Supporting Information

Druggability analysis and structural classification of bromodomain acetyl-lysine binding sites

Lewis R. Vidler,[1] Nathan Brown,[1] Stefan Knapp[2] and Swen Hoelder[1,]*

[1]Cancer Research UK Cancer Therapeutics Unit, Division of Cancer Therapeutics, The Institute of Cancer Research, 15 Cotswold Road, Sutton, Surrey SM2 5NG, United Kingdom; [2]Nuffield Department of Clinical Medicine, Structural Genomics Consortium, Oxford University, Old Road Campus Research Building, Headington, Oxford OX3 7DQ, United Kingdom.

Content:

Table S1. Bromodomain structures filtered out for unresolved binding site residues

Bromodomain	PDB	Chains	Unresolved Residues[a]
ATAD2A	3DAI	A	Lysine 985, Glutamate 1017
ATAD2B	3LXJ	A, B, C	Lysine 985
BRD1	3RCW	G	Glutamate 595
BRD4(A/B)(1)	3UW9	B	Leucine 92
BRD4(A/B)(1)	3UW9	C	Leucine 94
GCN5L2	3D7C	A	Lysine 758
MLL1	3LQH, 3LQI, 3LQJ	All	ZA-loop[b]
PCAF	3GG3	A	Lysine 753
TRIM33B	3U5M, 3U5N, 3U5O, 3U5P	All	BC-loop
WDR9(A/B)(2)	3Q2E	A	Lysine 1399

[a]UID residue numbering, [b]missing from protein construct

Table S2. Bromodomain structures filtered out for missing water molecules

Bromodomain	PDB	Chains	Resolution (Å)
ASH1L	3MQM	All	2.54
ATAD2B	3LXJ	D	2.33
BRDT(A/B)(1)	2RFJ	All	2.05
PB1(A/B/C)(3)	3K2J	All	2.20
PB1(A/B/C)(4)	3TLP	All	2.13
PB1A(6)	3IU6	All	1.79

Table S3. Details of structures included in analysis passing filters, output from SiteMap and water molecules included.

PDB	BRD	Bound State	Res. (Å)	SiteScore	Size	Dscore	Volume	Exposure	Enclosure	Contact	Phobic	Philic	Balance	Don/Acc	Water UID's[a]
3G0L	BAZ2B	Apo	2.03	0.718	39	0.700	104.615	0.711	0.612	0.767	0.690	0.780	0.885	0.433	5, 7, 20, 39, 44
3Q2F	BAZ2B	Ligand	2.06	0.672	31	0.519	92.267	0.563	0.694	0.998	0.400	1.289	0.310	0.322	5, 12, 14, 16, 21
3RCW_A	BRD1	Apo	2.21	0.848	65	0.774	161.210	0.567	0.684	0.858	0.413	1.208	0.342	0.571	18, 42, 104, 105, 46(3RCW_B)
3RCW_B	BRD1	Apo	2.21	0.849	56	0.834	141.659	0.588	0.709	0.980	0.792	0.904	0.877	0.449	46, 66, 68, 18(3RCW_A), 42(3RCW_A)
3RCW_C	BRD1	Ligand	2.21	0.846	66	0.818	124.509	0.569	0.674	0.918	0.484	1.073	0.451	0.585	38, 45, 132, 18(3RCW_A), 104(3RCW_A)
3RCW_D	BRD1	Apo	2.21	0.748	50	0.720	121.765	0.679	0.624	0.819	0.414	0.978	0.423	0.858	25, 78, 162, 171, 104(3RCW_A)
3RCW_E	BRD1	Apo	2.21	0.788	45	0.765	138.572	0.646	0.689	0.896	0.690	0.855	0.807	0.826	135, 164, 42(3RCW_A), 104(3RCW_A), 105(3RCW_A)
3RCW_F	BRD1	Apo	2.21	0.849	60	0.791	149.891	0.528	0.719	1.002	0.774	1.129	0.686	0.517	153, 18(3RCW_A), 42(3RCW_A), 104(3RCW_A), 46(3RCW_B)
3RCW_H	BRD1	Apo	2.21	0.744	40	0.669	113.533	0.619	0.718	0.978	0.447	1.092	0.409	0.684	98, 18(3RCW_A), 42(3RCW_A), 105(3RCW_A), 46(3RCW_B)
1X0J_A	BRD2(1)	Ligand	1.80	0.977	65	1.006	154.693	0.435	0.760	1.043	1.486	0.637	2.331	0.418	1303, 1304, 1305, 1307, 1323,
1X0J_B	BRD2(1)	Ligand	1.80	0.875	59	0.877	134.456	0.468	0.699	1.045	1.146	0.812	1.411	0.499	1303, 1305, 1306, 1313, 1320
1X0J_C	BRD2(1)	Ligand	1.80	0.800	48	0.766	122.790	0.543	0.711	1.019	0.993	0.957	1.038	0.627	1402, 1403, 1406, 1407, 1412
2DVQ_A	BRD2(1)	Peptide	2.04	1.009	76	1.065	160.181	0.465	0.713	1.012	1.923	0.559	3.438	1.855	197, 198, 199, 222, 200(2DVQ_B)
2DVQ_B	BRD2(1)	Peptide	2.04	1.009	88	1.066	149.548	0.460	0.676	0.952	1.325	0.678	1.953	1.053	195, 198, 200, 211, 214
2DVQ_C	BRD2(1)	Apo	2.04	0.789	41	0.786	132.055	0.658	0.670	0.977	1.219	0.669	1.822	0.511	197, 199, 203, 211, 216
2DVR_A	BRD2(1)	Peptide	2.30	0.976	68	1.025	157.094	0.460	0.711	1.026	1.905	0.543	3.508	1.174	131, 134, 129(2DVR_B),136(2DVR_B), 152(2VR_B),
2DVR_B	BRD2(1)	Peptide	2.30	0.946	66	0.978	152.978	0.532	0.709	1.003	1.255	0.647	1.942	1.036	129, 130, 136, 140, 152
2DVR_C	BRD2(1)	Apo	2.30	0.791	42	0.787	126.224	0.615	0.670	0.942	1.070	0.687	1.557	0.658	131, 135, 146, 149, 136(2DVR_B)
2DVS_A	BRD2(1)	Peptide	2.04	0.926	68	0.953	155.379	0.460	0.689	0.995	1.306	0.724	1.803	2.893	130, 136, 137, 138, 205
2DVS_B	BRD2(1)	Peptide	2.04	0.901	66	0.916	156.065	0.548	0.682	0.965	1.027	0.789	1.302	1.276	129, 132, 133, 152, 167
2DVS_C	BRD2(1)	Apo	2.04	0.864	53	0.906	128.968	0.586	0.633	0.892	1.322	0.486	2.719	0.646	131, 136, 137, 145, 147
2YDW_A	BRD2(1)	Ligand	1.90	0.853	59	0.823	154.350	0.546	0.731	1.027	0.725	1.037	0.699	0.598	2022, 2043, 2044, 2065, 2088
2YDW_B	BRD2(1)	Ligand	1.90	0.862	65	0.867	149.548	0.522	0.657	0.898	0.679	0.875	0.777	0.363	2016, 2026, 2027, 2038, 2059
2YDW_C	BRD2(1)	Ligand	1.90	0.873	66	0.863	157.780	0.504	0.693	0.930	0.802	0.971	0.827	0.503	2018, 2037, 2038, 2052, 2074
2YEK_A	BRD2(1)	Ligand	1.98	0.922	87	0.881	183.162	0.514	0.656	0.912	0.366	1.194	0.307	0.688	2027, 2070,2071, 2086, 2113
2YEK_B	BRD2(1)	Ligand	1.98	0.862	56	0.860	147.833	0.495	0.703	0.964	1.168	0.814	1.435	0.457	2015, 2048, 2049, 2058, 2092

