

SUPPLEMENTARY INFORMATION

Unveiling TP5 dual binding mechanism and structure-based search for potential dual inhibitors of Tubulin and PD-L1

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Table S1. Summary of the set of molecules included in this work

Complex	E_{vdW}	E_{Elec}	E_{GB}	E_{Surf}	ΔE_{gas}	ΔE_{solv}	$\Delta G_{\text{bind}} + \text{SD}$
Tub-TP5	-69.5	-24.2	41.8	-8.8	-93.6	33.0	-60.6 \pm 4.3
Tub-bf_1	-68.6	-25.7	37.0	-8.3	-94.3	28.7	-65.6 \pm 3.7
Tub-bf_13	-75.8	-37.2	55.5	-8.2	-112.9	47.3	-65.7 \pm 3.6
Tub-frag2_571	-66.3	-26.5	35.9	-8.3	-92.8	25.6	-65.2 \pm 5.4
Tub-frag2_1592	-60.6	-59.0	60.1	-8.1	-119.6	52.0	-67.6 \pm 4.9
Tub-frag2_3214	-62.6	-22.4	24.7	-7.9	-85.0	16.8	-68.2 \pm 5.2
Tub-frag2_3522	-63.3	-15.6	23.2	-7.3	-78.9	15.9	-63.0 \pm 3.3
Tub-frag2_7150	-67.4	-25.5	32.5	-7.8	-92.9	24.7	-68.2 \pm 4.2
Tub-frag2_8390	-71.0	-30.9	47.2	-8.9	-101.9	38.3	-63.6 \pm 4.8
Tub-frag2_8592	-73.2	-36.1	43.8	-8.4	-109.3	35.5	-73.8 \pm 4.8
dPD-L1-TP5	-55.8	-10.3	30.1	-7.1	-66.1	22.3	-43.1 \pm 4.5
dPD-L1-bf_1	-65.2	-19.2	34.6	-7.0	-84.3	27.6	-56.7 \pm 5.2
dPD-L1-bf_13	-65.8	-7.4	34.4	-7.3	-73.2	27.1	-46.1 \pm 4.1
dPD-L1-frag2_571	-69.0	-13.8	30.4	-7.1	-82.9	23.3	-59.5 \pm 4.6
dPD-L1-frag2_1592	-49.3	-48.0	57.9	-6.8	-97.4	51.1	-46.2 \pm 4.9
dPD-L1-frag2_3214	-62.1	-4.1	26.3	-6.4	-66.3	19.9	-46.3 \pm 2.9
dPD-L1-frag2_3522	-59.3	-12.4	27.7	-6.2	-71.7	21.5	-50.2 \pm 4.8
dPD-L1-frag2_7150	-70.2	-12.0	31.8	-7.2	-82.2	24.6	-57.6 \pm 3.8
dPD-L1-frag2_8390	-62.2	-24.6	44.4	-6.9	-86.7	37.5	-49.2 \pm 5.0
dPD-L1-frag2_8592	-63.4	-18.7	39.1	-7.8	-82.2	31.4	-50.8 \pm 5.6

