**The Genetic Code is Carried by a Messenger**

As we have learned, DNA contains the instructions for making all of the proteins needed by an organism. The sections coding for individual proteins are referred to as genes. But how does the cell actually use the instructions in genes to build proteins? It took scientists years to understand this process.

**I**

It had long been suspected that RNA was associated with protein synthesis in the cell because cells making large amounts of protein always contained large amounts of RNA. Some RNA is found in the cell nucleus but most RNA is found in the cytoplasm of the cell. By using techniques that split cells into their parts, biochemists found that the RNA in the cytoplasm was concentrated mainly in tiny granules called ribosomes. Later studies using amino acids tagged with radioactive isotopes showed that new strands of protein were in fact formed on the ribosomes. If proteins were formed on the ribosomes, then somehow the ribosomes must have been given the instructions for assembling the amino acids in the correct order. Scientists believed even then that these instructions were contained in the DNA in the nucleus. So how did they get to the ribosomes? One thing was certain – they could not come from the DNA directly, since it was known that DNA never left the nucleus.

**II**

When biochemists further investigated protein synthesis they learned that DNA does not form proteins directly. Instead, DNA works **through** RNA according to the scheme:

**Fig. 11**

DNA 🡪 RNA 🡪 protein

*(*this means*: DNA makes RNA and RNA makes protein.)*

They found that DNA acts as the master blueprint and is always kept securely locked in a safe place, the nucleus. From this master blueprint copies are made of individual protein recipes and carried to the ribosomes. These copies are in the form of special RNA molecules called **messenger RNA (mRNA)**. The genetic message contained in the DNA molecule is transcribed on the mRNA molecule and the mRNA in turn carries it to the ribosomes.

**III**

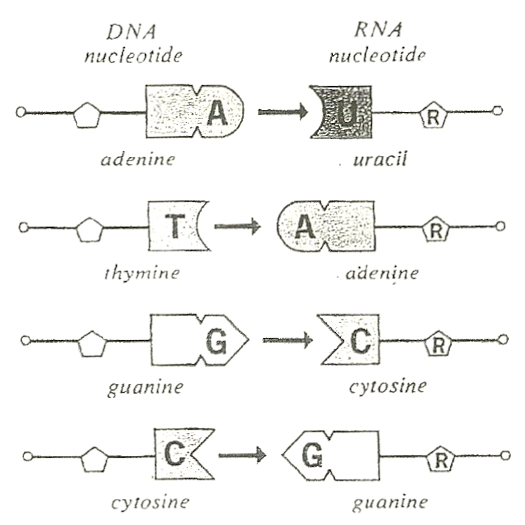
Messenger RNA strands are synthesized alongside a DNA strand in much the same way that a new strand of DNA is made in DNA replication. . This copying must be done very exactly. All messenger RNA molecules copied from one gene on a DNA strand must be alike. This ensures that all of the protein molecules made from that gene will be identical. In code language, this means that the nucleotides in the new strand of messenger

**IV**

RNA must match the nucleotides of the DNA perfectly. We have learned that the RNA alphabet of 4 nucleotides is very similar to that of DNA, the only differences being that they contain the sugar ribose instead of deoxyribose and that the T (thymine) of DNA is replaced by U (uracil) in RNA. Thymine and uracil differ slightly in their chemical make up but their shapes are almost identical. Recall that in DNA cytosine always pairs with guanine, and adenine always pairs with thymine. This same pairing must be followed when a DNA strand makes a strand of RNA except that now uracil pairs with adenine instead of thymine (see **Fig. 11**). Thus, whenever an adenine nucleotide is located on the DNA strand, a uracil nucleotide will be located on the RNA strand.

**IV**

**(cont.)**



**The Genetic Code is Finally Cracked**

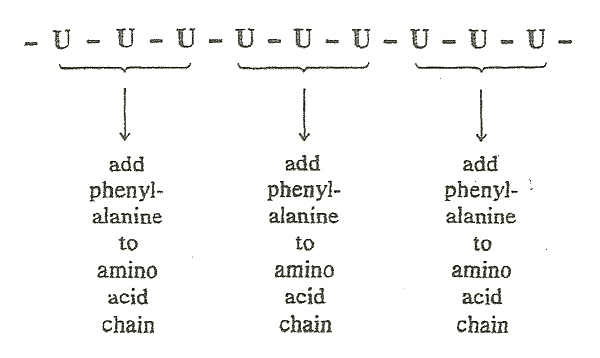
Another piece of the puzzle was determining how a particular sequence of nucleotides code for a particular sequence of amino acids. It was the mRNA that provided the clue to cracking this genetic code. A young American biochemist, Marshall Nirenberg, working at the National Institutes of Health, studied protein synthesis in an extract of bacterial cells that contained ribosomes. Nirenberg found that inserting messenger RNA from one kind of cell into another kind of cell increased protein synthesis by the ribosomes of the second cell. In other words, ribosomes started producing more protein molecules even when the instructions came from “foreign” RNA. This suggested an idea for an experiment. If ribosomes could follow instructions from a strange RNA, would they also follow instructions from a synthetic RNA, one made in the laboratory and never before present in a living cell?

