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## Supplemental information

## Structural basis for binding diversity

## of acetyltransferase p300 to the nucleosome

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Figure S1. Preparation of the NCP and the p300(BRPH $_{\Delta AIL}Z$ ) proteins and assay for p300(BRPH $_{\Delta AIL}Z$ )-DNA binding, related to Figures 1 and 3. (A) The 145 base-pair Widom 601 DNA and the purified NCP containing the DNA were analyzed by non-denaturing 6% polyacrylamide gel electrophoresis with ethidium bromide staining. (B) The nucleosomal histones were analyzed by 18% SDS-polyacrylamide gel electrophoresis with Coomassie Brilliant Blue staining. (C) Electrophoretic mobility shift assay of p300(BRPH $_{\Delta AIL}Z$ ) and the naked 145 base-pair Widom 601 DNA. The binding of p300(BRPH $_{\Delta AIL}Z$ ) and DNA was analyzed by non-denaturing 4% polyacrylamide gel electrophoresis with SYBR Gold staining. (D) The purified p300(BRPH $_{\Delta AIL}Z$ ) proteins were analyzed by 12% SDS-polyacrylamide gel electrophoresis with Coomassie Brilliant Blue staining.



Figure S2. Preparation and cryo-EM analysis of the p300(BRPH $_{\Delta AIL}Z$ )-NCP complexes, related to Figures 2 and 4. (A) The p300(BRPH $_{\Delta AIL}Z$ )-NCP complexes were purified by sucrose density gradient centrifugation, and the collected fractions were analyzed by non-denaturing 4% polyacrylamide gel electrophoresis with SYBR Gold staining. The fractions shown in the red frames were combined. (B) The purified NCP and p300(BRPH $_{\Delta AIL}Z$ )-NCP samples were analyzed by nondenaturing 4% polyacrylamide gel electrophoresis with SYBR Gold staining. Sample number 3 was used for the cryo-EM analysis. (C) A representative image from a digital cryo-EM micrograph of the p300(BRPH $_{\Delta AIL}Z$ )-NCP complexes. Scale bar indicates 100 nm. (D) Representative 2D class averages of the p300(BRPH $_{\Delta AIL}Z$ )-NCP complex from single particle images.



Figure S3. Workflow for cryo-EM processing of the p300(BRPH\_AILZ)-NCP complex related to

Figures 2 and 4. The particles contained in the classes enclosed by the red squares were used in

the subsequent processes.



Figure S4. Cryo-EM structure of the p300(BRPH $_{\Delta AIL}Z$ )-NCP complex I, related to Figure 2. (A) The overall structure of the p300(BRPH $_{\Delta AIL}Z$ )-NCP complex I. The crystal structures of the NCP and

the p300 catalytic core are superimposed on the cryo-EM map. (B) Gold-standard Fourier Shell Correlation (FSC) curve of the p300(BRPH<sub> $\Delta$ AIL</sub>Z)-NCP complex I. Its overall resolution is 3.95 Å at FSC = 0.143. (C) Angular distribution of model projections of the p300(BRPH<sub> $\Delta$ AIL</sub>Z)-NCP complex I. (D) Local resolution map of the p300(BRPH<sub> $\Delta$ AIL</sub>Z)-NCP complex I estimated by the RELION 3.1 postprocess, showing the resolution range across the map from 3.6 Å to 14.6 Å.



**Figure S5. Replicated experiments related to Figure 3.** (A) Electrophoretic mobility shift assay of the p300(BRPH<sub> $\Delta$ AIL</sub>Z) or p300(BRPH<sub> $\Delta$ AIL</sub>Z) BPD mutant (K1456A/K1459A/K1461A/R1462A) and the NCP. Complex formation was analyzed by non-denaturing 4% polyacrylamide gel electrophoresis with SYBR Gold staining. (B) Electrophoretic mobility shift assay of the p300(BRPH<sub> $\Delta$ AIL</sub>Z) or p300(BRPH<sub> $\Delta$ AIL</sub>Z) R1137A mutant and the NCP. Complex formation was analyzed by non-denaturing 4% polyacrylamide gel on-