CHAPTER 7
From DNA to Protein

DNA doesn’t direct protein synthesis itself, but acts rather like manger, delegating the various tasks required to a team of workers. When a particular proteins is needed by the cell, the nucleotide sequences of the appropriate portion of the immensely long DNA molecule in a chromosome is first copied into another type of nucleic acid- RNA. It is these RNA copies of short segments of DNA that are used as templates to direct DNA synthesis of protein. The flow of genetic information in cells is therefore from DNA to RNA to Protein.

From DNA to RNA

Transcription and translations are the means by which cells read out or express their genetic instructions (their genes). Genes can be expressed different efficiencies, which provide the cell with a way to make vas quantities of some proteins and tiny quantities of others.

Figure 7-1 Essential Cell Biology, 2nd (© 2004 Garland Science)
Portions of DNA Sequence Are Transcribed into RNA

The first step a cell takes in reading out part of its genetic instructions is to copy the required portion of the nucleotide sequence of DNA into a nucleotide sequence of RNA. This process is called transcription because the information, though copied into another chemical form.

Although their chemical differences are small, DNA and RNA differ dramatically in overall structure. Whereas DNA always occurs in cells as a double-strand helix, RNA is single stranded. This difference has important functional consequences. Because an RNA chain is single-stranded, it can fold up into variety of shapes, just as a polypeptide chain folds up to form a final shape of protein.
Transcription Produces RNA Complementary to ONE Strand of DNA

All of the RNA in a cell is made by transcription, a process that has certain similarities to DNA replication. Transcription begins with the opening and unwinding of a small portion of the DNA double helix to expose the bases on each DNA strand. One of the two strands of DNA double helix acts as template for the synthesis of RNA. Ribonucleotides are added, one-by-one, to the growing chain RNA. Transcription, however, differs from DNA replication in several crucial features.

1. RNA strand doesn’t remain hydrogen bonded to the DNA template strand
2. RNAs are copied from only limited region of DNA, these molecules are shorter than DNA molecules.

The enzymes that carry out transcription are called RNA polymerase. Like DNA polymerase, RNA polymerase catalyzes the formation of the phosphodiester bond that link nucleotides together and form sugar-phosphate backbone of the RNA chain.
Several Types of RNA Are Produced in Cells

The vast majority of genes in a cell’s DNA specify the amino acids sequences of proteins, and the RNA molecules that are copied from these genes are collectively called messenger RNA (mRNA).

Types of RNA Produced in Cells

<table>
<thead>
<tr>
<th>Type of RNA</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>mRNAs</td>
<td>codes for proteins</td>
</tr>
<tr>
<td>rRNAs</td>
<td>forms part of the structure of the ribosome and participates in protein synthesis</td>
</tr>
<tr>
<td>tRNAs</td>
<td>used in protein synthesis as an adaptor between mRNA and amino acids</td>
</tr>
<tr>
<td>Small RNAs</td>
<td>used in pre-mRNA splicing, transport of proteins to ER, and other cellular processes</td>
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</tbody>
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Signals in DNA Tell RNA Polymerase Where to Start and Finish

To begin transcription, RNA polymerase must be able to recognize the start of a gene and bind firmly to the DNA. The enzyme latches tightly onto the DNA once it encounters a region called PROMOTOR, which contains a sequence of nucleotides indicating the starting point for DNA synthesis. These nucleotides sequence are conserved in all prokaryote species with minor changes. After the RNA polymerase makes contact with the promoter DNA and binds tightly, the enzymes opens up the double helix immediately in front of it to expose the nucleotides on a short stretch of DNA on each strand. One of the two exposed DNA strands then acts as a template for complementary base-pairing with incoming ribonucleotides, two of which are joined together by the polymerase to begin RNA chain. Chain elongation then continues until the enzyme encounters a second signal in the DNA, the terminator where polymearse halts and releases both the DNA template and the newly made RNA chain.
A subunit of bacterial polymerase, called sigma factor, is primarily responsible for recognizing the promoter sequence on DNA. Once polymerase has latched onto the DNA at this site and has synthesized approximately 10 nucleotides of RNA, the sigma factor is released, enabling the polymerase to move forward and continue transcribing without it. The direction of transcription is determined by the orientation of the promoter at the beginning of each gene. Transcription can only proceed in the direction of 5' to 3'.

Eukaryotic RNAs Are Transcribed and Processed Simultaneously in the Nucleus

In bacteria, chromosomal DNA located within the cytoplasm where the ribosome on which protein synthesis takes place. As mRNA molecules in bacteria are transcribed, ribosome immediately attached to the 5'end of the RNA transcript and protein synthesis starts. On contrast, in eukaryotic cells DNA is enclosed is enclosed within the nucleus, but the protein synthesis takes place on ribosome in cytoplasm. So, before a eukaryotic mRNA can be translated, it must be transported out of the nucleus. Before a eukaryotic RNA can be exist in nucleus, it must go through several different RNA processing step.
1-RNA capping: this process involves a modification of the 5' end of the mRNA transcript.
2-Polyadenylation of mRNA: this process provides most newly transcribed mRNA with special structure at their 3' tail or ends.

These two processes are thought to increase the stability of the eukaryotic mRNA molecule. Also, these modifications on RNA help them to identify mRNA.

