Electronic Supplementary Material (ESI) for RSC Advances.

The effect of V155M mutation on the complex of hSTING and 2'3'-cGAMP: an in-silico study case

Bowen Tang[a,#], Baicun Li[a,#], Boqun Li[a], Zan Li[a], Jingbo Qin[a], Xiaoxiao Zhou[a], Yingkun Qiu[a], Zhen Wu[a,*] and Meijuan Fang[a,*]

[a] Fujian Provincial Key Laboratory of Innovative Drug Target Research, School of Pharmaceutical Sciences，Xiamen University, Xiamen 361000, China

[#] The first two authors are co-first authors.

* Corresponding authors. Tel.: +86-592-2189868; Fax: +86-592-2189868.

Correspondence and requests for materials should be addressed to wuzhen@xmu.edu.cn; fangmj@xmu.edu.cn.

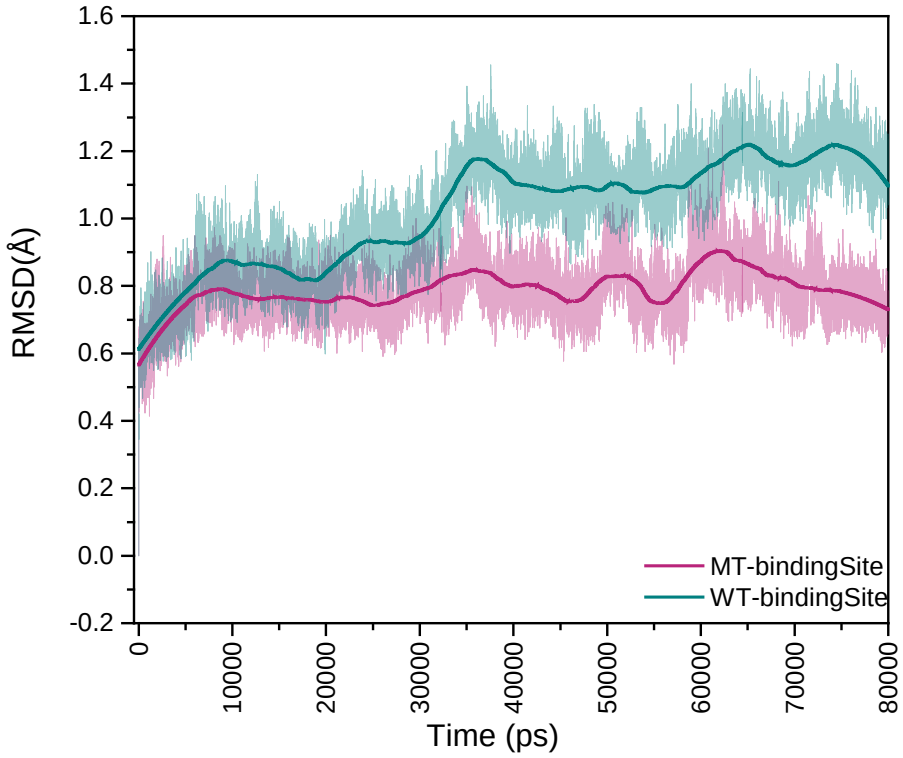

Figure S1. RMSD variation of the residues constructing the binding site (162, 163, 166, 167, 235, 238, 239, 240, 241, 260, 261, 263, 264, 267)

