Crystal Structure of the Chromodomain Helicase DNA-binding Protein 1 (Chd1) DNA-binding Domain in Complex with DNA*§

Received for publication, August 16, 2011, and in revised form, October 20, 2011 Published, JBC Papers in Press, October 27, 2011, DOI 10.1074/jbc.C111.294462

Amit Sharma†1, Katherine R. Jenkins†, Annie Héroux†, and Gregory D. Bowman‡1,2

From the †Thomas C. Jenkins Department of Biophysics, Johns Hopkins University, Baltimore, Maryland 21218 and the ‡Biology Department, Brookhaven National Laboratory, Upton, New York 11973

Background: The Chd1 DNA-binding domain is required for binding DNA outside the nucleosome core.

Results: The Chd1 DNA-binding domain primarily engages one strand of a straight DNA duplex.

Conclusion: Yeast Chd1 and Isw1 bind DNA with distinct geometries, yet contact the phosphate backbone using similar elements.

Significance: Knowledge of protein-DNA interactions is important for understanding how chromatin remodelers productively engage nucleosomes.

Chromatin remodelers are ATP-dependent machines that dynamically alter the chromatin packaging of eukaryotic genomes by assembling, sliding, and displacing nucleosomes. The Chd1 chromatin remodeler possesses a C-terminal DNA-binding domain that is required for efficient nucleosome sliding and believed to be essential for sensing the length of DNA flanking the nucleosome core. The structure of the Chd1 DNA-binding domain was recently shown to consist of a SANT and SLIDE domain, analogous to the DNA-binding domain of the ISWI family, yet the details of how Chd1 recognizes DNA were not known. Here we present the crystal structure of the Saccharomyces cerevisiae Chd1 DNA-binding domain in complex with a DNA duplex. The bound DNA duplex is straight, consistent with the preference exhibited by the Chd1 DNA-binding domain for extranucleosomal DNA. Comparison of this structure with the recently solved ISW1a DNA-binding domain bound to DNA reveals that DNA lays across each protein at a distinct angle, yet contacts similar surfaces on the SANT and SLIDE domains. In contrast to the minor groove binding seen for Isw1 and predicted for Chd1, the SLIDE domain of the Chd1 DNA-binding domain contacts the DNA major groove. The majority of direct contacts with the phosphate backbone occur only on one DNA strand, suggesting that Chd1 may not strongly discriminate between major and minor grooves.

The extensive packaging of eukaryotic DNA into nucleosomes plays a fundamental role in regulating DNA metabolism (replication, recombination, and repair) and gene transcription through the occlusion of functionally important DNA sequences. Reorganization of the nucleosomal barrier requires ATP-dependent enzymes called chromatin remodelers, which take part in the assembly, repositioning, exchange, and eviction of histones (1, 2). Chromodomain helicase DNA-binding protein 1 (Chd1), the founding member of the CHD remodeler family (3, 4), has been shown to be required for nucleosome disassembly in Schizosaccharomyces pombe (5), histone H3 variant exchange in S. pombe and Drosophila melanogaster (6, 7), and maintenance of stem cell pluripotency in mouse (8). Biochemically, Chd1 behaves similarly to another family of chromatin remodelers called ISWI (imitation switch) with its ability to center mononucleosomes on short DNA fragments and generate evenly spaced nucleosomal arrays (9, 10).

As for ISWI-type remodelers, the DNA-binding domain of Chd1 is believed to play a critical role in sensing the length of extranucleosomal DNA available for nucleosome sliding. The DNA-binding domain is required for Chd1 to stably associate with nucleosomes, and this interaction also requires flanking extranucleosomal DNA (11). The Chd1 DNA-binding domain was recently discovered to consist of a SANT (SWI3, ADA2, N-CoR, and TFIIIB) and SLIDE (SANT-like ISWI domain) domain, analogous to the SANT-SLIDE portion of the DNA-binding domain of ISWI (11–13). The SANT and SLIDE domains are related to the DNA-binding domains of c-Myb that bind DNA sequence-specifically through insertion of a C-terminal helix into the major groove (13, 14). The Chd1 DNA-binding domain is not a sequence-specific binding protein but has been shown to have preference for poly(dA-dT) and poly(dI-dC) sequences and proposed to interact with the DNA minor groove (11, 15). We have solved the crystal struc-

* This work was supported, in whole or in part, by National Institutes of Health Grant (R01 GM084192) (to G. D. B.).

