Amino acid to codon

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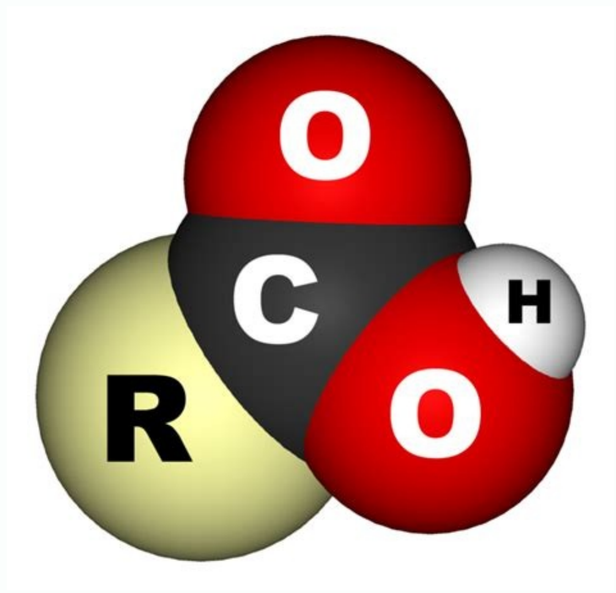

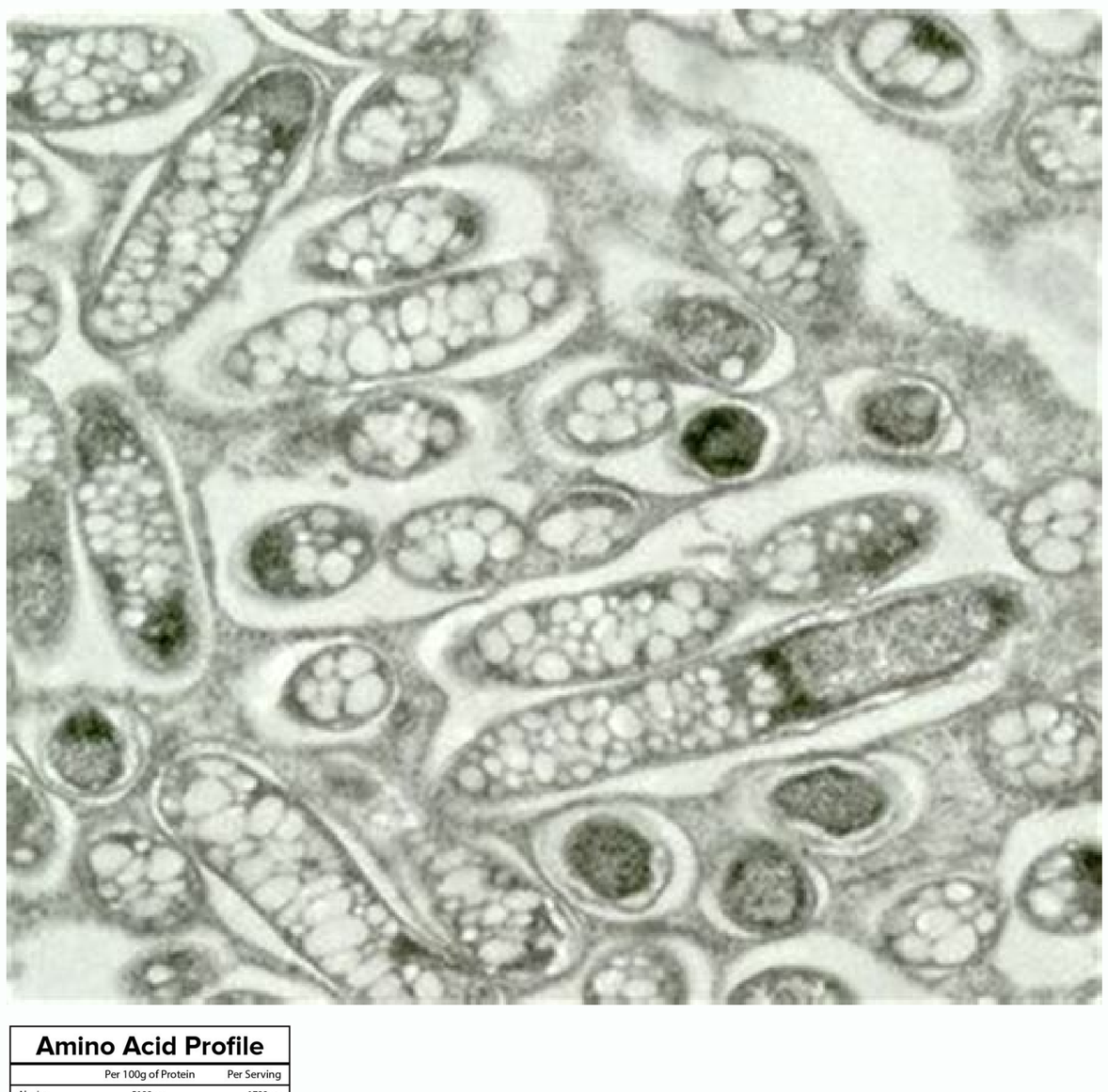

Amino Acid Profile		
	Per 100g of Protein	Per Serving
Alanine	5100mg	1700mg
Arginine	2600mg	780mg
Aspartic Acid	10700mg	3210mg
Cysteine	3100mg	930mg
Glutamic Acid	16700mg	5010mg
Glycine	1700mg	510mg
Histidine*	1800mg	540mg
Isoleucine**	5000mg	1500mg
Leucine**	12900mg	3870mg
Lysine*	10100mg	3030mg
Methionine*	2400mg	720mg
Phenylalanine*	3400mg	1020mg
Proline	4900mg	1470mg
Serine	3700mg	1110mg
Threonine*	4800mg	1440mg
Tryptophan	2600mg	780mg
Tyrosine	3700mg	1110mg
Valine**	5000mg	1500mg

** Branched Chain Amino Acid
* Essential Amino Acid

NOTE - starting VarNomen version 3 the '*' is used to indicate a translation stop codon, replacing the 'X' used previously (see Background). Nucleotide position in codon first second third U C A G U UUU - Phe UUC - Phe UUA - Leu UUG - Leu UCU - Ser UCC - Ser UCA - Ser UCG - Ser UAU - Tyr UAC - Tyr UAA - * UAG - * UGU - Cys UGC - Cys UGA - * UGG - Trp U C A G C CUU - Leu CUC - Leu CUA - Leu CUG - Leu CCU - Pro CCC - Pro CCA - Pro CCG - Pro CAU - His CAC - His CAA - Gln CAG - Gln CGU - Arg CGC - Arg CGA - Arg CGG - Arg U C A G A AUU - Ile AUC - Ile AUA - Ile AUG - Met ACU - Thr ACC - Thr ACA - Thr ACG - Thr AAU - Asn AAC - Asn AAA - Lys AAG - Lys AGU - Ser AGC - Ser AGA - Arg AGG - Arg U C A G G GUU - Val GUC - Val GUA - Val GUG - Val GCU - Ala GCC - Ala GCA - Ala GCG - Ala GAU - Asp GAC - Asp GAA - Glu GAG - Glu GGU - Gly GGC - Gly GGA - Gly GGG - Gly U C A G One letter code Three letter code Amino acid Possible codons A Ala Alanine GCA, GCC, GCG, GCT B Asx Asparagine or Aspartic acid AAC, AAT, GAC, GAT C Cys Cysteine TGC, TGT D Asp Aspartic acid GAC, GAT E Glu Glutamic acid GAA, GAG F Phe Phenylalanine TTC, TTT G Gly Glycine GGA, GGC, GGG, GGT H His Histidine CAC, CAT I Ile Isoleucine ATA, ATC, ATT K Lys Lysine AAA, AAG L Leu Leucine CTA, CTC, CTG, CTT, TTA, TTG M Met Methionine ATG N Asn Asparagine AAC, AAT P Pro Proline CCA, CCC, CCG, CCT Q Gln Glutamine CAA, CAG R Arg Arginine AGA, AGG, CGA, CGC, CGG, CGT S Ser Serine AGC, AGT, TCA, TCC, TCG, TCT T Thr Threonine ACA, ACC, ACG, ACT V Val Valine GTA, GTC, GTG, GTT W Trp Tryptophan TGG X X any codon NNN Y Tyr Tyrosine TAC, TAT Z Glx Glutamine or Glutamic acid CAA, CAG, GAA, GAG * * stop codon TAA, TAG, TGA Property Amino acids small Ala, Gly acidic / amide Asp, Glu, Asn, Gln charged negative Asp, Glu positive Lys, Arg polar Ala, Gly, Ser, Thr, Pro hydrophobic Val, Leu, Ile, Met size big Glu, Gln, His, Ile, Lys, Leu, Met, Phe, Trp, Tyr small Ala, Asn, Asp, Cys, Gly, Pro, Ser, Thr, Val aliphatic Ile, Leu, Val aromatic His, Phe, Tyr, Trp | Top of page | MutNomen homepage | Check-list | | Recommendations: DNA, RNA, protein, uncertain | | Discussions | Symbols, codons, etc. | FAQ's | History | | Example descriptions: QuickRef / symbols, DNA, RNA, protein | - Disclaimer Synthetic gene design made easy The Codon Optimization Tool converts the DNA, or protein sequence, from one organism for expression to another. The IDT algorithm provides the best sequence option by screening and filtering sequences to lower complexity and minimize secondary structures. Rebalance codon usage Decrease sequence complexity Avoid rare codons Proteins are synthesized from mRNA templates by a process that has been highly conserved throughout evolution (reviewed in Chapter 3). All mRNAs are read in the 5′ to 3′ direction, and polypeptide chains are synthesized from the amino to the carboxy terminus. Each amino acid is specified by three bases (a codon) in the mRNA, according to a nearly