CHROMOSOMES

Divisive Multiplication

from a Correspondent

BACTERIA and their viruses have provided us with highly rewarding model systems for helping us to understand some of the biological processes occurring in man. No doubt there is still much more to discover using these systems, but with the increasing rush into mammalian cell culture and animal virology it is easy to forget that there is an enormous range of other eukaryotic creatures less frighteningly complex, yet readily able to yield clues to the most challenging of problems if only we give them our attention.

One such problem is the organization and control of eukaryotic chromosomes, and the recent articles from Prescott's group in Boulder, Colorado (Kloetzel, *J. Cell Biol.*, **47**, 395; 1970; and Prescott *et al.*, *Chromosoma*, **34**, 355; 1971) highlight the fascinating vicissitudes of a protozoon's chromosomes. Their work was done on the ciliated protozoon *Stylonichia mytilus* which has a micronucleus which contains the genetic store, and a macronucleus whose DNA is used more like the DNA of a mammalian somatic cell —for phenotypic expression and metabolic control.

In certain conditions (such as a diminishing food supply) two protozoa will mate, whereupon their micronuclei undergo several meiotic divisions producing several haploid micronuclei, two of which fuse to give a zygote nucleus. This then further divides, giving two genetically identical sets of genes one of which becomes the new definitive micronucleus and the other begins a set of the most remarkable transformations to become the new macronucleus of the protozoon. It is on the nature of these transformations that the recent work has been done.

Ammerman (*Arch. Protistenk.*, **108**; 109; 1965) had previously shown that the formation of the new macronucleus from the diploid micronucleus was achieved by two separate periods of extensive DNA synthesis. In the first period, the DNA content increases to about fourteen times that in the original diploid micronucleus. Forty hours after conjugation this first period of DNA synthesis ends; and Kloetzel has produced some beautiful photographic evidence that the polytene chromosomes thus formed are transected between each of the bands. Indeed, if Crick (*Nature*, **234**, 25; 1971) is right, the chromosomes are divided into bags of multiple copies of separate genes, each with their globular control elements. Prescott *et al.* have isolated this transected DNA from the macronuclear region and have shown it to have a molecular weight of about 1.15×10^6 daltons, which fits in nicely with such an idea. (Micronuclear DNA at the same stage is much larger.)

The transected DNA is then broken down so that only five hours after the macronucleus had contained fourteen times the diploid amount it now contains only slightly more than the diploid amount. Thirty hours later still, there begin successive waves of DNA synthesis bringing the DNA content up to about thirty-two times the diploid content to complete the construction of the macronucleus.

Whether or not selective amplification or breakdown of genetic material has occurred is not yet known. But such questions can be answered if enough DNA can be isolated, and the question arises whether such a remarkable series of events has any counterpart in the mammalian cell.

REPLICATION

DNA in Hindsight

from our Cell Biology Correspondent

THE mysteries of the biochemistry of DNA replication continue to deepen. For as Fleischman and Richardson (*Proc US Nat. Acad. Sci.*, **68**, 2527; 1971) have now shown, the enzyme or enzymes which semiconservatively replicate the chromosome of *Escherichia coli* can apparently tell when the daughter duplexes behind the replication fork are cut and respond by ceasing to replicate any more of the parental chromosome. Precisely how the replicase at the replication fork recognizes the presence of double strand nicks in daughter duplexes behind it, is, needless to say, anyone's guess at present, but there can be no argument that the enzyme can do this and responds by ceasing to polymerize more DNA. Fleischman and Richardson's evidence comes from a particularly neat set of experiments which exploit host restriction enzymes and the recently developed toluenized cell system.

After exposure to toluene *E. coli* cells are rendered permeable to the deoxynucleoside triphosphates and in their presence, together with ATP, Mg^{2+}, K^+, the cells continue to synthesize DNA, using the triphosphates as precursors, by a reaction which has many of the characteristics of DNA replication. Indeed, it seems almost certain that in toluenized cells rounds of DNA replication, initiated before the cell is exposed to toluene, are completed by the same enzymatic machinery that was active before exposure to the solvent. The host restriction enzymes enable an *E. coli* cell to distinguish its own DNA from foreign DNA, such as that of an infecting phage, by virtue of differences in the pattern and extent to which different DNAs are methylated, glucosylated or otherwise modified.

Fleischman and Richardson's experiment was simply to allow toluenized cells of two strains of *E. coli* to incorporate hydroxymethyl deoxycytidine triphosphate (HMC) into their DNA and see what happens to further DNA replication. One of the strains they used is restrictive for the replication of T-even phages because it contains a restriction endonuclease which specifically recognizes nonglucosylated HMC residues in T-even phage DNA. The other strain lacks such an enzyme and supports the replication of T-even phages. The question Fleischman and Richardson were asking, in other words, was whether a restriction enzyme will attack its own

IMMUNOLOGY

Working Out Meetings

THE British Society for Immunology, with more than 1,100 members, 600 of whom attended the autumn meeting, has run into problems of how to organize its meetings. There have been several experiments in designing meetings of the BSI; the usual two day autumn meeting this year was preceded by a workshops' day. Seven workshops were accommodated by different host institutions in London and members had to choose only one to attend. For some people this was a difficult choice to make, for others it was predetermined no matter how green the grass seemed to be elsewhere. Attendance varied from about 20 (the complement meeting) to 120 (the cellular immunity mediators). Everyone agreed that the workshops were very successful and they will be held again next time, with no formal organization, except for the transplantation workshop.

A steering committee was formed comprising Dr H. Festenstein (London Hospital), Mr A. D. Barnes (Queen Elizabeth Hospital, Birmingham), Professor L. Brent (St Mary's Hospital Medical School, London), Professor R. Calne (Department of Surgery, Cambridge), Dr D. A. L. Davies (Searle Research Laboratories, High Wycombe) and Mr J. Hopewell (Royal Free Hospital), to organize a Transplantation Group (there is no British Transplantation Society), in the hope that it will attract the surgeons but remain firmly attached to the BSI in the same way meetings on virus research are organized as a subunit of the Society for General Microbiology.