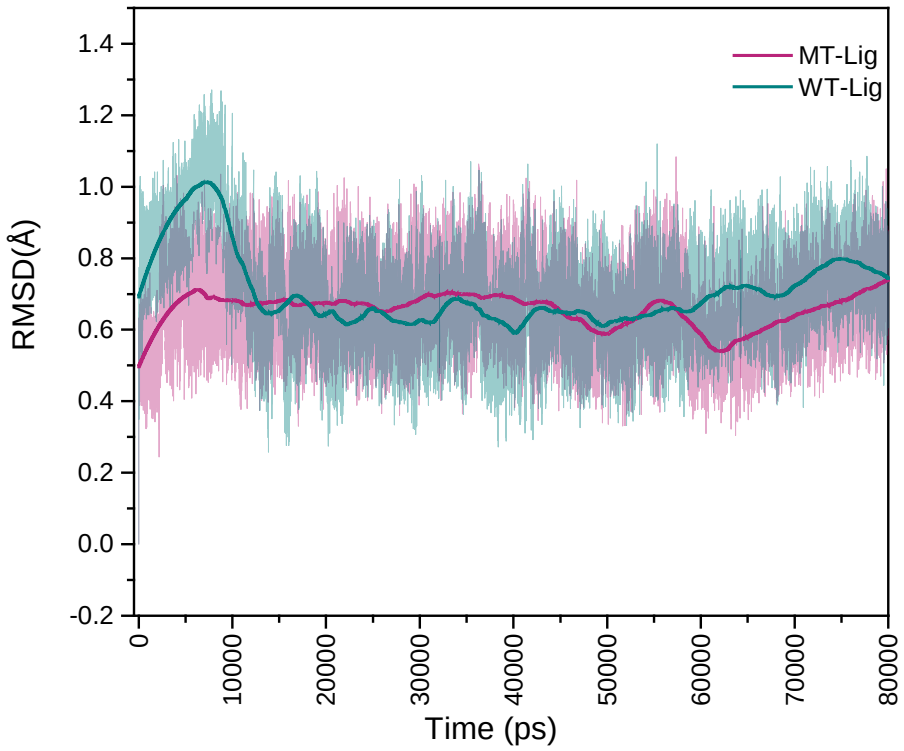

Figure S2. RMSD variation of the ligand 2'3'-cGAMP

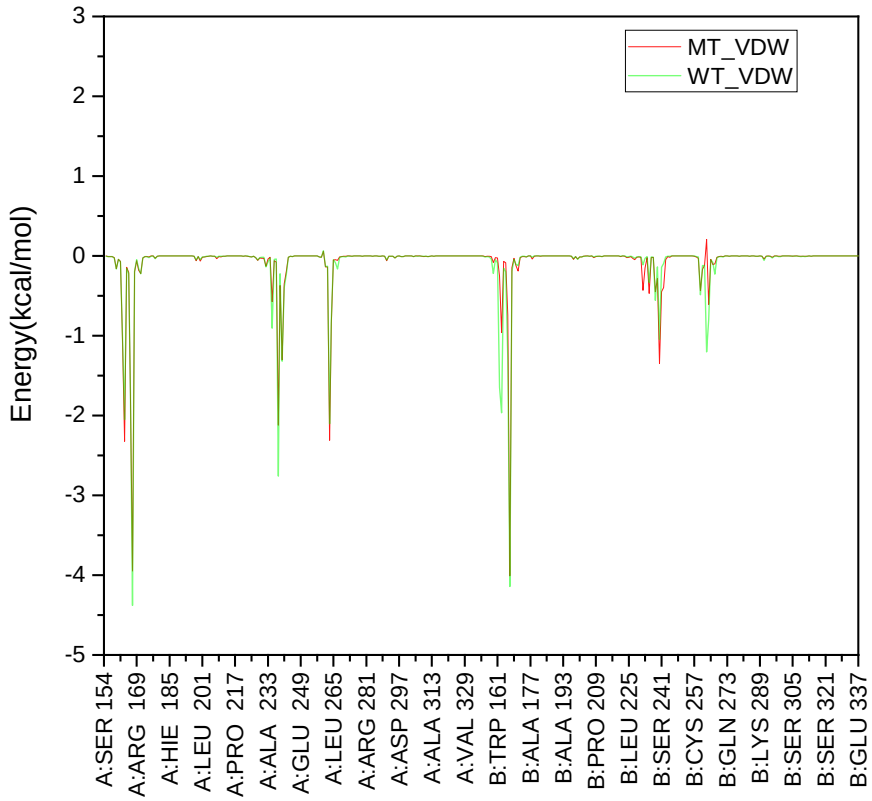

Figure S3. The average of van der Waals interaction energy decomposition of STING-ligand complex.

