The chromatin organization of eukaryotic telomeres is essential for telomeric function and is currently receiving great attention. In yeast, the structural organization of telomeres involves a complex interplay of telomeric proteins that results in the formation of heterochromatin. This telomeric heterochromatin involves homotypic and heterotypic protein interactions that have been summarized in a general model.

Recent analyses have focused on the study of the structural complexity at yeast telomeres to the level of specific nucleosomes and of the distribution of protein complexes in a natural telomeric region (LIII). In this report, we further analyze the structural complexity of LIII and the implication of this structure on telomeric silencing. It is shown that the establishment of repressive heterochromatin structures at LIII requires the recruitment of Sir3p through interaction with the N terminus of histone H4. The establishment of such structures does not require acetylation of any of four lysines located in the H4 N terminus (lysines 5, 8, 12, and 16).

Telomeres stabilize chromosomes, facilitate replication of chromosomal termini, and are functionally linked to aging and tumorigenesis (1, 2). The chromatin organization of telomeres is believed to be essential for their function and is currently receiving great attention. In particular, the chromatin structure of yeast telomeres is probably the best known among all eukaryotes because of their heterochromatic nature, required for transcriptional silencing in both artificial (3) and natural (4) contexts.

In Saccharomyces cerevisiae, the telomeric sequence is composed of about 350 base pairs containing the (C\textsubscript{1–3}A\textsubscript{n})\textsubscript{9} repeats. This element is followed by two main subtelomeric sequences: the X and the Y’ elements (5). X elements are present at all telomeres and can exist in two main forms, a complete form containing the X core and the STR-A, B, C, D elements or a short form containing the X core or part of it (5–8). Y’ elements are highly conserved and are present in about 70% of the telomeres (5–7). Thus, yeast telomeres contain tandem repetitions of the (C\textsubscript{1–3}A\textsubscript{n})\textsubscript{9} motif flanked by subtelomeric, middle repetitive sequences (reviewed in Ref. 9), internally followed by unique sequences.

As for the primary sequence, the chromatin structure of yeast telomeres is also organized in different domains. The terminal (C\textsubscript{1–3}A\textsubscript{n}) elements are organized into a nuclease-resistant structure called the telosome (10, 11) that does not contain nucleosomes and is firmly associated with the protein Rap1 (10–12). This protein binds to the repetitive (C\textsubscript{1–3}A\textsubscript{n})\textsubscript{9} sequences (13, 14) and interacts with other proteins including Rif1p, Rif2p, Sir3p, and Sir4p (15–17). In addition, Sir3p and Sir4p interact among them and with nucleosomes located in subtelomeric regions through the N termini of histones H3 and H4. The nature of the available evidence obtained so far for Sir3p-histone H4 interactions is genetic and biochemical (reviewed in Ref. 18).

The crystal structure of the nucleosome core particle has been recently resolved at 2.8 Å of resolution (19). This structure shows that the highly basic N-terminal tail of histone H4 (amino acids 1–25) potentially binds as an extended chain to a region of extreme acidity on the exposed face of the H2A-H2B dimer of a neighboring particle. The H4 residues involved in the interparticle contact are the amino acids 16–24, which are also involved in the binding to the silencing protein Sir3p. These data predict that Sir3p interacts with histone H4 at telomeres and alters nucleosomes interactions while participating in the formation of telomeric heterochromatin.

The complex interplay of telomeric proteins has been summarized in a model for telomeric heterochromatin (18). This general model applies to all 32 telomeres of S. cerevisiae and takes into account homotypic and heterotypic protein interactions. In summary, in a telomeric region, a telosome is internalized and takes into account homotypic and heterotypic protein interactions. This paper is available online at http://www.jbc.org
promoter region of Ty5–1 and releases Ty5–1 silencing. In contrast, Sir3p is not required to keep the overall tight organization of the X element (21). This previous analysis of LIII has focused the study of the structural complexity at telomeres to the level of specific nucleosomes and of the distribution of protein complexes. In addition, it has provided in vivo evidence linking the modification of heterochromatin structure with the loss of transcriptional telomeric silencing (4).

We describe in this report that the deletion of residues 4–28 of histone H4 disrupts the heterochromatin structure of LIII. This disruption mimics the rearrangement of heterochromatin caused by the absence of Sir3p (21). A previous report has shown that the 4–28 N-terminal domain of histone H4 contains residues that are required for Sir3p-H4 in vitro interaction (22). In addition, H4 residues 4–28 are required for the recruitment of Sir3p to telomeres and for telomeric silencing (4, 22).

