mTOR-mLST8 interaction: hot spots identification through quantum biochemistry calculations

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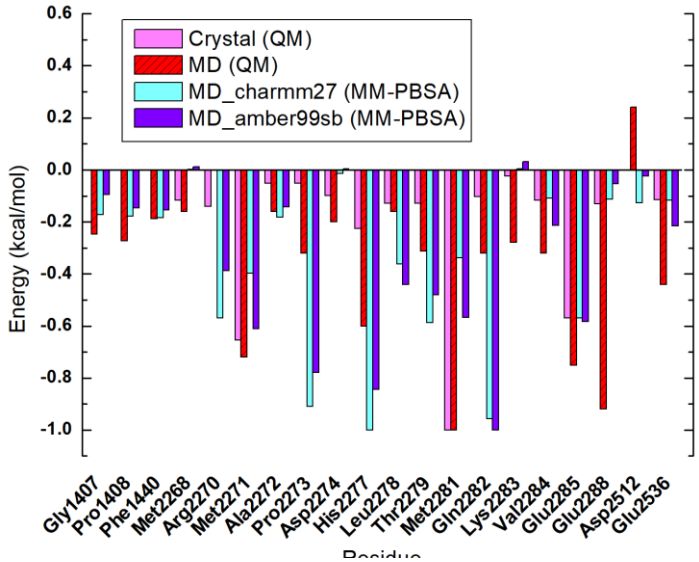
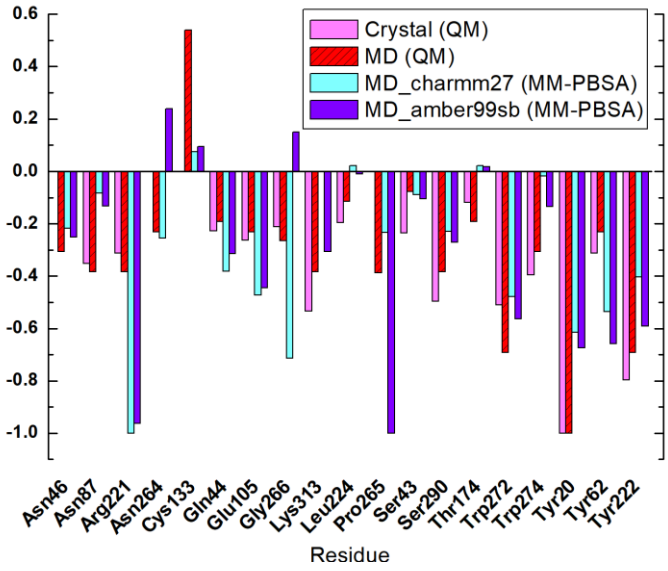
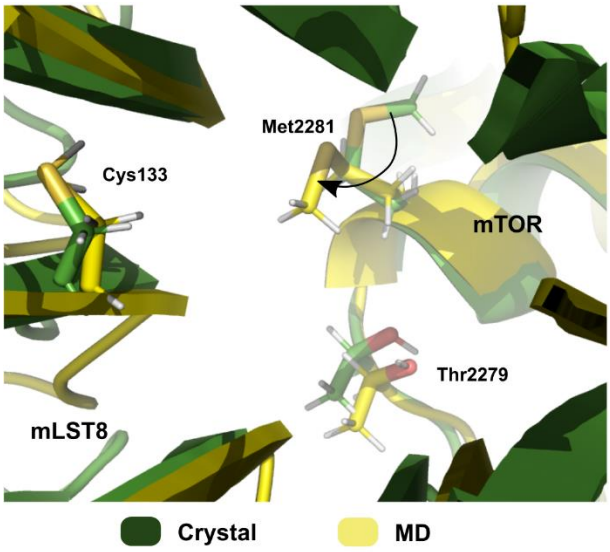
KEYWORDS: DFT, mTOR, mLST8, cancer, inhibitor, hot spots



Supplementary figure S1 – Interaction strength of mTOR residues using MFCC-QM or MM-PBSA approach. MM-PBSA was calculated from simulations with charmm27 or amber99sb force fields. Calculations were performed using SAV model and ε_{solute} = 40. To facilitate comparison between distinct methods, energy values were normalized.



Supplementary figure S2 – Interaction strength of mLST8 residues using MFCC-QM or MM-PBSA approach. MM-PBSA was calculated from simulations with charmm27 or amber99sb force fields. Calculations were performed using SAV model and ε_{solute} = 40. To facilitate comparison between distinct methods, energy values were normalized.



Supplementary figure S3 – Spatial relationship between residues Cys133 (mLST8) and Met2281(mTOR) in crystallographic (green) and MD (yellow) structures.

Table S1 – Calculated interaction energy (kcal.mol^{-1}) of individual mTOR amino acid residues along the interface of mTOR-mLST8 crystallographic structure.

