Supporting information

Effect of colchicine binding site inhibitors on the tubulin intersubunit interaction

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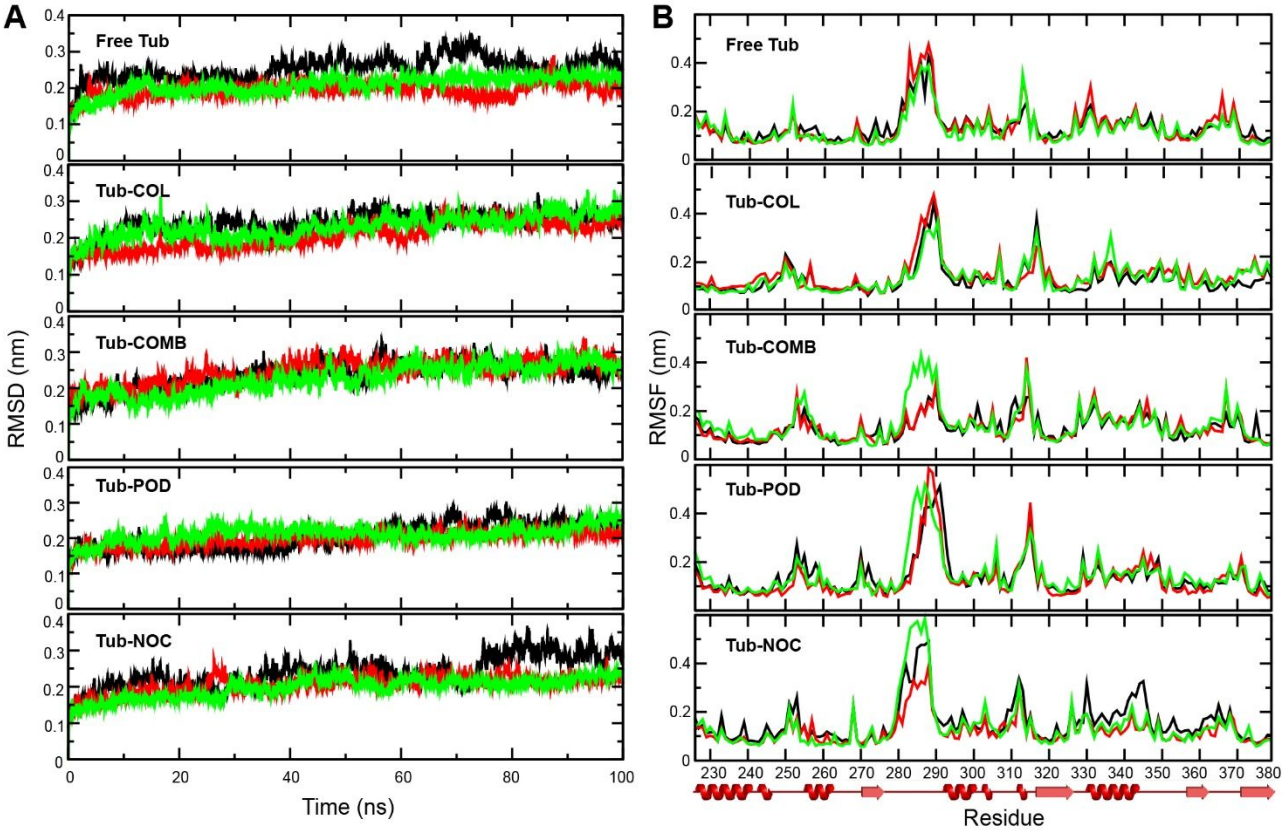

Figure S1. Protein-ligand complex stability in MD simulations. **A** Root-mean-square-deviation (RMSD) of tubulin dimer backbone atoms and ligand. **B** Root-mean-square-fluctuation (RMSF) of the C-terminal domain of beta-tubulin where the CBS is located.

