process would be much cheaper. Scientists working in the laser isotope separation project at Livermore are now analyzing a range of uranium compounds, probably including some newiy synthesized ones. The problem is to find a molecule with excited states that are less dense and overlap less than the states of uranium hexafluoride. For example, UF_5Cl might have a simpler spectrum than UF_6 because the replacement of one fluorine atom with chlorine would alter the molecular symmetry.

Besides the corrosiveness of uranium vapor, another problem with the Livermore process is that it is not very efficient. After the uranium vapor is produced in an oven "based on novel properties of uranium alloys," according to Snavely, it is illuminated with laser light at 5915.4 Å, a wavelength at which ^{235}U is relatively opaque but ^{238}U is transparent. (The corresponding absorption in ^{238}U occurs 0.1 Å lower.) At the same time, the stream of uranium vapor is bathed with an intense flood of ultraviolet light from an arc lamp (wavelengths 3000 Å or longer). The ultraviolet light is sufficiently energetic to ionize the ^{235}U atoms excited by the laser, but not the ^{238}U atoms. The ionized atoms are then deflected by an electric field and collected. One factor contributing to the inefficiency of the process is that the likelihood for the second step in the process to occur is three to four orders of magnitude less than for the first step. Another thing that tends to reduce the amount of ^{235}U actually produced is that the ionized atoms can become neutralized by collision with other gases, particularly ^{238}U, and thereby lose the charge identification tag that makes them separable. Excitation of the fissile isotope of uranium seems to be the easy part of an enrichment scheme. Keeping the excited molecules from transferring their energy before some physical or chemical process can be applied to isolate them appears to be more difficult.

Various processes besides the two-step ionization method can be used to separate isotopes, but they are not necessarily applicable to uranium compounds. V. S. Letokhov and R. V. Ambartzumian, at the Soviet Institute of Spectroscopy, Moscow, have reported separating ^{15}N from ^{14}N when the two isotopes are present in ammonia, by preferentially dissociating $^{15}NH_3$ with a two-step process. (The first photon excites NH_3 and the second dissociates it.) Researchers at Los Alamos recently reported success with the same technique for separating boron isotopes in BCl_3. In a two-photon process, photodissociation has the advantage over photoionization that the likelihood for absorption of the second photon is not so drastically suppressed. In some cases one-step dissociation is possible, however, so the problem of getting the second photon to be absorbed is circumvented. One-step dissociation of the deuterated component (D_2CO) of natural formaldehyde, which includes both H_2CO and D_2CO, was accomplished by C. B. Moore and E. S. Yeung at the University of California, Berkeley, and more recently Moore and Stephen Leone produced HBr enriched in the isotope ^{81}Br by a one-step dissociation of natural Br_2.

Another possibility is to find a chemical reaction that will proceed rapidly with the laser-excited molecules but not with the rest. So little is known about the chemistry of excited molecules that this approach has not yet been followed, but it could prove to be the cheapest method of laser enrichment.

Still another method is to try to make use of the small deflection undergone by the molecules that preferentially absorb laser light in order to separate them from the rest. A. Bernhardt and associates at Livermore recently showed that some separation of barium isotopes could be achieved by resonant scattering of laser light. A. Szoke at the University of Tel Aviv, Israel, and I. Nebenzahl have amplified this idea by suggesting that the laser light be reflected back and forth through the beam of vapor (uranium, for instance) several times. If the uranium vapor itself could be made to lase, absorbing a photon in one pass and reemitting it by stimulated emission on another pass, the deflection of the uranium atoms would be magnified, and in fact it might be possible to deflect more than one uranium atom per photon.

Almost all laser isotope separation schemes depend heavily on the detailed spectroscopic structures of molecules, first for finding suitable absorption frequencies and then for designing ways to physically separate the two species. Generally speaking, spectroscopic information with the resolution needed is not available in the literature, and can only be obtained by laser experiments. The best method, according to Snavely, will most likely be one that is particular to uranium, rather than a method generally applicable across the periodic table.