Thus, we conclude that the establishment of repressive heterochromatin structures at LIII requires the recruitment of Sir3p through interaction with the N terminus of histone H4. The establishment of such structures does not require acetylation of any of the four lysines located in the H4 N terminus (lysines 5, 8, 12, and 16).

**EXPERIMENTAL PROCEDURES**

**Yeast Strains and Culture Conditions**

All strains were provided by M. Grunstein.

*S. cerevisiae* STRA Studies—The following strains were used: wild type LKY153 and mutant LKY155 (isogenic to LKY153 and lacking Sir3p, indicated as sir3). LKY153: MATa ade2–101, his3–200, leu2–3, -112, lys2–801, Trp1–A301, ura 3–52, *Δhhy1/Δhis3*, with plasmid pRS424 (TRP1, 2 μm).

Additional details are provided in Refs. 22–24.

**H4 Studies**—The following strains were used: wt PKY501 and mutants PKY813 and LDY722. PKY501: MATa, ade2–101, his3–200, leu2–3, -112, lys2–801, Trp1–A301, ura 3–52, thr, arg4–1, *hhf1/Δhis3*, hph2-LU2, with pPK301 (CEN3, ARS1, URA3, HHF2). PKY813: isogenic to PKY501, with plasmid pPK613 (*hhf2* del4–28). For further descriptions of these strains, see Refs. 23 and 25. LDY722 is isogenic to PKY501 with plasmid pLD722 (CEN4, ARS1, URA3, HHF2-K5, 8, 12,16R) (26).

Strains LKY153 and LKY155 were grown at 28 °C on SC medium lacking tryptophan containing glucose to an *A*ₐₙ₀ of about 0.5/ml. Strains PKY501, PKY813, and LDY722 were grown similarly on SC medium lacking uracil.

**Nucleosome Sensitivity Analyses**

Cells from 50-ml cultures were collected by centrifugation, treated with zymolyase, and digested with micrococcal nuclease (Mnase) as described previously (27). After digestions of chromatin or naked DNA, the sensitivity to the enzyme was analyzed by the indirect end-labeling technique (28). The DNA samples were purified, digested with *Bam*HI, resolved in agarose gels, and transferred to nitrocellulose membranes. The cutting profile generated by Mnase was visualized after hybridization with the probe indicated in the map in Fig. 1. This probe abuts the *Bam*HI site selected for the analyses and extends in an outer direction from position 1495 to 1725 of *S. cerevisiae* chromosome III. Nucleosomal spacing analyses were performed with Mnase. After digestion of chromatin with Mnase, the purified DNA samples were directly resolved in agarose gels, generating a nucleosome ladder that could be visualized by staining with ethidium bromide. The DNA samples were then transferred to nitrocellulose membranes and hybridized with the probe indicated in the legend to Fig. 1.

**RESULTS**

**Deletion of Residues 4–28 of Histone H4 Disrupts Telomeric Heterochromatin Structure**—The chromatin structure of *S. cerevisiae* left telomeric region of chromosome 3 (LIII) has been analyzed in different wild type and mutant strains. Permeabilized cells were digested with increasing concentrations of Mnase, and the sensitivity to the enzyme was monitored by indirect end-labeling using the probe indicated in Fig. 1. This figure shows the Mnase digestion profiles of chromatin from the parental strain (PKY501) and from two derived H4 mutants (PKY813 and LDY722). PKY813 is isogenic to PKY501 and bears a deletion of residues 4–28 of histone H4 (termed ΔHtH4). LDY722 (termed Ac*Δ*HtH4) has the lysine residues 5, 8, 12, and 16 changed into arginine, thus preventing acetylation in these positions. The chromatin organization of LIII in the wild type strain has been previously reported (21). The digestion profile of this strain is shown in lanes 3–6. One fuzzy telomeric band is observed in the lane containing undigested chromatin from PKY501. Fuzziness is expected from the fact that the yeast population is length-heterogeneous for the (C₁₋₅₅₄₁)ₙ repeat (29). The X element shows low accessibility to Mnase, reflecting a closed overall chromatin structure organization. Inside the X element, this overall protection extends from the STRA sequences to the ACS binding site, a silenced origin of replication. Protein complexes and irregular, but well positioned nucleosomes coexist inside the X element. In contrast, the 5′ region of the Ty5–1 retrotransposon accommodates a regular array of nucleosomes that are associated with specific DNA sequences. The map at the sides of the gel images schematically depicts such organization both in the wild type (filled half-circles) and in the ΔHtH4 mutant (empty half-circles). Lanes 7–10 and 11–14 show the Mnase digestion profiles of the two histone H4 mutants (PKY813 and LDY722, respectively).