universal genetic code. The basic mechanics of protein synthesis are also the same in all cells: Translation is carried out on ribosomes, with tRNAs serving as adaptors between the mRNA template and the amino acids being incorporated into protein. Protein synthesis thus involves interactions between three types of RNA molecules (mRNA templates, tRNAs, and rRNAs), as well as various proteins that are required for translation.During translation, each of the 20 amino acids must be aligned with their corresponding codons on the mRNA template. All cells contain a variety of tRNAs that serve as adaptors for this process. As might be expected, given their common function in protein synthesis, different tRNAs share similar overall structures. However, they also possess unique identifying sequences that allow the correct amino acid to be attached and aligned with the appropriate codon in mRNA.Transfer RNAs are approximately 70 to 80 nucleotides long and have characteristic cloverleaf structures that result from complementary base pairing between different regions of the molecule (Figure 7.1). X-ray crystallography studies have further shown that all tRNAs fold into similar compact L shapes, which are likely required for the tRNAs to fit onto ribosomes during the translation process. The adaptor function of the tRNAs involves two separated regions of the molecule. All tRNAs have the sequence CCA at their 3′ terminus, and amino acids are covalently attached to the ribose of the terminal adenosine. The mRNA template is then recognized by the anticodon loop, located at the other end of the folded tRNA, which binds to the appropriate codon by complementary base pairing. The incorporation of the correctly encoded amino acids into proteins depends on the attachment of each amino acid to an appropriate tRNA, as well as on the specificity of codon-anticodon base pairing. The attachment of amino acids to specific tRNAs is mediated by a group of enzymes called aminoacyl tRNA synthetases, which were discovered by Paul Zamecnik and Mahlon Hoagland in 1957. Each of these enzymes recognizes a single amino acid, as well as the correct tRNA (or tRNAs) to which that amino acid should be attached. The reaction proceeds in two steps (Figure 7.2). First, the amino acid is activated by reaction with ATP to form an aminoacyl AMP synthetase intermediate. The activated amino acid is then joined to the 3′ terminus of the tRNA. The aminoacyl tRNA synthetases must be highly selective enzymes that recognize both individual amino acids and specific base sequences that identify the correct acceptor tRNAs. In some cases, the high fidelity of amino acid recognition results in part from a proofreading function by which incorrect aminoacyl AMPs are hydrolyzed rather than being joined to tRNA during the second step of the reaction. Recognition of the correct tRNA by the aminoacyl tRNA synthetase is also highly selective; the synthetase recognizes specific nucleotide sequences (in most cases including the anticodon) that uniquely identify each species of tRNA. After being attached to tRNA, an amino acid is aligned on the mRNA template by complementary base pairing between the mRNA codon and the anticodon of the tRNA. Codon-anticodon base pairing is somewhat less stringent than the standard A-U and G-C base pairing discussed in preceding chapters. The significance of this unusual base pairing in codon-anticodon recognition relates to the redundancy of the genetic code. Of the 64 possible codons, three are stop codons that signal the termination of translation; the other 61 encode amino acids (see Table 3.1). Thus, most of the amino acids are