

Supporting Information

Non-destructive Inhibition of Metallofullerenol Gd@C₈₂(OH)₂₂ on WW domain: Implication on Signal Transduction Pathway

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Figure S1. **a)** Root-mean square deviation (rmsd) and **b)** root-mean square fluctuation (rmsf) of the WW domain in the binary system with four Gd@C₈₂(OH)₂₂ molecules. **c)** rmsd and **d)** rmsf of the WW domain when with both Gd@C₈₂(OH)₂₂ and the PRM.

Figure S2. **a)** The residue types of WW domain. Colors represent residue type depending on polarity: blue for positively charged, red for negatively charged, green for polar, white for non-polar and yellow for key binding site residues. **b)** Electrostatic potential around the WW domain with blue for positive and red for negative fields calculated by APBS tool.¹ T1 and T2 indicate the first and second turn of the WW domain, respectively. The two PRM binding grooves are indicated with arrows, to which Gd@C₈₂(OH)₂₂ also binds. The first two Pro's of the PPxY motif are packed into the groove-1, and the Tyr of the PPxY is accommodated by the groove-2.

Figure S3. Binding free energy landscape between the full sequence of WW domain (46 residues) with Gd@C₈₂(OH)₂₂ (a), and PRM (b). The total number of atoms in the ternary system is ~20,000. The solvated system was also run 5 times, with simulation length about 150ns each. All the other simulation details are the same as the truncated system with the functional unit (L13-P42) only. Similarly, **D** and **S** of two axes in the free energy diagrams indicate distance and contact area. The subscripts P, K, L and M represent protein, key residues, PRM ligand and Gd@C₈₂(OH)₂₂, respectively. The local energy minima are indicated with free energy numbers. With the full sequence of WW domain, Gd@C₈₂(OH)₂₂ again wins the competition over the native ligand PRM in its binding with the WW domain, with $\Delta\Delta G \approx -0.53$ kcal/mol, despite the more flexible terminal residues (which affect the shapes and details of the free energy landscapes somewhat). These findings are consistent with the results from the functional unit (L13-P42) only, indicating Gd@C₈₂(OH)₂₂ can potentially inhibit the WW domain function.

Figure S1.

