Electronic Supplementary Information

Energy landscape quantifications of histone H3.3 recognition by chaperon DAXX reveal an uncoupled binding specificity and affinity

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1 Hamiltonian

The Hamiltonian is given by the expression:

$$U_{Total} = U_{Local} + U_{Attraction} + U_{Repulsive}$$

1.1 Attraction term

The $U_{Attraction}$ is give by the expression: $U_{Attracition} = U_{LJ}(native contacts)$

$$U_{LJ} = \epsilon_{LJ}[5(\frac{\sigma_{ij}}{r_0})^{12} - 6(\frac{\sigma_{ij}}{r_0})^{10}]$$

We build a native contacts library by collecting all the pairs in the contact map obtained from the reference crystal structures (PDB ID: 4HGA).

1.2 Repulsive interactions

The σ_{NC} is the excluded distance between non-native pairs to provide excluded volume repulsion. The repulsive rail is 4.0 $\mathring{A}$, the $\epsilon_{NC} = 1KJ/mol$. All pairs in γ^{all} were not considered in this term.

$$U_{Repulsive} = \epsilon_{NC}(\frac{\sigma_{NC}}{r_{ij}})^{12}$$

1.3 Local Potential

The Local potential is divided into bond stretching, angle bending, torsion energy.

$$U_{Local} = U_{Bonds} + U_{Angles} + U_{Dihedrals}$$

$$U_{Bonds} = \sum_{bonds} K_b(r - r_0)^2 = 0$$

$$U_{Angles} + U_{Dihedral} = K_\theta(\theta - \theta_0)^2 + K_\phi[(1 - \cos(\phi - \phi_0)) + 0.5(1 - \cos(\phi - \phi_0))]$$

The bonded energies U_{Bonds} are summed over the energy of all co-valent bonds. $K_r = 10000KJ/(mol\ nm^2)$ is the bond constant. The angle constant $K_\theta = 20kJ/mol$. The $K_\phi = 0.8kJ/mol$.
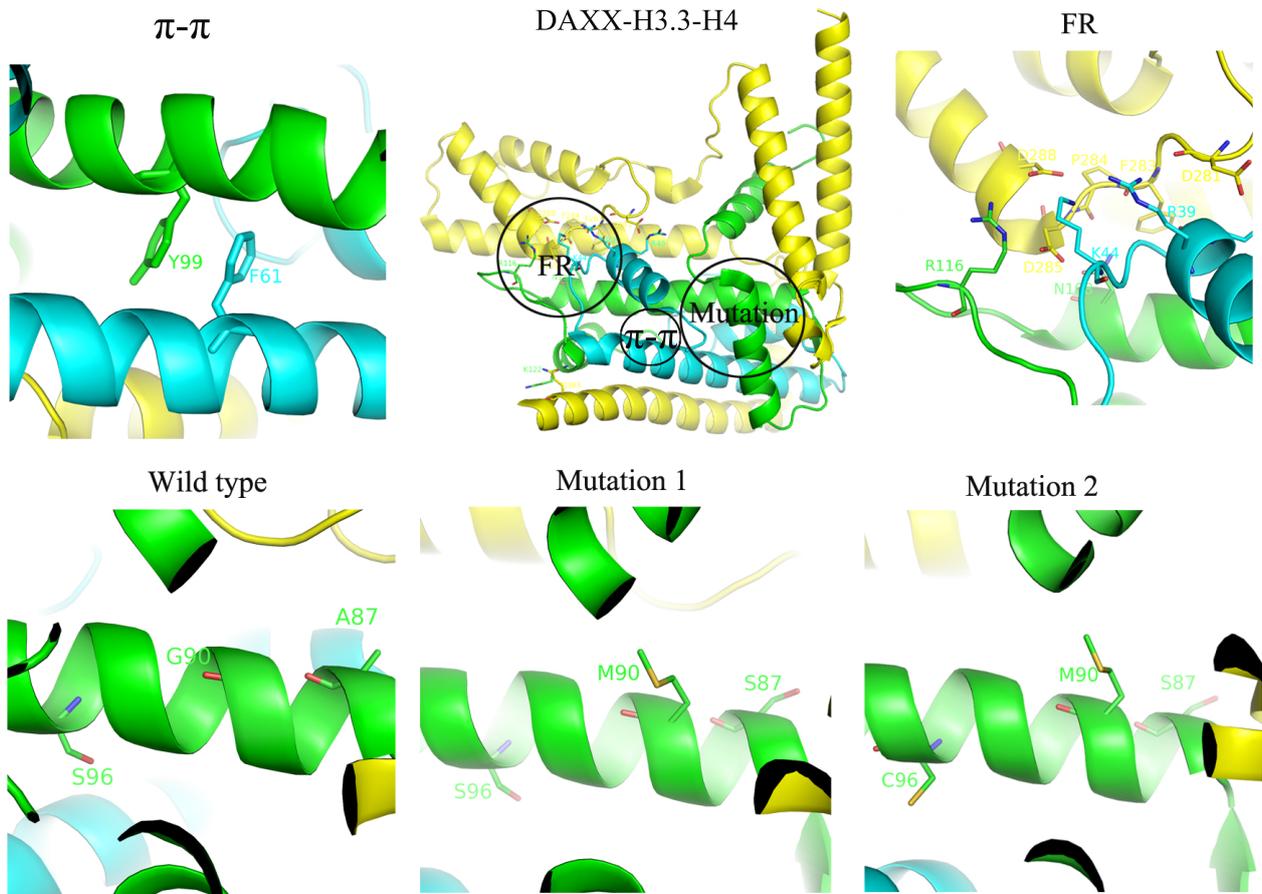
2   Supplementary Figure

