NEWS AND VIEWS

Antigens Unmasked

EVEN the most imperceptive observer must have realized that research into the structure, composition and function of cell membranes is very much in vogue. Numerous molecular biologists, bored with *E. coli* and its viruses, can be found toying with red blood cells, retina, synapses and the like, all of them materials which only two or three years ago were strictly left to the physiologists. At the same time tumour virologists are beginning to pay increasing attention to the changes in the cell surface that accompany the transformation of cells by oncogenic viruses. It is now clear that transformation by the small DNA viruses SV40 and polyoma, the genomes of which specify probably less than ten proteins, results in surprisingly complex changes in the surface antigens of the transformed cells.

One of the more interesting ideas that has emerged to account for the complexity of these changes is that SV40 and polyoma viruses somehow induce the specific uncovering of antigenic components which are present in the membranes of untransformed cells but are masked and therefore not accessible to the immune system. Häyry and Defendi (*Virology*, **41**, 22; 1970), for example, report the detection, by mixed haemagglutination and indirect immunofluorescence, of a specific surface (S) antigen on SV40 transformed cells. This antigen is present neither on the untransformed cells nor on cells of the same lines transformed by polyoma virus. To that extent the S antigen is specific to SV40 transformation, but it is not apparently a product of an SV40 gene. Mild short term digestion of untransformed or polyoma transformed cells with trypsin or chymotrypsin, but not papain, ficin or neuraminidase, exposes the S antigen characteristic of SV40 transformation.

The S antigen does not seem to be related to other changes in the cell surface which accompany transformation. It does not, for example, cross react with the Forsmann antigen, the amount of which is known to increase after transformation with polyoma or SV40 viruses. It is not apparently related to the sites which bind wheat germ lipase agglutinin and it is not hematoside, which is present in a masked form on the surfaces of untransformed cells and in an incomplete form on transformed cells.

Ben-Bassat, Inbar and Sachs (*Virology*, **40**, 854; 1970) have followed the appearance of another change in the surface of cells transformed with SV40. Last year Sachs's group reported that 85 per cent of the sites capable of binding concanavalin A are cryptic on untransformed cells but become exposed after transformation. They now claim that cells must divide at least once after SV40 infection and reach a density of 10^5 cells per cm^2 before this exposure of cryptic sites occurs. After infection with SV40 many of the cells which bind concanavalin A are abortively rather than stably transformed. As these abortively transformed cells continue to divide they lose the transformed cell phenotype and the binding sites revert to the cryptic state. If, however, they are maintained in conditions which inhibit cell division they retain the capacity to bind concanavalin. The exposure of these binding sites is a phenotypic characteristic of all transformation by SV40 but a genotypic character only of stably transformed cells. Obviously, just how a small oncogenic viral genome brings about such striking changes in the surface of its host will be one of the chief preoccupations of tumour virologists in the next few years.

PROTEINS

Assorted Assembly

from our Molecular Biology Correspondent

SELF-ASSEMBLY is still probably one of the most potent totems to let slip in one's grant applications, and T4 phage is a favoured example. The phage head is a system of considerable complexity, and the interdependence of its several protein components has been demonstrated by the study of mutants with a malfunction in one or other gene. The latest chapter in this long story, unfolded over the years largely by Kellenberger and his associates, is to be found in an article by Yanagida *et al.* (*J. Mol. Biol.*, **50**, 35; 1970). Seven genes have been implicated in defining the phage head structure, and the function, or at least the consequences of malfunction, of five of them has been determined. One gene, designated 23, is responsible for the predominant subunit protein, whereas others determine the elongation and shape of the head, and one seems to prevent a non-specific aggregation of the 23-protein. Among other deviant forms that have been recognized, an error in gene 22 causes the formation of long tubes, or "polyheads".

Yanagida *et al.* have studied the structure of the tubes by optical diffraction of electron microscope images. Earlier discrepancies are resolved by the demonstration that the tubes consist for the most part of several concentric layers, but that these tend to separate on lysing the cells, so that electron micrographs give the impression of particles of variable diameter. In the intact structures one sees always an inner shell of some 290 Å inside diameter. Successive layers number up to seven or more in some particles, and their separation is about 70 Å. The tubes bear a helical lattice pattern of variable pitch and a right-handed screw-sense.

Evidence has now appeared, however, of some unsuspected depths in the self-assembly process. For example, Larcom, Bendit and Mumma (*Virology*, **41**, 1; 1970) have been exercised to establish the molecular weights of the proteins. Molecular weight determinations on a polydisperse mixture of unfractionated