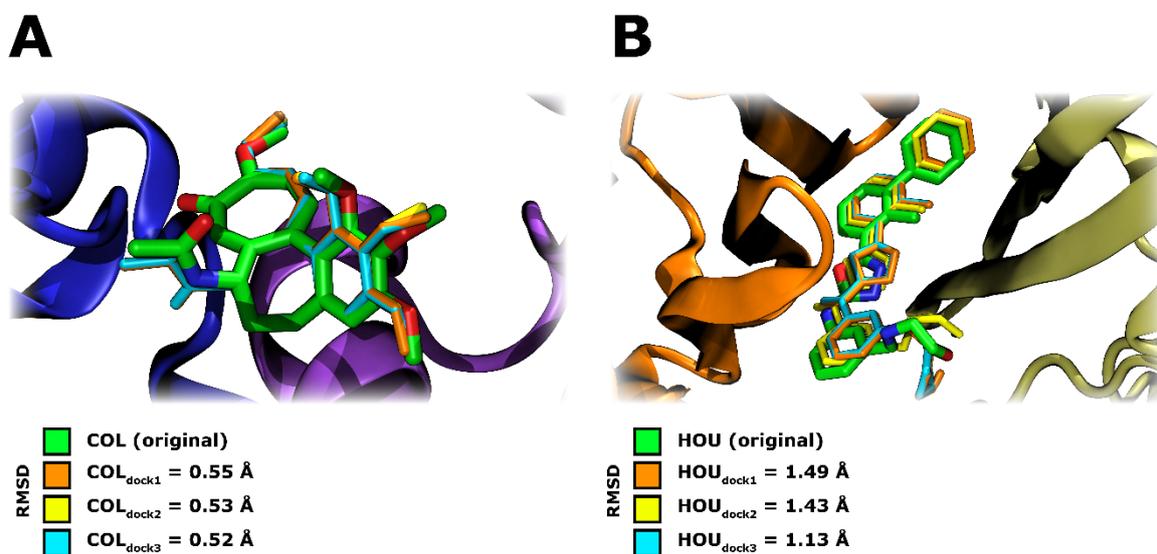


Figure S1. Superposition of A) colchicine ; and B) 2-[[3-[[5-(2-methyl-3-phenyl-phenyl)-1,3,4-oxadiazol-2-yl]amino]phenyl]methylamino]ethanol docking results.

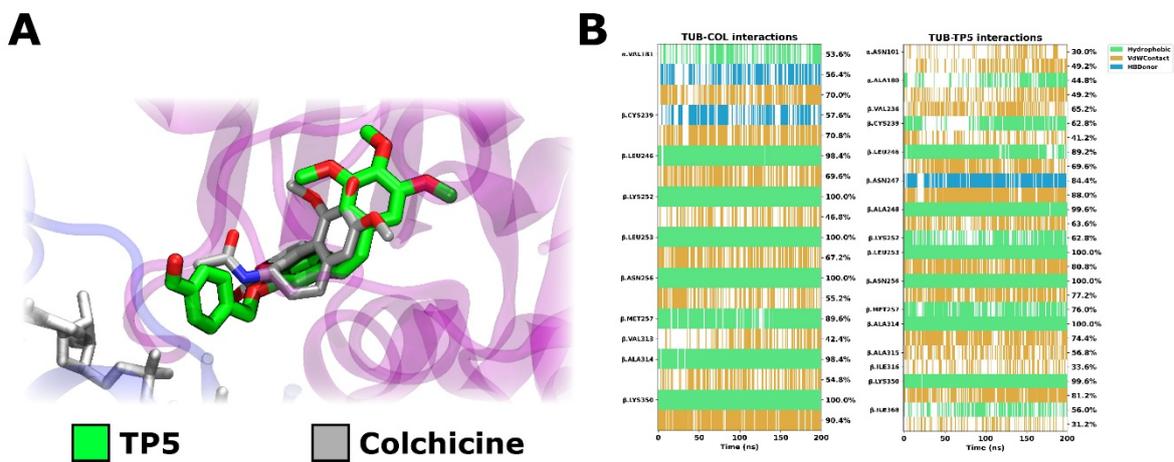


Figure S2. A) Superposition of TP5 and COL within the colchicine binding site. B) COL and TP5 residue interaction decomposition with $\alpha\beta$ -tubulin.