In PKY813 the length of the band detected in the absence of Mnase digestion is higher (lane 7) than in the wild type strain (lane 3). This is because of the fact that the subpopulation of cells from PKY813 used in this study bears a 5.5 kilobase Y′-short subtelomeric element inserted into the (C₁₋₅₅₄₁)ₙ repeat at ~150 base pairs from the X element border (to be detailed elsewhere; see the map on the right side of Fig. 1). This insertion is favored by the ΔHtH4 mutation,² is stable (being constantly observed for at least 100 generations), and is not present in all the subpopulations derived from the original mutated clone (see below).

The digestion profiles in lanes 7–10 show that the Y′-short element inserted into the (C₁₋₅₅₄₁)ₙ repeat of PKY813 has a complex Mnase digestion pattern, too distant from the probe to allow any detailed analysis. Two separate (C₁₋₅₅₄₁)ₙ tracts are present in LIII in these cells: one terminal and one internal, between the Y′ and X elements. The terminal (C₁₋₅₅₄₁)ₙ tract is organized into the so-called telosomic structure and is expected to be Mnase-inaccessible, as actually observed. In addition, also the internal 150-base pairs long (C₁₋₅₅₄₁)ₙ tract is Mnase-inaccessible, thus suggesting a closed heterochromatic and telosome-like organization.

Moving inward from the internal (C₁₋₅₅₄₁)ₙ repeat, the X element of the ΔHtH4 mutant (lanes 7–10) shows, as in the wild type strain, overall protection against Mnase. Thus, the 4–28 residues from the N terminus of histone H4 are not essential to keep the closed overall organization of the X element. In addition, the digestion pattern of the X element is quite similar in the wild type and the ΔHtH4 strains (see also next sections), suggesting that the lack of H4 N terminus does not cause major changes in the specific chromatin structure of the X element.

The digestion pattern generated by Mnase inside the X element is in general more smeared in the ΔHtH4 mutant than in the wild type strain. This can be explained assuming that most nucleosomes and protein complexes within the X element are in a more relaxed conformation in the mutant. The digestion pattern generated by Mnase in the promoter region of

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¹ The abbreviations used are: Mnase, micrococcal nuclease; wt, wild type.

² S. Venditti, M. A. Vega-Palas, and E. Di Mauro, unpublished results.
Ty5–1 is altered in the ΔNh4 mutant, suggesting a change of nucleosome distribution.

To analyze whether the insertion of Y'S element had any effect on the chromatin structure of LIII, the MNase digestion profiles of Y'S-short-bearing and Y'S-less subpopulations of the PKY813 strain were analyzed. The analysis was made possible by the existence of subpopulations bearing or devoid of Y'S elements that are stable for a sufficient number of generations. The digestion profiles in both the X elements and in the Ty5–1 sequences were essentially indistinguishable in the various subpopulations analyzed, pointing to the independence of the heterochromatin organization of these sequences upon proximity of the telosome structure that characterizes the C1–3A tracts. The digestion profile of these tracts is always the same, independently on the presence (see the profile shown in Fig. 1, lanes 7–10, and in Fig. 2, lanes 7–9) or absence of Y' elements in distal position.

Our restriction analyses of LIII (Refs. 4 and 21, this paper, and unpublished results) have revealed no differences between the sequence of the parental and of the mutant strains analyzed in this work for the region encompassed between the (C1–3A)n repeat/X element border and the BamHI restriction site used for indirect end-labeling are also indicated. S. cerevisiae wild type (wt) strain PKY501 (lanes 3–6) and mutants PKY813 (lacking the N-terminal tail: ΔNh4) (lanes 7–10) and LDY722 (substituted in the N-terminal tail acetylatable Lys residues: Ac Nh4) (lanes 11–14) were grown in 50-ml cultures, collected, treated with zymolyase, and digested with MNase as described previously (27). Indirect end-labeling analysis is shown. Samples 1 and 2 show purified PKY501 DNA (10 µg) digested with 1.2 and 2.5 units/ml MNase, respectively. Samples 3, 7, and 11; 4, 8, and 12; 5, 9, and 13; and 6, 10, and 14 show chromatin digested with 0, 4, 12, and 40 units/ml, respectively. The size marker lane (M) contains a 123-base pair ladder from Life Technologies, Inc. A scaled representation of LIII is shown both on the right and on the left-sides. The representation on the left side depicts a wt LIII, and the right side representation shows the same LIII when bearing a 5.5-kilobase Y' element inserted into the (C1–3A)n repeat at about 0.15 kilobases from the X element border. This insertion is stably present in a subpopulation of the ΔNh4 mutant. Half-circles along these maps represent the translationally phased nucleosomes on the Ty5–1 sequences (filled, PKY501 wt; empty, PKY813 mutant). The lower intensity of the digestion patterns shown in lanes 11–14 is because of an occasional lower yield of the LDY722 samples.

