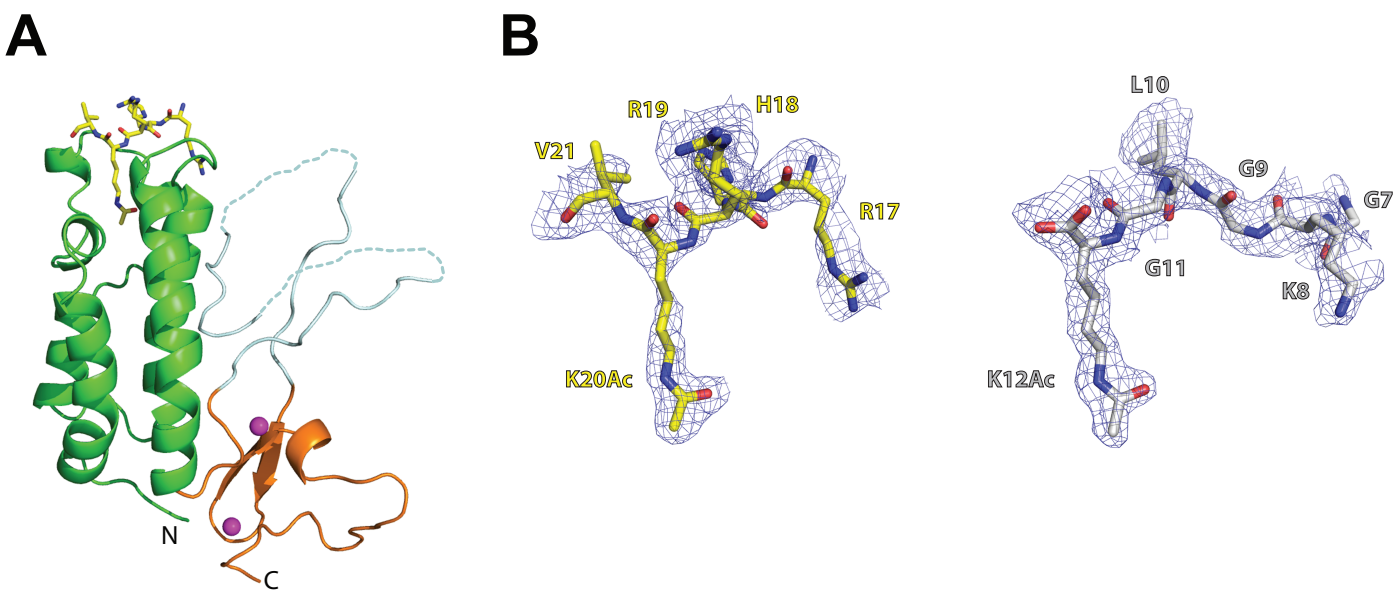


Figure S1. Crystal structures of human CBP BrD-PHD bound to lysine-acetylated H4 peptides. Related to Figure 1.

(A) Cartoon representation of 3D structure of the tandem BrD (green) and PHD finger (orange) of CBP bound to a histone H4K20ac peptide (shown in sticks with carbon atoms in yellow). The linker of the BrD-PHD module is colored in light cyan and regions that are lack of electron density is indicated by dots. Zn atoms are shown in magenta spheres.

B) Electron density map of H4K20ac and H4K12ac peptides. The Fo-Fc maps are computed after simulated annealing with H4 peptides omitted from the atomic model and shown in mesh (contoured to 1.0 σ). H4 peptides are presented in the same orientation as in panel ***(A)***.

