sion that the molecule hunters are gathering data with no attempt at interpretation. This is emphatically not the case, and a wealth of information is concealed in the line measurements. In this particular case Weliachew has estimated the abundance of OH relative to neutral hydrogen, and for M82 and NGC 253 this is comparable with representative regions in the Galaxy. There is, however, a note of caution: both galaxies have strong radio sources in their centres and so the excitation conditions may not be similar to the Galaxy. Nevertheless the evidence does not point to any completely new type of excitation mechanism for the OH in these energetic galaxies.

VIROLOGY

Links and Rings

from our Cell Biology Correspondent

WHEN small covalently closed, circular DNA molecules replicate, there seems to be an inherent tendency to generate a small proportion of oligomeric complex forms, either continuous ring-shaped DNA molecules two or more times the size of the monomer, or catenated forms, consisting of two or more monomeric rings interlocked like the links of a chain. Such oligomeric forms of the genomes of the bacteriophages φX174, P22 and M13 have been described, as have oligomers of circular mitochondrial DNA from a variety of mammalian cells and kinetoplast DNA from the protozoan *Trypanosoma cruzi*. It comes as no surprise, therefore, that Cuzin and his colleagues have detected complex forms of polyoma virus DNA and Rush, Eason and Vinograd (*Biochim. Biophys. Acta*, **228**, 585; 1971) and Jaenisch and Levine (*Virology*, **44**, 408; 1971) now report both ring-shaped and interlinked oligomeric forms of simian virus 40 DNA among the molecules which can be extracted from African green monkey cells supporting the replication of this virus.

Rush *et al.* find that rings and interlinked oligomers each constitute about 1 per cent of the total DNA extractable from cells supporting SV40 replication. Most of these molecules are dimers but there may also be trimers mixed with mitochondrial DNA which happens to have an identical size. Rush and his colleagues, following the lead of Riou and Delain, who reported that low concentrations of ethidium bromide markedly alter the frequency of oligomeric forms of kinetoplast DNA, added 10 μg ml.$^{-1}$ of this drug to their cultures of SV40 infected cells but there was no significant effect; oligomers were found at the same frequency as in untreated cultures. As Eason and Vinograd have reported elsewhere (*J. Virol.*, **7**, 1; 1971), however, ethidium bromide does affect the superhelical coiling of intracellular SV40 DNA; it causes the progeny viral molecules to have a homogeneous superhelix density, the same as that of DNA extracted from SV40 particles, instead of being heterogeneous in this respect.

Similarly to Rush and his colleagues, Jaenisch and Levine report the detection of about 1–2 per cent of circular and interlinked oligomeric SV40 DNAs in infected cells (their electron micrographs of the interlinked forms are particularly elegant and convincing) and they claim some of the ring forms are up to six times the size of monomers. Infectivity tests reveal that each different class of oligomer is infectious and the specific infectivity of these complex forms is more or less that expected; dimeric DNA, for example, has a specific infectivity half that of monomeric DNA.

Cuzin *et al.* detected about 1–2 per cent oligomeric polyoma DNA in mouse 3T3 cells supporting the replication of this virus, but they also found oligomers at a much higher frequency in 3T3 cells that had been transformed by the polyoma virus mutant *tsa* and then induced to allow replication of the mutant. This observation led Cuzin and his colleagues to speculate that oligomeric polyoma DNAs might be produced by the excision of multiple copies of the polyoma genome, which had integrated in tandem in one or more of the host cell chromosomes. It is of course impossible that oligomeric SV40 DNAs are also produced in this way although there is as yet no good reason to believe that the SV40 genome is ever integrated into its host's genome during replication. The high proportion of oligomers in induced *tsa* transformants may therefore be a unique situation and currently it seems more likely that SV40 oligomers arise either by some aberrant event during replication of the free viral genome or perhaps as a result of some recombination event. Certainly Jaenisch and Levine are thinking along these latter lines, for they are apparently infecting cells with pairs of SV40 mutants in an attempt to decide whether dimeric molecules are produced at replication or by recombination. No doubt we shall not have long to wait to know their answer.

Towards the Genetics of Hormone Action

THE ability of the molecular biologist studying bacterial control mechanisms to isolate and recombine regulatory mutants is a constant source of envy for his counterparts working with animal cells, for whom such techniques are not readily available. As some consolation, however, it is being recognized that a number of inherited diseases in man and other animals may involve regulatory functions. β-Thalassaemia has already been successfully exploited from this point of view (see, for example, Nienhaus *et al.*, *Nature New Biology*, **231**, 205; 1971). In a forthcoming article in *Nature New Biology*, Ulrich Gehring and Gordon Tomkins turn with characteristic perspicacity to the inherited defect known as "testicular feminization" for insight into the mechanism of action of steroid hormones. Individuals with this abnormality have an external female phenotype, but an *XY* genotype, and are insensitive to androgenic hormones, including 5-α-dihydrotestosterone, the presumed active metabolite of testosterone. The defect has also been described in mice, where it is known to be *X*-linked.

Susumo Ohno, with whom Gehring and Tomkins collaborated, had previously shown that normal mouse kidney is a target tissue for sex hormones, and responds to testosterone injection with the induction of a number of specific enzymes, including alcohol dehydrogenase. It is worth noting here that this kidney enzyme is coded for by the same autosomal gene as in liver, where it is not under steroid control (Ohno *et al.*, *Biochem. Genet.*, **4**, 565; 1970). In all steroid-sensitive tissues so far studied it had been assumed that the first step in the action of the hormone was its combination with specific cytoplasmic receptor proteins, followed by their association with the nucleus. Gehring *et al.* show that such complexes are indeed formed with dihydrotestosterone in the kidneys of normal X^+Y and X^+X^+ males and females but are present in very reduced amounts in the cytoplasm and nuclei of $X^{Tfem}Y$ mice. It is not yet known if the X^{Tfem} mutation involves a structural alteration, or loss, of one or a class of cytoplasmic dihydrotestosterone-binding protein(s), but what these results do establish is that the combination of the steroid with such molecules is a prerequisite for its correct biological action. The number of these cytoplasmic receptors, their uptake and specific binding to chromatin, and the relation between these steps and transcriptional and translational control are obviously problems that will, in the absence of further regulatory mutants, continue to tax everyone's ingenuity for a long time.

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