Supplementary Table 1a. Patient Clinical History: East Asians

Patient ID	Age	Sex	Smoker	Tumor type	TNM	Stage
14	80	M	Y	Adenocarcinoma	T2N0M0	IB
16	53	F	N	Adenocarcinoma	T4N2M0	IIIB
18	75	F	N	Adenocarcinoma	T2N0M0	IB
30	77	F		Adenocarcinoma	T2N1M0	IIB
34	65	M	Y	Squamous cell carcinoma	T2N2M0	IIIA
36	73	M	Y	Squamous cell carcinoma	T3N0M0	IIB
37	62	M	Y	Adenocarcinoma	T1N0M0	IA
38	47	F	N	Adenocarcinoma	T2N2M0	IIIA
39	68	M	Y	Squamous cell carcinoma	T2N1M0	IIB
40	67	M	Y	Large cell carcinoma	T2N2M0	IIIA
41	74	M	Y	Squamous cell carcinoma	T2N2M0	IIIA
43	56	M		Adenocarcinoma	T2N2M0	IIIA
44	60	M	Y	Adenocarcinoma	T2N2M1	IV
45	56	M	Y	Squamous cell carcinoma	T2N2M0	IIIA
51	66	F		Adenocarcinoma	T2N0M0	IB
52	53	M		Adenocarcinoma	T2N2M0	IIIA
54	47	M		Adenocarcinoma	T2N0M0	IB
55	63	M	Y	Squamous cell carcinoma	T2N2M0	IIIA
57	55	F		Adeno/Squamous	T3N0M0	IIB
62	90	M		Adenocarcinoma	T2N1M1	IV
63	79	M	Y	Adenocarcinoma, mixed subtypes	T4N2M0	IIIB
66	68	M		Adenocarcinoma	T2N2M0	IIIA
67	80	M	Y	Large cell carcinoma	T2N0M0	IB
68	68	M	Y	Adenocarcinoma	T3N0M0	IIB
69	44	M	Y	Adenocarcinoma	T2N2M0	IIIA
70	78	M		Small cell carcinoma	T2N2M0	IIIA
75	74	M	Y	Adenocarcinoma	T2N0M0	IB
76	75	M	Y	Squamous cell carcinoma	T1N0M0	IA
79	73	M	Y	Adenocarcinoma	T2N0M0	IB

80	69	M	Y	Adenocarcinoma	T2N2M0	IIIA
81	57	F	N	Adenocarcinoma	T4N2M0	IIIB
83	77	M	Y	Large cell carcinoma	T2N0M0	IB
85	66	M	Y	Adenocarcinoma	T2N0M0	IB
89	76	M	Y	Adenocarcinoma	T2N0M0	IB
92	65	M	Y	Squamous cell carcinoma	T3N2M0	IIIA
96	74	M	Y	Adenocarcinoma	T2N0M0	IB
101	73	F	Y	Squamous cell carcinoma	T2N3M0	IIIB
103	62	M	Y	Squamous cell carcinoma	T3N2M0	IIIA
104	69	M	Y	Adenocarcinoma	T2N1M0	IIB
113	79	M	Y	Adenocarcinoma	T4N2M0	IIIB
115	74	M	Y	Squamous cell carcinoma	T2N0M0	IB
118	77	M	Y	Adenocarcinoma	T2N0M0	IB
119	56	M	Y	Adenocarcinoma	T2N0M0	IB
121	70	M		Adenocarcinoma	T2N0M1	IV
126	45	M	Y	Adenocarcinoma	T2N2M0	IIIA
127	67	M	Y	Squamous cell carcinoma	T2N0M0	IB
128	43	M	Y	Large cell carcinoma	T1N2M0	IIIA
132	72	F		Adenocarcinoma	T1N1M0	IIA
134	71	M	Y	Adenocarcinoma	T2N2M0	IIIA
139	67	M	Y	Squamous cell carcinoma	T4N0M0	IIIB
140	74	M	Y	Adenocarcinoma	T2N0M1	IV
142	70	F		Adenocarcinoma	T3N2M0	IIIA
143	81	M	Y	Squamous cell carcinoma	T2N0M0	IB
144	62	M	Y	Adenocarcinoma	T2N1M0	IIB
146	69	F	N	Adenocarcinoma	T2N0M0	IB
147	80	M		Squamous cell carcinoma	T2N0M0	IB
148	78	M		Adenocarcinoma	T2N2M1	IV
152	79	M	Y	Adenocarcinoma	T1N0M0	IA
156	53	M	Y	Adenocarcinoma	T2N1M0	IIB
157	84	M	Y	Squamous cell carcinoma	T2N0M0	IB
161	59	F		Adenocarcinoma	T2N0M0	IB
162	71	F		Adenocarcinoma	T2N0M1	IV
163	55	M	Y	Large cell carcinoma	T3N0M0	IIB
164	73	M		Adenocarcinoma	T2N0M0	IB

