Electronic Supplementary Material (ESI) for Physical Chemistry Chemical Physics.

Supporting Information

Atomistic Insight into Inhibition Mechanisms of Suppressors of Cytokine Signaling on Janus Kinase

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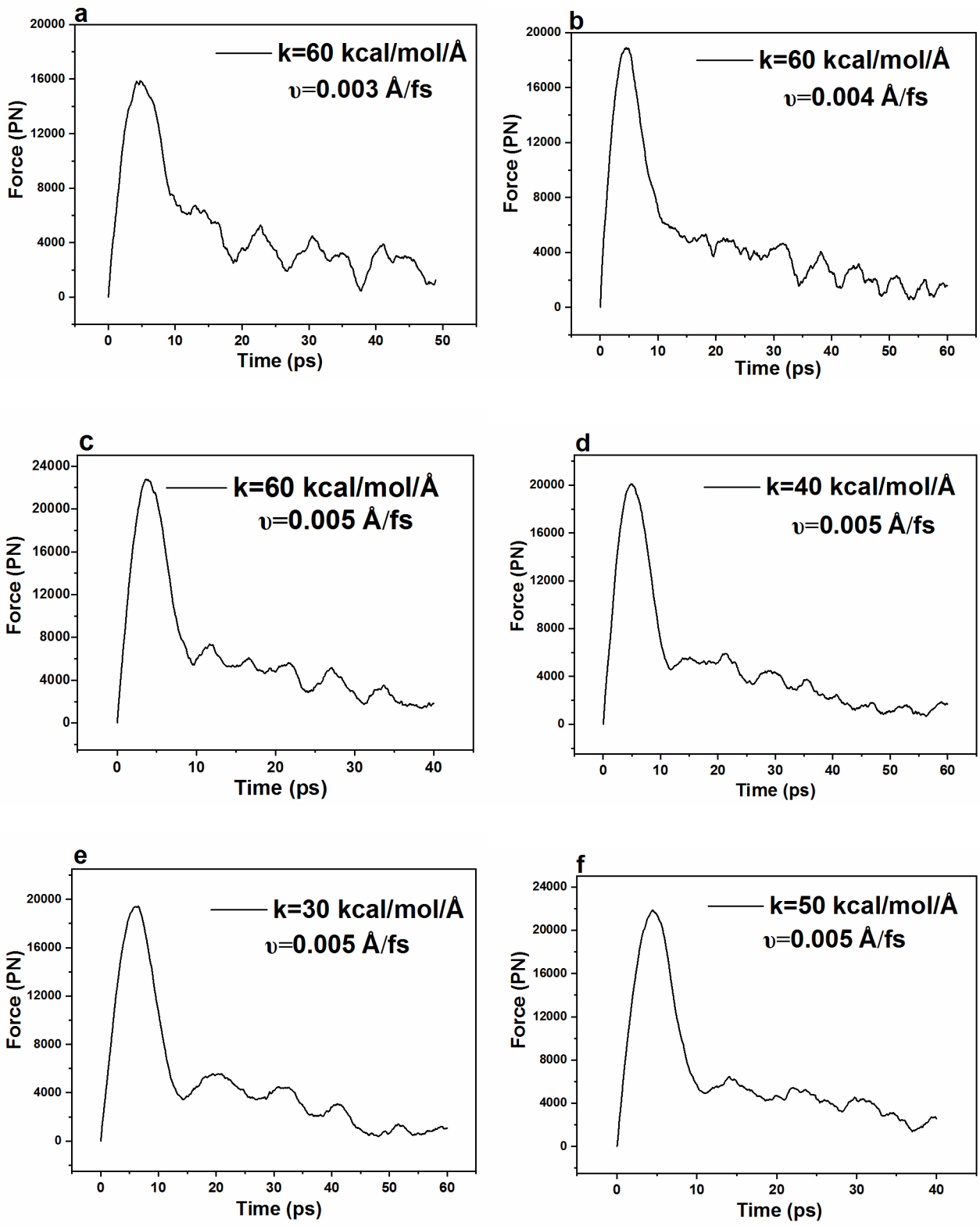


Fig S1. The test of a series of spring constants K and speed υ.

