The impact of high-speed computers with large memories on the exploration business was substantial even before the advent of stratigraphic techniques. A typical seismic record contains about 2 million bits of information, and an exploration ship may take 60 records per mile all along a line that is part of a grid. By the time the whole grid has been covered, so that a three-dimensional picture of a region can be built up, the amount of data is truly phenomenal and its analysis would be impossible without modern computers. Interestingly enough, however, practitioners of seismic analysis report that it takes little more computer time to do a bright spot analysis than to do the cruder structural analysis. All in all, the effort amounts to the largest and perhaps the most sophisticated exploration of the earth's crust that geophysicists have yet undertaken.

Academic seismologists have for the most part had little to do with stratigraphic analysis of the bright spot type. For one thing, interest in plate tectonics has led to a focus on techniques applicable to exploration in deep water rather than the shallower offshore areas of the continental margin. For another, multichannel digital amplifiers are expensive, $160,000 for one instrument alone and more than $0.5 million to outfit a ship with all the needed gear. University research laboratories are just now beginning to put this equipment in use. But interest is growing. Some researchers have noted the potential overlap of the bright spot technique and those used in earthquake prediction despite the fact that crystalline rather than sedimentary rocks are involved. The zone of swollen, dilatant rock thought to surround a fault prior to a quake is, like a gas reservoir, characterized by an anomalously low value for the speed of sound. Others think that still more can be done to extend the bright spot technique itself. They note that so far only compressional seismic waves are used, and propose that shear waves may also find a use. It seems clear that digital data-gathering techniques and stratigraphic analysis will find uses outside the oil industry.

—ALLEN L. HAMMOND

Control of Protein Synthesis (I): Poly (A) in the Cytoplasm

One of the most enigmatic substances in cells of higher organisms is polyadenylate [poly(A)], a nucleotide sequence believed to play an important, but as yet unknown, role in protein synthesis. Recent experiments have provided evidence that poly(A) is associated with those intracellular events leading to protein synthesis that take place in the cytoplasm. These experiments have brought into question existing views about the role of poly(A) and have led to the advancement of several new hypotheses.

When proteins are synthesized in cells of higher organisms (eukaryotes) a portion of the cell's DNA is transcribed into a collection of RNA molecules. A sequence of poly(A) consisting of about 200 nucleotides is then added to one end of certain of those RNA molecules. Next, some of the RNA molecules that contain poly(A) are transported through the nuclear membrane to the cytoplasm. Those RNA molecules that enter the cytoplasm are called messenger RNA's (mRNA's). The mRNA molecules in the cytoplasm are translated into specific proteins. While they are in the cytoplasm, their poly(A) sequences gradually become shorter until they consist, on the average, of about 100 nucleotides.

The gradual decrease in the lengths of poly(A) sequences in mRNA's was first noticed about 2 years ago, but only recently have investigators shown that adenylate can be added to mRNA molecules in cytoplasms. This phenomenon has now been demonstrated in four kinds of cells with three different experimental techniques. Since many investigators had previously believed that adenylate is only added to RNA molecules in the nucleus of a cell and had based theories of the function of poly(A) on this belief, the details of these experiments are of more than ordinary interest.

The addition of adenylate molecules to mRNA's in sea urchin embryos was demonstrated by I. Slater and D. Slater of the National Institute of Child Health and Human Development at Baltimore City Hospital. The unfertilized sea urchin egg has in its cytoplasm both mRNA's that contain poly(A) and mRNA's that lack poly(A). The Slaters showed that, upon fertilization, the mRNA's that lack poly(A) have poly(A) added to them and are subsequently translated.

In the Slaters' experiments, sea urchin eggs were fertilized and grown in the presence of two radioactive nucleotides: namely, adenosine, which would be incorporated into newly synthesized poly(A) molecules, and uridine, which would be incorporated into newly synthesized mRNA molecules. They showed that, just after fertilization, only the poly(A) portion of mRNA's in the eggs was labeled, and, hence, poly(A) was added to preexisting, rather than newly synthesized, mRNA's. Since they believe that preexisting mRNA's are only found in the cytoplasm, they interpret their results as indicating that poly(A) was added to mRNA's in the cytoplasms of the eggs.

R. Perry of the Fox Chase Center for Cancer Research in Philadelphia used a different technique to obtain evidence that he believes is consistent with the hypothesis that poly(A) sequences are synthesized in the cytoplasms, as well as the nuclei, of cells. Perry grew mouse L cells in the presence of radioactive adenylate and measured the rate at which the labeled adenylate appears in poly(A) sequences in the nucleus and in the cytoplasm. The initial rate of synthesis of poly(A) in the nucleus was considerably less than would be predicted if all poly(A) sequences in the cytoplasm originated in the nucleus.

J. Diez of the Children's Cancer Research Foundation in Boston together with G. Brawerman of Tufts University Medical School in Boston suppressed RNA synthesis in the nuclei of Chinese hamster cells and mouse sarcoma 180 ascites cells with actinomycin D in order to observe the addition of adenylate to poly(A) sequences in the cytoplasms of these cells. Since poly(A) is normally added to RNA molecules in the nucleus after transcription, blocking transcription greatly reduces the rate at which radioactive adenylate is added to nuclear poly(A) sequences. The rate of nuclear incorporation of radioactive adenylate is slow and linear for at least an hour after actinomycin D is added, an indication that the lengths of preexisting poly(A) se-

quences in the nucleus are gradually increased. The rate of incorporation of radioactive adenylate in the cytoplasm, on the other hand, is initially rapid; but eventually it slows down and decreases to zero when a steady state is reached. The steady state occurs, the investigators believe, when the rate at which the labeled adenylate molecules are added to poly(A) sequences in the cytoplasm reaches the rate at which they are removed as the poly(A) sequences are degraded.