165	69	M		Adenocarcinoma	T2N0M1	IV
168	65	F		Adenocarcinoma	T4N0M0	IIIB
169	48	M	Y	Adenocarcinoma	T2N2M0	IIIA
171	64	M	Y	Squamous cell carcinoma	T2N1M0	IIB
173	61	M	Y	Squamous cell carcinoma	T2N0M0	IB
176	50	M	Y	Adenocarcinoma	T2N2M1	IV
179	79	M	Y	Adenocarcinoma	T4N0M0	IIIB
204	57	F		Adenocarcinoma	T2N0M0	IB
206	71	M	Y	Adenocarcinoma	T1N0M0	IA
207	73	F		Squamous cell carcinoma	T2N0M0	IB
208	72	M	N	Adenocarcinoma	T2N0M0	IB
209	64	F	N	Adenocarcinoma	T1N0M0	IA
210	50	M	Y	Squamous cell carcinoma	T2N0M0	IB
211	54	F		Adenocarcinoma	T2M0N0	IB
212	52	F	N	Adenocarcinoma	T2N1M0	IIB
215	68	F	Y	Adenocarcinoma	T2N0M0	IB
217	66	M	Y	Adeno/Squamous	T2N1M0	IIB
219	69	M	Y	Squamous cell carcinoma	T2N0M0	IB
220	53	M	Y	Adenocarcinoma	T2N2M0	IIIA
221	79	M	Y	Adenocarcinoma	T2N0M0	IB
223	50	M	Y	Adenocarcinoma	T2N0M0	IB
224	54	F		Adenocarcinoma	T1N0M0	IA
225	73	M	Y	Squamous cell carcinoma	T3N0M0	IIB
226	74	M	Y	Adenocarcinoma	T2N0M0	IB
227	74	M	N	Adenocarcinoma	T2N*M0	IB
229	83	M	Y	Adenocarcinoma	T2N0M0	IB
231	55	M	N	Adenocarcinoma	T2N2M0	IIIA
232	59	M	Y	Adenocarcinoma	T2N2M0	IIIA
233	75	M	Y	non-small cell carcinoma	T2N0M0	IB
235	58	F	N	Adenocarcinoma, mixed subtype	T2N2M0	IIIA
242	73	M	N	Adenocarcinoma	T2N2M0	IIIA
248	78	M	Y	Adenocarcinoma	T1N2M0	IIIA
249	83	M	Y	Adenocarcinoma	T1N1M0	IIA
250	64	F		Squamous cell carcinoma	T2N2M0	IIIA
256	73	M		Adenocarcinoma	T2N2M0	IIIA

