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Principles of nucleosome recognition by chromatin factors and enzymes

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Abstract

The recent torrent of structures of chromatin complexes determined by cryoelectron microscopy provides an opportunity to discern general principles for how chromatin factors and enzymes interact with their nucleosome substrate. We find that many chromatin proteins employ strikingly similar arginine anchor and variant arginine interactions to bind to the nucleosome acidic patch. We also observe that many chromatin proteins target the H3 and H2B histone fold α1-loop1 elbows and the H2B C-terminal helix on the nucleosomal histone face. These interactions with the histones can be complemented with interactions with and distortions of nucleosomal DNA.

Keywords

nucleosome; chromatin; histone; acidic patch; arginine anchor; structural biology

Introduction

When we reviewed how chromatin factors and enzymes recognize the nucleosome in 2016 [1], there were published atomic structures for only 6 proteins or peptides bound to the nucleosome, all determined by X-ray crystallography, and one docking model based on low resolution cryoelectron microscopy (cryo-EM) data [2–8]. Five years later, the resolution revolution in cryo-EM has produced an explosion of new chromatin complex structures. It is therefore an opportune time to examine the more than 40 unique chromatin complex structures now available to identify general principles for how chromatin factors and enzymes recognize the nucleosome.

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Our 2016 review highlighted two general principles for nucleosome recognition: multivalent interactions and the arginine anchor paradigm. We noted that chromatin factors and enzymes often interacted with multiple subunits of the nucleosome across multiple nucleosome surfaces. We also observed that 5 of the then 7 available chromatin complex structures employed an arginine residue from the chromatin protein to engage the histone H2A-H2B dimer acidic patch on the nucleosome surface in essentially an identical manner. We termed this the arginine anchor nucleosome binding motif [5]. The availability of many new chromatin complex structures confirms these two key principles of multivalency and the arginine anchor, but also allows us to identify new structural paradigms for interactions with both the histone and DNA components of the nucleosome (Fig. 1).

The arginine anchor and variant arginines interact with the acidic patch

Early nucleosome complex structures exposed the H2A-H2B acidic patch as a hot spot for nucleosome recognition based on the shared motif of interaction, the arginine anchor [9,10]. Despite this emerging paradigm of nucleosome recognition, it was unclear how many nucleosome binding proteins required the acidic patch for nucleosome engagement and whether other hot spots existed and remained undiscovered. Recent studies have demonstrated the pervasiveness of acidic patch binding proteome-wide and heightened our understanding of the molecular details underlying acidic patch interactions. The nucleosome acidic patch is formed by an evolutionarily conserved cluster of acidic amino acids in histones H2A (E56, E61, E64, D90, E91, and E92) and H2B (E105, E113) [11]. These acidic residues line a depression that is split into two halves by a low ridge (Fig. 2a). In 2020, one of us (R.K.M.) reported an unbiased proteomic analysis of the nucleosome interactome to establish the fundamental principles governing recognition of the nucleosome disk surface [12]. Consistent with early structural studies, the region centered on the acidic patch, including the surface that interacts with the arginine anchor, emerged as a clear hot spot, contributing to nucleosome binding by the majority of proteins overall and more than 90% of the subset of proteins that interact with the nucleosome disk face in this study.

The surge of new nucleosome complex structures solved by cryo-EM not only reinforces the acidic patch as a primary hot spot for nucleosome binding (23 of 41 structures that interact with the histone components of the nucleosome) and provides additional examples of the arginine anchor motif, but also illuminates several new patterns for acidic patch recognition. It is now clear that most proteins use two or more arginines to bind to the acidic patch. Alignment of all acidic patch-interacting arginines from unique structures demonstrates that the canonical arginine anchor is the most common arginine position, but many arginines in variant positions also participate in acidic patch binding (Fig. 2a). With more than twenty examples, the canonical arginine anchors (green) insert with strikingly similar conformations into a narrow cavity bounded by the α2 and α3 helices of H2A and the C-terminal helix of H2B (Fig. 2b). The arginine anchor cavity is formed from three layers: 1) the floor (H2A L93, H2B L106); 2) the middle ring comprising the acidic triad (H2A E61, D90, and E92); and 3) the side wall (H2B E105 and H109) that corrals the arginine anchor and orients it for interaction with the acidic triad. Recently, a de novo R95Q mutation was reported in the arginine anchor of the Polycomb Repressive Complex 1 (PRC1) component RING1A [13]. This mutation is causative in an epigenetic

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neurodevelopmental disorder due to aberrant developmental gene regulation, underscoring the fundamental importance of arginine anchors in health and disease.

Analysis of variant arginines demonstrates a diversity of side chain orientations and binding positions within the acidic patch in addition to the canonical arginine anchor (Fig. 2a). However, a subset of variant arginines converge on one of two acidic patch surfaces, herein described as type 1 and type 2. Type 1 variant arginines (light blue) bind on the opposite half of the acidic patch and commonly interact with H2A E56 and/or H2B E113 (Fig. 2b). The type 1 variant arginine depression is wider that the arginine anchor cavity but equally deep, and like the arginine anchor cavity contains three layers: 1) the floor (H2A A60 and mainchain atoms of the H2A α2 helix); 2) the middle ring of acidic residues (H2A E56, E61, and E64; H2B E113); and 3) two side walls, one constructed by the H2B C-terminal helix (H2B E113 and K116) and the other by the H2B α1L1 elbow (H2B Q47 and V48, see next section). Similar to the arginine anchor cavity, these side walls corral the type 1 variant arginine side chains and direct them to the bottom of the depression. In contrast, type 2 variant arginines (cyan) project their side chain guanidinium groups into a shallow cleft formed by H2A E61, E64, and L65 that is immediately adjacent to the canonical arginine anchor binding cavity (Fig. 2b). We refer to all other variant arginines as atypical variant arginines due to the absence of clear patterns of acidic patch binding.