mTOR	mLST8	E	d
Ala2272	Gly19	0.09	7.5
	Tyr20	-2.30	3.0
	Asp21	-0.16	6.5
	His22	-0.19	7.0
	Gln44	-0.10	5.0
	Trp274	-0.01	8.0
	Ser290	-0.02	8.0
	Lys313	0.11	4.5
	Ala314	-0.06	5.5
	Val316	-0.01	7.5
Ala2290	Ser268	-0.02	7.5
Ala2266	Lys313	0.75	7.5
Arg2270	Tyr20	-0.04	6.0
	Asp21	-0.72	7.5
	Asn292	-0.05	7.5
	Gln312	-0.18	6.5
	Lys313	-6.1	2.0
	Ala314	-0.02	6.5
Asn2292	Arg221	0.14	4.5
	Gly266	0.01	7.5
	Glu267	-0.17	6.5
	Ser268	-0.66	3.0
	Ser269	0.02	4.5
	Arg270	-0.02	7.5
	Gly271	0.01	7.5
	Trp272	-0.03	6.0
Asn2293	Gly266	0.01	8.0
	Glu267	0.06	6.0
	Ser268	-2.09	2.5
	Ser269	-0.1	5.5
	Arg270	-0.13	6.5
	Gly271	0.01	8.0
Asn2537	Tyr222	-0.10	7.0
Asp2274	Gly19	0.01	6.5
	Tyr20	0.12	4.5
	Asp21	0.95	7.0
	His22	-1.04	2.5
	His40	-0.05	6.5
	Gln41	-0.33	6.5
	Asp42	2.01	4.5
	Ser43	-5.11	3.0
	Gln44	-0.42	2.5
	Val45	0.07	7.0
	Asn46	0.05	8.0
	Tyr62	-0.09	6.0
	His64	0.05	7.5
	Asn87	-0.02	6.5
	Lys313	-1.23	6.5
Asp2276	Gln44	0.05	6.5
	Tyr62	-0.50	5.0
	Lys86	-1.01	7.5
	Asn87	0.10	6.0
	Glu105	1.13	7.5
Cys2539	Tyr222	-3.81	7.0
	Trp272	-0.02	7.5
Glu2285	Tyr20	-0.38	3.5
	Arg221	-1.72	5.0
	Tyr222	-0.01	6.0
	Leu224	-0.14	6.0
	Ser239	0.01	8.0
	Ala240	0.01	5.5
	Gln242	-0.23	7.0
	Ile260	0.01	8.0
	Ser268	0.04	7.5
	Ser269	0.04	5.0
	Arg270	-1.00	6.5
	Gly271	-4.42	3.5
	Trp272	-5.59	2.5
	Met273	-2.22	6.5
	Trp274	-4.42	2.5
	Ser289	-1.43	6.5
	Ser290	-8.41	2.5
	Asp291	1.38	6.5
	Asn292	0.06	8.0
	Ala314	-0.21	5.5
	Val315	0.07	7.0
	Val316	-0.06	5.0
Glu2288	Arg221	-4.94	2.5
	Tyr222	-0.40	4.0
	Ala240	-0.01	5.5
	Ser268	0.01	6.0
	Ser269	0.04	5.5
	Trp272	-1.28	2.5
Glu2369	Asn85	-0.07	8.0
	Lys86	-1.52	7.0
Glu2536	Gln148	-0.10	4.0
	Glu170	1.24	8.0
	Val171	-0.22	7.5
	Ser172	-0.20	5.5
	Thr174	-0.01	7.5
	Ser190	0.01	4.5
	Thr191	0.05	8.0
	Tyr222	-6.52	2.5
	Trp272	-0.02	7.0
His2277	Tyr20	-0.12	8.0
	His22	-0.03	7.0
	Asp42	-0.28	4.0
	Ser43	-0.30	4.5
	Gln44	-1.61	2.5
	Asn46	-0.15	5.0
	Gly61	-0.13	6.5
	Tyr62	-6.36	3.0
	Gln63	-0.18	6.0
	His64	-0.05	7.0
	Lys86	-0.61	6.0
	Asn87	-1.76	2.0
	Ile88	0.06	7.0
	Glu105	0.19	5.5
His2289	Tyr20	-0.05	7.5
	Arg221	-0.02	7.0
Leu2280	Gln44	-0.02	8.0
	Asn46	0.01	7.5
	Lys86	0	8.0
	Asn87	-0.12	5.0
	Ala89	-0.01	7.0
	Glu105	-0.2	5.0
	Ala129	0	8.0
	Pro130	-0.1	6.0
	Asn132	-0.11	6.0
	Gln148	-1.09	3.0
	Ser172	-0.09	5.0
	Thr174	0	7.0
	Ser190	-0.03	6.5
	Tyr222	-0.26	5.0
	Leu224	-0.04	8.0
	Trp272	-0.04	6.0
	Trp274	0.18	6.0
Leu2527	Glu170	0.03	7.5
Lys2283	Tyr20	-0.13	5.5
	Gln44	-0.03	7.0
	Asn46	-0.08	8.0
	Tyr62	-0.1	6.0
	Lys86	1.26	7.5
	Asn87	0.1	5.5
	Glu105	-1.79	6.0
	Tyr222	-0.07	8.0
	Trp272	-0.12	6.0
	Trp274	-0.16	5.5
	Val316	-0.02	8.0
Lys2370	Tyr62	-0.16	5.0
	Gln63	-0.15	8.0
	Lys86	1.22	7.0
Lys2374	Lys86	1.39	6.5
	Glu105	-1.39	8.0
	Pro130	0	7.0
	Gln148	-0.14	8.0
Met2268	Tyr20	-4	6.5
	Lys313	-1.93	7.0
Met2271	Gly19	-0.73	8.0
	Tyr20	-5.25	2.5
	Asp21	-2.49	6.5
	Gln44	-2.04	7.5
	Ser269	-1.24	7.0
	Arg270	-2.69	7.5
	Gly271	-0.62	5.0
	Trp272	-0.15	5.5
	Trp274	-0.08	5.5
	Ser289	-1.09	7.5
	Ser290	-1.85	3.0
	Asp291	-2.59	6.5
	Asn292	-1.94	6.5
	Gln312	-2.4	7.0
	Lys313	-4.36	3.5
	Ala314	-1.51	3.5
	Val315	-1.88	7.0
Phe2513	Glu170	0.00	7.5
Pro2273	Gly19	0.03	6.5
	Tyr20	-1.30	2.5
	Asp21	0.00	4.0
	His22	-1.08	3.5
	Thr23	-0.02	8.0
	Gln41	-0.02	7.5
	Asp42	-0.14	7.0
	Ser43	0.07	6.5
	Gln44	-0.16	5.0
	Val45	-0.02	8.0
	Gln312	0.05	7.5
	Lys313	0.03	3.0
	Ala314	-0.08	6.0
Pro2372	Lys86	-0.06	7.0
Ser2514	Glu170	-0.08	7.5
Ser2534	Tyr222	-0.03	6.5
Thr2279	Tyr20	-0.08	6.0
	Ser43	-0.01	8.0
	Gln44	-0.11	4.0
	Val45	-0.05	7.0
	Asn46	-0.78	3.0
	Ala47	-0.02	7.5
	Ala60	-0.01	7.5
	Gly61	-0.05	6.5
	Tyr62	-0.13	6.0
	Gln63	-0.01	8.0
	Lys86	0.10	6.5
	Asn87	-2.53	3.0
	Ile88	-0.08	5.5
	Ala89	-0.55	3.5
	Ser90	-0.03	7.0
	Gly103	-0.01	7.5
	Gly104	0.00	7.0
	Glu105	-1.35	3.5
	Asp106	-0.07	8.0
	Pro130	-0.03	7.0
	Ile131	-0.05	6.5
	Asn132	-0.16	5.5
	Gln148	-0.14	6.5
	Ser172	0.00	8.0
	Thr174	-0.04	7.5
	Leu224	-0.03	7.5
	Trp272	-0.02	7.0
	Trp274	-0.21	5.0
	Val136	-0.07	5.5
Thr2294	Ser268	-0.03	6.5
Tyr2275	Tyr20	-0.15	6.5
	His22	-0.05	7.5
	Ser43	-0.08	7.5
	Gln44	-0.08	5.5
	Tyr62	-0.05	8.0
	Asn87	-0.05	7.0
Val2284	Tyr20	-0.02	7.5
	Gln148	-0.02	8.0

Gln2282	Ala18	-0.02	7.5
	Gly19	-0.04	5.5
	Tyr20	-2.29	3.0
	Ser43	-0.07	6.5
	Gln44	0.44	3.0
	Val45	0.16	4.0
	Asn46	-0.06	2.5
	Ala47	-0.08	6.0
	Ala60	-0.04	6.5
	Gly61	-0.03	6.0
	Tyr62	-0.05	7.0
	Asn87	-0.15	4.5
	Ile88	-0.04	7.0
	Ala89	-0.06	6.5
	Glu105	-0.02	7.0
	Asn132	-0.03	8.0
	Thr174	-0.03	8.0
	Tyr222	-0.04	8.0
	Leu224	-0.10	6.0
	Ala240	-0.01	8.0
	Trp272	-0.02	4.5
	Trp274	-2.98	2.5
	Ser290	-0.07	6.5
	Ala314	-0.04	7.0
	Val315	0.20	7.0
	Val316	0.44	2.0
	Cys317	-0.14	5.0
Gln2540	Lys86	-0.26	7.0
	Glu105	0.22	6.5
	Pro130	-0.03	7.5
	Gln148	-0.01	7.0

	Glu267	-0.06	6.0
	Ser268	-0.30	4.5
	Ser269	-0.11	4.0
	Arg270	-0.11	5.5
	Gly271	-0.02	6.5
	Trp272	-0.13	6.5
	Ser290	-0.03	7.0
	Asp291	-0.02	8.0
His2535	Arg221	1.38	6.5
	Tyr222	-0.10	5.0
	Trp272	-0.03	6.0
Ile2267	Ser268	-0.02	8.0
	Lys313	-0.26	7.0
Leu2269	Tyr20	-0.03	7.0
	Lys313	0.30	4.0
Leu2278	Gly19	-0.04	7.0
	Tyr20	-2.82	3.0
	His22	-0.02	8.0
	Ser43	-0.11	6.5
	Gln44	-1.34	2.0
	Val45	-0.04	6.0
	Asn46	-0.18	5.0
	Gly61	-0.07	7.5
	Tyr62	0.01	5.0
	Lys86	-0.12	7.0
	Asn87	-1.96	3.0
	Ile88	-0.04	8.0
	Glu105	0.48	4.5
	Trp274	-0.10	6.5
	Lys313	0.01	8.0
	Ala314	-0.03	7.0
	Val316	-0.12	5.0