258	40	F	N	Adenocarcinoma	T3N0M0	IIB
260	75	M		Adenocarcinoma, mixed subtypes	T4N2M0	IIIB
264	76	F	N	Adenocarcinoma	T2N2M0	IIIA
271	67	M	Y	Squamous cell carcinoma	T2N2M0	IIIA
272	63	M	Y	Squamous cell carcinoma	T2N2M0	IIIA
274	62	M		Large cell carcinoma	T2N1M0	IIB
282	73	M	Y	Squamous cell carcinoma	T2N0M0	IB
290	50	F		Adenocarcinoama, multifocal	T4N0M0	IIIB
291	49	M		Adenocarcinoma	T2N0M0	IB
293	73	M	N	Pleomorphic carcinoma	T2N0M0	IB
294	58	M	N	Adenocarcinoma	T4N2M1	IV
295	70	M		Adenocarcinoma	T1N0M0	IA
297	78	M	Y	Adenocarcinoma	T2N0M0	IB
299	78	M	Y	Squamous cell carcinoma	T2N2M0	IIIA
300	71	M	Y	Squamous cell carcinoma	T2N0M0	IB
302	79	M	Y	Adenocarcinoma	T2N2M0	IIIA
305	77	F		Adenocarcinoma	T1N0M0	IA
306	75	M	Y	Large cell carcinoma	T2N0M0	IB
309	80	M	Y	Squamous cell carcinoma	T2N2M0	IIIA
311	71	F	N	Mucoepidermoid carcinoma	T2N2M0	IIIA
312	69	M	N	Adenocarcinoma	T2N0M0	IB
314	67	M	Y	Squamous cell carcinoma	T2N0M0	IB
317	76	F		Adenocarcinoma	T1N1M0	IIA
324	75	M	Y	Squamous cell carcinoma	T3N0M0	IIB
329	77	M	Y	Squamous cell carcinoma	T2N0M1	IV
330	78	M	Y	Adenocarcinoma	T2N0M0	IB
335	79	M	Y	Squamous cell carcinoma	T1N2M0	IIIA
336	73	M	Y	Squamous cell carcinoma	T1N0M0	IA
341	43	F		Adenocarcinoma	T2N0M0	IB
345	75	M	Y	Adenocarcinoma	T2N0M0	IB
349	50	M	Y	Adenocarcinoma	T1N2M0	IIIA
360	78	F		Adenocarcinoma	T4N0M0	IIIB
370	42	F		Mucoepidermoid carcinoma	T4N*M0	IIIB
372	81	M	Y	Squamous cell carcinoma	T2N1M0	IIB
375	75	M		Adenocarcinoma	T2N0M0	IB

378	79	M	Y	Adenocarcinoma	T2N0M0	IB
382	71	F	N	Adenocarcinoma	T2N0M0	IIB
383	63	F	N	Adenocarcinoma	T2N0M0	IB
385	75	M	Y	Squamous cell carcinoma	T2N0M0	IIA
386	81	M	Y	Adenocarcinoma	T4N0M0	IIIB
389	76	M	Y	Squamous cell carcinoma	T2N0M0	IB
390	80	M	Y	Squamous cell carcinoma	T2N0M0	IIIB
391	71	M	N	Adenocarcinoma	T2N0M0	IB
392	44	F	N	Adenocarcinoma	T2N1M0	IIB
404	61	F	N	Adenocarcinoma	T2N0M0	IA

Open boxes: information not available

Supplementary Table 1b. Patient Clinical History: Caucasians

Patient ID	Age	Sex	Smoker	Tumor Type	Stage
US 1	67	M	Y	Adenocarcinoma	
US 2	70	M	Y	Adenocarcinoma	IV
US 4	72	M	Y	Adenocarcinoma	IIIA
US 5	72	F	Y	Adenocarcinoma(Acinar cell)	IB
US 6	63	M	Y	Adenocarcinoma	IA
US 8	67	M	Y	Adenocarcinoma	IIIA
US 13	51	M	Y	Adenocarcinoma	IIIB
US 14	91	M	Y	Adeno with large cell neuroendocrine	IA
US 15	60	M	Y	Adenocarcinoma	IA
US 16	53	M	Y	Adenocarcinoma	IIB
US 18	70	M	Y	Adenocarcinoma	IIIA
US 20	79	F	Y	Adenocarcinoma	IB
US 21	77	M	Y	Adenocarcinoma	IA
US 22	74	M	Y	Adenocarcinoma	IB
US 24	70	M	Y	Adenocarcinoma	IB
US 25	66	F	Y	Adenocarcinoma	IB
US 26	55	F	Y	Adenocarcinoma	IB
US 27	37	M	N	Adenocarcinoma	IB
US 28	66	F	N	Adenocarcinoma	IA
US 30	69	M	Y	Adenocarcinoma	IA
US 31	62	M	Y	Adenocarcinoma	IIIA
US 35	63	M	Y	Adenocarcinoma	IA
US 36	49	M	Y	Adenocarcinoma	IA

