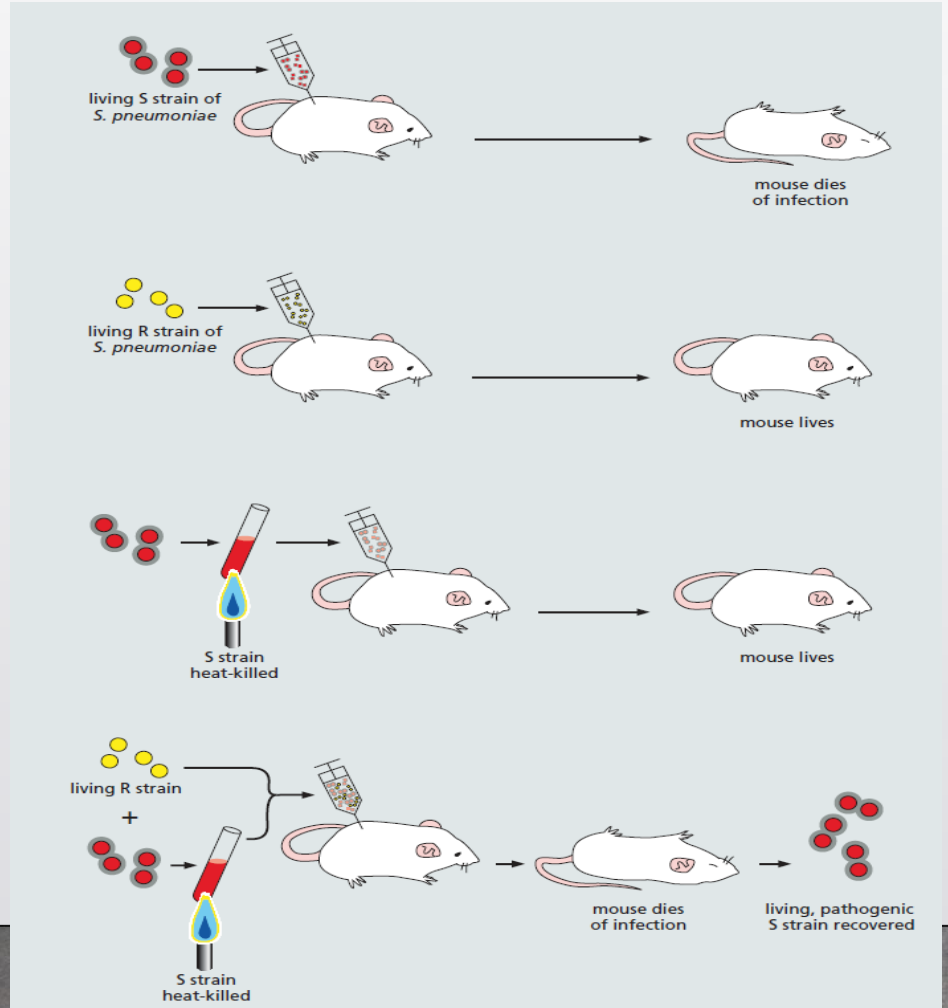
Kuliah Biologi Sel

Program Studi Ilmu dan Teknologi Pangan

Sejarah Penemuan DNA

- Kehidupan sangat bergantung pada kemampuan sel untuk menyimpan dan menterjemahkan informasi genetik
- Penelitian tentang DNA dimulai sekitar awal abad 20 → awal mula ilmu genetik
- Tahun 1940 → DNA merupakan pembawa informasi genetik
- Tahun 1953, James Watson & Francis Crick menetapkan struktur DNA

DNA Sebagai Pembawa Informasi Genetik



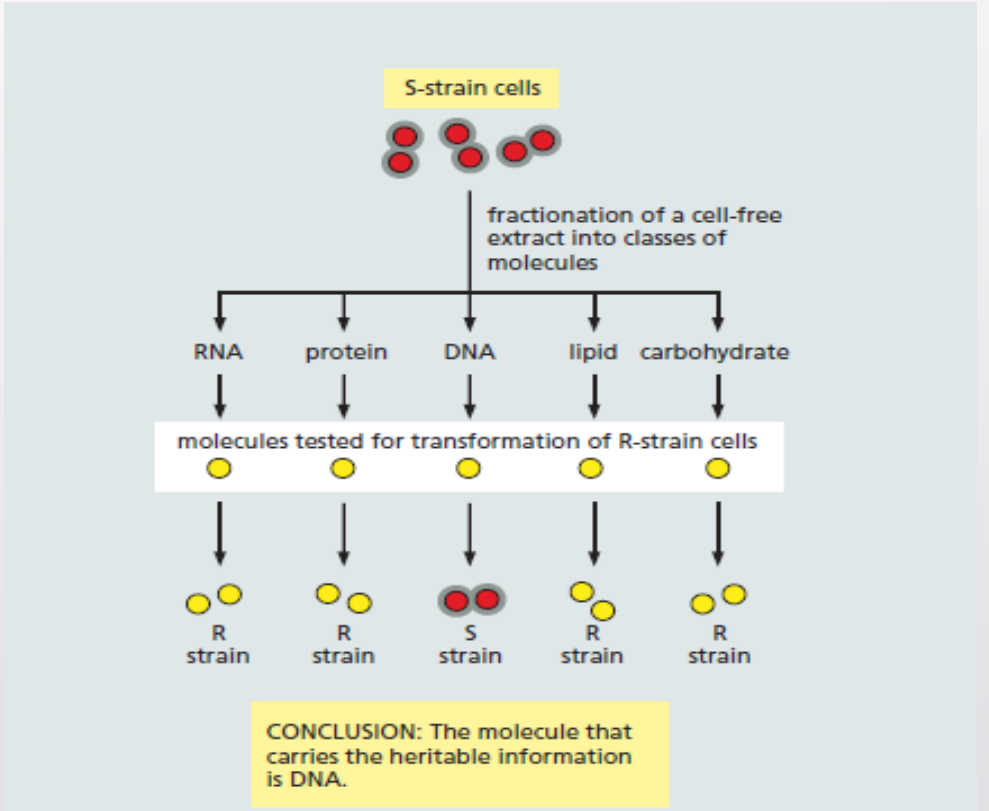


Figure 5–4 Avery, MacLeod, and McCarty demonstrated that DNA is the genetic material. The researchers prepared an extract from the disease-causing S strain of pneumococci and showed that the "transforming principle" that would permanently change the harmless R-strain pneumococci into the pathogenic S strain is DNA. This was the first evidence that DNA could serve as the genetic material.

Struktur DNA

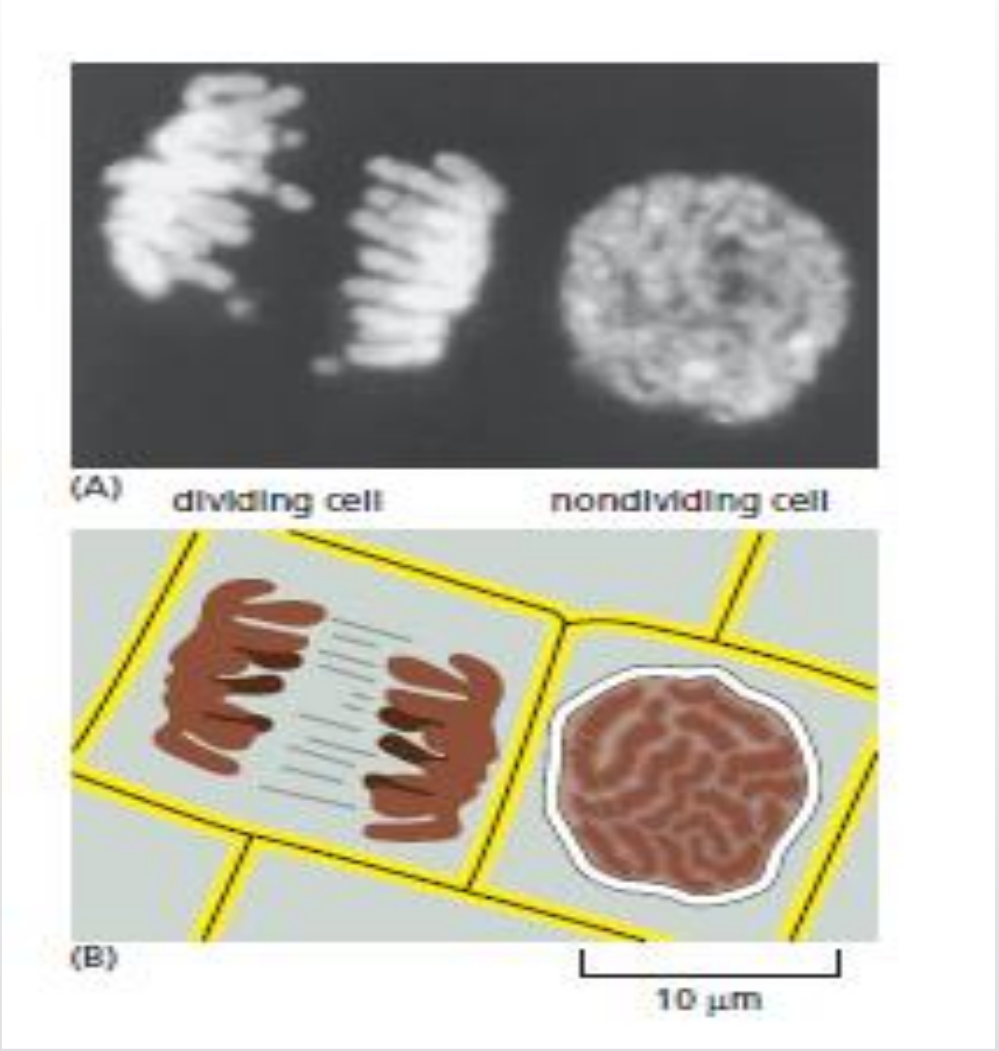


Figure 5–1 Chromosomes become visible as eukaryotic cells prepare to divide. (A) Two adjacent plant cells photographed in a fluorescence microscope. The DNA is labeled with a fluorescent dye (DAPI) that binds to it. The DNA is packaged into chromosomes, which become visible as distinct structures only when they condense in preparation for cell division, as shown on the *left*. The cell on the *right*, which is not dividing, contains the identical chromosomes, but they cannot be distinguished as individual entities because the DNA is in a much more extended conformation at this phase in the cell's life cycle. (B) Schematic diagram of the outlines of the two cells and their chromosomes. (A, courtesy of Peter Shaw.)