Based on existing structures, arginine anchors and variant arginines are found roughly equally in structured protein loops, α-helices, and/or extended protein chains (Fig. 2c). For example, cGAS, a cytosolic double-stranded DNA sensor that functions in the innate immune system, is negatively regulated by binding the nucleosome acidic patch using two adjacent loops, one with an arginine anchor and an atypical variant arginine, and the other, a type 2 variant arginine [14–19]. In another example, the histone H3 K79 methyltransferase Dot1L binds the acidic patch using a loop containing a type 1 variant arginine along with an atypical variant arginine [20–23]. Two orthologs of the SWI/SNF family of remodeling complexes, the human BAF complex [24] and the yeast RSC complex [25,26], bind the acidic patch using a single α-helix with four or five arginines all aligned on the nucleosome-facing surface of the helix. These helices include an arginine anchor, type 1 and type 2 variant arginines, and one or more atypical variant arginines. Interestingly, the Set1 catalytic subunit of the yeast COMPASS H3 K4 methyltransferase complex employs a helix with near identical orientation and arginine composition, suggesting evolutionary convergence on a nucleosome binding mechanism [27,28]. Finally, some proteins use arginines in extended peptide chains to interact with the acidic patch, including the H4 K20 methyltransferase Set8 that interacts with its target sequence in the H4 tail and projects an N-terminal extension with an arginine anchor that interacts with the acidic patch [29].

In some instances, related domains use nearly identical modes of acidic patch recognition. Two examples are the RING domains of E3 ligases PRC1 [5] and BRCA1 [30], which both have an arginine anchor imbedded within a similar loop sequence, and the Bromo-associated homology (BAH) domains of yeast proteins Sir3 [6] and Orc1 [31] that interact with the acidic patch using loops with an arginine anchor and a type 1 variant arginine. Interestingly, while several orthologous proteins have been shown to interact similarly with the acidic patch, this is by no means a requirement, as in the case of human Dot1L and its yeast

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ortholog Dot1p that utilize a type 1 variant arginine and a canonical arginine anchor, respectively [20–23,32]. Even with an increasing set of examples of acidic patch-interacting proteins, this structural variability presents challenges to prediction of new arginine anchors and variant arginines except in select cases.

Several questions regarding acidic patch interactions remain. The relative contributions of each arginine to nucleosome binding and/or enzymatic activity has only been reported for a few nucleosome complexes [5,15,16,20,27]. These studies suggest a hierarchy of importance for acidic patch-binding: arginine anchor > type 1/type 2 variant arginines >> atypical variant arginines, but further detailed analysis is required to confirm this hypothesis. Moreover, given the convergence of many chromatin proteins on one surface, it is largely unclear how nucleosome acidic patch binding is regulated. Nearby histone post-translational modification can tune acidic patch interactions, but this may only provide crude regulation [20,33]. A recent discovery that methylation of an acidic patch binding arginine in RCC1 enhances its chromatin interaction, presents a more elegant solution [34]. It remains unclear if arginine methylation or other modifications are used broadly to positively or negatively regulate acidic patch binding. However, there is now no doubt that arginine-acidic patch interactions are extraordinarily pervasive in nucleosome recognition and critical to diverse genome-templated processes.

Interactions with the histone elbow

The arginine anchor is the most prominent structural paradigm used by chromatin proteins and enzymes to engage the nucleosome, but it is not the only one. The plethora of new chromatin complex structures now makes it possible to recognize other structural motifs on the nucleosome targeted by chromatin proteins. Two structural motifs we would like to highlight here are what we term the histone elbow and the histone H2B C-terminal helix.

The histone fold, which enables the pairing of histones H3 with H4 and histones H2A with H2B, is composed of three α-helices separated by two loops. The resulting H3/H4 and H2A/H2B histone fold pairs form crescent structures with outer surfaces that bind DNA in the nucleosome [35] (Fig. 1). The junction of the H3 histone fold α1 helix and L1 loop (H3 α1L1) is exposed on the nucleosome surface and we observe that chromatin proteins interact with this region in multiple nucleosome complex structures. The α1 helix and the L1 loop combination resembles an elbow, and we therefore call this the H3 α1L1 elbow. Over 40% of unique structures where chromatin proteins interact with histones (18 of 41) make close contact with the H3 α1L1 elbow (Fig. 3a).

Although the specific interactions at the H3 α1L1 elbow interface differ among the different chromatin proteins, common themes do emerge. The chromatin proteins that bind the H3 α1L1 elbow usually make close contact through a combination of van der Waal interactions, hydrogen bonding and ionic interactions without significantly altering the structure of the H3 α1L1 elbow. The exceptions to the absence of conformational change are the yeast Dot1p and the human Dot1L proteins where the H3 α1L1 elbow is distorted to position the H3 K79 target of the Dot1 methyltransferase into the enzyme's active site [21,32]. Many of the interactions are made to the L1 loop at the tip of the H3 α1L1 elbow region

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corresponding to H3(76-81) with the sequence QDFKTD. H3 D77 and K79 can make charged interactions with the chromatin protein [5,6,21,29,31,36]. In contrast, the side chain of H3 F78 between these two residues does not appear to interact with chromatin proteins and instead packs against the H4 α2 helix.

The catalytic subunit of several chromatin remodeling enzymes, including Chd1, Chd4, Snf2, Snf2h and ISWI also interact with the H3 α1L1 elbow [37–42]. These enzymes, which share the Snf2 family ATPase domain, bind to the nucleosome at DNA positions SHL2 and SHL6. When bound at SHL2, the ATPase domains are positioned similarly through extensive interactions with the DNA and additional contacts with the H4 N-terminal tail and the H3 α1L1 elbow which is adjacent to SHL2.

