

Supplementary Materials

Supplementary Figure Legends

Fig. S1. A close-up stereo view of the BRD2-BD2 dimer interface region. The intermolecular interactions occur through buried water molecules.

Fig. S2. A close-up view of the H4K5ac/K12ac complex in the BRD2-BD2 complex. (A) A close-up view of the H4K5ac/H12ac tail Q with its 2mFo-DFc map contoured at 1.0σ . The two BD2 chains A_1 and A_2 which associate with the H4 tail are shown in the background. (B) A close-up view of the H4K5ac/H12ac tail R with its 2mFo-DFc map contoured at 1.0σ . The two BD2 chains B_1 and B_2 which associate with the H4 tail are shown in the background.

Fig. S3. The electrostatic surface potential of the BD2 chains in the BD2 complex. The H4K5ac/K12ac tail bound to the protein is shown as sticks. The surface is colored red and blue for potential values below $-5k_B T$ and above $+5k_B T$, respectively, where k_B is the Boltzmann constant and T is the room temperature.

Fig. S4. Superposition of the two H4 tails, Q and R, in the BRD2-BD2 complex with respect to K5ac.

Fig. S5. Sequence comparison of the BET and non-BET bromodomains. The alignment was produced by ClustalW [1] and was manually modified. The red characters indicate identical residues in the BET family (group 1) of BRD2, BRD4 and mBRDT bromodomains. The white characters on the blue background indicate completely conserved amino acids among the BET family (group 1) and non-BET

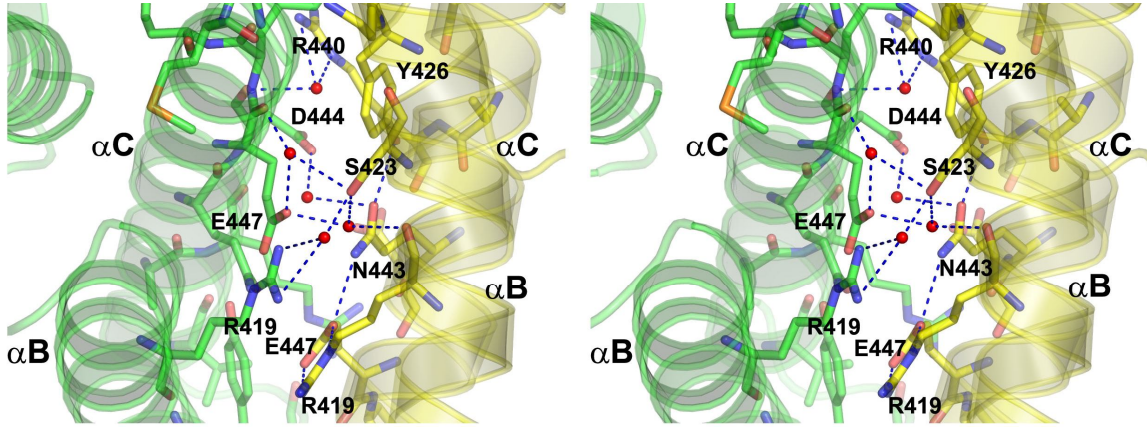
family (group 2) bromodomains. Red star denotes the residue that interacts with the acetylated histone H4 tail residues (except for the K5ac and K12ac side chain interactions, for clarity). The figure was generated by ESript [2].

Fig. S6. Comparison of the BRD2-BD1 and BRD2-BD2 complexes. (A) Superposition of the BD2 complex over the BD1 complex, with respect to K12ac in the BD2 complex. In this superposition, the H4 tails in the BD1 and BD2 complexes are oriented in opposite directions. (B) Superposition of the BD2 complex over the BD1 complex with respect to K5ac in the BD2 complex. In this superposition, the H4 tails are oriented in the same direction.

References

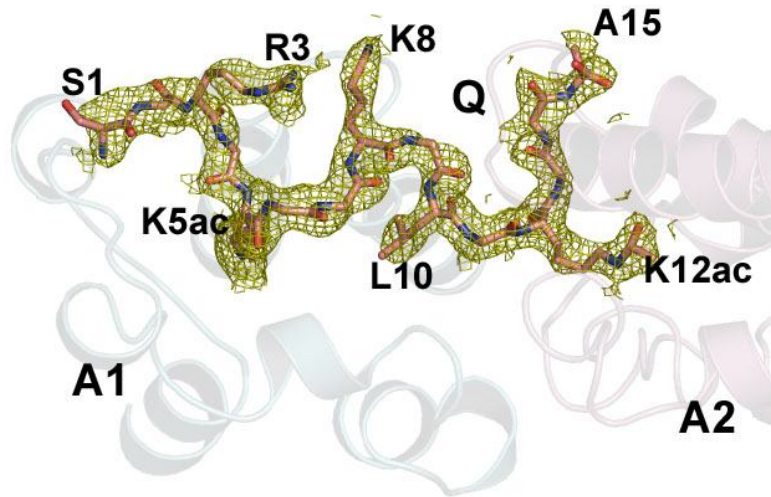
- [1] Higgins, D. G., Bleasby, A. J., & Fuchs, R. (1992). CLUSTAL W: improved software for multiple sequence alignment. *Comput. Applic. Biosci.* **8**, 189–191.
- [2] Gouet, P., Courcelle, E., Stuart, D., & Metoz, F. (1999). ESript: multiple sequence alignments in postscript. *Bioinformatics* **15**, 305–308.

