news and views

Digesting DNA and chromatin

ALTHOUGH the basic double-helical structure of DNA has been known for many years its sequence arrangements and spatial organisation in chromatin have remained poorly understood. The discovery of restriction enzymes, which cleave double-stranded DNA at specific target sites, has given a much needed boost to sequence analysis of DNA. Recently some interesting results concerning the organisation of satellite DNAs have been obtained using the restriction enzyme EcoRI, which cleaves DNA at the sequence GAATTC. The size of DNA fragments generated by the enzyme reflects the separation of target sites and so a limited base sequence complexity, as exists in satellite DNAs, would tend to result in infrequent cleavage.

Botchan *et al.* (*Cold Spring Harb. Symp. quant. Biol.*, **38**, 383; 1974) found that mouse satellite DNA could be separated from the rest of the DNA by cleavage with EcoRI. The satellite DNA formed a slow migrating band on electrophoresis whose fragments ranged in molecular weight from 4×10^6 to 20×10^6, indicating that it is composed of inexact repeating units. In contrast, Botchan (in this issue of Nature, page 288) finds that the same enzyme cleaves bovine satellite I DNA into highly repetitious units of 1,400 base pairs. Renaturation kinetics indicate that these units are internally repetitious. He proposes that two stages were involved in the evolution of satellite I DNA. The first stage involved small duplications, indicated by the renaturation rate, to yield the 1,400 base pair unit, and the second stage involved the production of large tandem repeats of this unit. Such analysis of other satellites should give a clearer picture of how satellite DNAs are organised and perhaps confirm this hypothesis. Mouse satellite DNA, if further analysis does not reveal some higher order of repeating units, may be a case where subsequent divergence has obscured the homogeneity of the tandem arrays.

On another level of DNA organisation recent work points to a highly repetitive association of protein with DNA in chromatin. Olins and Olins (*Science*, **183**, 330; 1974) reported linear arrays of chromatin particles, which they termed ν bodies, each about 70 Å in diameter. They calculated that each ν particle could contain at least one, possibly two, molecule of each of the five main histones and a stretch of DNA of molecular weight between 80,000 and 160,000. Sahasrabuddhe and Van Holde (*J. biol. Chem.*, **249**, 152; 1974) isolated micrococcal nuclease resistant particles constituting 50% of the total DNA from calf thymus chromatin with sedimentation coefficients of between 10S and 12S. These particles contained approximately 100 base pairs and had an estimated diameter of about 80 Å. Similarly Clark and Felsenfeld (*Biochemistry* **13**, 3622; 1974) have found that, on digestion with micrococcal nuclease, 50% of the DNA in chromatin remains as protected areas containing roughly 100 base pairs. Hewish and Burgoyne (*Biochem. biophys. Res. Commun.*, **52**, 504; 1973), on the basis of nuclease digestion studies using an endogenous Ca^{2+}–Mg^{2+} dependent endonuclease of rat liver chromatin, have proposed a simple, basic, repeating structure for chromatin. Kornberg (*Science*, **184**, 868; 1974) has elaborated this into a theory of chromatin structure based on a repeating unit containing two each of the main histones (excluding F1 histone) and about 200 base pairs of DNA forming a flexibly jointed chain. Support for this theory now comes from the work of Noll (*Nature*, **251**, 249; 1974) who finds that using both the endogenous Ca^{2+}–Mg^{2+} dependent endonuclease and micrococcal nuclease approximately 85% of rat liver chromatin can be digested into 11S fragments containing about 200 base pairs. Further digestion, however, causes a breakdown of DNA in these fragments. The isolated fragments contain all five major histones and some nonhistone proteins.

Thus evidence is accumulating for a regular spatial arrangement of proteins in chromatin, the proteins protecting stretches of DNA from nuclease attack. Further studies may show a simple relationship between the 200 and 100 base pair fragments, for example a totally protected 100 base pair unit associated with 100 base pairs which are partially protected. T. BARRETT

Termination and the juggernaut polymerase

GENE expression seems in general to be controlled at the initiation of transcription. An alternative mechanism operates, however, during the development of some phages. Initially 'early' genes are transcribed by a host (bacterial) polymerase which is halted by termination signals. Subsequently an anti-termination protein is synthesised to allow transcription beyond these signals. The mechanisms of termination and of anti-termination have not been well defined and their role within the uninfected bacterium remains particularly unclear. Adya, Gottesman and De Crombrugghe (*Proc. natn. Acad. Sci. U.S.A.*, **71**, 2534–2538; 1974) now suggest that the mode of termination may be dictated by events taking place at initiation; their work with polar mutants also reveals a new aspect of the connection between translation and transcription.

Expression of the galactose operon of *Escherichia coli* is different when caused by readthrough from a prophage instead of the normal initiation at a galactose promotor. When prophage lambda is induced, constitutive ('escape') synthesis of the nearby galactose enzymes ensues, for two reasons: (1) replication of the galactose structural genes together with the prophage increases the number of operators so that insufficient repressor is present in the cell to prevent transcription; (2) transcription is initiated at the p_I (*sex*) promotor and proceeds from the prophage, through the intervening bacterial genes, into the galactose operon. Certain mutations permit only the second mechanism to operate, by preventing the replication and the excision from the chromosome of the prophage.

Adya *et al.* used an increase in temperature from 32° C to 41° C to induce prophage bearing such mutations. They found a seven-fold increase in the specific activity of galactokinase, the enzyme coded by *galK*, the last of the three structural genes of the galactose operon. Since the addition of fucose, an inducer of the galactose operon, causes a further increase in galactokinase synthesis, apparently to the same extent as usual, expression by induction and expression by readthrough seem to be additive. This suggests that they take place by different