Supplementary Materials: L1198F Mutation Resensitizes Crizotinib to ALK by Altering the Conformation of Inhibitor and ATP Binding Sites

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Table S1. Predicted binding energy of anaplastic lymphoma kinase (ALK)–crizotinib and ALK–lorlatinib complexes.

PDB ID	Mutation	Inhibitor	Ki	IC_{50}	AUTODOCK (kJ/mol)	Hawkins_GB/SA (kJ/mol)	MM/PBSA (kJ/mol)
5AA8	C1156Y L1198F	Lorlatinib	61	67	123.7	−77.44	−26.66
5AAB	C1156Y L1198F	Crizotinib	0.6	0.6	25.9	−472.74	−231.88
Folds of change (crizotinib/lorlatinib)	C1156Y L1198F	-	111.7	111.7	4.8	6.1	8.7

GB/SA: Generalized Born surface area; MM/PBSA: Molecular mechanics Poisson–Boltzmann surface area; PDB: Protein Data Bank.

Table S3. Key amino acid residues contributing to the electrostatic energy.

Position	PDB ID	Electrostatic Energy (kcal/mol)			Folds of Change			Average
		5–10 ns	20–25 ns	25–30 ns	5–10 ns	20–25 ns	25–30 ns	
1124	5AA8	−10.74	−10.98	−10.90	−10.90	6.73	5.74	5.60
	5AAb	−46.58	−73.95	−62.56				
1150	5AA8	−79.38	−69.78	−72.11	1.24	1.08	1.09	1.14
	5AAb	−64.01	−64.55	−66.09				
1119	5AA8	−7.22	−8.98	−8.61	1.26	1.07	1.07	1.14
	5AAb	−9.1	−9.63	−9.25				
1203	5AA8	−1.67	−5.4	−2.28	11.63	3.68	8.28	7.86
	5AAb	−19.42	−19.88	−18.87				
1210	5AA8	4.65	13.43	16.47	2.74	3.82	24.58	8.55
	5AAb	−12.73	3.52	0.67				

Table S4. Trends of root-mean-square fluctuation (RMSF) change of the key amino acid residues in ALK.

Position	PDB ID	RMSF (nm)			Interval Coefficient		RMSF Coefficient	Relative Folds of Change			Average
		5–10 ns	20–25 ns	25–30 ns	5-10 ns/20–25 ns	20–25 ns/25–30 ns		5–10 ns	20–25 ns	25–30 ns	
1270	5AA8	0.0413	0.0365	0.036	−1	1	0				
	5AAB	0.0401	0.0376	0.0397							
1124	5AA8	0.1004	0.102	0.0985	1	1	2	1.53	2.34	1.53	1.80
	5AAB	0.1538	0.2382	0.1511							
1150	5AA8	0.0496	0.0496	0.0461	1	−1	−2				
	5AAB	0.0483	0.0462	0.051							
1119	5AA8	0.0512	0.0455	0.0548	−1	−1	0				
	5AAB	0.0501	0.0591	0.0414							
1203	5AA8	0.0405	0.042	0.0448	1	−1	2				
	5AAB	0.0462	0.0537	0.0422							
1210	5AA8	0.0652	0.0612	0.0544	1	1	0	1.04	1.67	1.16	1.29
	5AAB	0.0678	0.1023	0.063							
1249	5AA8	0.0412	0.0393	0.0367	−1	1	0				
	5AAB	0.0366	0.0433	0.0384							
1278	5AA8	0.0812	0.0739	0.0781	−1	1	0				
	5AAB	0.0773	0.1089	0.088							
1279	5AA8	0.1008	0.098	0.0845	−1	1	0				
	5AAB	0.0915	0.1336	0.113							