Supplementary Fig. S1

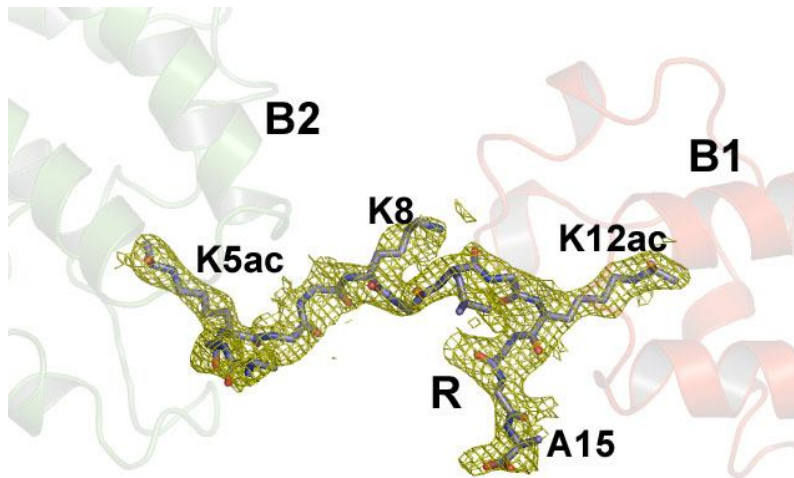


Supplementary Fig. S2

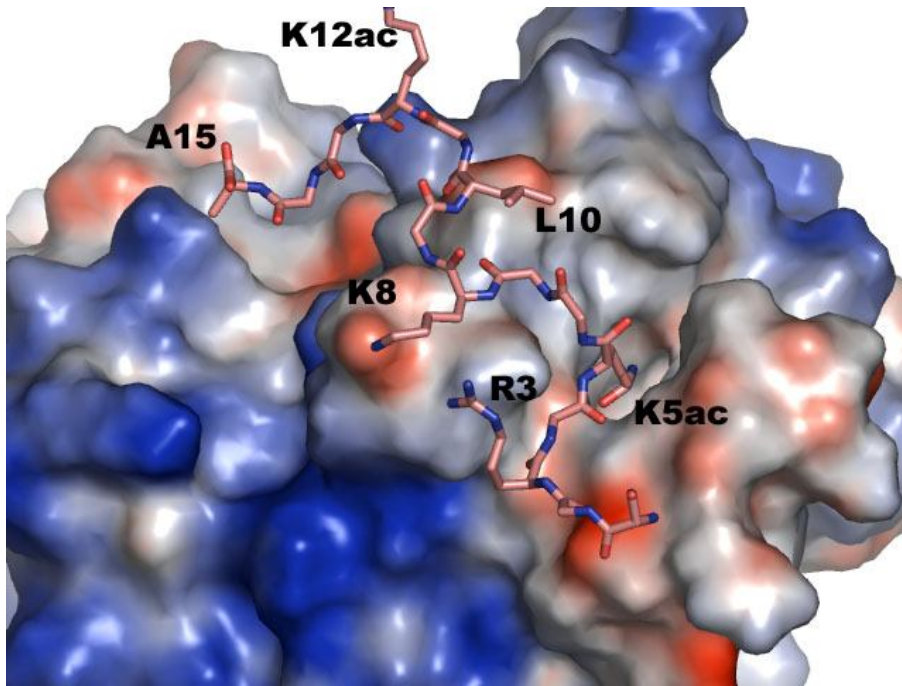
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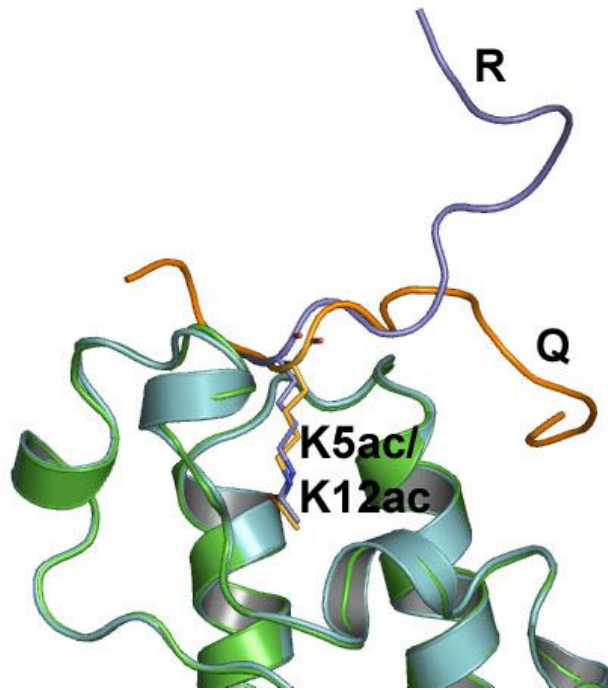
B