† The online version of this article (available at http://www.jbc.org) contains supplemental Table 1, Fig. S1, and Movies S1 and S2.

‡ The atomic coordinates and structure factors (code 3TED) have been deposited in the Protein Data Bank, Research Collaboratory for Structural Bioinformatics, Rutgers University, New Brunswick, NJ (http://www.rcsb.org/).

§ Present address: Astbury Centre for Structural Molecular Biology, University of Leeds, LS2 9JT, United Kingdom.

‖ To whom correspondence should be addressed: Thomas C. Jenkins Dept. of Biophysics, Johns Hopkins University, 3400 N. Charles St., Baltimore, MD 21218. Tel.: 410-516-7850; Fax: 410-516-4118; E-mail: gdbowman@jhu.edu.

‡1 Thomas C. Jenkins Department of Biophysics, Johns Hopkins University, Baltimore, Maryland 21218 and the ‡2 Biology Department, Brookhaven National Laboratory, Upton, New York 11973

The abbreviations used are: Chd1, chromodomain helicase DNA-binding protein 1; r.m.s.d., root mean square deviation; Bis-Tris, 2-(bis(2-hydroxyethyl)amino)-2-(hydroxymethyl)propane-1,3-diol; Vvn, V. vulnificus nuclease; N-CoR, nuclear receptor corepressor.
Chd1 DNA-binding Domain in Complex with DNA

ture of the *Saccharomyces cerevisiae* Chd1 DNA-binding domain in complex with a DNA duplex to 2.0 Å resolution, and here we present an analysis of the structure and comparison with the recently solved complex of the Isw1 DNA-binding domain with DNA (16).

**EXPERIMENTAL PROCEDURES**

The DNA-binding domain of *S. cerevisiae* Chd1 (residues 1006–1274) was TOPO-cloned into pDEST17 (Invitrogen), with a PreScission protease cleavage site (LEVLFQ/GP) introduced immediately preceding residue 1006. Protein expression was carried out in BL21 Star (DE3) cells (Invitrogen) containing the pRARE2 plasmid for rare tRNA codons (EMD Biosciences). Cell cultures were grown to an *A*$_{600}$ of 0.8–1.2, induced with 0.3 mM isopropyl-1-thio-β-D-galactopyranoside, and grown for an additional 18 h at 18 °C before harvesting. Cell pellets were resuspended in His-Bind buffer (10 mM imidazole, 500 mM NaCl, 30 mM Tris, pH 7.8, 10% glycerol, 5 mM β-mercaptoethanol) supplemented with 10 μg/ml DNase and 0.2 mM phenylmethylsulfonyl fluoride and lysed with 0.2 mg/ml lysozyme and sonication. After centrifugation of the cell slurry, the Histagged Chd1 DNA-binding domain was separated from the soluble fraction of the lysate using a HisTrap FF crude column followed by a cation exchange (SP Sepharose Fast Flow) column (GE Healthcare). The His tag was removed by overnight incubation with PreScission protease followed by a second passage over a HisTrap column. The final step of purification was passage over an S75 16/60 Superdex size exclusion column (GE Healthcare). Fractions containing the Chd1 DNA-binding domain were pooled, concentrated to 30–40 mg/ml, dialyzed overnight against buffer containing 10 mM Bis-Tris, pH 6.5, and 5 mM β-mercaptoethanol, and then stored at −80 °C.