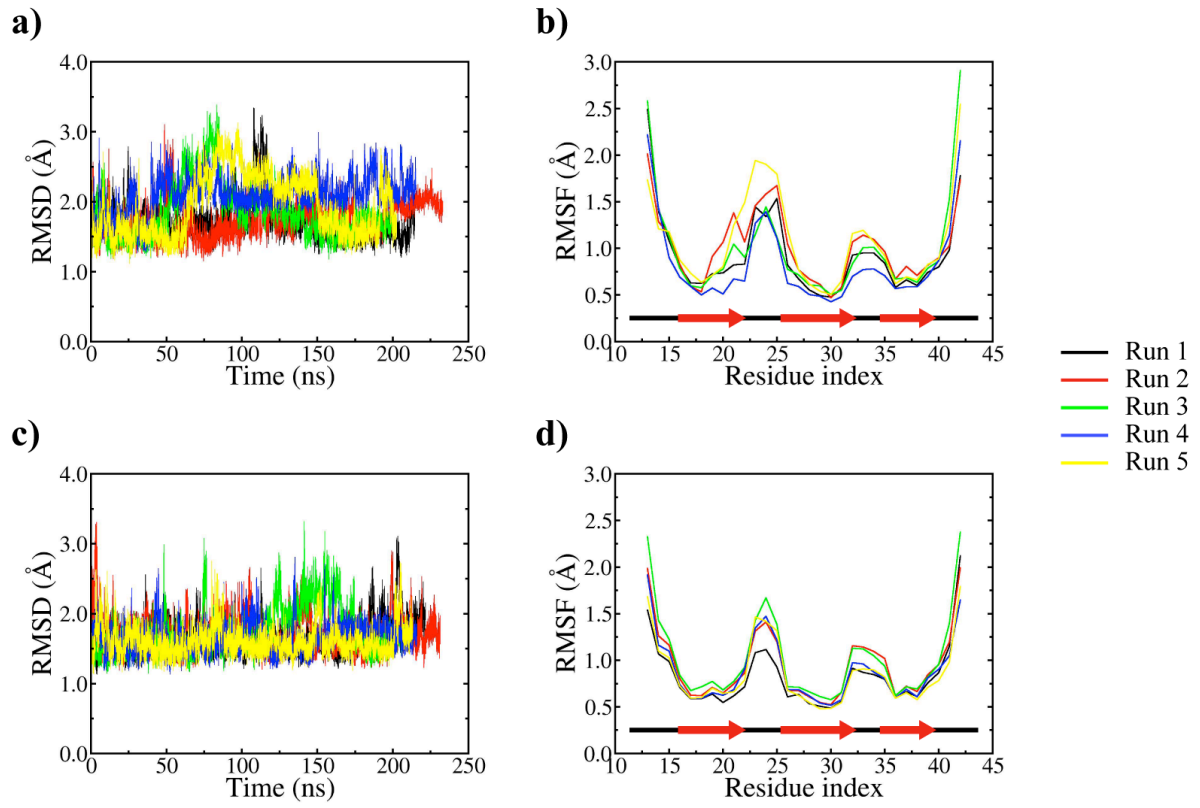


Figure S2.

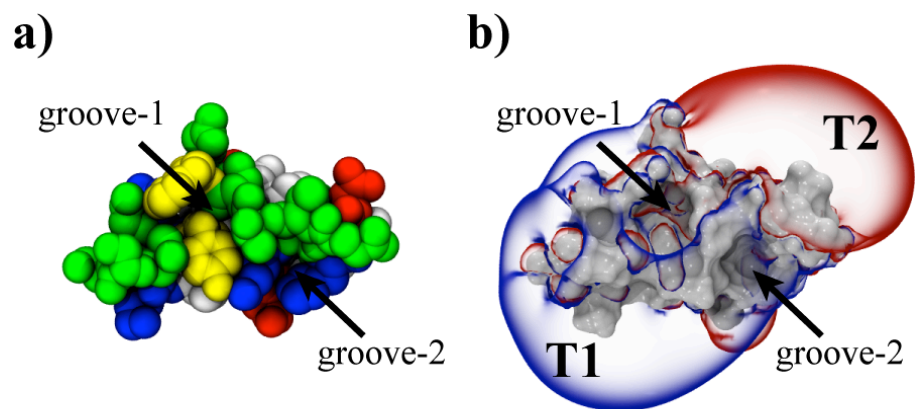
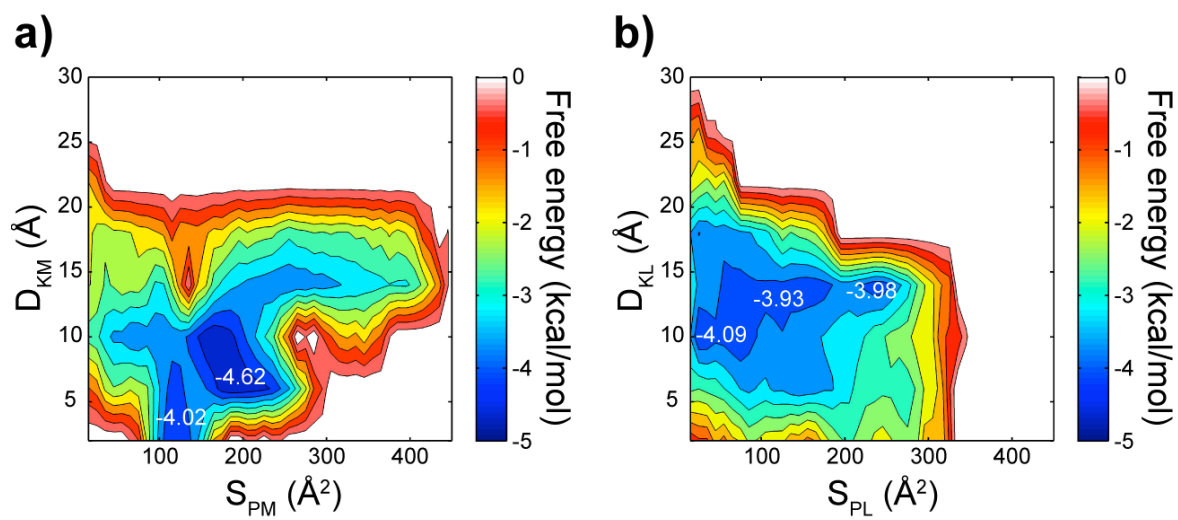


Figure S3.



References

- ¹ Baker, N. A., Sept, D., Joseph, S., Holst, M. J. & McCammon, J. A. Electrostatics of nanosystems: application to microtubules and the ribosome. *Proc Natl Acad Sci USA* **98**, 10037-10041, (2001).