Biochimie 81 (1999) 727–732

The site of binding of linker histone to the nucleosome does not depend upon the amino termini of core histones

Woojin An[a], Jordanka Zlatanova[a,b]*, Sanford H. Leuba[a]**, Kensal van Holde[a]

[a]*Department of Biochemistry and Biophysics, Oregon State University, Corvallis, OR 97331-7305, USA*
[b]*Institute of Genetics, Bulgarian Academy of Sciences, 1113 Sofia, Bulgaria*

(Received 17 December 1998; accepted 16 April 1999)

Abstract — Using nucleosomes reconstituted on a defined sequence of DNA, we have investigated the question as to whether the N-terminal tails of core histones play a role in determining the site of binding of a linker histone. Reconstitutes used histone cores of three types: intact, lacking the N-terminal H3 tails, or lacking all tails. In each case the same, single defined position for the histone core was observed, using high-resolution mapping. The affinity for binding of linker histone H1° was highest for the intact cores, lowest for the tailless cores. However, the location of the linker histone, as judged by micrococcal nuclease protection, was exactly the same in each case, an asymmetric site of about 17 bp to one side of the core particle DNA. © 1999 Société française de biochimie et biologie moléculaire / Éditions scientifiques et médicales Elsevier SAS

core histone tails / H3 tails / linker histone / nucleosome

1. Introduction

Recent years have produced overwhelming evidence for the involvement of chromatin structure in transcription regulation [1-3], at both the initiation and elongation steps. The strong inhibition of transcription initiation attributed to the binding of the histone octamer to DNA is augmented by the additional binding of linker histones (LHs) and seems to involve direct repression of transcription factor binding to chromatin DNA. Exactly how these two elements of chromatin structure, the core nucleosome and LHs, exert their action is far from understood. Part of the problem lies in our poor knowledge of how LHs interact with chromatin, despite years of intensive research (reviewed in [4, 5]).

It has long been recognized that LHs bind to linker DNA, at or near the point where DNA enters and exits from the core nucleosome [4, 5]. This binding protects an additional 20 bp of linker DNA, immediately contiguous to the 146 bp of the DNA in the core nucleosome against nuclease attack. The exact binding site is still under debate [5], although recent analyses of LH-containing mono- and di-nucleosomes reconstituted on defined-sequence DNA fragments seem to indicate that, in many cases, the protection conferred by LH binding is totally asymmetric, with the protected DNA being located on one side of the particle only [6-9].

That LH lies close to the nucleosome core has been directly demonstrated by protein/DNA [10] and protein/protein cross-linking (for references see [4]). The major contacts identified were with H2A (e.g., [11]), but cross-linking to the other core histones has been also reported [12, 13]. These early studies did not address the question of which portions of the respective histone molecules were involved in the cross-linking. More recent studies used H1 addition onto H1-depleted native or reconstituted oligonucleosomes that contained either intact core histones, core histones whose N-terminal tails were highly acetylated, or core histones which lacked these tails altogether. Both mobility shift assays and analyses of the products of micrococcal nuclease (MNase) digestion indicated beyond doubt that core histone amino termini were not absolutely required for LH binding to the nucleosome core [14-18]. Although the lack of such a requirement seems to be generally agreed upon, there is still a difference in opinion of whether the affinity of LH binding is the same for both kinds of chromatin templates - those containing intact core histones and those possessing acetylated (or truncated) core histone amino termini (compare [18] with [19], for example).

In order to clarify this issue, we performed further analysis of LH binding to mononucleosomes reconstituted on defined-sequence DNA fragments. Three different reconstitution substrates were employed: i) nucleosome cores that contained intact core histones; ii) cores which

* Correspondence and reprints: Argonne National Laboratory, 9700 S. Cass Ave., Bldg. 202-A253, Argonne, IL 60439-4833, USA.