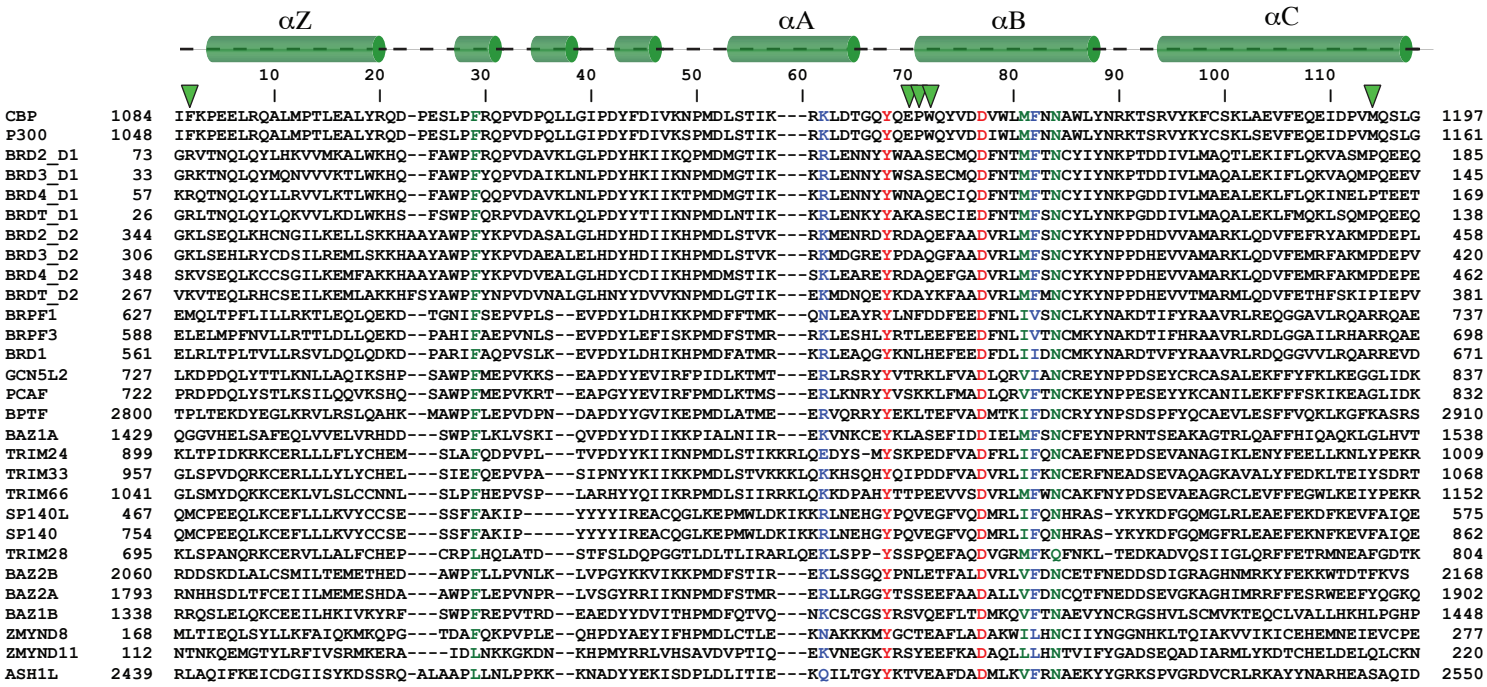


Figure S2. Structure-based sequence alignment of representative members of human BrD proteins. Related to Figure 2.

Identical, highly similar and similar residues are colored in red, green and blue respectively. Secondary structure elements of human CBP BrD are assigned by the PROCHECK program (1) and are shown above the sequences: the helices are shown as cylinders. The residues interacting with the PHD finger are labeled with green arrowheads. The alignment was generated using ClustalW (2). The sequences shown are ASH1L (NP_060959), BAZ1A (NP_038476), BAZ1B (NP_115784), BAZ2B (NP_038478), BPTF (NP_872579), BRD1 (NP_055392), BRD2 (NP_005095), BRD3 (NP_031397), BRD4 (NP_490597), BRDT (NP_872579), BRPF1 (NP_001003694), BRPF3 (NP_056510), CBP (NP_004371), GCN5L2 (NP_066564), P300 (NP_001420), PCAF (NP_003875), SP140 (NP_009168), SP140L (NP_612411), TRIM24 (NP_056989), TRIM28 (NP_005753), TRIM33 (NP_056990), TRIM66 (NP_055633), ZMYND8 (NP_898868), and ZMYND11 (NP_006615).