The DNA oligomers used for crystallization (5′-CCA TAT ATA TGC-3′ and 5′-GCA TAT ATA TGG-3′) were purchased from Integrated DNA Technologies with standard desalting and used without further purification. The two DNA strands were annealed by heating equimolar amounts to 95 °C for 10 min in 10 mM HEPES, pH 7.5, 10 mM NaCl followed by slow cooling to room temperature. Prior to crystallization, protein and DNA were incubated together ~30 min on ice at a 1:1.2 ratio with a final protein concentration of 20 mg/ml. The complex was crystallized by hanging drop vapor diffusion at 4 °C with a well solution of 100 mM Bis-Tris, pH 6.5, and 17–20% PEG 400. Crystals were cryoprotected in buffer containing 35% PEG 400 and cooled in liquid nitrogen. Diffraction data to 2.0 Å were collected at National Synchrotron Light Source (NSLS) beamlines X25 and X29 at Brookhaven National Laboratory. Due to the low symmetry (monoclinic) of the crystal, 900 frames of 1° oscillations were recorded to achieve high (~18-fold) redundancy. The beam was reduced to a 50 × 50-μm profile, and exposure time was limited to 0.5 s/frame to minimize radiation damage. The crystal was not translated during data collection, but it did not show obvious signs of radiation damage as the first and second halves of the dataset showed nearly identical statistics after scaling.

Diffraction data were integrated and scaled using HKL2000 (17). The structure was solved by molecular replacement using MOLREP (18) as part of the CCP4 program suite (19), with the core SANT and SLIDE domains of uncomplexed Chd1 (Protein Data Bank [PDB] code 2X80 (11)) used as a search model. The complex crystallized in space group P2$_1$ with one protein-DNA complex in the asymmetric unit. After generating a mask for the protein-DNA complex by docking an idealized duplex onto phosphate peaks in initial electron density maps, solvent flattening using DM (20) starting with phases from the protein alone produced electron density of excellent quality for all 12 DNA base pairs. Building was carried out using Coot (21), and the structure was refined with REFMAC (22). The final model contained all 24 DNA nucleotides, protein residues 1006–1212 and 1245–1266, and 169 water molecules. Similar to the structure of the uncomplexed Chd1 DNA-binding domain (11), a large loop consisting of residues 1213–1244 failed to show continuous electron density and was not modeled. Analysis with PROCHECK (23) confirmed that all residues are in favorable and additionally allowed regions of Ramachandran space, and the model was refined to 2.0 Å resolution with *R*$_{work}$/R$_{free}$ values of 19.3/24.9%. Additional data collection and refinement statistics are given in supplemental Table 1. Calculation of DNA structural parameters and analysis was carried out using the program 3DNA (24). Structural alignments and root mean square deviation (r.m.s.d.) values were calculated using Isqman (25). All figures were generated using PyMOL (26).

**RESULTS AND DISCUSSION**

To gain insight into how Chd1 interacts with extranucleosomal DNA, we crystallized and solved the structure of the *S. cerevisiae* Chd1 DNA-binding domain in complex with a dodecameric DNA duplex (see supplemental Table 1 for data collection and refinement statistics). The core SANT and SLIDE domains of Chd1 show little deviation in the presence and absence of DNA (r.m.s.d. of 1.12 Å over 160 Cα atoms), suggesting a rigid unit similar to what has been proposed for the HAND-SANT-SLIDE domains of ISW1 (13, 16). Comparison with the DNA-bound structure of the yeast ISW1a remodeler complex, which consists of Isw1 and Ioc3p (16), revealed distinct orientations of DNA duplexes (Fig. 1). In the ISW1a complex, the DNA is oriented at an acute angle to the long axis of the SANT-SLIDE unit, extending toward the HAND domain at one end and toward a DNA-binding surface of the Ioc3p partner subunit at the other. Relative to the SLIDE domain, the trajectory of the DNA duplex bound to Chd1 differs by ~35° and aligns with a variable length loop following the C-terminal helix of the SANT domain. In yeast Chd1, this loop forms a long helix (named helical linker-1, HL1; Fig. 1A, yellow) that extends ~50 Å away from the SANT-SLIDE core. This HL1 extension contains two residues previously shown to be important for DNA binding, Arg-1113 and Lys-1115 (11), that contact one end of the DNA duplex. In the structure, HL1 extends past the end of the DNA duplex, yet the common trajectory of HL1 with DNA suggests that other residues such as Arg-1086, Lys-1090, and Lys-1112 could also play a role in DNA binding.