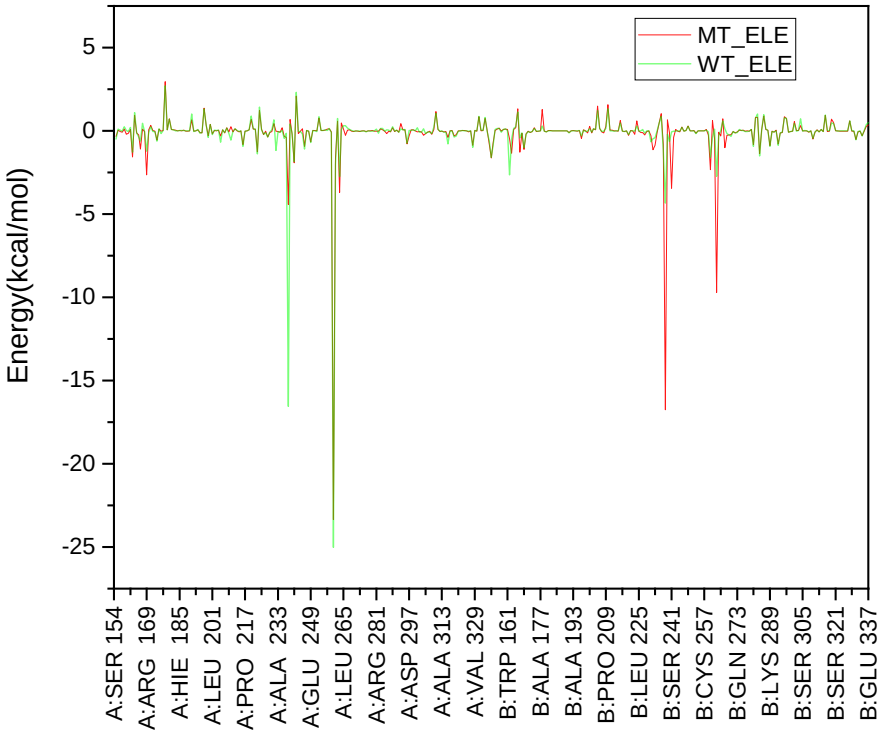

Figure S4. The average of electrostatic energy decomposition of STING-ligand complex.

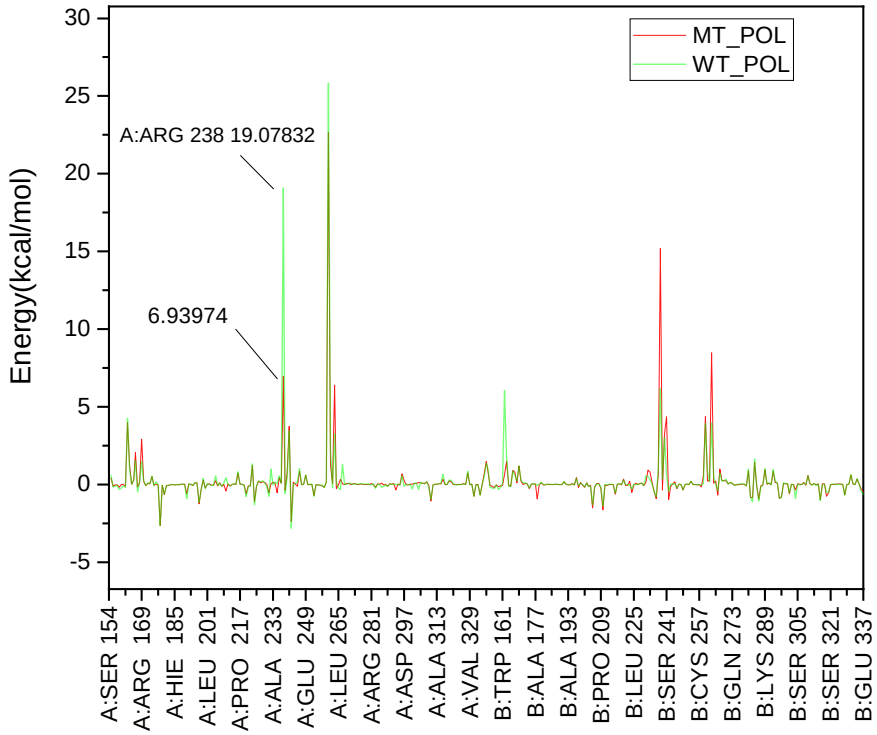

Figure S5. The average of polar contribution solvation free energy decomposition of STING-ligand complex.