** Presently NCI scholar at Laboratory of Receptor Biology and Gene Expression, Bldg 41, Room B602, NCI, NIH, Bethesda, MD 20892-5055, USA

Abbreviations: bp, base pair(s); LH, linker histone; MNase, micrococcal nuclease; SDS, sodium dodecyl sulfate.

lacked the amino termini of all core histones; and iii) cores that contained intact H2A, H2B and H4, and histone H3 missing its N-terminal tail. The latter reconstitution was included in this study in view of our recent scanning force microscopy (SFM) results showing that the tails of H3 and those of H5 are structurally redundant in the extended chromatin fiber [20-22]. The N-tails of H3 could not be substituted for by the tails of any of the other core histones in determining the three-dimensional organization of nucleosome in the fiber [20-22]. The H3 tails are situated closer to the dyad axis of the core nucleosome, as compared to the unstructured tails of the other core histones [23], and could, in view of this, more easily interact with the linker DNA and/or with the LH which binds close to the dyad.

These three types of reconstituted particles were analyzed by mobility shift assays, MNase digestion, and mapping of the LH binding site by a combination of MNase digestion and restriction nuclease cleavage. Our results confirm previous reports that the tails of the core histones are dispensable for LH binding. More importantly, they show for the first time that the site of LH binding is not in any way dependent on the presence of the core histone amino termini, although the affinity of LH binding is somewhat reduced in tailless mononucleosomes.

2. Materials and methods

2.1. Expression of human H1° and DNA fragment used for reconstitution

The human H1° gene was obtained by polymerase chain reaction of pWH312 [24], and cloned into pET-15b expression vector, as recently detailed in [8]. The native status of the purified recombinant protein was checked by circular dichroism. The 235 bp DNA fragment used for nucleosome reconstitution contained 30 bp and 20 bp extensions on the 5'- and 3'-sides of the 179 bp pGUB fragment [25] and was cloned and purified as described elsewhere [8].

2.2. Preparation of intact, H3-tailless or totally-tailless histone octamers

The preparation of intact histone octamer was previously described [7]. Tailless histone octamers were prepared by mild trypsin digestion of chicken erythrocyte chromatin (at 0.1 mg of DNA/mL) using immobilized trypsin [26]. Membranes with immobilized trypsin were immersed in the reaction solution (10 mM Tris-HCl, pH 7.5) 15 min prior to the addition of the chromatin substrate. Chromatin was digested for 5–7 h or for 10–12 h at 37 °C to prepare H3-tailless or totally-tailless histone octamer, respectively. Digestion was stopped by removal of the membranes, adding phenyl methyl sulfonyl fluoride to a final concentration of 0.5 mM, and chilling the sample on ice. Digestion products were analyzed on 15% SDS-polyacrylamide gel electrophoresis [27]. Digested chromatin was stripped of linker histones by CM Sephadex C-25 [28, 29], and H3-tailless or totally-tailless histone octamers were purified by hydroxyapatite column by the standard procedure for histone octamer purification [30].

2.3. Reconstitution of core nucleosomes and chromatosomes

Reconstitutions were carried out by the salt dialysis methods of Tatchell and van Holde [31] at 4 °C as described recently [7]. The success of reconstitution was monitored by electrophoresis in 0.9% agarose gels in 0.5 × TBE (0.045 M Tris·borate, pH 8.0, 1 mM EDTA). The intactness of the histones following nucleosome reconstitution was monitored by 15% SDS-polyacrylamide gels [27]: no signs of proteolysis were detected. The stoichiometry of bound linker histones was determined by densitometry of Coomassie-stained gels and comparisons with staining patterns of total chicken erythrocyte histones run in parallel. H1° was added to the reconstitution mixture at a molar ratio ranging from 1.3 to 2.5 molecules of H1° per mole of core histone octamer, depending on the reconstitution substrate (see legend to *figure 2*). Such additions resulted in one molecule of linker histone bound per nucleosome.

2.4. MNase digestion of reconstituted nucleosomes and mapping of the LH binding site

These procedures were recently described [7, 8].