H2B is the only other core histone with an exposed α1L1 elbow and like H3, the H2B α1L1 elbow interacts with multiple chromatin proteins (Fig. 3b). (The α1L1 regions of the other core histones, H2A and H4, are buried in the interior of the nucleosome and not solvent accessible.) The tip of the H2B α1L1 elbow corresponding to H2B(47-51) with the sequence QVHPD interacts in almost 30% of the unique chromatin complex structures containing histone interactions (12 of 41). Q47 often hydrogen bonds or makes van der Waal contact with interacting chromatin proteins, while H49 can hydrogen bond or stack with residues from the chromatin protein [2,4,14,24,25,27,43–45]. In addition, P50 and D51 residues in the H2B L1 loop interact with several chromatin proteins [14,27,43–46].

Unlike the histone acidic patch with its well defined residues that can be targeted for study by mutating to alanine or basic residues, the variety of interactions made by chromatin proteins to the H3 and H2B α1L1 elbows make it more difficult to recommend specific mutations to disrupt such interactions. Furthermore, given the multivalent interactions made by most chromatin proteins to multiple surfaces on the nucleosome, more study will be needed to determine how critical the observed histone elbow interactions are. One possible strategy to investigate potential interactions of a chromatin protein with the H3 α1L1 elbow might be to swap the charges on H3 D77 and K79. Similarly, the H2B α1L1 elbow could be targeted by mutating Q47, H49 and D51.

Interactions with the H2B C-terminal helix

The other major protein feature on the nucleosome targeted by chromatin proteins is the H2B C-terminal helix (Fig. 4). It is perhaps not surprising that this helix is contacted in about half of the unique structures with histone interactions (20 of 41) given its prominently exposed position on the surface of the nucleosome and its proximity to the acidic patch targeted by the arginine anchor. However it should be noted that most chromatin proteins do not simply tangentially contact the H2B C-terminal helix as a consequence of the arginine anchor binding to the histone acidic patch. Many make multiple contacts along the H2B C-terminal helix, including chromatin proteins that do not employ an arginine anchor to bind to the histone acidic patch. Some like COMPASS nearly engulf the entire length of the H2B C-terminal helix [27,28]. The interactions made by chromatin proteins to the H2B C-terminal helix include van der Waals interactions, hydrogen bonding and ionic interactions and there does not appear to be a predominant mode of binding employed.

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The fore mentioned nucleosome interactome study from the McGinty laboratory provides experimental evidence of widespread interactions with the H2B and H3 α1L1 elbows and the H2B C-terminal helix proteome-wide [12]. Besides the acidic patch, the two nucleosome disk regions that are most critical for protein binding include a face of the H2B C-terminal helix and parts of either the H2B or H3 α1L1 elbow.

Conformational changes to nucleosomal DNA

In addition to binding to exposed histone surfaces of the nucleosome, many proteins interact with the contorted DNA wrapping the histone octamer and/or to linker DNA projecting from the nucleosome core particle. While typically only minor conformational rearrangements are observed in histone disk surfaces upon protein binding, in several cases, substantial rearrangements are observed in nucleosomal and linker DNA. The majority of these DNA rearrangements can be classified into three categories: 1) unwrapping of entry/exit DNA, 2) bulging of DNA away from the histone octamer surface, and 3) translocation of the DNA sequence around the histone octamer surface (Fig. 5).

To date, the most commonly observed DNA conformational change upon protein-nucleosome interaction is unwrapping of entry/exit DNA. The entry/exit DNA is known to spontaneously unwrap [47] and such DNA end breathing is observed in single particle cryo-EM analysis of nucleosomes [48]. However, several structures demonstrate that nucleosome binding proteins can interact with DNA ends and/or linker DNA to stabilize an unwrapped conformation to elicit specific effects. Examples include H3 K36 methyltransferases Set2 and NSD3 that gain access to their targeted lysine upon DNA unwrapping [49,50], remodelers like SWR1 that unwrap DNA to facilitate histone exchange [51], RNA PolII with elongation factors Elf1 and Spt4/5 transcribing through a nucleosome [52], the inner kinetochore CCAN complex [53], and pioneer transcription factors Sox2 and Oct4, when their sequence recognition motifs are imbedded in positions near the DNA entry/exit site [54]. Interestingly, DNA bulging is induced by Sox2 and Oct4, instead of unwrapping, when motifs are positioned at internal locations. Frequently observed DNA unwrapping, contrasts with nucleosome-bound structures of linker histones [7,55–60] and the H3 K4 demethylase LSD1 [61], which engage linker DNA and stabilize a fully wrapped DNA conformation. A more unique DNA rearrangement is observed for the DNA damage recognition complex UV-DDB. While binding to surface exposed lesions in nucleosomal DNA without altering the nucleosome structure, UV-DDB recognizes occluded lesions by engaging and stabilizing a translocated DNA conformation that relocalizes the lesion to an accessible, exposed position [62]. One noteworthy mechanism of nucleosomal DNA recognition is used by PARP2, whose contacts do not cause major DNA conformational changes, but rather bridges two nucleosomes through recognition of DNA ends to function in double strand break repair [63,64]. As more structures are solved especially with native DNA sequences, we anticipate that these and other DNA conformational changes will be commonplace.