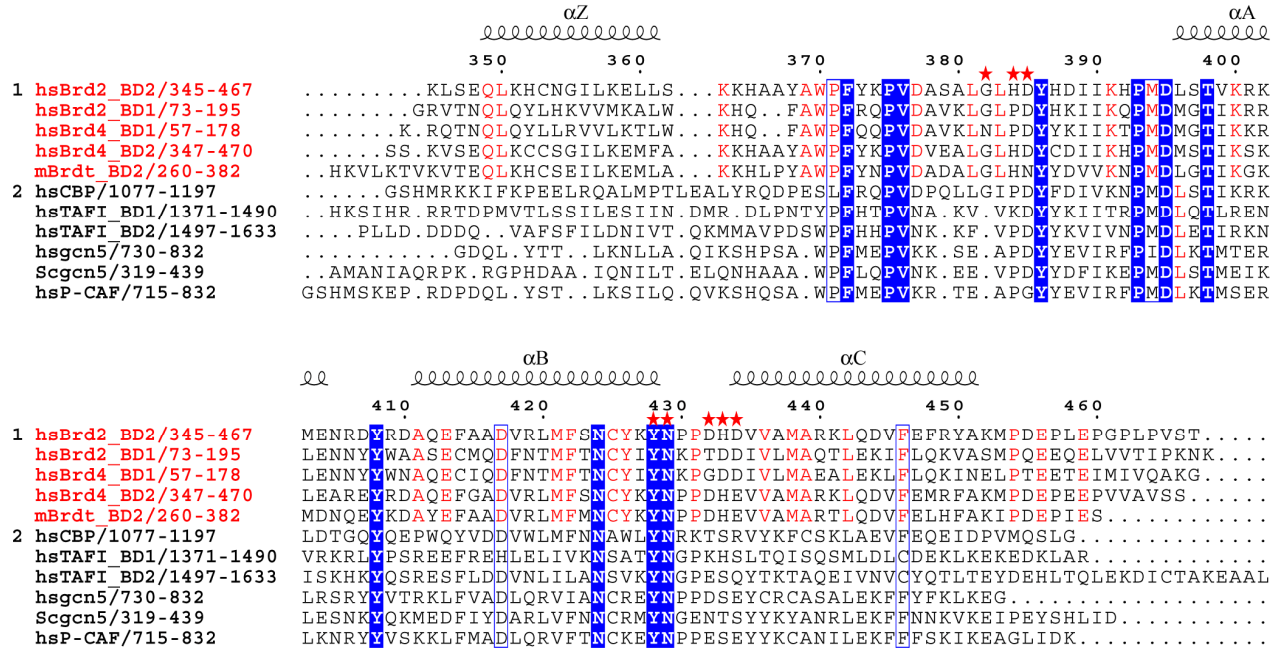
Supplementary Fig. S3



Supplementary Fig. S4

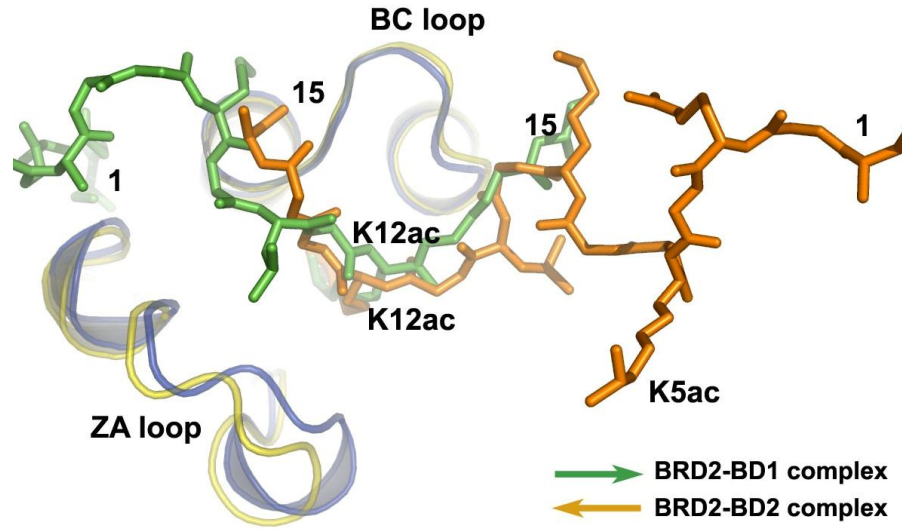


Supplementary Fig. S5



Supplementary Fig. S6

A



B