Struktur DNA

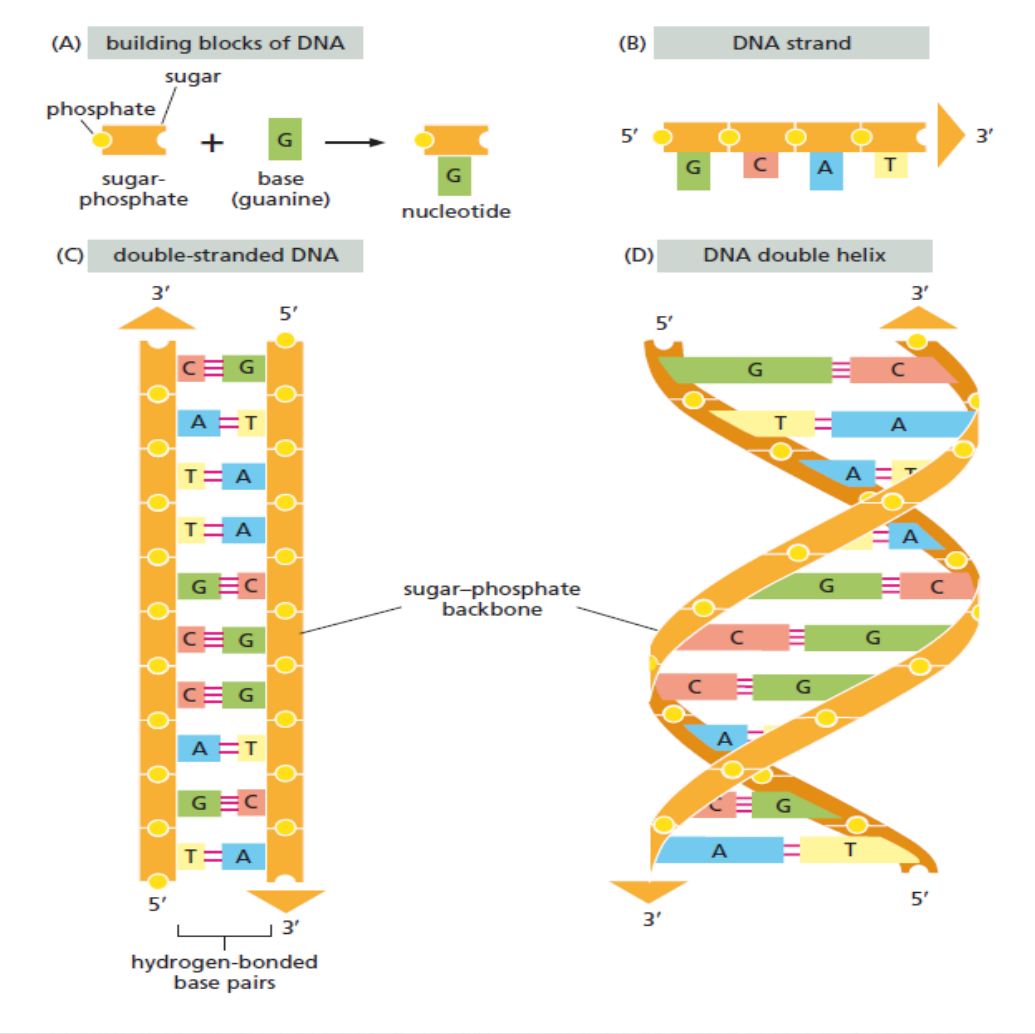
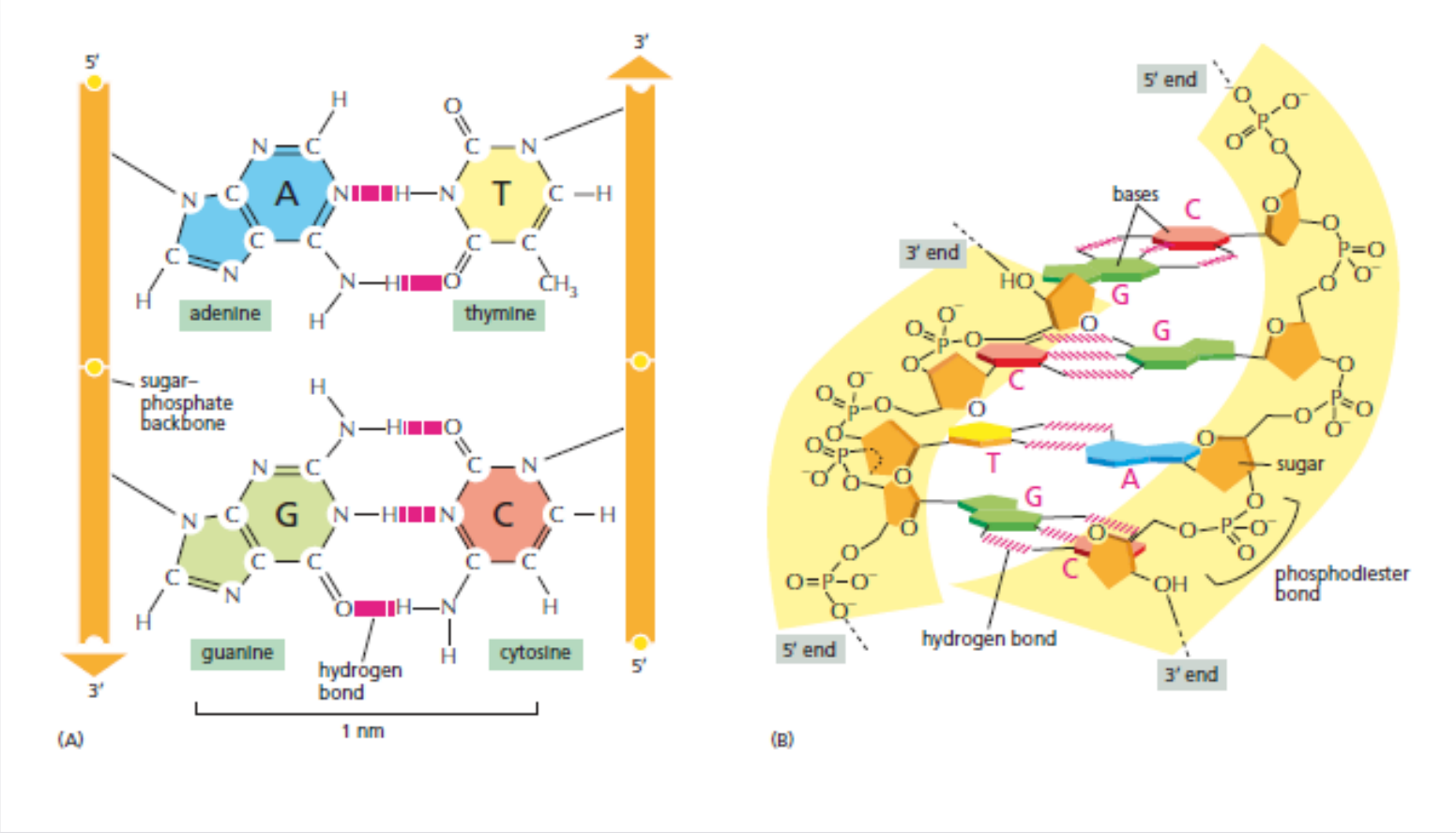


Figure 5–2 DNA is made of four nucleotide building blocks. (A) Each nucleotide is composed of a sugar–phosphate covalently linked to a base—guanine (G) in this figure. (B) The nucleotides are covalently linked together into polynucleotide chains, with a sugar–phosphate backbone from which the bases (A, C, G, and T) extend. (C) A DNA molecule is composed of two polynucleotide chains (DNA strands) held together by hydrogen bonds between the paired bases. The *arrows* on the DNA strands indicate the polarities of the two strands, which run antiparallel to each other in the DNA molecule. (D) Although the DNA is shown straightened out in (C), in reality, it is wound into a double helix, as shown here.

Antipair, double helix DNA



Struktur Chromosome Eukariotik

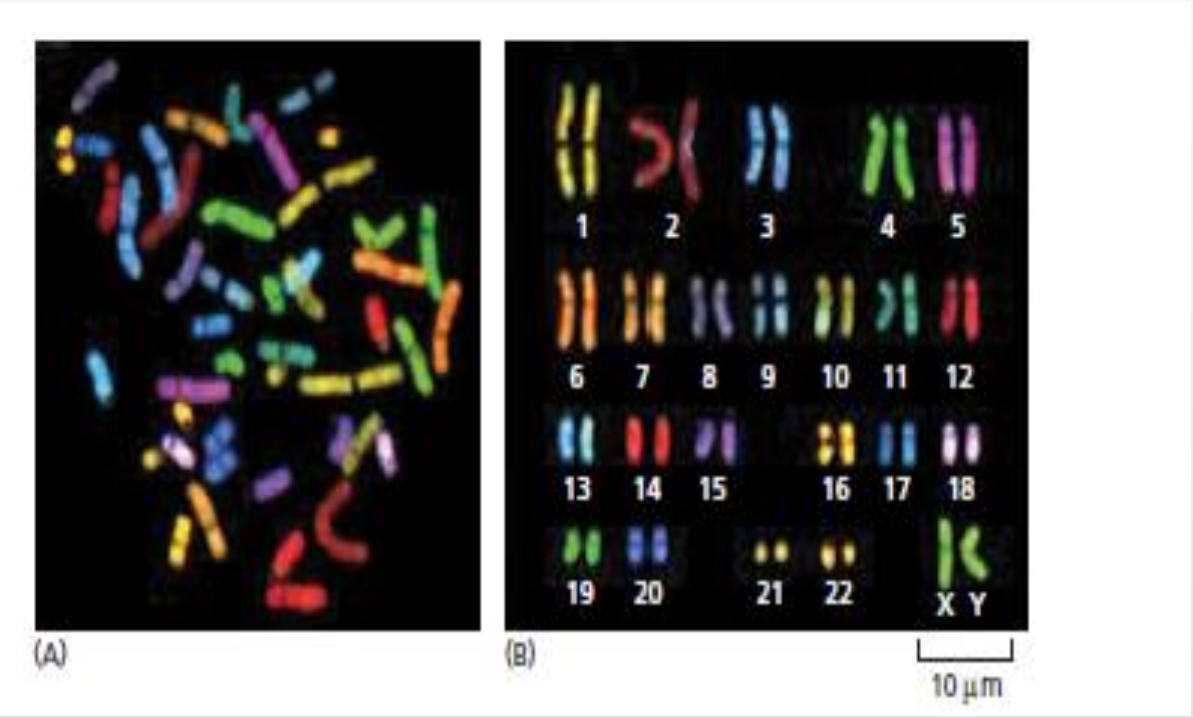


Figure 5–10 Each human chromosome can be "painted" a different color to allow its unambiguous identification. The chromosomes shown here were isolated from a cell undergoing nuclear division (mitosis) and are therefore in a highly compact (condensed) state. Chromosome painting is carried out by exposing the chromosomes to a collection of human DNA molecules that have been coupled to a combination of fluorescent dyes. For example, DNA molecules derived from Chromosome 1 are labeled with one specific dye combination, those from Chromosome 2 with another, and so on. Because the labeled DNA can form base pairs (hybridize) only to its chromosome of origin (discussed in Chapter 10), each chromosome is differently colored. For such experiments, the chromosomes are treated so that the individual strands of the double-helical DNA molecules partly separate to enable base-pairing with the labeled, single-stranded DNA, while keeping the chromosome structure relatively intact. (A) Micrograph shows the array of chromosomes as they originally spilled from the lysed cell. (B) The same chromosomes have been artificially lined up in order. In this so-called *karyotype*, the homologous chromosomes are numbered and arranged in pairs; the presence of a Y chromosome reveals that these chromosomes came from a male. (From E. Schröck et al., *Science* 273:494–497, 1996. With permission from the AAAS.)

Human karyotype

Gene & Genomes in Chromosome

- Gene → bagian segment DNA yang berisi instruksi untuk membuat protein atau RNA
- Total genetic information carried by chromosome in all cell or organism → Genomes

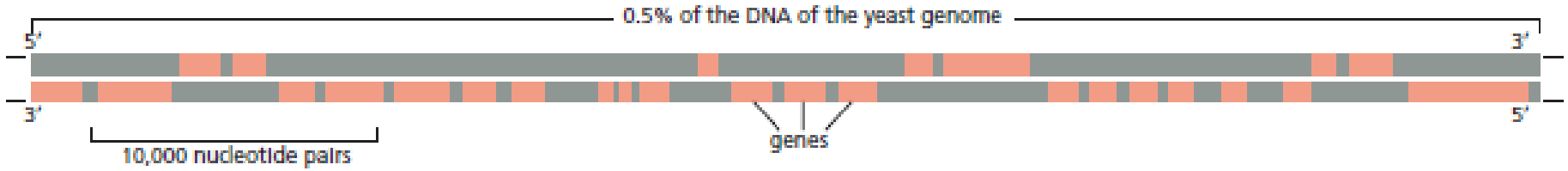


Figure 5–12 Genes are arranged along chromosomes. This figure shows a small region of the DNA double helix in one chromosome from the budding yeast *S. cerevisiae*. The *S. cerevisiae* genome contains about 12 million nucleotide pairs and 6600 genes—spread across 16 chromosomes. Note that, in each gene, only one of the two DNA strands actually encodes the information to make an RNA molecule, and this can be either strand, as indicated by the *light red* bars. However, a gene is generally denoted to contain both the "coding strand" and its complement, as in Figure 5–9. The high density of genes is characteristic of *S. cerevisiae*.