The DNA duplex bound to Chd1 displays roll, tilt, and twist parameters within ranges expected for B-form DNA (24, 27) and is relatively straight. Chd1 contacts one face of the DNA duplex, spanning a 9-bp segment. Spanning almost a full helical turn of the duplex, this interaction may indicate a preference
of the DNA-binding domain in relaying the availability of DNA outside the nucleosome core.

Individually, the folds of the SANT and SLIDE domains of Chd1 match up with those of ISWI (11), although the best alignments are achieved when only the N- and C-terminal helices of each domain are used for superpositioning (for SANT domains of yeast Chd1 and Isw1, r.m.s.d. of 1.22 Å over 32 Ca atoms, and for SLIDE domains, r.m.s.d. of 0.84 Å over 34 Ca atoms). Comparison of Chd1 and Isw1 structures revealed that despite the different directions of the DNA duplexes, both Chd1 and Isw1 contact DNA using residues from the N-terminal helix of the SANT domain and C-terminal helix of the SLIDE domain (Fig. 1). Previous sequence analysis of SANT domains identified basic residues in the first helix shared by ISWI and Chd1 proteins that were predicted to interact with DNA (11). Chd1 residues Arg-1016 and Lys-1020 and Isw1 residues Lys-889, Arg-893, Lys-894, and Thr-897 on this N-terminal helix make direct or water-mediated interactions with the DNA phosphate backbone (Fig. 2A). On the C-terminal helix of the SLIDE domains, both yeast remodelers possess a pair of consecutive arginine residues (Chd1 Arg-1255/Arg-1256, Isw1 Arg-1044/1045) that straddle the phosphate backbone in a similar fashion (Fig. 2B). The different directions for the DNA duplexes bound to Chd1 and Isw1, despite similar contacts on both the SANT and the SLIDE domains, correlate with the different lengths of the spacer helix connecting these two domains. Due to a shorter spacer helix, the SANT and SLIDE domains are ~15 Å closer together in Chd1 than in ISWI proteins (11). Because the spacer helix is approximately perpendicular to the DNA axis in Chd1, maintaining these two points of contact with a relative displacement of SANT and SLIDE domains effectively changes the angle at which DNA crosses the binding domains.

A notable difference in the Chd1 and Isw1 structures is the register of the DNA duplex on the SLIDE domain; in Isw1, the SLIDE C-terminal helix lies parallel to the minor groove, whereas in Chd1, this SLIDE helix aligns with the major groove (Fig. 2B). This difference in the register of the DNA grooves corresponds to a relative swap in polarity (3’ to 5’ versus 5’ to 3’) of DNA strands. From the nature of the DNA duplex, aligning a strand oriented 3’ to 5’ from one duplex with a strand oriented 5’ to 3’ from another duplex effectively places the major groove of each duplex on top of the minor groove of the other. For Chd1 and Isw1, aligning DNA strands of opposite polarity is required for matching analogous protein elements in the SANT and SLIDE domains while maintaining similar trajectories of the DNA duplexes.

In addition to associating with different DNA grooves, the C-terminal SLIDE helices also show distinct orientations with respect to the DNA duplex. This SLIDE helix is analogous to the C-terminal helices of the R2 and R3 DNA-binding domains of c-Myb that sit in the major groove and make base-specific contacts with DNA (14). In Isw1, the C-terminal helix of the SLIDE domain is oriented similarly to the C-terminal helices of the c-Myb R2 and R3 domains with respect to the DNA axis but shows a relative displacement away from the DNA axis by ~5.5 Å and thus cannot reach beyond the phosphate backbone of the minor groove (Fig. 2B). In Chd1, the N-terminal portion of the SLIDE helix sits in the major groove at a depth similar to the

for DNA that is not geometrically constrained by the histone core. Binding to DNA in a straight conformation agrees with the finding that extranucleosomal DNA is required for Chd1 to stably bind to nucleosomes (11) and is consistent with the role