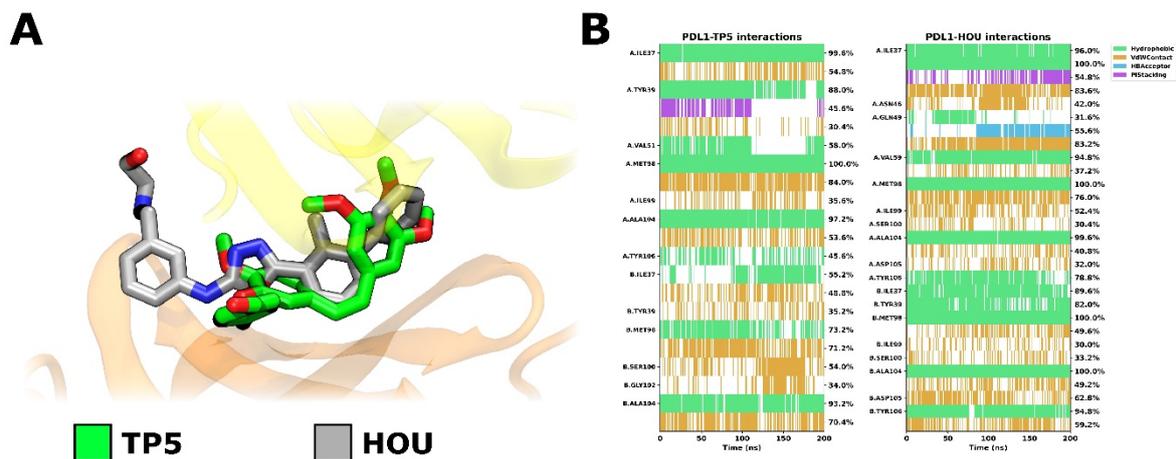


Figure S3. A) Superposition of TP5 and HOU within the dPD-L1 binding site. B) HOU and TP5 residue interaction decomposition with dPD-L1.