Perspective

Despite the availability of so many new structures of chromatin factors and enzymes in complex with the nucleosome, we still lack structures for many unique classes of

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nucleosome-binding proteins. Moreover, most structures have been solved with artificially stable nucleosome positioning DNA sequences and histones with one, or most often, no histone modifications. Pivoting toward structures with native DNA sequences and established patterns of histone modifications can capture chromatin complexes in a more physiological context. We also need more information about the dynamics of chromatin complexes. Increasingly, cryo-EM data analysis allows dynamic motions of macromolecular complexes to be inferred from conformational heterogeneity. It is clear that most chromatin factors and enzymes engage nucleosomes through flexible and dynamic interactions. Selecting a highly homogeneous subset of particles may enable high resolution reconstructions, but neglects the true dynamic nature of the complexes. Finally, while the accessibility of cryo-EM has provided much needed structural insights, comprehensive functional characterization has lagged behind. While less flashy than increasingly ambitious structures, a greater emphasis on careful mechanistic investigation is necessary to fully leverage the rapidly growing set of structures towards biomedical innovations.

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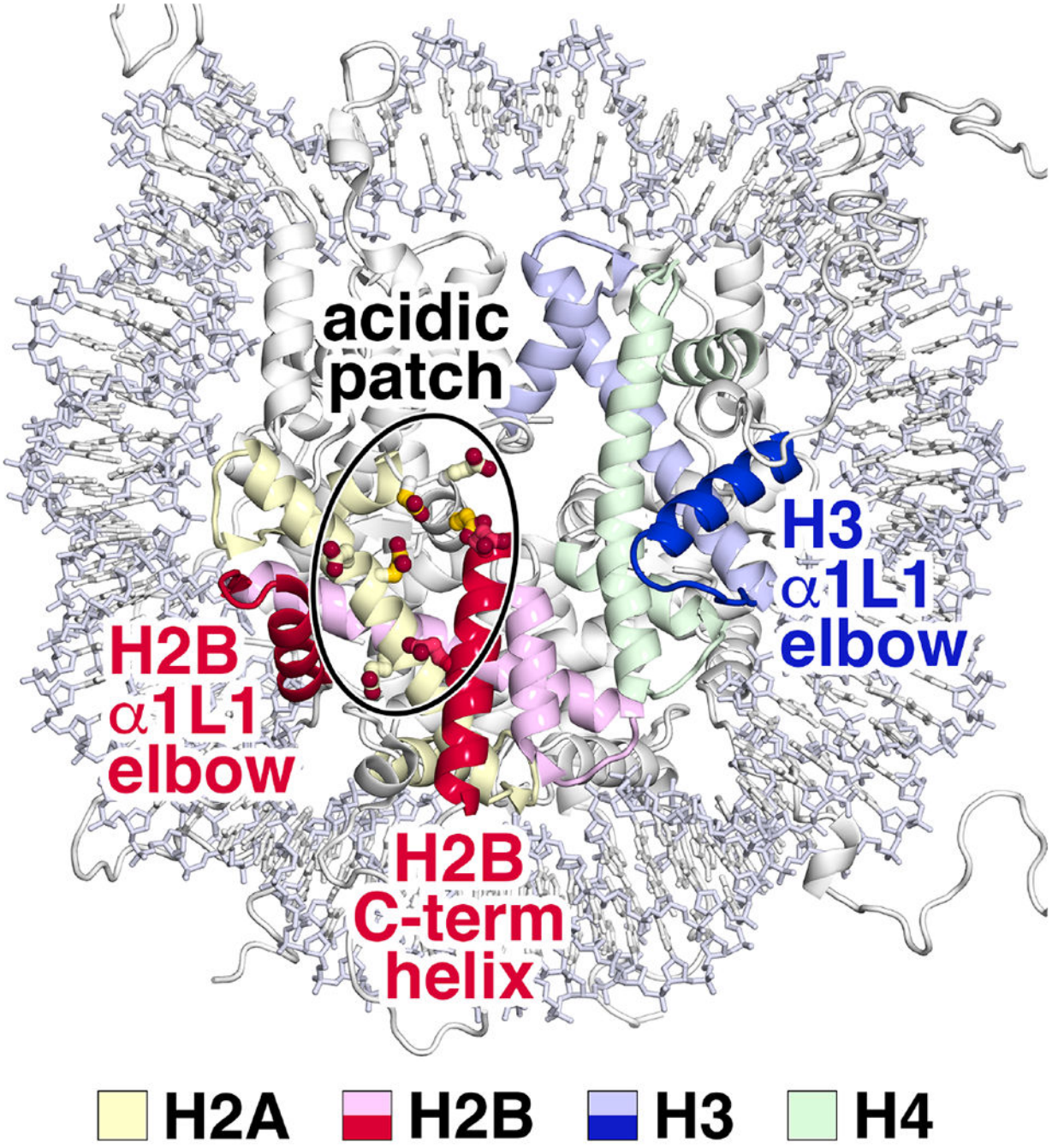

Fig. 1:

Nucleosome features targeted by chromatin proteins. The nucleosome acidic patch created by histone H2A and H2B acidic residues (encircled) is frequently contacted by chromatin protein arginine residues. In addition, the histone H3 α1L1 elbow region of the histone fold (blue), the corresponding histone H2B α1L1 elbow (red) and the histone H2B C-terminal helix are sites of interaction by multiple chromatin proteins. The H2A, H2B, H3 and H4 core histones are shown in shades of yellow, red, blue and green respectively. The carbon

side chain atoms of H2A acidic patch residues E61, D90 and E92 are shown in a more saturated yellow color.