2YEK_C	BRD2(1)	Ligand	1.98	0.852	60	0.841	147.147	0.492	0.690	0.990	0.850	0.924	0.920	0.433	2023, 2046, 2047, 2063, 2088
3AQA_A	BRD2(1)	Ligand	2.39	0.900	53	0.902	165.669	0.518	0.755	1.055	1.411	0.722	1.955	0.567	7, 10, 22, 198, 204
3AQA_B	BRD2(1)	Apo	2.39	0.981	77	1.009	151.263	0.462	0.726	1.012	1.271	0.771	1.649	0.517	12, 17, 21, 57, 208
3AQA_C	BRD2(1)	Apo	2.39	0.828	56	0.814	134.799	0.537	0.679	0.985	0.763	0.910	0.839	0.955	40, 48, 50, 52, 197
4A9E_A	BRD2(1)	Ligand	1.91	0.867	65	0.766	147.833	0.570	0.712	0.999	0.560	1.287	0.435	0.846	2027, 2059, 2060, 2087, 2117
4A9E_B	BRD2(1)	Ligand	1.91	0.885	63	0.894	136.857	0.519	0.684	0.938	0.991	0.804	1.233	0.451	2021, 2043, 2044, 2061, 2084
4A9E_C	BRD2(1)	Ligand	1.91	0.787	52	0.751	133.084	0.581	0.682	1.002	0.948	1.031	0.919	1.185	2017, 2029, 2030, 2040, 2060
4A9F_A	BRD2(1)	Ligand	1.73	0.939	76	0.940	156.065	0.476	0.725	1.030	1.108	0.964	1.149	0.501	2029, 2078, 2079, 2117, 2118
4A9F_B	BRD2(1)	Ligand	1.73	0.870	70	0.863	159.838	0.545	0.671	0.894	0.667	0.999	0.668	0.691	2021, 2051, 2052, 2073, 2098
4A9F_C	BRD2(1)	Ligand	1.73	0.791	62	0.776	142.688	0.622	0.610	0.795	0.568	1.011	0.562	0.772	2022, 2044, 2045, 2061, 2062
4A9H_A	BRD2(1)	Ligand	2.05	0.918	75	0.889	162.239	0.483	0.723	1.062	0.739	1.101	0.671	0.492	2027, 2060, 2061, 2076, 2077
4A9H_B	BRD2(1)	Ligand	2.05	0.922	73	0.874	168.756	0.416	0.741	1.041	0.874	1.148	0.761	0.930	2019, 2039, 2040, 2057, 2077
4A9H_C	BRD2(1)	Ligand	2.05	0.917	82	0.792	184.877	0.503	0.677	0.958	0.229	1.428	0.160	1.147	2014, 2032, 2033, 2045, 2068
4A9I_A	BRD2(1)	Ligand	2.25	0.861	60	0.820	149.548	0.483	0.738	1.076	0.815	1.076	0.757	0.511	2015, 2036, 2037, 2049, 2071
4A9I_B	BRD2(1)	Ligand	2.25	0.856	63	0.870	147.147	0.588	0.638	0.813	0.718	0.796	0.902	0.448	2016, 2032, 2033, 2051, 2070
4A9I_C	BRD2(1)	Ligand	2.25	0.783	60	0.766	152.292	0.691	0.612	0.811	0.409	1.012	0.404	1.321	2008, 2015, 2016, 2022, 2039
4A9J_A	BRD2(1)	Ligand	1.90	0.824	58	0.803	144.060	0.583	0.679	0.966	0.591	0.983	0.601	0.922	2027, 2051, 2052, 2068, 2096
4A9J_B	BRD2(1)	Ligand	1.90	0.820	48	0.810	147.833	0.597	0.692	0.968	1.044	0.789	1.325	0.875	2016, 2041, 2042, 2059, 2078
4A9J_C	BRD2(1)	Ligand	1.90	0.781	52	0.753	133.084	0.570	0.660	0.949	0.814	0.984	0.827	1.201	2013, 2026, 2027, 2036, 2056
4A9M_A	BRD2(1)	Ligand	2.06	0.935	83	0.948	176.302	0.556	0.676	0.967	0.802	0.964	0.832	1.044	2026, 2058, 2059, 2072, 2097
4A9M_B	BRD2(1)	Ligand	2.06	0.886	61	0.886	157.094	0.523	0.711	0.981	1.139	0.843	1.351	0.426	2018. 2039, 2040, 2058, 2081
4A9M_C	BRD2(1)	Ligand	2.06	0.825	55	0.814	147.490	0.574	0.672	0.921	0.837	0.876	0.955	0.249	2011, 2024, 2025, 2037, 2058
4A9N_A	BRD2(1)	Ligand	1.85	0.955	83	0.928	164.640	0.435	0.728	1.021	0.619	1.121	0.552	0.435	2018, 2050, 2051, 2065, 2087
4A9N_B	BRD2(1)	Ligand	1.85	0.919	69	0.927	164.297	0.514	0.710	0.974	0.940	0.857	1.097	0.554	2015, 2028, 2029, 2046, 2063
4A9N_C	BRD2(1)	Ligand	1.85	0.870	67	0.876	176.645	0.553	0.656	0.921	0.745	0.879	0.847	1.056	2013, 2025, 2026, 2034, 2051
4A9O_A	BRD2(1)	Ligand	1.78	0.948	79	0.853	160.181	0.415	0.742	1.061	0.514	1.313	0.392	0.656	2035, 2081, 2082, 2104, 2136
4A9O_B	BRD2(1)	Ligand	1.78	0.914	72	0.835	160.867	0.395	0.736	0.995	0.627	1.239	0.506	0.642	2023, 2045, 2046, 2072, 2100
4A9O_C	BRD2(1)	Ligand	1.78	0.901	75	0.837	161.553	0.472	0.696	0.951	0.462	1.210	0.382	0.605	2015, 2035, 2036, 2052, 2079
4ALH_A	BRD2(1)	Ligand	1.97	0.962	86	0.894	162.239	0.456	0.720	1.002	0.495	1.258	0.394	0.835	2031, 2065, 2066, 2082, 2103
4ALH_B	BRD2(1)	Ligand	1.97	0.970	86	0.913	163.954	0.415	0.733	1.004	0.701	1.224	0.573	0.424	2017, 2033, 2034, 2052, 2072
4ALH_C	BRD2(1)	Ligand	1.97	0.888	70	0.840	157.437	0.481	0.709	1.021	0.560	1.141	0.491	0.568	2013, 2028, 2029, 2040, 2058
2DVV	BRD2(2)	Ligand	1.80	0.917	70	0.946	156.751	0.527	0.666	0.924	1.039	0.737	1.410	0.312	457, 460, 467, 590, 4(3ONI)
2E3K_A	BRD2(2)	Apo	2.30	0.946	78	0.989	172.529	0.602	0.651	0.879	0.944	0.712	1.327	0.977	462, 463, 496, 470(2E3K_B), 473 (2E3K_B)