	Val316	-0.05	6.5
Met2281	Tyr20	-3.88	6.5
	Asn46	-2.00	7.5
	Asn87	-1.99	7.5
	Ala89	-1.25	7.0
	Glu105	-3.52	7.5
	Pro130	-1.76	8.0
	Asn132	-0.32	5.0
	Gln148	-2.34	5.5
	Ser172	-1.46	5.0
	Ile173	-2.41	7.0
	Thr174	-2.77	3.0
	Ser175	-1.08	7.5
	Val188	-1.75	8.0
	Asn189	-1.79	7.0
	Ser190	-1.71	4.5
	Thr191	-1.63	8.0
	Arg221	-2.24	7.0
	Tyr222	-5.23	2.5
	Ala223	-1.28	5.5
	Leu224	-4.31	3.0
	Ser239	-0.04	7.5
	Ala240	-1.36	4.5
	Trp272	-1.42	2.5
	Trp274	-1.47	2.5
	Ser290	-1.36	8.0
	Val316	0.02	7.0
Met2287	Tyr20	-0.04	8.0
	Tyr222	-0.03	8.0
	Trp272	-0.05	7.0
	Trp274	-0.02	8.0
Phe2371	Lys86	0.04	8.0

	Ser190	-0.03	7.5
	Arg211	-0.04	5.5
	Tyr222	-2.40	2.5
	Leu224	-0.04	7.0
	Ala240	-0.03	6.0
	Trp272	-3.26	2.5
	Trp274	-0.07	6.0
Val2286	Tyr20	-1.07	3.0
	Gln44	-0.02	7.0
	Trp272	0.02	6.0
	Trp274	-0.10	5.5
	Ser290	-0.10	6.5
	Lys313	-0.04	8.0
	Ala314	-0.04	6.0
	Val316	-0.02	7.5
Val2291	Ser268	-0.12	7.5

Table S2 – Calculated interaction energy (kcal.mol^{-1}) of individual mLST8 amino acid residues along the interface of mTOR-mLST8 crystallographic structure.

mLST8	mTOR	E	d
Tyr20	Ala2272	-2.30	3.0
	Arg2270	-0.04	6.0
	Asp2274	0.12	4.5
	Gln2282	-2.29	3.0
	Glu2285	-0.38	3.5
	His2277	-0.12	8.0
	His2289	-0.05	7.5
	Leu2269	-0.03	7.0
	Leu2278	-2.82	3.0
	Lys2283	-0.13	5.5
	Met2268	-4.00	6.5
	Met2271	-5.25	2.5
	Met2281	-3.88	6.5

mLST8	mTOR	E	d
Gln44	Ala2272	-0.10	5.0
	Asp2274	-0.42	2.5
	Asp2276	0.05	6.5
	Gln2282	0.44	3.0
	His2277	-1.61	2.5
	Leu2278	-1.34	2.0
	Leu2280	-0.02	8.0
	Lys2283	-0.03	7.0
	Met2271	-2.04	7.5
	Pro2273	-0.16	5.0
	Thr2279	-0.11	4.0
	Tyr2275	-0.08	5.5
	Val2286	-0.02	7.0

mLST8	mTOR	E	d
His40	Asp2274	-0.05	6.5
Gln41	Asp2274	-0.33	6.5
	Pro2273	-0.02	7.5
Asp42	Asp2274	2.01	4.5
	His2277	-0.28	4.0
	Pro2273	-0.14	7.0
Ser43	Asp2274	-5.11	3.0
	Gln2282	-0.07	6.5
	His2277	-0.30	4.5
	Leu2278	-0.11	6.5
	Pro2273	0.07	6.5
	Thr2279	-0.01	8.0
	Tyr2275	-0.08	7.5

mLST8	mTOR	E	d
Asn132	Gln2282	-0.03	8.0
	Leu2280	-0.11	6.0
	Met2281	-0.32	5.0
	Thr2279	-0.16	5.5
Thr174	Gln2282	-0.03	8.0
	Glu2536	-0.01	7.5
	Leu2280	0.00	7.0
	Met2281	-2.77	3.0
	Thr2279	-0.04	7.5
Leu224	Gln2282	-0.10	6.0
	Glu2285	-0.14	6.0
	Leu2280	-0.04	8.0
	Met2281	-4.31	3.0