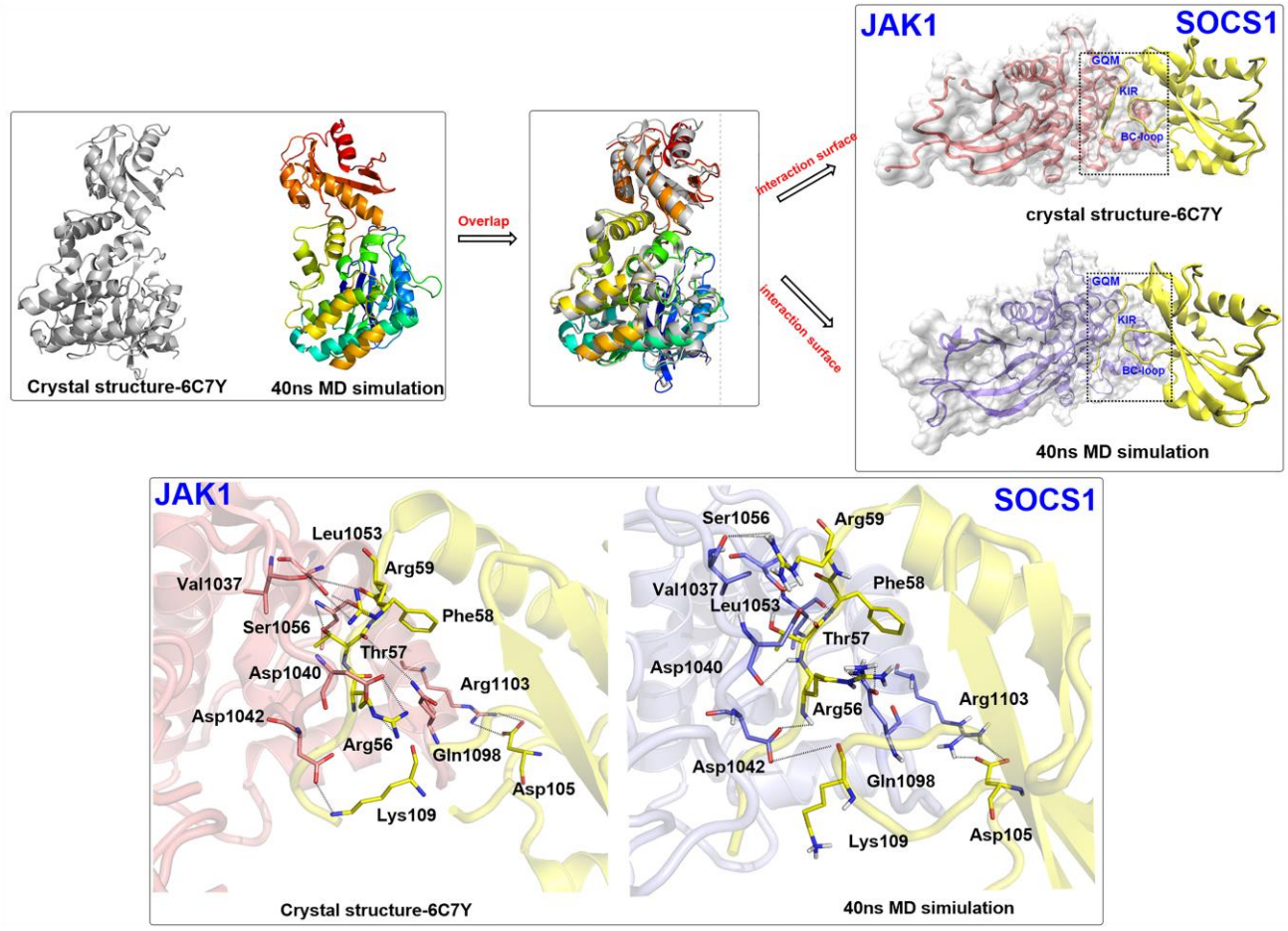


Fig S2. The overlap and interface of crystal structure observed by experiment and equilibrium structure obtained by MM MD simulations.

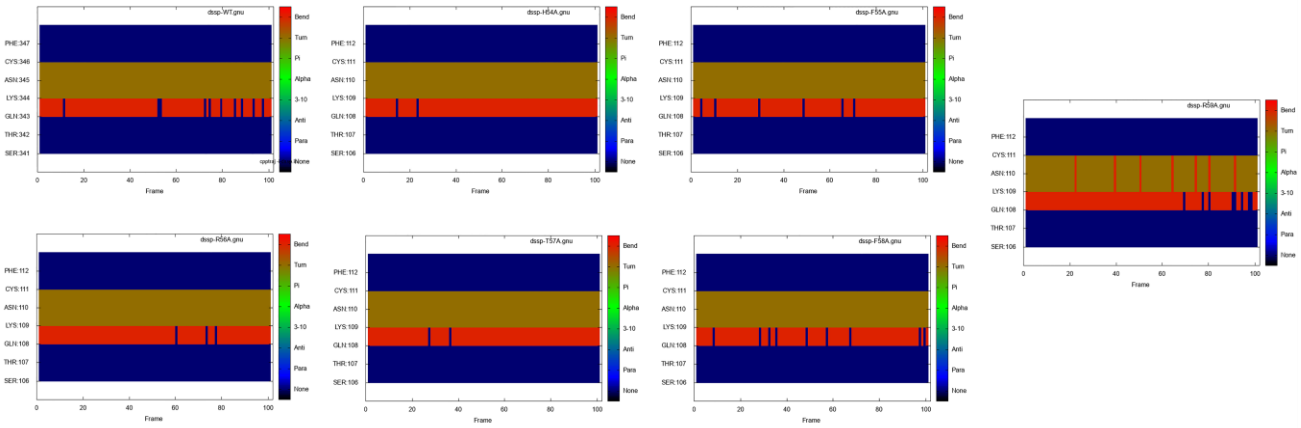
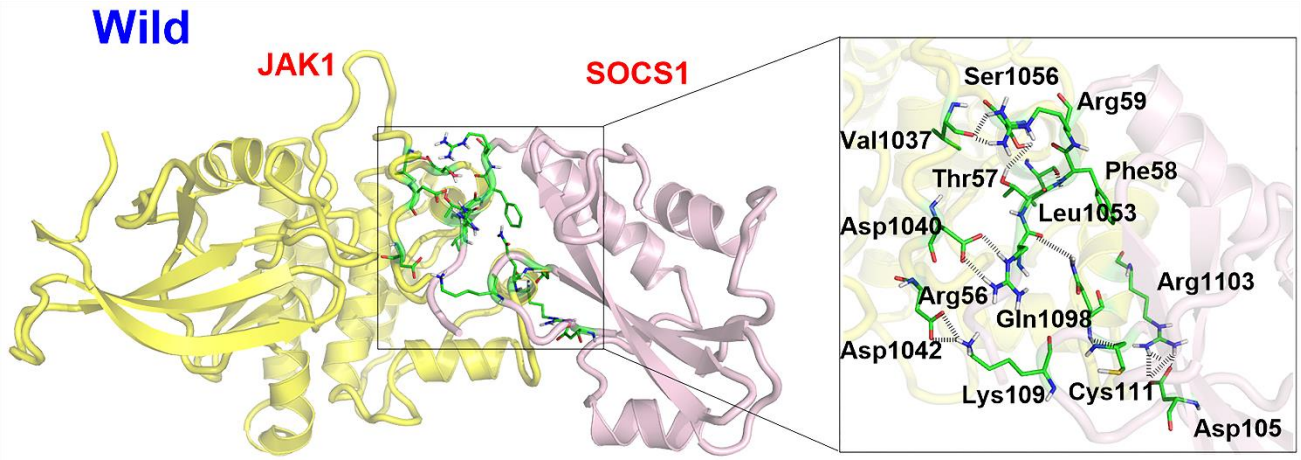