2E3K_B	BRD2(2)	Peptide	2.30	0.692	22	0.643	102.557	0.662	0.725	0.948	1.308	0.715	1.831	0.811	459, 465, 470, 473, 496(2E3K_A)
2E3K_C	BRD2(2)	Peptide	2.30	0.845	56	0.863	160.524	0.624	0.643	0.863	0.794	0.694	1.144	0.870	459, 460, 464, 508, 473(2E3K_B)
2E3K_D	BRD2(2)	Peptide	2.30	0.927	71	0.983	162.239	0.606	0.624	0.831	1.281	0.563	2.276	1.023	459, 461, 496(2E3K_A), 470(2E3K_B), 473 (2E3K_B)
3ONI	BRD2(2)	Ligand	1.61	0.803	55	0.809	151.263	0.621	0.614	0.836	0.587	0.786	0.748	0.400	3, 4, 30, 34, 460
2NXB_A	BRD3(1)	Apo	1.40	0.794	46	0.798	142.345	0.657	0.641	0.760	0.965	0.688	1.402	0.559	325, 337, 351, 382, 386
2NXB_B	BRD3(1)	Apo	1.40	0.967	66	1.009	162.925	0.538	0.721	0.999	1.846	0.575	3.209	0.944	337, 342, 340, 345, 457
3S91	BRD3(1)	Ligand	2.06	0.871	69	0.862	170.471	0.507	0.678	0.971	0.508	1.000	0.508	0.688	5, 6, 12, 15, 147
2OO1_A	BRD3(2)	Apo	1.70	0.917	63	0.944	163.611	0.526	0.692	0.988	1.445	0.667	2.167	0.824	2970, 2973, 2977, 2982, 2985
2OO1_B	BRD3(2)	Apo	1.70	0.795	44	0.800	159.152	0.633	0.648	0.866	0.764	0.650	1.175	0.385	2969, 2970, 2980, 2984, 2992
2OO1_C	BRD3(2)	Apo	1.70	0.933	67	0.986	166.698	0.573	0.650	0.883	1.548	0.532	2.909	0.660	5099, 5100, 5103, 5107, 5110
2OO1_D	BRD3(2)	Apo	1.70	0.895	70	0.904	165.326	0.542	0.674	0.949	0.740	0.880	0.841	0.369	2970, 2974, 2977, 2081, 2997
3S92	BRD3(2)	Ligand	1.36	0.929	65	0.966	187.964	0.504	0.681	0.979	1.320	0.616	2.141	0.466	2, 5, 10, 19, 20
2OSS	BRD4(A/B)(1)	Apo	1.35	0.891	59	0.938	131.026	0.590	0.637	0.850	1.621	0.508	3.192	0.732	311, 320, 326, 334, 2101(2YEL)
2YEL	BRD4(A/B)(1)	Ligand	1.65	0.854	53	0.854	133.770	0.470	0.699	0.988	1.239	0.766	1.618	0.297	2101, 2126, 2127, 2135, 2167
3MUK	BRD4(A/B)(1)	Peptide	1.75	0.973	68	1.016	144.060	0.414	0.719	1.029	2.064	0.583	3.541	0.601	2, 3, 4, 5, 169
3MUL	BRD4(A/B)(1)	Peptide	1.65	0.938	70	0.992	173.215	0.591	0.644	0.907	1.694	0.556	3.045	1.355	2, 3, 4, 5, 169
3MXF	BRD4(A/B)(1)	Ligand	1.60	0.934	64	0.976	143.031	0.511	0.683	0.928	1.802	0.570	3.160	0.577	9, 12, 15, 33, 209
3P5O	BRD4(A/B)(1)	Ligand	1.60	0.942	63	0.990	143.374	0.533	0.685	0.907	1.590	0.512	3.106	0.763	9, 10, 27, 29, 33
3SVF	BRD4(A/B)(1)	Ligand	1.98	0.884	60	0.886	133.084	0.459	0.709	1.009	1.236	0.820	1.508	0.243	1, 8, 13, 31, 54
3SVG	BRD4(A/B)(1)	Ligand	1.68	0.933	86	0.963	219.177	0.664	0.632	0.900	0.815	0.885	0.921	0.725	3, 8, 18, 22, 40
3JVJ	BRD4(A/B)(1)	Ligand	1.55	0.985	83	1.049	176.645	0.605	0.646	0.853	1.311	0.599	2.190	1.172	9, 10, 11, 12, 172
3JVK	BRD4(A/B)(1)	Ligand	1.80	0.890	62	0.924	143.374	0.622	0.646	0.844	1.193	0.625	1.909	0.519	6, 14, 15, 16, 17
3U5J	BRD4(A/B)(1)	Ligand	1.60	0.918	86	0.948	197.225	0.650	0.612	0.858	0.745	0.893	0.834	0.510	7, 11, 16, 170, 178
3U5K_A	BRD4(A/B)(1)	Ligand	1.80	0.927	75	0.955	181.447	0.583	0.661	0.958	1.042	0.785	1.327	0.650	5, 188, 198, 175(3U5K_C), 204(3U5K_C)
3U5K_B	BRD4(A/B)(1)	Ligand	1.80	0.861	54	0.866	139.258	0.530	0.694	0.969	1.231	0.741	1.663	0.776	1, 4, 9, 169, 171(3U5K_C)
3U5K_C	BRD4(A/B)(1)	Ligand	1.80	0.924	72	0.864	143.717	0.419	0.750	1.042	0.900	1.178	0.764	0.386	28, 171, 175, 186, 204
3U5K_D	BRD4(A/B)(1)	Ligand	1.80	0.857	67	0.844	143.374	0.538	0.676	0.955	0.859	1.014	0.846	0.583	37, 170, 187, 175(3U5K_C), 186(3U5K_C)
3U5L	BRD4(A/B)(1)	Ligand	1.39	0.869	62	0.881	138.229	0.534	0.663	0.872	1.175	0.788	1.490	0.239	3, 9, 13, 16, 219
3UVW	BRD4(A/B)(1)	Peptide	1.37	0.921	81	0.945	217.805	0.667	0.641	0.913	0.827	0.875	0.946	0.700	4, 11, 15, 21, 170
3UVX	BRD4(A/B)(1)	Peptide	1.91	0.939	76	0.965	172.186	0.566	0.680	0.983	0.890	0.804	1.107	0.879	4, 6, 10, 21, 41
3UVY	BRD4(A/B)(1)	Peptide	2.02	0.913	64	0.912	137.886	0.423	0.736	1.039	1.079	0.863	1.250	0.465	11, 20, 26, 30, 170
3UW9_A	BRD4(A/B)(1)	Peptide	2.30	0.913	78	0.904	182.476	0.439	0.696	1.047	0.681	1.054	0.646	0.808	2, 12, 38, 169, 173