Genome

- Sequence genome ribuan organisme sudah berhasil diidentifikasi
- Jumlah gen dalam genome tiap organisme bervariasi
- > 500 gen untuk simple bacteria; 30.000 gen untuk manusia
- Gen pada bakteri lebih kompak (dense)
- Gen manusia mengandung deretan yang bukan gen → Junk DNA

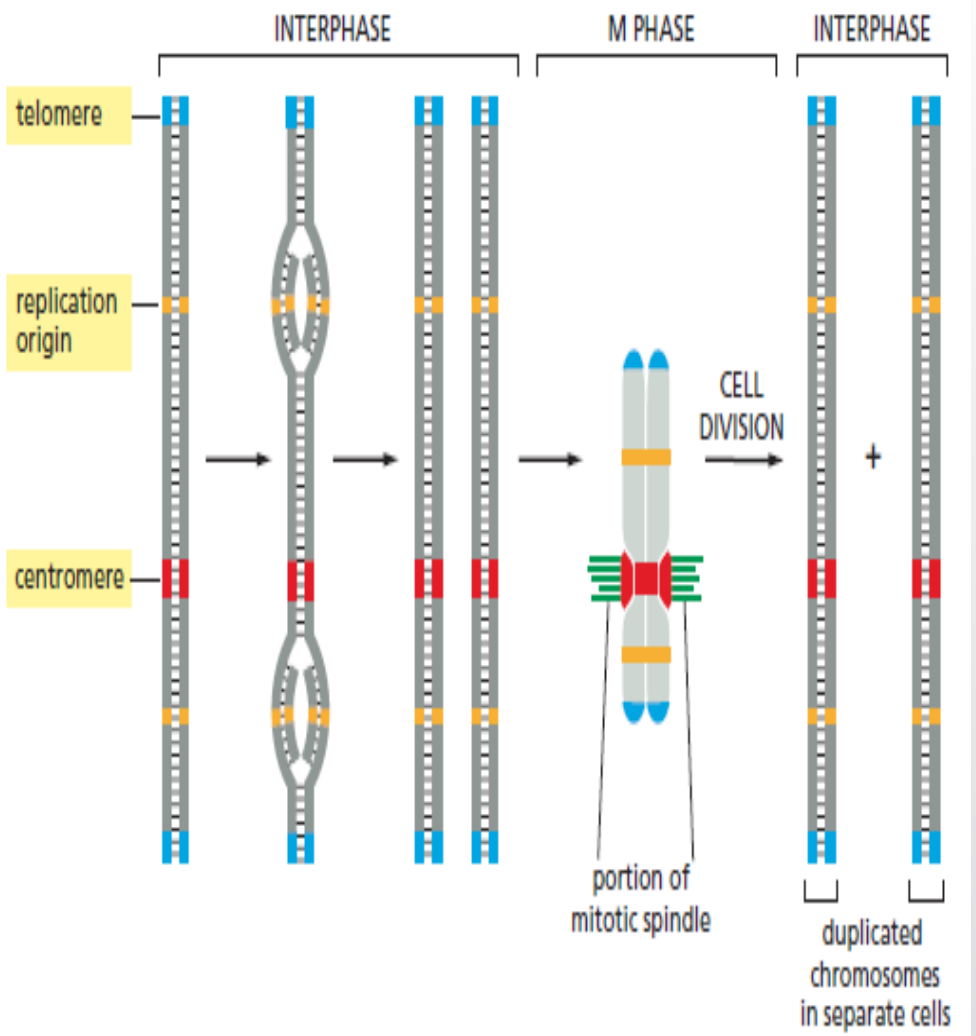
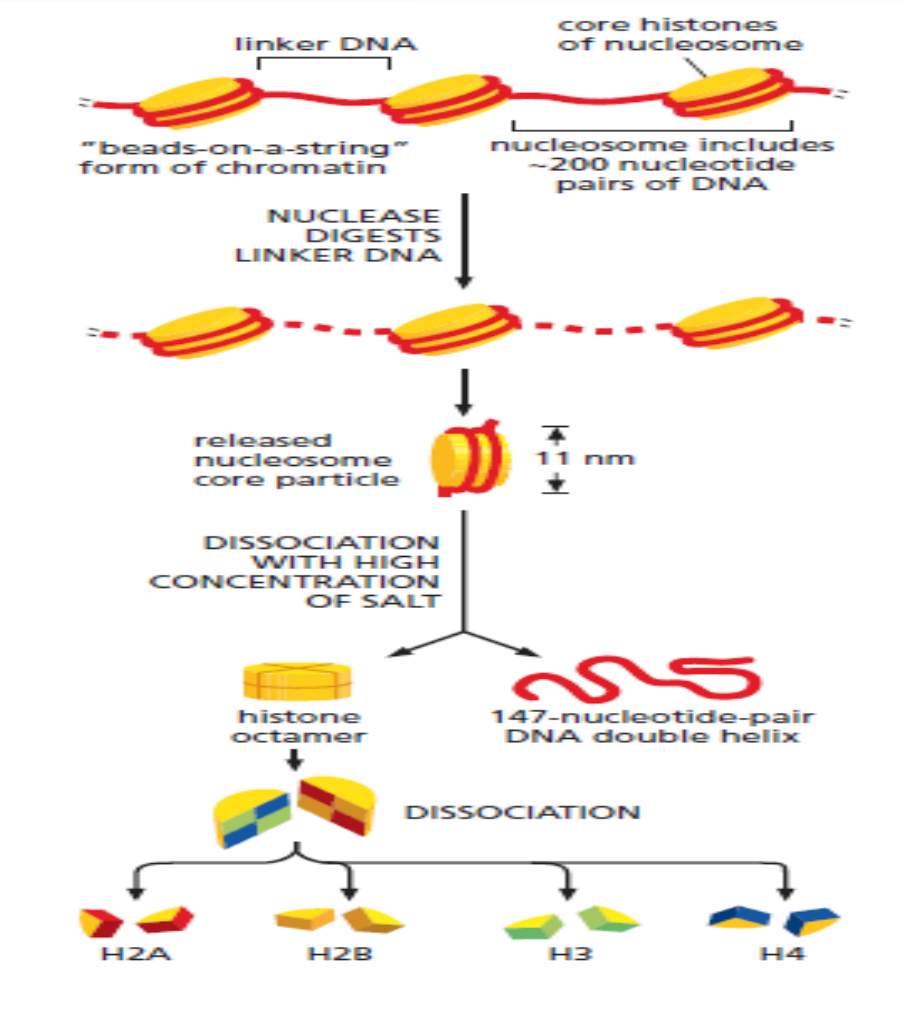


Figure 5–15 Three DNA sequence elements are needed to produce a eucaryotic chromosome that can be replicated and then segregated at mitosis. Each chromosome has multiple origins of replication, one centromere, and two telomeres. The sequence of events that a typical chromosome follows during the cell cycle is shown schematically. The DNA replicates in interphase, beginning at the origins of replication and proceeding bidirectionally from the origins across the chromosome. In M phase, the centromere attaches the duplicated chromosomes to the mitotic spindle so that one copy is distributed to each daughter cell when the cell divides. Prior to cell division, the centromere also helps to hold the compact, duplicated chromosomes together until they are ready to be pulled apart. Telomeres, which form special caps at the tips of each chromosome, aid in the replication of chromosome ends.

DNA dan Histone



- Protein pengikat DNA pada chromosome eukariot → Histone dan non histone
- Jumlah histone lebih banyak → 60 jt tiap sel

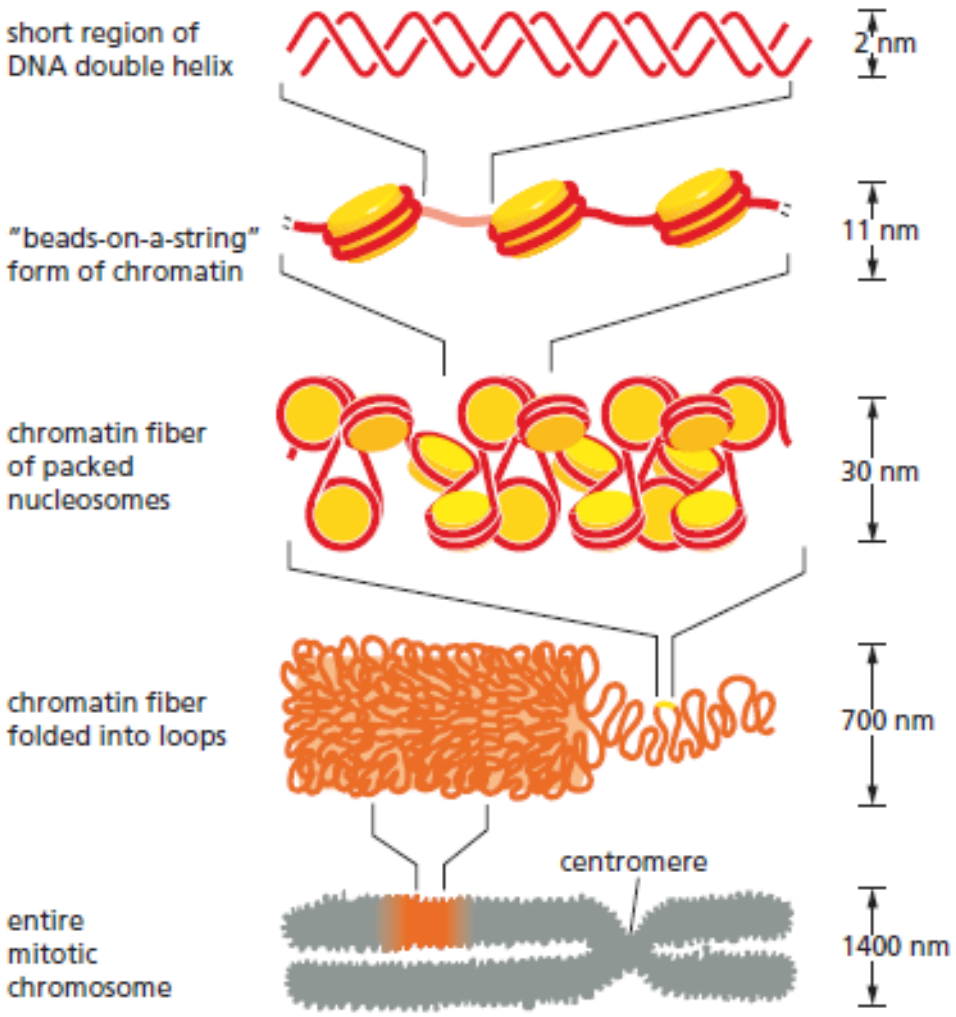
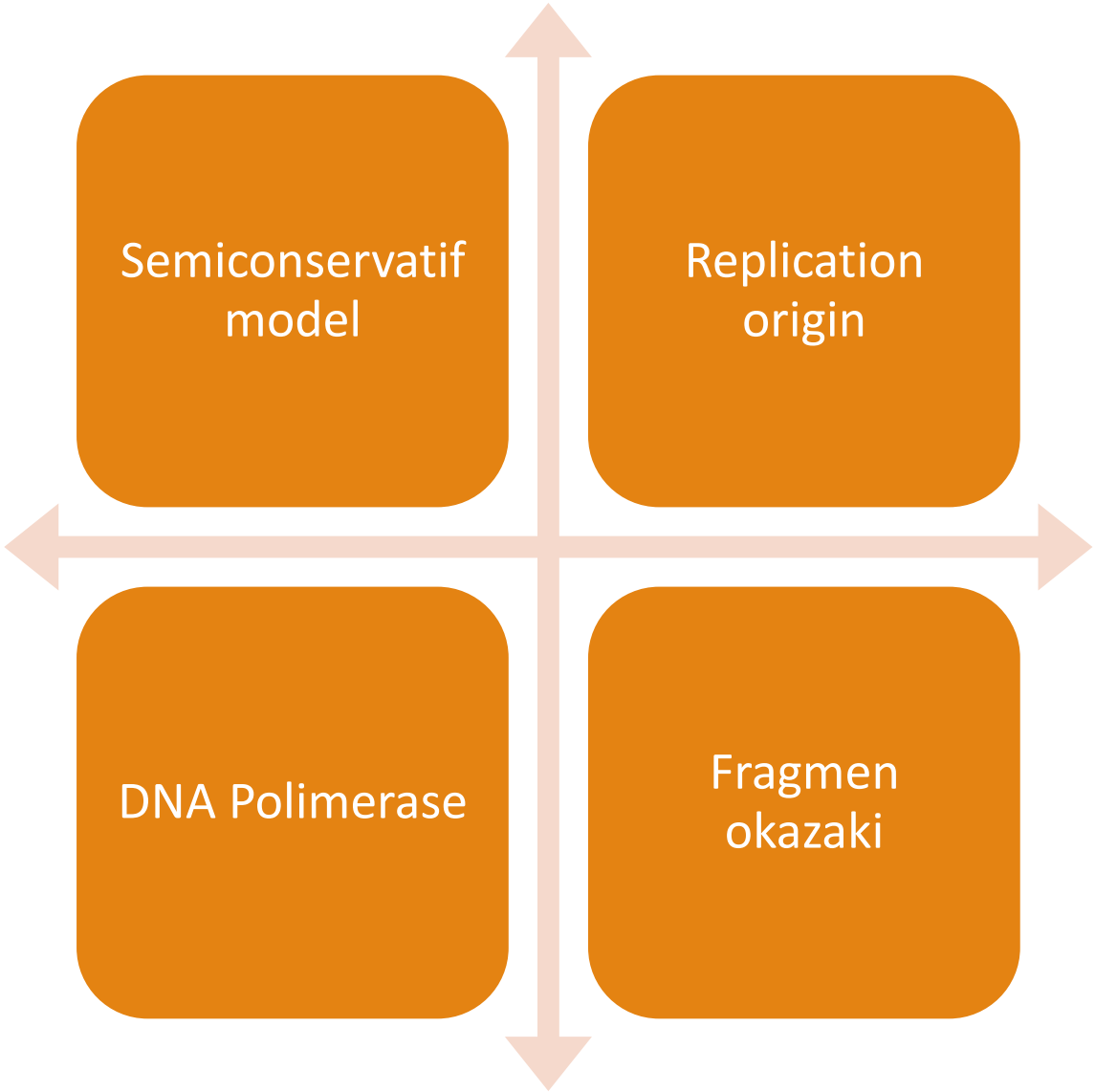


Figure 5–24 DNA packing occurs on several levels in chromosomes. This schematic drawing shows some of the levels thought to give rise to the highly condensed mitotic chromosome. The actual structures are still uncertain.

