

# Supporting Information

## Effect of Single-Residue Mutations on CTCF Binding to DNA: Insights from Molecular Dynamics Simulations

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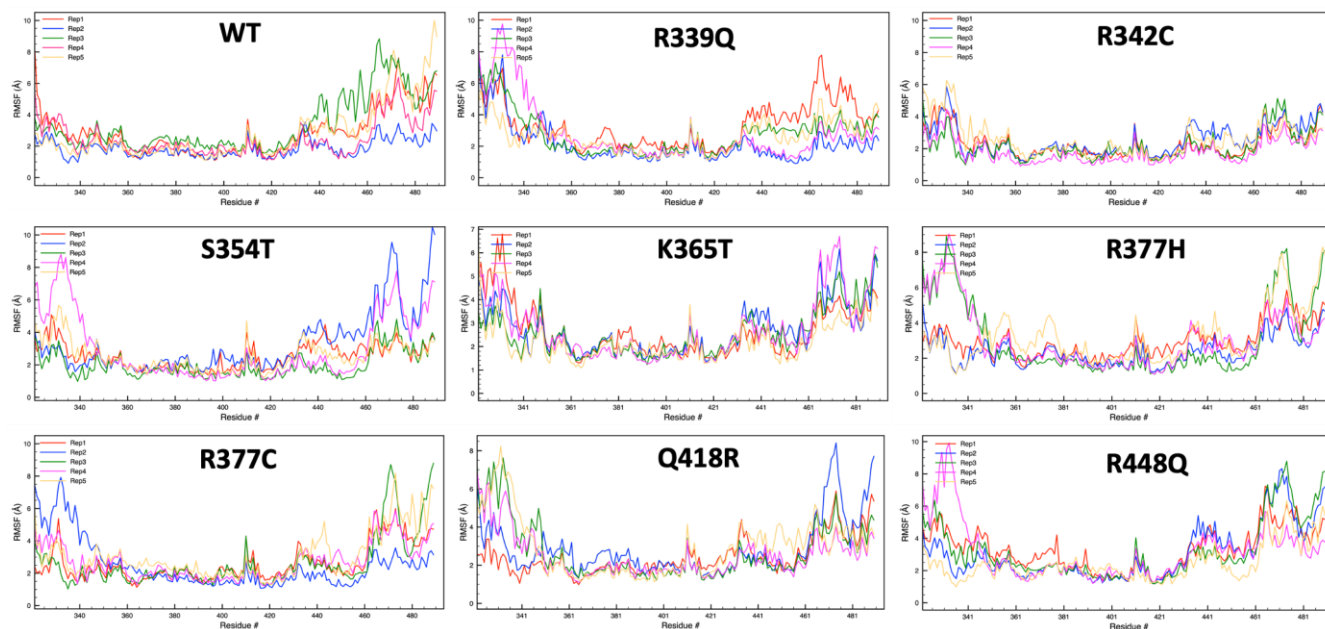
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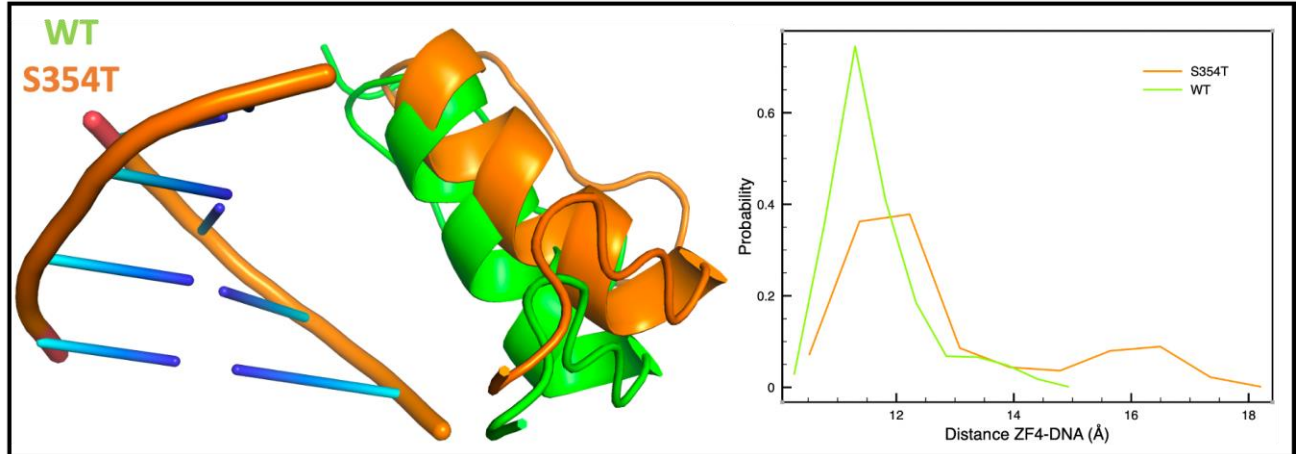
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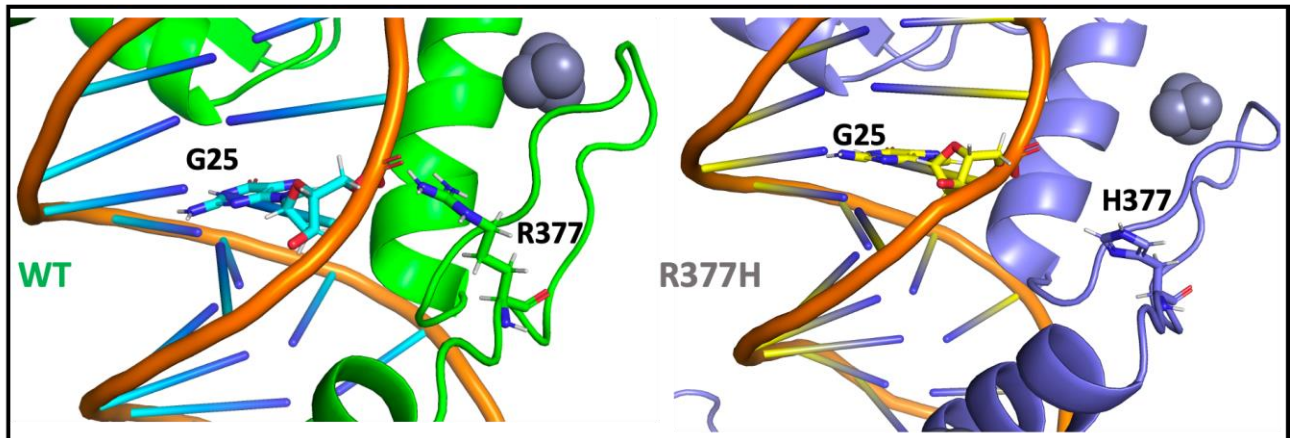
### 1) Supporting Figures