Fig S3. Secondary structures of Ser106-Phe112 of SOCS1 in JAK1-SOCS1 systems (100 snapshots) during molecular dynamics (MD) simulation by using DSSP method.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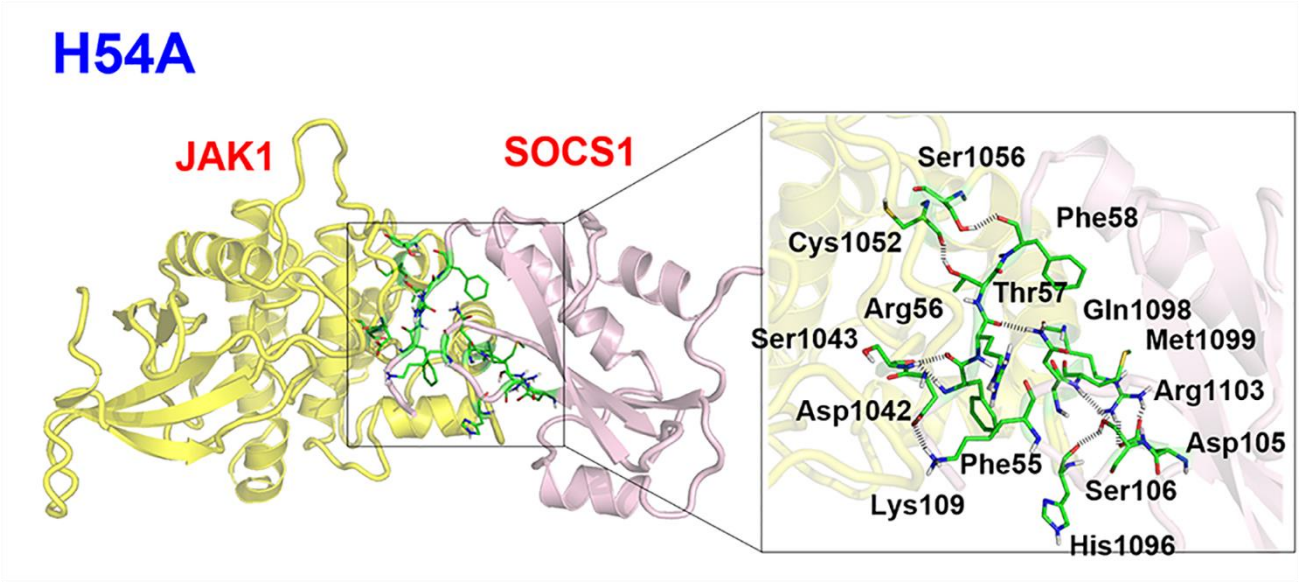