3UW9_D	BRD4(A/B)(1)	Peptide	2.30	0.834	55	0.806	142.688	0.518	0.718	1.031	0.984	0.986	0.997	0.293	8, 15, 177, 178, 169(3UW9_A)
3ZYU_A	BRD4(A/B)(1)	Ligand	1.50	0.934	80	0.976	213.003	0.631	0.631	0.885	0.725	0.748	0.968	0.522	2100, 2136, 2137, 2145, 2178
3ZYU_B	BRD4(A/B)(1)	Ligand	1.50	0.918	71	0.896	167.041	0.418	0.748	1.084	0.897	1.059	0.847	0.325	2077, 2108, 2109, 2120, 2153
4A9L	BRD4(A/B)(1)	Ligand	1.60	1.006	102	1.062	220.549	0.622	0.636	0.905	0.964	0.795	1.212	0.612	2094, 2130, 2131, 2146, 2181
4E96	BRD4(A/B)(1)	Ligand	1.92	0.862	59	0.852	135.828	0.572	0.706	0.969	1.143	0.902	1.268	0.610	308, 309, 315, 326, 333
2DWW	BRD4(A/B)(2)	Apo	1.80	0.809	53	0.835	147.147	0.688	0.593	0.845	0.887	0.629	1.411	1.906	207, 209, 221, 224, 11(2OUO)
2OUO	BRD4(A/B)(2)	Apo	1.89	0.816	48	0.819	170.814	0.667	0.663	0.903	0.915	0.706	1.296	0.701	8, 11, 15, 147, 148
2YEM_A	BRD4(A/B)(2)	Ligand	2.30	0.890	67	0.901	172.529	0.544	0.672	0.985	0.975	0.831	1.172	0.842	2019, 2033, 2034, 2039, 2062
2YEM_B	BRD4(A/B)(2)	Ligand	2.30	0.817	64	0.811	180.418	0.644	0.620	0.878	0.541	0.961	0.563	0.628	2005, 2020, 2021, 2024, 2034
3JVL	BRD4(A/B)(2)	Apo	1.20	0.914	70	0.939	168.413	0.521	0.668	0.920	0.739	0.763	0.968	0.569	4, 5, 15, 20, 26
3JVM	BRD4(A/B)(2)	Apo	1.20	0.895	65	0.897	167.727	0.522	0.702	0.999	0.980	0.863	1.135	0.611	3, 4, 10, 72, 468
3HME_A	BRD9	Apo	2.23	0.850	66	0.858	130.340	0.548	0.630	0.840	0.611	0.872	0.700	0.870	9, 138, 141, 160, 163(3HME_B)
3HME_B	BRD9	Apo	2.23	0.786	50	0.777	140.973	0.618	0.639	0.829	0.552	0.832	0.663	0.577	4, 7, 163, 164, 169
3NXB_A	CECR2	Apo	1.83	0.964	73	1.015	125.881	0.532	0.676	0.989	1.592	0.594	2.679	1.345	2, 30, 171, 172, 173
3NXB_B	CECR2	Apo	1.83	0.958	86	0.994	170.128	0.530	0.652	0.848	0.727	0.826	0.881	0.648	5, 11, 21, 28, 36
3DWY_A	CREBBP	Apo	1.98	0.728	41	0.658	109.074	0.568	0.685	0.967	0.625	1.089	0.574	0.716	1199, 1210, 1211, 1213, 1246
3DWY_B	CREBBP	Apo	1.98	0.768	43	0.763	136.171	0.672	0.637	0.844	0.988	0.723	1.366	0.887	4, 76, 85, 130, 160
3P1C_A	CREBBP	Peptide	1.82	0.754	45	0.722	111.818	0.587	0.661	0.929	0.947	0.935	1.013	0.279	3, 4, 5, 18, 44
3P1C_B	CREBBP	Peptide	1.82	0.870	55	0.892	131.026	0.574	0.671	0.913	1.544	0.636	2.427	1.067	23, 32, 47, 49, 72
3P1D_A	CREBBP	Ligand	1.86	0.730	41	0.688	117.992	0.610	0.666	0.922	0.796	0.961	0.828	0.367	7, 9, 13, 18, 42 (3P1D_B)
3P1D_B	CREBBP	Ligand	1.86	0.802	47	0.795	126.224	0.580	0.669	0.922	0.962	0.769	1.250	0.621	36, 42, 56, 76, 7 (3P1D_A)
3P1E_A	CREBBP	Ligand	1.80	0.747	40	0.707	117.992	0.619	0.688	0.964	0.865	0.916	0.944	0.544	15, 18, 21, 28, 88
3P1E_B	CREBBP	Ligand	1.80	0.827	53	0.821	137.886	0.569	0.675	0.927	1.007	0.824	1.222	0.716	12, 27, 32, 81, 117
3P1F_A	CREBBP	Ligand	1.63	0.857	68	0.843	120.736	0.514	0.674	0.962	0.570	1.031	0.553	0.425	4, 7, 11, 18, 1200
3P1F_B	CREBBP	Ligand	1.63	0.757	43	0.711	115.248	0.598	0.701	0.996	0.771	1.000	0.770	0.616	22, 39, 45, 1199, 1200
3SVH_A	CREBBP	Ligand	1.80	0.812	51	0.817	125.195	0.602	0.641	0.888	0.865	0.732	1.181	0.551	7, 16, 18, 27, 23(3SVH_B)
3SVH_B	CREBBP	Ligand	1.80	0.820	56	0.824	117.992	0.566	0.636	0.869	0.725	0.802	0.904	0.463	20, 23, 45, 102, 144
4A9K_A	CREBBP	Ligand	1.81	0.717	35	0.669	115.591	0.624	0.688	0.996	0.809	0.921	0.879	0.287	2050, 2066, 2067, 2082, 2083
4A9K_B	CREBBP	Ligand	1.81	0.787	42	0.733	132.741	0.523	0.757	1.126	1.031	1.015	1.015	0.406	2041, 2059, 2070, 2058, 2088
3I3J_A	EP300	Apo	2.33	0.745	42	0.671	102.557	0.517	0.702	0.981	0.669	1.103	0.606	0.497	6, 105, 126, 145, 181(3I3J_C)
3I3J_B	EP300	Apo	2.33	0.791	46	0.756	109.760	0.495	0.708	1.049	1.074	0.940	1.142	0.461	81, 99, 205, 373, 108(3I3J_C)
3I3J_C	EP300	Apo	2.33	0.782	41	0.721	112.161	0.438	0.766	1.098	1.002	1.044	0.960	0.230	72, 108, 181, 304, 353
3I3J_D	EP300	Apo	2.33	0.767	40	0.690	106.330	0.467	0.752	1.080	1.105	1.090	1.014	0.248	59, 218, 322, 181(3I3J_C), 304(3I3J_C)