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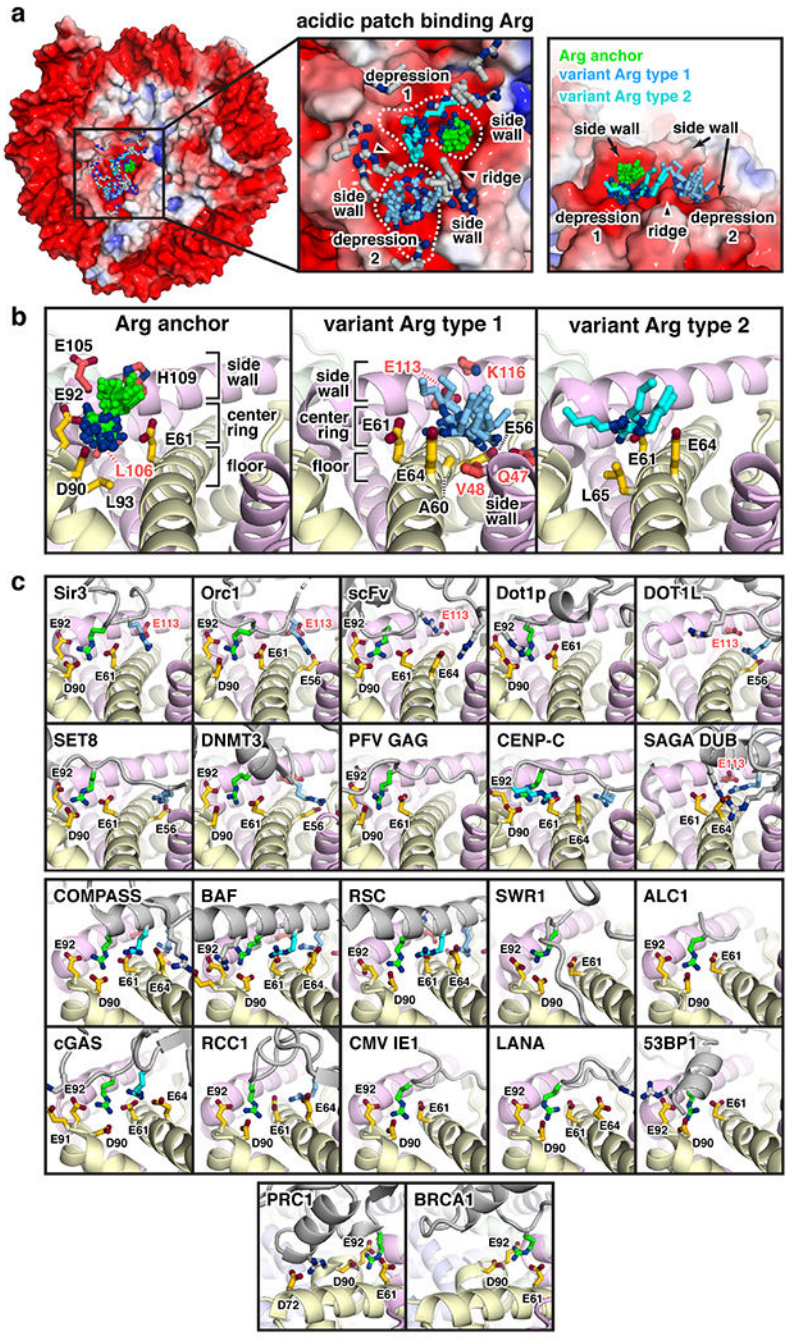

Fig. 2:

Arginine-acidic patch interactions. (a) Left, electrostatic surface disk view of nucleosome generated with APBS (PDB id 3MVD [3]) overlaid with all chromatin protein acidic patch-binding arginines colored by type – arginine anchors (green), type 1 variant arginines (light blue), type 2 variant arginines (cyan), and atypical variant arginines (gray). Center, zoomed top view with atypical variant arginines from Dot1L (PDB id 6NJ9; R278 [21]), SAGA DUB (PDB id 4ZUX; R91 [44]), and COMPASS (PDB id 6VEN; R936 [27]) omitted for clarity. Right, zoomed side view of all arginine anchors and type 1 and 2 variant arginines.

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(b) All arginine anchors (left), type 1 variant arginines (center), and type 2 variant arginines (right) with nearby histone residues annotated. (c) Interactions of chromatin proteins (gray), highlighting arginines (colored as in panels a and b) that interact with the nucleosome acidic patch. Structures are clustered in groups with identical views and shown in cartoon representation with key side chains depicted. Acidic patch binding proteins and protein complexes are Sir3 (PDB id 3TU4; R29 (anchor); R28 (type1) [6]), Orc1 (PDB id 6OM3; R31 (anchor); R29 (type1) [31]), scFV (PDB id 6DZT; R124 (anchor); R126/188 (atypical) [65]), Dot1p (PDB id 7K6Q; R571 (anchor); R572 (atypical) [32]), Dot1L (PDB id 6NJ9; R282 (anchor); R278 (atypical) [21]), Set8 (PDB id 7D1Z; R192 (anchor); R188 (type 1) [29]), DNMT3 (PDB id 6PA7; R743 (anchor); R740 (type 1) [66]), PFV GAG (PDB id 5MLU; R540 (anchor) [67]), CENP-C (PDB id 4X23; R717 (anchor); R714 (type 1); R719 (type 2) [4]), SAGA DUB (PDB id 4ZUX; Sgf11 R84 (type 1); R78/91 (atypical) [44]), COMPASS (PDB id 6VEN; Set1 R901 (anchor); R908 (type 1); R904 (type 2); R936 (atypical) [27]), BAF (PDB id 6LTJ; SMARCB1 R370 (anchor); R377 (type 1); R373 (type 2); R366/374 (atypical) [24]), RSC (PDB id 6TDA; Sfh1 R397 (anchor); R404 (type 1); R400 (type 2); R401/408 (atypical) [25]), SWR1 (PDB id 6GEN; Swc6 R44 (anchor) [51]), ALC1 (PDB id 6ZHX; R9 (anchor) [68]), cGAS (PDB id 7JO9; R241 (anchor); R222 (type 2); R244 (atypical) [14]), RCC1 (PDB id 3MVD; R223 (anchor); R216 (type 1) [3]), CMV IE1 (PDB id 5E5A; R486 (anchor) [43]), LANA (PDB id 1ZLA; R9 (anchor); R12 (atypical) [2]), 53BP1 (PDB id 5KGF; R1627 (anchor); R1630 (atypical) [69]), PRC1 (PDB id 4R8P; Ring1B R98 (anchor); R81 (atypical) [5]), and BRCA1 (PDB id 7JZV; R71 (anchor) [30]).