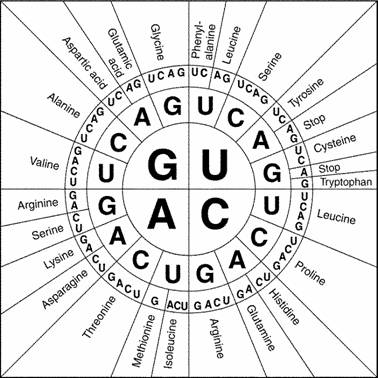
**V**

To keep matters simple, Nirenberg prepared RNA molecules that consisted of only one ribonucleotide, uracil, repeated over and over again. A custom-made chain of uracil nucleotides (U-U-U-U-U-U-U-U) was added to each of twenty different test tubes, each containing ribosomes, enzymes, and other factors needed for protein synthesis. However each test tube contained a different radioactive amino acid. The results were astonishing. In nineteen of the test tubes nothing happened, but in the twentieth the radioactive amino acid was incorporated into polypeptide chains. The radioactive amino acid was phenylalanine. When the polypeptide was analyzed, it was found to consist only of the phenylalanine units, one joined to another as shown in **Fig.12**.

**VI**

**Fig. 12**

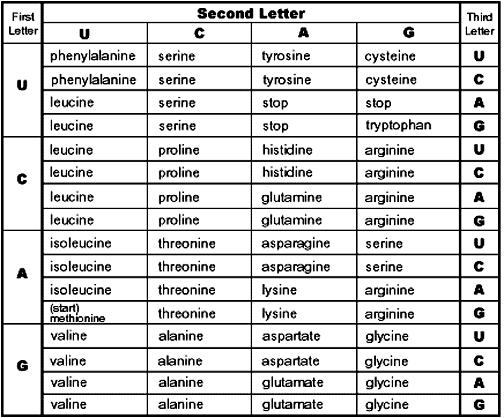


Biochemists had previously concluded that a sequence of three of nucleotides (a “triplet”) might represent a code word that specifies one particular amino acid to be incorporated into protein. Nirenberg discovered the first triplet. It was UUU and it meant: attach one molecule of the amino acid phenylalanine to the polypeptide chain (see Figure 2). This was a remarkable discovery for which Nirenberg later received the Nobel Prize.

**VII**

Nirenberg’s work electrified the scientific world. Soon Severo Ochoa in New York, Francis Crick in England and others (along with Nirenberg) followed this first breakthrough with other experiments. They made many different molecules of mRNA and tested to see what amino acids they would add to a polypeptide chain. In this way the triplet code words (now called “**codons**”)

**VIII**

for the rest of the amino acids were found. **Fig. 13** shows the complete genetic code – all of the possible mRNA codons and the amino acids they specify. **Fig. 14** shows the same information organized in a different way.

Remarkably scientists have found that the genetic code is the same in all organisms studied. Each triplet means exactly the same thing to every organism on Earth. This means an organism can read and follow the directions on any DNA strand even if it is from a different species than its own. This is among our most powerful evidence that all life is related and that all organisms evolved from a common ancestor.