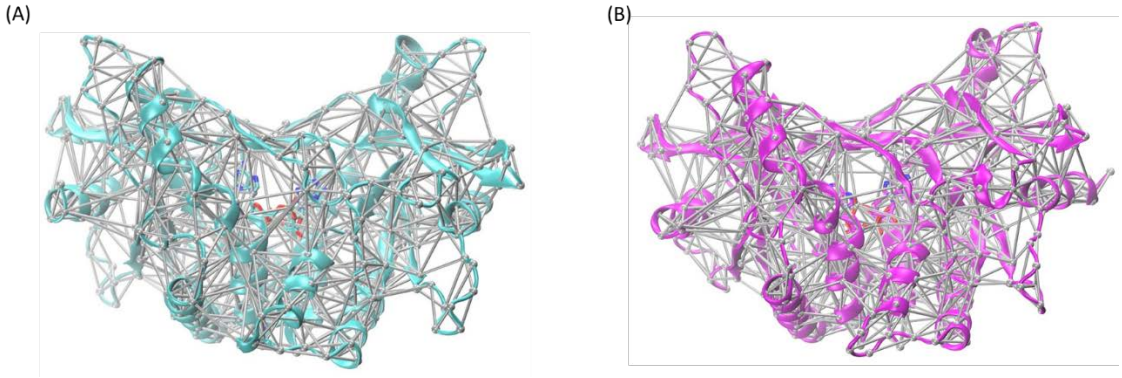

Figure S6. The overall networks in WT and MT. (A) the whole network in WT system. (B) the whole network in MT system.

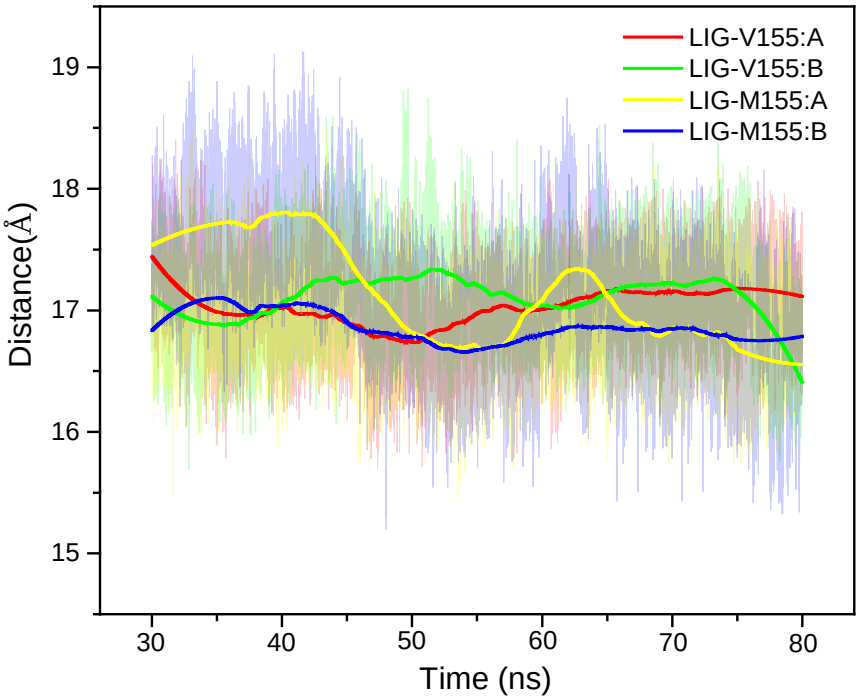

Figure S7. The distance between the mass center of the ligand and the Cα of the residue 155.