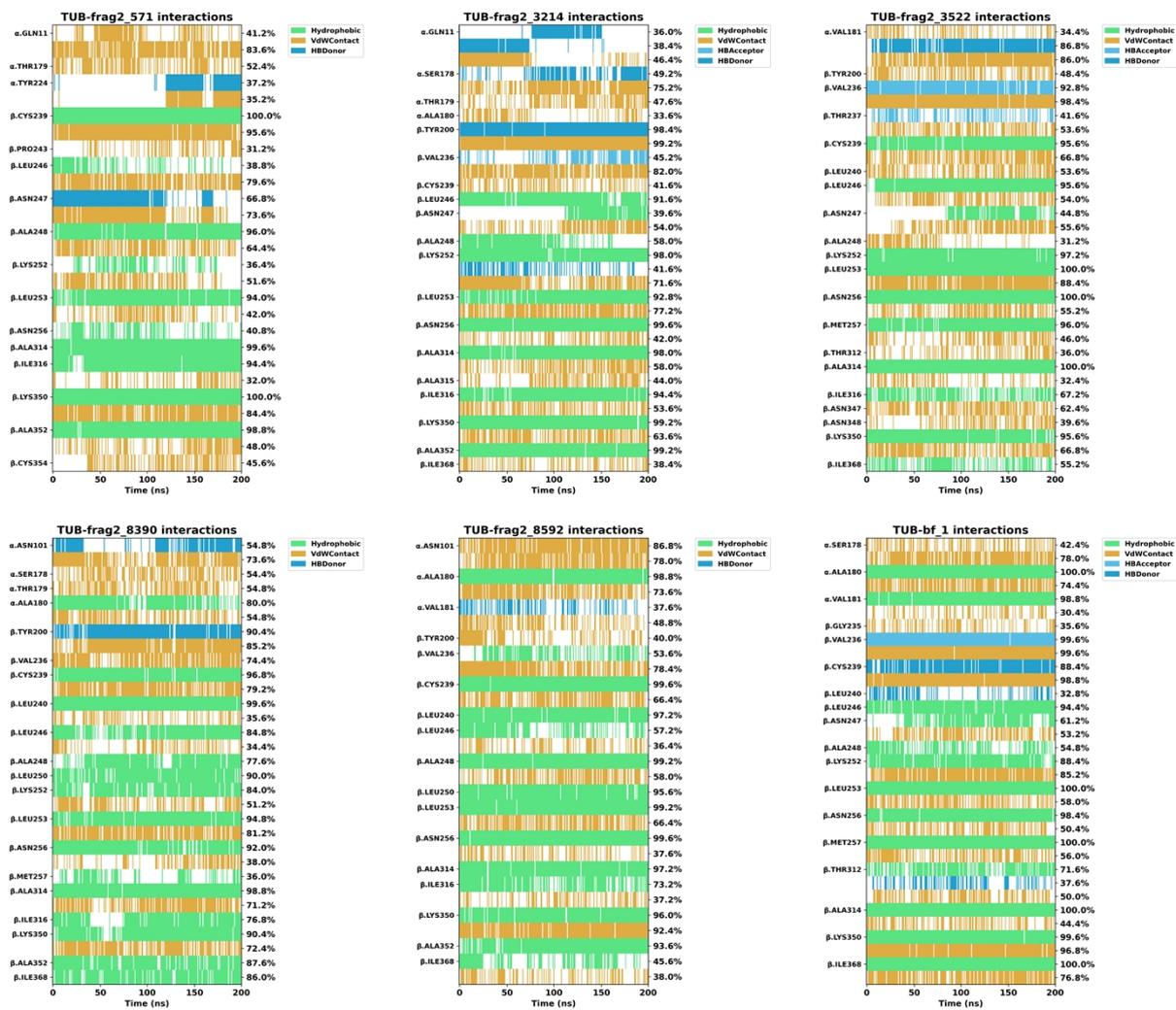
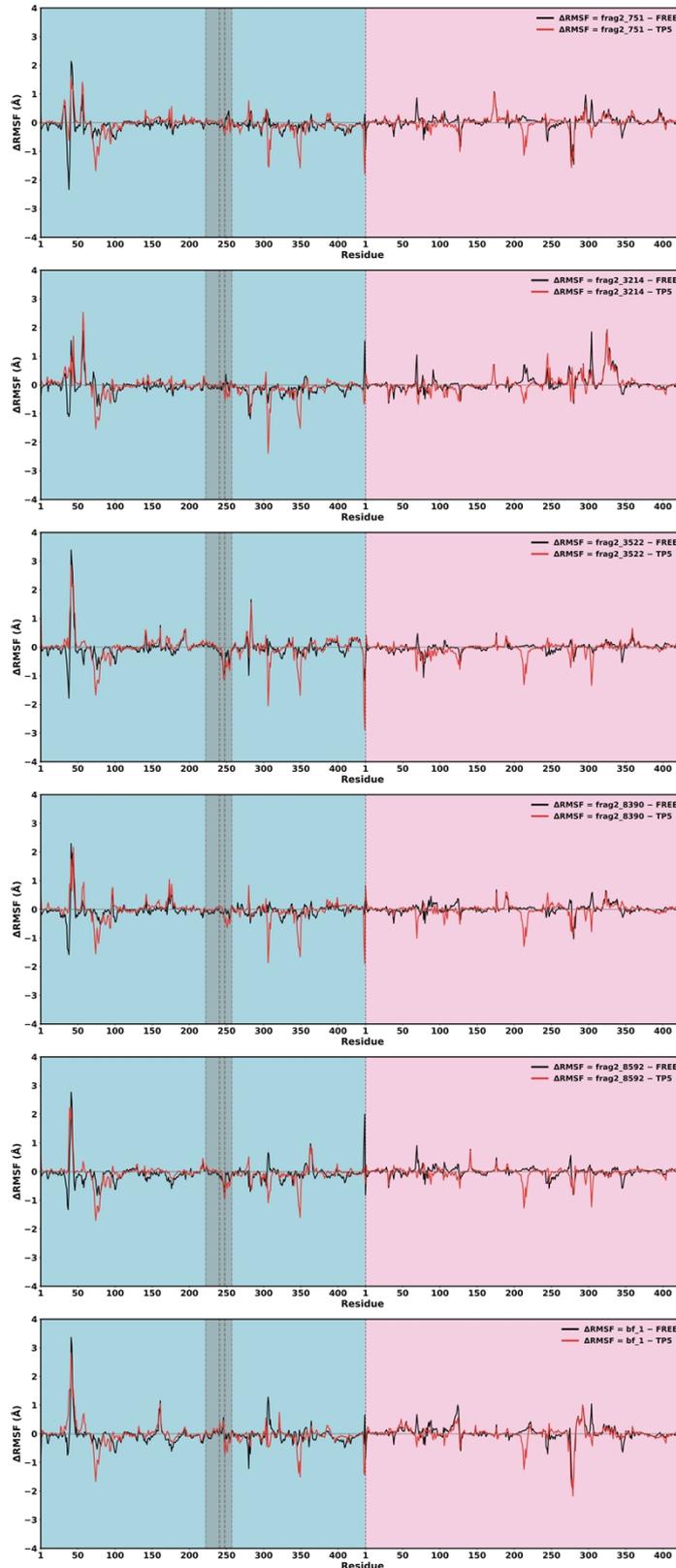


Figure S4. Residue-level interaction profiles of frag2_571, frag2_3214, frag2_3522, frag2_8390, frag2_8592, and bf_1 with $\alpha\beta$ -tubulin.