1. Laskowski RA, MacArthur MW, Moss DS, Thornton JM (1993) PROCHECK: A program to check the stereochemical quality of protein structures. *J Appl Cryst* 26:283–291.

2. Thompson JD, Higgins DG, Gibson TJ (1994) CLUSTAL W: Improving the sensitivity of progressive multiple sequence alignment through sequence weighting, position-specific gap

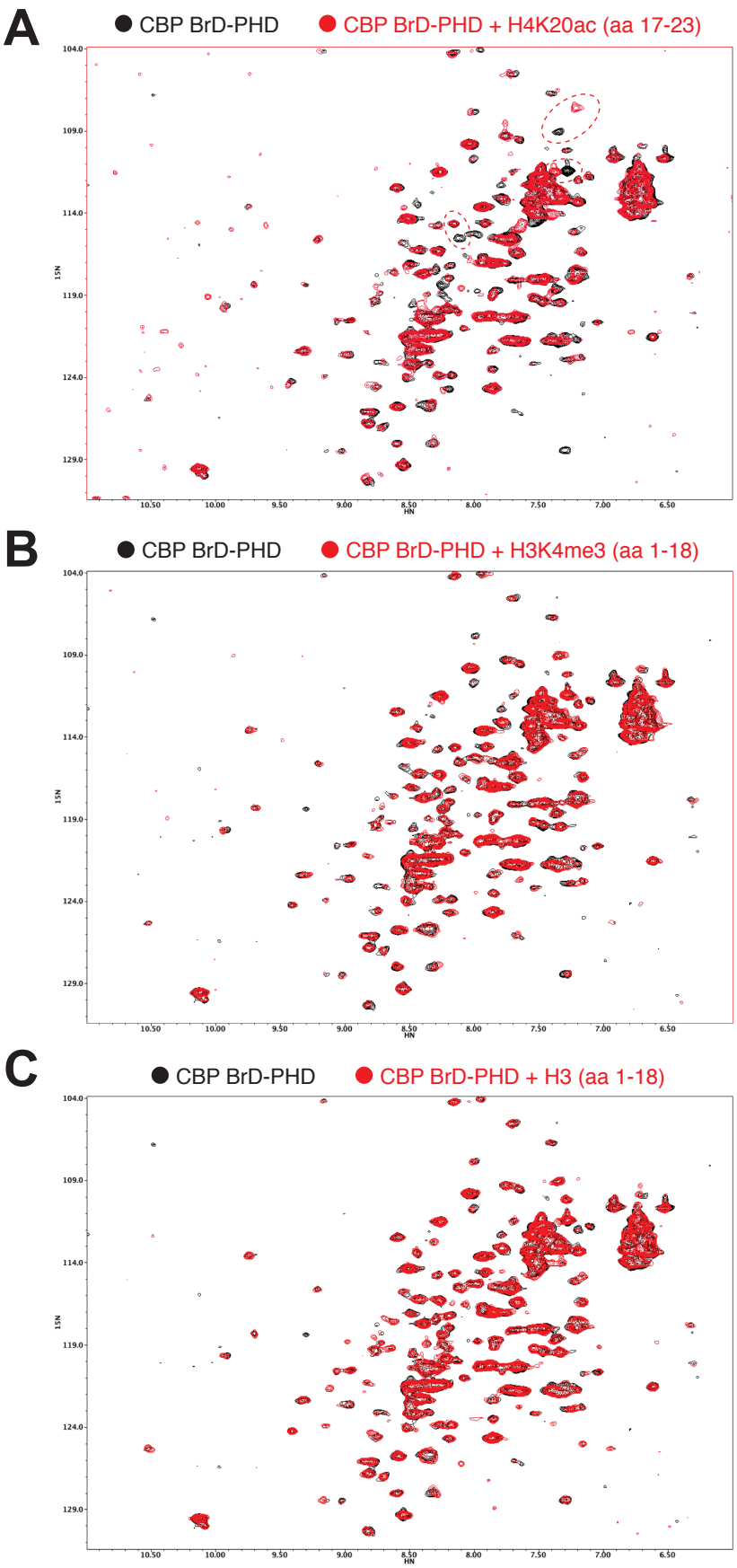
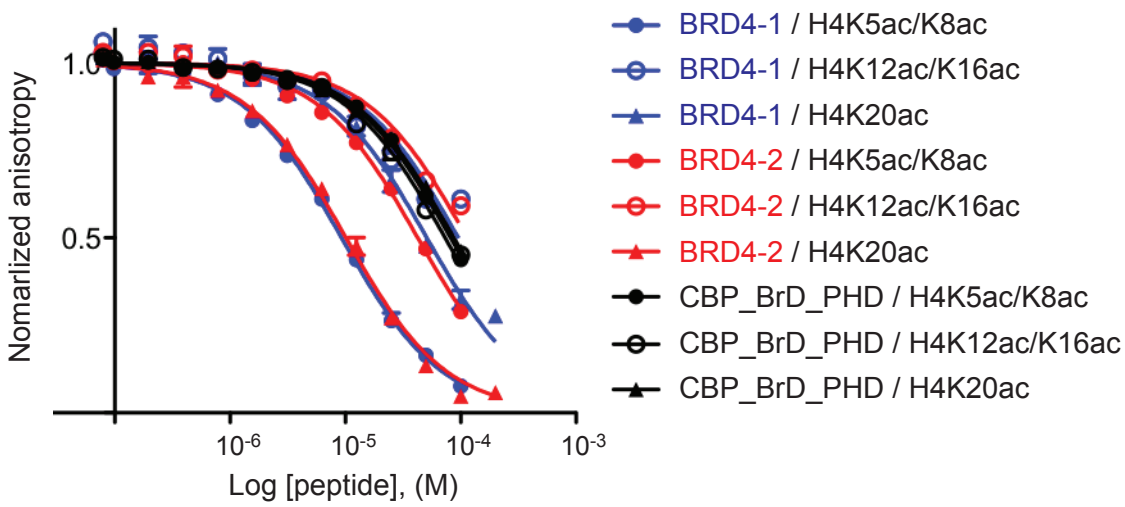