3. Results

3.1. Production and characterization of intact, H3-tailless, and totally-tailless histone octamers

In order to study the possible involvement of core histone amino termini in the binding of LH to the nucleosome, we performed binding experiments with three types of reconstitution substrates: core mononucleosomes which contained intact histone octamers, mononucleosomes in which H2A, H2B and H4 were intact but H3 lacked its N-terminal tail, and mononucleosomes in which all core histones were missing their amino termini. These LH binding substrates were obtained by reconstitution of the 235 pGUB DNA fragment with core histones isolated from chicken erythrocyte chromatin that had been mildly digested with immobilized trypsin to different degrees. Trypsinization for ≈6 h led to selective cleavage of 20 or 26 amino acids from the N-terminal portion of histone H3, with the production of P1' and P1 proteolytic fragments

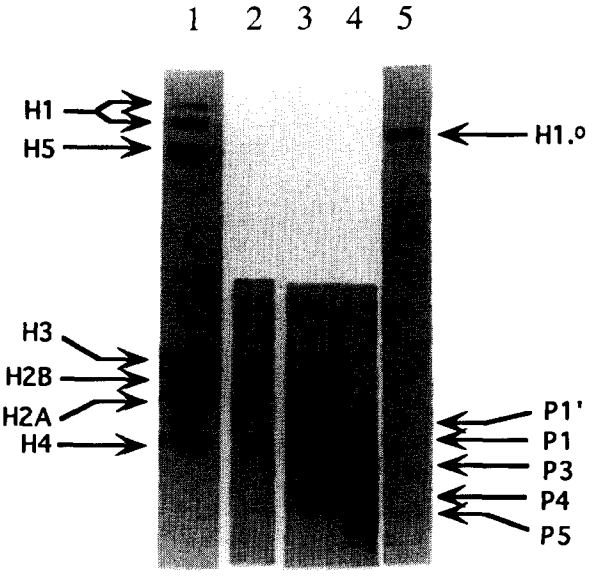

Figure 1. 15% SDS-polyacrylamide electrophoretic patterns of the histones used in this work. Lanes 1–4, 2–3 μg of the respective protein preparations; lane 5, 1 μg. Lane 1, chicken erythrocyte total histones as markers. Lanes 2, 3, and 4, intact histone octamers, H3-tailless histone octamers, and totally-tailless histone octamers, respectively, used for nucleosome reconstitution. The arrows on the right hand side show the products of immobilized trypsin cleavage: P1' and P1 represent truncated H3 molecules, missing 20 and 26 amino acids from the N-termini, respectively (see text). Note that in lane 3 histone H3 has been proteolyzed but the other core histones are still intact, in contrast to the situation presented in lane 4, where all core histones lack their N-termini. Lane 5, recombinant human H1° used as a representative of the LH class.

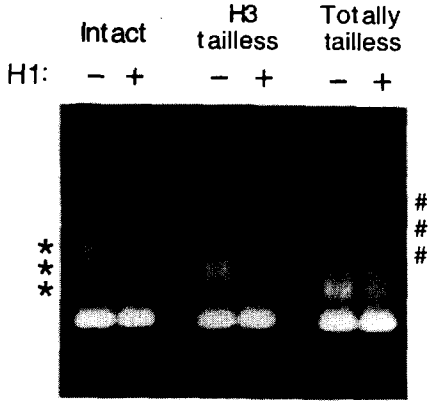

Figure 2. Mobility shift assay to follow the success of reconstitution. The 235 bp DNA fragment was reconstituted with the respective histone octamers only (first lane of each pair) or with the respective octamer followed by addition of H1° (second lane of each pair). Histone H1° was added to a molar ratio with respect to the nucleosome cores of 1.3, 1.7, and 2.5, respectively, for the three different types of reconstitutes. The products of reconstitution were analyzed by 0.9% agarose gels and visualized by ethidium bromide staining. The three asterisks on the left-hand side point to the core nucleosomes containing intact, H3-tailless, and totally-tailless histone octamers. The three pound signs on the right-hand side indicate the respective H1°-containing nucleosomes.

(lane 3 in *figure 1*). The other core histones were still intact at this point (lane 3 in *figure 1*). Overnight digestion resulted in proteolytic removal of the tails of all core histones (lane 4 in *figure 1*). *Figure 1* also shows the purity of recombinant histone H1° used as a LH.