Dna : replikasi, repair & recombination

BIOLOGI SEL

S1 ILMU DAN TEKNOLOGI PANGAN


Semiconservatif model
Replication origin
DNA Polimerase
Fragmen okazaki

Replikasi DNA

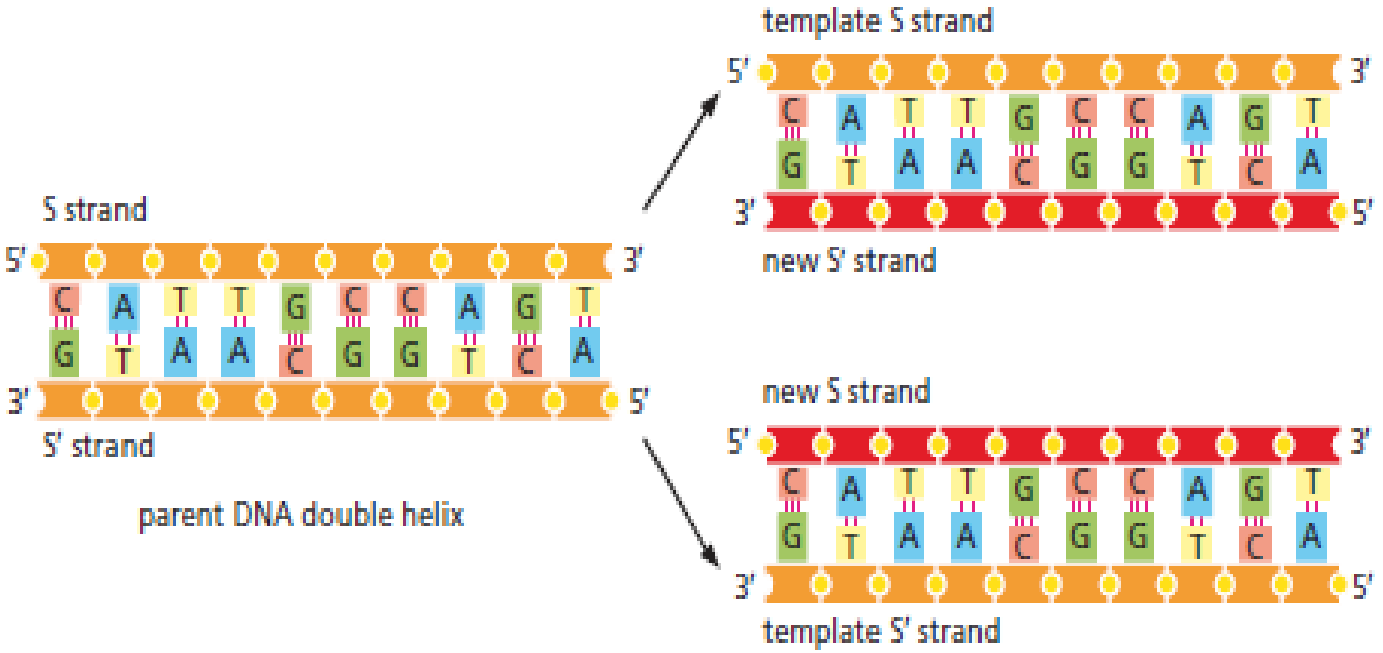


Figure 6–2 DNA acts as a template for its own duplication. Because the nucleotide A will successfully pair only with T, and G with C, each strand of a DNA double helix—labeled here as the S strand and its complementary S′ strand—can serve as a template to specify the sequence of nucleotides in its complementary strand. In this way, both strands of a DNA double helix can be copied precisely.

Replication Origin

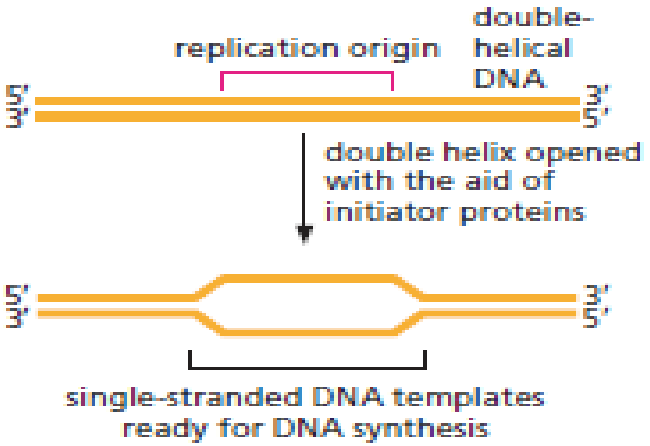


Figure 6–4 A DNA double helix is opened at replication origins. DNA sequences at replication origins are recognized by initiator proteins (not shown), which locally pry apart the two strands of the double helix. The exposed single strands can then serve as templates for copying the DNA.

- ✓ Sintesis DNA dimulai oleh "initiator protein" yang terikat pada specific DNA sequence yang disebut Replication Origin
- ✓ Mengandung lebih banyak pasangan basa A-T
- ✓ Replication origin pada bakteri dan yeast → 100 nukleotida, single replication origin
- ✓ Human genome mempunyai sekitar 10.000 replication origin→ rata-rata 220 origin per chromosome

Replication Fork

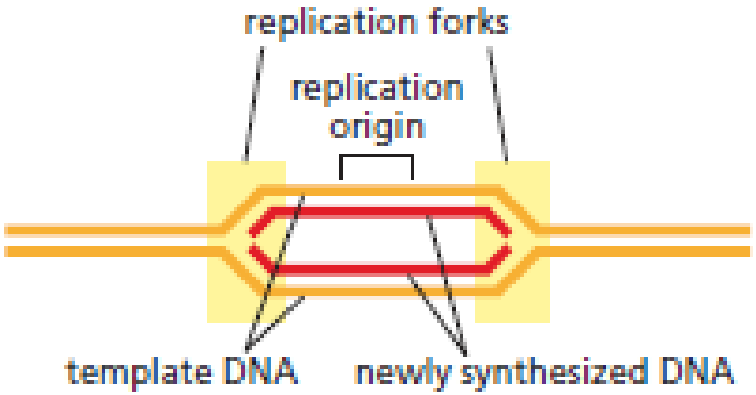


Figure 6–8 DNA synthesis occurs at Y-shaped junctions called replication forks. Two replication forks are formed at each replication origin.

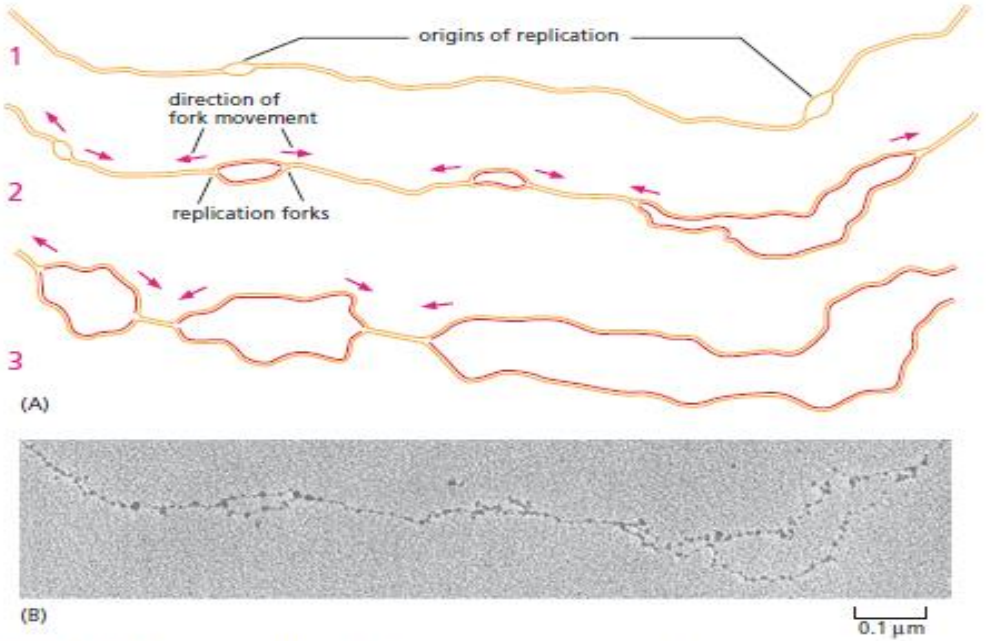


Figure 6–9 The two replication forks move away in opposite directions at each replication origin. (A) These drawings represent the same portion of a DNA molecule as it might appear at different times during replication. The *orange* lines represent the two parental DNA strands; the *red* lines represent the newly synthesized DNA strands. (B) An electron micrograph showing DNA replicating in an early fly embryo. The particles visible along the DNA are nucleosomes, structures made of DNA and the protein complexes around which the DNA is wrapped (discussed in Chapter 5). The chromosome in this micrograph is the one that was redrawn in sketch (2) above. (Electron micrograph courtesy of Victoria Foe.)

DNA Polimerase

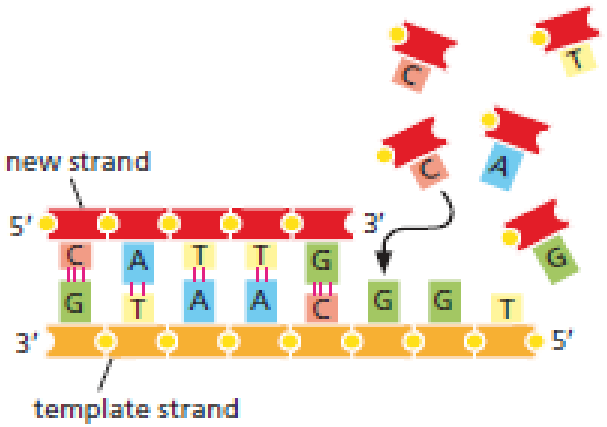


Figure 6–10 A new DNA strand is synthesized in the 5′–to–3′ direction. At each step, the appropriate incoming nucleotide is selected by forming base pairs with the next nucleotide in the template strand: A with T, T with A, C with G, and G with C. Each is added to the 3′ end of the growing new strand, as indicated.

- enzim yang bekerja menggabungkan basa nukleotida pada strand DNA baru dengan arah 5’ ke 3’
- enzim ini sangat akurat → 1 kesalahan setiap 10 jt nukleotida
- kontrol yang dilakukan adalah memonitor basa nukleotida yang akan menempel apakah sesuai dengan DNA template
- Dna polymerase dapat memperbaiki kesalahan dengan mekanisme PROOFREADING

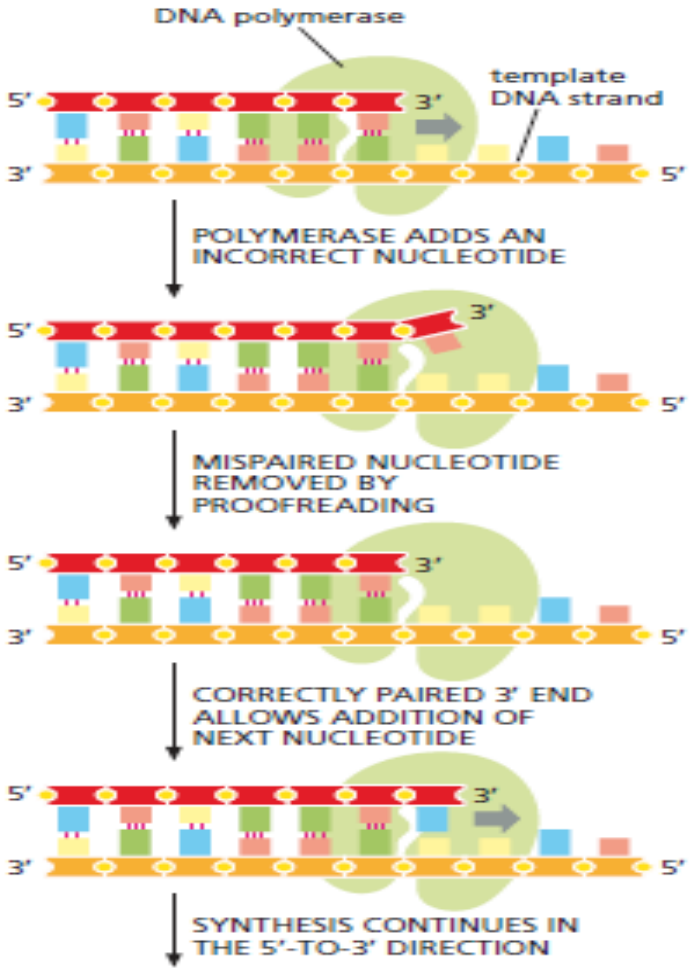


Figure 6–14 During DNA synthesis, DNA polymerase proofreads its own work. If an incorrect nucleotide is added to a growing strand, the DNA polymerase cleaves it from the strand and replaces it with the correct nucleotide before continuing.