Eukaryotic Genes Are Interrupted by Noncoding Sequences
Most eukaryotic RNAs have to undergo an additional processing step before they are functional. In bacteria, most proteins are encoded by an uninterrupted stretch of DNA sequence that is transcribed into an RNA without any further modifications. Most eukaryotic genes, in contrast, have their coding sequences interrupted by long noncoding sequences called intron. The scattered pieces of coding sequences or expressed sequences called exons.
Introns Are Removed by RNA Splicing

To produce an mRNA in a eukaryotic cell, the entire length of the gene (introns and exon) is transcribed into RNA. After capping, as the RNA polymerase continues to transcribe gene, the process RNA splicing begin.
Mature mRNAs Are Selectively Exported From the Nucleus

Each mRNA molecule is eventually degraded into nucleotides by cellular RNase, but the lifetime of mRNA molecules differ considerably depending on mRNA type. Most mRNAs produced in bacteria are degraded rapidly having a typical lifetime of about 3 minutes. The mRNAs in eukaryotic cells usually persists for longer amounts of time. For example B-globin mRNA’s life time is about 10 hours. The life time of each mRNA is determined by nucleotide sequences located in the 3 region of mRNA.

FROM RNA TO PROTEIN

mRNA Molecules Are Eventually Degraded by the Cell

An mRNA Sequence Is Decoded in Sets of Three Nucleotides

The conversion of the information in RNA into protein represents a translation of the information into another language that uses quite different symbols. The rules by which the nucleotide sequence of a gene, through the medium of RNA, is translated into the amino acid sequence of protein is known Genetic code. The sequence of nucleotides in the mRNA molecule is read consecutively in groups of three. Each group of three consecutive nucleotides in RNA is called a codon, and each specifies one amino acids.
tRNA Molecules Match Amino Acids to Codons in mRNA

Each amino acid is represented by at least one codon that consists of a nucleotides triplet in the mRNA. These codons in mRNA molecule do not directly recognize the amino acids they specify. Rather, the translation of mRNA into protein depends on adaptor molecules that recognize and binds both the codon and, at another site on their surface, to the amino acids. These amino acids consist of a set of small RNA molecules known as transfer RNA (tRNA).

Specific Enzymes Couple tRNAs to the Correct Amino Acid

Each amino acid are linked to corresponding amino acids by enzymes called aminoacyl tRNA synthases, which covalently couple each amino acid to its appropriate set of tRNA molecules. There is a different synthase enzyme for each amino acid; one attaches to glycine to all tRNAs that recognize codons for glycine, another attaches alanine to all tRNA that recognize codons for alanine and so on... The synthase-catalyzed reaction that attaches the amino acid at 3’end of the tRNA by utilizing energy for this reaction.
The RNA Massage Is Decoded on Ribosomes

The recognition of a codon by the anticodon on a tRNA molecule depends on the same type of complementary base pairing used in DNA replication and transcription. The protein-manufacturing machine is the ribosome. Ribosomes are made up of more than 50 different proteins and several RNA molecules called ribosomal RNA (rRNA). In a eukaryote, the ribosomal subunits are made in the nucleus by the association of newly transcribed rRNAs with ribosomal proteins.

Each ribosome contains three binding sites for tRNA molecules, called the A-site, the P-sites, and the E-sites. Because tRNA molecules have the same basic shape, they are all capable of fitting into these sites. A tRNA molecule is held tightly at the A- and P-sites, however, only if it is anticodon forms base pairs with a complementary codon on the mRNA molecule that is bound to the ribosome.
Once protein synthesis has been initiated, each new amino acid is added to the elongation chain in a cycle of reactions.

Step 1. A tRNA carrying the next amino acid chain has been bound to the vacant ribosomal A-site by forming base pairs with the codon in mRNA exposed at the A-site.

Step 2. The carboxyl end of the polypeptide chain is uncoupled from the tRNA at the P-site and joined by a peptide bond to the free amino group of the amino acid linked to the tRNA at the A-site.

Step 3. The small subunit moves exactly three nucleotides along the mRNA molecule, bringing it back to its original position relative to the large subunit, and the RNA occupying the E-site dissociates.

Codons in mRNA Signal Where to Start and to Stop Protein Synthesis

The site where protein synthesis begins on the mRNA is crucial, because it sets the reading frame for the whole length of the message. An error of one nucleotide either way at this stage will cause every subsequent codon in the message to be misread, so that a nonfunctional protein with a garbled sequence of the amino acids will result. The translation of an mRNA begins with the codon AUG, and a special tRNA is required to initiate translation. This initiator mRNA always carries the amino acid methionine so that newly made proteins all have met as the first amino acid at their N-terminal end.
The mechanism for selecting a start codon is different in bacteria. Bacterial mRNAs have no 5' caps to tell the ribosome where to begin searching for the translation. Instead, they contain specific ribozyme binding sequences, up to six nucleotides long, that are located a few nucleotides upstream of AUGs at which translation is to begin. Unlike a eukaryotic ribosome, a prokaryotic ribosome can readily bind directly to a start codon that lies in the interior of an mRNA, as long as a ribosome-binding sequence, are necessary in bacteria.

Inhibitors of Prokaryotic Protein Synthesis Are Used as Antibiotics

Many of our most effective antibiotics are compounds that act by inhibiting bacterial but not eukaryotic, protein synthesis. Some of these drugs exploit the small structural and functional differences between bacterial and eukaryotic ribosomes, so they interfere preferentially with bacterial protein synthesis.