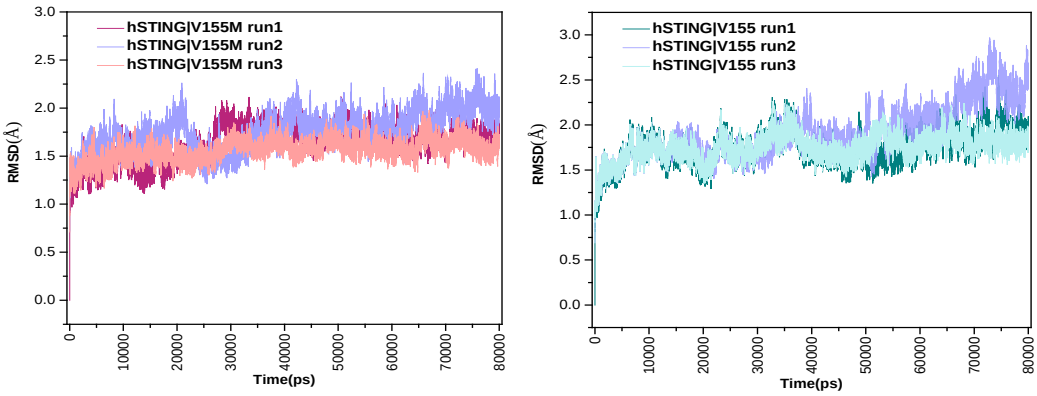

Figure S8. Total 480 ns simulation time for WT/MT systems. (A) The RMSD of each parallel calculation for MT system. (B) The RMSD of each parallel calculation for WT system.

Table S1. The hydrogen bonds between substrate 2'3'-cGAMP and residues of hSTING

Acceptor	DonorH	Donor	Frac(%)	AvgDist(Å)	AvgA(°)
V155M					
1SY_369@O4	ARG_238:B@HH22	ARG_238:B@NH2	0.9614	2.7588	160.7150
1SY_369@O9	THR_263:B@HG1	THR_263:B@OG1	0.8601	2.6752	163.2070
1SY_369@O13	ARG_238:B@HH12	ARG_238:B@NH1	0.7482	2.8300	159.5663
1SY_369@O6	THR_263:A@HG1	THR_263:A@OG1	0.7385	2.8047	157.7942
THR_263:B@OG1	1SY_369@H2	1SY_369@O2	0.5230	2.7881	155.0825
GLU_260:A@OE2	1SY_369@H22	1SY_369@N9	0.3299	2.7715	146.0754
1SY_369@O10	1SY_369@H2	1SY_369@O2	0.1648	2.7245	155.0298
1SY_369@O4	ARG_238:B@HH12	ARG_238:B@NH1	0.1406	2.8689	144.7982
SER_241:B@O	1SY_369@H15	1SY_369@N1	0.1224	2.8654	147.1997
SER_241:B@O	1SY_369@H16	1SY_369@N1	0.0576	2.8634	147.1672
1SY_369@O10	ARG_238:A@HH22	ARG_238:A@NH2	0.0417	2.7734	156.8930
VAL_239:B@O	1SY_369@H16	1SY_369@N1	0.0317	2.8341	158.6317
SER_241:B@OG	1SY_369@H15	1SY_369@N1	0.0270	2.8936	157.5028
1SY_369@O10	ARG_238:A@HH12	ARG_238:A@NH1	0.0256	2.8468	147.4947
1SY_369@O13	TYR_240:B@HH	TYR_240:B@OH	0.0202	2.7969	153.2701
1SY_369@O10	THR_263:B@HG1	THR_263:B@OG1	0.0165	2.8096	151.9879
1SY_369@N3	ARG_238:A@HH21	ARG_238:A@NH2	0.0163	2.9072	150.0176
1SY_369@O5	THR_263:A@HG1	THR_263:A@OG1	0.0156	2.8956	149.7981
1SY_369@O13	ARG_238:B@HH22	ARG_238:B@NH2	0.0148	2.8787	148.6733
1SY_369@O9	1SY_369@H2	1SY_369@O2	0.0144	2.8353	161.2447
SER_241:B@OG	1SY_369@H16	1SY_369@N1	0.0062	2.882	149.7300
1SY_369@O2	ARG_238:A@HH21	ARG_238:A@NH2	0.0056	2.9042	143.0939
VAL_239:B@O	1SY_369@H15	1SY_369@N1	0.0042	2.8736	155.2484
1SY_369@N1	VAL_239:A@H	VAL_239:A@N	0.0035	2.9377	163.9936
1SY_369@O2	THR_263:B@HG1	THR_263:B@OG1	0.0021	2.8532	159.8019
1SY_369@N1	SER_241:B@H	SER_241:B@N	0.0018	2.9339	151.4319
1SY_369@O8	1SY_369@H2	1SY_369@O2	0.0010	2.5438	137.5876
1SY_369@N10	THR_263:A@HG1	THR_263:A@OG1	0.0006	2.8883	145.8508
GLU_260:A@OE2	1SY_369@H21	1SY_369@N9	0.0002	2.8314	143.2454
1SY_369@O8	THR_263:B@HG1	THR_263:B@OG1	0.0002	2.9049	155.3679
THR_263:A@OG1	1SY_369@H21	1SY_369@N9	0.0001	2.8387	147.2601
GLU_260:A@OE1	1SY_369@H22	1SY_369@N9	0.0001	2.8708	150.0491
THR_263:A@OG1	1SY_369@H3	1SY_369@O6	0.0001	2.8763	142.0449
1SY_369@N7	ARG_238:A@HH21	ARG_238:A@NH2	0.0001	2.9508	139.7689
1SY_369@O2	ARG_238:A@HH22	ARG_238:A@NH2	0.0001	2.9111	142.0244
1SY_369@O12	SER_241:A@H	SER_241:A@N	0.0001	2.9793	146.9359
1SY_369@O13	THR_263:A@HG1	THR_263:A@OG1	0.0000	2.8203	155.5455