specified by more than one codon. In part, this redundancy results from the attachment of many amino acids to more than one species of tRNA. E. coli, for example, contain about 40 different tRNAs that serve as acceptors for the 20 different amino acids. In addition, some tRNAs are able to recognize more than one codon in mRNA, as a result of nonstandard base pairing (called wobble) between the tRNA anticodon and the third position of some complementary codons (Figure 7.3). Relaxed base pairing at this position results partly from the formation of G-U base pairs and partly from the modification of guanosine to inosine in the anticodons of several tRNAs during processing (see Figure 6.38). Inosine can base-pair with either C, U, or A in the third position, so its inclusion in the anticodon allows a single tRNA to recognize three different codons in mRNA templates. Ribosomes are the sites of protein synthesis in both prokaryotic and eukaryotic cells. First characterized as particles detected by ultracentrifugation of cell lysates, ribosomes are usually designated according to their rates of sedimentation: 70S for bacterial ribosomes and 80S for the somewhat larger ribosomes of eukaryotic cells. Both prokaryotic and eukaryotic ribosomes are composed of two distinct subunits, each containing characteristic proteins and rRNAs. The fact that cells typically contain many ribosomes reflects the central importance of protein synthesis in cell metabolism. E. coli, for example, contain about 20,000 ribosomes, which account for approximately 25% of the dry weight of the cell, and rapidly growing mammalian cells contain about 10 million ribosomes.The general structures of prokaryotic and eukaryotic ribosomes are similar, although they differ in some details (Figure 7.4). The small subunit (designated 30S) of E. coli ribosomes consists of the 16S rRNA and 21 proteins; the large subunit (50S) is composed of the 23S and 5S rRNAs and 34 proteins. Each ribosome contains one copy of the rRNAs and one copy of each of the ribosomal proteins, with one exception: One protein of the 50S subunit is present in four copies. The subunits of eukaryotic ribosomes are larger and contain more proteins than their prokaryotic counterparts have. The small subunit (40S) of eukaryotic ribosomes is composed of the 18S rRNA and approximately 30 proteins; the large subunit (60S) contains the 28S, 5.8S, and 5S rRNAs and about 45 proteins. A noteworthy feature of ribosomes is that they can be formed in vitro by self-assembly of their RNA and protein constituents. As first described in 1968 by Masayasu Nomura, purified ribosomal proteins and rRNAs can be mixed together and, under appropriate conditions, will reform a functional ribosome. Although ribosome assembly in vivo (particularly in eukaryotic cells) is considerably more complicated, the ability of ribosomes to self-assemble in vitro has provided an important experimental tool, allowing analysis of the roles of individual proteins and rRNAs.Like tRNAs, rRNAs form characteristic secondary structures by complementary base pairing (Figure 7.5). In association with ribosomal proteins the rRNAs fold further, into distinct three-dimensional structures. Initially, rRNAs were thought to play a structural role, providing a scaffold upon which ribosomal proteins assemble. However, with the discovery of the catalytic activity of other RNA molecules (e.g., RNase P and the self-splicing introns discussed in Chapter 6), the possible catalytic role of rRNA became widely considered. Consistent with this hypothesis, rRNAs were found to be absolutely required for the in vitro assembly of functional