Genetical Society in Dublin

from a Correspondent

THE 172nd meeting of the Genetical Society held at Trinity College, Dublin, from July 11 to 13 included a special session on the genetics of transcriptional and translational systems and a symposium on the structure and function of eukaryotic genes.

Dr J. D. Smith (MRC Laboratory of Molecular Biology, Cambridge) introduced the special session with a review of his analysis of the tyrosine tRNA molecule. Five mutants of the tyrosine tRNA structural gene su_{III}, each of which alters a base in the amino acid acceptor stem and apparently allows the tRNA to be loaded with glutamine *in vivo*, have been isolated; this was confirmed *in vitro* with purified mutant tyrosine tRNA and glutaminyl-tRNA synthetase. These observations show clearly that the recognition site on the tRNA for the synthetase at least includes the acceptor arm. So far the rules of the recognition process are not known—but with five different mutations causing a switch from tyrosyl to glutaminyl-tRNA synthetase they will no doubt be complicated.

Dr S. Ryce who, together with J. F. Atkins of Trinity College, Dublin, had been the first to describe external suppressors of frameshift mutations, presented some further analysis of single suppressor mutations which suppress both UGA and frameshift mutations. These suppressors were mapped in the region of *supK* at minute 95 and have properties similar to *supK* mutants previously isolated. It is now thought that *supK* codes for a tRNA methylase, so that it is possible that a change in the methylase activity could cause one tRNA to read UGA and another to read frameshift mutants.

Dr D. L. Riddle (MRC, Cambridge) reviewed a scheme for the classification of external frameshift suppressors in *Salmonella typhimurium*. Six distinct types (*sufA–F*) suppress particular combinations of a set of frameshift mutations in the histidine operon. *SufD* has been shown to be the structural gene for a minor glycine tRNA and the *sufD* mutants code for a tRNA with a quadruplet anticodon CCCC instead of the wild type CCC. *SufA* mutations affect the principal proline tRNA. When this work is considered along with that of Yourno and others it seems likely that external suppression of frameshift mutations will occur most readily when the coding sequence at the frameshift involves a homopolymeric codon as GGG or CCC.

The five other presentations in the special session dealt with the RNA polymerase-promoter interaction. A non-genetic approach to this problem is under way in Dr D. J. McConnell's laboratory in Dublin. The object is the purification and sequencing of the promoter region of T7 which, as shown recently by Dunn and Studier (*Proc. natn. Acad. Sci. U.S.A.*, **70**, 1559; 1973), is more complex than was suggested by earlier work. Dr McConnell has isolated DNA fragments with affinity for *Escherichia coli* RNA polymerase and showed that it will be possible to determine whether these fragments are derived from the early region of T7: he has split T7 DNA into fifty fragments by digestion with the restriction enzyme, endonuclease R, and so will be able to show which of these carries the promoter region.

Dr W. J. Brammar (University of Edinburgh) discussed a most interesting series of experiments by means of which he has been able to select mutants of the promoter of the *trp* operon. Essentially the techniques involved the juxtaposition of the *trp* and *lac* operons, deletion of the *lac* promoter and the *trp* terminator, so making the expression of *lac* dependent on readthrough from *trp*. Then *lac* technology could be used to select mutants with decreased β-galactosidase activity which mapped at the proximal region of *trp*.

The symposium on the structure and function of eukaryotic genes was organized to bring together exponents of several disciplines all ultimately interested in the working of the genes of the higher organisms. The famous dictum of Monod "if you understand *E. coli* you can explain an elephant" no longer holds except at the most superficial level. That became clear when Britten discovered repetitive DNA, Judd and others showed that the chromomeres or bands of *Drosophila* polytene chromosomes apparently only contain one complementation group or functional genetic unit each, and several laboratories established that about 90% of the rapidly-labelled RNA, most of which is synthesized as very large molecules, does not leave the nucleus, and that which does is considerably smaller.

So it was a pleasure to hear Dr A. Chovnick (University of Connecticut) start the day with a review of his work on the fine structure of the rosy (*ry*) and maroon-like (*ma-l*) loci of *Drosophila*. The band with which *ry* is correlated is large, about 10,000 base pairs in length, whereas *ma-l* is small, perhaps only 1,000 units long. Fine structural analysis can be carried out on these systems, at a level usually only possible in fungi or prokaryotes, because *ry* and *ma-l* mutations are conditionally lethal so that very rare wildtype recombinants between closely linked markers can be selected. Moreover, *ry* is the structural gene for xanthine dehydrogenase so that by mapping mutations which cause changes in the electrophoretic properties of the enzyme it is possible to establish regions of the genetic map which fall in the coding sequence. At present this system is the best prospect for an extension to a eukaryotic genome of Yanofsky's classical analysis of *trpA* in *E. coli*. At a guess the 10,000 base pairs of *ry* must code for more than one polypeptide and the question is what?

Dr R. A. Firtel (University of California, San Diego) and Dr J. Paul (Beatson Institute, Glasgow) essentially produced the same answer, the first with slime moulds and the second with haemoglobin messenger RNA. The basic model proposes that the precursor to a particular mRNA is a larger molecule of heterogeneous nuclear RNA, which may represent the transcript of a large proportion of the DNA in a chromomere. Most of the non-coding sequences which are repetitive are removed from the 5′ end, and a short poly (A) sequence is added to the 3′ end before the molecule leaves the cytoplasm. Dr D. S. Holmes (California Institute of Technology) discussed an analysis of the arrangement of repetitive and unique sequences in the rat genome as revealed in electron micrographs of DNA which had been partly renatured to allow large molecules of total DNA to reassociate with small molecules of middle repetitive DNA. Double and single stranded DNA were distinguished by the formamide technique. Dr Holmes's model suggests that middle repetitive (300 ± 200 bases long) and unique sequences (800 ± 400 bases long) are interspersed. The interesting corollary of this model is that a chromomere (average 10–20 kilobases) would presumably contain more than one unique sequence. If unique sequences are always coding sequences then chromomeres would be expected to contain more than one complementation group. This is not what is observed by Judd and others.

The alternative approach to unravelling this Gordian knot of eukaryotic genetics was touched on in the discussion. All mutations in eukaryotic systems may be polar and antipolar within a chromomere, so that a mutation anywhere in a chromomere which may contain several cistrons (in the bacterial sense) renders them all inactive.

Dr H. G. Callan (University of St Andrews), Dr C. Pelling (Max Planck Institute, Tübingen), Dr J. Bonner (California Institute of Technology) and Dr E. M. Bradbury (Portsmouth Polytechnic) also made many interesting contributions to a fascinating day.