Electronic Supplementary Material (ESI) for RSC Advances.

Molecular Modeling of Structural and Functional Variance in the SAGA Deubiquitinating Module Caused by Sgf73 Y57A Mutation

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Supplementary Material

Equations to estimate RMSD, RMSF, and PCA

Root-Mean-Square Deviation

RMSD measures the deviation of a target structure to a reference structure. Higher RMSD values imply the evaluated structures are very different from the reference structure. RMSD is calculated as:

$$RMSD = \sqrt{\frac{\sum_{i=0}^{N}\left[m_i * (x_i - y_i)^2\right]}{M}}$$

where N is the number of atoms taken into consideration for RMSD calculation for structure comparison, m_i is the mass of atom i, x_i is the coordinate for target atom i, y_i is the coordinate for reference atom i, and M is the sum of m_i. In this work, we considered only the backbone atoms for RMSD calculation.

Root-Mean-Square Fluctuation

RMSF is calculated as

$$RMSF = \sqrt{\frac{1}{T}\sum_{t_j=1}^{T}(x_i(t_j) - \tilde{x}_i)^2}$$

where T is the number of the time steps in the simulation duration; $x_i(t_j)$ the coordinates of atom x_i at time t_j; $\tilde{x}_i$ is the mean coordinate x_i. Next we divide the sum to T and extract the root of it. Hence we are able to calculate the fluctuation of an atom with its mean in trajectory files. In this work, he RMSF was computed from the coordinates of the backbone and residue atoms.

Principal component analysis

PCA is based on the covariance matrix

$$Cov(i, j) = \left\langle (r_i(t) - \langle r_i \rangle_t) \cdot (r_j(t) - \langle r_j \rangle_t) \right\rangle_t$$

where r_i and r_j are Cartesian coordinates of atoms i and j, respectively, and $\langle r \rangle_t$ is the average of the variable over duration t in the collected MD trajectory. The eigenvectors and eigenvalues of this matrix represent the collective dynamic modes and amplitudes, respectively. PCA is an common tool for investigating the recorded motion of each atom on a reduced dimension manner and represents the trajectories in several combinational modes by separating large collective motions from random thermal fluctuations. We used ProDy program to conduct the PCA.