ribosomes. On the other hand, the omission of many ribosomal proteins resulted in a decrease, but not a complete loss, of ribosome activity. Direct evidence for the catalytic activity of rRNA first came from experiments of Harry Noller and his colleagues in 1992. These investigators demonstrated that the large ribosomal subunit is able to catalyze the formation of peptide bonds (the peptidyl transferase reaction) even after approximately 95% of the ribosomal proteins have been removed by standard protein extraction procedures. In contrast, treatment with RNase completely abolishes peptide bond formation, providing strong support for the hypothesis that the formation of a peptide bond is an RNA-catalyzed reaction. Further studies have confirmed and extended these results by demonstrating that the peptidyl transferase reaction can be catalyzed by synthetic fragments of 23S rRNA in the total absence of any ribosomal protein. Thus, the fundamental reaction of protein synthesis is catalyzed by ribosomal RNA. Rather than being the primary catalytic constituents of ribosomes, ribosomal proteins are now thought to facilitate proper folding of the rRNA and to enhance ribosome function by properly positioning the tRNAs.The direct involvement of rRNA in the peptidyl transferase reaction has important evolutionary implications. RNAs are thought to have been the first self-replicating macromolecules (see Chapter 1). This notion is strongly supported by the fact that ribozymes, such as RNase P and self-splicing introns, can catalyze reactions that involve RNA substrates. The role of rRNA in the formation of peptide bonds extends the catalytic activities of RNA beyond self-replication to direct involvement in protein synthesis. Additional studies indicate that the Tetrahymena rRNA ribozyme can catalyze the attachment of amino acids to RNA, lending credence to the possibility that the original aminoacyl tRNA synthetases were RNAs rather than proteins. The ability of RNA molecules to catalyze the reactions required for protein synthesis as well as for self-replication may provide an important link for understanding the early evolution of cells.Although the mechanisms of protein synthesis in prokaryotic and eukaryotic cells are similar, there are also differences, particularly in the signals that determine the positions at which synthesis of a polypeptide chain is initiated on an mRNA template (Figure 7.6). Translation does not simply begin at the 5′ end of the mRNA; it starts at specific initiation sites. The 5′ terminal portions of both prokaryotic and eukaryotic mRNAs are therefore noncoding sequences, referred to as 5′ untranslated regions. Eukaryotic mRNAs usually encode only a single polypeptide chain, but many prokaryotic mRNAs encode multiple polypeptides that are synthesized independently from distinct initiation sites. For example, the E. coli lac operon consists of three genes that are translated from the same mRNA (see Figure 6.8). Messenger RNAs that encode multiple polypeptides are called polycistronic, whereas monocistronic mRNAs encode a single polypeptide chain. Finally, both prokaryotic and eukaryotic mRNAs end in noncoding 3′ untranslated regions. In both prokaryotic and eukaryotic cells, translation always initiates with the amino acid methionine, usually encoded by AUG. Alternative initiation codons, such as GUG, are used occasionally in bacteria, but when they occur at the beginning of a polypeptide chain, these codons direct the incorporation of methionine rather than of the amino acid they normally encode (GUG normally encodes valine). In most bacteria, protein synthesis is initiated with a