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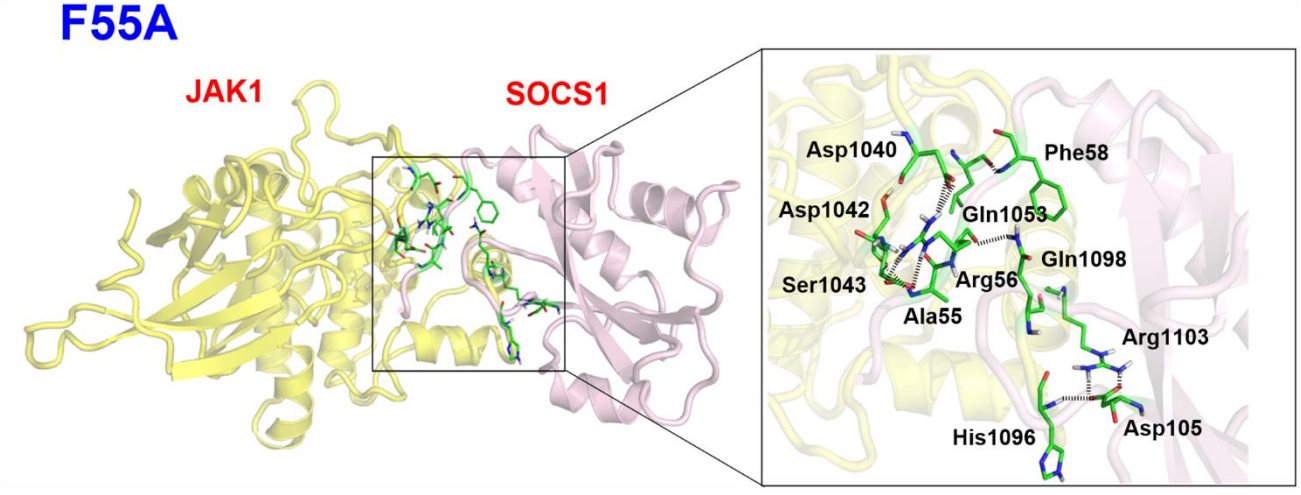
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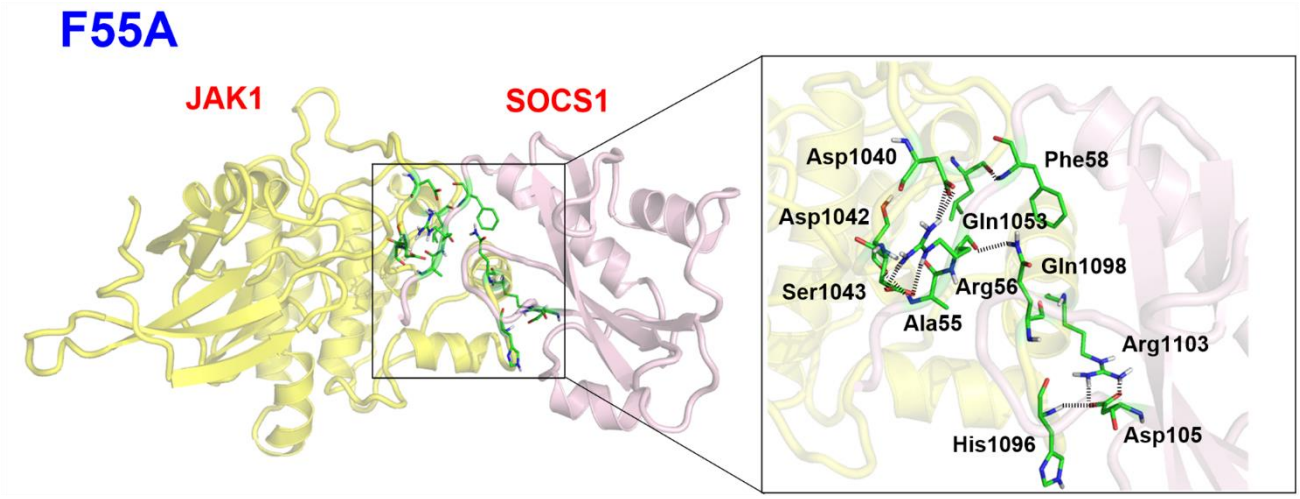
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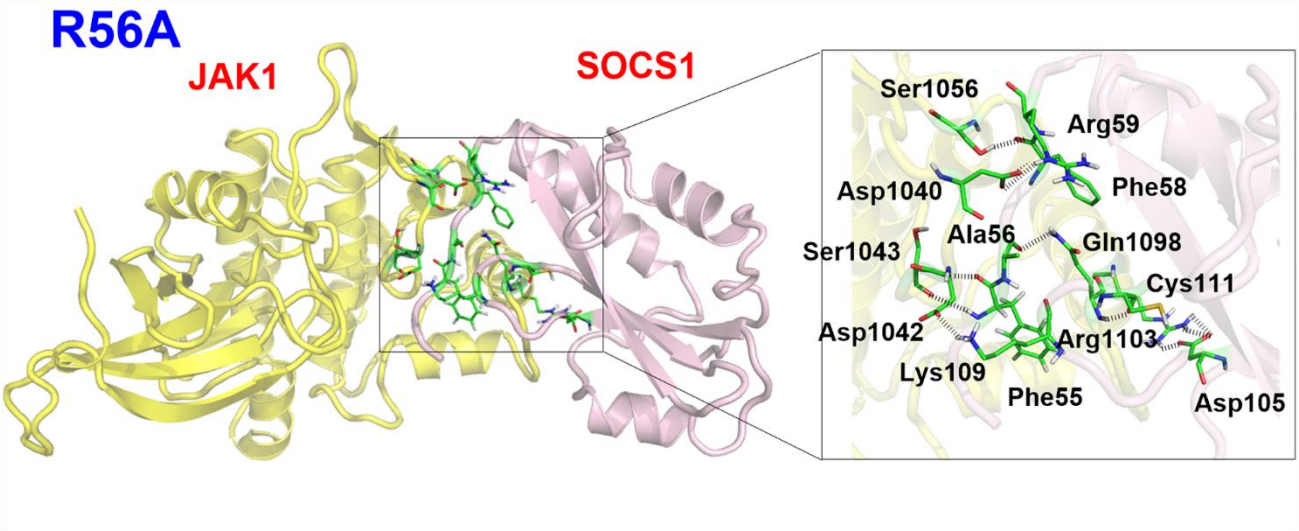