	Met2287	-0.04	8.0
	Pro2273	-1.30	2.5
	Thr2279	-0.08	6.0
	Tyr2275	-0.15	6.5
	Val2284	-0.02	7.5
	Val2286	-1.07	3.0
Tyr222	Asn2537	-0.10	7.0
	Cys2539	-3.81	7.0
	Gln2282	-0.04	8.0
	Glu2285	-0.01	6.0
	Glu2288	-0.40	4.0
	Glu2536	-6.52	2.5
	His2535	-0.10	5.0
	Leu2280	-0.26	5.0
	Lys2283	-0.07	8.0
	Met2281	-5.23	2.5
	Met2287	-0.03	8.0
	Ser2534	-0.03	6.5
	Val2284	-2.40	2.5
Lys313	Ala2272	0.11	4.5
	Ala2266	0.75	7.5
	Arg2270	-6.10	2.0
	Asp2274	-1.23	6.5
	Ile2267	-0.26	7.0
	Leu2269	0.30	4.0
	Leu2278	0.01	8.0
	Met2268	-1.93	7.0
	Met2271	-4.36	3.5
	Pro2273	0.03	3.0
	Val2286	-0.04	8.0
Ser290	Ala2272	-0.02	8.0
	Gln2282	-0.07	6.5
	Glu2285	-8.41	2.5
	His2289	-0.03	7.0
	Met2271	-1.85	3.0
	Met2281	-1.36	8.0
	Val2286	-0.10	6.5
Trp272	Asn2292	-0.03	6.0
	Cys2539	-0.02	7.5
	Gln2282	-0.02	4.5
	Glu2285	-5.59	2.5
	Glu2288	-1.28	2.5
	Glu2536	-0.02	7.0
	His2289	-0.13	6.5
	His2535	-0.03	6.0
	Leu2280	-0.04	6.0
	Lys2283	-0.12	6.0
	Met2271	-0.15	5.5
	Met2281	-1.42	2.5
	Met2287	-0.05	7.0
	Thr2279	-0.02	7.0
	Val2284	-3.26	2.5
	Val2286	0.02	6.0
Gly19	Ala2272	0.09	7.5
	Asp2274	0.01	6.5
	Gln2282	-0.04	5.5
	Leu2278	-0.04	7.0
	Met2271	-0.73	8.0
	Pro2273	0.03	6.5
Asp21	Ala2272	-0.16	6.5
	Arg2270	-0.72	7.5
	Asp2274	0.95	7.0
Trp274	Ala2272	-0.01	8.0
	Gln2282	-2.98	2.5
	Glu2285	-4.42	2.5
	Leu2278	-0.10	6.5
	Leu2280	0.18	6.0
	Lys2283	-0.16	5.5
	Met2271	-0.08	5.5
	Met2281	-1.47	2.5
	Met2287	-0.02	8.0
	Thr2279	-0.21	5.0
	Val2284	-0.07	6.0
	Val2286	-0.10	5.5
Ala314	Ala2272	-0.06	5.5
	Arg2270	-0.02	6.5
	Gln2282	-0.04	7.0
	Glu2285	-0.21	5.5
	Leu2278	-0.03	7.0
	Met2271	-1.51	3.5
	Pro2273	-0.08	6.0
	Val2286	-0.04	6.0
Val316	Ala2272	-0.01	7.5
	Gln2282	0.44	2.0
	Glu2285	-0.06	5.0
	Leu2278	-0.12	5.0
	Lys2283	-0.02	8.0
	Met2271	-0.05	6.5
	Met2281	0.02	7.0
	Thr2279	-0.07	5.5
	Val2286	-0.02	7.5
Ser268	Ala2290	-0.02	7.5
	Asn2292	-0.66	3.0
	Asn2293	-2.09	2.5
	Glu2285	0.04	7.5
	Glu2288	0.01	6.0
	His2289	-0.30	4.5
	Ile2267	-0.02	8.0
	Thr2294	-0.03	6.5
	Val2291	-0.12	7.5
Asn292	Arg2270	-0.05	7.5
	Glu2285	0.06	8.0
	Met2271	-1.94	6.5
Gln312	Arg2270	-0.18	6.5
	Met2271	-2.40	7.0
	Pro2273	0.05	7.5
Arg221	Asn2292	0.14	4.5
	Glu2285	-1.72	5.0
	Glu2288	-4.94	2.5
	His2289	-0.02	7.0
	His2535	1.38	6.5
	Met2281	-2.24	7.0
	Val2284	-0.04	5.5
Gly266	Asn2292	0.01	7.5
	Asn2293	0.01	8.0
Glu267	Asn2292	-0.17	6.5
	Asn2293	0.06	6.0
	His2289	-0.06	6.0
Ser269	Asn2292	0.02	4.5
	Asn2293	-0.10	5.5
	Glu2285	0.04	5.0
	Glu2288	0.04	5.5
	His2289	-0.11	4.0
	Met2271	-1.24	7.0
Val45	Asp2274	0.07	7.0
	Gln2282	0.16	4.0
	Leu2278	-0.04	6.0
	Pro2273	-0.02	8.0
	Thr2279	-0.05	7.0
Asn46	Asp2274	0.05	8.0
	Gln2282	-0.06	2.5
	His2277	-0.15	5.0
	Leu2278	-0.18	5.0
	Leu2280	0.01	7.5
	Lys2283	-0.08	8.0
	Met2281	-2.00	7.5
	Thr2279	-0.78	3.0
Tyr62	Asp2274	-0.09	6.0
	Asp2276	-0.50	5.0
	Gln2282	-0.05	7.0
	His2277	-6.36	3.0
	Leu2278	0.01	5.0
	Lys2283	-0.10	6.0
	Lys2370	-0.16	5.0
	Thr2279	-0.13	6.0
	Tyr2275	-0.05	8.0
His64	Asp2274	0.05	7.5
	His2277	-0.05	7.0
Asn87	Asp2274	-0.02	6.5
	Asp2276	0.10	6.0
	Gln2282	-0.15	4.5
	His2277	-1.76	2.0
	Leu2278	-1.96	3.0
	Leu2280	-0.12	5.0
	Lys2283	0.10	5.5
	Met2281	-1.99	7.5
	Thr2279	-2.53	3.0
	Tyr2275	-0.05	7.0
Lys86	Asp2276	-1.01	7.5
	Gln2540	-0.26	7.0
	Glu2369	-1.52	7.0
	His2277	-0.61	6.0
	Leu2278	-0.12	7.0
	Leu2280	0.00	8.0
	Lys2283	1.26	7.5
	Lys2370	1.22	7.0
	Lys2374	1.39	6.5
	Phe2371	0.04	8.0
	Pro2372	-0.06	7.0
	Thr2279	0.10	6.5
Glu105	Asp2276	1.13	7.5
	Gln2282	-0.02	7.0
	Gln2540	0.22	6.5
	His2277	0.19	5.5
	Leu2278	0.48	4.5
	Leu2280	-0.20	5.0
	Lys2283	-1.79	6.0
	Lys2374	-1.39	8.0
	Met2281	-3.52	7.5
	Thr2279	-1.35	3.5
Ala18	Gln2282	-0.02	7.5
Ala47	Gln2282	-0.08	6.0
	Thr2279	-0.02	7.5
Ala60	Gln2282	-0.04	6.5
	Thr2279	-0.01	7.5
Gly61	Gln2282	-0.03	6.0
	Thr2279	-0.03	7.5
	Val2284	-0.04	7.0
Ala240	Gln2282	-0.01	8.0
	Glu2285	0.01	5.5
	Glu2288	-0.01	5.5
	Met2281	-1.36	4.5
	Val2284	-0.03	6.0
Val315	Gln2282	0.20	7.0
	Glu2285	0.07	7.0
	Met2271	-1.88	7.0
Cys317	Gln2282	-0.14	5.0
Pro130	Gln2540	-0.03	7.5
	Leu2280	-0.10	6.0
	Lys2374	0.00	7.0
	Met2281	-1.76	8.0
	Thr2279	-0.03	7.0
Gln148	Gln2540	-0.01	7.0
	Glu2536	-0.10	4.0
	Leu2280	-1.09	3.0
	Lys2374	-0.14	8.0
	Met2281	-2.34	5.5
	Thr2279	-0.14	6.5
	Val2284	-0.02	8.0
Ser239	Glu2285	0.01	8.0
	Met2281	-0.04	7.5
Gln242	Glu2285	-0.23	7.0
Ile260	Glu2285	0.01	8.0
Met273	Glu2285	-2.22	6.5
Ser289	Glu2285	-1.43	6.5
	Met2271	-1.09	7.5
Asp291	Glu2285	1.38	6.5
	His2289	-0.02	8.0
	Met2271	-2.59	6.5
Asn85	Glu2369	-0.07	8.0
Glu170	Glu2536	1.24	8.0
	Leu2527	0.03	7.5
	Phe2513	0.00	7.5
	Ser2514	-0.08	7.5
Val171	Glu2536	-0.22	7.5
Ser172	Glu2536	-0.20	5.5
	Leu2280	-0.09	5.0
	Met2281	-1.46	5.0
	Thr2279	0.00	8.0
Ser190	Glu2536	0.01	4.5
	Leu2280	-0.03	6.5
	Met2281	-1.71	4.5
	Val2284	-0.03	7.5
Thr191	Glu2536	0.05	8.0
	Met2281	-1.63	8.0
Ala129	Leu2280	0.00	8.0
Gln63	His2277	-0.18	6.0
	Lys2370	-0.15	8.0
	Thr2279	-0.01	8.0
Ile173	Met2281	-2.41	7.0
Ser175	Met2281	-1.08	7.5
Val188	Met2281	-1.75	8.0
Asn189	Met2281	-1.79	7.0
Ala223	Met2281	-1.28	5.5
Thr23	Pro2273	-0.02	8.0
Ser90	Thr2279	-0.03	7.0
Gly103	Thr2279	-0.01	7.5
Gly104	Thr2279	0.00	7.0

	Met2271	-2.49	6.5
	Pro2273	0.00	4.0
His22	Ala2272	-0.19	7.0
	Asp2274	-1.04	2.5
	His2277	-0.03	7.0
	Leu2278	-0.02	8.0
	Pro2273	-1.08	3.5
	Tyr2275	-0.05	7.5

Arg270	Asn2292	-0.02	7.5
	Asn2293	-0.13	6.5
	Glu2285	-1.00	6.5
	His2289	-0.11	5.5
	Met2271	-2.69	7.5
Gly271	Asn2292	0.01	7.5
	Asn2293	0.01	8.0
	Glu2285	-4.42	3.5
	His2289	-0.02	6.5
	Met2271	-0.62	5.0

	His2277	-0.13	6.5
	Leu2278	-0.07	7.5
	Thr2279	-0.05	6.5
Ile88	Gln2282	-0.04	7.0
	His2277	0.06	7.0
	Leu2278	-0.04	8.0
	Thr2279	-0.08	5.5
Ala89	Gln2282	-0.06	6.5
	Leu2280	-0.01	7.0
	Met2281	-1.25	7.0
	Thr2279	-0.55	3.5

Asp106	Thr2279	-0.07	8.0
Ile131	Thr2279	-0.05	6.5
Gly192	Met2281	0.00	8.5
Asp192	Met2281	13.0	8.5

Table S3 – Calculated interaction energy (kcal.mol^{-1}) of mTOR amino acid residues along the interface of mTOR-mLST8 MD structure.