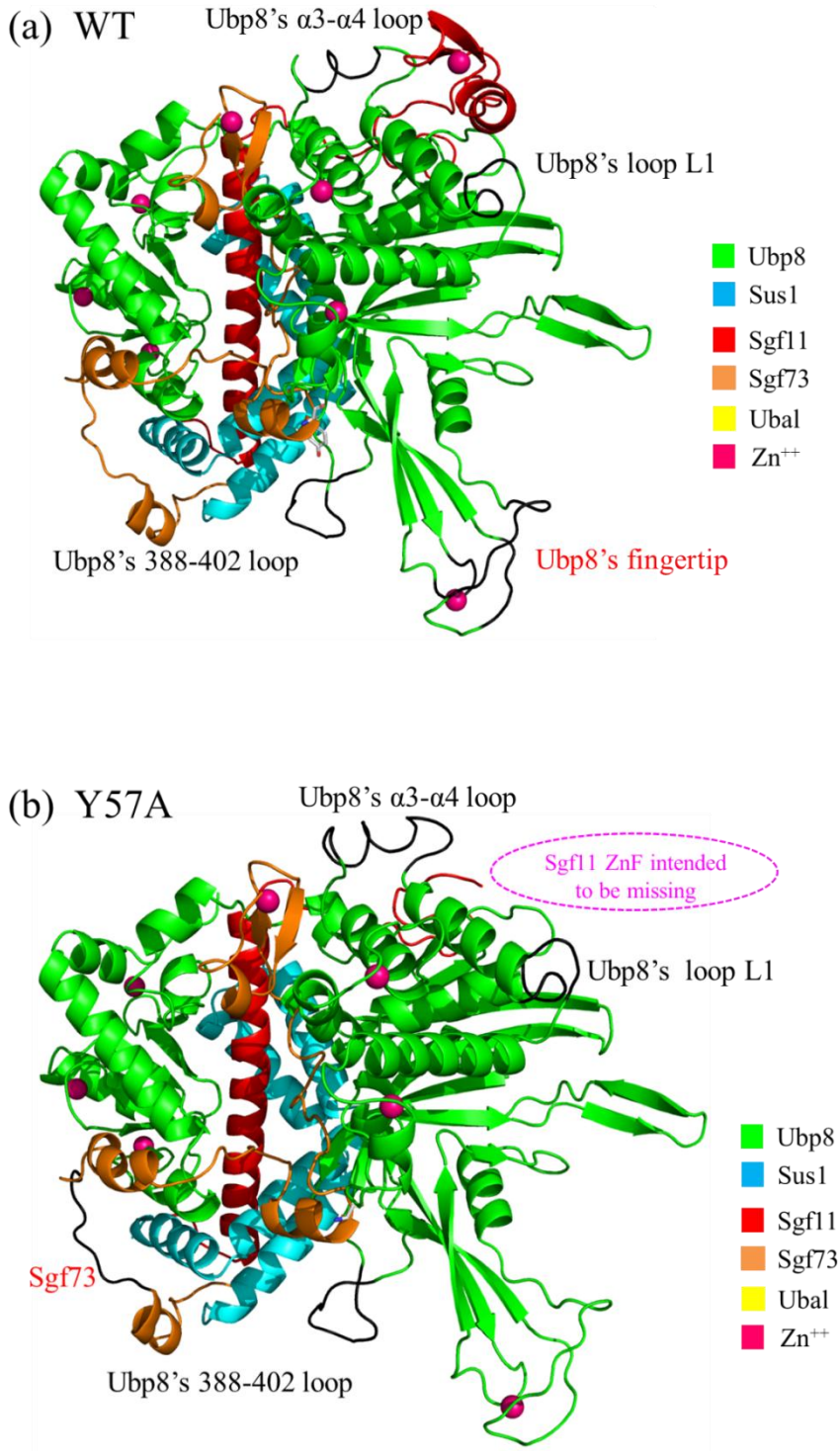

Figure S1 Missing segments specified in black lines for the initial structures in this study: (a) WT and (b) Y57A.