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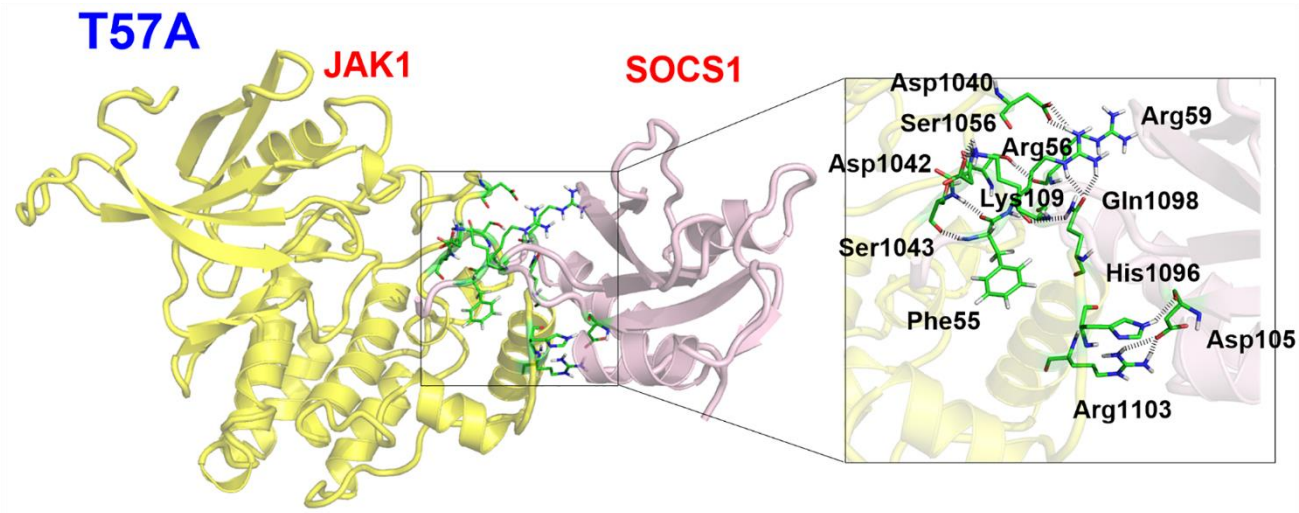
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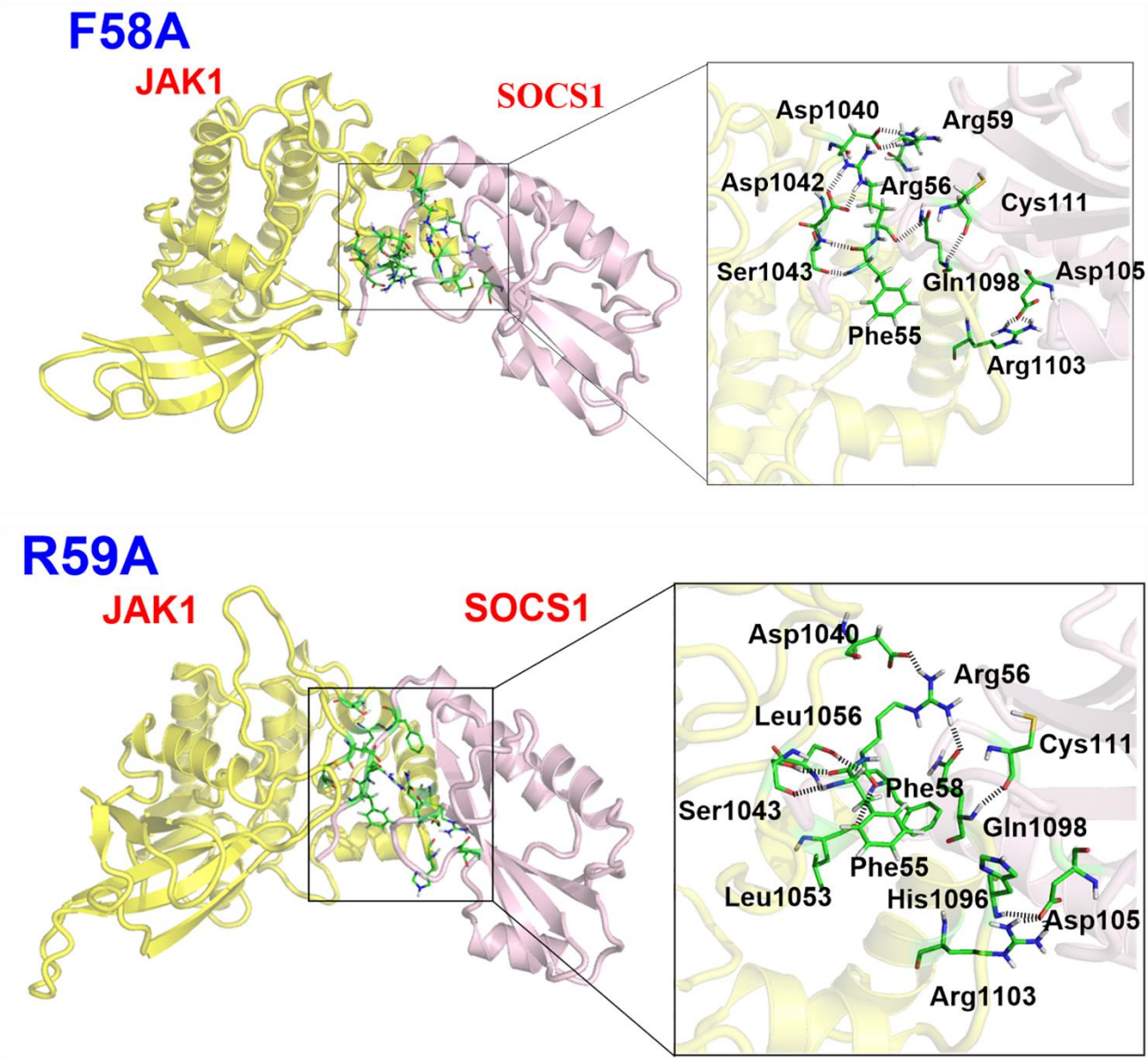
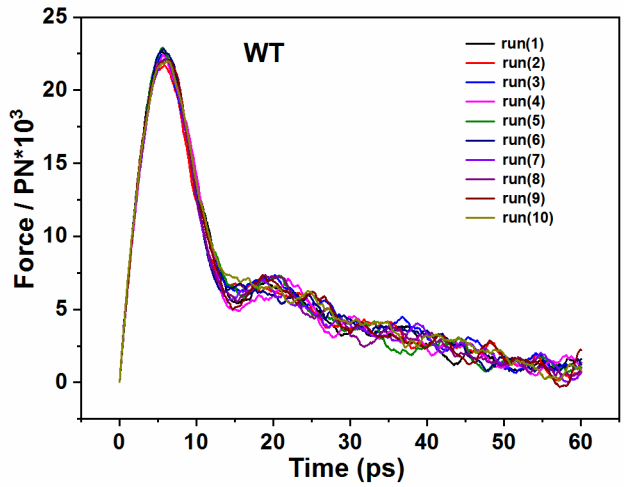