1SY_369@N4	ARG_238:B@HH21	ARG_238:B@NH2	0.0000	2.9285	141.7094
1SY_369@N9	ARG_238:B@HH21	ARG_238:B@NH2	0.0000	2.9779	138.5177
1SY_369@O4	ARG_238:B@HH21	ARG_238:B@NH2	0.0000	2.9992	138.9237
WT					
1SY_369@O10	ARG_238:A@HH22	ARG_238:A@NH2	0.9122	2.773	155.321
1SY_369@O10	ARG_238:A@HH12	ARG_238:A@NH1	0.7360	2.8068	149.4667
THR_263:B@OG1	1SY_369@H2	1SY_369@O2	0.6578	2.6815	162.6218
GLU_260:A@OE2	1SY_369@H22	1SY_369@N9	0.3733	2.7716	154.3358
1SY_369@O9	THR_263:B@HG1	THR_263:B@OG1	0.2811	2.7517	155.6128
GLU_260:A@OE1	1SY_369@H21	1SY_369@N9	0.2670	2.7681	156.9044
1SY_369@O13	ARG_238:B@HH12	ARG_238:B@NH1	0.2536	2.7855	157.3767
1SY_369@O4	ARG_238:B@HH22	ARG_238:B@NH2	0.2093	2.818	158.4829
1SY_369@O13	ARG_238:B@HH22	ARG_238:B@NH2	0.1834	2.8311	151.2463
THR_263:A@OG1	1SY_369@H22	1SY_369@N9	0.1472	2.8779	156.7584
THR_263:A@OG1	1SY_369@H21	1SY_369@N9	0.1404	2.8822	154.4363
GLU_260:A@OE1	1SY_369@H22	1SY_369@N9	0.1142	2.7796	151.3976
1SY_369@O6	THR_263:A@HG1	THR_263:A@OG1	0.1103	2.8425	154.199
1SY_369@O9	1SY_369@H2	1SY_369@O2	0.0800	2.8495	159.6839
SER_241:B@O	1SY_369@H16	1SY_369@N1	0.0600	2.8688	151.0012
SER_241:B@O	1SY_369@H15	1SY_369@N1	0.0541	2.8622	150.849
1SY_369@O5	THR_263:A@HG1	THR_263:A@OG1	0.0490	2.8680	151.1628
1SY_369@O10	THR_263:B@HG1	THR_263:B@OG1	0.0279	2.8047	150.5096
1SY_369@O2	THR_263:B@HG1	THR_263:B@OG1	0.0205	2.7424	160.3301
VAL_239:B@O	1SY_369@H16	1SY_369@N1	0.0140	2.8802	146.8333
1SY_369@O13	1SY_369@H3	1SY_369@O6	0.0136	2.7794	154.2457
1SY_369@N3	THR_263:B@HG1	THR_263:B@OG1	0.0120	2.8627	156.0307
VAL_239:B@O	1SY_369@H15	1SY_369@N1	0.0118	2.8706	146.8435
1SY_369@O4	ARG_238:B@HH12	ARG_238:B@NH1	0.0070	2.8679	144.9294
1SY_369@N1	SER_241:B@H	SER_241:B@N	0.0066	2.9424	160.389
1SY_369@O13	TYR_240:B@HH	TYR_240:B@OH	0.0041	2.8244	148.6829
1SY_369@O13	THR_263:A@HG1	THR_263:A@OG1	0.0029	2.8546	160.3011
1SY_369@O13	ARG_238:B@HH21	ARG_238:B@NH2	0.0025	2.7957	149.6247
1SY_369@N10	THR_263:A@HG1	THR_263:A@OG1	0.0016	2.9178	145.3472
1SY_369@O4	ARG_238:B@HH21	ARG_238:B@NH2	0.0011	2.8383	141.4117
1SY_369@O8	1SY_369@H2	1SY_369@O2	0.0009	2.5373	137.5116
GLU_260:A@OE2	1SY_369@H21	1SY_369@N9	0.0007	2.7795	144.5728
1SY_369@O10	1SY_369@H2	1SY_369@O2	0.0002	2.6797	148.2064
SER_241:B@OG	1SY_369@H16	1SY_369@N1	0.0002	2.8470	144.0061
1SY_369@O4	ARG_238:A@HH22	ARG_238:A@NH2	0.0002	2.8539	145.3348
1SY_369@O9	ARG_238:A@HH12	ARG_238:A@NH1	0.0001	2.9069	163.0682