mTOR	mLST8	E	d
Glu1403	Asn264	-1.00	6.5
	Gly266	1.00	8.0
	Glu267	1.00	7.5
Phe1404	Asn264	0.00	7.5
	Gly266	0.00	6.0
	Glu267	1.00	7.0
Gln1405	Gly266	0.00	7.5
	Glu267	0.00	6.5
	Ser268	1.00	8.0
	Arg270	1.00	7.0
Lys1406	Gly263	0	7.0
	Asn264	0	4.5
	Pro265	0	8.0
	Gly266	0	6.0
	Glu267	-1	3.0
	Ser268	0	6.5
	Arg270	1	5.0
Gly1407	Lys261	0	7.0
	Gly263	-1	7.0
	Asn264	-2	3.0
	Pro265	-0.2	6.0
	Gly266	-1	3.5
	Glu267	-1	2.5
	Ser268	0	5.5
	Arg270	-1	5.5
Pro1408	Lys261	0	7.0
	Gly263	1	7.5
	Asn264	-1	3.0

mTOR	mLST8	E	d
Ala2272	Gly19	0.00	7.0
	Tyr20	-3.00	3.0
	Asp21	-1.00	6.5
	His22	1.00	7.0
	Gln44	0.00	5.0
	Val45	0.00	8.0
	Asn46	0.00	7.5
	Ser290	0.00	8.0
	Lys313	-1.00	3.5
	Ala314	0.00	5.5
	Val316	0.00	6.5
Pro2273	Gly19	0.00	5.5
	Tyr20	-2.00	2.5
	Asp21	0.00	5.0
	His22	-1.00	3.0
	Thr23	0.00	7.5
	His40	-1.00	6.5
	Gln41	0.00	7.0
	Asp42	0.00	5.0
	Ser43	-2.00	5.0
	Gln44	-2.00	3.0
	Val45	0.00	6.0
	Asn46	-1.00	7.5
	Tyr62	0.00	7.0
	His64	0.00	8.0
	Lys313	-1.00	4.0
	Ala314	1.00	7.0
	Val316	1.00	7.5

mTOR	mLST8	E	d
Met2281	Tyr20	-3.00	6.5
	Asn46	-1.00	7.0
	Ala89	-1.00	5.5
	Ser90	0.00	6.5
	Glu105	-2.00	8.0
	Pro130	-2.00	8.0
	Ile131	-2.00	6.5
	Asn132	-1.00	3.0
	Cys133	14.00	5.5
	Gly146	-1.00	7.5
	Asp147	-2.00	7.5
	Gln148	-2.00	4.5
	Ser172	-1.00	4.0
	Ile173	-2.00	5.5
	Thr174	-4.00	3.0
	Ser175	-1.00	5.0
	Ala176	-1.00	8.0
	Val188	-1.00	7.0
	Asn189	-1.00	7.5
	Ser190	-1.00	5.5
	Arg221	-1.00	8.0
	Tyr222	-3.00	3.5
	Ala223	0.00	6.0
	Leu224	-5.00	3.5
	Gln225	0	6.5
	Ala240	-1	7.0
	Trp272	0	3.0
	Trp274	-1	2.5

mTOR	mLST8	E	d
Glu2288	Arg221	-15	2
	Tyr222	0	5.5
	Leu224	0	8
	Ala240	0	4
	Asp241	2	6
	Gln242	0	7.5
	Ser268	0	7.5
	Ser269	0	3.5
	Arg270	-1	6.5
	Gly271	-1	5
	Trp272	-8	2
	Trp274	0	7.5
	Ser290	0	6.5
His2289	Tyr20	0	6.5
	Arg221	1	7.5
	Gln242	0	6.5
	Ser269	1	5.5
	Arg270	1	5.5
	Gly271	-1	3.5
	Trp272	0	4.5
	Trp274	1	6
	Ser289	1	6.5
	Ser290	0	2.5
	Asp291	-3	4.5
	Asn292	0	5.5
	Leu293	0	8
	Lys313	2	7.5
	Ala314	0	4.5

	Pro265	-2.6	3.5	Asp2274	Tyr20	-1.00	5.5		Val316	1	7.5		Val315	1	7.5
	Gly266	-3.9	2.5		His22	-2.00	5.5	Gln2282	Ala18	0.00	7.5		Val316	0	8
	Glu267	-0.3	4.5		Asp42	1.00	5.5		Gly19	1.00	5.5	Ala2290	Ser290	1	8
	Ser268	0	7.0		Ser43	-1.00	5.5		Tyr20	-3.00	2.0	Val2291	Arg221	-1	7.5
Thr1409	Gly263	0.00	6.5		Gln44	0.00	3.5		Gln44	0.00	4.0		Ser269	0	6
	Asn264	-2	3.0		Asn46	1.00	7.5		Val45	-1.00	4.5	Asn2292	Arg221	0	6.5
	Pro265	0	3.0		Tyr62	-1.00	6.0		Asn46	-4.00	2.0		Ser268	0	5
	Gly266	-1	4.5		Asn87	-1.00	7.0		Ala47	-1.00	6.5		Ser269	-1	3
	Glu267	0	7.0		Lys313	-1.00	7.5		Ala60	0.00	7.5		Arg270	0	5
Pro1410	Gly263	0	7.5	Tyr2275	Tyr20	0.00	7.5		Gly61	1.00	7.0		Gly271	0	6
	Asn264	1	5.0		Gln44	1.00	6.5		Tyr62	0.00	7.0		Trp272	0	6.5
	Pro265	-2	2.5		Asn87	0.00	7.5		Asn87	1.00	6.5	Asn2293	Ser269	0	6.5
	Gly266	-1	5.0	Asp2276	Gln44	0.00	6.5		Ile88	0.00	7.0		Arg270	0	6
	Glu267	0	7.5		Tyr62	0.00	6.5		Ala89	0.00	6.0		Gly271	1	6.5
Ala1411	Asn264	0	7.5		Lys86	-2.00	7.5		Asn132	0.00	7.5		Ser290	1	7
	Pro265	-0.3	6.5		Asn87	0.00	6.0		Gln148	0.00	7.5		Asp291	1	7.5
Ile1412	Asn264	0	5.5		Glu105	1.00	6.5		Thr174	0.00	8.0		Asn292	1	8
	Pro265	0.1	7.0	His2277	Tyr20	0.00	7.0		Tyr222	1.00	8.0	Arg2503	Glu170	-1	7
	Gly266	0	7.5		Asp42	-2.00	6.5		Leu224	1.00	6.0	Arg2511	Pro169	-1	8
	Glu267	-0.6	8.0		Ser43	0.00	6.5		Trp272	0.00	5.0		Glu170	-1	7
Leu1413	Asn264	-1.00	7.5		Gln44	-1.00	2.5		Trp274	-3.00	3.0	Asp2512	Pro169	1	7
	Pro265	-0.40	5.0		Asn46	0.00	5.0		Ser290	0.00	7.5		Glu170	5	3.5
	Gly266	1.00	5.5		Gly61	0.00	7.5		Ala314	0.00	6.5	Phe2513	Pro169	0	5
Tyr1435	Lys261	-1.00	7.5		Tyr62	-5.00	3.0		Val315	1.00	7.5		Glu170	3	3.5
	Asn264	0.00	8.0		Gln63	-1.00	5.5		Val316	-1.00	2.5	Ser2514	Pro169	1	5
	Pro265	0	6.0		Lys86	1.00	6.0		Cys317	-1.00	6.0		Glu170	-1	6
	Gly266	-1	3.5		Asn87	-3.00	2.0	Lys2283	Tyr20	-1.00	5.5	His2515	Pro169	-1	5
	Glu267	0.00	5.5		Ile88	-1.00	8.0		Gln44	0.00	8.0		Glu170	-1	7
	Ser268	0.00	5.0		Glu105	-3.00	5.0		Asn46	-1.00	7.0	Asp2516	Glu168	2	8
Ala1436	Pro265	0.00	7.5	Leu2278	Gly19	1	8.0		Asn87	0.00	7.5		Pro169	0	5
	Gly266	0.00	7.5		Tyr20	-2	3.0		Glu105	-2.00	7.5	Asp2517	Pro169	0	8
Met1437	Thr220	-1.00	8.0		Ser43	1	8.0		Gln148	0.00	8.0	Glu2526	Thr220	0	8
Lys1438	Thr220	1.00	5.0		Gln44	-1	3.0		Tyr222	0.00	8.0	Leu2527	Glu170	-1	7.5
	Arg221	2.00	7.5		Val45	0	8.0		Trp272	-1.00	6.5		Thr191	1	7
	Ser268	1.00	8.0		Asn46	0	4.0		Trp274	-1.00	6.0	Lys2530	Val171	1	8
His1439	His219	1.00	7.5		Tyr62	0	5.5		Val316	-1.00	7.5		Ser190	0	7.5
	Thr220	-1.00	5.0		Lys86	0	7.5	Val2284	Tyr20	0.00	7.5		Thr191	0	4.5
	Arg221	1.00	7.0		Asn87	-3	4.0		Gln148	0.00	8.0		Gly192	0	7.5
	Asp241	-1.00	6.0		Glu105	1	4.5		Ser172	-1.00	8.0		Asn193	0	6.5
	Lys261	1.00	6.0		Pro130	0	8.0		Ser190	0.00	6.5		His219	1	7.5
	Pro265	0.00	5.5		Gln148	0	7.0		Arg221	-1.00	3.5		Thr220	0	4
	Gly266	0.00	5.0		Trp274	-1	7.5		Tyr222	-2.00	3.0		Arg221	2	5
	Glu267	0.00	7.5		Ala314	0	8.0		Leu224	0.00	6.0		Tyr222	-1	7.5
	Ser268	1.00	5.0		Val316	0	6.0		Ala240	0.00	6.0	Gln2531	Glu170	-1	5.5