Fig S4. The details of the interaction between JAK1 and SOCS1 for wild and mutant systems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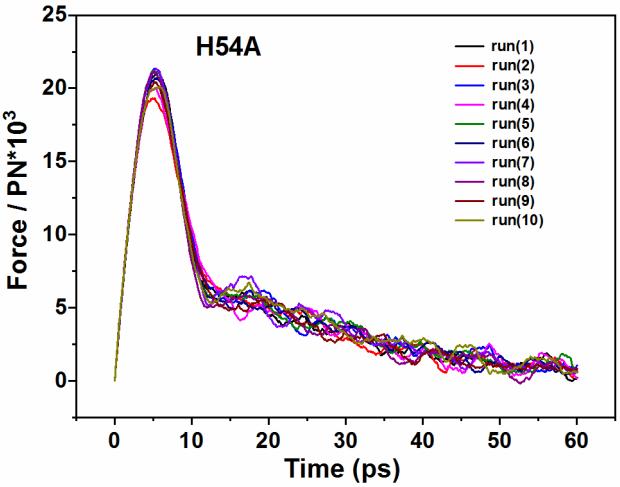
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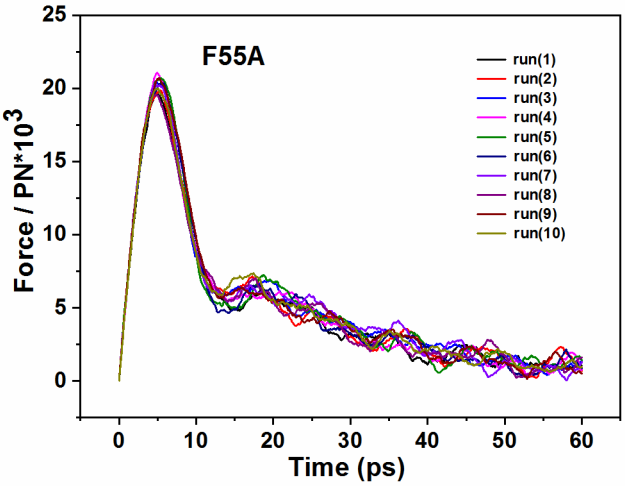
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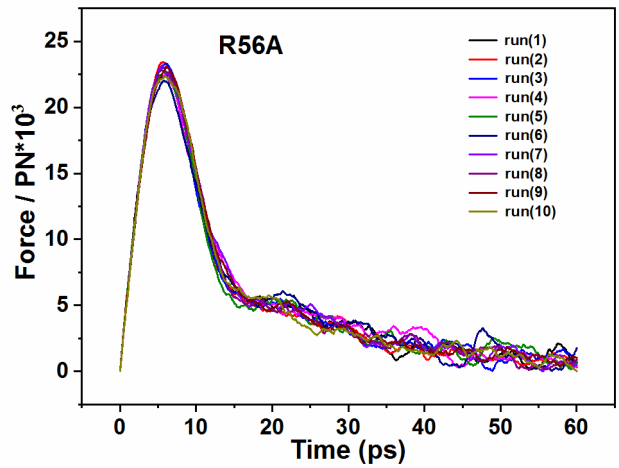
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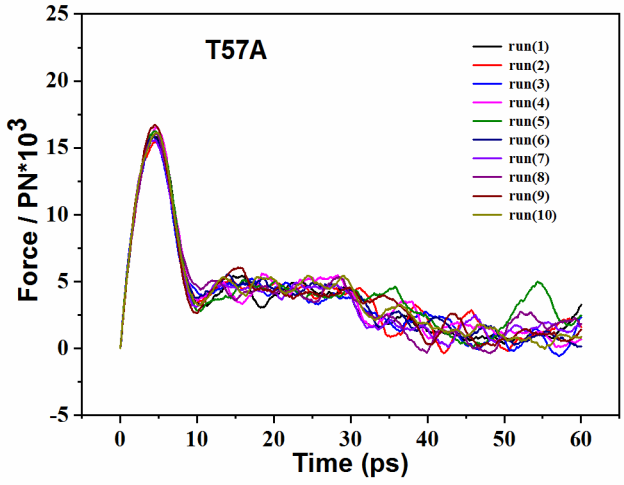
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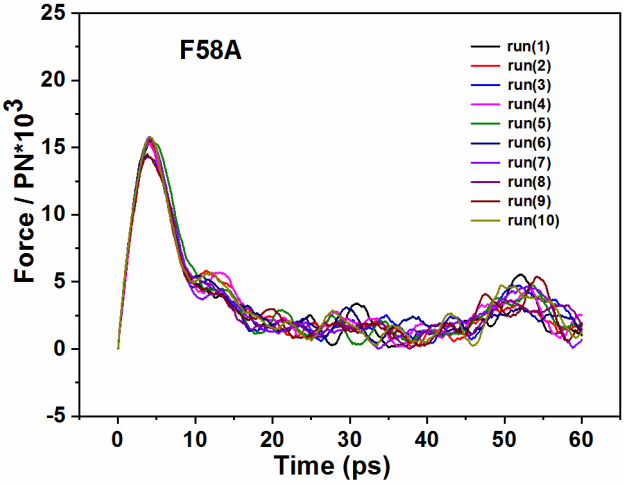
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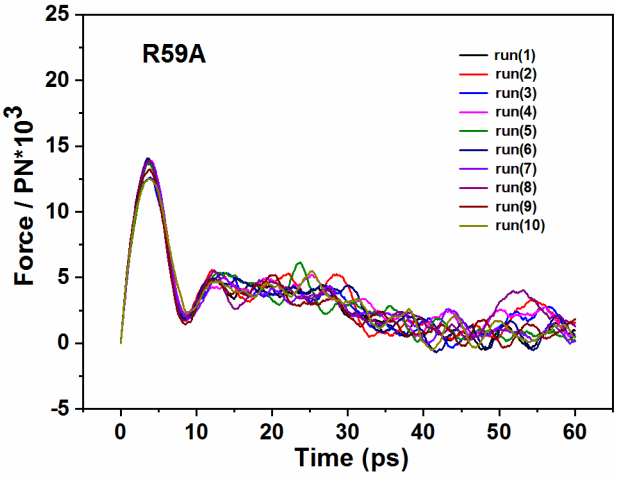