![Fig. 1. Chromatin structure of LIII in histone H4 N terminus mutants.](https://example.com/f1.png)

- **Fig. 1. Chromatin structure of LIII in histone H4 N terminus mutants.** The bottom map is a representation of LIII. The position of the (C1–3A)n repeats (filled bar), the X element, and the Ty5–1 retrotransposon are indicated as well as the TBF1 (gray oval), ABF1 (filled oval), and ACS (empty oval) binding sites (determined in Ref. 21). The STR A-D sequence elements are localized in the left part of the X element. The 5' and 3' long terminal repeats (LTR) of Ty5–1 are also shown. The three arrowed rectangles with decreasingly gray shades represent the open reading frames previously defined by sequencing (44): YCL76w, 75w, and 74w (from left to right). The positions of the probe (black bar) and the BamHI restriction site used for indirect end-labeling are also indicated. S. cerevisiae wild type (wt) strain PKY501 (lanes 3–6) and mutants PKY813 (lacking the N-terminal tail: ΔNh4) (lanes 7–10) and LDY722 (substituted in the N-terminal tail acetylatable Lys residues: Ac Nh4) (lanes 11–14) were grown in 50-ml cultures, collected, treated with zymolyase, and digested with MNase as described previously (27). Indirect end-labeling analysis is shown. Samples 1 and 2 show purified PKY501 DNA (10 µg) digested with 1.2 and 2.5 units/ml MNase, respectively. Samples 3, 7, and 11; 4, 8, and 12; 5, 9, and 13; and 6, 10, and 14 show chromatin digested with 0, 4, 12, and 40 units/ml, respectively. The size marker lane (M) contains a 123-base pair ladder from Life Technologies, Inc. A scaled representation of LIII is shown both on the right and on the left-sides. The representation on the left side depicts a wt LIII, and the right side representation shows the same LIII when bearing a 5.5-kilobase Y' element inserted into the (C1–3A)n repeat at about 0.15 kilobases from the X element border. This insertion is stably present in a subpopulation of the ΔNh4 mutant. Half-circles along these maps represent the translationally phased nucleosomes on the Ty5–1 sequences (filled, PKY501 wt; empty, PKY813 mutant). The lower intensity of the digestion patterns shown in lanes 11–14 is because of an occasional lower yield of the LDY722 samples.
deregression of Ty5–1 and disruption of LIII heterochromatin structures. On the contrary, mutations that mimic the hypoacetylated state of histone H4 N terminus do not significantly alter LIII chromatin structure nor Ty5–1 silencing.

The Lack of Histone H4 N-terminal Tail and the Absence of Sir3p Cause Similar Changes of Heterochromatin Structure—

Fig. 2 compares the MNase digestion profiles of LIII in two different mutant strains: LJY155 (lacking Sir3p) and PKY813 (ΔH4) (lanes 4–6), PKY813 (ΔNH4) (lanes 7–9), and PKY501 (wt, lanes 10–12). Lane D, naked DNA digestion. The similarity of the alterations produced by the sir3 and ΔNH4 mutations is shown by the comparison of lanes 4–6 versus lanes 7–9. M, size markers; LTR, long terminal repeat.

The indirect end-labeling analyses shown in Fig. 2 do not absolutely demonstrate that the change of MNase digestion pattern observed for the ΔNH4 mutants is because of a shift of nucleosomes positions. Such conclusions can be further sustained by a “nucleosomal spacing” analysis in vivo, as already reported for the wt LJY153 (21), to show that nucleosomes are actually present on the Ty5–1 promoter region of the ΔNH4 mutant. Fig. 3 shows the results obtained performing the nucleosomal spacing analyses on all the strains studied in the present report.