3.2. Linker histone is capable of binding to core nucleosomes containing core histones lacking their amino termini

Reconstitution of the core nucleosomes and LH binding were monitored by band shift analysis of the kind illustrated in *figure 2*. Interestingly, our gels could discriminate among the three kinds of core nucleosomes, the absence of the H3 tails or the tails of all core histones leading to successively higher electrophoretic mobilities of the respective particles as compared to the reconstitute containing intact octamers *(figure 2)*. Addition of LH to the these core nucleosomes produced further retardation of the particles, again different for the three different reconstitution substrates. Titration of the amount of LH needed to achieve comparable extents of LH binding showed a somewhat reduced affinity of the LH for the H3 tailless material, and even more so for the totally tailless material, since more LH was required in these latter cases (see legend to *figure 2*). This result confirms similar observations from Workman's group [18].

The successful reconstitution of LH to the three types of core nucleosomes was further tested by MNase digestion. In all three cases, the kinetic intermediate of 168 bp in length characteristic of the chromatosome was clearly seen on the gels (marked Chr. in *figure 3a* and *b*). In accordance with our previous results [7], the control digestion of the naked DNA used for reconstitution did not produce prominent bands in the core- or chromatosome-sized DNA regions of the gel *(figure 3c)*.

3.3. Linker histone binds to the same site in nucleosomes containing intact or tailless core histones

Finally, we mapped the position of the reconstituted core nucleosomes and chromatosomes on the DNA fragment in the control, the H3-tailless, and the totally tailless material by the method originally introduced by Dong et

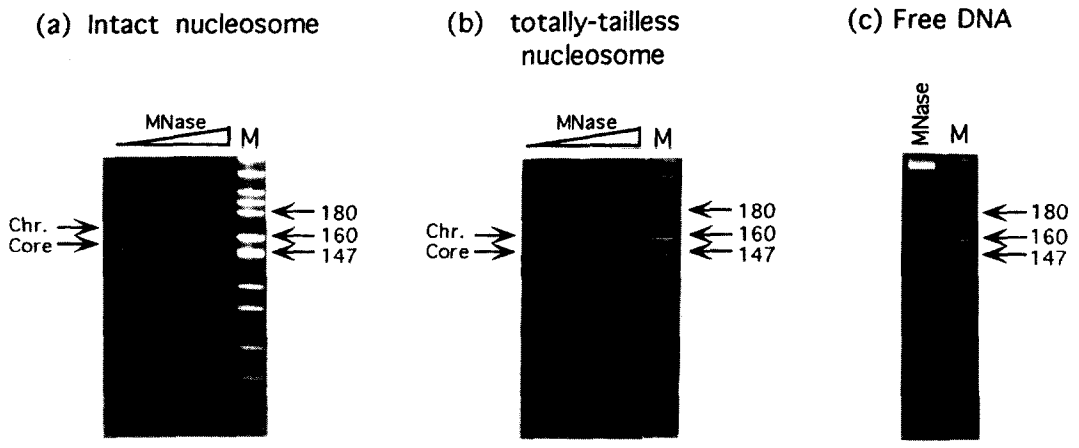

Figure 3. Products of MNase digestion of the H1°-intact nucleosome (**a**), the H1°-totally tailless nucleosome (**b**), and the naked DNA fragment used for the above reconstitutions (**c**). The digestion patterns were visualized by ethidium bromide staining. Note that the free DNA present in the incubation mixtures subjected to MNase digestion will not contribute to the patterns observed with the reconstituted particles, since under the conditions of digestion used to obtain DNA from these particles naked DNA was completely digested to small fragments unobservable on gels. Lanes marked M contain pBR322/*Msp*I size markers. The arrows on the left-hand side of panels (**a**) and (**b**) denote the positions of the DNA bands resulting from MNase digestion of linker DNA to the chromatosome and core particle.

al. [32]. In this approach, the reconstituted particles were subjected to MNase digestion to trim down the unprotected linker DNA, the digested DNA was purified and fractionated on DNA electrophoretic gels. DNA bands of defined lengths (146 bp representing the core particle and 168 bp representing the chromatosome) were eluted from the gels, end-labeled, subjected to restriction nuclease digestion and the lengths of the resulting DNA fragments were determined by electrophoresis on polyacrylamide sequencing gels.