modified methionine residue (N-formylmethionine), whereas unmodified methionines initiate protein synthesis in eukaryotes (except in mitochondria and chloroplasts, whose ribosomes resemble those of bacteria).The signals that identify initiation codons are different in prokaryotic and eukaryotic cells, consistent with the distinct functions of polycistronic and monocistronic mRNAs (Figure 7.7). Initiation codons in bacterial mRNAs are preceded by a specific sequence (called a Shine-Delgarno sequence, after its discoverers) that aligns the mRNA on the ribosome for translation by base-pairing with a complementary sequence near the 3′ terminus of 16S rRNA. This base-pairing interaction enables bacterial ribosomes to initiate translation not only at the 5′ end of an mRNA but also at the internal initiation sites of polycistronic messages. In contrast, ribosomes recognize most eukaryotic mRNAs by binding to the 7-methylguanosine cap at their 5′ terminus (see Figure 6.39). The ribosomes then scan downstream of the 5′ cap until they encounter an AUG initiation codon. Sequences that surround AUGs affect the efficiency of initiation, so in many cases the first AUG in the mRNA is bypassed and translation initiates at an AUG farther downstream. However, eukaryotic mRNAs have no sequence equivalent to the Shine-Delgarno sequence of prokaryotic mRNAs. Translation of eukaryotic mRNAs is instead initiated at a site determined by scanning from the 5′ terminus, consistent with their functions as monocistronic messages that encode only single polypeptides. Translation is generally divided into three stages: initiation, elongation, and termination (Figure 7.8). In both prokaryotes and eukaryotes the first step of the initiation stage is the binding of a specific initiator methionyl tRNA and the mRNA to the small ribosomal subunit. The large ribosomal subunit then joins the complex, forming a functional ribosome on which elongation of the polypeptide chain proceeds. A number of specific nonribosomal proteins are also required for the various stages of the translation process (Table 7.1). The first translation step in bacteria is the binding of three initiation factors (IF-1, IF-2, and IF-3) to the 30S ribosomal subunit (Figure 7.9). The mRNA and initiator N-formylmethionyl tRNA then join the complex, with IF-2 (which is bound to GTP) specifically recognizing the initiator tRNA. IF-3 is then released, allowing a 50S ribosomal subunit to associate with the complex. This association triggers the hydrolysis of GTP bound to IF-2, which leads to the release of IF-1 and IF-2 (bound to GDP). The result is the formation of a 70S initiation complex (with mRNA and initiator tRNA bound to the ribosome) that is ready to begin peptide bond formation during the elongation stage of translation. Initiation in eukaryotes is more complicated and requires at least ten proteins (each consisting of multiple polypeptide chains), which are designated eIFs (eukaryotic initiation factors; see Table 7.1). The factors eIF-1, eIF-1A, and eIF-3 bind to the 40S ribosomal subunit, and eIF-2 (in a complex with GTP) associates with the initiator methionyl tRNA (Figure 7.10). The mRNA is recognized and brought to the ribosome by the eIF-4 group of factors. The 5′ cap of the mRNA is recognized by eIF-4E. Another factor, eIF-4G, binds to both eIF-4E and to a protein (poly-A binding protein or PABP) associated with the poly-A tail at the 3′ end of the mRNA. Eukaryotic initiation factors thus recognize both the 5′ and 3′ ends of mRNAs, accounting for the stimulatory effect of polyadenylation on translation. The initiation factors eIF-4E and eIF-4G, in association