	Ser269	0.00	7.5	Thr2279	Tyr20	0	6.0		Trp272	-4.00	2.5	Thr2533	Arg221	1	6
Phe1440	Lys261	-1.00	4.0		Gln44	0	4.5		Trp274	0.00	5.5		Tyr222	0	8
	Asn264	0.00	6.0		Val45	0	8.0	Glu2285	Tyr20	0.00	4.0	Ser2534	Ser190	0	7.5
	Pro265	-2.70	3.0		Asn46	-1	3.0		Arg221	-1.00	6.0		Thr191	0	8
	Gly266	-1.00	3.0		Ala47	0	7.0		Tyr222	0.00	7.0		Arg221	0	4.5
	Glu267	0.00	5.5		Gly61	0	6.0		Leu224	0.00	5.5		Tyr222	0	4.5
	Ser268	0.00	6.5		Tyr62	0	5.5		Ser239	0.00	7.5	His2535	Arg221	4	3
Glu1442	Pro217	1.00	8.0		Lys86	0	6.5		Ala240	0.00	5.5		Tyr222	1	5
	Ala218	0.00	6.5		Asn87	-3	3.0		Asp241	1.00	8.0		Ala240	0	7
	His219	-1.00	7.0		Ile88	1	5.0		Gln242	0.00	7.0		Ser269	0	5.5
	Thr220	0	8.0		Ala89	-1	3.5		Ser269	0.00	7.5		Trp272	-1	5
	Thr243	-1	7.5		Ser90	-1	6.5		Arg270	0.00	6.5	Glu2536	Asn132	-1	8
	Lys245	-2	4.5		Gly103	0.2	7.5		Gly271	-1.00	3.5		Gln148	0	6.5
	Trp247	1	7.5		Gly104	1	6.5		Trp272	-5.00	2.5		Glu170	2	8
	Leu254	0	5.0		Glu105	-1	3.5		Met273	-2.00	6.0		Val171	0	7.5
	Glu257	1	5		Asp106	0	8.0		Trp274	-2.00	3.0		Ser172	0	5.5
Leu1443	Glu257	0.00	7.5		Pro130	0	6.0		Ser289	0.20	7.0		Thr174	0	7.5
	Ser259	0.00	8.0		Ile131	-1	6.0		Ser290	-9.00	2.0		Ser190	0	4.5
	Lys261	0.00	5.5		Asn132	-1	5.0		Asp291	1.00	6.5		Thr191	0	8
	Asn264	0.00	7.5		Gln148	-1	5.0		Asn292	0.00	8.0		Arg221	-1	4.5
	Pro265	-1.00	3.5		Ser172	0	8.0		Ala314	0.00	4.5		Tyr222	-11	2
	Gly266	0.00	7.0		Trp272	0	8.0		Val315	0.00	7.5		Trp272	0	6
Glu1444	Pro265	-1.00	8.0		Trp274	0	6.5		Val316	-1.00	5.5	Asn2537	Arg221	0	7
Trp1449	Pro265	0.00	8.0		Val316	0	6.5	Val2286	Tyr20	-2.00	3.0		Tyr222	0	6
Ile2267	Lys313	0.00	6.5	Leu2280	Asn46	-1	7.0		Gln44	0.00	7.5	Leu2538	Arg221	0	7.5
Met2268	Tyr20	-3.00	8.0		Asn87	-1	6.5		Gly271	0.00	7.5	Cys2539	Tyr222	-3	7
	Lys313	-1.00	7.0		Ala89	0	7.0		Trp272	0.00	6.5		Trp272	0	7.5
Leu2269	Tyr20	-1.00	7.5		Glu105	0	5.0		Trp274	0.00	5.5	Gln2540	Gln148	0	6.5
	Lys313	0.00	5.5		Ala129	0	8.0		Ser290	-1	6		Tyr222	0	7
Arg2270	Tyr20	0.00	6.0		Pro130	0	6.0		Lys313	-1	7.5				
	Asp21	0.00	7.5		Ile131	0	7.5		Ala314	0	5.5				
	Gln312	1.00	7.0		Asn132	0	5.0		Val316	0	6				
	Lys313	-3.00	2.0		Gln148	-1	3.0	Phe2287	Tyr20	-1	7.5				
	Ala314	0.00	7.0		Ser149	1	8.0		Arg221	-1	7				
Met2271	Gly19	0.00	8.0		Val171	1	8.0		Trp272	0	7				
	Tyr20	-4.00	3.5		Ser172	0	4.0		Trp274	-1	8				
	Asp21	-2.00	7.0		Ile173	-1	8.0								
	Gln44	-2.00	8.0		Thr174	-1	7.0								
	Ser290	-2.00	6.5		Ser190	1	6.5								
	Asn292	-1.00	7.5		Tyr222	0	5.0								
	Gln312	-2.00	7.0		Leu224	1	8.0								
	Lys313	-4.00	3.0		Trp272	1.00	6.0								
	Ala314	-1.00	4.5		Trp274	0.00	6.0								
	Val316	0.00	8.0												

Table S4 – Calculated interaction energy (kcal.mol^{-1}) of individual mLST8 amino acid residues along the interface of mTOR-mLST8 MD structure.

mLST8	mTOR	E	d
Ala129	Leu2280	0.00	8.0
Ala176	Met2281	-1.00	8.0
Ala18	Gln2282	0.00	7.5
Ala218	Glu1442	0.00	6.5
Ala223	Met2281	0.00	6.0
Ala240	Met2281	-1.00	7.0
	Val2284	0.00	6.0
	Glu2285	0.00	5.5
	Glu2288	0.00	4.0
	His2535	0.00	7.0
Ala314	Arg2270	0	7.0
	Met2271	-1	4.5
	Ala2272	0	5.5
	Pro2273	1	7.0
	Leu2278	0	8.0
	Gln2282	0	6.5
	Glu2285	0	4.5
	Val2286	0	5.5
	His2289	0	4.5
Ala47	Thr2279	0	7.0
	Gln2282	-1	6.5
Ala60	Gln2282	0	7.5
Ala89	Thr2279	-1	3.5
	Leu2280	0	7.0
	Met2281	-1	5.5
	Gln2282	0	6.0
Arg221	Lys1438	2	7.5
	His1439	1	7.0
	Met2281	-1	8.0
	Val2284	-1	3.5
	Glu2285	-1	6.0
	Phe2287	-1	7.0
	Glu2288	-15.00	2.0
	His2289	1	7.5
	Val2291	-1	7.5
	Asn2292	0	6.5
	Lys2530	2	5.0
	Thr2533	1	6.0
	Ser2534	0	4.5
	His2535	4	3.0