Chromatin from these strains was digested with increasing concentrations of MNase. The purified DNA samples were resolved in agarose gels, visualized after staining with ethidium bromide (panel B), transferred, and hybridized with probe 1 (panel A). Lanes 1–3, LJY153 (wt); lanes 4–6, LJY155 (sir3); lanes 7–9, PKY501 (wt); lanes 10–12, PKY813 (ΔNH4); lanes 13–15, LDY722 (Ac NH4).

DISCUSSION

Repressive Heterochromatin Structures Require Recruitment of Sir3p through Histone H4 Interaction—

The model derived from the 2.8-Å crystal structure of the nucleosome suggests that an H4-based internucleosome connection in the higher

FIG. 2. The absence of Sir3p and of the histone H4 N-terminal tail cause similar alterations of LIII heterochromatin. Indirect end-labeling analysis (MNase digestion patterns, obtained as described in Fig. 1) of strains LJY153 (wt, lanes 1–3), LJY155 (sir3) (lanes 4–6), PKY813 (ΔNH4) (lanes 7–9), and PKY501 (wt, lanes 10–12). Lane D, naked DNA digestion. The similarity of the alterations produced by the sir3 and ΔNH4 mutations is shown by the comparison of lanes 4–6 versus lanes 7–9. M, size markers; LTR, long terminal repeat.

FIG. 3. Nucleosomes are present on the Ty5–1 sequences of histone H4 mutants. Nucleosomal spacing analysis. After digestion of chromatin with increasing concentrations of MNase (0, 20, and 40 units/ml for the left-to-right samples in each group), the purified DNA samples were resolved in agarose gels, visualized after staining with ethidium bromide (panel B), transferred, and hybridized with probe 1 (panel A). Lanes 1–3, LJY153 (wt); lanes 4–6, LJY155 (sir3); lanes 7–9, PKY501 (wt); lanes 10–12, PKY813 (ΔNH4); lanes 13–15, LDY722 (Ac NH4).
Sir3p and Histone H4 Interaction in Yeast Telomeres

order structure is replaced in heterochromatin by an interaction with Sir3p (19, 30). The region of histone H4 that binds to the silencing factor localizes in its N terminus and is also required for telomeric silencing. Consequently, it has been suggested (30) that the binding of Sir3p to telomeric areas and the establishment of telomeric silencing would require the disruption of nucleosome-nucleosome interactions. These considerations highlight the interest of analyzing the direct in vivo interaction between Sir3p and the H4 N-terminal tail and its structural consequences.

Studies on natural, nonengineered telomeres often yield population-averaged data because they rely on probes for repetitive sequences; hence, the difficulty of establishing precise boundaries among the various structural compartments of the chromosomal extremities and precise mapping of nucleosomes and other proteins.

We compare in this report the in vivo structural consequences of mutations that affect two different heterochromatin components (histone H4 and Sir3p). The deletion of residues 4–28 of histone H4 cause modifications of LIII heterochromatin that are similar to those caused by the absence of Sir3p. Interestingly, both kinds of mutations release Ty5–1 silencing and silencing at the HM loci (4, 22). In addition, the 4–28 N-terminal domain of histone H4 is required for the recruitment of Sir3p to the telomeres and contains residues required for Sir3p–H4 in vitro interaction (22, 23). Thus, the present data show that the establishment of repressive heterochromatin structures at LIII requires the recruitment of Sir3p through interaction with the N terminus of histone H4.

The most interesting attribute of the structural alterations caused by the lack of Sir3p and by the deletion of histone H4 N terminus is that they are undistinguishable. The major changes observed in both mutant strains is an alternate localization of nucleosomes on the Ty5–1 sequences. To our knowledge, this is an unprecedented observation.

Nucleosomes are known to undergo in vivo destabilization or loss, but not displacement. Their structural modification can reach various degrees of severity and occurs in different genetic processes, the most thoroughly analyzed being the activation of transcription (31–33). A limited ability of translational displacement has been described in vitro, in artificial conditions (34). Multiple alternate positions on the same rotational phase (reviewed in Ref. 35) can be occupied in vitro, ranging usually from 1 to 5 different positions (an extreme case of 15 different positions occupied being provided by the 5 S rDNA gene (36). Thus, the occupation of different positions is documented both as a static possibility in vivo by alternate locations along the same rotational frame and as a temperature-driven dynamic process in vitro in the “mobile nucleosomes” experiments (34), not as an actual process in vivo. Interestingly, two among the mutations known to relieve transcriptional silencing at telomeres (4, 37–39) cause the differential localization of in vivo nucleosomes (Figs. 1–3).