Figure S3. NMR analysis of CBP BrD-PHD tandem module binding to histone peptides. Related to Figure 2.

The protein/peptide binding was assessed by 2D ^{1}H-^{15}N-HSQC NMR spectra of the ^{15}N-labeled protein (0.2 mM) in the free form (black) and in the presence of a histone peptide (1.2 mM) (red) of (**A**) H4K20ac (aa 17-23); (**B**) H3K4me3 (aa 1-18); or (C) H3 (aa 1-18).



	CBP-BrD-PHD			BRD4-BrD1			BRD4-BrD2		
	IC_{50}	IC_{50} 95% confidence	K_i	IC_{50}	IC_{50} 95% confidence	K_i	IC_{50}	IC_{50} 95% confidence	K_i
H4K5ac/K8ac	818	731 to 917	383	92.8	82.3 to 104.7	26	424	347 to 518	142
H4K12ac/K16ac	732	652 to 822	343	952	755 to 1200	270	1139	985 to 1317	380
H4K20ac	874	708 to 1078	315	508	454 to 571	145	101.3	91.5 to 112.3	34

Figure S4. Fluorescence anisotropy measurement of binding affinity of the bromodomains of CBP and BRD4 to lysine-acetylated histone H4 peptides. Related to Figure 3.
Upper, fluorescence anisotropy competition plots of the CBP and BRD4 bromodomains binding to various histone H4 peptides. Lower, a Table summarizes the binding affinity values. Ki was calculated as described in Supplementay Information. The errors in IC_{50} values recovered from fitting competition curves reflect 95% of confidence intervals.