with eIF-4A and eIF-4B, then bring the mRNA to the 40S ribosomal subunit, with eIF-4G interacting with eIF-3. The 40S ribosomal subunit, in association with the bound methionyl tRNA and eIFs, then scans the mRNA to identify the AUG initiation codon. When the AUG codon is reached, eIF-5 triggers the hydrolysis of GTP bound to eIF-2. Initiation factors (including eIF-2 bound to GDP) are then released, and a 60S subunit binds to the 40S subunit to form the 80S initiation complex of eukaryotic cells. After the initiation complex has formed, translation proceeds by elongation of the polypeptide chain. The mechanism of elongation in prokaryotic and eukaryotic cells is very similar (Figure 7.11). The ribosome has three sites for tRNA binding, designated the P (peptidyl), A (aminoacyl), and E (exit) sites. The initiator methionyl tRNA is bound at the P site. The first step in elongation is the binding of the next aminoacyl tRNA to the A site by pairing with the second codon of the mRNA. The aminoacyl tRNA is escorted to the ribosome by an elongation factor (EF-Tu in prokaryotes, eEF-1α in eukaryotes), which is complexed to GTP. The GTP is hydrolyzed to GDP as the correct aminoacyl tRNA is inserted into the A site of the ribosome and the elongation factor bound to GDP is released. The requirement for hydrolysis of GTP before EF-Tu or eEF-1α is released from the ribosome is the rate-limiting step in elongation and provides a time interval during which an incorrect aminoacyl tRNA, which would bind less strongly to the mRNA codon, can dissociate from the ribosome rather than being used for protein synthesis. Thus, the expenditure of a high-energy GTP at this step is an important contribution to accurate protein synthesis; it allows time for proofreading of the codon-anticodon pairing before the peptide bond forms. Once EF-Tu (or eEF-1α) has left the ribosome, a peptide bond can be formed between the initiator methionyl tRNA at the P site and the second aminoacyl tRNA at the A site. This reaction is catalyzed by the large ribosomal subunit, with the rRNA playing a critical role (as already discussed). The result is the transfer of methionine to the aminoacyl tRNA at the A site of the ribosome, forming a peptidyl tRNA at this position and leaving the uncharged initiator tRNA at the P site. The next step in elongation is translocation, which requires another elongation factor (EF-G in prokaryotes, eEF-2 in eukaryotes) and is again coupled to GTP hydrolysis. During translocation, the ribosome moves three nucleotides along the mRNA, positioning the next codon in an empty A site. This step translocates the peptidyl tRNA from the A site to the P site, and the uncharged tRNA from the P site to the E site. The ribosome is then left with a peptidyl tRNA bound at the P site, and an empty A site. The binding of a new aminoacyl tRNA to the A site then induces the release of the uncharged tRNA from the E site, leaving the ribosome ready for insertion of the next amino acid in the growing polypeptide chain.As elongation continues, the EF-Tu (or eEF-1α) that is released from the ribosome bound to GDP must be reconverted to its GTP form (Figure 7.12). This conversion requires a third elongation factor, EF-Ts (eEF-1βγ in eukaryotes), which binds to the EF-Tu/GDP complex and promotes the exchange of bound GDP for GTP.