US 37	80	M	Y	Adenocarcinoma	IA
US 39	69	M	Y	Adenocarcinoma	IB
US 40	48	M	Y	Adenocarcinoma	IIIA
US 41	67	M	Y	Adenocarcinoma	IIIA
US 42	55	F	Y	Adenocarcinoma	IA
US 44	68	M	Y	Adenocarcinoma	IA
US 45	44	F	Y	Large cell carcinoma	IV
US 49	73	F	Y	Large cell carcinoma	IA
US 50	71	M	Y	Large cell carcinoma	IA
US 51	59	M	Y	Large cell carcinoma	IA
US 53	46	F	Y	Large cell carcinoma	IB
US 54	62	M	Y	Large cell carcinoma	IB
US 55	72	M	Y	Large cell carcinoma	IB
US 56	69	M	Y	Large cell carcinoma	IB
US 60	70	M	Y	Large cell carcinoma	IIIA
US 61	72	M	Y	Large cell carcinoma	IIIA
US 63	55	F	Y	Large cell carcinoma	IB
US 64	60	M	Y	Large cell carcinoma	IB
US 65	77	F	Y	Large cell carcinoma	Unknown
US 66	64	M		Large cell carcinoma	Unknown
US 68	70	M	Y	Squamous cell carcinoma	IV
US 69	66	F	Y	Squamous cell carcinoma	IA
US 72	66	F	Y	Squamous cell carcinoma	IA
US 74	79	M	Y	Squamous cell carcinoma	IA
US 77	69	M	Y	Squamous cell carcinoma	IA
US 78	70	M	Y	Squamous cell carcinoma	IA
US 79	67	M	Y	Squamous cell carcinoma	IA
US 80	68	M	Y	Squamous cell carcinoma	IA
US 81	83	F	Y	Squamous cell carcinoma	IB
US 83	80	F	Y	Squamous cell carcinoma	IB
US 85	60	M	Y	Squamous cell carcinoma	IB
US 87	77	M	Y	Squamous cell carcinoma	IB
US 88	66	M	Y	Squamous cell carcinoma	IB
US 89	73	M	Y	Squamous cell carcinoma	IB
US 91	69	F	Y	Squamous cell carcinoma	IIB
US 92	75	F	Y	Squamous cell carcinoma	IIB
US 94	60	F	Y	Squamous cell carcinoma	IIIA
US 95	63	F	Y	Squamous cell carcinoma	IIIA
US 96	56	M	Y	Squamous cell carcinoma	IIIA
US 98	59	M	Y	Squamous cell carcinoma	IIIA
US 100	71	M	Y	Squamous cell carcinoma	IIIA

US 101	61	M	Y	Squamous cell carcinoma	IIIA
US 102	69	F	N	Squamous cell carcinoma	Metastases from bladder
US 103	62	F	Y	Squamous cell carcinoma	Metastases from cervix
US 104	55	M	Y	Small cell carcinoma	Metatsatic
US 105	59	M	Y	Small cell carcinoma	Extensive
US 106	69	M	Y	Small cell carcinoma	Limited
US 107	80	M	Y	Small cell carcinoma	Extensive
US 108	65	F	Y	Small cell carcinoma	Extensive
US 109	75	M	Y	Small cell carcinoma	Extensive
US 110	67	M		Large/Adeno	IB
US 111	66	M	Y	Small/Adeno	IB
US 112	65	M	Y	Small/Adeno/Large cell	IIIB

Supplementary Table 1c. Patient Clinical History: African Americans

Patient ID	Age	Sex	Smoker	Tumor Type	Stage
US 3	84	F	Y	Adenocarcinoma	IV
US 7	60	F	Y	Adenocarcinoma	IA
US 9	54	F	Y	Adenocarcinoma	IIB
US 10	59	F	Y	Adenocarcinoma	IIIA
US 11	40	F	Y	Adenocarcinoma	IIIA/IIIB
US 12	69	M	Y	Adenocarcinoma	IB
US 17	81	F	Y	Adenocarcinoma	IA
US 19	71	F	Y	Adenocarcinoma	IB
US 23	59	M	Y	Adenocarcinoma	IA
US 29	80	F	N	Adenocarcinoma	IIIA
US 32	59	M	Y	Adenocarcinoma	IIIA
US 33	71	M	Y	Adenocarcinoma	IA
US 34		M	Y	Adenocarcinoma	IB
US 38	69	F	Y	Adenocarcinoma	IIIA
US 43	73	M	Y	Adenocarcinoma	IIIA
US 46	43	F	Y	Large cell carcinoma	IV
US 47	47	F	Y	Large cell carcinoma	IV
US 48	51	F	Y	Large cell carcinoma	IV
US 52	70	F	N	Large cell carcinoma	IB
US 57	77	F	N	Large cell carcinoma	IIA
US 58	75	M	Y	Large cell carcinoma	IIA
US 59	63	M	Y	Large cell carcinoma	IIB
US 62	46	F	Y	Large cell carcinoma	IIIB
US 67	60	M	Y	Large cell carcinoma	