S5. Δ RMSF profiles of the $\alpha\beta$ -tubulin dimer upon frag2_571, frag2_3214, frag2_3522, frag2_8390, frag2_8592, and bf_1, calculated as $\text{RMSF}_{\text{ligand}} - \text{RMSF}_{\text{Free}}$ (black) and $\text{RMSF}_{\text{ligand}} - \text{RMSF}_{\text{TP5}}$ (red). The blue-shaded region corresponds to α -tubulin, while the pink-shaded region represents β -tubulin.

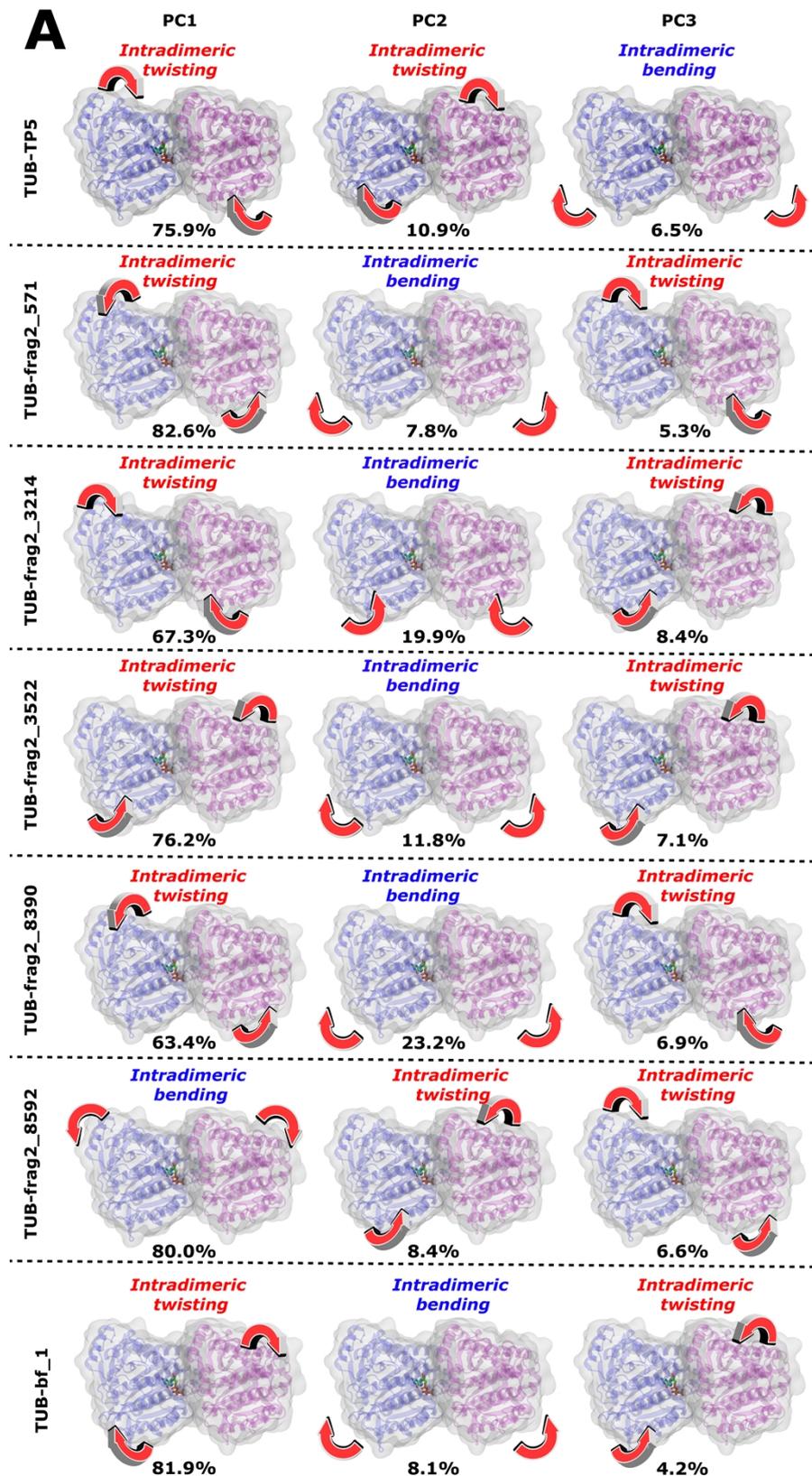


Figure S6. Principal component analysis (PCA) of the $\alpha\beta$ -tubulin dimer in complex with TP5 and selected candidate compounds.