3I3J_E	EP300	Apo	2.33	0.748	48	0.711	113.190	0.571	0.650	0.919	0.812	1.013	0.801	0.422	14, 107, 134, 179, 224
3I3J_F	EP300	Apo	2.33	0.808	45	0.746	98.098	0.423	0.771	1.062	1.257	1.065	1.180	0.167	72(3I3J_C), 108(3I3J_C), 181(3I3J_C), 304(3I3J_C), 353(3I3J_C)
3I3J_G	EP300	Apo	2.33	0.780	36	0.706	102.214	0.379	0.807	1.180	1.079	1.049	1.028	0.348	5, 24, 58, 62, 217
3I3J_H	EP300	Apo	2.33	0.824	51	0.825	102.900	0.528	0.666	0.916	1.148	0.755	1.522	0.226	27, 108(3I3J_C), 181(3I3J_C), 304(3I3J_C), 353(3I3J_C)
3I3J_I	EP300	Apo	2.33	0.764	34	0.628	103.586	0.469	0.803	1.137	0.891	1.234	0.722	0.213	54, 102, 180, 192, 281
3I3J_J	EP300	Apo	2.33	0.786	42	0.736	100.499	0.475	0.750	0.987	1.033	0.993	1.041	0.149	7, 30, 80, 195, 353(3I3J_C)
3I3J_K	EP300	Apo	2.33	0.755	39	0.703	108.045	0.500	0.726	1.040	0.568	0.980	0.580	0.513	4, 135, 163, 108(3I3J_C), 181(3I3J_C)
3I3J_L	EP300	Apo	2.33	0.804	39	0.794	104.272	0.519	0.712	0.966	1.157	0.673	1.718	0.212	72(3I3J_C), 108(3I3J_C), 181(3I3J_C), 304(3I3J_C), 353(3I3J_C)
2F6J_A	FALZ(A/B)	Apo	2.00	0.915	67	0.949	142.002	0.591	0.663	0.896	1.208	0.670	1.802	0.915	1007, 1010, 1013, 1039, 1045
2F6J_B	FALZ(A/B)	Apo	2.00	0.842	53	0.863	149.548	0.637	0.642	0.845	1.111	0.634	1.753	0.984	1008, 1026, 1032, 1035, 1007(2F6J_A)
2F6J_C	FALZ(A/B)	Apo	2.00	0.795	47	0.793	152.978	0.671	0.649	0.860	0.922	0.737	1.250	0.890	1012, 1044, 1007(2F6J_A), 1010(2F6J_A), 1013(2F6J_A)
2F6N_A	FALZ(A/B)	Apo	2.00	0.767	48	0.728	153.664	0.613	0.679	0.957	0.572	1.012	0.565	0.470	1006, 1011, 1023, 1032, 1035
2F6N_B	FALZ(A/B)	Apo	2.00	0.897	66	0.938	152.292	0.566	0.630	0.832	1.155	0.625	1.847	0.744	1012, 1025, 1059, 1071, 1032(2F6N_A)
2FSA_A	FALZ(A/B)	Apo	1.90	0.916	71	0.962	146.461	0.618	0.628	0.822	1.041	0.634	1.643	0.955	505, 513, 516, 529, 1045(2F6J_A)
2FSA_B	FALZ(A/B)	Apo	1.90	0.834	53	0.848	150.234	0.660	0.648	0.865	1.189	0.692	1.718	0.804	203, 204, 205, 209, 1007(2F6J_A)
2FSA_C	FALZ(A/B)	Apo	1.90	0.762	51	0.733	147.147	0.673	0.643	0.782	0.471	0.995	0.473	0.492	349, 351, 355, 384, 1039(2F6J_A)
2RI7	FALZ(A/B)	Ligand	1.45	0.793	52	0.811	138.572	0.714	0.589	0.725	0.790	0.675	1.172	0.882	797, 799, 812, 820, 1007(2F6J_A)
3QZS_A	FALZ(A/B)	Peptide	1.80	0.986	91	1.015	141.316	0.435	0.689	0.992	0.977	0.905	1.079	0.680	175, 176, 180, 182, 189
3QZS_B	FALZ(A/B)	Peptide	1.80	0.940	80	0.961	141.659	0.490	0.677	0.972	0.952	0.877	1.086	0.753	175, 176, 180, 182, 190
3QZT	FALZ(A/B)	Peptide	1.50	0.938	83	0.967	128.282	0.503	0.648	0.901	0.824	0.853	0.967	0.788	175, 177, 180, 181, 232
3QZV	FALZ(A/B)	Peptide	2.00	0.890	71	0.892	137.200	0.500	0.677	0.961	0.835	0.938	0.890	0.450	193, 205, 207, 209, 217
3UV2	FALZ(A/B)	Ligand	1.58	0.921	71	0.930	124.166	0.510	0.705	1.018	1.244	0.876	1.421	0.634	12, 14, 15, 25, 26
3D7C_B	GCN5L2	Apo	2.06	0.976	82	1.012	163.954	0.457	0.690	0.970	1.028	0.776	1.324	0.502	18, 20, 21, 37, 56
3IU5	PB1(A/B/C)(1)	Apo	1.63	0.473	14	0.377	61.054	0.827	0.581	0.689	0.025	0.992	0.026	0.964	2, 3, 10, 11, 19
3HMF	PB1(A/B/C)(2)	Apo	1.63	0.751	27	0.752	113.190	0.654	0.681	0.898	1.321	0.447	2.958	0.712	22, 63, 77, 103, 5(3LJW_B)
3LJW_A	PB1(A/B/C)(2)	Apo	1.50	0.762	45	0.726	112.504	0.567	0.679	0.966	0.837	0.959	0.874	0.959	3, 21, 43, 59, 406
3LJW_B	PB1(A/B/C)(2)	Apo	1.50	0.756	46	0.747	113.876	0.649	0.617	0.826	0.751	0.800	0.940	0.656	2, 5, 52, 53, 388
3G0J_A	PB1(A/B/C)(5)	Apo	1.78	0.794	31	0.771	75.117	0.483	0.759	1.103	2.192	0.637	3.443	0.554	12, 36, 53, 166, 221
3MB4_A	PB1(A/B/C)(5)	Ligand	1.66	0.704	18	0.678	79.919	0.617	0.723	0.969	1.673	0.476	3.518	0.770	15, 20, 71, 78, 132
3MB4_B	PB1(A/B/C)(5)	Ligand	1.66	0.808	37	0.786	85.750	0.549	0.749	1.035	1.549	0.722	2.146	0.578	16, 18, 26, 37, 50