This exchange results in the regeneration of EF-Tu/GTP, which is now ready to escort a new aminoacyl tRNA to the A site of the ribosome, beginning a new cycle of elongation. The regulation of EF-Tu by GTP binding and hydrolysis illustrates a common means of the regulation of protein activities. As will be discussed in later chapters, similar mechanisms control the activities of a wide variety of proteins involved in the regulation of cell growth and differentiation, as well as in protein transport and secretion. Elongation of the polypeptide chain continues until a stop codon (UAA, UAG, or UGA) is translocated into the A site of the ribosome. Cells do not contain tRNAs with anticodons complementary to these termination signals; instead, they have release factors that recognize the signals and terminate protein synthesis (Figure 7.13). Prokaryotic cells contain two release factors that recognize termination codons: RF-1 recognizes UAA or UAG, and RF-2 recognizes UAA or UGA (see Table 7.1). In eukaryotic cells a single release factor (eRF-1) recognizes all three termination codons. Both prokaryotic and eukaryotic cells also contain release factors (RF-3 and eRF-3, respectively) that do not recognize specific termination codons but act together with RF-1 (or eRF-1) and RF-2. The release factors bind to a termination codon at the A site and stimulate hydrolysis of the bond between the tRNA and the polypeptide chain at the P site, resulting in release of the completed polypeptide from the ribosome. The tRNA is then released, and the ribosomal subunits and the mRNA template dissociate. Messenger RNAs can be translated simultaneously by several ribosomes in both prokaryotic and eukaryotic cells. Once one ribosome has moved away from the initiation site, another can bind to the mRNA and begin synthesis of a new polypeptide chain. Thus, mRNAs are usually translated by a series of ribosomes, spaced at intervals of about 100 to 200 nucleotides (Figure 7.14). The group of ribosomes bound to an mRNA molecule is called a polyribosome, or polysome. Each ribosome within the group functions independently to synthesize a separate polypeptide chain. Although transcription is the primary level at which gene expression is controlled, the translation of mRNAs is also regulated in both prokaryotic and eukaryotic cells. One mechanism of translational regulation is the binding of repressor proteins, which block translation, to specific mRNA sequences. The best understood example of this mechanism in eukaryotic cells is regulation of the synthesis of ferritin, a protein that stores iron within the cell. The translation of ferritin mRNA is regulated by the supply of iron: More ferritin is synthesized if iron is abundant (Figure 7.15). This regulation is mediated by a protein which (in the absence of iron) binds to a sequence (the iron response element, or IRE) in the 5′ untranslated region of ferritin mRNA, blocking its translation. In the presence of iron, the repressor no longer binds to the IRE and ferritin translation is able to proceed. It is interesting to note that the regulation of translation of ferritin mRNA by iron is similar to the regulation of transferrin receptor mRNA stability, which was discussed in the previous chapter (see Figure 6.48). Namely, the stability of transferrin receptor mRNA is regulated by protein binding to an IRE in its 3′ untranslated region. The same protein binds to the IREs of both ferritin and transferrin receptor mRNAs. However, the consequences of protein binding to the two IREs are quite different. Protein bound to the transferrin receptor IRE protects the mRNA from degradation rather than inhibiting its translation. These distinct effects presumably result from the different locations of the IRE in the two mRNAs. To function as a repressor-binding site, the IRE must be located within 70 nucleotides of the 5′ cap of ferritin mRNA, suggesting that protein binding to the IRE blocks