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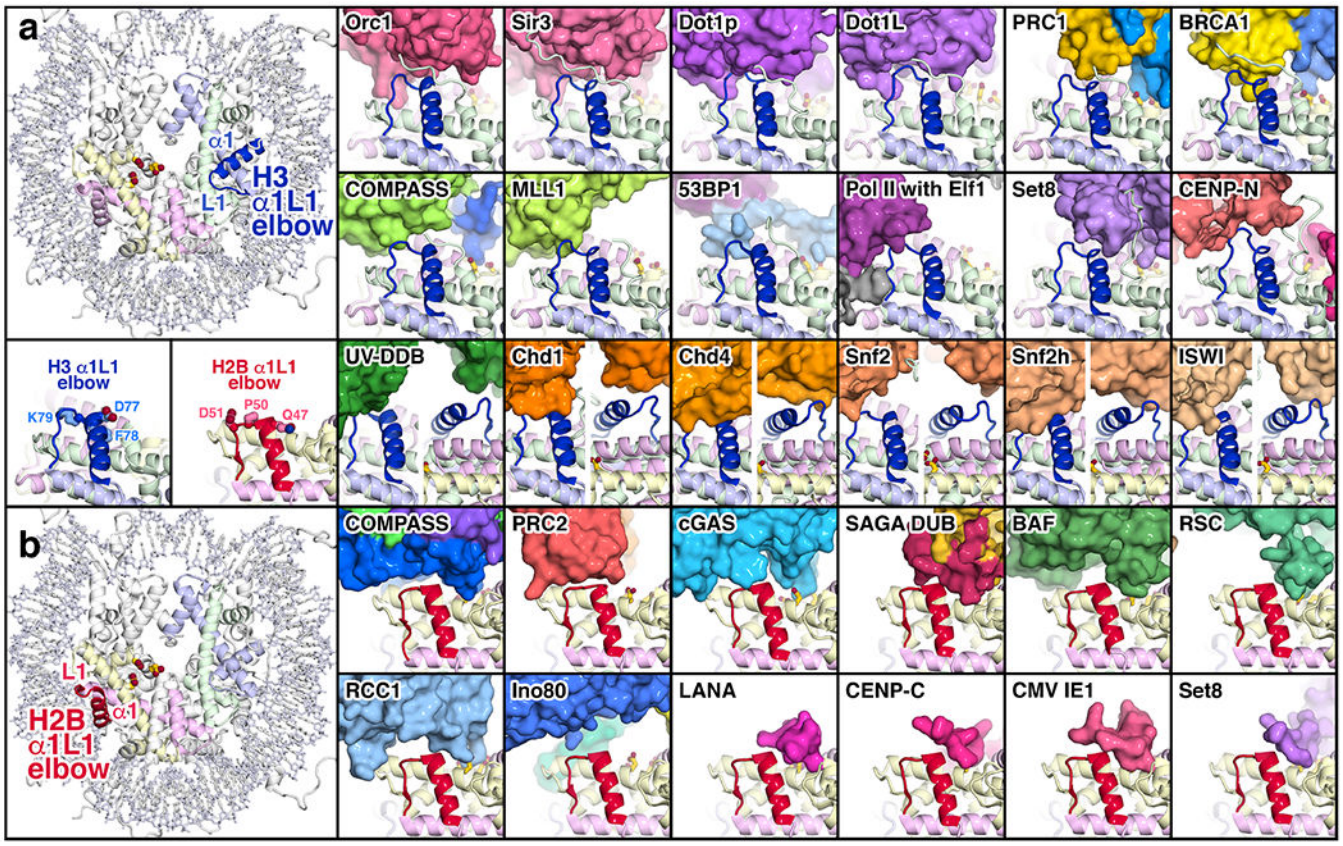

Fig. 3:

Interactions of chromatin proteins with the histone H3 and H2B α1L1 elbows. (a) Interactions with the H3 α1L1 elbow. The location of the H3 α1L1 elbow is shown on the left in the nucleosome crystal structure (PDB id 1KX5 [70]) together with the H2A acidic patch residues E61, D90 and E92. To the right are shown proteins and protein complexes in surface representation that interact with the H3 α1L1 elbow (blue): Orc1 (PDB id 6OM3 [31]), Sir3 (PDB id 3TU4 [6]), Dot1p (PDB id 7K6Q [32]), Dot1L (PDB id 6NQA [21]), PRC1 (PDB id 4R8P [5]), BRCA1 (PDB id 7JZV [30]), COMPASS (PDB id 6VEN [27]), MLL1 (PDB id 6KIU [36]), 53BP1 (PDB id 5KGF [69]), PolII elongation complex with Elf1 (PDB id 6IR9 [52]), Set8 (PDB id 7D1Z [29]), CENP-N (PDB id 6MUP [71]), UV-DDB (PDB id 6R8Y [62]), Chd1 (PDB id 6FTX [38]), Chd4 (PDB id 6RYR [39]), Snf2 (PDB id 5X0Y [40]), Snf2h(PDB id 6NE3 [41]) and ISWI (PDB id 6K1P [42]). In the CENP-CN structure, the α1L1 elbow of the centromeric histone variant, CENP-A, contains two extra residues compared to the histone H3 it replaces. The histones are shown in cartoon representation, and the nucleosomal DNA omitted for clarity. The H3 α1L1 elbow as it occurs in the nucleosome crystal structure is shown in blue in the same orientation together with elbow residues D77, F78 and K79 on the left below the full nucleosome structure. An additional view from the back is provided for Chd1, Chd4, Snf2, Snf2h and ISWI. (b) Interactions with the H2B α1L1 elbow. The location of the H2B α1L1 elbow is shown on the left in the nucleosome crystal structure (PDB id 1k5x) together with the H2A acidic patch residues E61, D90 and E92. Proteins and protein complexes shown that interact with the H2B α1L1 elbow (red) are COMPASS (PDB id 6VEN [27]), PRC2 (PDB id 6WKR