mLST8	mTOR	E	d
Gln148	Leu2278	0.00	7.0
	Thr2279	-1.00	5.0
	Leu2280	-1.00	3.0
	Met2281	-2.00	4.5
	Gln2282	0.00	7.5
	Lys2283	0.00	8.0
	Val2284	0.00	8.0
	Glu2536	0.00	6.5
	Gln2540	0.00	6.5
Gln225	Met2281	0.00	6.5
Gln242	Glu2285	0.00	7.0
	Glu2288	0.00	7.5
	His2289	0.00	6.5
Gln312	Arg2270	1.00	7.0
	Met2271	-2.00	7.0
Gln41	Pro2273	0.00	7.0
Gln44	Met2271	-2.00	8.0
	Ala2272	0.00	5.0
	Pro2273	-2.00	3.0
	Asp2274	0.00	3.5
	Tyr2275	1.00	6.5
	Asp2276	0.00	6.5
	His2277	-1.00	2.5
	Leu2278	-1.00	3.0
	Thr2279	0.00	4.5
	Gln2282	0.00	4.0
	Lys2283	0.00	8.0
	Val2286	0.00	7.5
Gln63	His2277	-1.00	5.5
Glu105	Asp2276	1.00	6.5
	His2277	-3.00	5.0
	Leu2278	1.00	4.5
	Thr2279	-1.00	3.5
	Leu2280	0.00	5.0
	Met2281	-2.00	8.0
	Lys2283	-2.00	7.5
Glu168	Asp2516	2.00	8.0
Glu170	Arg2503	-1.00	7.0
	Arg2511	-1.00	7.0
	Asp2512	5.00	3.5

mLST8	mTOR	E	d
Leu224	Leu2280	1.00	8.0
	Met2281	-5.00	3.5
	Gln2282	1.00	6.0
	Val2284	0.00	6.0
	Glu2285	0.00	5.5
	Glu2288	0.00	8.0
Leu254	Glu1442	0.00	5.0
Leu293	His2289	0.00	8.0
Lys245	Glu1442	-2.00	4.5
Lys261	Gly1407	0.00	7.0
	Pro1408	0.00	7.0
	Tyr1435	-1.00	7.5
	His1439	1.00	6.0
	Phe1440	-1.00	4.0
	Leu1443	0.00	5.5
Lys313	Ile2267	0.00	6.5
	Met2268	-1.00	7.0
	Leu2269	0.00	5.5
	Arg2270	-3.00	2.0
	Met2271	-4.00	3.0
	Ala2272	-1.00	3.5
	Pro2273	-1.00	4.0
	Asp2274	-1.00	7.5
	Val2286	-1.00	7.5
	His2289	2	7.5
Lys86	Asp2276	-2	7.5
	His2277	1	6.0
	Leu2278	0	7.5
	Thr2279	0	6.5
Met273	Glu2285	-2.00	6.0
Pro130	Leu2278	0.00	8.0
	Thr2279	0.00	6.0
	Leu2280	0.00	6.0
	Met2281	-2.00	8.0
Pro169	Arg2511	-1.00	8.0
	Asp2512	1.00	7.0
	Phe2513	0.00	5.0
	Ser2514	1.00	5.0
	His2515	-1.00	5.0
	Asp2516	0.00	5.0

mLST8	mTOR	E	d
Thr220	Met1437	-1	8
	Lys1438	1	5
	His1439	-1	5
	Glu1442	0	8
	Glu2526	0	8
	Lys2530	0	4
Thr23	Pro2273	0	7.5
Thr243	Glu1442	-1	7.5
Trp247	Glu1442	1	7.5
Trp272	Thr2279	0	8
	Leu2280	1	6
	Met2281	0	3
	Gln2282	0	5
	Lys2283	-1	6.5
	Val2284	-4	2.5
	Glu2285	-5	2.5
	Val2286	0	6.5
	Phe2287	0	7
	Glu2288	-8	2
	His2289	0	4.5
	Asn2292	0	6.5
	His2535	-1	5
	Glu2536	0	6
	Cys2539	0	7.5
Trp274	Leu2278	-1	7.5
	Thr2279	0	6.5
	Leu2280	0	6
	Met2281	-1	2.5
	Gln2282	-3	3
	Lys2283	-1	6
	Val2284	0	5.5
	Glu2285	-2	3
	Val2286	0	5.5
	Phe2287	-1	8
	Glu2288	0	7.5
	His2289	1	6
Tyr20	Met2268	-3	8
	Leu2269	-1	7.5
	Arg2270	0	6
	Met2271	-4	3.5

	Glu2536	-1	4.5		Phe2513	3.00	3.5		Asp2517	0.00	8.0	
	Asn2537	0	7.0		Ser2514	-1.00	6.0	Pro217	Glu1442	1.00	8.0	
	Leu2538	0	7.5		His2515	-1.00	7.0	Pro265	Lys1406	0.00	8.0	
Arg270	Gln1405	1	7.0		Leu2527	-1.00	7.5		Gly1407	-0.20	6.0	
	Lys1406	1	5.0		Gln2531	-1.00	5.5		Pro1408	-2.60	3.5	
	Gly1407	-1	5.5		Glu2536	2.00	8.0		Thr1409	0.00	3.0	
	Glu2285	0	6.5	Glu257	Glu1442	1.00	5.0		Pro1410	-2.00	2.5	
	Glu2288	-1	6.5		Leu1443	0.00	7.5		Ala1411	-0.30	6.5	
	His2289	1.00	5.5	Glu267	Glu1403	1.00	7.5		Ile1412	0.10	7.0	
	Asn2292	0.00	5.0		Phe1404	1.00	7.0		Leu1413	-0.40	5.0	
	Asn2293	0.00	6.0		Gln1405	0.00	6.5		Tyr1435	0.00	6.0	
Asn132	Thr2279	-1.00	5.0		Lys1406	-1.00	3.0		Ala1436	0.00	7.5	
	Leu2280	0.00	5.0		Gly1407	-1.00	2.5		His1439	0.00	5.5	
	Met2281	-1	3.0		Pro1408	-0.30	4.5		Phe1440	-2.70	3.0	
	Gln2282	0	7.5		Thr1409	0.00	7.0		Leu1443	-1.00	3.5	
	Glu2536	-1.00	8.0		Pro1410	0.00	7.5		Glu1444	-1.00	8.0	Tyr222
Asn189	Met2281	-1.00	7.5		Ile1412	-0.60	8.0		Trp1449	0.00	8.0	
Asn193	Lys2530	0.00	6.5		Tyr1435	0	5.5	Ser149	Leu2280	1.00	8.0	
Asn264	Glu1403	-1.00	6.5		His1439	0	7.5	Ser172	Thr2279	0.00	8.0	
	Phe1404	0.00	7.5		Phe1440	0	5.5		Leu2280	0.00	4.0	
	Lys1406	0.00	4.5	Gly103	Thr2279	0.2	7.5		Met2281	-1.00	4.0	
	Gly1407	-2.00	3.0	Gly104	Thr2279	1	6.5		Val2284	-1.00	8.0	
	Pro1408	-1.00	3.0	Gly146	Met2281	-1	7.5		Glu2536	0.00	5.5	
	Thr1409	-2.00	3.0	Gly19	Met2271	0	8.0	Ser175	Met2281	-1.00	5.0	
	Pro1410	1.00	5.0		Ala2272	0	7.0	Ser190	Leu2280	1.00	6.5	
	Ala1411	0.00	7.5		Pro2273	0	5.5		Met2281	-1.00	5.5	
	Ile1412	0.00	5.5		Leu2278	1	8.0		Val2284	0.00	6.5	
	Leu1413	-1.00	7.5		Gln2282	1	5.5		Lys2530	0.00	7.5	
	Tyr1435	0.00	8.0	Gly192	Lys2530	0	7.5		Ser2534	0.00	7.5	
	Phe1440	0.00	6.0	Gly263	Lys1406	0	7.0		Glu2536	0.00	4.5	
	Leu1443	0.00	7.5		Gly1407	-1	7.0	Ser239	Glu2285	0.00	7.5	Tyr62
Asn292	Met2271	-1.00	7.5		Pro1408	1	7.5	Ser259	Leu1443	0.00	8.0	
	Glu2285	0.00	8.0		Thr1409	0	6.5	Ser268	Gln1405	1.00	8.0	
	His2289	0.00	5.5		Pro1410	0	7.5		Lys1406	0.00	6.5	
	Asn2293	1.00	8.0	Gly266	Glu1403	1	8.0		Gly1407	0.00	5.5	
Asn46	Ala2272	0.00	7.5		Phe1404	0	6.0		Pro1408	0.00	7.0	
	Pro2273	-1.00	7.5		Gln1405	0	7.5		Tyr1435	0.00	5.0	
	Asp2274	1.00	7.5		Lys1406	0	6.0		Lys1438	1.00	8.0	Val171
	His2277	0.00	5.0		Gly1407	-1	3.5		His1439	1.00	5.0	
	Leu2278	0.00	4.0		Pro1408	-3.9	2.5		Phe1440	0.00	6.5	
	Thr2279	-1.00	3.0		Thr1409	-1	4.5		Glu2288	0.00	7.5	Val188
	Leu2280	-1.00	7.0		Pro1410	-1	5.0		Asn2292	0.00	5.0	Val315
	Met2281	-1	7.0		Ile1412	0	7.5	Ser269	His1439	0.00	7.5	
	Gln2282	-4	2.0		Leu1413	1	5.5		Glu2285	0.00	7.5	
	Lys2283	-1	7.0		Tyr1435	-1	3.5		Glu2288	0.00	3.5	Val316