3GG3_B	PCAF	Apo	2.25	1.032	103	1.084	162.582	0.452	0.678	0.900	0.864	0.807	1.071	0.702	7, 19, 34, 87, 88
3MB3	PHIP(2)	Ligand	2.25	0.866	71	0.869	145.775	0.587	0.643	0.833	0.358	0.947	0.378	0.756	25, 27, 29, 34, 151
2GRC	SMARCA4	Apo	1.50	0.715	36	0.658	97.412	0.514	0.696	0.937	1.116	0.992	1.125	1.147	2, 3, 11, 13
3UVD	SMARCA4	Ligand	1.85	0.720	33	0.545	84.035	0.522	0.746	1.010	0.665	1.358	0.490	0.707	2, 4, 19, 58
1EQF	TAF1(A/B)(1)	Apo	2.10	0.724	41	0.689	120.393	0.643	0.644	0.849	0.557	0.918	0.606	0.409	13, 14, 16, 18, 20
3UV5	TAF1(A/B)(1)	Apo	2.03	0.685	36	0.628	117.306	0.640	0.659	0.927	0.693	1.016	0.682	0.530	34, 72, 120, 128, 158
1EQF	TAF1(A/B)(2)	Apo	2.10	0.873	72	0.886	162.239	0.586	0.631	0.918	0.728	0.889	0.819	0.729	1, 5, 7, 21, 321
3UV4_B	TAF1(A/B)(2)	Ligand	1.89	0.979	79	1.002	155.379	0.436	0.728	1.058	1.097	0.829	1.323	0.588	3, 10, 22, 26, 262
3UV4_B	TAF1(A/B)(2)	Ligand	1.89	0.858	59	0.780	154.693	0.478	0.739	1.089	0.607	1.182	0.514	0.298	36, 39, 70, 245, 246
3UV5	TAF1(A/B)(2)	Apo	2.03	0.888	72	0.892	148.176	0.510	0.667	0.973	0.638	0.937	0.680	0.434	11, 16, 33, 82, 165
3HMH	TAF1L(2)	Apo	2.05	0.760	43	0.728	148.862	0.659	0.678	0.895	0.644	0.907	0.709	0.207	3, 5, 8, 12, 35
2YYN_A	TRIM24	Apo	2.50	0.645	23	0.602	74.431	0.657	0.646	0.842	0.595	0.726	0.820	0.539	138, 146, 150, 156, 147(2YYN_B)
2YYN_B	TRIM24	Apo	2.50	0.702	37	0.706	83.006	0.697	0.562	0.687	0.574	0.622	0.923	0.705	136, 147, 138(2YYN_A), 146(2YYN_A), 156(2YYN_A)
2YYN_C	TRIM24	Apo	2.50	0.643	30	0.625	93.982	0.758	0.559	0.711	0.599	0.690	0.869	1.606	136, 145, 138(2YYN_A), 146(2YYN_A), 147(2YYN_B)
2YYN_D	TRIM24	Apo	2.50	0.702	35	0.725	89.523	0.729	0.534	0.648	1.025	0.463	2.213	0.817	139, 150, 151, 146(2YYN_A), 147(2YYN_B)
3O33_A	TRIM24	Apo	2.00	0.690	30	0.657	79.576	0.639	0.648	0.905	0.848	0.756	1.121	0.469	109, 111, 117, 127, 121(3O33_D)
3O33_B	TRIM24	Apo	2.00	0.679	26	0.639	80.948	0.653	0.670	0.962	0.731	0.745	0.981	1.098	115, 135, 136, 139, 130(3O33_D)
3O33_C	TRIM24	Apo	2.00	0.718	30	0.709	73.745	0.630	0.641	0.813	0.902	0.582	1.549	0.893	107, 120, 124, 126, 130(3O33_D)
3O33_D	TRIM24	Apo	2.00	0.761	50	0.761	116.277	0.675	0.589	0.806	0.622	0.787	0.790	0.722	108, 115, 118, 121, 130
3O35_A	TRIM24	Peptide	1.76	0.648	30	0.610	89.866	0.714	0.603	0.820	0.526	0.817	0.644	2.197	100, 102, 112, 113, 131
3O35_B	TRIM24	Peptide	1.76	0.796	50	0.827	135.142	0.718	0.576	0.805	0.744	0.562	1.324	1.048	100, 101, 120, 130, 198
3O36_A	TRIM24	Peptide	1.70	0.684	32	0.674	92.267	0.738	0.588	0.797	0.578	0.645	0.897	1.372	104, 108, 116, 122, 144
3O36_B	TRIM24	Peptide	1.70	0.770	50	0.765	122.108	0.675	0.609	0.776	0.764	0.812	0.942	0.713	103, 106, 139, 145, 166
3O37_B	TRIM24	Apo	2.00	0.605	26	0.570	83.006	0.790	0.562	0.703	0.403	0.758	0.531	1.039	108, 109, 144, 150, 134(3O37_D)

[a]Water molecules included from structures other than indicated with PDB code for structure from which they were taken in brackets. UID's correspond to numbering from the other structure.

Table S4. Output from SiteMap for structures that have been excluded from Figure 4 Figure 5 and Table 1(see main text), but have been subsequently used in analysis. Details of water molecules included where appropriate.

PDB	BRD	Bound State	Res. (Å)	SiteScore	Size	Dscore	Volume	Exposure	Enclosure	Contact	Phobic	Philic	Balance	Don/Acc	Water UID's[a]
3MQM_A	ASH1L	Apo	2.54	0.866	43	0.790	79.576	0.317	0.874	1.435	0.835	1.352	0.618	0.812	
3MQM_B	ASH1L	Apo	2.54	0.875	47	0.697	84.378	0.365	0.855	1.349	0.913	1.412	0.647	1.418	
3LXJ_D	ATAD2B	Apo	2.33	0.668	36	0.636	136.857	0.765	0.588	0.696	0.358	0.863	0.415	0.432	67, 68, 70, 1231(3DAI), 1253(3DAI)
2D9E_A	BRPF1B	Apo		1.032	100	1.103	201.684	0.639	0.641	0.863	0.819	0.680	1.205	2.280	
2D9E_B	BRPF1B	Apo		1.011	82	1.052	162.582	0.523	0.726	0.996	1.388	0.719	1.931	1.585	
2D9E_C	BRPF1B	Apo		0.969	81	0.984	145.432	0.487	0.722	1.004	0.931	0.906	1.028	1.687	
2D9E_D	BRPF1B	Apo		1.001	82	1.043	140.973	0.523	0.711	1.012	1.361	0.720	1.891	2.206	
2D9E_E	BRPF1B	Apo		1.000	76	1.028	152.635	0.522	0.754	1.037	1.720	0.749	2.297	1.410	
2D9E_F	BRPF1B	Apo		1.046	92	1.100	164.640	0.533	0.717	1.018	1.514	0.711	2.129	1.569	
2D9E_G	BRPF1B	Apo		1.051	96	1.092	160.867	0.475	0.736	1.060	1.182	0.831	1.422	1.199	
2D9E_H	BRPF1B	Apo		1.037	89	1.084	155.722	0.486	0.726	1.017	1.555	0.730	2.130	2.505	
2D9E_I	BRPF1B	Apo		0.965	76	0.990	158.466	0.571	0.714	1.010	1.266	0.790	1.603	3.074	
2D9E_J	BRPF1B	Apo		0.988	87	1.015	155.722	0.547	0.705	0.992	1.045	0.874	1.196	1.665	
2D9E_K	BRPF1B	Apo		0.969	85	0.987	152.292	0.538	0.705	1.020	0.778	0.929	0.838	1.403	
2D9E_L	BRPF1B	Apo		0.951	65	0.964	130.683	0.492	0.755	1.053	1.417	0.756	1.873	2.034	
2D9E_M	BRPF1B	Apo		1.078	92	1.136	155.379	0.477	0.750	1.058	2.167	0.663	3.269	2.073	
2D9E_N	BRPF1B	Apo		1.067	88	1.122	162.239	0.500	0.755	1.037	1.649	0.653	2.526	1.660	
2D9E_O	BRPF1B	Apo		0.981	73	1.004	152.635	0.552	0.749	1.001	1.485	0.761	1.953	1.933	
2D9E_P	BRPF1B	Apo		0.870	67	0.858	156.065	0.599	0.689	0.932	0.260	0.996	0.261	1.918	
2D9E_Q	BRPF1B	Apo		0.980	88	1.010	166.012	0.542	0.688	0.899	0.775	0.875	0.886	2.050	
2D9E_R	BRPF1B	Apo		1.057	102	1.099	163.954	0.487	0.730	1.040	1.203	0.854	1.408	1.833	
2D9E_S	BRPF1B	Apo		1.036	79	1.073	158.466	0.466	0.776	1.068	1.437	0.700	2.054	1.016	
2D9E_T	BRPF1B	Apo		0.997	92	1.043	156.751	0.572	0.668	0.903	0.714	0.797	0.895	1.845	
3K2J_A	PB1(A/B/C)(3)	Apo	2.20	0.623	23	0.553	96.040	0.689	0.669	0.842	0.751	0.918	0.818	0.665	23, 46, 3(3LJW_A), 43(3LJW_A), 406(3LJW_A)
3K2J_B	PB1(A/B/C)(3)	Apo	2.20	0.653	25	0.595	96.040	0.632	0.674	0.868	0.954	0.857	1.113	0.611	3, 20, 55, 43(3LJW_A), 406(3LJW_A)
3TLP_A	PB1(A/B/C)(4)	Apo	2.13	0.717	41	0.687	112.161	0.650	0.626	0.870	0.804	0.892	0.900	0.404	2, 15, 20, 43, 406(3LJW_A)
3TLP_B	PB1(A/B/C)(4)	Apo	2.13	0.727	41	0.706	112.847	0.680	0.621	0.803	0.768	0.822	0.933	0.477	7, 9, 54, 43(3TLP_A), 406(3LJW_A)