FIGURE 1. Overview of the Chd1 DNA-binding domain bound to DNA and comparison with the Isw1-DNA structure. A, backbone (left) and graphic (right) representations of the S. cerevisiae Chd1 DNA-binding domain bound to a dodecameric DNA duplex. Four residues that make up part of the DNA-binding surface are highlighted as magenta spheres (shown also in Figs. 2 and 3). In the graphic, the dotted lines represent the expected position of the DNA backbone continued in a straight trajectory from the duplex observed in the crystal. Residues on the HL1 extension unique to Chd1 that appear positioned to contact DNA are shown as yellow sticks. The orange circles on the DNA graphic indicate common points of contact from the SANT and SLIDE domains of Chd1 and Isw1. B, backbone (left) and graphic (right) representations for the S. cerevisiae Isw1 DNA-binding domain in complex with a DNA duplex (PDB code 2Y9Z (16)), shown in an orientation that aligns the Isw1 SLIDE domain with that of Chd1 in A. Four residues that appear to be structurally analogous to those highlighted for Chd1 in A are shown as magenta spheres. Note that the loc3p subunit of the ISW1a complex, which is bound beneath the HAND-SANT-SLIDE domain in this orientation, is not shown for clarity.
c-Myb domains. However, this helix differs from both Isw1 and the c-Myb domains by projecting away from the DNA duplex.

The structure of the Chd1 DNA-binding domain bound to DNA provides a high-resolution view of residues previously predicted to be involved in DNA binding (11). Residues Arg-1016, Lys-1020, Arg-1113, Lys-1115, and Arg-1255, which were shown by alanine substitutions to contribute to DNA binding, all interact with the same DNA strand. Based on their involvement in DNA binding, these residues were used to provide interaction restraints for modeling a DNA duplex (11). The highest scoring modeled DNAs show duplex trajectories that are similar to the duplex in the crystal structure and match the phosphate backbone most closely in the vicinity of Arg-1255 in the structure. When compared with the DNA in the crystal structure, however, these models have the opposite strand polarity. This difference in strand polarity means that, similar to Isw1, the minor grooves of the modeled DNAs align with the major groove of the DNA in the crystal structure.

Despite the opposite polarity of DNA strands from the crystal structure and modeled DNAs, we believe that both groove registers could be compatible with binding to Chd1. The majority of protein contacts occur along the DNA sugar-phosphate backbone in a manner that would not discriminate strand polarity. Only three interactions are observed outside the DNA backbone: van der Waals contacts between the C5-methyl of T6 and Ile-1251, van der Waals contacts between the C5-methyl, C5, and C6 of T4 and Arg-1255, and potentially influenced by crystal packing, hydrogen bonding between the O6 of G1 and Arg-1113. Although DNA binding is typically dominated through interactions with the sugar-phosphate backbone, the vast majority of DNA-binding proteins, including those that bind sequence nonspecifically, often make significant contacts within one or both nucleic acid grooves, likely used to determine groove register. One notable exception, however, is the Vibrio vulnificus nuclease, Vvn, which can digest DNA and RNA nonspecifically and primarily makes contacts to the sugar-phosphate backbone outside the grooves (28, 29). Vvn was shown to bridge one major and one minor groove of DNA, yet the manner in which Vvn recognizes DNA in a groove-specific manner is presently unclear. Another family of nucleases with an active site arrangement similar to Vvn yet with a distinct fold is the colicin nuclease family, which shows sequence selectivity in cleavage yet also binds DNA in a largely sequence-nonspecific fashion (29). Although crystal structures of the colicin E7 nuclease domain show extensive sequence-nonspecific interactions with both major and minor grooves in one register (1ZN5, 2IVH; Ref. 30), a recent computational study of the colicin E7
nuclease domain has proposed that binding to either groove register would be energetically favorable (31).