The experiments of the Slaters, Perry, and Diez and Brawerman thus provide evidence that the addition of adenylate to RNA molecules is not confined to the nuclei of cells. Although poly(A) may be a regulatory agent for events that take place in the nucleus, such as the selection of RNA molecules to be transported to the cytoplasm and the passage of such molecules into the cytoplasm, several hypotheses concerning the role of poly(A) in the control of mRNA translation and degradation are being reevaluated. Of these theories, two have been shown to be incorrect, predictions from another have been verified, and others are as yet untested.

One hypothesis is that mRNA molecules with short poly(A) sequences are more likely to be degraded. This theory was proposed on the basis of the observation that poly(A) sequences decreased in length as mRNA molecules remain in the cytoplasm. By labeling newly synthesized mRNA's with one radioactive nucleotide and old mRNA's with another, Perry and his colleagues demonstrated that the degradation of mRNA molecules from each class is a random event. Thus the likelihood that an mRNA will be degraded does not increase with the age of the mRNA. The poly(A) sequences on the newly synthesized mRNA's consist of about 180 nucleotides, whereas those on the old mRNA's are much shorter and are often as short as 50 nucleotides.

A variation of the previous hypothesis is that mRNA's with poly(A) sequences may be more stable than those without them. This hypothesis can be interpreted in two ways. One interpretation is that mRNA molecules without poly(A) are translated inefficiently, if at all. Thus the probability that an mRNA without poly(A) would be translated would be small. A second interpretation is that mRNA molecules without poly(A) will be degraded sooner than those with poly(A). Over the lifetime of a cell, an mRNA with poly(A) would be translated many thousands of times, whereas one without poly(A) would be translated far fewer times.

The first interpretation of this hypothesis—that an mRNA molecule without poly(A) will be translated inefficiently—was tested by several groups of researchers, including Perry's group and a group headed by R. Williamson of the Beatson Institute for Cancer Research in Glasgow, Scotland. Perry and his colleagues compared the translations in vitro of a collection of mRNA's whose poly(A) sequences had been removed by an enzyme to those of a collection of mRNA's whose poly(A) sequences were intact. His group found no apparent differences in the amounts of protein synthesized by translations of the two classes of mRNA's. However, only two or three translations of an mRNA can occur in vitro.

Williamson and his associates performed experiments similar to those of Perry but with a specific mRNA—the mRNA that codes for rabbit globin—rather than with the whole collection of mRNA's in a cell. They interpret their results as indicating that, in vitro, the lack of poly(A) does not prevent translation of an mRNA molecule.

Poly(A) Confers Stability

Although mRNA molecules that lack poly(A) can still be translated a few times in vitro, experiments such as those performed by Perry and Williamson and their associates do not rule out the possibility that a different phenomenon may occur over the course of the thousands of translations of an mRNA that take place in living cells. Now, G. Huez and G. Marbaix of the University of Brussels in Belgium have designed an in vivo experiment with results that support the second interpretation of the hypothesis that an mRNA is translated more times when it contains poly(A) than when it does not.

Huez's group injected rabbit globin mRNA molecules into the egg cells of the African toad *Xenopus*. They detected translation of these mRNA's by measuring production of hemoglobin by these cells. (Hemoglobin is not produced by uninjected, normal *Xenopus* oocytes.) For the first hour after the mRNA's were injected, the *Xenopus* cells with globin mRNA molecules that lacked poly(A) produced as much hemoglobin as those with the globin mRNA that contained the poly(A). However, the rate of hemoglobin production in cells with the mRNA without poly(A) began to decline after the first hour until, 5 to 10 hours later, the rate of hemoglobin synthesis was only about half the original rate. Hemoglobin synthesis that resulted from translations of globin mRNA's that contained poly(A) continued at the initial rate for at least 48 hours after these mRNA's were injected into the *Xenopus* cells.

Most conjectures about how poly(A) might facilitate translation or prevent degradation of mRNA molecules are untested. Perry has proposed that there may be one or several critical periods in a cell's lifetime when all mRNA molecules that do not contain poly(A) are destroyed. He has shown that the destruction of poly(A)-containing mRNA's in a cell is apparently random. However, the mRNA molecules that are translated into histones are all destroyed at a certain time in the cell cycle. [Histone mRNA's lack poly(A).]

Brawerman believes that proteins associated with poly(A) sequences may be important to the function of poly(A) in cells. He postulates that poly(A) sequences of different mRNA's may have different proteins bound to them. When the protein dissociates from a given poly(A) sequence, the corresponding mRNA would be destroyed. Although both Brawerman and Gunther Blobel of Rockefeller University in New York have found that cytoplasmic poly(A) sequences have proteins bound to them and that apparently only one protein is bound to a given poly(A) sequence, these proteins and their relation to poly(A) sequences are as yet uncharacterized.

While these conjectures about how poly(A) affects the translation of mRNA molecules remain unresolved, many believe that they may lead to some testable predictions. However, before an understanding of the role of poly(A) in the control of protein synthesis is obtained, the problem of explaining why adenylate is added to and removed from poly(A) sequences in the cytoplasm must be solved. Much attention is now focused on the cytoplasms of cells since here, it is believed, the discovery of the role of poly(A) may provide the most useful new insight into the control of protein synthesis.—GINA BARI KOLATA

Additional Reading

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