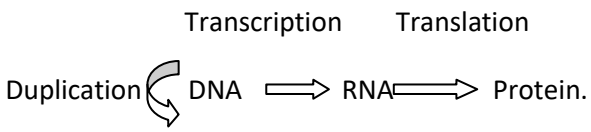
THE CENTRAL DOGMA

By the fall of 1953, the working hypothesis was adopted that chromosomal DNA functions as the template for RNA molecules, which subsequently move to the cytoplasm, where they determine the arrangement of amino acids within proteins. In 1956 Francis Crick referred to this pathway for the flow of genetic information as the central dogma:



Here the arrows indicate the directions proposed for the transfer of genetic information. The arrow encircling DNA signifies that DNA is the template for its self-replication. The arrow between DNA and RNA indicates that RNA synthesis (called transcription) is directed by a DNA template. Correspondingly, the synthesis of proteins (called translation) is directed by an RNA template. Most importantly, the last two arrows were presented as unidirectional; that is, RNA sequences are never determined by protein templates nor was DNA then imagined ever to be made on RNA templates. The idea that proteins never serve as templates for RNA has stood the test of time. RNA templates sometimes do act as templates for DNA chains of complementary sequence. Such reversals of the normal flow of information are very rare events compared with the enormous number of RNA molecules made on DNA templates. Thus, the Central dogma as originally proclaimed more than 50 years ago still remains essentially valid.

The Adaptor Hypothesis of Crick

At first it seemed simplest to believe that the RNA templates forprotein synthesis were folded upto create cavities on their outer surfaces specific for the 20 different amino acids. The cavities would be so shaped that only one given amino acid would fit,and in this way RNA would provide the information to order amino acids during protein synthesis.By 1955,however,Crick became disenchanted with this conventional wisdom, arguing that it would never work. In the first place, the specific chemical groups on the four bases of RNA (A, U, G, and C) should mostly interact with water-soluble groups. Yet, the specific side groups of many amino acids (e.g., leucine, valine, and phenylalanine) strongly prefer interactions with water-insoluble (hydrophobic) groups. In the second place, even if somehow RNA could be folded so as to display some hydrophobic surfaces, it seemed at the time unlikely that an RNA template would be used to discriminate accurately between chemically very similar amino acids like glycine and alanine or valine and isoleucine, both pairs differing only by the presence of single methyl (CH_3) groups. Crick thus proposed that prior to incorporation into proteins,amino acids are first attached to specific adaptor molecules,which in turn possess unique surfaces that can bind specifically to bases on the RNA templates.

Discovery of Messenger RNA (mRNA)

Cells infected with phage T4 provided the ideal system to find the true template.Following infection by this virus, cells stop synthesizing E.coli RNA; the only RNA synthesized is transcribed off the T4 DNA. Most strikingly,not only does T4 RNA have a base composition very similar to T4 DNA, but it does not bind to the ribosomal proteins that normally associate with rRNA to form ribosomes.

Instead, after first attaching to previously existing ribosomes, T4 RNA moves across their surface to bring its bases into positions where they can bind to the appropriate tRNA–amino acid precursors for protein synthesis (Fig. 2-15). In so acting, T4 RNA orders the amino acids andisthusthelong-sought-forRNAtemplateforproteinsynthesis.Because it carries the information from DNA to the ribosomal sites of protein synthesis,it is called messenger RNA(mRNA).The observation of T4 RNA binding to E.coli ribosomes,first made in the spring of 1960,was soon followed with evidence for a separate messenger class of RNA within uninfected E. coli cells, thereby definitively ruling out a template role for any rRNA. Instead, the rRNA components of ribosomes, together with some 50 different ribosomal proteins that bind to them, serve as the factories for protein synthesis, functioning to bring the tRNA–amino acid precursors into positions where they can read off the information provided by the mRNA templates. Only a few percent of total cellular RNA is mRNA. This RNA shows the expected large variations in length and nucleotide composition required to encode the many different proteins found in a given cell. Hence, it is easy to understand why mRNA was first overlooked. Because only a small segment of mRNA is attached at a given moment to a ribosome, a single mRNA molecule can simultaneously be read by several ribosomes. Most ribosomes are found as parts of polyribosomes(groups of ribosomes translating the same mRNA), which can include more than 50 members(Fig.2-16).

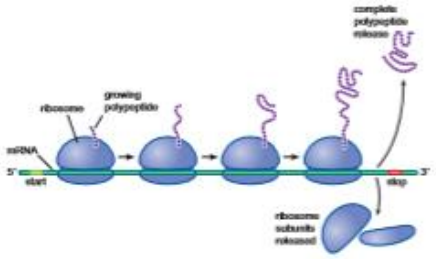


FIGURE 2-16 Diagram of a polyribosome. Each ribosome attaches at a start signal at the 5′ end of an mRNA chain and synthesizes a polypeptide as it proceeds along the molecule. Several ribosomes may be attached to one mRNA molecule at one time; the entire assembly is called a polyribosome.

NOTE:

- Dear students along with notes I have attached previous year question paper of Molecular biology. You are required to read the questions carefully and try to solve all, especially which deals with the Units 1/2/3/4(my portion). In case of any query you can mail me.
- Please be prepared for your molecular biology class test which I will take immediately as soon as the college reopens because the exams are very near and already a lot of delay has occurred. Depending on circumstances The class test can be written or oral. Be prepared for both. All the best and be safe.