A possible explanation for the shift of nucleosome positioning caused by the lack of Sir3p or the deletion of histone H4 N terminus is that, in the absence of a staple-like function provided by the Sir3p or by its H4 amino-tail counterpart, the tight structure of heterochromatin (in which nucleosomes are constrained in certain positions) does not occur. Under these unconstrained conditions, a more accessible unpressed configuration (with differently located nucleosomes) is organized that allows transcription to start. In addition, the recruitment of the transcriptional preinitiation complex to the Ty5–1 promoter region could also favor the shift of nucleosome positioning in the absence of Sir3p–H4 interaction.

One of the features defined by the 2.8-Å resolution model of the nucleosome structure is that one H4 N-terminal tail segment has the potential to make a strong interparticle connection, perhaps relevant to the higher-order structure of chromatin (19). Because this H4 domain is also required for the binding of Sir3p, the similarity of the effects caused by the lack of Sir3p or of its reacting counterpart in histone H4 is coherent, with the possibility that binding of Sir3p locks down nucleosomes by changing the normal nucleosome-nucleosome interactions.

It was suggested that the R1 domain of histone H4 is involved in stabilizing the bend caused on DNA by the interaction with the histone octamer (25) at the site defined as dyad. The R1 domain is functionally defined as a basic region spanning residues 16–19 (24, 30), very sensitive to mutations that alter charge and lead to derepression at HML and at telomeres (37–39). R1 was also shown to be necessary for nucleosome positioning by the a2 repressor (15). Thus, it is likely that the lack of these residues weakens the DNA-H4 tail interactions, allowing a more relaxed and accessible heterochromatin configuration.

In conclusion, the similarity of the modifications caused by the lack of Sir3p and by the deletion of H4 N-terminal tail supports the in vivo interaction of these components at LIII, which agrees with the nucleosome high resolution model. This interaction is required to keep the repressed heterochromatin configuration of the Ty5–1 retrotransposon (4).

The Role of H4 N-terminal Acetylation in Heterochromatin—As mentioned above, the establishment of heterochromatic repressive structures at LIII requires the N terminus of histone H4. In contrast, the simultaneous mutation of the four acetylable lysines (5, 8, 12, 16) of histone H4 to arginines does not significantly affect it.

Previous in vitro binding analyses suggest that the K to R mutation of the four H4 N-terminal lysines does not impair Sir3p-histone H4 interaction (22). In addition, studies on the HM loci have demonstrated that, as in other eukaryotes, heterochromatin in yeast is hypoacetylated at the H4 lysines 5, 8, and 16 but not at lysine 12 (41). However, lysine 12 is not required for the interaction with Sir3p or for the establishment of functional heterochromatin (22, 23).

We have shown that the K to R mutation of the four acetylable lysines does not affect Ty5–1 silencing. In addition, although these mutations moderately inhibit mating (42), they do not lead to derepression of the HMLa locus, as analyzed by Northern hybridization (data not shown), which suggests that they exert a minimal effect of HM repression. Taken together, these data prompt us to propose that the recruitment of Sir3p to telomeres and the consequent establishment of heterochromatic-repressive structures do not require acetylation of any of the H4 N-terminal lysines.

It is interesting to note that the two mutations of histone H4 analyzed in this report (ΔN1H4 and Ac–N1H4) exert a negative effect on the activation of regular non-telomeric polymerase II genes (26). Such gene activation failure has been correlated with the establishment of a closed chromatin structure (43). In addition, the N terminus of histone H4 has been shown to be required for α2 to position nucleosomes and repress gene expression (15). In summary, the N terminus of histone H4 plays an essential role in gene activation and silencing through the establishment of specific chromatin structure organizations. The role of the acetylable lysines differs depending on the specific process and probably on the proteins with which they interact.

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Heterochromatin Organization of a Natural Yeast Telomere: RECRUITMENT OF Sir3p THROUGH INTERACTION WITH HISTONE H4 N TERMINUS IS REQUIRED FOR THE ESTABLISHMENT OF REPRESSIVE STRUCTURES

Sabrina Venditti, Miguel A. Vega-Palas and Ernesto Di Mauro

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