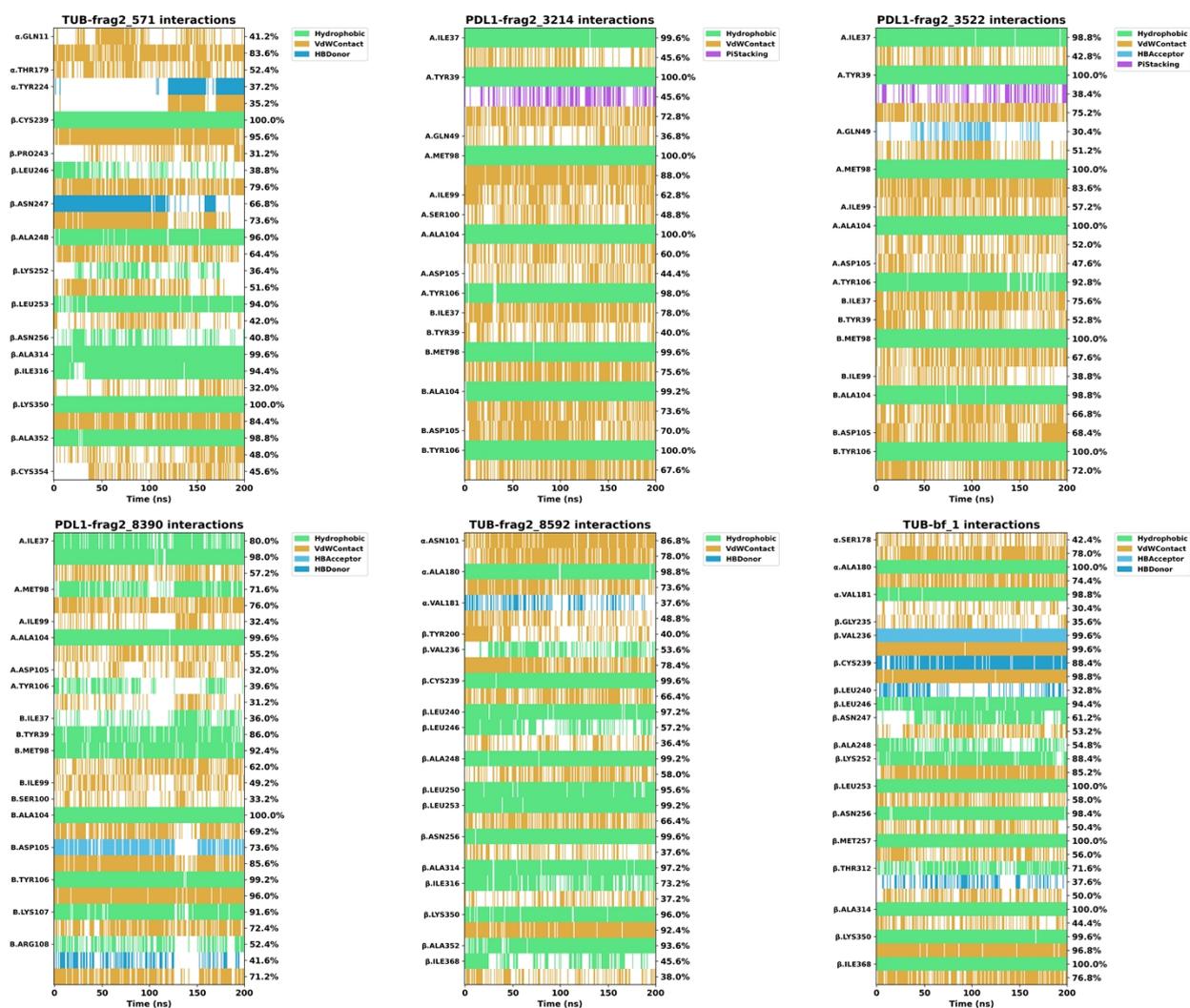


Figure S7. Residue-level interaction profiles of frag2_571, frag2_3214, frag2_3522, frag2_8390, frag2_8592, and bf_1 with dPD-L1.