The electrophoretic patterns of *Xbo*I fragments on such gels define one major position of the core particle located between bp 34 and 181 (see DNA bands of 108 and 39 bp in *figure 4*, lanes 2 in (a) and (b)). This is also the major core position determined by Adams and Workman [25], and in our previous study [7]. The core position was the same for the three kinds of reconstitutes, in conformity with earlier data indicating that the histone tails are not determinants of nucleosome positioning [32]. Addition of LH to the intact *(figure 4a)*, or the totally tailless core nucleosome particles *(figure 4b)* led to the production of two major *Xbo*I bands, 108 bp and 56 bp in length, which indicates that LH protects linker DNA highly asymmetrically, on one side of the core particle only *(figure 4c)*. The protection result with the H3 tailless reconstitute was exactly the same as that with the intact or the totally tailless material (not shown). Thus, LH does not require the amino termini of the core histones for its binding to the nucleosome; moreover, it binds to exactly the same location in the presence or absence of these termini.

4. Discussion

Acetylation of core histones and partial depletion of LH are considered characteristic features of transcriptionally active chromatin. That the two processes may be interrelated is suggested by the correlation between core histone acetylation and LH deficiency in newly replicated [33] or transcriptionally active [34] chromatin. However, the exact molecular mechanisms underlying this correlation and its functional consequences vis-a-vis binding of general and gene-specific transcription factors remain elusive.

In an attempt to look more closely into this issue, we studied LH binding to nucleosomes subtly differing in the composition of their histone octamers. Core histones truncated at their N-termini have been widely used by numerous laboratories for nucleosome reconstitution to mimic the effect of histone tail acetylation, a modification that drastically reduces the affinity of their binding to DNA (e.g. [35]). Our studies with nucleosomes containing intact core histones, core histones specifically devoid of the N-terminal portion of histone H3, or all core histones lacking their amino termini indicate that LH binds less stably to nucleosomes containing truncated core histones. This result agrees with some earlier reports [18]. More importantly, the site of LH binding is not dependent on these termini: LH binding protects linker DNA in exactly the same way in nucleosomal particles containing intact core histones and those containing truncated core histones.

What could be the molecular basis for the reduced affinity of LH to nucleosomes possessing acetylated core