Fig S5. The SMD simulations of wild and mutant systems.

Table S1. The Binding Information of the Wild Systems

	Binding couples		MD	
Wild	DONOR	ACCEPTORH	Distance(Å)	Binding type
	Arg56@O	HE22-NE2@Gln1098	2.90	H-bond
	Ser1056@OG	HG1-OG1@Thr57	1.87	H-bond
	Val1037@O	HH22-NH2@Arg59	1.71	H-bond
	Val1037@O	HH12-NH1@Arg59	1.91	H-bond
	Asp105@OD2	HH12-NH1@ Arg1103	2.75	SB
	Cys111@O	H- N@Gln1098	2.84	H-bond
	Asp105@OD2	HH22- NH2@Arg1103	2.80	SB
	Leu1053@O	H- N@Phe58	2.87	H-bond
	Asp105@OD1	HH22- NH2@Arg1103	2.84	SB
	Asp1042@OD2	HZ3-NZ@Lys109	2.12	SB
	Asp1042@OD1	HZ3-NZ@Lys109	1.85	SB
	Asp105@OD1	HH12- NH1@Arg1103	2.87	SB
	Asp1040@OD2	HH21-NH2@Arg56	1.95	SB
	Asp1040@OD1	HE -NE@Arg56	1.85	SB

Table S2. The Binding Information of the H54A Systems

Binding couples			MD	
H54A	DONOR	ACCEPTORH	Distance(Å)	Binding type
	Ser1043@O	H-O @Phe55	1.98	H-bond
	Phe55@O	H-O @Ser1043	2.05	H-bond
	Cys1052@OG	HG1-OG1@Thr57	2.19	H-bond
	Phe58@O	HG-OG @ Ser1056	1.83	H-bond
	Arg56@O	HE22-NE2@ Gln1098	2.03	H-bond
	Asp1042@OD2	HZ3-NZ @ Lys109	1.88	SB
	His1096@O	HG-OG @ Ser106	1.97	H-bond
	Ser106@OG	H-N @ Met1099	2.20	H-bond
	Asp105@OD1	HH22-NH2@ Arg1103	1.77	SB
	Asp105@OD2	HH12-NH1@ Arg1103	2.13	SB