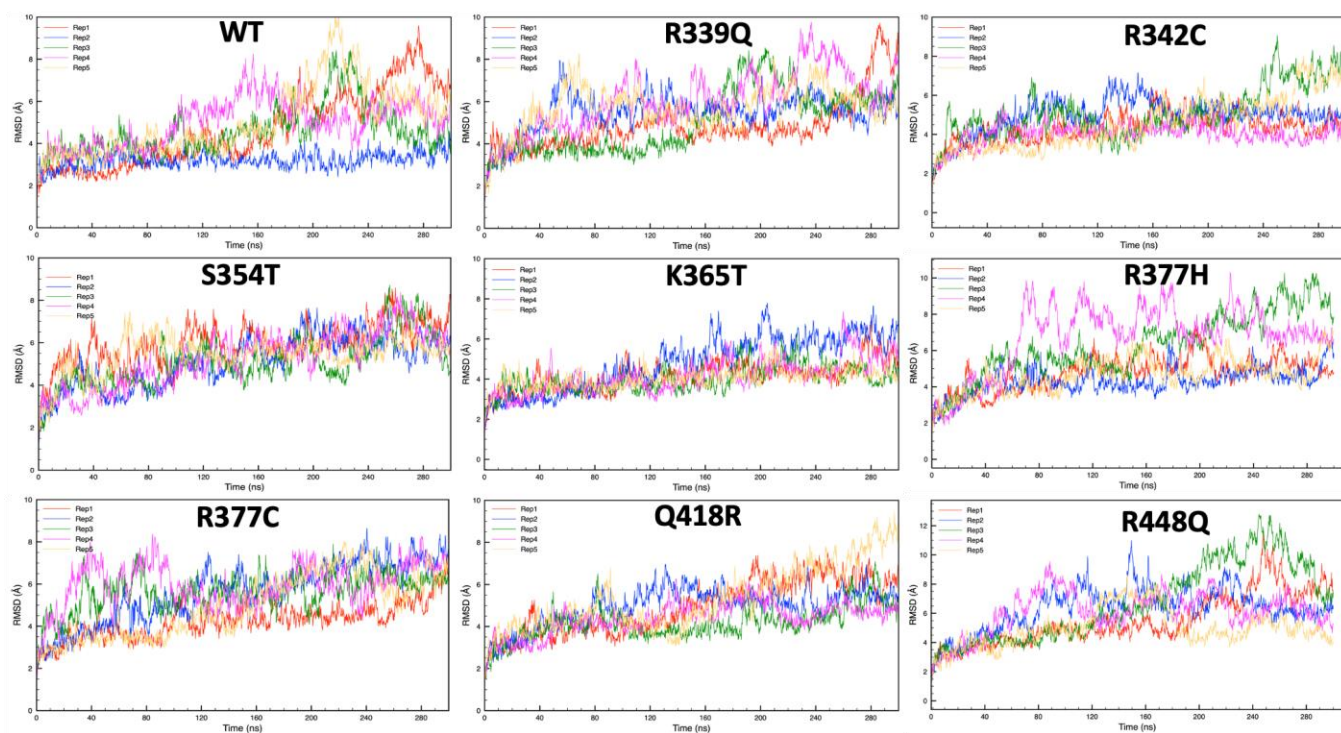
**Supplementary Figure S1.** Root mean squared fluctuation calculated using the last 100 ns of simulation of each of the five replicas of the wildtype and mutant proteins.