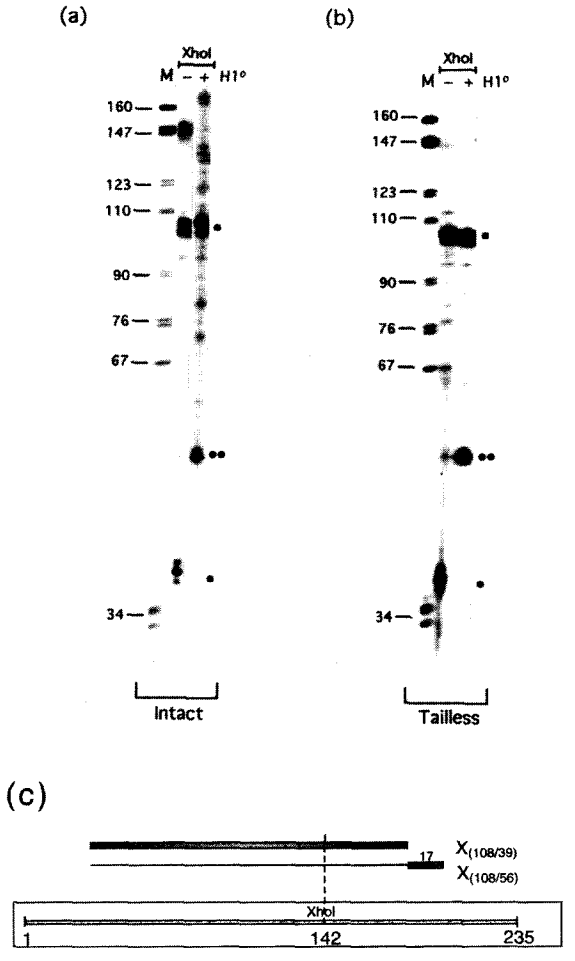

Figure 4. Linker histone-induced protection of linker DNA against MNase digestion. Autoradiography of the labeled DNA fragments obtained following restriction nuclease digestion of DNA bands of 146 bp and 168 bp in length (*figure 3*). Lanes labeled M contain pBR322/*Msp*I size markers. Main digestion products identified as representing core or chromatosome positions (see text) are marked by dots. One dot designates fragments seen in either the core nucleosome or in both the core and the chromatosome; two dots designate new fragments observed in chromatosome digests only. **a.** Reconstitutes containing intact histone octamers. **b.** Reconstitutes containing totally-tailless histone octamers. **c.** Scheme summarizing the protection data. The positions of the core particle is denoted as a gray bar, and those of the chromatosomes as a plain line with a stippled gray box at the end, representing the DNA stretch protected by LH binding. The number above this box denotes the length of the protected region (in bp). The framed bar in the middle of the scheme represents the DNA fragment used for reconstitution, with the site for *Xbo*I cleavage marked.

histone tails or lacking these tails altogether? The location of the LH in the nucleosome is determined entirely by factors other than the tails of the core histones. However, these tails may still affect the affinity of LH binding, by either direct interaction with the protein, or by conformational changes they may confer on the particle, depending on their interactions with the DNA (which, in turn, may be a function of their state of post-synthetic modifications). At this point, it is difficult to see exactly how the tails may affect LH binding, since the crystal structure of the core particle [23] shows that these tails are disorganized and probably extend away from the nucleosomal core. The amino termini, though, may influence the conformation of the particle by loosely associating with the outside of the DNA supercoil [36]. Such changes, if they occur, must be subtle, for neither neutron scattering [37] nor sedimentation [38] reveal significant dimensional changes in core particles upon tail cleavage. It is becoming increasingly clear, however, that the nucleosome core is capable of significant conformational changes (see for example, [39-41]), not all of which would by necessity produce observable changes in dimensions.

Finally, we note that virtually all of these physical studies of the effects of either tail removal or acetylation have utilized core particles. Even if most of the core histone tails (except H3, see figure 7 in [20]) cannot reach a significant portion of the linker, they are potentially capable of interacting with that 20 or so base pairs which are needed to extend the 146 bp of core particle DNA to create the binding site for the LH. It must be emphasized that the X-ray diffraction studies do not show any specific roles for theses termini in the core particle [36]. They may, instead find their true roles in the full nucleosome, or chromatosome; stabilization of this region may be essential for strong binding of LHs.

It remains difficult to believe that structures so highly conserved as the core histone tails do not have very special structural functions. One of these may well reside in modulation of the stability of linker histones binding to the chromatin fiber. The finding of Juan et al. [18] that acetylation or removal of the tails weakens H1-nucleosome interaction so as to stimulate transcription factor binding is certainly supportive of this concept.

Acknowledgments

We are indebted to Drs. D. Doenecke and J. Workman for providing plasmids pWH312 and pGUB, respectively. This research was supported by NIH Grant GM50276 and by TW00568 FIRCA (Fogarty International Research Cooperation Award) to K. v. H. and J.Z.

References

[1] Felsenfeld G., Chromatin as an essential part of the transcriptional mechanism, Nature 355 (1992) 219–224.

