

**S1 Table. SB269652 interacting residues.** The means and standard deviations of the interaction frequencies for each residue were calculated using 3 sets of 500 MSM Bayesian samples, each set containing 1500 frames per MS. Residues having contact frequencies above 25% in at least one of the MS are listed and the contact frequencies above 25% are in bold. The OBS and SBP residues identified in [7] are highlighted in cyan and yellow, respectively.

Index	D2R/WT			D3R/WT		
	Residue	green (%)	orange (%)	Residue	green (%)	orange (%)
NT	<b>MET1</b>	<b>39.3 ± 1.0</b>	<b>25.7 ± 1.7</b>	<b>LEU7</b>	<b>60.7 ± 0.9</b>	<b>51.9 ± 0.8</b>
	<b>TRP18</b>	<b>25.0 ± 1.6</b>	<b>11.4 ± 0.7</b>	<b>LEU11</b>	<b>38.2 ± 2.3</b>	<b>31.5 ± 1.3</b>
	<b>PHE22</b>	<b>33.9 ± 0.6</b>	<b>23.5 ± 1.3</b>	<b>TYR13</b>	<b>21.4 ± 0.6</b>	<b>32.7 ± 1.9</b>
	<b>ASN23</b>	<b>25.2 ± 0.8</b>	<b>20.0 ± 0.4</b>			
1.32	TYR34	28.6 ± 0.2	6.6 ± 0.8	HIS29	29.5 ± 2.1	45.5 ± 1.4
2.61	VAL91	93.1 ± 0.2	84.2 ± 0.7	VAL86	94.9 ± 0.8	93.9 ± 1.3
2.64	LEU94	96.2 ± 0.3	87.8 ± 0.8	LEU89	100.0 ± 0.1	99.8 ± 0.1
2.65	GLU95	94.7 ± 0.2	91.4 ± 0.5	GLU90	99.5 ± 0.2	98.6 ± 0.2
EL1	GLY98	93.8 ± 0.4	76.2 ± 1.6	GLY93	99.4 ± 0.1	99.1 ± 0.3
EL1	GLU99	54.6 ± 0.7	39.5 ± 0.9	GLY94	99.4 ± 0.0	98.8 ± 0.3
3.28	PHE110	88.9 ± 0.6	80.4 ± 1.3	PHE106	77.0 ± 0.8	82.5 ± 0.8
3.32	ASP114	100.0 ± 0.0	100.0 ± 0.0	ASP110	100.0 ± 0.0	100.0 ± 0.0
3.33	VAL115	99.9 ± 0.1	100.0 ± 0.1	VAL111	99.9 ± 0.2	99.7 ± 0.1
3.36	CYS118	95.8 ± 0.2	99.0 ± 0.3	CYS114	83.4 ± 1.9	90.6 ± 0.8
EL2.50	CYS182	27.9 ± 0.2	9.0 ± 0.2	CYS181	33.3 ± 0.8	52.1 ± 0.5
EL2.51	ILE183	97.2 ± 0.3	99.7 ± 0.2	SER182	77.0 ± 0.6	72.7 ± 0.9
EL2.52	ILE184	27.5 ± 0.5	0.6 ± 0.1	ILE183	97.0 ± 0.4	96.0 ± 0.7
5.38	PHE189	11.0 ± 0.4	4.9 ± 0.5	PHE188	96.2 ± 0.6	95.8 ± 0.4
5.39	VAL190	93.5 ± 0.9	96.6 ± 0.4	VAL189	99.6 ± 0.1	99.6 ± 0.1
5.42	SER193	92.9 ± 0.3	99.8 ± 0.1	SER192	100.0 ± 0.1	99.9 ± 0.1
5.43	SER194	88.3 ± 0.3	99.7 ± 0.1	SER193	14.1 ± 1.0	14.0 ± 0.5
5.46	SER197	82.4 ± 0.9	97.5 ± 0.4	SER196	15.6 ± 2.1	17.6 ± 0.9
6.48	TRP357	100.0 ± 0.0	100.0 ± 0.0	TRP342	99.8 ± 0.2	99.8 ± 0.1
6.51	PHE360	100.0 ± 0.0	100.0 ± 0.0	PHE345	100.0 ± 0.0	100.0 ± 0.0
6.52	PHE361	99.8 ± 0.1	99.8 ± 0.2	PHE346	94.3 ± 0.9	95.1 ± 0.5
6.55	HIS364	80.4 ± 0.8	94.3 ± 0.3	HIS349	62.6 ± 1.5	43.0 ± 1.5
7.32	PRO376	3.9 ± 0.4	16.9 ± 0.7	PRO362	46.3 ± 0.7	74.2 ± 0.3
7.33	VAL377	3.0 ± 0.4	14.4 ± 0.6	GLU363	28.3 ± 0.5	46.2 ± 1.3
7.35	TYR379	29.4 ± 0.8	33.7 ± 0.8	TYR365	95.3 ± 0.3	97.0 ± 0.6
7.36	SER380	5.6 ± 0.5	21.7 ± 0.4	SER366	60.8 ± 0.6	81.7 ± 1.4
7.39	THR383	99.6 ± 0.1	100.0 ± 0.1	THR369	100.0 ± 0.0	100.0 ± 0.0
7.43	TYR387	99.7 ± 0.1	99.9 ± 0.1	TYR373	98.1 ± 0.4	97.1 ± 0.2