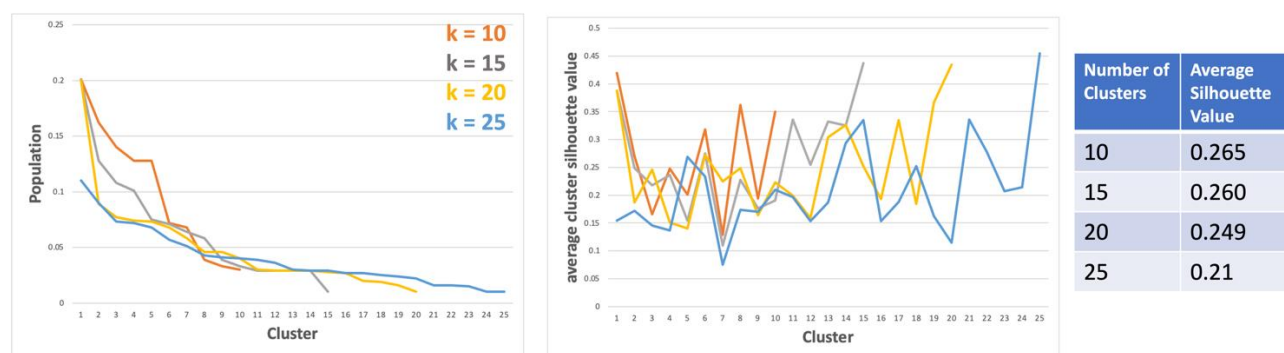
**Supplementary Figure S2.** Left: overlapping between WT and S354T protein showing the movement of ZF4. Right: Probability distribution for the distance between ZF4 and DNA segment containing nucleotides G25, A26, G27, G28, and G29.