[2] Adams C.C., Workman J.L., Nucleosome displacement in transcription, Cell 72 (1993) 305–308.
[3] Wolffe A.P., Wong J., Pruss D., Activators and repressors: making use of chromatin to regulate transcription, Genes Cells 2 (1997) 291–302.
[4] Zlatanova J., van Holde K., The linker histones and chromatin structure: new twists, Prog. Nucleic Acids Res. Mol. Biol. 52 (1996) 217–259.
[5] Crane-Robinson C., Where is the globular domain of linker histone located on the nucleosome?, Trends Biochem. Sci. 22 (1997) 75–77.
[6] Wong J., Li Q., Levi B.-Z., Shi Y.-B., Wolffe A.P., Structural and functional features of a specific nucleosome containing a recognition element for the thyroid hormone receptor, EMBO J. 16 (1997) 7130–7145.
[7] An W., Leuba S.H., van Holde K., Zlatanova J., Linker histone protects linker DNA on only one side of the core particle and in a sequence dependent manner, Proc. Natl. Acad. Sci. USA 95 (1998) 3396–3401.
[8] An, W., van Holde K., Zlatanova J., Linker histone protection of chromatosomes reconstituted on 5S rDNA from *Xenopus borealis*: A reinvestigation, Nucleic Acids Res. 26 (1998) 4042–4047.
[9] Sera T., Wolffe A.P., Role of histone H1 as an architectural determinant of chromatin structure and as a specific repressor of transcription on *Xenopus* oocyte 5S rRNA genes, Mol. Cell. Biol. 18 (1998) 3668–3680.
[10] Belyavsky A.V., Bavykin S.G., Goguadze E.G., Mirzabekov A.D., Primary organization of nucleosomes containing all five histones and DNA 175 and 165 base-pairs long, J. Mol. Biol. 139 (1980) 519–536.
[11] Boulikas T., Wiseman J.M., Garrard W.T., Points of contact between histone H1 and the histone octamer, Proc. Natl. Acad. Sci. USA 77 (1980) 127–131.
[12] Glotov B.O., Itkes A.V., Nikolaev L.G., Severin E.S., Evidence for the close proximity of histones H1 and H3 in chromatin of intact nuclei, FEBS Lett. 91 (1978) 149–152.
[13] Ring D., Cole R.D., Chemical cross-linking of H1 histone to the nucleosomal histones, J. Biol. Chem. 254 (1979) 11688–11695.
[14] Allan J., Harborne N., Rau D.C., Gould H., Participation of core histone 'tails' in the stabilization of the chromatin solenoid, J. Cell Biol. 93 (1982) 285–297.
[15] Allan J., Mitchell T., Harborne N., Böhm L., Crane-Robinson C., Roles of H1 domains in determining higher order chromatin structure and H1 location, J. Mol. Biol. 187 (1986) 591–601.
[16] Ura K., Wolffe A.P., Hayes J.J., Core histone acetylation does not block linker histone binding to a nucleosome including a *Xenopus borealis* 5S rRNA gene, J. Biol. Chem. 269 (1994) 27171–27174.
[17] Ura K., Kurumizaka H., Dimitrov S., Almouzni G., Wolffe A.P., Histone acetylation: influence on transcription, nucleosome mobility and positioning, and linker histone-dependent transcriptional repression, EMBO J. 16 (1997) 2096–2107.
[18] Juan L.J., Utley R.T., Adams C.C., Vettese-Dadey M., Workman J.L., Differential repression of trancription factor binding by histone H1 is regulated by the core histone amino termini, EMBO J. 13 (1994) 6031–6040.
[19] Krajewski W.A., Becker P.B., Reconstitution of hyperacetylated, DNase I-sensitive chromatin characterized by high conformational flexibility of nucleosomal DNA, Proc. Natl. Acad. Sci. USA 95 (1998) 1540–1545.
[20] Zlatanova J., Leuba S.H., Vanholde K., Chromatin fiber structure: morphology, molecular determinants, structural transitions, Biophys. J. 74 (1998) 2554–2566.
[21] Leuba S.H., Bustamante C., Zlatanova J., van Holde K., Contribution of linker histones and histone H3 to chromatin structure: SFM studies on trypsinized fibers, Biophys. J. 74 (1998) 2823–2829.