US 70	76	F	Y	Squamous cell carcinoma	IA
US 71	72	F	Y	Squamous cell carcinoma	IA
US 73	83	M	Y	Squamous cell carcinoma	IA
US 75	63	M	Y	Squamous cell carcinoma	IA
US 76	69	M	Y	Squamous cell carcinoma	IA
US 82	53	F	Y	Squamous cell carcinoma	IB
US 84	72	M	Y	Squamous cell carcinoma	IB
US 86	82	M	Y	Squamous cell carcinoma	IB
US 90	60	F	Y	Squamous cell carcinoma	IIA
US 93	61	M	Y	Squamous cell carcinoma	IIB
US 97	69	M	Y	Squamous cell carcinoma	IIIA
US 99	68	M	Y	Squamous cell carcinoma	IIIA
US 113	72	M	Y	Large/Adeno	IB
US 114	72	M	Y	Adeno/Squamous	IIB
US 115	52	M	Y	Adeno/Squamous	IIIA
US 116	59	M	Y	Adenocarcinoma	
US 117	73	F	Y	Adenocarcinoma	
US 118	70	F	Y	Adenocarcinoma	
US 119	78	F	N	Adenocarcinoma	
US 120	70	F	Y	Carcinoid tumor	
US 121	65	F	Y	Squamous cell carcinoma	
US 122	59	F	Y	Adenocarcinoma	
US 123	63	M	Y	Adenocarcinoma	
US 124	65	M	Y	Squamous cell carcinoma	
US 125	53	F	Y	Adenocarcinoma	
US 126	74	F	N	Carcinoid tumor	
US 127	61	M	Y	Squamous cell carcinoma	
US 128	67	M	Y	Squamous cell carcinoma	
US 129	58	M	Y	Squamous cell carcinoma	
US 130	79	M	N	Adenocarcinoma	
US 131	63	F	Y	Adenocarcinoma	
US 132	73	F	Y	Adenocarcinoma	
US 133	64	F	Y	Squamous cell carcinoma	
US 134	64	M	Y	Squamous cell carcinoma	
US 135	66	M	Y	Squamous cell carcinoma	
US 136	78	F	Y	Squamous cell carcinoma	
US 137	75	F	Y	Squamous cell carcinoma	
US 138	64	F	Y	Squamous cell carcinoma	
US 139	65	F	Y	Squamous cell carcinoma	
US 140	49	M	Y	Squamous cell carcinoma	
US 141	64	M	N	Squamous cell carcinoma	

US 142	66	M	N	Squamous cell carcinoma	

Open boxes: information not available

Supplementary Table 2. Multiplex PCR-amplification primers

Gene	Exon #	Forward (5′to 3′)	Reverse (5′to 3′)
MET	2	GACAACTGAACTGCTCTCGCCTTGAACC	GAGAATATGCAGTGAACCTCCGACTGTATG
	2	GACTGGGCCTGTGCTGGAACACC	GATGAAAGGACTTTGGCTCCCAGGGC
	2	GCCCTGGGAGCCAAAGTCCTTTCATC	CACTCCAGAGGCATTTCCATGTAGGAATGC
	2	CATGTCTTTCCCCACAATCATACTGCTGA	CTTTTCTGTGAGAATACACTCCAGAGGC
	2	CAGGTTCTGTTCCATAAACTCTGGATTGC	CCTATTAAAGCAGTGCTCATGATTGGGTCCG
	3	TGATTATCCTTGCCATTATCCTCCAGGCTCTG	ACCAGATAGAACAGACACAGCTACTCTCAG
	4	GGTCTTCAGTTCAAACACCCACAAGC	GCCAAGTGACACTGGTTGTAAATATGC
	14	GGGCCCATGATAGCCGTCTTTAACAAGC	TGTGTCAAATACTTACTTGGCAGAGGTAAATACTTCC
	15	GCTCTTCCTGTTTCAGTCCCCATTAAATGAGG	CACCATTGTCTAAGTTCCTAATCTGCAAAGGCC
	16	CCCCCTTACTAATGAGGGCTCTGAGGG	GTTACGCAGTGCTAACCAAGTTCTTTC
	17	CCCTCAGGACAAGATGCTAACTGTGTGG	GGGATGGCTGGCTTACAGCTAGTTTGC
	18	ACTCCTGGCCTCAAGCCATCCTCTC	GGATTGTGGCACAGAGATTCTGATACTTAC
	19	CTCAGCCTGTTGAATTGGCAATGTCAATGTC	CAGAGATAACCAATACATTACCACATCTGACTTGG
	20	GAGACCCTTTGAAGGCAGGCATTTC	GCCAAGTTTAGTTACCAAGACCTACTGATTTC
EGFR	18	TGCTTTCCAGCATGGTGAGGGCTG	ATATACAGCTTGCAAGGACTCTGGGCTCC
	19	CAGCATGTGGCACCATCTCACAATTGC	GCAGCTGCTCTGCTCTAGACCCTG
	20	ACCATGCGAAGCCACACTGACGTG	AGACCGCATGTGAGGATCCTGGCTC
	21	CTTCCCATGATGATCTGTCCCTCACAGC	GGAGAGCATCCTCCCCTGCATGTGT