Okazaki Fragmen

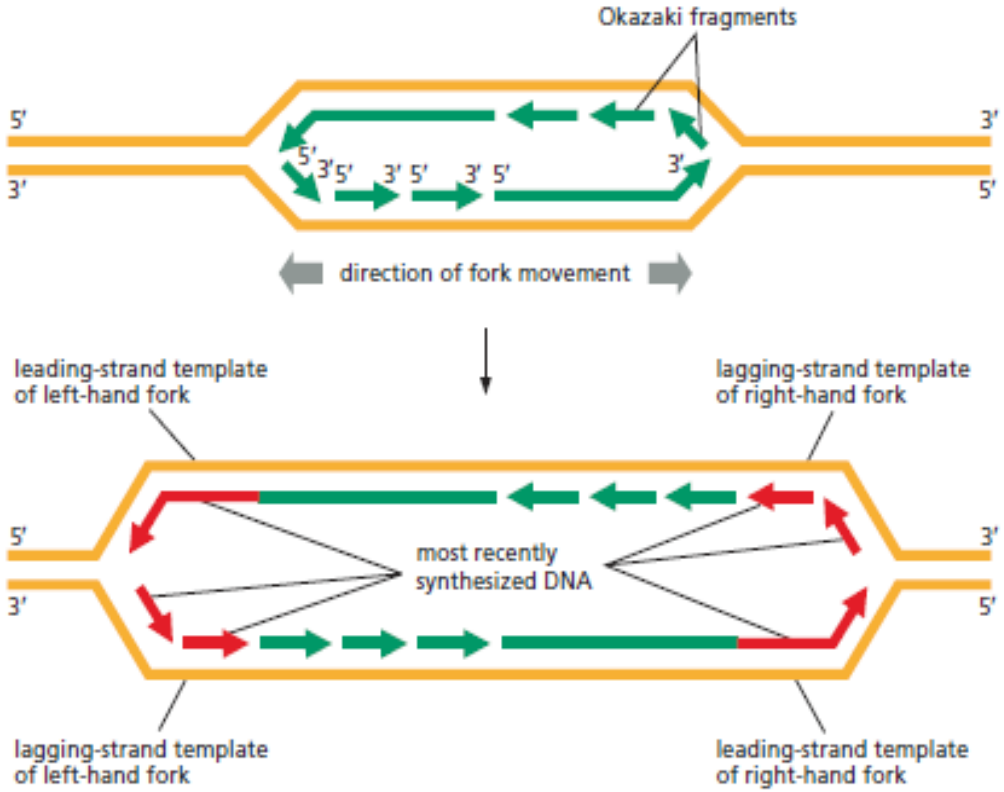


Figure 6–13 At each replication fork, the lagging DNA strand is synthesized in pieces. Because both of the new strands at a replication fork are synthesized in the 5′-to-3′ direction, the lagging strand of DNA must be made initially as a series of short DNA strands, which are later joined together. The upper diagram shows two replication forks moving in opposite directions; the lower diagram shows the same forks a short time later. To replicate the lagging strand, DNA polymerase uses a backstitching mechanism: it synthesizes short pieces of DNA (called Okazaki fragments) in the 5′-to-3′ direction and then moves back along the template strand (toward the fork) before synthesizing the next fragment.

RNA Primer (Primase)

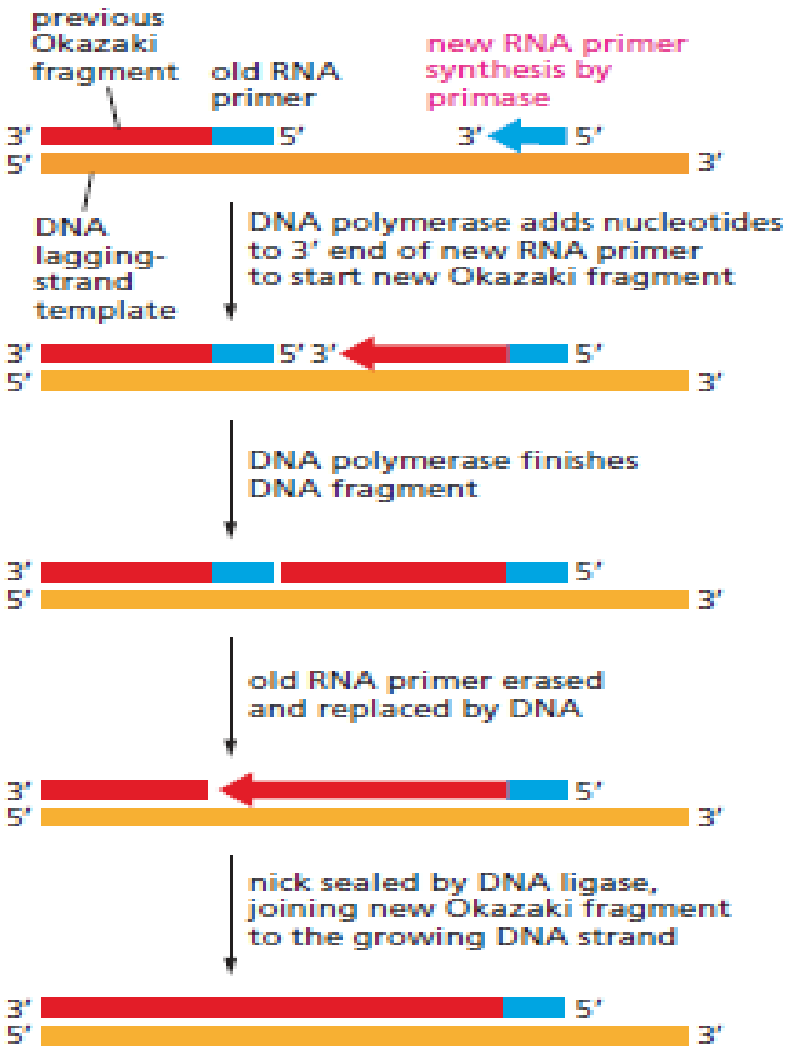


Figure 6–17 Multiple enzymes are required to synthesize Okazaki fragments on the lagging DNA strand. In eukaryotes, RNA primers are made at intervals of about 200 nucleotides on the lagging strand, and each RNA primer is approximately 10 nucleotides long. Primers are removed by nucleases that recognize an RNA strand in an RNA/DNA helix and degrade it; this leaves gaps that are filled in by a repair DNA polymerase that can proofread as it fills in the gaps. The completed fragments are finally joined together by an enzyme called DNA ligase, which catalyzes the formation of a phosphodiester bond between the 3′-OH end of one fragment and the 5′-phosphate end of the next, thus linking up the sugar–phosphate backbones. This nick-sealing reaction requires an input of energy in the form of ATP (not shown; see Figure 6–18).

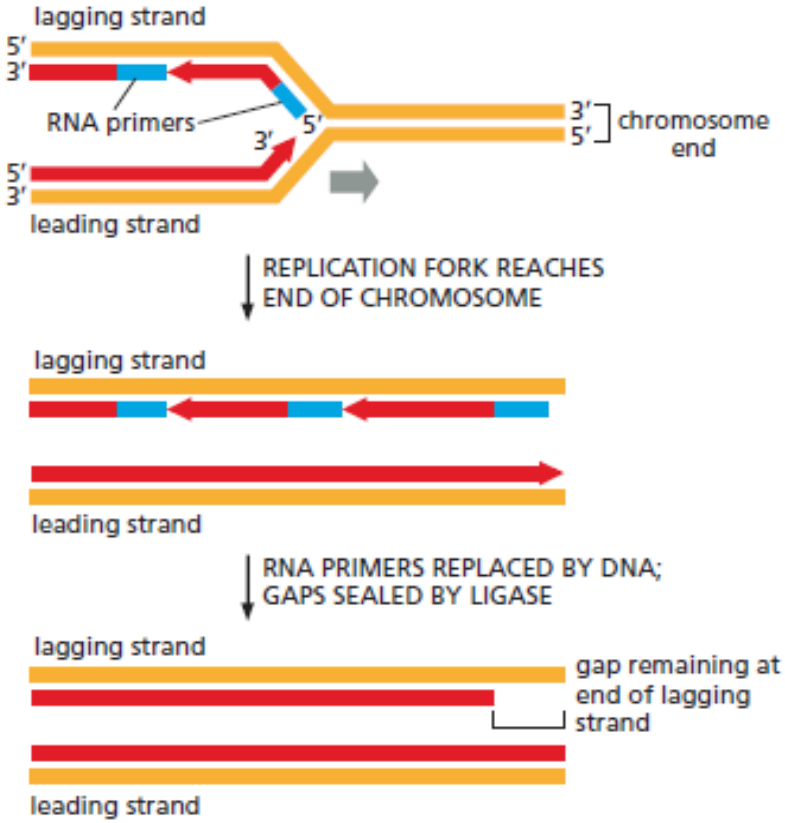


Figure 6–21 Without a special mechanism to replicate the ends of linear chromosomes, DNA would be lost during each round of cell division. DNA synthesis begins at origins of replication and continues until the replication machinery reaches the ends of the chromosome. The leading strand is reproduced in its entirety. But the ends of the lagging strand can't be completed, because once the final RNA primer has been removed there is no way to replace it with DNA. These gaps at the ends of the lagging strand must be filled in by a special mechanism to keep the chromosome ends from shrinking with each cell division.

DNA Repair

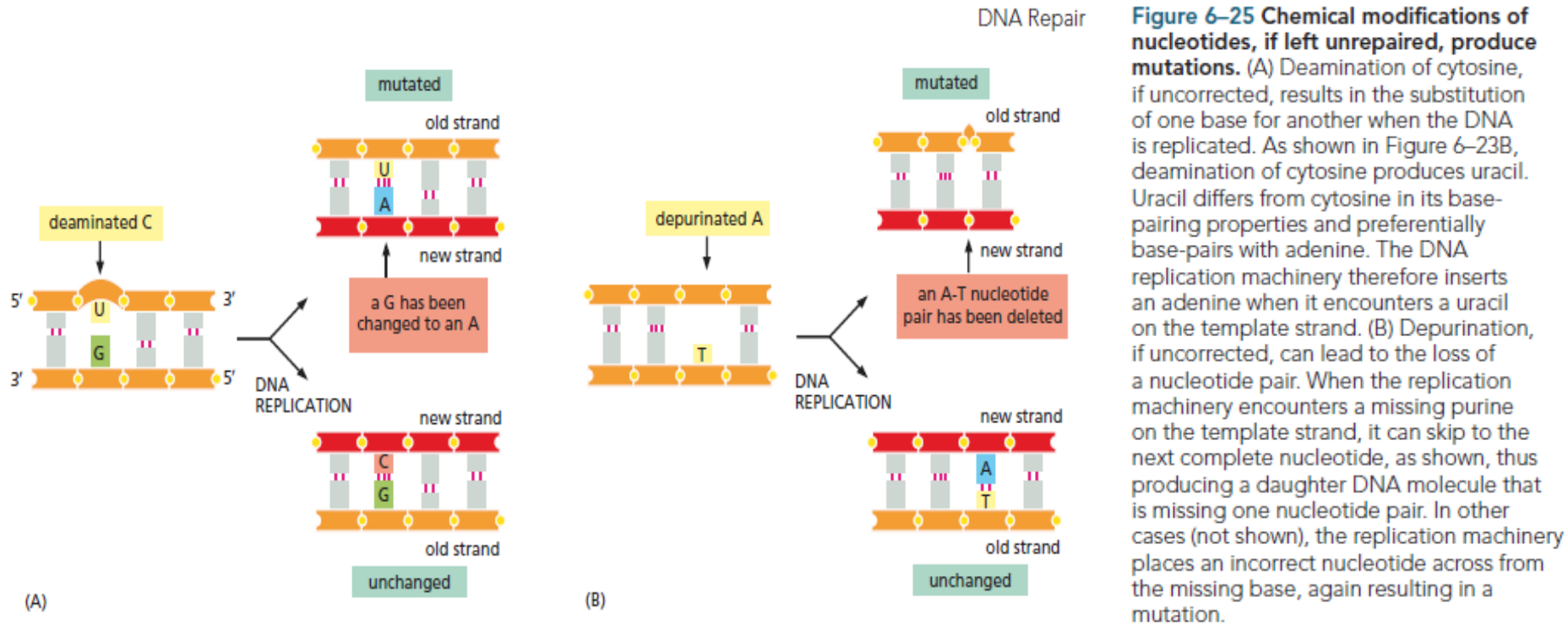


Figure 6–25 Chemical modifications of nucleotides, if left unrepaired, produce mutations. (A) Deamination of cytosine, if uncorrected, results in the substitution of one base for another when the DNA is replicated. As shown in Figure 6–23B, deamination of cytosine produces uracil. Uracil differs from cytosine in its base-pairing properties and preferentially base-pairs with adenine. The DNA replication machinery therefore inserts an adenine when it encounters a uracil on the template strand. (B) Depurination, if uncorrected, can lead to the loss of a nucleotide pair. When the replication machinery encounters a missing purine on the template strand, it can skip to the next complete nucleotide, as shown, thus producing a daughter DNA molecule that is missing one nucleotide pair. In other cases (not shown), the replication machinery places an incorrect nucleotide across from the missing base, again resulting in a mutation.