[22] Leuba S.H., Bustamante C., van Holde K., Zlatanova J., Linker histone tails and the N-tails of histone H3 are redundant: SFM studies of reconsitututed fibers, Biophys. J. 74 (1998) 2830–2839.
[23] Luger K., Mäder A.W., Richmond R.K., Sargent D.F., Richmond T.J., Crystal structure of the nucleosome core particle at 2.8 Å resolution, Nature 389 (1997) 251–260.
[24] Doenecke D., Tönjes R., Differential distribution of lysine and arginine residues in the closely related histone H1o and H5, J. Mol. Biol. 187 (1986) 461–464.
[25] Adams C.C., Workman J.L., Binding of disparate transcriptional activators to nucleosomal DNA is inherently cooperative, Mol. Cell. Biol. 15 (1995) 1405–1421.
[26] Leuba S., Zlatanova J., van Holde K., On the location of histones H1 and H5 in the chromatin fiber: studies with immobilized trypsin and chymotrypsin, J. Mol. Biol. 229 (1993) 917–929.
[27] Laemmli U.K., Cleavage of structural proteins during the assembly of the head of bacteriophage T4, Nature 227 (1970) 680–685.
[28] Garcia-Ramirez M., Leuba S.H., Ausio J., One-step fractionation method for isolating H1 histones from chromatin under nondenaturing conditions, Protein Exp. Purif. 1 (1990) 40–44.
[29] Leuba S.H., A one-step preparative method to reconstitute linker histones onto linker histone-stripped chromatin fibers, Methods. Mol. Cell. Biol. 6 (1997) 125–133.
[30] Simon R.H., Felsenfeld G., A new procedure for purifying histone pairs H2A + H2B and H3 + H4 from chromatin using hydroxylapatite, Nucleic Acids Res. 6 (1979) 689–696.
[31] Tatchell K., van Holde K.E., Reconstitution of core particles, Biochemistry 16 (1977) 5295–5303.
[32] Dong F., Hansen J.C., van Holde K.E., DNA and protein determinants of nucleosome positioning on sea urchin 5S rRNA gene sequences *in vitro*, Proc. Natl. Acad. Sci. USA 87 (1990) 5724–5728.
[33] Perry C.A., Annunziato A.T., Histone acetylation reduces H1-mediated nucleosome interactions during chromatin assembly, Exp. Cell Res. 196 (1991) 337–345.
[34] Ridsdale J.A., Hendzel M.J., Delcuve G.P., Davie J.R., Histone acetylation alters the capacity of the H1 histones to condense transcriptionally active/competent chromatin, J. Biol. Chem. 265 (1990) 5150–5156.
[35] Hong L., Schroth G.P., Matthews H.R., Yau P., Bradbury E.M., Studies of the DNA binding properties of histone H4 amino terminus. Thermal denaturation studies reveal that acetylation markedly reduces the binding constant of the H4 'tail' to DNA, J. Biol. Chem. 268 (1993) 305–314.
[36] Luger K., Richmond T.J., The histone tails of the nucleosome, Curr. Opin. Genet. Dev. 8 (1998) 140–146.
[37] Imai B.S., Yau P., Baldwin J.P., Ibel K., May R.P., Bradbury E.M., Hyperacetylation of core histones does not cause unfolding of nucleosomes. Neutron scatter data accords with disc shape of the nucleosome, J. Biol. Chem. 261 (1986) 8784–8792.
[38] Ausio J., Dong F., van Holde K.E., The use of selectively trypsinized nucleosome core particles to analyze the role of histone 'tails' in the stabilization of the nucleosome, J. Mol. Biol. 206 (1989) 451–463.
[39] Usachenko S.I., Gavin I.M., Bavykin S.G., Alterations in nucleosome core structure in linker histone-depleted chromatin, J. Biol. Chem. 271 (1996) 3831–3836.
[40] Hamiche A., Carot V., Alilat M., De Lucia F., O'Donohue M.F., Révet B., Prunell A., Interaction of the histone (H3-H4) 2 tetramer of the nucleosome with positively supercoiled DNA minicircles: Potential flipping of the protein from a left- to a right-handed superhelical form, Proc. Natl. Acad. Sci. USA 93 (1996) 7588–7593.
[41] Walia H., Chen H.Y., Sun J.M., Holth, L.T., Davie, J.R., Histone acetylation is required to maintain the unfolded nucleosome structure associated with transcribing DNA, J. Biol. Chem. (1998) 14516–14522.