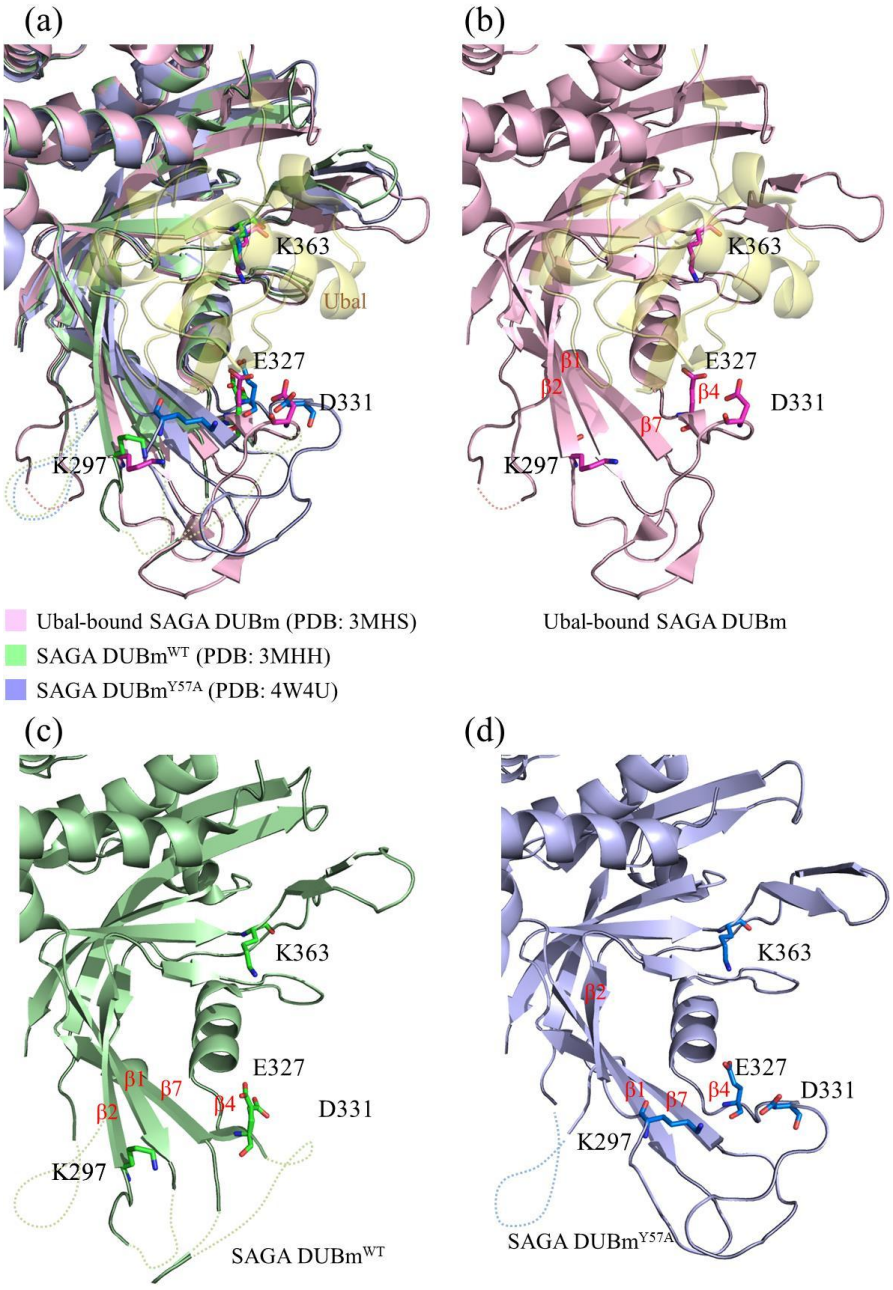

Figure S2 (a) Reproduced structural alignment of three available SAGA DUBm structures according to the binding pocket for the Ubal globular portion. Separated views for the (b) Ubal-bound SAGA DUBm, (c) SAGA DUBm^{WT}, and (d) SAGA DUBm^{Y57A}. The undetermined fragments are indicated by dashed lines.

Table S1 Hydrogen bond occupancy between the long helix of Sgf11 and its surroundings according to the collected 300 conformations for each of WT and Y57A mutant.

Hydrogen bond occupancy				
Sgf11	**Ubp8**	**WT**	**Y57A**	**DUBm-Ubal**[a]
T21:OG1	N70:HD21	32%		
T22:HG1	N53:OD1	64%		
T22:OG1	N53:HD21		19%	
T22:HG1	G55:O			●
Q25:OE1	A56:H	88%	85%	●
Q25:OE1	W69:HE1	39%		
Q25:HE21	N70:OD1	28%		
D26:OD2	N90:HD22	13%	54%	
D26:OD2	N91:HD21	13%		
D26:OD1	N91:HD22		33%	
D26:OD2	N91:HD22	33%	64%	
D26:OD1	N91:HD21			●
R30:HH21	N90:O			●
T33:O	N105:HD21	32%		
Q34:HE21	G436:O		20%	
Q36:HE21	Y102:O	66%		
Q36:OE1	S2:HG		12%	
Q36:OE1	G104:H			●
Q36:OE1	N105:HD22	31%		
T40:OG1	S2:H		14%	
T40:HG1	N105:OD1		11%	
T40:HG1	N105:O	28%		
T40:OG1	N105:HD21			●
R41:HH21	D107:O	11%		
R41:HH21	D107:OD1	14%		●
R41:HH21	D107:OD2	14%		
R41:HH22	D107:OD1	14%		
R41:HH22	D107:OD2	11%		

Sgf11	**Sgf73**	**WT**	**Y57A**	**DUBm-Ubal**[a]
R30:HH12	D67:OD2	21%		
R30:HH11	D70:OD1	23%	39%	●
R30:HH11	D70:OD2	48%		●
R30:HH12	D70:OD1	16%	13%	
R30:HH12	D70:OD2	20%	17%	
Q34:HE21	Q74:OE1	14%		
R41:HH12	Q74:OE1	45%		
R41:HH22	Q74:OE1	23%	16%	

Sgf11	Sus1	WT	Y57A	DUBm-Ubal[a]
Q25:HE21	E66:OE2			●
Q25:HE22	E66:OE2	12%		
Q25:HE22	E66:OE1		30%	
E31:OE1	K47:HZ3			●
E31:OE2	K43:HZ1		26%	
E31:OE2	K43:HZ2		22%	
E31:OE2	K43:HZ3		11%	

[a] The appearance of hydrogen bond in the X-ray crystallography solved SAGA DUBm-Ubal complex structure (PDB code: 3MHS).