NEWS AND VIEWS

Nucleic Acids and Interferon

THE discovery of a new type of double-stranded RNA (page 940, this issue) has two important implications. First, the new RNA may play a part in the induction of interferon production—interferon is the protein, discovered at the National Institute for Medical Research, Mill Hill, by the late Dr Alec Isaacs, which has the property of inhibiting the replication of a wide range of DNA and RNA viruses in animal cells. Second, it may mean that virologists will have to modify their ideas about the way in which DNA viruses replicate in mammalian cells.

Viral infection can induce infected cells to produce interferon which is a defence against the virus. Both DNA and RNA viruses share this property, but all attempts to track down the active principle introduced by the virus have led to the conclusion that the inducer is double-stranded RNA. Neither single nor double-stranded DNA nor single-stranded RNA have much capacity for interferon induction. For the past two years, this result has puzzled virologists because, although DNA viruses induce interferon, there has been neither reason to assume nor evidence to suggest that DNA viruses manufacture double-stranded RNA during their replicative cycle.

Colby and Duesberg, however, now report that the DNA vaccinia virus does make a viral specific double-stranded RNA during growth in cultured chick cells. They infected chick cells with vaccinia and simultaneously fed either radioactively labelled uridine (to pick out newly synthesized RNA) or labelled thymidine (which indicated newly synthesized DNA) and then extracted and fractionated the nucleic acids of the infected cells. About 3 per cent of the RNA labelled by uridine turned out to be resistant to digestion by ribonucleases. This property is characteristic of double-stranded RNA. This interpretation is borne out by the chromatographic properties of this fraction, its resistance to digestion by deoxyribonucleases, its density as measured by density gradient centrifugation and by the fact that heating to 100° C, which destroys the double-stranded structure of DNA, makes the nucleic acid sensitive to RNase.

Hybridization experiments with vaccinia virus DNA prove that the double-stranded RNA is specified by the vaccinia genome, and it seemed that at low concentrations this RNA can induce the production of interferon and, moreover, that the ability to do so is lost when it is converted to single-stranded RNA by heating to 100° C. All these experiments indicate that a DNA virus can synthesize a double-stranded RNA (or at least an RNA which after extraction from the cells by a technique which removes all protein is double-stranded) which induces interferon. It is important to add this proviso because Colby and Duesberg's experiments do not prove that the RNA is double-stranded in the cell and work on RNA bacteriophages has shown that single-stranded RNA may be converted to a double-stranded form during extraction.

Saying that, of course, in no way minimizes the work of Colby and Duesberg, which seems to prove that DNA viruses induce interferon by way of an RNA molecule. It also raises an interesting question about DNA virus replication; if, as seems likely, it turns out that the RNA they have isolated is in fact double-stranded *in vivo*, what is its function in viral multiplication? There is no obvious reason why replication of a DNA virus should involve the production of a double-stranded RNA. But another observation made by Colby and Duesberg, which confirms experiments published last year by Montagnier, is that even uninfected animal cells contain a small proportion of RNA which is double-stranded after extraction. All this suggests that double-stranded RNAs are more widely distributed than has previously been realized. So far, there is not much to suggest what they may do.

MYOSIN

Off with its Head

from our Molecular Biology Correspondent

THE construction of the myosin molecule is now broadly agreed: it consists of a long shaft, terminating at one end in two globular heads. This end also probably contains two small polypeptide chains, which are liberated on denaturation. The results of a detailed study of the gross structure of the molecule are reported by Lowey *et al.* (*J. Mol. Biol.*, **42**, 1; 1969).

Proteolytic enzymes cleave the molecule at a region in the rod, giving rise in the first instance to light and heavy meromyosin, which are respectively a section of the rod, and the truncated remainder, bearing the two heads. Further proteolysis can cause the heads to become detached, and in this state they are known as subfragment-1. By using papain for the proteolysis, it is possible to isolate not only subfragment-1, but also subfragment-2—the rod-like part of heavy meromyosin—without the formation of any substantial low molecular weight debris. Moreover, when digestion is carried out on precipitated, filamentous myosin, cleavage of the rod is inhibited, so that the molecule is merely made shorter by a head. The subfragments-1 are liberated and intact rods remain.

It is now possible to define the size of the various constituents with good precision, for all the fragments turn out to be remarkably homogeneous. Molecular weights have been determined by sedimentation equilibrium, and the lengths in the electron microscope have been measured. In all cases the weight-average and number-average lengths are essentially identical. Measurements on 300–600 molecules have shown that the length of the shaft in intact myosin is the same as that of the isolated rods, namely, 1350 Å, subfragment-