SER_162:B@OG	1SY_369@H3	1SY_369@O6	0.0000	2.7200	160.5636
1SY_369@O13	SER_162:B@HG	SER_162:B@OG	0.0000	2.7782	163.6858
SER_241:B@OG	1SY_369@H15	1SY_369@N1	0.0000	2.8162	153.8604
THR_263:A@OG1	1SY_369@H3	1SY_369@O6	0.0000	2.8231	143.4397
1SY_369@O4	THR_263:A@HG1	THR_263:A@OG1	0.0000	2.8820	159.4654
1SY_369@O12	SER_241:A@H	SER_241:A@N	0.0000	2.8915	150.1505
TYR_167:A@OH	1SY_369@H22	1SY_369@N9	0.0000	2.9548	147.6834

Angle cutoff for hydrogen bonds > 135º, distance cutoff for hydrogen bonds <3.5 Å

Table S2. The information of the red subnetwork

Sources	Targets	Number of paths	Sources	Targets	Number of paths
V155M			Wild type		
155:A	303:B	3	155:A	303:B	3
155:A	304:B	2	155:A	304:B	13
155:A	305:B	4	155:A	305:B	18
155:A	306:B	1	155:A	306:B	18
155:A	307:B	4	155:A	307:B	7
155:A	308:B	4	155:A	308:B	18
155:B	303:B	3	155:B	303:B	9
155:B	304:B	3	155:B	304:B	11
155:B	305:B	1	155:B	305:B	4
155:B	306:B	2	155:B	306:B	16
155:B	307:B	5	155:B	307:B	6
155:B	308:B	2	155:B	308:B	4
Sum		34	Sum		127

The edge length offset was 10 and the suboptimal paths were no longer than optimal plus 10.

Table S3. The information of the blue subnetwork

Nodes in the path						
V155M						
155:A	159:A	162:A	LIG-Node1	238:B		
155:A	158:A	162:A	167:A	341:B	238:B	
155:B	158:B	162:B	LIG-Node3	238:B		
155:B	271:B	267:B	165:A	167:A	341:B	238:B
Wild type						
155:A	268:A	266:A	233:B	235:B	238:B	
155:B	169:B	163:B	LIG-Node3	238:B		
155:B	169:B	162:B	166:B	232:B	238:B	
155:B	168:B	162:B	166:B	232:B	238:B	

The edge length offset was 10 and the suboptimal paths were no longer than optimal plus 10.

LIG-Node1 = [N6 N7 N10 N9 N8 C20 C17 C18 C19 C16 O12]. It was centered N6.

LIG-Node2 = [P2 O10 O9 O7 O11 O6 O5 C15 C11 C12 C13 C14]. It was centered P2.

LIG-Node3 = [P1 O4 O13 O3 O1 O2 O8 C1 C2 C3 C4 C10]. It was centered P1.

LIG-Node4 = [N5 N4 N3 N1 N2 C9 C7 C6 C8 C5]. It was centered N5.