**IX**

**Fig. 13**

**mRNA codons and the amino acids for which they code**

**Fig. 14**

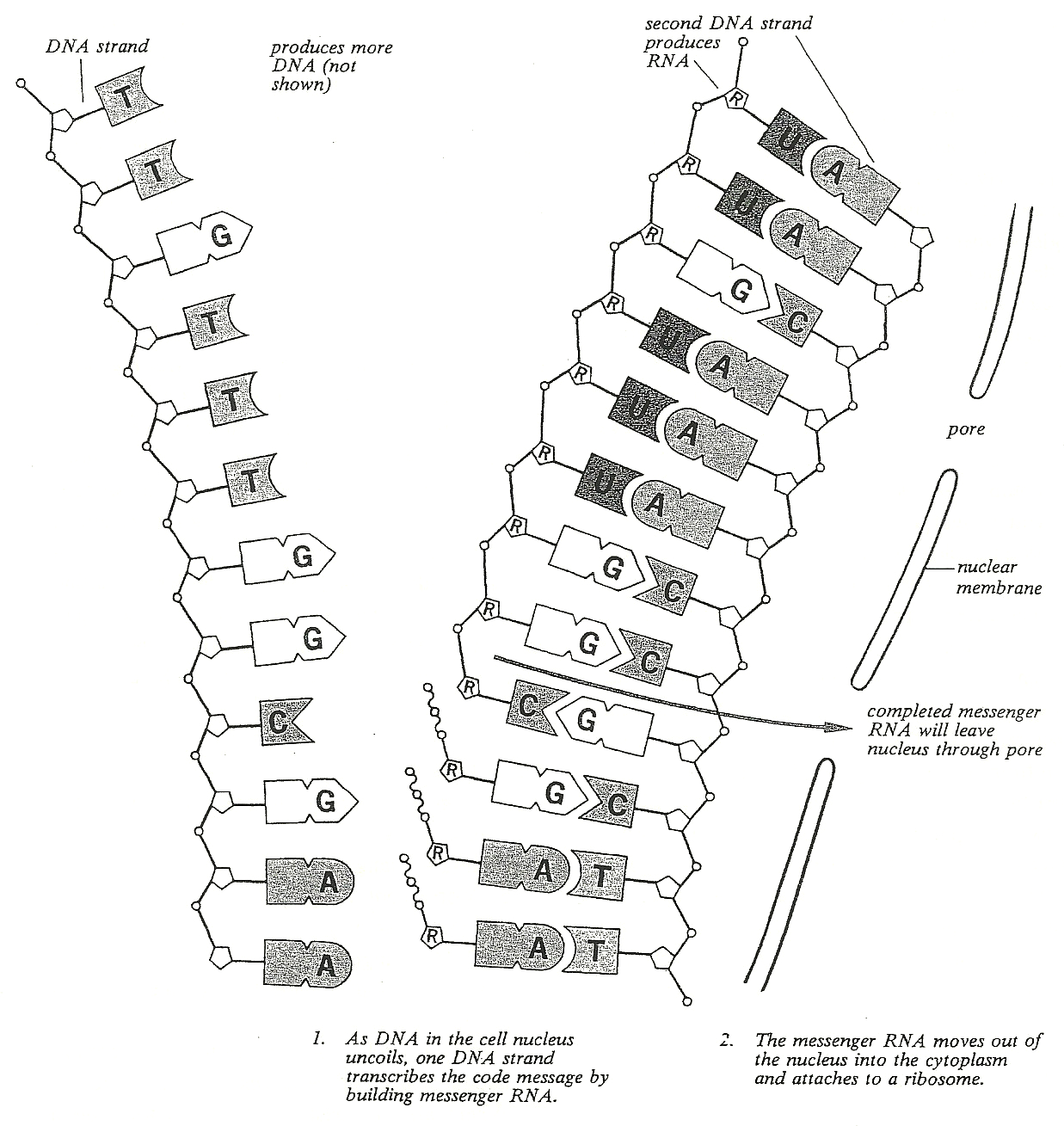
**mRNA codons and the amino acids for which they code**

**Building Protein Molecules**

We are now ready to bring together the knowledge about protein synthesis and the DNA code to see how the process occurs in cells. Step 1 has already been discussed in more detail above. Other steps will now be discussed for the first time. Beginning with the DNA, here is our understanding of the process. Each step is made possible by the action of specific enzymes.

**1.** The instructions for forming new proteins are coded in the DNA molecules in the nucleus. These instructions are transcribed (copied) when a particular gene (section of the DNA coding for one protein) is unzipped by an enzyme. RNA nucleotides match up to the exposed region of the DNA molecule and another enzyme bonds these nucleotides together to form a strand that is now called messenger RNA or mRNA. The DNA may close back up or more mRNA molecules can be formed. (**Fig. 15**)