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[45]), cGAS (PDB id 7JO9 [14]), SAGA DUB (PDB id 4ZUX [44]), BAF (PDB id 6LTJ [24]), RSC (PDB id 6TDA [25]), RCC1 (PDB id 3MVD [3]), Ino80 (PDB id 6FML [46]), LANA (PDB id 1ZLA [2]), CENP-C (PDB id 4X23 [4]), CMV IE1 (PDB id 5E5A [43]) and Set8 (PDB id 7D1Z [29]). The H2B α1L1 elbow as it occurs in the nucleosome crystal structure is shown in red in the same orientation together with elbow residues Q47, P50 and D51 on the left above the full nucleosome structure.

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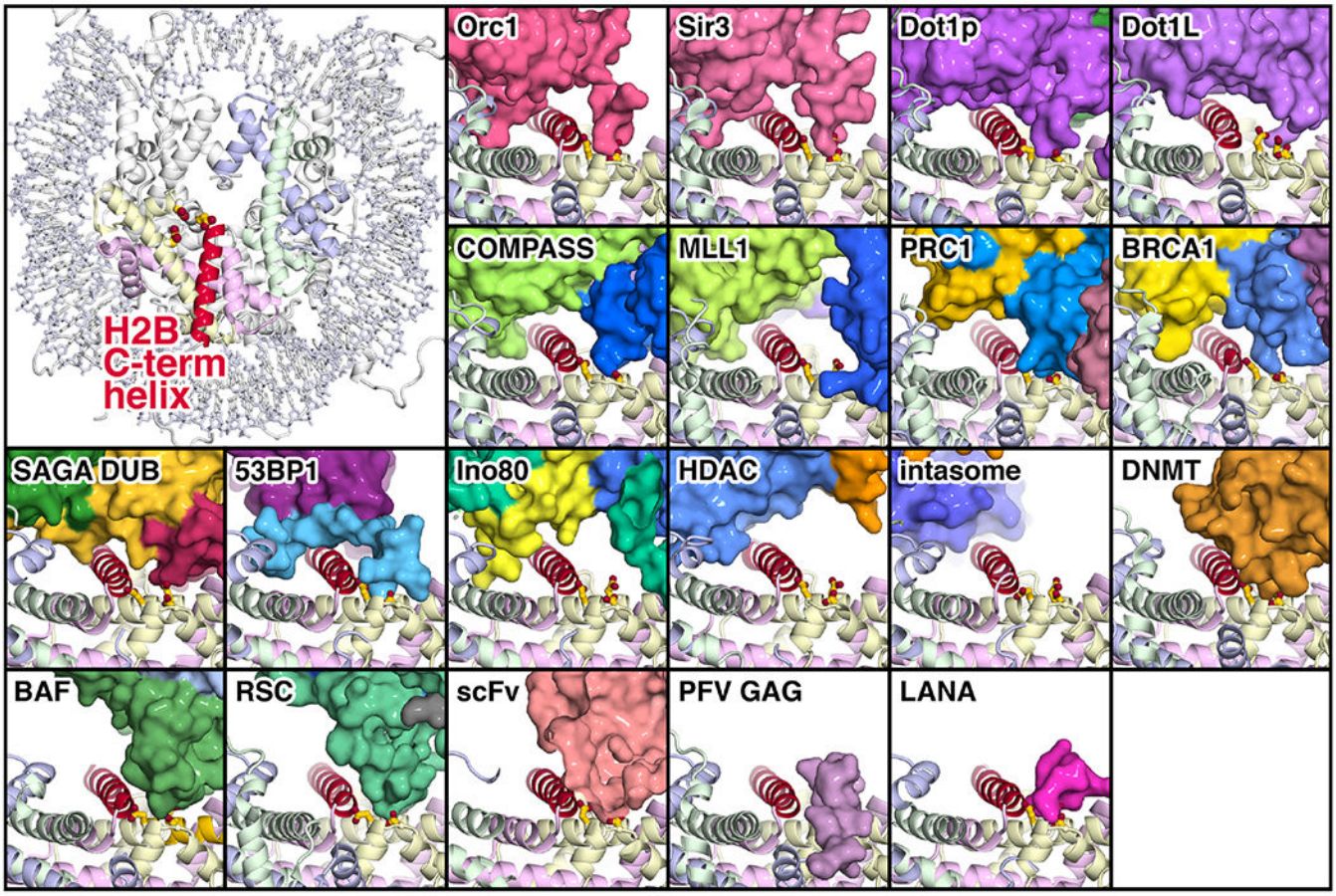

Fig. 4:

Interactions of chromatin proteins with the histone H2B C-terminal helix. The location of the H2B C-terminal helix is shown in the upper left in the nucleosome crystal structure (PDB id 1KX5 [70]) together with the adjacent H2A acidic patch residues E61, D90 and E92. Proteins and protein complex shown in surface representation that interact with the H2B C-terminal helix (red) are Orc1 (PDB id 6OM3 [31], Sir3 (PDB id 3TU4 [6]), Dot1p (PDB id 7K6Q [32]), Dot1L (PDB id 6NQA [21]), COMPASS (PDB id 6VEN [27]), MLL1 (PDB id 6KIU [36]), PRC1 (PDB id 4R8P [5]), BRCA1 (PDB id 7JZV [30]), SAGA DUB (PDB id 4ZUX [44]), 53BP1 (PDB id 5KGF [69]), Ino80 (PDB id 6FML [46]), HDAC (PDB id 6Z6P [72]), intasome (PDB id 6RNY [73]), DNMT (PDB id 6PA7 [66]), BAF (PDB id 6LTJ [24]), RSC (PDB id 6TDA [25]), scFv (PDB id 6DZT [65]), PFV GAG (PDB id 5MLU [67]) and LANA (PDB id 1ZLA [2]). The histones are shown in cartoon representation, and the nucleosomal DNA omitted for clarity.