Mutasi Gen

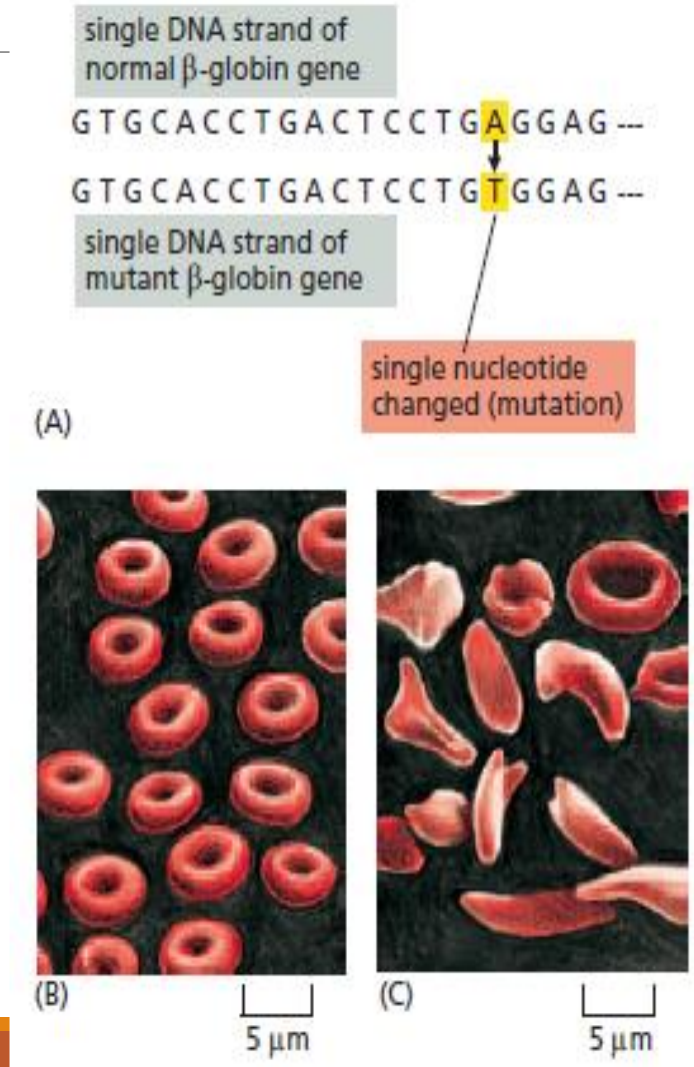


Figure 6–31 A single nucleotide change causes the disease sickle-cell anemia. (A) β-globin is one of the two types of protein subunits that form hemoglobin (see Figure 4–24). A single nucleotide change (mutation) in the β-globin gene produces a β-globin subunit that differs from normal β-globin only by a change from glutamic acid to valine at the sixth amino acid position. (Only a small portion of the gene is shown here; the β-globin subunit contains a total of 146 amino acids.) Humans carry two copies of each gene (one inherited from each parent); a sickle-cell mutation in one of the two β-globin genes generally causes no harm to the individual, as it is compensated for by the normal gene. However, an individual who inherits two copies of the mutant β-globin gene will have sickle-cell anemia. Normal red blood cells are shown in (B), and those from an individual suffering from sickle-cell anemia in (C). Although sickle-cell anemia can be a life-threatening disease, the mutation responsible can also be beneficial. People with the disease, or those who carry one normal gene and one sickle-cell gene, are more resistant to malaria than unaffected individuals, because the parasite that causes malaria grows poorly in red blood cells that contain the sickle-cell form of hemoglobin.

Sintesis Protein dan ekspresi gen

Kuliah Biologi Sel

S1 Ilmu dan Teknologi Pangan

Fakultas Pertanian, Universitas Sebelas Maret

From DNA to Protein

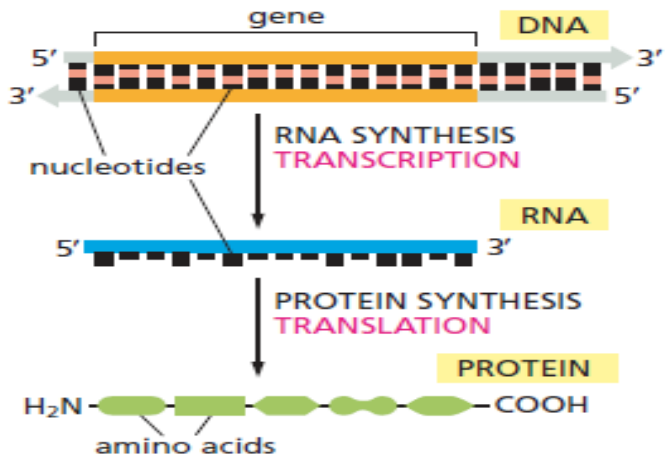
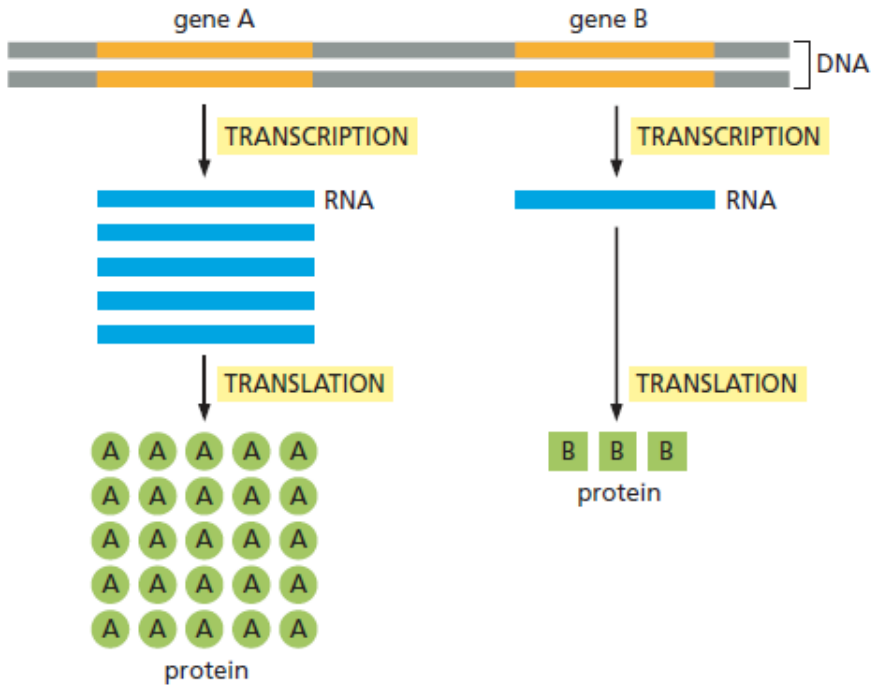


Figure 7–1 Genetic information directs the synthesis of proteins. The flow of genetic information from DNA to RNA (transcription) and from RNA to protein (translation) occurs in all living cells. It was Francis Crick who dubbed this flow of information "the central dogma." The segments of DNA that are transcribed into RNA are called genes.

- Sejak struktur DNA ditemukan → penelitian tentang hereditas menjadi semakin jelas
- DNA → informasi genetic yang diturunkan melalui REPLIKASI
- DNA merupakan "manager" untuk sintesa protein
- Jenis protein ditentukan oleh deretan asam amino yang diterjemahkan dari deretan basa nitrogen

From DNA to RNA

- Transkripsi & Translasi → sel membaca atau express instruksi dari gen
- Beberapa RNA identik berasal dari gen yang sama
- Kecepatan transkripsi hingga translasi disesuaikan dengan kebutuhan protein yang disintesis → Ekspresi gen



Perbedaan DNA dan RNA

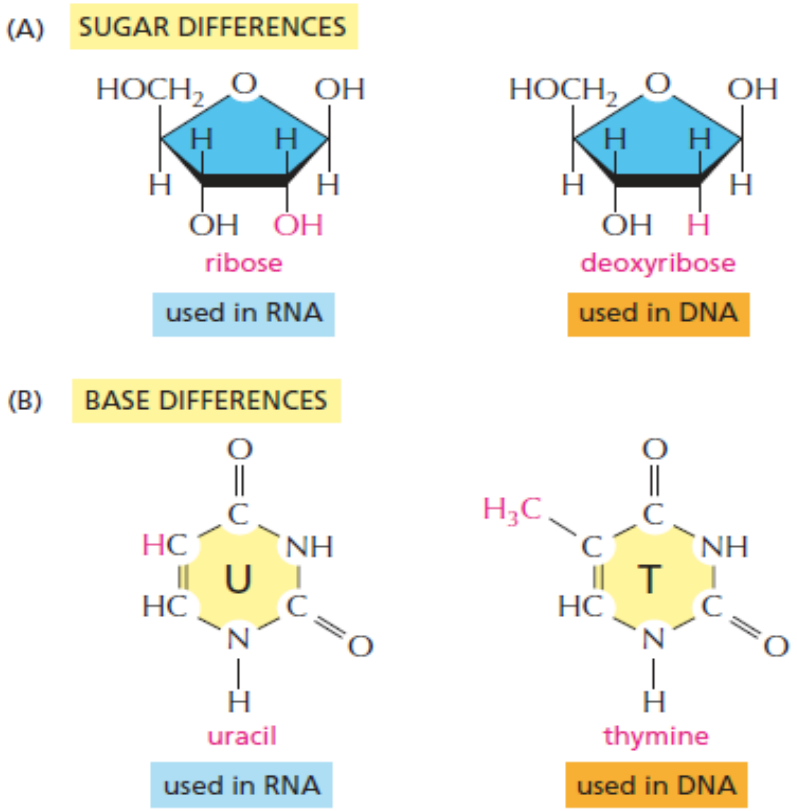


Figure 7–3 The chemical structure of RNA differs slightly from that of DNA. (A) RNA contains the sugar ribose, which differs from deoxyribose, the sugar used in DNA, by the presence of an additional –OH group. (B) RNA contains the base uracil, which differs from thymine, the equivalent base in DNA, by the absence of a $–CH_3$ group. (C) A short length of RNA. The chemical linkage between nucleotides in RNA—a phosphodiester bond—is the same as that in DNA.

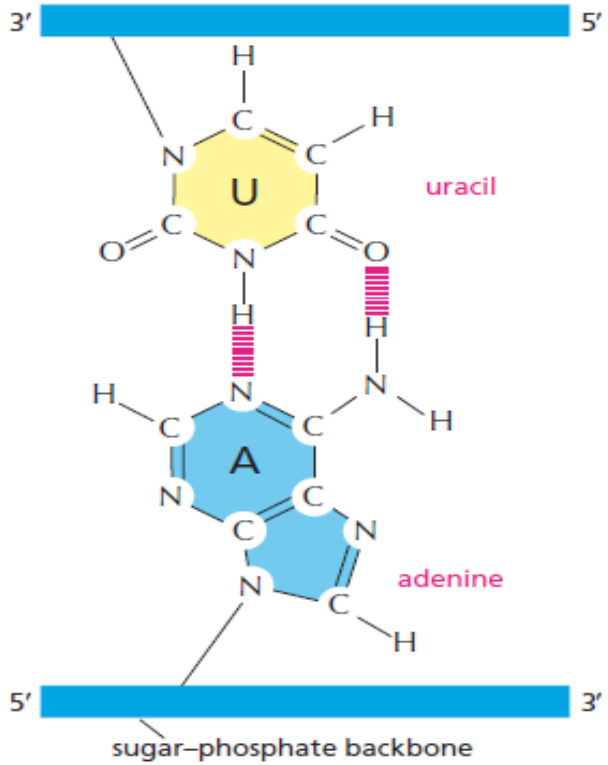


Figure 7–4 Uracil forms a base pair with adenine. The hydrogen bonds that hold the base pair together are shown in *red*. Uracil has the same base-pairing properties as thymine. Thus U-A base pairs in RNA closely resemble T-A base pairs in DNA (see Figure 5–6A).