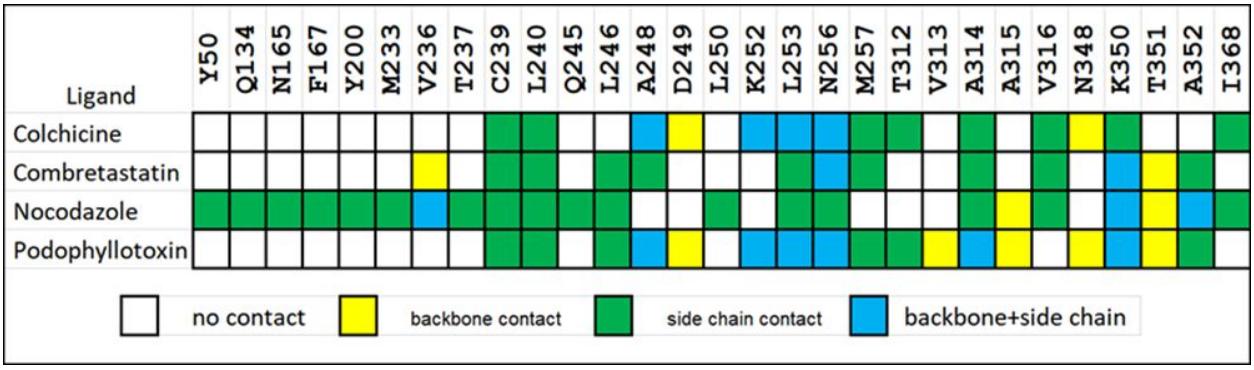

Figure S2. Interaction of different tubulin polymerization inhibitors with colchicine binding site. Data was collected from the Pocketome database.

Table S1. MMPBSA energy components for each complex. **EEL** electrostatic energy calculated from force filed, **EPB** electrostatic contribution to the solvation free energy calculated by PB model, **VDWAALS** van der Waals contribution, **ENPOLAR** polar contribution to the solvation free energy, **Δ G Gas/Solv** estimated binding free energy in vacuum and solvent, **ΔG Total** final binding free energy calculated from all terms.

	EEL	EPB	VDWAALS	ENPOLAR	ΔG Gas	ΔG Solv	ΔG Total
tub-gtp_1	1124.16	-1031.21	-124.32	-13.16	999.83	-1045.19	-45.36
tub-gtp_2	1084.23	-975.00	-141.28	-12.38	942.95	-991.26	-48.31
tub-gtp_3	1063.24	-966.50	-133.33	-12.51	929.92	-981.79	-51.87
AVR	1090.54	-990.90	-132.98	-12.68	957.57	-1006.08	-48.51
SD	25.26	28.71	6.93	0.34	30.36	27.92	2.66
SEM	14.59	16.58	4.00	0.20	17.53	16.12	1.54
tub-col_1	1203.30	-1105.26	-119.98	-13.13	1083.31	-1118.41	-35.10
tub-col_2	1296.53	-1198.32	-116.15	-13.47	1180.38	-1210.70	-30.32
tub-col_3	1302.48	-1215.23	-116.22	-13.58	1186.27	-1227.74	-41.47
AVR	1267.44	-1172.94	-117.45	-13.40	1149.99	-1185.62	-35.63
SD	45.42	48.35	1.79	0.19	47.21	48.03	4.57
SEM	26.22	27.91	1.03	0.11	27.25	27.73	2.64
tub-comb_1	1576.54	-1478.36	-119.30	-13.98	1457.24	-1491.49	-34.25
tub-comb_2	1667.92	-1548.44	-120.41	-16.27	1547.51	-1561.91	-14.40
tub-comb_3	1553.28	-1457.73	-117.37	-15.29	1435.91	-1471.31	-35.40
AVR	1599.25	-1494.84	-119.03	-15.18	1480.22	-1508.24	-28.02
SD	49.48	38.82	1.26	0.94	48.37	38.84	9.64
SEM	28.57	22.42	0.73	0.54	27.93	22.42	5.56
tub-pod_1	1498.07	-1388.13	-131.64	-14.70	1366.44	-1402.83	-36.39
tub-pod_2	1551.81	-1439.64	-139.12	-15.50	1412.69	-1455.14	-42.45
tub-pod_3	1589.80	-1462.83	-144.76	-15.69	1445.04	-1478.53	-33.49
AVR	1546.56	-1430.20	-138.51	-15.30	1408.06	-1445.50	-37.44
SD	37.63	31.22	5.37	0.43	32.26	31.65	3.73
SEM	21.73	18.02	3.10	0.25	18.62	18.27	2.16
tub-noc_1	1343.80	-1279.82	-117.12	-13.97	1226.68	-1293.79	-67.10
tub-noc_2	1266.45	-1186.54	-124.94	-14.62	1141.51	-1201.15	-59.65
tub-noc_3	1215.52	-1131.32	-128.32	-14.92	1087.20	-1146.23	-59.03
AVR	1275.26	-1199.22	-123.46	-14.50	1151.80	-1213.72	-61.93
SD	52.74	61.28	4.69	0.39	57.41	60.89	3.67
SEM	30.45	35.38	2.71	0.23	33.14	35.16	2.12

Movies S1-S5. Visualization of tubulin subunits disassociation during steered molecular dynamics: S1 Free TUB, S2 Tub-COL, S3 Tub-CA4, Tub-POD', Tub-NOC.