**X**



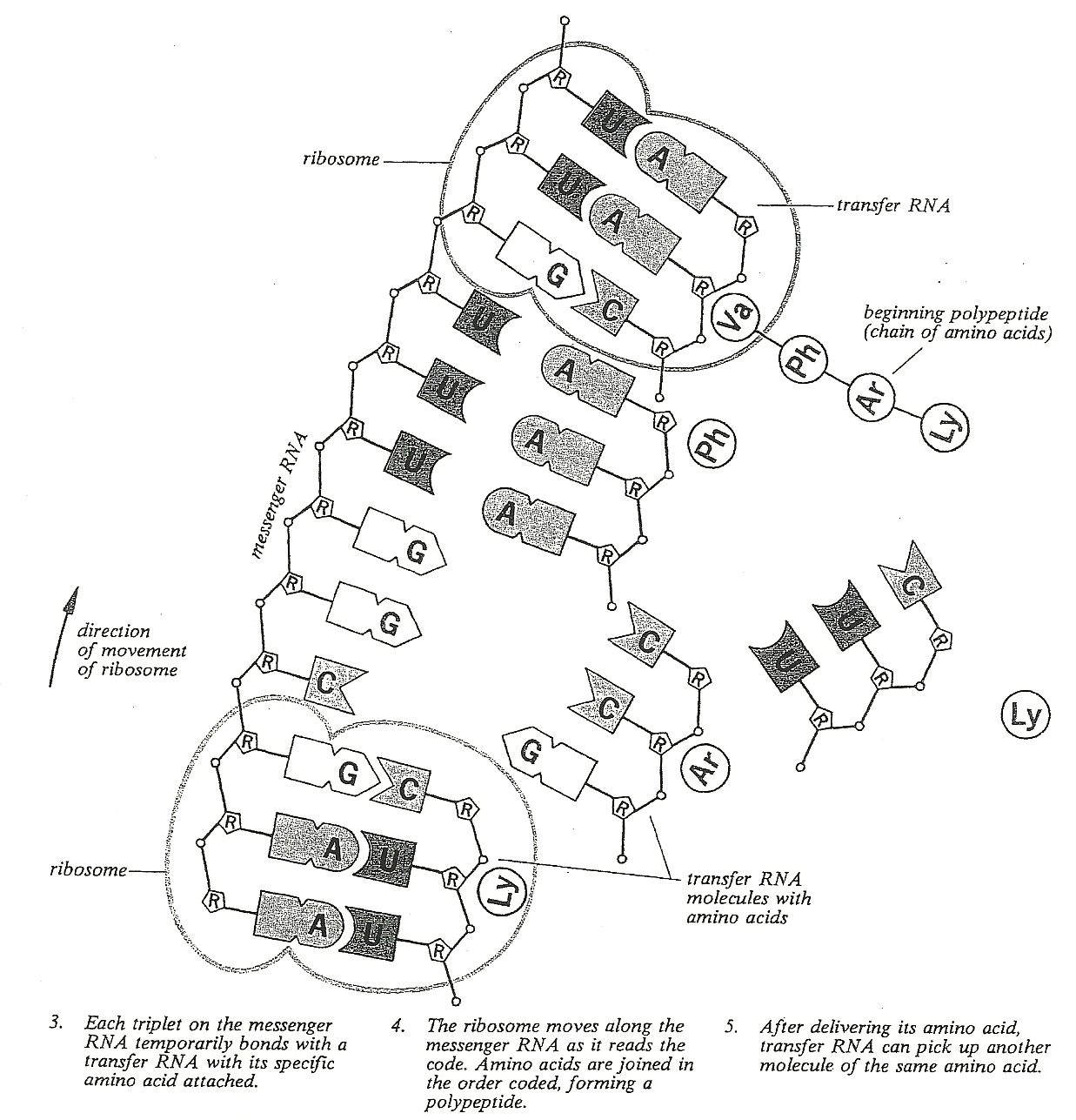
**Fig. 15**

**2.** The mRNA carries the instructions from the nucleus through pores in the nuclear membrane to ribosomes in the cytoplasm. In the ribosomes, a protein will be made from amino acids following the instructions given in the mRNA.

**XI**

3. Amino acids are found throughout the cytoplasm. They are carried to the ribosomes by special RNA molecules called **transfer (or “taxi”) RNA**, or **tRNA**. Each tRNA has 3 nucleotides and a unique shape that fits with a specific amino acid. Since there are 20 different amino acids there must be at least 20 different tRNA’s, one for each amino acid. The 3 bases of the tRNA temporarily attach to complementary three base sequences on the mRNA at the ribosome. Enzymes bond the amino acids carried by the tRNAs together and a chain of amino acids begins to form. When all specified amino acids have been added a complete protein or polypeptide has been built (**Fig.** **6**).

**XII**

4. The synthesis of a peptide chain thus occurs as the ribosome moves along the mRNA reading its code and matching up with tRNA’s carrying amino acids in the sequence specified. (**Fig. 16**)

**XIII**

**Fig. 16**

5. tRNAs, after delivering their amino acids, are free to go once again and pick up another of their specific amino acids from the cytoplasm. (**Fig. 6**)

**XIV**

The complexity of the process of protein synthesis may surprise you. This complexity is believed to be nature’s insurance against errors in carrying out the genetic instructions in the DNA. Even the misplacement of a single amino acid out of several hundreds or thousands in a protein can change its shape and thereby alter its function. Depending on the role of that protein in the organism this can have devastating, even lethal, consequences

**XV**