Perbedaan DNA dan RNA

DNA

- Gula deoksiribosa dengan gugus ‘H”
- Basa nitrogen terdiri dari Adenin, Timin, Guanin, Sitosin
- Double strands → satu struktur saja → double helix
- Memiliki fungsi penyimpan informasi genetik

RNA

- Gula ribose dengan gugus “OH”
- Basa nitrogen terdiri dari Adenin, Urasil, Guanin, Sitosin
- Single strand → strukturnya bias bermacam-macam seperti polipeptida (protein)
- Berfungsi structural, regulatory dan berperan sebagai katalis

Struktur RNA

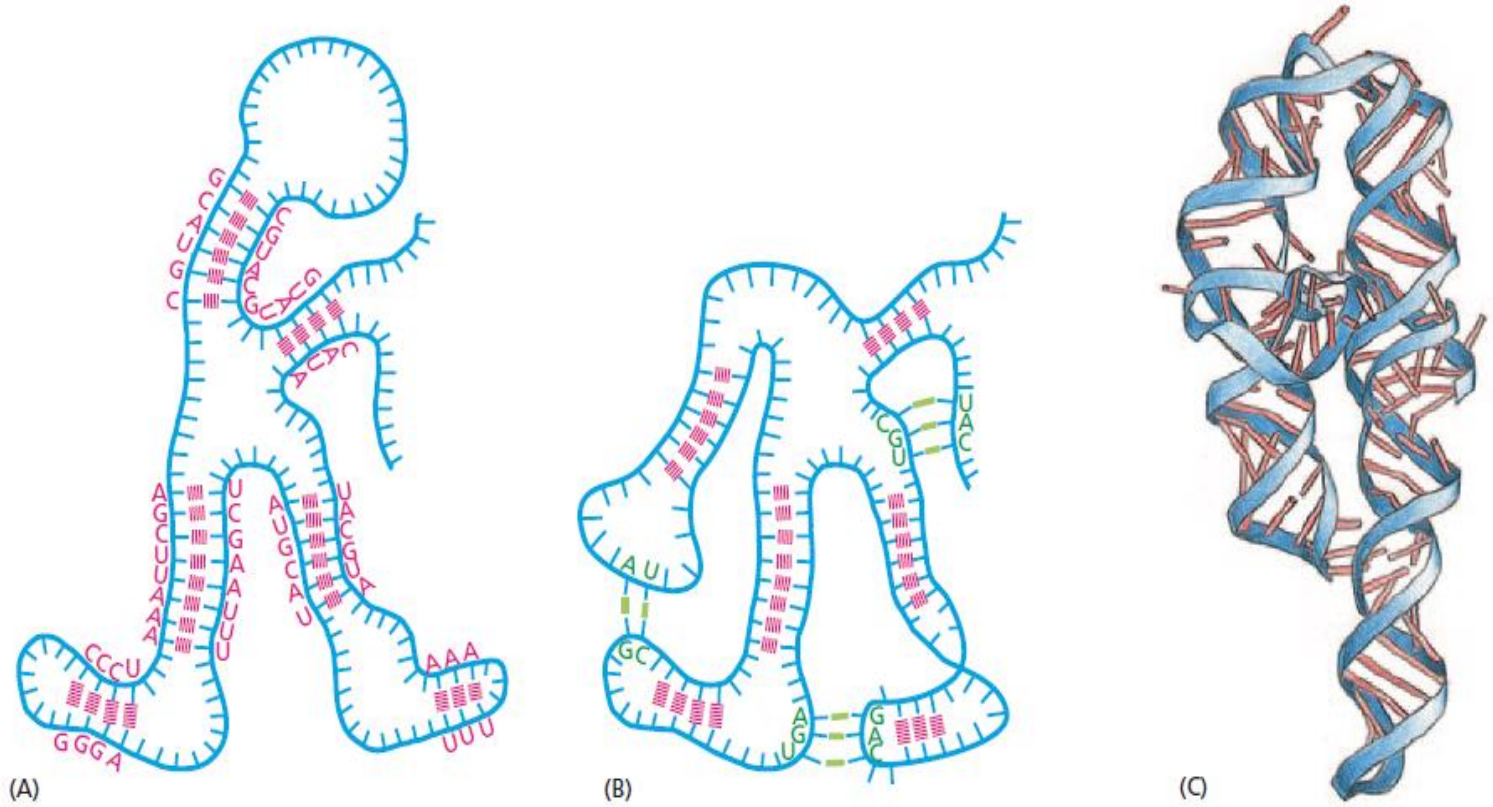
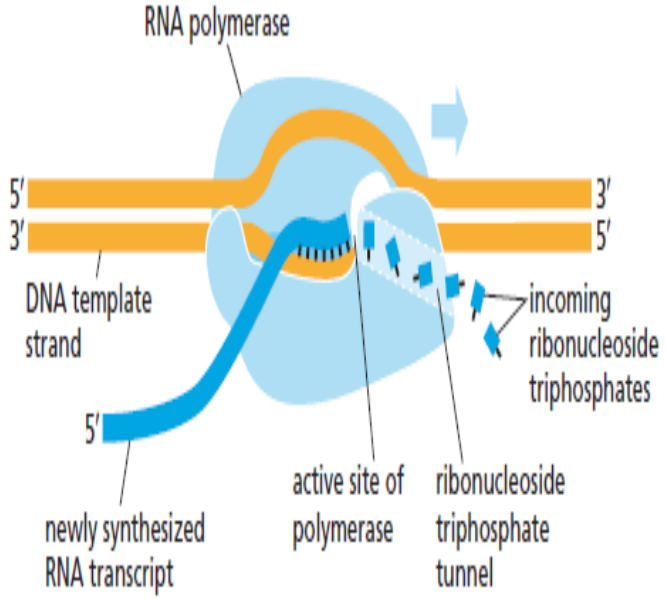


Figure 7–5 RNA molecules can form intramolecular base pairs and fold into specific structures. RNA is single-stranded, but it often contains short stretches of nucleotides that can base-pair with complementary sequences found elsewhere on the same molecule. These interactions—along with some "nonconventional base-pair interactions (e.g., A-G)—allow an RNA molecule to fold into a three-dimensional structure that is determined by its sequence of nucleotides. (A) A diagram of a hypothetical, folded RNA structure showing only conventional (G-C and A-U) base-pair interactions. (B) Incorporating nonconventional base-pair interactions (*green*) changes the structure of the hypothetical RNA shown in (A). (C) Structure of an actual RNA molecule that is involved in RNA splicing. This RNA contains a considerable amount of double-helical structure. The sugar–phosphate backbone is *blue* and the bases are *red*; the conventional base-pair interactions are indicated by red "rungs" that are continuous, and nonconventional base pairs are indicated by broken red rungs. For an additional view of RNA structure, see Movie 7.1.

TRANSKRIPSI

- Transkripsi mirip replikasi DNA
- Salah satu strand DNA menjadi template
- Transkripsi tidak memerlukan ikatan hydrogen dengan basa nitrogen DNA → RNA hanya single strand
- Penggabungan nukleotida oleh RNA polimerase



TRANSKRIPSI

- RNA polymerase bekerja spesifik dengan substrat ribonukleosida
- Tidak memerlukan primer, kesalahan RNA tidak memiliki dampak besar bagi sel
- Kesalahan traanskripsi → 1 kesalahan dalam 10^4 nukleotida
- Dalam satu gene, transkripsi bida dilakukan berulang dengan kecepatan yang berbeda tiap gen

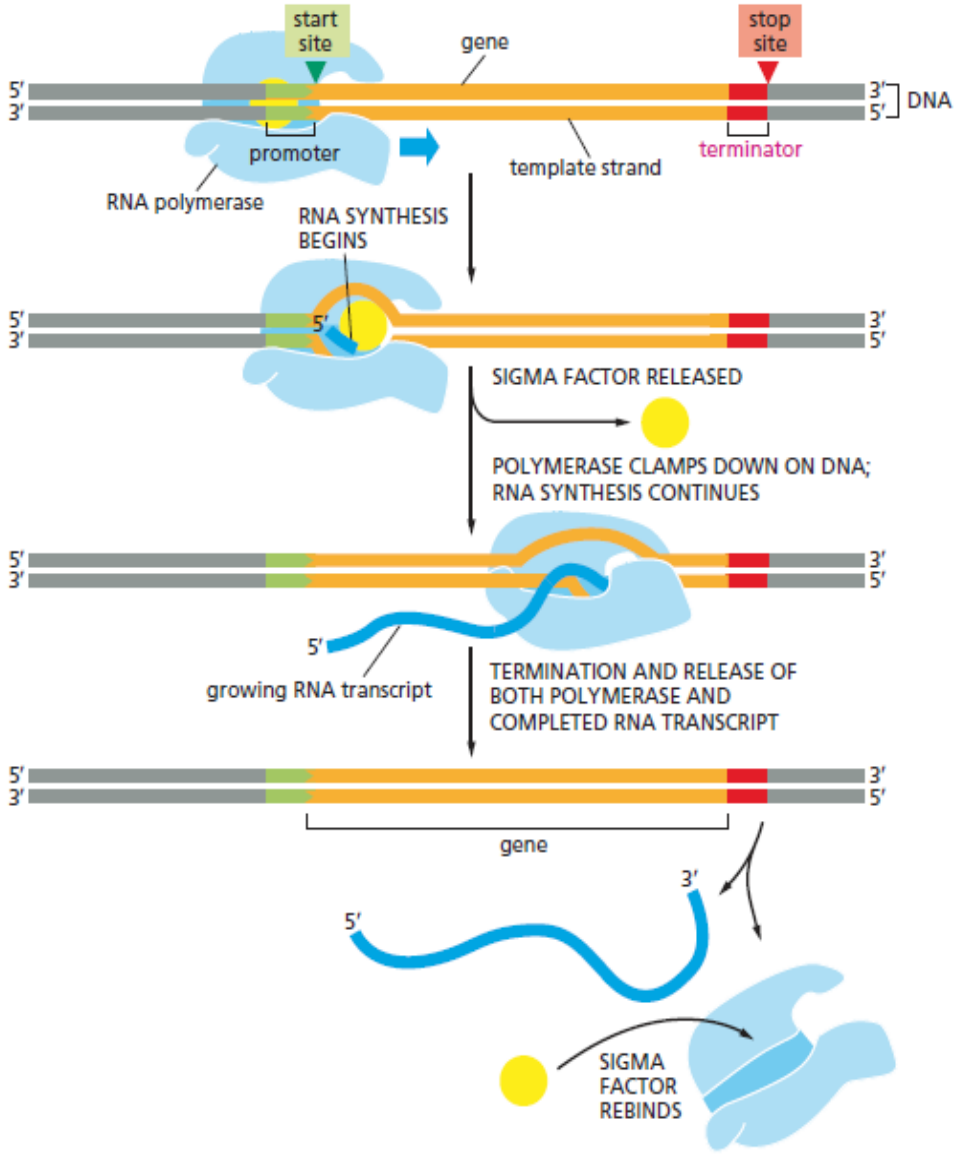


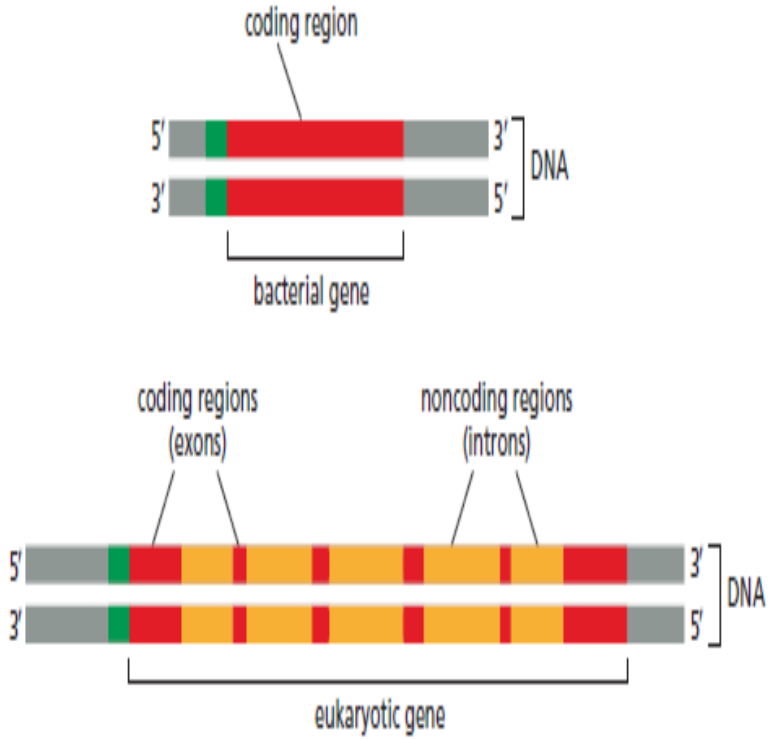
Figure 7–9 Signals in the nucleotide sequence of a gene tell bacterial RNA polymerase where to start and stop transcription. Bacterial RNA polymerase (*light blue*) contains a subunit called sigma factor (*yellow*) that recognizes the promoter of a gene (*green*). Once transcription has begun, sigma factor is released, and the polymerase moves forward and continues synthesizing the RNA. Chain elongation continues until the polymerase encounters a sequence in the gene called the terminator (*red*). There the enzyme halts and releases both the DNA template and the newly made RNA transcript. The polymerase then reassociates with a free sigma factor and searches for another promoter to begin the process again.

