The Structure and Function of Chromatin

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Edited by D. W. Fitzsimons and G. E. W. Wolstenholme
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Meetings concerned with chromatin have an infamous reputation. Whilst to the devotee the morass of apparently contradictory detail is a stimulating intellectual challenge, the interested bystander finds the situation perplexing and a little irritating. After all, so much work has been done and so many papers have been published in this area that surely a little light should be emerging by now. I am happy to report that such is the case. This collection of papers given during April, 1974 at the 28th Ciba Foundation Symposium by members of virtually all the important research groups in this area is a fair review of the new situation. Also, since trouble has been taken to introduce most topics clearly and simply, it will, I am sure, please those readers who do not have much previous knowledge of the subject. The discussions reported make fascinating reading for all. Unfortunately, the book is doomed to a short life. Progress is rapid, particularly with regard to the structural organization of histones and the configuration of DNA in chromosomes. For example, the word 'supercoil' used so frequently at the Symposium is probably not applicable now. The simple histone nomenclature adopted by the meeting is listed below in the hope that its widespread adoption will be encouraged. The new designations are listed, followed by previous names in parentheses: *H1* (F1, 1a, 1b, KAP); *H2A* (F2a2, IIb1, ALK); *H2B* (F2b, IIb2, KSA); *H3* (F3, III, ARK); *H4* (F2a1, IV, GRK); and the special histones, *H5* (F2c, KAS); and *H6* (T, AKP).

Much of thenew understanding has come from studies on the interaction of native histones and from gentle nuclease degradation of chromatin. These results are described by R. Kornberg on behalf of the Cambridge Group. In the native form, histones H3 and H4 are found mainly as an $(H3)_2$ $(H4)_2$ tetramer. Similarly, H2A and H2B also associate. Evolutionary data and behaviour during salt extraction from chromatin confirm these pairings. Gentle nuclease digestion generates a particle containing approximately 200 base-pairs of DNA. The X-ray diffraction data which shows the presence of a 10 nm repeat in chromosome structure is obtained only with native material or using chromatin reconstituted with all four histones, H2A, H2B, H3 and H4. These results, together with the stoichiometry of histone/DNA ratios (one of each per 100 base-pairs of DNA) led Kornberg to put forward the 'string of beads' structure for chromatin. Each 200 base-pair unit of DNA is wrapped up into a globular bead containing 2 molecules of each of the four histones mentioned above. The role of H1 is not certain, but could cover interbead DNA. The weight of supporting evidence is such that this model is now widely accepted.

A clearer picture of histone structure is also emerging from amino acid sequence studies. H3 and H4 have basic DNA binding regions at the $-NH_2$ terminal portion whereas these areas are located at both ends of the other histone molecules. The hydrophobic regions are located at the -COOH terminal part of the H3 and H4 molecules and in the central area of the other histone proteins. These probably represent sites of protein–protein interaction. G. H. Dixon et al. find that histones are both phosphorylated and acetylated immediately after synthesis in trout testes. This may prevent non-specific DNA binding. When they are orientated correctly on the chromosome, dephosphorylation and deacetylation occur to lock them in position. H1 phosphorylation appears to be associated with any activation of chromosomes for replication or transcription. It may be involved with the relaxing of the interbead DNA. H. Weintraub et al., working with duck erythrocyte chromatin find that the histones are digested by trypsin in pairs and sequentially: H1 + H5 first; H3 + H4 second; and H2A and H2B third. Hence the latter pair may be located at the inside of the bead. H5 is a special H1 substitute in avian reticulocytes.

The complexity of the non-histone proteins and the difficulty of separating them preparatively are still major problems. However, the results reported here indicate that two major functional classes occur. As shown by E. W. Johns et al., certain non-histone proteins are present in many tissues and probably have a structural function. Non-histone proteins described by V. G.

Allfrey et al., by L. S. Anilica, and by R. Baserga appear when tissues are stimulated to change and have a tissue specificity, for example, in immunological tests. These could be the regulatory proteins. That such a class can be isolated in crude form at least is clearly shown by the experiments reported by J. Paul and R. S. Gilmour. The expression of the haemoglobin gene in reconstituted chromatin is turned-on by including a specific set of non-histone proteins. This important result has been confirmed recently by H. Gould's group at King's College.

It is clear that one can begin, at last, to think in detailed terms about eucaryotic gene expression and chromatin structure. This book will be of great help to all who need to do this. A background to the field is provided by 'Gene Expression II. Eucaryotic Chromosomes' by B. Lewin (1974) published by Wiley in paperback. Though the work discussed is about 2–3 years out of date, Lewin's style is easy to read and the subject matter is comprehensive and clearly laid-out. These two books together with two recent reviews by the same author (Cell, 4, 11–20, 77–93, 1975) will convert the willing reader to quite an armchair expert in modern eucaryotic molecular biology.

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Membrane-Active Complexones

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by Yu. A. Ovchinnikov, V. T. Ivanov and A. M. Shkrob
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This book will be widely welcomed. The authors, from the Shemyakin Institute for Chemistry of Natural Products, USSR Academy of Sciences, Moscow, have brought together an immense amount of recent information about the chemistry of a somewhat diverse group of naturally-occuring, alkali metal, binding macrocyclic compounds – peptides, depsipeptides, depsides, polyethers – as well as about some non-cyclic compounds – the nigericin and gramicidin antibiotics – that also bind metal ions, the resulting complexes being folded into a pseudocyclic conformation. The biochemical properties and uses of these compounds are also dealt with. The thoroughness with which the work has been done is testified to by the 1115 references mentioned in the text and the list of 208 additional, mostly very recent ones.

The first chapter contains descriptions of the chemical structures of 340 compounds and for many of them details are given of some of their physical, physicochemical and antibiotic properties. Chapter 2 briefly describes the methods available for studying the complexing reaction. It includes accounts of the application of spectral, conductimetric, relaxation, and other techniques, the study of two-phase systems and the mass spectrometry of complexes. While the treatment is not detailed enough to serve as a laboratory handbook, it does tell the reader the sorts of information the various methods will yield and the references should lead him rapidly to more detailed descriptions.

The largest section of the book is devoted to the spatial structures and complexing properties of macrocyclic compounds. This chapter brings out very clearly how these properties are due not only to the number and nature of the groups directly interacting