VIROLOGY

Inside Adenoviruses

from our Cell Biology Correspondent

THE elegant electron micrographs of core structures isolated from adenoviruses, which are published in the latest issue of the *J. Mol. Biol.* (**37**, 379; 1968) by Laver, Pereira, Russell and the late Robin Valentine, of the National Institute for Medical Research at Mill Hill, will surely convince even the most dyed in the wool sceptics that these viruses are not simply a nucleic acid molecule wrapped up in coat protein. They also give some indication of the extent of the loss to the Mill Hill laboratory and to molecular biology in Britain caused by the sudden death of Valentine.

The paper in *J. Mol. Biol.* is in essence a description of the methods developed by the group for isolating the cores which consist of a family of proteins in association with the viral DNA. It contains, however, a few preliminary results about the properties of these core proteins, and in a recent issue of *Nature* (**219**, 1127; 1968) Russell, Laver and Sanderson reported on their chemistry. It appears that the core proteins have several properties in common with the basic protamines, which characteristically occur associated with the DNA of sperm, and also with the F^3 arginine rich histones of higher organisms.

The core proteins, like the arginine rich histones, contain about 15 per cent of arginine, can be extracted with an acid ethanol solvent system and are precipitated by absolute ethanol; furthermore, both groups have the same major N-terminal amino-acid, alanine. On the other hand, two of the core proteins, separated by polyacrylamide gel electrophoresis, are devoid of tryptophan and much richer in arginine than the others. These two may be more closely related to the protamines than the arginine rich histones. All this does not, of course, mean that the core proteins are identical to histones or protamines. Preliminary analyses of their total amino-acid composition have apparently revealed that they contain less of the other two basic amino-acids, lysine and histidine, than the protamines and histones. Nonetheless, the obvious interpretation of the core proteins is that they have the same role as histones in higher organisms. If this can be established, then the core proteins of adenovirus will provide a comparatively simple model system in which to study the basic questions of the interactions of nucleic acids and basic proteins. And if the definition of a chromosome is an association of nucleic acid and basic protein, then adenovirus may be said to have a true chromosome.

One of the first questions that has yet to be answered is whether or not the core proteins are specified by viral genes or derived from host cell components. Serological experiments indicate that the core proteins are at least induced by the virus after infection, but that says nothing of their genetic specificity.

PROTEINS

Functions of Transfer Factors

from our Molecular Biology Correspondent

THE recent successes in separating the steps involved in protein synthesis, and identifying the components implicated in them, offer hopes of understanding more precisely the function of metabolically active substances. An interesting result on these lines was the evidence adduced last year by Collier that diphtheria toxin acts on mammalian cells by inactivating one of the supernatant transfer factors, transferase II.

Johnson *et al.* (*J. Bact.*, **96**, 1089; 1968) have elaborated this discovery, using cell-free systems from toxin-susceptible guinea-pig and resistant rat liver. In both cases protein synthesis was strongly inhibited by the toxin, but only in conjunction with NAD. A bacterial system was by contrast unaffected. Experiments with heterologous systems from bacteria and mammalian cells confirmed that the site of action of the toxin is in the soluble fraction of the latter, and not in the ribosomes. Moreover, in the rat liver system, with poly U as messenger, they found that the addition of phenylalanyl-*t*RNA does not reverse the action of the toxin, which must therefore operate at a later stage in peptide bond formation. NAD is found to be absolutely required for inhibition, and is entrapped together with the transfer factors, transferase I and II, in the floccules formed when antitoxin is added to the entire system.

The rest is more speculative: the toxin, which is a protein of molecular weight 74,000, is thought to bind to transferase II without any detrimental effect on its function. The NAD, which does not become reduced and is not therefore functioning in its normal mode, is thereby enabled somehow to form a ternary complex with both the transferases so that their function is destroyed. A final point is the response of the cells from the resistant animal to the toxin: the resistance is evidently a question of selective permeability of the cell membrane.

Two further studies on the function of the same transferases come from Skogerson and Moldave (*J. Biol. Chem.*, **243**, 5354 and 5361; 1968). It has been found that preincubation of ribosomes with isolated transferase II, together with a thiol and GTP, enables them to catalyse the aminoacyl-transfer reaction when transferase I, GTP and aminoacyl-*t*RNA are added, no further transferase II being then required. Evidently the ribosomes are somehow prepared to receive the aminoacyl-*r*RNA, perhaps by virtue of translocation of the incumbent peptidyl-*t*RNA from the aminoacyl to the peptidyl site. Once translocation has occurred, only transferase I is needed for the formation of a peptide bond with the new aminoacyl-*t*RNA.

The transfer factors of micro-organisms differ in a number of respects from those of animal cells. Active factors, termed G, T_u and T_s, were identified in *E. coli* in Lipmann's laboratory, and experiments on heterologous systems, notably yeast and *E. coli*, showed that yeast transfer enzymes appeared to be incompatible with *E. coli* ribosomes. Attempts have been made to localize the source of the species specificity, and Ciferri *et al.* (*J. Mol. Biol.*, **37**, 529; 1968) have now tested the ability of *E. coli* ribosomes to incorporate phenylalanine in the presence of fractionated yeast transfer enzymes. It seems that the yeast G and T_u factors will function in the *E. coli* system, but that T_s is strictly specific for its own ribosomes. Since T_u and T_s function by forming a ternary complex with GTP, which is able to interact with the aminoacyl-*t*RNA, Ciferri *et al.* suggest that T_s may well be responsible for the recognition process by which the aminoacyl-*t*RNA enters its site on the ribosome.