TABLE 7–1 TYPES OF RNA PRODUCED IN CELLS	
Type of RNA	**Function**
messenger RNAs (mRNAs)	code for proteins
ribosomal RNAs (rRNAs)	form the core of the ribosome's structure and catalyze protein synthesis
microRNAs (miRNAs)	regulate gene expression
transfer RNAs (tRNAs)	serve as adaptors between mRNA and amino acids during protein synthesis
other noncoding RNAs	used in RNA splicing, gene regulation, telomere maintenance, and many other processes

TABLE 7–2 THE THREE RNA POLYMERASES IN EUKARYOTIC CELLS

Type of Polymerase	Genes Transcribed
RNA polymerase I	most rRNA genes
RNA polymerase II	all protein-coding genes, miRNA genes, plus genes for other noncoding RNAs (e.g., those in spliceosomes)
RNA polymerase III	tRNA genes 5S rRNA gene genes for many other small RNAs

Transkripsi Prokariot Vs Eukariot



- Prokariot melibatkan 1 RNA Polimerase, Eukariot 3 jenis RNA polymerase
- Gene Eukariot terletak berjauhan sehingga pada RNA nya terdapat daerah intron (noncode sequence) dan exon (code sequence)
- Pada Pre-mRNA intron dihapus dengan mekanisme RNA splicing

RNA Splicing

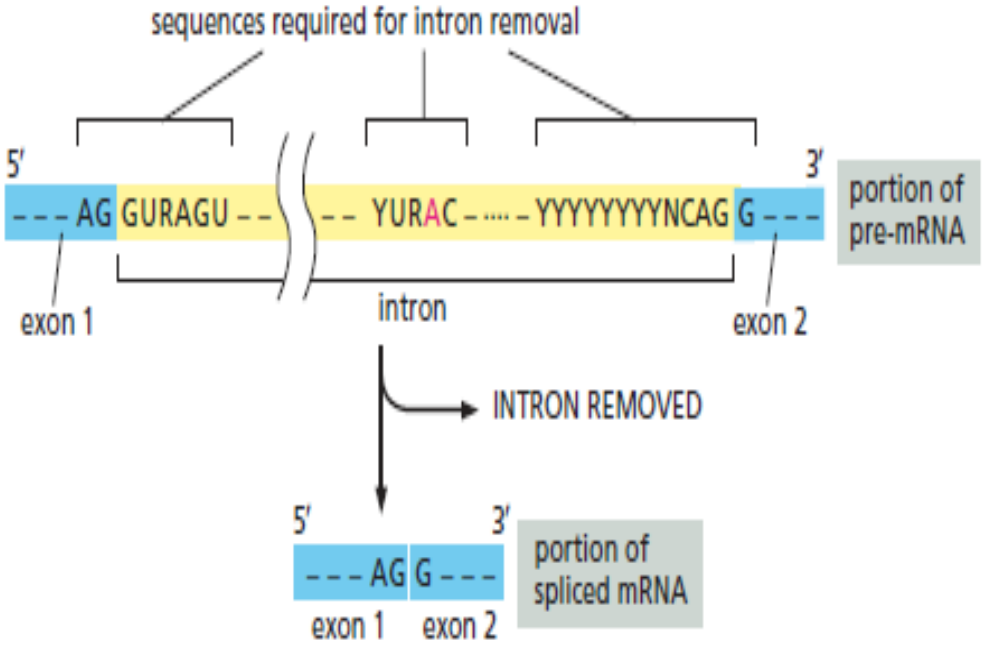
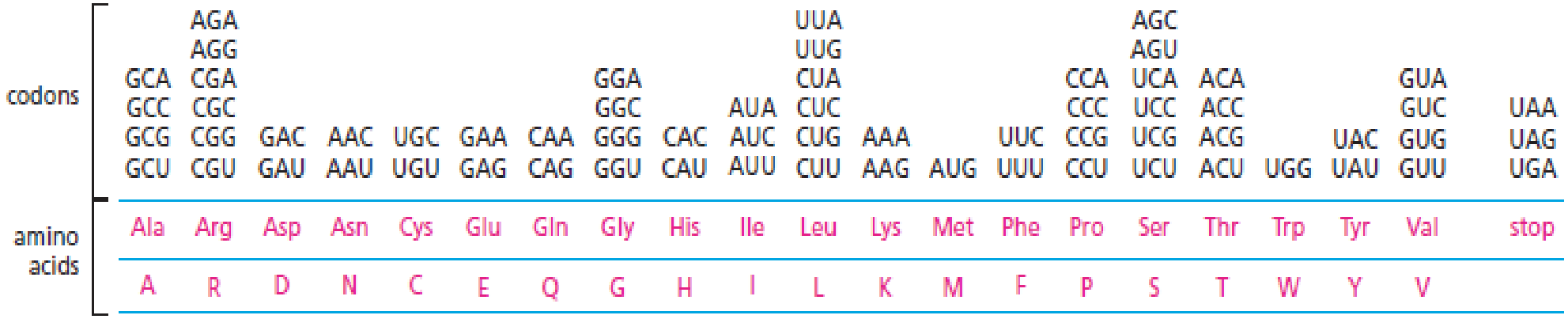


Figure 7–19 Special nucleotide sequences in a pre-mRNA transcript signal the beginning and the end of an intron. Only the nucleotide sequences shown are required to remove an intron; the other positions in an intron can be occupied by any nucleotide. The special sequences are recognized primarily by small nuclear ribonucleoproteins (snRNPs), which direct the cleavage of the RNA at the intron–exon borders and catalyze the covalent linkage of the exon sequences. Here, in addition to the standard symbols for nucleotides (A, C, G, U), R stands for either A or G; Y stands for either C or U; N stands for any nucleotide. The A shown in *red* forms the branch point of the lariat produced in the splicing reaction shown in Figure 7–20. The distances along the RNA between the three splicing sequences are highly variable; however, the distance between the branch point and the 5′ splice junction is typically much longer than that between the 3′ splice junction and the branch point (see Figure 7–20). The splicing sequences shown are from humans; similar sequences direct RNA splicing in other eukaryotes.

Translasi



codons	GCA GCC GCG GCU	AGA AGG CGA CGC CGG CGU	GAC GAU	AAC AAU	UGC UGU	GAA GAG	CAA CAG	GGA GGC GGG GGU	CAC CAU	AUA AUC AUU	UUA UUG CUA CUC CUG CUU	AAA AAG	AUG	UUC UUU	CCA CCC CCG CCU	AGC AGU UCA UCC UCG UCU	ACA ACC ACG ACU	UGG	UAC UAU	GUA GUC GUG GUU	UAA UAG UGA
amino acids	Ala	Arg	Asp	Asn	Cys	Glu	Gln	Gly	His	Ile	Leu	Lys	Met	Phe	Pro	Ser	Thr	Trp	Tyr	Val	stop
	A	R	D	N	C	E	Q	G	H	I	L	K	M	F	P	S	T	W	Y	V	

Figure 7–25 The nucleotide sequence of an mRNA is translated into the amino acid sequence of a protein via the genetic code. All the three-nucleotide codons in mRNAs that specify a given amino acid are listed above that amino acid, which is given in both its three-letter and one-letter abbreviations (see Panel 2–5, pp. 74–75, for the full name of each amino acid and its structure). Like RNA molecules, codons are always written with the 5′-terminal nucleotide to the left. Note that most amino acids are represented by more than one codon, and there are some regularities in the set of codons that specify each amino acid. Codons for the same amino acid tend to contain the same nucleotides at the first and second positions and to vary at the third position. There are three codons that do not specify any amino acid but act as termination sites (*stop codons*), signaling the end of the protein-coding sequence in an mRNA. One codon—AUG—acts both as an initiation codon, signaling the start of a protein-coding message, and as the codon that specifies the amino acid methionine.

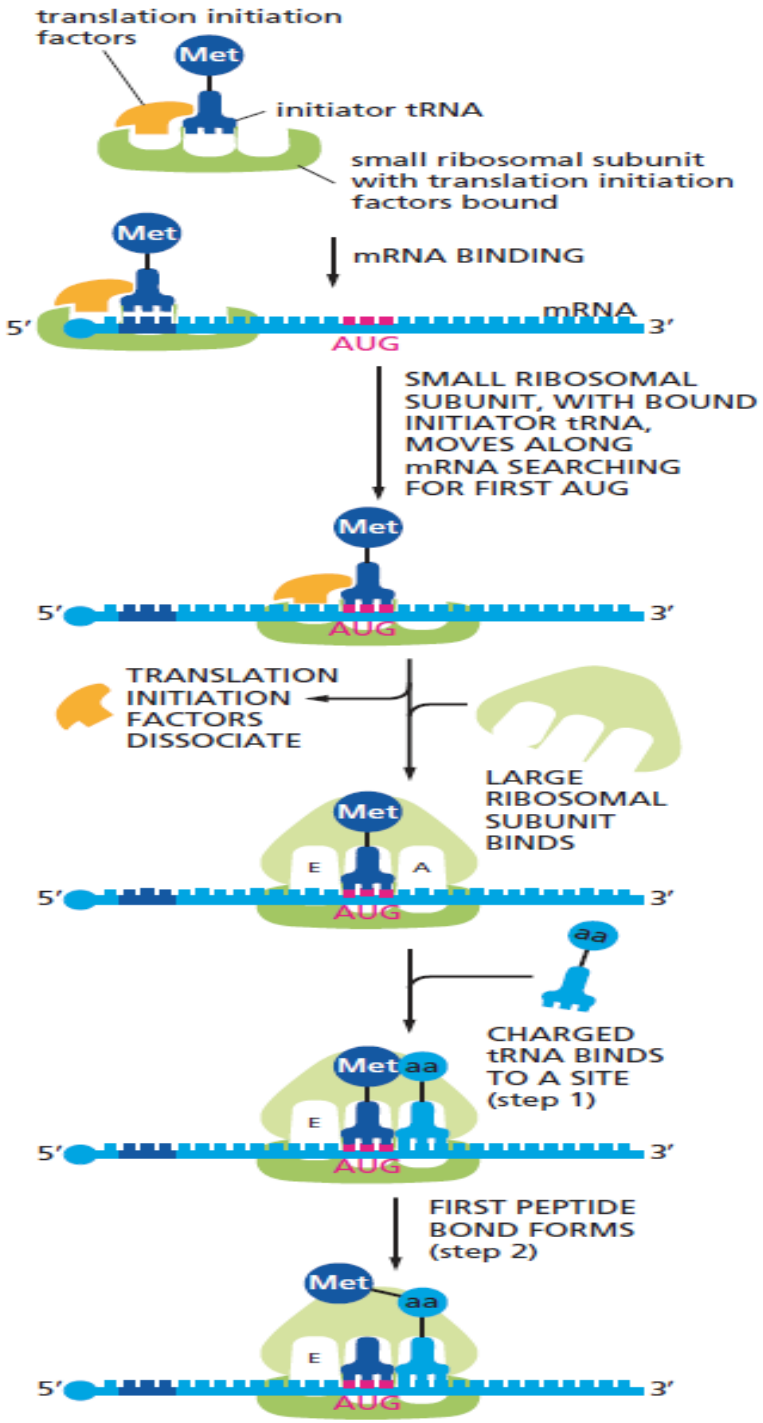


Figure 7–36 Initiation of protein synthesis in eukaryotes requires translation initiation factors and a special initiator tRNA. Although not shown here, efficient translation initiation also requires additional proteins that are bound at the 5′ cap and poly-A tail of the mRNA (see Figure 7–23). In this way, the translation apparatus can ascertain that both ends of the mRNA are intact before initiating translation. Following initiation, the protein is elongated by the reactions outlined in Figure 7–34.