Further support for the idea that the Chd1 DNA-binding domain may bind either groove register comes from the observation that the majority of direct contacts to DNA occur on one strand. The SANT domain is positioned to only contact one of the two DNA strands. The strand contacted by the SANT domain also makes direct contact with residues on the SLIDE domain: Lys-1166, Trp-1171, His-1252, and Arg-1255 make hydrogen bonds and Val-1247 and Tyr-1259 make van der Waals clashes with phosphate oxygens (Fig. 3A). The other DNA strand makes hydrogen bonds with the backbone amide of Ala-1117 and the side chain of Asn-1129 on the β-linker and spacer helix, respectively, but contacts the SLIDE domain primarily through water-mediated hydrogen bonds (Fig. 3B). These indirect contacts may indicate a relaxed geometric requirement for the spacing between the two strands. In the ISW1a complex, several features hint at the possibility of the protein preferentially recognizing one of the two DNA strands as observed for Chd1; however, the lower resolution of that structure (3.6 Å) precludes a detailed analysis of protein-DNA interactions.

To show the extent to which the Chd1-DNA complex may be able to accommodate DNA with reversed polarity, we superimposed an ideal B-form DNA duplex onto the DNA in the crystal structure (supplemental Fig. S1). The idealized duplex was aligned using the DNA strand in the crystal structure that makes direct contacts with the SLIDE domain. Despite having reversed polarity, the phosphates of the aligned DNA strand closely match those of the crystal structure, and therefore, in this orientation, a chemically similar structure would be presented to Chd1. By effectively placing the minor groove of the idealized duplex on top of the major groove of the crystallographic DNA, the other strand of the idealized duplex, which corresponds to the water-mediated strand in the crystal structure, makes a closer approach to the protein. This alignment of idealized DNA results in two regions of van der Waals clashes with Chd1: the beginning of the C-terminal SLIDE helix and an extended portion of the HL1/β-linker (supplemental Fig. S1). Therefore, for the Chd1 DNA-binding domain to recognize the minor groove, some adjustments in orientations and conformations of the protein and/or DNA would be required, which may include a widening of the minor groove and, as observed for Isw1, a shift in the position of the SLIDE domain relative to the DNA.

In conclusion, the structure presented here extends our knowledge of how the Chd1 DNA-binding domain can bind straight DNA duplexes. The backbone-dominant recognition suggests an insensitivity for DNA strand polarity, a feature that may also be shared by ISWI remodelers. Integration of this information with the nucleosome centering and spacing abilities of Chd1 will be important for revealing how the DNA-binding domain participates in regulating remodeler activity that is necessary for generating evenly spaced nucleosomal arrays.

Acknowledgments—We thank T. Owen-Hughes and D. Ryan for providing us with the coordinates for the uncomplexed Chd1 DNA-binding domain prior to publication (2XB0) and Chd1-DNA models. We greatly appreciate G. Hauk for help with data collection and I. Nodelman for critical comments on the manuscript. Support for beamlines X25 and X29 of the National Synchrotron Light Source comes principally from the Offices of Biological and Environmental Research and Basic Energy Sciences of the United States Department of Energy and from the National Center for Research Resources (NCRR), National Institutes of Health (Grant P41RR012408).

REFERENCES

1. Gangaraju, V. K., and Bartholomew, B. (2007) Mutat. Res. 618, 3–17
2. Ryan, D. P., and Owen-Hughes, T. (2011) Curr. Opin. Chem. Biol. 15, 649–656
3. Delmas, V., Stokes, D. G., and Perry, R. P. (1993) Proc. Natl. Acad. Sci. U.S.A. 90, 2414–2418
4. Marfella, C. G., and Imbalzano, A. N. (2007) Mutat. Res. 618, 30–40
5. Walfridsson, J., Khorosjutina, O., Matikainen, P., Gustafsson, C. M., and Eckwall, K. (2007) EMBO J. 26, 2868–2879
6. Walfridsson, J., Bjerling, P., Thalen, M., Yoo, E. J., Park, S. D., and Eckwall, K. (2005) Nucleic Acids Res. 33, 2868–2879
7. Konev, A. Y., Tribus, M., Park, S. Y., Podhraski, V., Lim, C. Y., Emelyanov,
Chd1 DNA-binding Domain in Complex with DNA