translation by interfering with cap recognition and binding of the 40S ribosomal subunit. Rather than inhibiting translation, protein binding to the same sequence in the 3′ untranslated region of transferrin receptor mRNA protects the mRNA from nuclease degradation. Binding of the same regulatory protein to different sites on mRNA molecules can thus have distinct effects on gene expression, in one case inhibiting translation and in the other stabilizing the mRNA to increase protein synthesis.Another mechanism of translational regulation in eukaryotic cells, resulting in global effects on overall translational activity rather than on the translation of specific mRNAs, involves modulation of the activity of initiation factors, particularly eIF-2. As already discussed, eIF-2 (complexed with GTP) binds to the initiator methionyl tRNA, bringing it to the ribosome. The subsequent release of eIF-2 is accompanied by GTP hydrolysis, leaving eIF-2 as an inactive GDP complex. To participate in another cycle of initiation, the eIF-2/GTP complex must be regenerated by the exchange of bound GDP for GTP. This exchange is mediated by another factor, eIF-2B. The control of eIF-2 activity by GTP binding and hydrolysis is thus similar to that of EF-Tu (see Figure 7.12). However, the regulation of eIF-2 provides a critical control point in a variety of eukaryotic cells. In particular, eIF-2 can be phosphorylated by regulatory protein kinases. This phosphorylation blocks the exchange of bound GDP for GTP, thereby inhibiting initiation of translation. One type of cell in which such phosphorylation occurs is the reticulocyte, which is devoted to the synthesis of hemoglobin (Figure 7.16). The translation of globin mRNA is controlled by the availability of heme: The mRNA is translated only if adequate heme is available to form functional hemoglobin molecules. In the absence of heme, a protein kinase that phosphorylates eIF-2 is activated, and further translation is inhibited. Similar mechanisms have been found to control protein synthesis in other cell types, particularly virus-infected cells in which viral protein synthesis is inhibited by interferon. Other studies have implicated eIF-4E, which binds to the 5′ cap of mRNAs, as a translational regulatory protein. For example, the hormone insulin stimulates protein synthesis in adipocytes and muscle cells. This effect of insulin is mediated, at least in part, by phosphorylation of proteins associated with eIF-4E, resulting in stimulation of eIF-4E activity and increased rates of translational initiation.Translational regulation is particularly important during early development. As discussed in Chapter 6, a variety of mRNAs are stored in oocytes in an untranslated form; the translation of these stored mRNAs is activated at fertilization or later stages of development. One mechanism of such translational regulation is the controlled polyadenylation of oocyte mRNAs. Many untranslated mRNAs are stored in oocytes with short poly-A tails (approximately 20 nucleotides). These stored mRNAs are subsequently recruited for translation at the appropriate stage of development by the lengthening of their poly-A tails to several hundred nucleotides. In addition, the translation of some mRNAs during development appears to be regulated by repressor proteins that bind to specific sequences in their 3′ untranslated regions. These regulatory proteins may also direct mRNAs to specific regions of eggs or embryos, allowing localized synthesis of the encoded proteins during embryonic development.Key Experiment: Catalytic Role of Ribosomal RNA. Molecular Medicine: Antibiotics and Protein Synthesis.