2DAT_A	SMARCA2B	Apo		0.893	57	0.880	126.910	0.500	0.759	1.039	1.237	0.876	1.412	0.951	
2DAT_B	SMARCA2B	Apo		0.882	51	0.868	136.171	0.500	0.770	1.044	1.235	0.815	1.516	1.239	
2DAT_C	SMARCA2B	Apo		0.952	65	0.938	145.089	0.414	0.809	1.105	1.106	0.936	1.181	0.994	
2DAT_D	SMARCA2B	Apo		0.873	92	0.798	174.587	0.699	0.552	0.804	0.198	1.334	0.149	0.811	
2DAT_E	SMARCA2B	Apo		0.828	51	0.674	112.504	0.510	0.754	1.076	0.574	1.380	0.416	1.060	
2DAT_F	SMARCA2B	Apo		0.880	53	0.874	119.707	0.485	0.744	1.006	1.538	0.787	1.954	1.173	
2DAT_G	SMARCA2B	Apo		0.869	57	0.755	115.934	0.441	0.771	1.063	0.914	1.278	0.715	0.984	
2DAT_H	SMARCA2B	Apo		0.812	47	0.654	109.074	0.548	0.762	1.033	0.618	1.375	0.449	0.880	
2DAT_I	SMARCA2B	Apo		0.877	60	0.852	119.364	0.429	0.748	1.008	1.342	0.996	1.347	1.651	
2DAT_J	SMARCA2B	Apo		0.792	45	0.711	112.161	0.545	0.748	1.046	1.036	1.131	0.916	1.394	
2DAT_K	SMARCA2B	Apo		0.760	43	0.701	110.103	0.583	0.717	0.941	0.433	1.060	0.409	0.912	
2DAT_L	SMARCA2B	Apo		0.903	57	0.867	121.765	0.367	0.814	1.192	1.847	1.016	1.817	1.138	
2DAT_M	SMARCA2B	Apo		0.841	47	0.815	120.736	0.539	0.755	1.026	1.044	0.868	1.202	1.018	
2DAT_N	SMARCA2B	Apo		0.836	49	0.702	117.992	0.505	0.782	1.067	0.383	1.304	0.293	1.031	
2DAT_O	SMARCA2B	Apo		0.796	43	0.674	101.185	0.511	0.770	1.188	0.923	1.239	0.745	0.934	
2DAT_P	SMARCA2B	Apo		0.864	52	0.818	137.886	0.458	0.799	1.121	0.829	1.040	0.797	1.126	
2DAT_Q	SMARCA2B	Apo		0.849	52	0.827	128.968	0.552	0.736	0.986	1.037	0.899	1.154	1.302	
2DAT_R	SMARCA2B	Apo		0.814	42	0.776	117.649	0.533	0.763	1.072	1.464	0.892	1.641	0.673	
2DAT_S	SMARCA2B	Apo		0.841	54	0.812	121.765	0.550	0.732	0.964	0.801	0.974	0.823	1.043	
2DAT_T	SMARCA2B	Apo		0.869	49	0.845	111.475	0.473	0.780	1.067	1.226	0.862	1.423	0.743	
3O34	TRIM24	Peptide	1.90	0.965	112	1.018	315.217	0.718	0.589	0.802	0.602	0.845	0.713	1.378	101, 107, 110, 121, 185
3O37_A	TRIM24	Apo	2.00	0.904	86	0.949	268.912	0.774	0.566	0.742	0.453	0.805	0.563	1.277	103, 113, 128, 150(3O37_B), 134(3O37_D)
3O37_C	TRIM24	Apo	2.00	0.903	88	0.946	251.419	0.760	0.564	0.720	0.334	0.842	0.397	1.083	104, 115, 150, 144(3O37_B), 150(3O37_B)
3O37_D	TRIM24	Apo	2.00	0.799	66	0.823	182.476	0.751	0.535	0.728	0.357	0.803	0.445	1.054	105, 106, 122, 134, 150(3O37_B)

[a]Water molecules included from structures other than indicated with PDB code for structure from which they were taken in brackets. UID's correspond to numbering from the other structure.

Table S5. Eight identified binding site residues, representative PDB code and median druggability for each bromodomain.

Bromodomain	Structure[a]	W81	L92	L94	N140	D144	D145	I146	M149	Median Dscore
BRD2(1)	1X0J	W	L	L	N	D	D	I	M	0.87
BRD2(2)	3ONI	W	L	L	N	H	D	I	M	0.90
BRD3(1)	2NXB	W	L	L	N	D	D	I	M	0.86
BRD3(2)	2OO1	W	L	L	N	H	E	I	M	0.94
BRD4(A/B)(1)	2OSS	W	L	L	N	D	D	I	M	0.93
BRD4(A/B)(2)	2OUO	W	L	L	N	H	E	I	M	0.87
BRDT(A/B)(1)	-	W	L	L	N	D	D	I	M	
BRDT(A/B)(2)	-	W	L	L	N	H	E	I	M	
CECR2	3NXB	W	Y	A	N	S	E	Y	M	1.00
FALZ(A/B)	2F6J	W	D	A	N	S	P	F	C	0.91
GCN5L2	3D7C	W	E	A	N	S	E	Y	Y	1.01
PCAF	3GG3	W	E	A	N	S	E	Y	C	1.08
TAF1(A/B)(2)	1EQF	W	F	V	N	S	Q	Y	T	0.89
TAF1L(2)	3HMH	W	F	V	N	S	Q	Y	T	0.73
BRD1	3RCW	R	E	V	N	T	V	F	A	0.77
BRD7	-	A	I	A	N	T	I	Y	A	
BRD9	3HME	G	I	A	N	T	V	Y	L	0.82
BRPF1A	-	N	E	V	N	T	I	F	A	
BRPF1B	2D9E[c]	N	E	V	N	T	I	F	A	0.91-0.97[d]
BRPF3	-	H	E	V	N	T	I	F	A	
BAZ1A(A/B)	-	W		V	N	T	S	E	A	
BAZ1B	-	W		A	N	S	H	V	C	
BAZ2A(A/B)	-	W		V	N	S	E	I	A	
BAZ2B	3G0L	W		V	N	S	D	I	A	0.61
TRIM24	2YYN	L		V	N	S	E	V	A	0.67[e]
TRIM33B	-	I		I	N	S	E	V	A	
TRIM66[b]	-	L		H	N	S	E	V	A	
PB1(A/B/C)(2)	3HMF	E		Y	N	S	Q	V	D	0.75
PB1(A/B/C)(3)	3K2J[c]	E		Y	N	S	A	I	R	0.57[d]
PB1(A/B/C)(4)	3TLP[c]	D		Y	N	S	Q	V	D	0.70[d]
PB1A(6)	-	D		F	N	S	E	I	D	
PHIP(2)	3MB3	E	E	Y	T	S	R	I	M	0.87
WDR9(A/B)(2)	-	E	E	Y	T	S	K	I	M	
BRWD3(1)	-	S	A	Y	N	K	A	A	V	
PHIP(1)	-	S	A	Y	N	K	S	A	V	
WDR9(A/B)(1)	-	A	T	Y	N	R	S	A	I	
PB1(A/B/C)(5)	3G0J	A	E	L	N	S	L	I	D	0.77
SMARCA2A	-	E	E	L	N	S	Q	I	D	
SMARCA2B	2DAT[c]	E	E	L	N	S	Q	I	D	0.53-0.64[d]
SMARCA4	2GRC	E	E	L	N	S	L	I	D	0.60
ASH1L	3MQM[c]	A	K	N	Y	S	P	V	D	
MLL1[b]	-				D	P	E	I	A	
LOC93349[b]	-	S	K	I	Y	K	D	F	M	
PB1(A/B/C)(1)	3IU5	E	N	Q	Y	S	P	E	A	0.38
SP100A[b]	-	C		E	Y	D	K	F	L	
SP110A[b]	-		I	R	Y	S	D	F	V	
SP110C[b]	-	S	I	R	Y	S	D	F	V	
SP140A[b]	-	S	K	I	Y	K	D	F	M	
ZMYND11(A/B)	-	I	K	H	Y	S	E	Q	I	
CREBBP	3DWY	L	L	I	N	S	R	V	F	0.75
EP300	3I3J	L	L	I	N	S	R	V	Y	0.72
ATAD2A	-	R	E	V	N	D	L	I	R	
ATAD2B	3LXJ[c]	N	E	V	N	D	I	I	R	0.64[d]
TAF1 (1)	1EQF	Y	V	V	N	H	S	L	I	0.66