**Supplementary Figure S3.** WT and R377H proteins showing the position of the link region between ZF4 and ZF5 shifted away upon the R377H mutation.

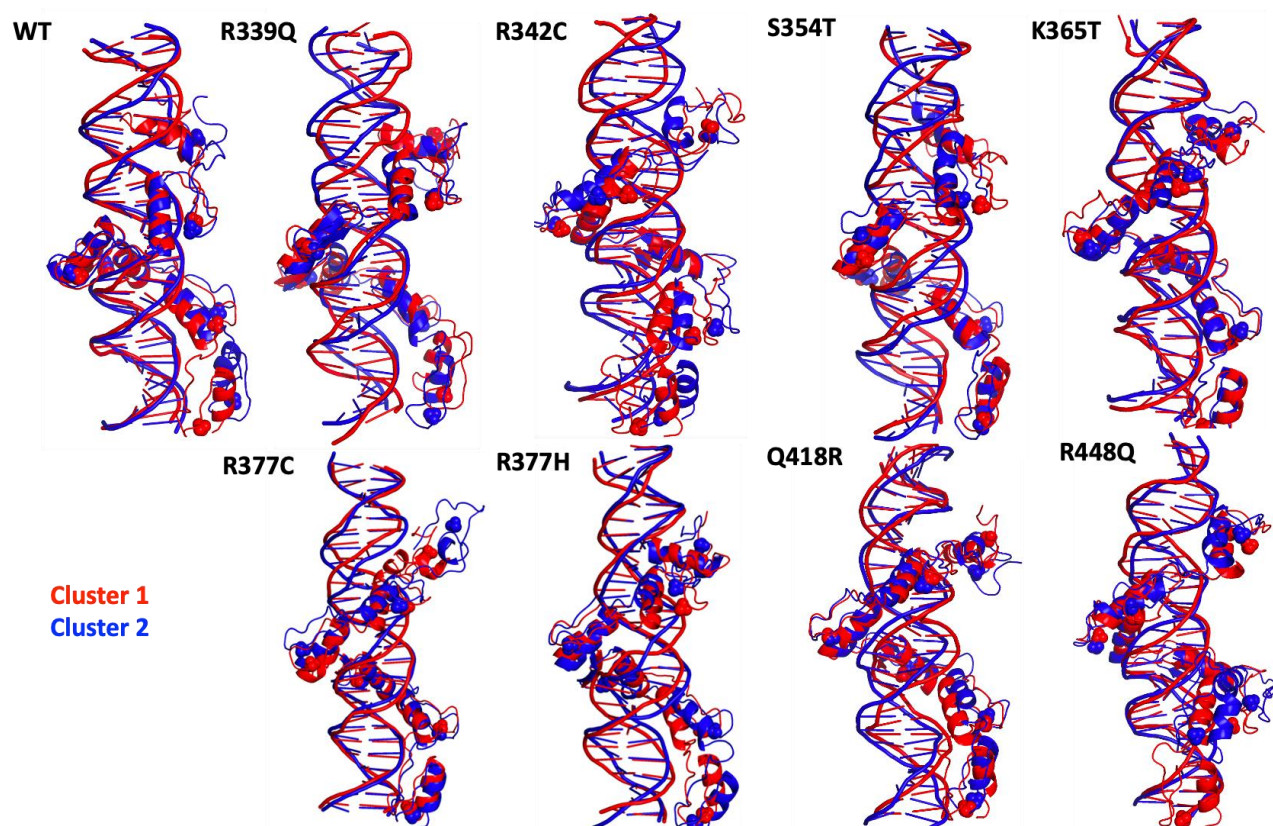


**Supplementary Figure S4.** Backbone root mean squared deviation across each trajectory for each simulated system.

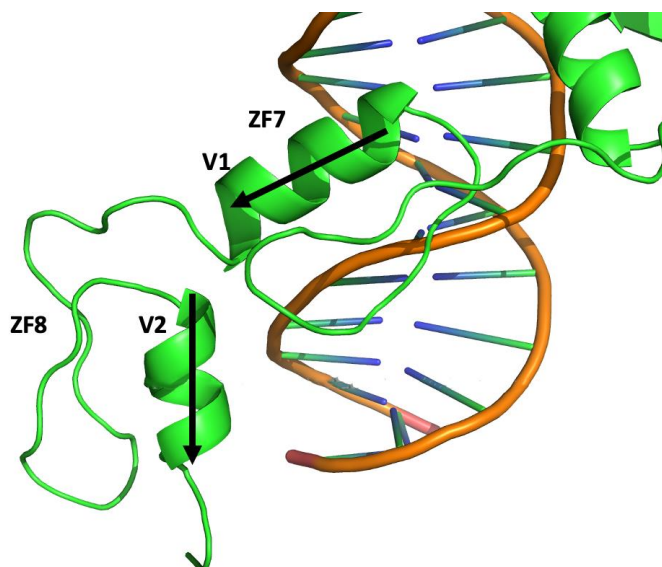


**Supplementary Figure S5.** Clustering analysis with increasing number of clusters. Population and average silhouette value.





**Supplementary Figure S6.** Superposition of the representative structures of clusters 1 and 2 for each system.



**Supplementary Figure S7.** Vectors defined in the  $\alpha$ -helices of ZF7 and ZF8 used to calculate the angle formed between the two fingers.

## 2) Supplementary Tables

**Supplementary Table S1. Secondary structure percentage of ZF3's  $\alpha$ -helix.**

Total Secondary Structure		
Residue	WT	R342C
G335	0.9999	0.6505
E336	0.9956	0.4312
L337	0.9929	0.5263
V338	0.9996	0.9973
