

this meeting his opponents were distinctly subdued, especially after his allied concept of the megalithic yard had received Professor Kendall's blessing.

Some at least of the participants also felt that the meeting took on a life of its own, as an unintended (and therefore all the more sincere) tribute to those nameless but ingenious proto-scientists of antiquity: the Babylonians and Egyptians who gave us our timing systems; the Polynesian navigators; the neolithic European engineers and miners; the Maya, who timed Venus so exactly; and, perhaps most of all, the ancient Britons who found how to measure the lunar inclination. Although presumably illiterate, they seem to have developed methods of astronomical measurement fundamentally much more accurate than any devised by an ancient literate society.

#### PROTEIN SYNTHESIS

### End of Message

from our Molecular Biology Correspondent

In a fast moving field, like control of eukaryotic protein synthesis, there is a tendency to make a little, in the way of results, go a long way. New discoveries do not in consequence hit the literature with a solid and reassuring thud that draws the reader's attention, but come instead in the form of a continuous spatter of grapeshot. This makes all efforts to keep abreast of progress doubly irksome, yet from time to time some small advance may actually be discernible from the outside. An interesting aspect, about which there has been a considerable effusion of articles in the past year or two, is the run of polyadenylic acid, which seems to occur at the 3'-end of nearly all eukaryotic messengers, is not translated, and has no obvious function. Now Kwan and Brawerman (*Proc. US Nat. Acad. Sci.*, **69**, 3247; 1972) have found evidence that it is the anchoring point of some at least of the protein that accompanies the messenger into the cytoplasm and on to the polysomes, and stays with it when it is dissociated from the polysomes by treatment with EDTA for example.

The poly A segment is easily enough prepared from the isolated (protein-free) messenger by treatment with pancreatic ribonuclease and sediments at about 4S. Working with the ascites cell system, Kwan and Brawerman find that the particle remaining, after an extensive nuclease digestion of the polysomes, sediments at 12-15S, and when deproteinized with detergent yields the 4S poly A fragment. Its complement of proteins has not evidently been picked up from the debris of polysomes and degraded messenger, for the poly A

piece derived from  $^{14}\text{C}$ -labelled messenger, digested with nuclease in the presence of tritium-labelled polysomes did not generate a 15S particle. (Some interaction with the protein mixture does nevertheless occur, for a fraction sedimenting somewhat faster than 4S seems to be generated.) The inference is that the poly A end of the messenger does indeed carry proteins. These are sufficient to afford the poly A at least partial protection against the A-specific  $\text{T}_2$ -ribonuclease. The poly A, or a part of it at least, is yet sufficiently unimpeded to form a complex with added polyuridylic acid.

The functional relevance of these results, of course, remains unexplained, for nothing is in fact known about the role of the messenger-bound proteins, neither does the fact of their association with the poly A end throw much light on any role that this may have in the process of messenger migration. Moreover, Kwan and Brawerman have not ascertained whether the protein fraction in the poly A particle accounts for all the recognizable proteins that are carried by the messenger. The high sedimentation rate (30-150S compared with 10-30S for the messenger RNA alone) of the messenger-protein complex, and its high buoyant density, indicate, as Kwan and Brawerman point out, that it may not.

When cells in culture are treated with 3'-deoxyadenosine, the turnover of messenger largely ceases, and it now seems, from some results of Adesnik *et al.* (*J. Mol. Biol.*, **71**, 21; 1972), that this may arise from a disturbance in the mechanism of grafting the poly A onto the newly transcribed messenger RNA. The deoxyadenosine does not bring

about the complete disappearance of messenger: the concentration of a nucleotide label in the product of EDTA-dissociation of the total polysomes indicates that the messenger content of the cytoplasm is 10-20 per cent of the normal level. Of this some 70 per cent binds to captive poly U, covalently attached to a column matrix, and is little different from the fraction that binds in normal cells. It thus seems that the poly A is present in the existing messenger. After nuclease digestion, however, the total proportion of nucleotide retained on the poly U column was a good deal less than that from normal messenger. Analysis by polyacrylamide gel electrophoresis of this nuclease-resistant residuum showed that the messenger in the polysomes of the poisoned cells had a smaller and more polydisperse complement of poly A than that of normal cells.

The abnormal messenger is, all the same, incorporated into polysomes to the normal extent. A chase experiment with actinomycin, which stops all RNA synthesis in the nucleus, indicated that the 3'-deoxyadenosine operates by preventing the migration of messenger into the cytoplasm. It is known to inhibit the incorporation of A residues into RNA, so that one may suppose that it strangles the supply of nucleotides needed for the addition of poly A to the completed messenger, and further that a critical length of poly A is indispensable for the transport process. It would be of some interest to establish whether this might not also be the length required for the retention of one or more of the proteins that, according to the results of Kwan and Brawerman, travel on the poly A.

### What Generates the Cohesive Ends of Lambda?

DURING various stages of the life cycle of bacteriophage lambda the circular duplex DNA genome of the phage is converted into a linear duplex molecule which, because of its cohesive ends, can return to its circular duplex form. Several pieces of evidence indicate that these changes are neatly achieved by introducing single chain scissions, staggered by twelve bases, in the complementary strands of the circular duplex DNA. But what endonuclease, or endonuclease complex, presumably specified by the lambda genome, is responsible for this specific nucleolytic attack? This question has yet to be fully answered, but experiments reported in *Nature New Biology* next Wednesday (January 3) by Wang and Kaiser indicate that a product of the lambda gene A is required.

Using a biological assay system for linear lambda DNA molecules, Kaiser and Wang have shown that extracts of

*Escherichia coli* infected with wild type lambda contain an activity which *in vitro* will convert circular monomeric and dimeric lambda DNAs into linear molecules with cohesive ends. This reaction depends on a supply of ATP, which is a characteristic requirement of many endonucleases. Furthermore, it also depends on an activity specified by gene A—extracts of cells infected with lambda carrying a mutated gene A or a gene A deletion do not convert circular DNA into linear DNA.

The A gene product required for this reaction is almost certainly a protein because it is temperature sensitive and because amber mutants of the A gene have been isolated. Wang and Kaiser suggest, from these and other data, that the A gene product is a specific endonuclease responsible for generating cohesive ends, but proof that this is the case will depend on the isolation and purification of the gene A protein.