Selecting Messengers for Survival

by our Molecular Genetics Correspondent

THE question of how messenger RNA is degraded has proved to be one of the thornier problems of molecular biology. The kinetics of the life of bacterial messengers are clear enough; shortly after synthesis of the messenger has begun, ribosomes attach to it and move along the RNA very closely behind the RNA polymerase synthesizing it. Degradation takes place soon after the last of the tightly packed bunch of ribosomes has passed by.

But in spite of the instability of the messenger, the enzymes which degrade mRNA have proved difficult to pin down. One idea is to suppose that a proportion of the ribosomes of the cell carries some enzyme, so that when one of these "killer" ribosomes attaches to a messenger, it degrades the RNA as it moves along. Another idea is that the number of ribosomes attaching to any particular message is controlled in some other way and that, once the last ribosome has passed, the exposed message is vulnerable to nucleases which may first cleave the chain into fragments and then degrade the pieces into nucleotides. But be that as it may, most researchers have at least been looking for just one degradation system which would work with all messenger RNAs.

The idea that there is some central control for degrading messenger RNA was supported by the finding of Sumners and his colleagues (*J. Mol. Biol.*, **51**, 671; 1971) that messenger RNAs are stable when *Escherichia coli* is infected by bacteriophage T7. The messengers specified by the phage genome itself are stable and measurements on the total fraction of messenger RNA in the bacterial cells suggested that this stability is achieved by switching off whatever mechanism exists in the cell to degrade messengers. This idea was supported by the further finding (*Nature New Biology*, **230**, 208; 1971) that T7 messengers which are not translated have an enhanced stability in *E. coli* cells which carry a mutation in the *suA* gene; this locus changes patterns of survival of bacterial messengers and one theory is that it may code for an enzyme involved in degrading messengers (see *Nature New Biology*, **232**, 161; 1971).

Ideas about a central control system, however, will need to be rethought in view of the experiments which Marrs and Yanofsky report on page 168 of this issue of *Nature New Biology*. They have looked at the fate of the messenger RNA of the tryptophan operon of the host bacterium after infection with phage T7. They have used a mutant of the phage which cannot make its own RNA polymerase so that treating infected cells with rifampicin, to inhibit *E. coli* RNA polymerase, prevents synthesis of any RNA; in these conditions, it is possible to follow the degradation of labelled RNA molecules.

When the stability of phage messenger molecules was compared with that of tryptophan mRNA, the T7 species proved to be stable with a half life of some 6–20 minutes whereas the tryptophan mRNA suffered degradation with its usual half life of about 80 seconds. Infection with T7 evidently fails to interfere with whatever are the usual systems for degrading tryptophan messengers, at least, although the general kinetics of mRNA survival are changed. The implication of these results is that the messenger degradation system(s) can discriminate between different messenger RNA species.

How might this be achieved? If there are killer ribosomes, their action must in some way depend on the particular messenger which they are about to attack; it cannot be random, which removes one of the most attractive aspects of this scheme. Presumably, the attachment of killer ribosomes to messenger would need to be different from that of other ribosomes, perhaps depending in some way on the base sequence at the beginning of the messenger. It is even more difficult to reconcile models for internal snipping of messengers with Marr and

COLICIN DNA

Replication through Catenation

WHEN minicells were discovered, one molecular biologist commented that if they had been available ten years earlier, they would have been useful for solving many of the then outstanding problems of nucleic acid and protein synthesis. For minicells are mutants of *Escherichia coli* which lack DNA of their own and are therefore particularly good cells in which to study the behaviour of DNA introduced from other sources.

The idea that they were discovered too late has been refuted by the use to which they have been put in the past year or so for studying the episomes of *E. coli*. The replication of the DNA of colicin E1 in minicells has been reported recently by Inselburg and Fuke (*Proc. US Nat. Acad. Sci.*, **68**, 2839; 1971); they find that the absence of the bacterial genome enables them to pick out the colicin DNA with no difficulty.

They have previously identified double-forked circular structures of the type isolated by Cairns in *E. coli*. They now report that they can identify twisted circular DNA and replicating catenating molecules, bringing the total number of replicative intermediates to four. The photograph shows some of the catenated molecules; the reason for the production of these molecules, which consist of more than one colicin DNA joined end to end, is quite mysterious, but may yet throw new light on the structure and function of colicin DNA.