KRAS2	1	GGTACTGGTGGAGTATTTGATAGTG	GAATGGTCCTGCACCAGTAATATG
TP53	1, 2	TGACCCAGGGTTGGAAGTGTCTCATG	CCCAGCCCAACCCTTGTCCTTAC
	3	AGGGTGAAGAGGAATCCCAAAGTTCCAAAC	GGTCCTCTGACTGCTCTTTTCACCCATC
	4, 5	GGGAGGTCAAATAAGCAGCAGGAGAAAGC	GTGCCCTGACTTTCAACTCTGTCTCCTTC
	6	TGGAGCTTGCAGTGAGCTGAGATCAC	GGATGTGATGAGAGGTGGATGGGTAGTAG
	7, 8	GACAAGGGTGGTTGGGAGTAGATGGAG	GGAAACTTTCCACTTGATAAGAGGTCCCAAG
	9	GTCAGCTGTATAGGTACTTGAAGTGCAG	AGCTGCCTTTGACCATGAAGGCAG
	10	TGGGCAACAAGAGTGAAACTCCGTC	GACCCAAAACCCAAAATGGCAGGG

Supplementary Table 3. MET mutations with known SNP IDs

MET Mutation	SNP ID	SNP type
S178S	rs35775721	Synonymous
N375S	rs33917957	Non-synonymous
I377I	rs28444388	Synonymous
R988C	rs34589476	Non-synonymous
D1304D	rs41736	Synonymous

Supplementary Table 4. Computational analysis of MET sema domain non-synonymous mutations

Mutations		Amino acid property	Potential H-bond (n)	ω value /z score [a]	Probability to be binding Residue [b]	Δ Potential energy (DOPE) [c]	RMSD (Å)[d]
168	E	Polar/negative	2	0.132/0.07	0.71	-0.002	0.15
	D	Polar/negative	1				
229	L	Hydrophobic	0	0.113/0.18	0.59	0.003	0.70
	F	Hydrophobic/aromatic	0				
323	S	Polar	3	0.125/0.11	0.21	0	0.71
	G	Hydrophobic	2				
347	A	Hydrophobic	0	0.040/0.59	0.0	0.003	0.70
	T	Hydrophobic/polar	0				
355	E	Polar/negative	2	0.078/0.37	0.08	0.002	0.68
	K	Polar/positive	2				
362	M	Hydrophobic	0	0.078/0.37	0.94	0.004	0.70
	T	Hydrophobic/polar	0				
375	N	Polar	2	0.039/0.60	0.62	0	0.25
	S	Polar	1				
431	M	Hydrophobic	0	0.072/0.41	0.82	0	0.60
	V	Hydrophobic	0				
454	N	Polar	3	0.107/0.21	0.37	-0.006	0.60
	I	Hydrophobic	2				

Using 1SHY chain B as template, mutations are modeled by MODELLER and SWISS-model.

[a] The nonsynonymous/synonymous rate ratio ($\omega = d_N/d_S$) was calculated by PAML package, an implementation of the maximum likelihood method for estimating ω values. Homologous sequences were collected from HSSP database and PSI-Blast searching. We repeatedly estimated ω (20 times) using different initial v value that is assigned to all amino acid sites. The initial ω values range from 0.01 to 2.00, at an interval of 0.1.

[b] We used Promate, an interface prediction program which combined many significant interface properties, to predict potential protein binding sites.

[c] Discrete Optimized Protein Energy (DOPE) was used to evaluate the accuracy of models. DOPE is a distance-dependent statistical potential based on a physical reference state that accounts for the finite size and spherical shape of proteins.

[d] Root Mean Square Deviation (RMSD) values were calculated from Cα carbon of 1SHY B chain and mutation models.