The AEC laser isotope separation program has been expanding rapidly in scope since it began in 1971. The Los Alamos program, called Project Jumper, has a staff of 90 and a budget of $5.6 million for fiscal 1975. Livermore's funding during the same period will be $3.1 million, and the staff will be at least 40. Only about a year ago, the total AEC research budget for laser isotope separation was said to be just over $1 million. At both laboratories, the laser enrichment programs are embedded in the much larger and also expanding laser fusion programs. They undoubtedly draw intellectual if not material support from the $66 million fusion efforts. One can surmise that laser enrichment efforts are not being expanded so rapidly without some solid progress in the research, although this could not be published in the scientific journals because most work on uranium enrichment is classified. A successful laser process for uranium enrichment could bring a bonanza to U.S. industry, if not a wealth of cheap energy, and some scientists are predicting that the AEC laser enrichment program will prove successful long before laser fusion does.—WILLIAM D. METZ

Control of Protein Synthesis (II): RNA in the Nucleus

Although the cytoplasm is the site of protein synthesis in the cell, new evidence tends to support the notion that large RNA molecules in the cell nucleus have a role in regulating protein synthesis. Moreover, results from recent experiments indicate that fragments from these large RNA molecules in the nucleus may be a source of messenger RNA's (mRNA's) that carry genetic information to the cytoplasm.

In the 10 years since the large RNA molecules in the nucleus were discovered, investigators have tried to determine whether some of those molecules are precursors for mRNA's. Experiments to test this hypothesis directly with radioactively labeled nuclear RNA, however, have failed to solve the problem. But investigators have been able to show that nucleotide sequences of certain mRNA's occur in the large RNA's of the nucleus. These results are consistent with, but do not prove, the hypothesis that mRNA's are derived from large nuclear RNA's.

In one group of experiments, de-

signed to show that mRNA sequences are found in large nuclear RNA's, R. Wall, then at J. Darnell's laboratory at Columbia University in New York, and his associates, studied mRNA's that are translated into proteins of a virus. They used cells in which the DNA of a virus had become integrated into the cells' DNA and found that sequences copied from viral DNA are part of large nuclear RNA molecules. Those same viral sequences are found in the cytoplasm as mRNA's.

The experiments by Wall and his colleagues were possible because the DNA from a virus can be isolated and can serve as a molecular probe for viral sequences that are part of RNA molecules. If an RNA molecule is copied (transcribed) from a DNA segment that includes viral DNA, it will contain sequences that are complementary to the viral DNA. When viral DNA and either nuclear RNA molecules or mRNA's from the cytoplasm are mixed together, the viral DNA will bind to complementary sequences on the RNA's

Unfortunately, it is much more difficult to ascertain whether mRNA molecules that are translated into cellular—as opposed to viral—proteins are present as part of large nuclear RNA molecules. Individual cellular mRNA's are generally present in such minute quantities that it is impossible to identify specific mRNA sequences. However, there are several exceptions to this phenomenon. For example, duck globin mRNA is present in large quantities in duck immature red blood cells (reticulocytes). Thus this mRNA can be isolated, making it possible to do experiments similar to those with viral mRNA sequences.

Two groups of investigators, T. Imaizumi and her colleagues at the laboratory of K. Scherrer at the Swiss Institute for Cancer Research in Lausanne and M. Macnaughton and his colleagues at J. Bishop's laboratory at the University of Edinburgh in Scotland, have shown that the sequence of duck globin mRNA is present in large RNA molecules in the nuclei of duck reticulocytes. The two groups agree that these nuclear RNA molecules are larger than globin mRNA's, although the question of their actual size is open to debate. They were able to synthesize a molecular probe for this mRNA sequence by isolating the mRNA and transcribing it with an enzyme—a reverse transcriptase—into a DNA molecule that is complementary to it. Like the viral molecular probe, these DNA molecules will bind to sequences of nuclear RNA molecules to which they are complementary.