Figure S1. The pi-pi interaction region, folding region (FR) and AAMD with mutations.
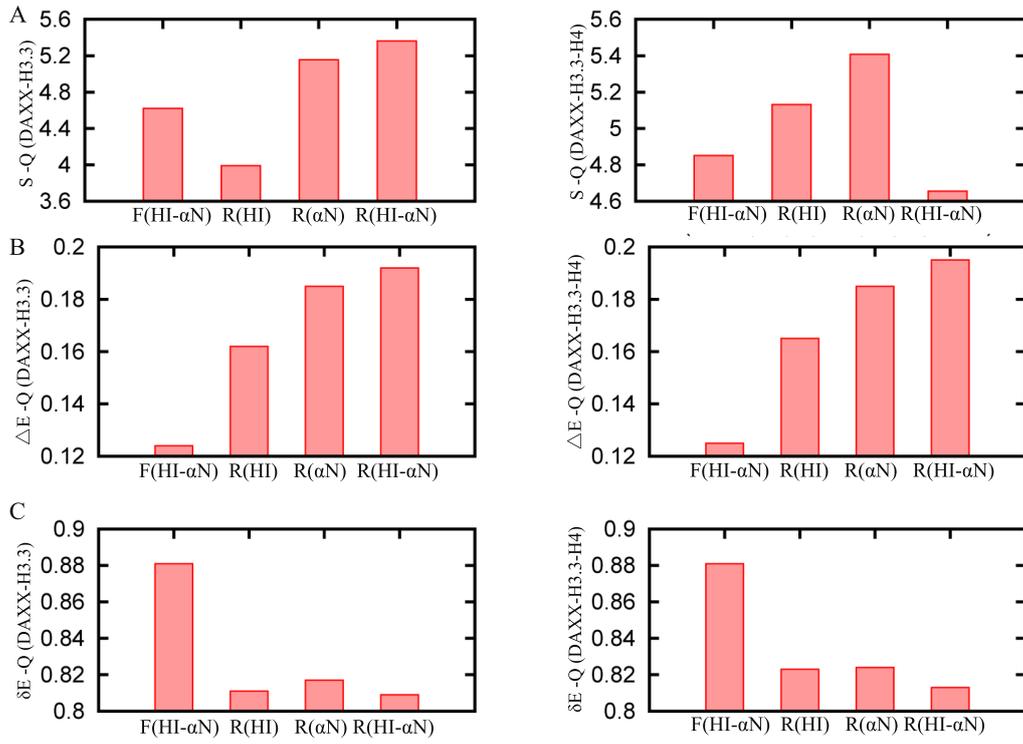
Figure S2. The phase transition temperature of binding is measured by the equation $1/T_f = S/(E_n\text{-}E_D)$, where the S is quantified by $\ln(E_D)$. The energy gap δE is quantified by $E_n\text{-}E_D$ and the energy roughness ΔE is got by calculating the standard deviation of non-native state ensemble. The Λ can be got by equation $\Lambda = \delta\text{E}/(\Delta\text{E}\sqrt{2S})$. The Q values between DAXX and H3.3 as well as between DAXX and H3.3-H4 complex are used to define the location of the native and nonnative basins within the density of states during the binding and binding-folding process of DAXX and H3.3-H4.
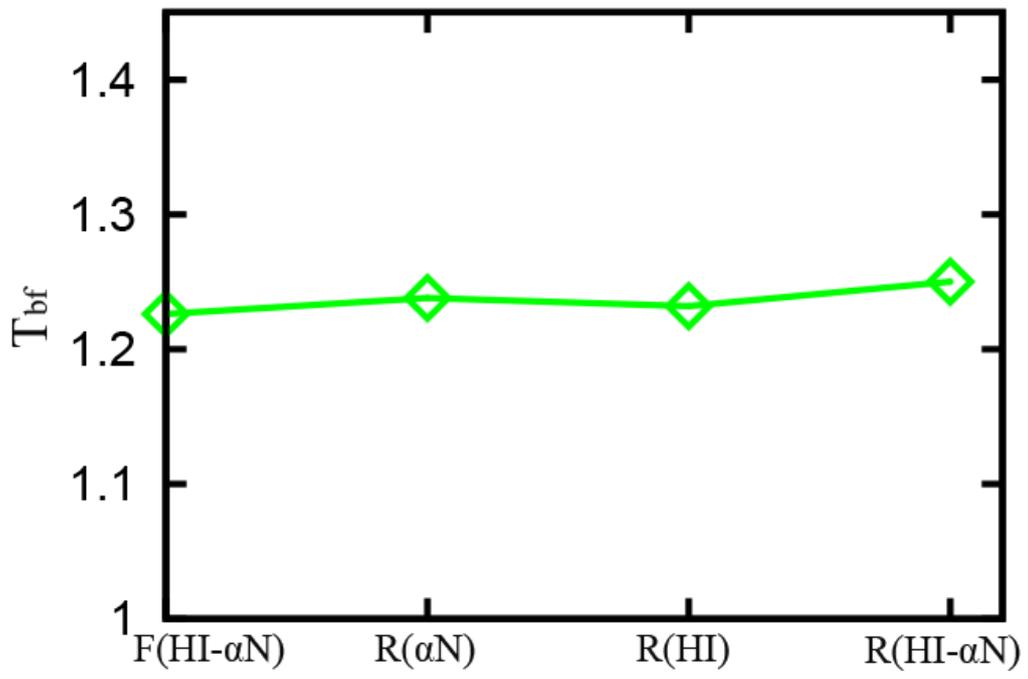
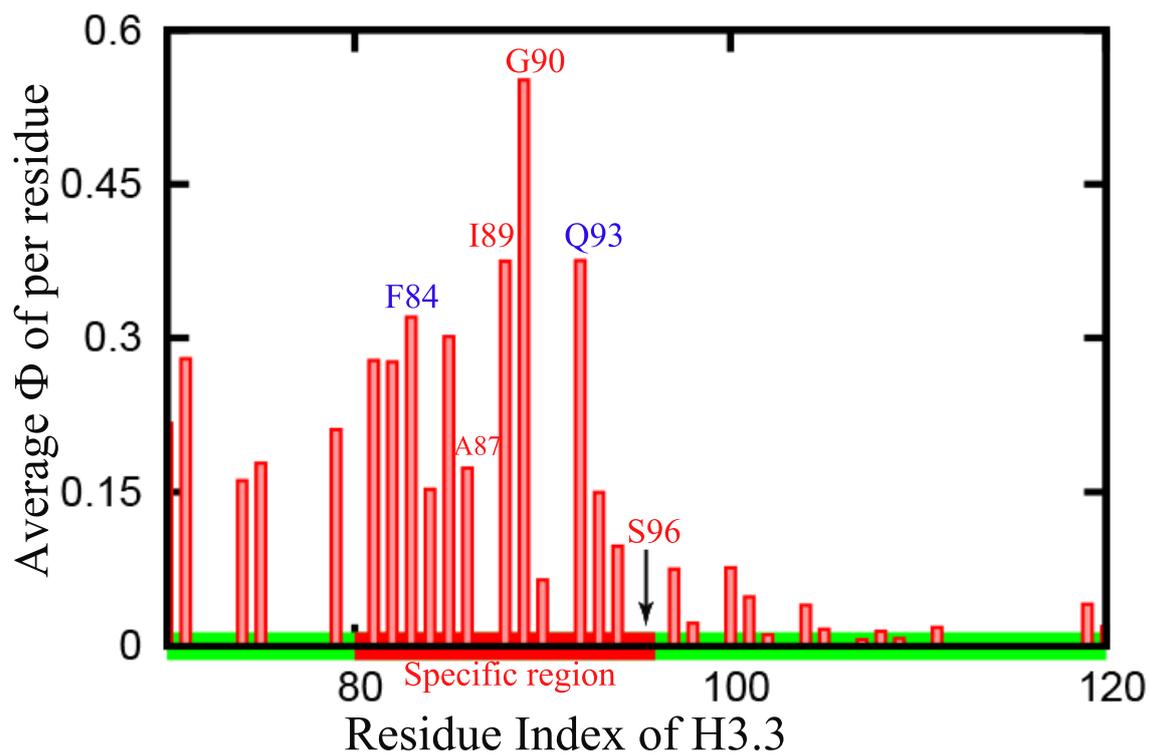Figure S3.The phase transformation temperature Tbf of simulation in each local flexibility simulation.