A. V., Vershilova, E., Pirrotta, V., Kadonaga, J. T., Lusser, A., and Fyodorov, D. V. (2007) Science 317, 1087–1090
8. Gaspar-Maia, A., Alajem, A., Polesso, F., Sridharan, R., Mason, M. J., Heidersbach, A., Ramalho-Santos, J., McManus, M. T., Plath, K., Mesher, E., and Ramalho-Santos, M. (2009) Nature 460, 863–868
9. Lusser, A., Urwin, D. L., and Kadonaga, J. T. (2005) Nat. Struct. Mol. Biol. 12, 160–166
10. Stockdale, C., Flaus, A., Ferreira, H., and Owen-Hughes, T. (2006) J. Biol. Chem. 281, 16279–16288
11. Ryan, D. P., Sundaramoorthy, R., Martin, D., Singh, V., and Owen-Hughes, T. (2011) EMBO J. 30, 2596–2609
12. Aasland, R., Stewart, A. F., and Gibson, T. (1996) Trends Biochem. Sci. 21, 87–88
13. Grüne, T., Brzeski, J., Eberharter, A., Clapier, C. R., Corona, D. F., Becker, P. B., and Müller, C. W. (2003) Mol. Cell 12, 449–460
14. Tahirov, T. H., Sato, K., Ichikawa-Iwata, E., Sasaki, M., Inoue-Bungo, T., Shiina, M., Kimura, K., Takata, S., Fujikawa, A., Morii, H., Kumasaka, T., Yamamoto, M., Ishii, S., and Ogata, K. (2002) Cell 108, 57–70
15. Stokes, D. G., and Perry, R. P. (1995) Mol. Cell. Biol. 15, 2745–2753
16. Yamada, K., Frouws, T. D., Angst, B., Fitzgerald, D. J., DeLuca, C., Schimmel, K., Sargent, D. F., and Richmond, T. J. (2011) Nature 472, 448–453
17. Carter, C. W., Jr., and Sweet, R. M. (1997) Methods Enzymol. 276, 307–326
18. Vagin, A., and Teplyakov, A. (2010) Acta Crystallogr. D Biol. Crystallogr. 66, 22–25
19. Collaborative Computational Project Number 4 (1994) Acta Crystallogr. D Biol. Crystallogr. 50, 760–763
20. Cowtan, K. (1994) CCP4 Newsletter, Vol. 31, pp. 34–38, Collaborative Computational Project Number 4, CCLRC Daresbury Laboratory, Daresbury, UK
21. Emsley, P., and Cowtan, K. (2004) Acta Crystallogr. D Biol. Crystallogr. 60, 2126–2132
22. Murshudov, G. N., Vagin, A. A., and Dodson, E. J. (1997) Acta Crystallogr. D Biol. Crystallogr. 53, 240–255
23. Laskowski, R. A., MacArthur, M. W., Moss, D. S., and Thornton, J. M. (1993) J. Appl. Crystallogr 26, 283–291
24. Lu, X. J., and Olson, W. K. (2003) Nucleic Acids Res. 31, 5108–5121
25. Kleywegt, G. J., and Jones, T. A. (1994) CCP4 Newsletter, Vol. 31, 9–14, Collaborative Computational Project Number 4, CCLRC Daresbury Laboratory, Daresbury, UK
26. DeLano, W. L. (2010) The PyMOL Molecular Graphics System, version 1.3r1, Schrödinger, LLC, New York
27. Yuan, H., Quintana, J., and Dickerson, R. E. (1992) Biochemistry 31, 8009–8021
28. Li, C. L., Hor, L. I., Chang, Z. F., Tsai, L. C., Yang, W. Z., and Yuan, H. S. (2003) EMBO J. 22, 4014–4025
29. Wang, Y. T., Yang, W. J., Li, C. L., Doudeva, L. G., and Yuan, H. S. (2007) Nucleic Acids Res. 35, 584–594
30. Doudeva, L. G., Huang, H., Hsia, K. C., Shi, Z., Li, C. L., Shen, Y., Cheng, Y. S., and Yuan, H. S. (2006) Protein Sci. 15, 269–280
31. Chen, C., and Pettitt, B. M. (2011) Biophys. J. 101, 1139–1147