Role of Large RNA's

Assuming that large RNA molecules in cell nuclei are indeed converted into mRNA molecules, H. Abelson, L. Johnson, and their associates at the laboratories of H. Green and S. Penman at the Massachusetts Institute of Technology in Cambridge have conjectured that this posttranscriptional modification is involved in the control of protein synthesis. They arrive at this conjecture from a comparison of rates of RNA synthesis and degradation in resting and growing cells. Mouse fibroblast cells that were not dividing were exposed to an environment in which they began to grow rapidly. During the transition between rest and active growth, a great deal of mRNA accumulated in the cytoplasms of these cells. However, with the exception of ribosomal and transfer RNA's which do not contain mRNA precursors, there was no corresponding increase in the amount of RNA being synthesized in the nuclei of the cells, and there was no change in the rate of degradation of mRNA molecules when the cells began to grow rapidly. Thus, these investigators conclude, the rate at which mRNA appears in the cytoplasms of these cells is most likely regulated by the rate at which RNA in their nuclei is processed to mRNA.

One way to study the formation of mRNA from nuclear RNA is to study the structure of nuclear RNA molecules that contain polyadenylate [poly(A)]. This nucleotide sequence is found on one end of both mRNA molecules and certain large RNA molecules in the nucleus. Thus it is presumed by many investigators that nuclear RNA's that contain poly(A) include precursors of mRNA's.

G. Molloy and his colleagues in Darnell's laboratory find that molecules from a collection of poly(A)-containing nuclear RNA's bear a structural resemblance that may provide clues to the way they are degraded. Such molecules contain double-stranded loops and stems near what may be the junction between the mRNA section of the molecule and the remainder of the molecule. The longest of these nuclear RNA's also have sequences consisting of uridylate molecules (that is, oligouridylate), each about 30 nucleotides long, that are located at the end of the molecule opposite to the end where the poly(A) is located and, presumably, where the mRNA sequences are located. Molloy proposes that these structural features may be recognized by enzymes that break up nuclear RNA's.

It may be possible to examine the fate of nuclear RNA molecules that contain mRNA sequences by isolating these molecules from cell components not directly involved in the formation of mRNA's, thereby obtaining nuclear RNA's before they are degraded. For example, W. Jelinek of Columbia University plans to study RNA in vitro. He has succeeded in synthesizing RNA from purified cell nuclei. Poly(A) is added to a subset of these molecules just as it is added in vivo. Jelinek has found no indications that RNA transcribed in vitro differs from that transcribed in vivo.

Another approach to studying nuclear RNA molecules in isolation from the rest of the cell is being taken by Penman and his associates. Penman and his group have isolated a subset of nuclear RNA that contains 50 percent of the poly(A) in the nucleus but only 10 percent of the RNA. This subset does not contain the largest nuclear RNA molecules; rather, it contains only those that are two to three times the size of mRNA molecules. This subset differs from the remainder of nuclear RNA in ways that cause Penman to suggest that it may indeed consist of mRNA precursors. For example, when cells are exposed to a drug that prevents the addition of poly(A) to nuclear RNA's, all the poly(A) on molecules of this subset disappears, whereas the poly(A) remains on other nuclear RNA's. Others have shown that, if the addition of poly(A) to nuclear RNA is blocked by this drug, no new mRNA molecules appear in the cytoplasm.

According to Penman, studies of the nuclear RNA are now complicated by the discovery by Bishop and his colleagues that there are three different classes of mRNA. Each class consists of about one-third of a mammalian cell's mRNA molecules, but one class consists of about 17 different mRNA sequences (molecules transcribed from about 17 different genes), one has about 350 different sequences, and the third has about 35,000 different sequences. The recognition of this phenomenon, namely that different abundance classes of mRNA's exist, may influence the interpretation of research on nuclear RNA's and the relation of nuclear RNA to the control of protein synthesis.

—GINA BARI KOLATA