Figure S4. The average Φ values of residues within the specific region at barrier height S2. When the average Φ values increase, there is a corresponding augmentation in the positive contribution to each state.
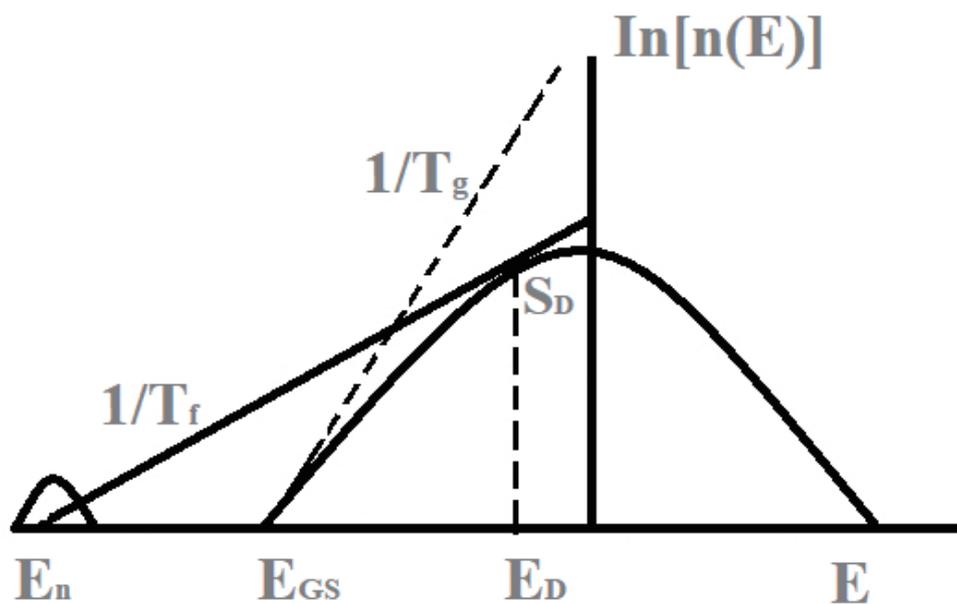
Figure S5.Quantify Intrinsic Energy Funnel.