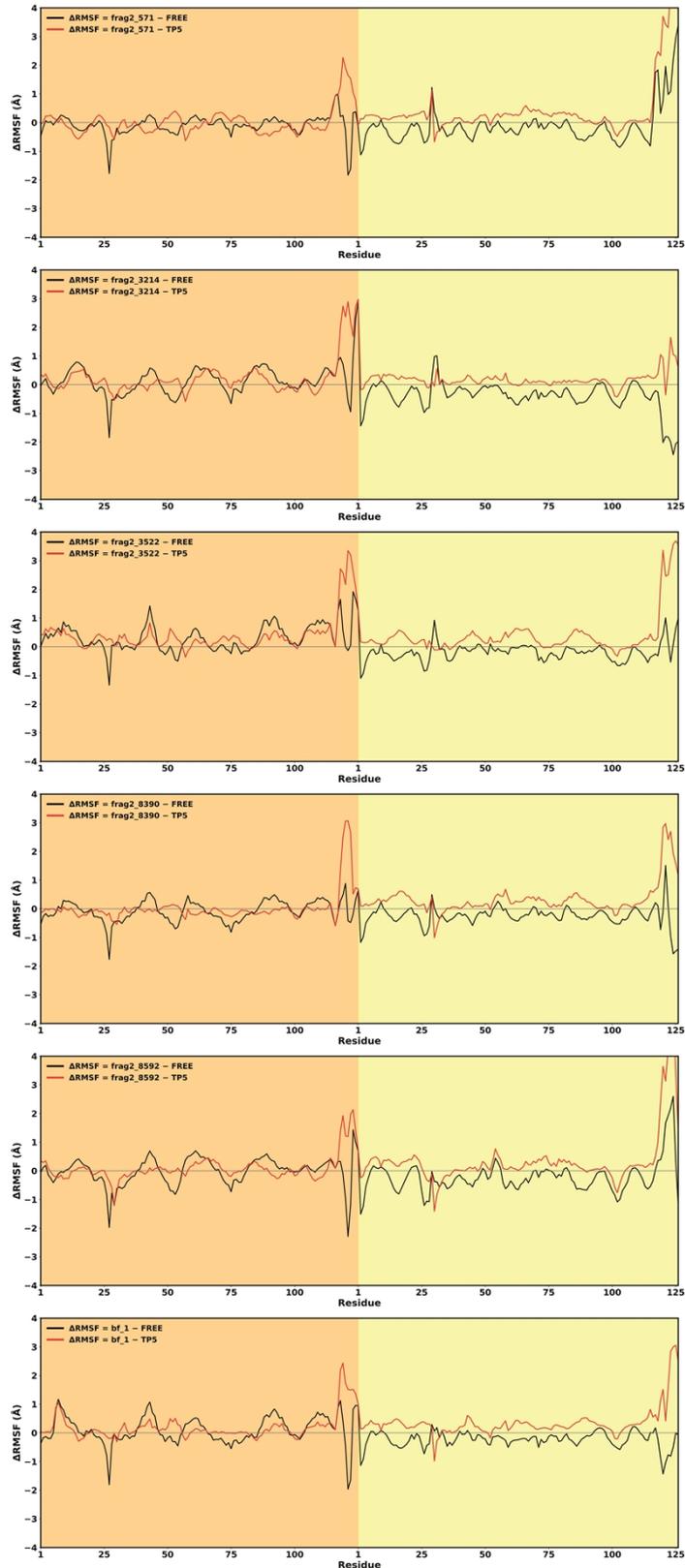


Figure S8. S5. ΔRMSF profiles of the PD-L1 dimer upon frag2_571, frag2_3214, frag2_3522, frag2_8390, frag2_8592, and bf_1, calculated as $\text{RMSF}_{\text{ligand}} - \text{RMSF}_{\text{Free}}$ (black) and $\text{RMSF}_{\text{ligand}} - \text{RMSF}_{\text{TP5}}$ (red). The orange-shaded region corresponds to monomer A, while the yellow-shaded region represents monomer B.