	Ala2272	-3	3
	Pro2273	-2	2.5
	Asp2274	-1	5.5
	Tyr2275	0	7.5
	His2277	0	7
	Leu2278	-2	3
	Thr2279	0	6
	Met2281	-3	6.5
	Gln2282	-3	2
	Lys2283	-1	5.5
	Val2284	0	7.5
	Glu2285	0	4
	Val2286	-2	3
	Phe2287	-1	7.5
	His2289	0	6.5
	Leu2280	0	5
	Met2281	-3	3.5
	Gln2282	1	8
	Lys2283	0	8
	Val2284	-2	3
	Glu2285	0	7
	Glu2288	0	5.5
	Lys2530	-1	7.5
	Thr2533	0	8
	Ser2534	0	4.5
	His2535	1	5
	Glu2536	-11	2
	Asn2537	0	6
	Cys2539	-3	7
	Gln2540	0	7
	Pro2273	0	7
	Asp2274	-1	6
	Asp2276	0	6.5
	His2277	-5	3
	Leu2278	0	5.5
	Thr2279	0	5.5
	Gln2282	0	7
	Leu2280	1	8
	Lys2530	1	8
	Glu2536	0	7.5
	Met2281	-1	7
	Gln2282	1	7.5
	Glu2285	0	7.5
	His2289	1	7.5
	Met2271	0	8

Asn87	Asp2274	-1	7.0		Ala1436	0	7.5		His2289	1.00	5.5		Ala2272	0	6.5
	Tyr2275	0	7.5		His1439	0	5.0		Val2291	0.00	6.0		Pro2273	1	7.5
	Asp2276	0	6		Phe1440	-1	3.0		Asn2292	-1.00	3.0		Leu2278	0	6
	His2277	-3.00	2.0		Leu1443	0	7.0		Asn2293	0.00	6.5		Thr2279	0	6.5
	Leu2278	-3.00	4.0	Gly271	Glu2285	-1	3.5		His2535	0.00	5.5		Met2281	1	7.5
	Thr2279	-3.00	3.0		Val2286	0	7.5	Ser289	Glu2285	0.20	7.0		Gln2282	-1	2.5
	Leu2280	-1.00	6.5		Glu2288	-1	5.0		His2289	1.00	6.5		Lys2283	-1	7.5
	Gln2282	1.00	6.5		His2289	-1	3.5	Ser290	Met2271	-2.00	6.5		Glu2285	-1	5.5
	Lys2283	0.00	7.5		Asn2292	0	6.0		Ala2272	0.00	8.0		Val2286	0	6
Asp106	Thr2279	0.00	8.0		Asn2293	1	6.5		Gln2282	0.00	7.5		His2289	0	8
Asp147	Met2281	-2.00	7.5	Gly61	His2277	0	7.5		Glu2285	-9.00	2.0	Val45	Ala2272	0	8
Asp21	Arg2270	0.00	7.5		Thr2279	0	6.0		Val2286	-1.00	6.0		Pro2273	0	6
	Met2271	-2.00	7.0		Gln2282	1	7.0		Glu2288	0.00	6.5		Leu2278	0	8
	Ala2272	-1.00	6.5	His219	His1439	1	7.5		His2289	0.00	2.5		Thr2279	0	8
	Pro2273	0.00	5.0		Glu1442	-1	7.0		Ala2290	1.00	8.0		Gln2282	-1	4.5
Asp241	His1439	-1.00	6.0		Lys2530	1	7.5		Asn2293	1	7				
	Glu2285	1.00	8.0	His22	Ala2272	1	7.0	Ser43	Pro2273	-2	5				
	Glu2288	2.00	6.0		Pro2273	-1	3.0		Asp2274	-1	5.5				
Asp291	Glu2285	1.00	6.5		Asp2274	-2	5.5		His2277	0	6.5				
	His2289	-3.00	4.5	His40	Pro2273	-1	6.5		Leu2278	1	8				
	Asn2293	1.00	7.5	His64	Pro2273	0	8.0	Ser90	Thr2279	-1	6.5				
Asp42	Pro2273	0.00	5.0	Ile131	Thr2279	-1	6.0		Met2281	0	6.5				
	Asp2274	1.00	5.5		Leu2280	0	7.5	Thr174	Leu2280	-1	7				
	His2277	-2.00	6.5		Met2281	-2	6.5		Met2281	-4	3				
Cys133	Met2281	14.00	5.5	Ile173	Leu2280	-1	8.0		Gln2282	0	8				
Cys317	Gln2282	-1.00	6.0		Met2281	-2	5.5		Glu2536	0	7.5				
				Ile88	His2277	-1	8.0	Thr191	Leu2527	1	7				
					Thr2279	1	5.0		Lys2530	0	4.5				
					Gln2282	0.00	7.0		Ser2534	0	8				
									Glu2536	0	8				

Supplementary Methods

MM-PBSA calculation

MM-PBSA calculations were performed using the g_mmpbsa code[1]. Ionic concentration was set to 0.150 M to match the MD simulation and atomic bondi radii was employed. Dielectric constant inside the protein was set to 40, while the dielectric constant for the solvent was set to 80. Linearized Poisson-Boltzmann equation was employed using grid resolution of 0.5 Å. Nonpolar solvation energy calculations were performed using the solvent accessible volume model with the number of dots per sphere set to 200. For calculations, 100 snapshots from the last 10ns of 100 ns simulations with charmm27 amber99sb [2] force fields were employed. Trajectory with charmm27 force field is the same used for mfcc-QM calculations. Trajectory with amber9sb force field was

produced as follow: crystallographic structure of human mTOR-mLST8 complex (PDB ID: 4JSN)[3] was prepared using the PDB2PQR[4] server with the protonation state of residues calculated at the pH 7.2 with the help of the Propka[5] algorithm. Molecular dynamics simulation was performed using GROMACS 2019 [6,7] package with amber99sb [2] force field. The simulation consisted in ~365,000 atoms which included the mTOR-mLST8 system, 114,042 water molecules, 345 ions Na+ and 334 ions Cl−. Restraint was applied to the mTOR backbone (except for the loop making close contact with mLST8) while the whole mLST8 was free to move. Before the MD production step, the total energy minimization was accomplished by combining the steepest-descent algorithm followed by a step using conjugate gradient approach. Long-range electrostatics was modelled with the Particle Mesh Ewald (PME) method [8], temperature coupling was done at 310.15 K in reference pressure of 1 bar with compressibility of 4.5×10^{-5}/bar applied for pressure control. TIP3P water model was used to describe water molecules [9] and bond links controlled by the LINCS algorithm [10]. The integration steps of all simulations were set to 2 fs. The production step generates a 100-ns trajectory, from which the last 10ns were extracted to be used during the MM-PBSA calculations.

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