R339	1	1
H340	0.9714	0.9977
R341	1	1.0001
R342	1	1.0001
Y343	0.9999	1
K344	0.9999	1
Y345	0.9997	0.9973
K346	0.3008	0.2607
H347	0.1072	0.4617
T348	0.0263	0.2233

**Supplementary Table S2. Cluster populations in fraction for each system simulated.**

	WT	R339Q	R342C	S354T	K365T	R377H	R377C	Q418R	R448Q
<b>Cluster 1</b>	0.201	0.2	0.2	0.2	0.193	0.257	0.17	0.246	0.183
<b>Cluster 2</b>	0.162	0.2	0.199	0.2	0.146	0.117	0.158	0.123	0.173
<b>Cluster 3</b>	0.14	0.141	0.135	0.103	0.142	0.112	0.132	0.111	0.141
<b>Cluster 4</b>	0.128	0.107	0.101	0.102	0.109	0.098	0.128	0.104	0.127
<b>Cluster 5</b>	0.128	0.092	0.076	0.097	0.094	0.086	0.1	0.096	0.119
<b>Cluster 6</b>	0.072	0.075	0.07	0.079	0.091	0.086	0.099	0.085	0.073
<b>Cluster 7</b>	0.068	0.065	0.066	0.066	0.085	0.083	0.071	0.077	0.059
<b>Cluster 8</b>	0.039	0.059	0.065	0.06	0.069	0.059	0.066	0.068	0.05
<b>Cluster 9</b>	0.033	0.033	0.054	0.054	0.05	0.059	0.042	0.053	0.044
<b>Cluster 10</b>	0.03	0.029	0.034	0.039	0.021	0.043	0.034	0.036	0.031