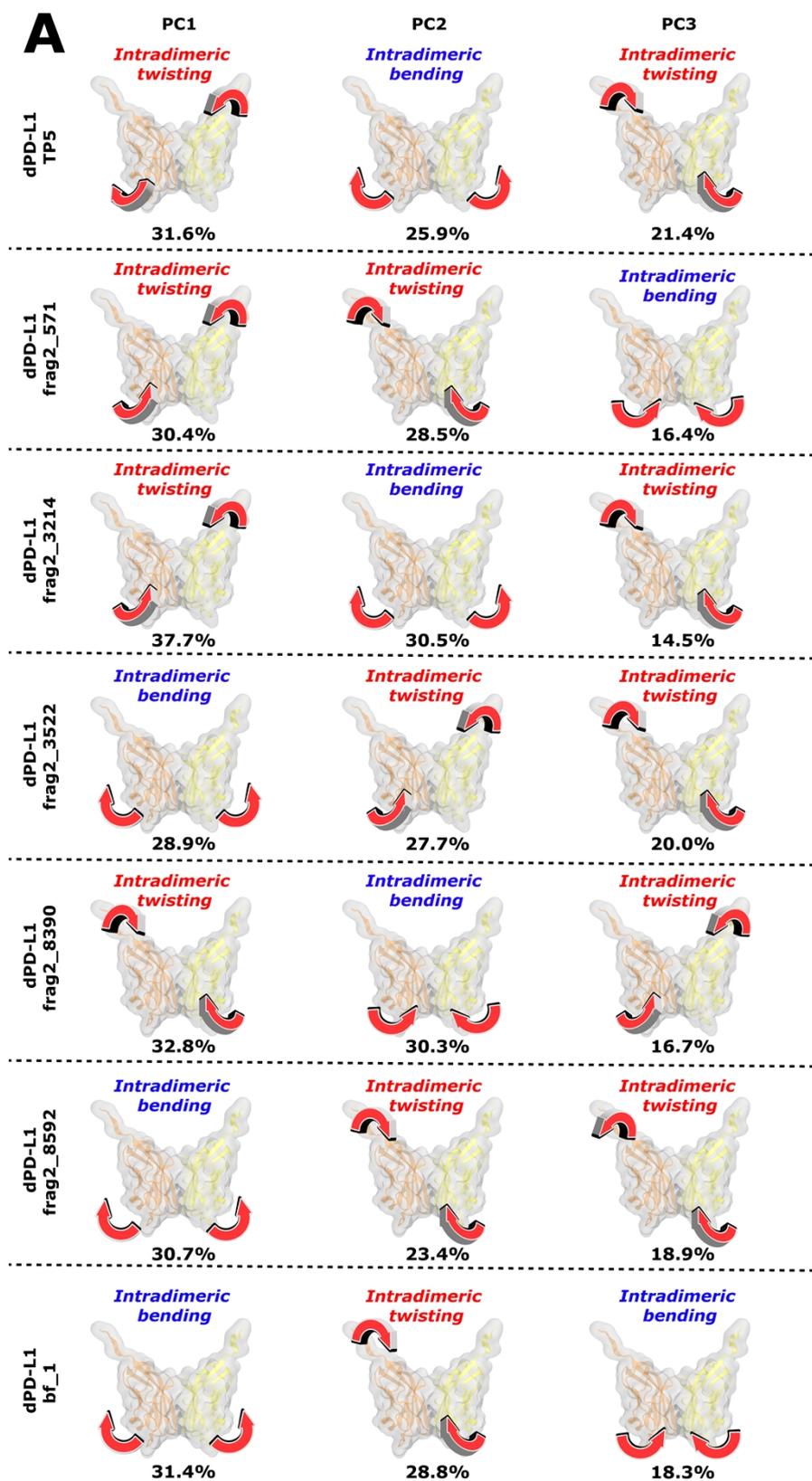


Figure S9. Principal component analysis (PCA) of the PD-L1 dimer in complex with TP5 and selected candidate compounds.