TAF1L (1)	-	H	V	V	N	H	S	L	I	
BRD8(A/B)(1)[b]	-	N	I	A	N	H	D	V	M	
BRD8B(2)[b]	-	S	Q	A	N	H	H	V	M	
BRWD3(2)[b]	-	E			T	S	R	I	M	
TRIM28[b]	-	R			T	A	D	V	I	
TRIM33A[b]	-	I		I	N	V	Q	V	D	
PRKCBP1[b]	-	D	Q	H	N	H	K	L	I	

[a]Representative structure for bromodomain passing imposed filters, [b]Prediction of ZA loop residues difficult due to variation in length and lack of structure, [c]Structure did not pass imposed filters, but has been used in analysis, [d]Estimated Dscore from structures without conserved water molecules, [e]Median Dscore with four outliers removed (See Group 4 text)

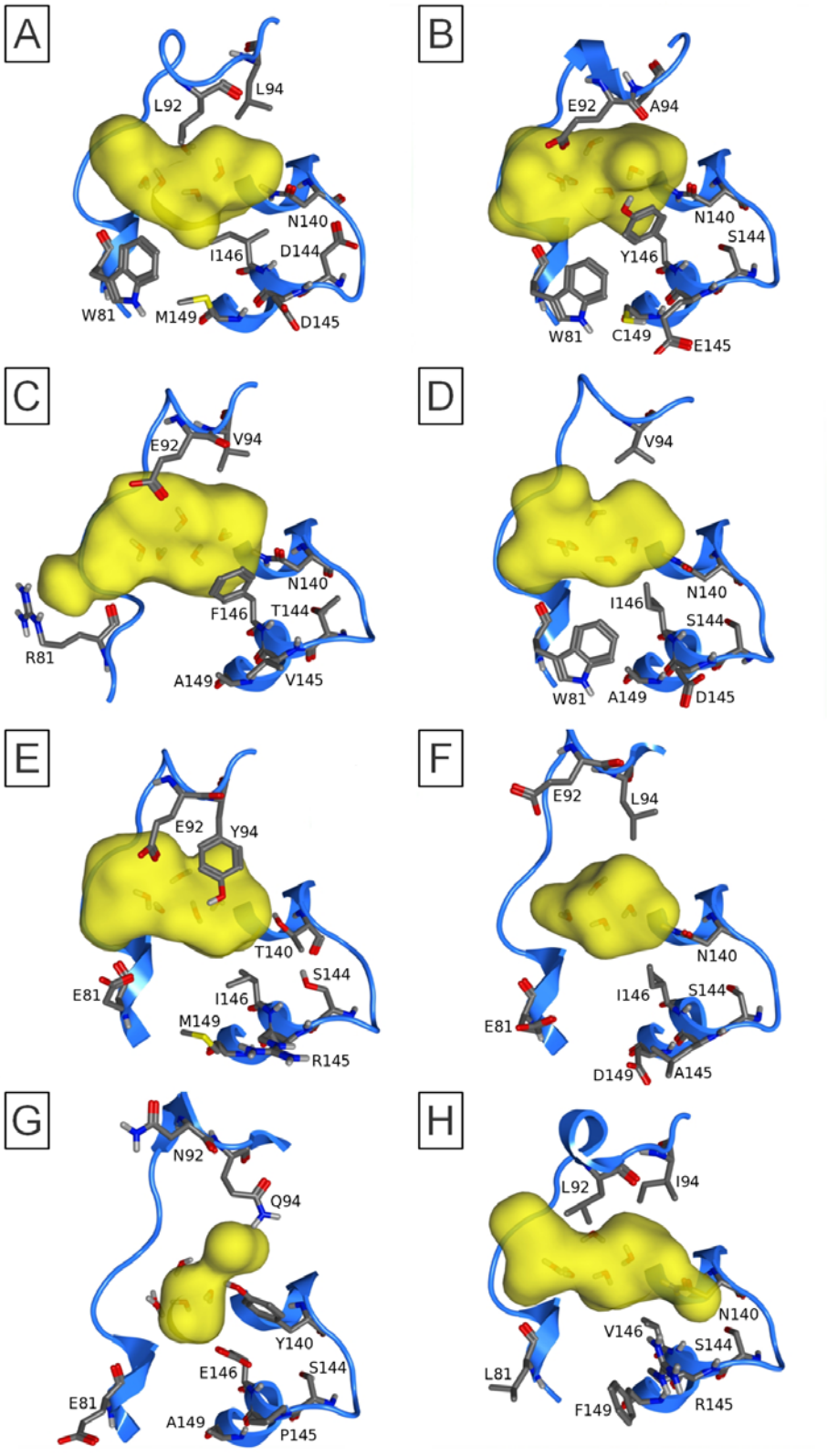

Figure S1. Eight binding site residues used in classification for representative bromodomain of each group and conserved water molecules. Pocket identified by SiteMap shown in yellow. All images captured from the same viewpoint. Bromodomain structures the same as Figure 9. (A) BRD4(A/B)(1)

PDB 3MXF structure representative of Group 1. (B) PCAF PDB 3GG3_B structure representative of Group 2. (C) BRD1 PDB 3RCW_A structure representative of Group 3. (D) BAZ2B PDB 3G0L structure representative of Group 4. (E) PHIP(2) PDB 3MB3 structure representative of Group 5. (F) SMARCA4 PDB 2GRC structure representative of Group 7. (G) PB1(A/B/C)(1) PDB 3IU5 structure representative of Group 8. (H) CREBBP PDB 3P1C_B structure.