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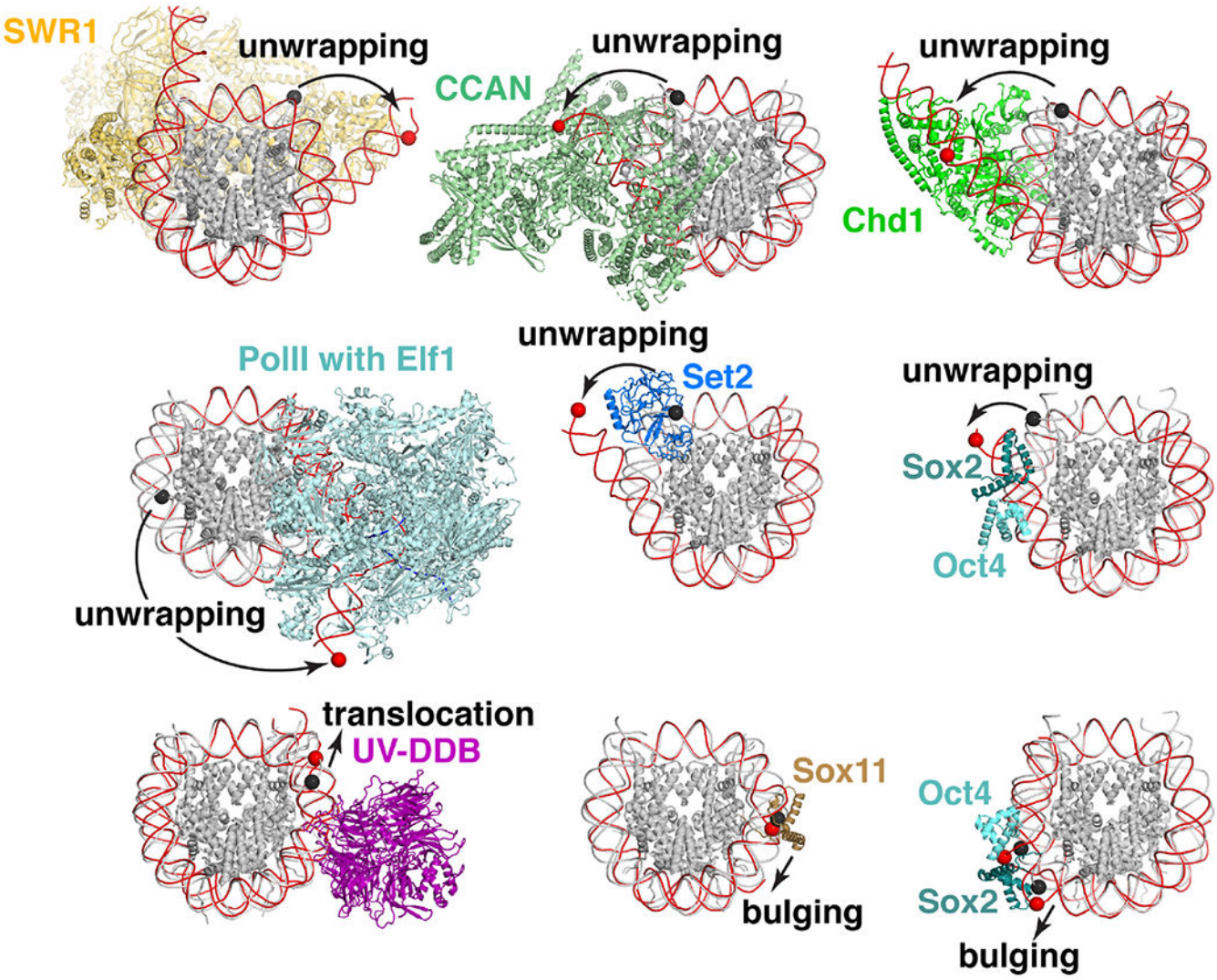

Fig. 5:

DNA conformational changes upon nucleosome binding. Chromatin proteins and complexes induce conformational changes to DNA. Overlay of nucleosome-bound (red DNA) and nucleosome only (white DNA) structures with identical DNA positions for bound and nucleosome only structures highlighted with red and black spheres, respectively. Nucleosome only structure PDB id 6PX1 used when matched structure is unavailable. Conformational changes include unwrapping as depicted for SWR1 (PDB id 6GEN [51]), CCAN (PDB id 6QLD [53]), Chd1 (PDB id 5O9G [37]), PolII with Elf1 and Spt4/5 stalled at SHL-1 (PDB id 6IR9 [52]), Set2 (PDB id 6NZO, nucleosome only 6PX1 [49]), and Sox2/Oct4 at SHL-6 (PDB id 6T90, nucleosome only 6T93 [54]); translocation as depicted for UV-DDB with THF2 lesion at -3 position (PDB id 6R91, nucleosome only 6R94 [62]); and bulging with Sox11 (PDB id 6T7A, nucleosome only 6T79 [74]) and Sox2/Oct4 at SHL+6 (PDB id 6YOV, nucleosome only 6T93 [54]).