Table S3. The Binding Information of the F55A Systems

	Binding couples		MD	
F55A	DONOR	ACCEPTORH	Distance(Å)	Binding type
	Asp1040@OD2	HH11-NH1@Arg56	1.98	SB
	Asp1040@OD1	HH12-NH1@Arg56	2.98	SB
	Asp1042@OD2	HH21-NH2@ Arg56	1.93	SB
	Asp1042@OD1	HE-NE@Arg56	2.18	SB
	Ala55@O	H-O@Ser1043	2.01	H-bond
	Ser1043@O	H-O@Ala55	2.16	H-bond
	Arg56@O	HE22-NE@Gln1098	1.36	H-bond
	Lue1053@O	H-O@Phe58	2.07	H-bond
	Asp105@OD2	H-N@His1096	1.94	SB
	Asp105@OD1	HH22-NH2@Arg1103	1.68	SB
	Asp105@OD2	HH12-NH1@Arg1103	1.66	SB

Table S4. The Binding Information of the R56A Systems

	Binding couples		MD	
R56A	DONOR	ACCEPTORH	Distance(Å)	Binding type
	Asp1040@OD1	HH21-NH2@Arg59	2.26	SB
	Asp1040@OD1	HE-NE@ Arg59	1.81	SB
	Ser1043@O	H-O @Phe55	2.59	H-bond
	Phe55@O	H-O@ Ser1043	2.05	H-bond
	Phe58@O	H-O@ Ser1056	1.64	H-bond
	Ala56@OD2	HE22-NE2@Gln1098	2.38	H-bond
	Asp1042@OD1	HZ2-NZ@ Lys109	2.01	SB
	Lys111@O	H-N@ Gln1098	1.96	H-bond
	Asp105@OD2	HH12-NH1@Arg1103	1.83	SB
	Asp105@OD2	HH22-NH2@Arg1103	1.75	SB
	Asp105@OD1	HH22-NH2@Arg1103	2.61	SB

Table S5. The Binding Information of the T57A Systems

	Binding couples		MD	
T57A	DONOR	ACCEPTORH	Distance(Å)	Binding type
	Asp1040@OD2	HH11-NH1@ Arg56	2.11	SB
	Asp1040@OD1	HH11-NH1@ Arg56	2.17	SB
	Ser1043@O	H-O@Phe55	1.91	H-bond
	Phe55@O	H-O@Ser1043	1.67	H-bond
	Arg59@O	HG-OG@Ser1056	2.14	H-bond
	Gln1098@OE1	HE-NE@Arg56	2.01	H-bond
	Gln1098@OE1	HH21-NH2@Arg56	2.01	H-bond
	Arg56@O	HE22-NE@Gln1098	2.87	H-bond
	Asp1042@OD1	HZ3-NZ@Lys109	1.93	SB
	Asp105@O	HE2-NE@His1096	2.05	SB
	Asp105@OD2	HH12-NH1@Arg1103	2.39	SB
	Asp105@OD2	HH22-NH2@Arg1103	1.79	SB

Table S6. The Binding Information of the F58ASystems

Binding couples			MD	
F58A	DONOR	ACCEPTORH	Distance(Å)	Binding type
	Asp1040@OD1	Arg59@HH21-NH2	1.93	SB
	Asp1040@OD2	Arg59@HE-NE	2.00	SB
	Asp1042@OD2	Arg56@HH21-NH2	1.76	SB
	Asp1042@OD1	Arg56@HE-NE	1.92	SB
	Phe55@O	Ser1043@H-N	1.79	H-bond
	Ser1043@O	Phe55@H-N	1.97	H-bond
	Arg56@O	Gln1098@HE22-NE	2.44	H-bond
	Asp105@OD2	Arg1103@HH12-NH1	1.68	SB
	Asp105@OD1	Arg1103@HH22-NH2	2.27	SB
	Cys111@O	Gln1098@H-N	2.36	H-bond

Table S7. The Binding Information of the R59A Systems

	Binding couples		MD	
R59A	DONOR	ACCEPTORH	Distance(Å)	Binding type
	Ser1043@O	H-O@ Phe55	1.94	H-bond
	Asp1040@OD2	HH11-NH1@Arg56	1.74	SB
	Phe55@O	HG-OG@ Ser1043	2.11	H-bond
	Leu1053@O	H-O@ Phe58	2.13	H-bond
	Phe58@O	HG-OG@ Leu1056	1.89	H-bond
	Gln1098@OE1	HH21-NH2 @Arg56	1.81	H-bond
	Asp105@OD2	H-N @ His1096	2.32	SB
	Asp105@OD1	HH22-NH2@ Arg1103	2.22	SB
	Asp105@OD1	HH12-NH1@ Arg1103	1.75	SB
	Cys111@O	H-N @ Gln1098	1.85	H-bond