Supplementary Information for

In silico screening of LRRK2 WDR domain inhibitors using deep docking and free energy simulations

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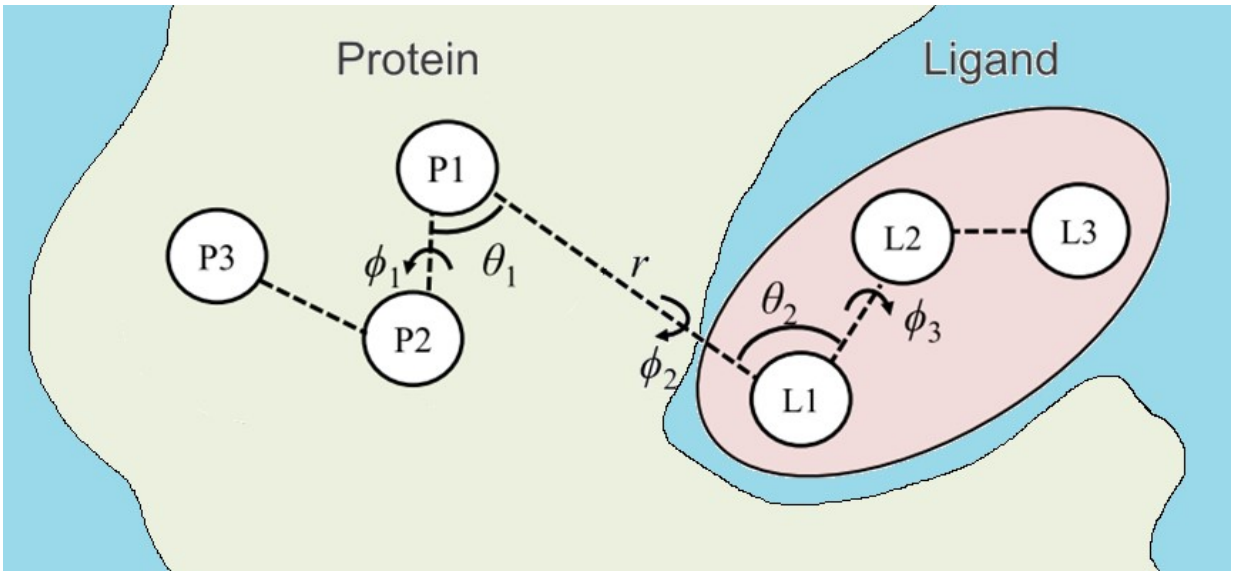

Figure S1. Schematic representation of the virtual bond (1) used for restraining the orientation of ligand in protein. P1, P2, P3 are L1, L2, L3 are atoms of protein and ligand used for specifying six degrees of freedom: distance r, angles θ_1 and θ_2, and torsion angles ϕ_1, ϕ_2, and ϕ_3.

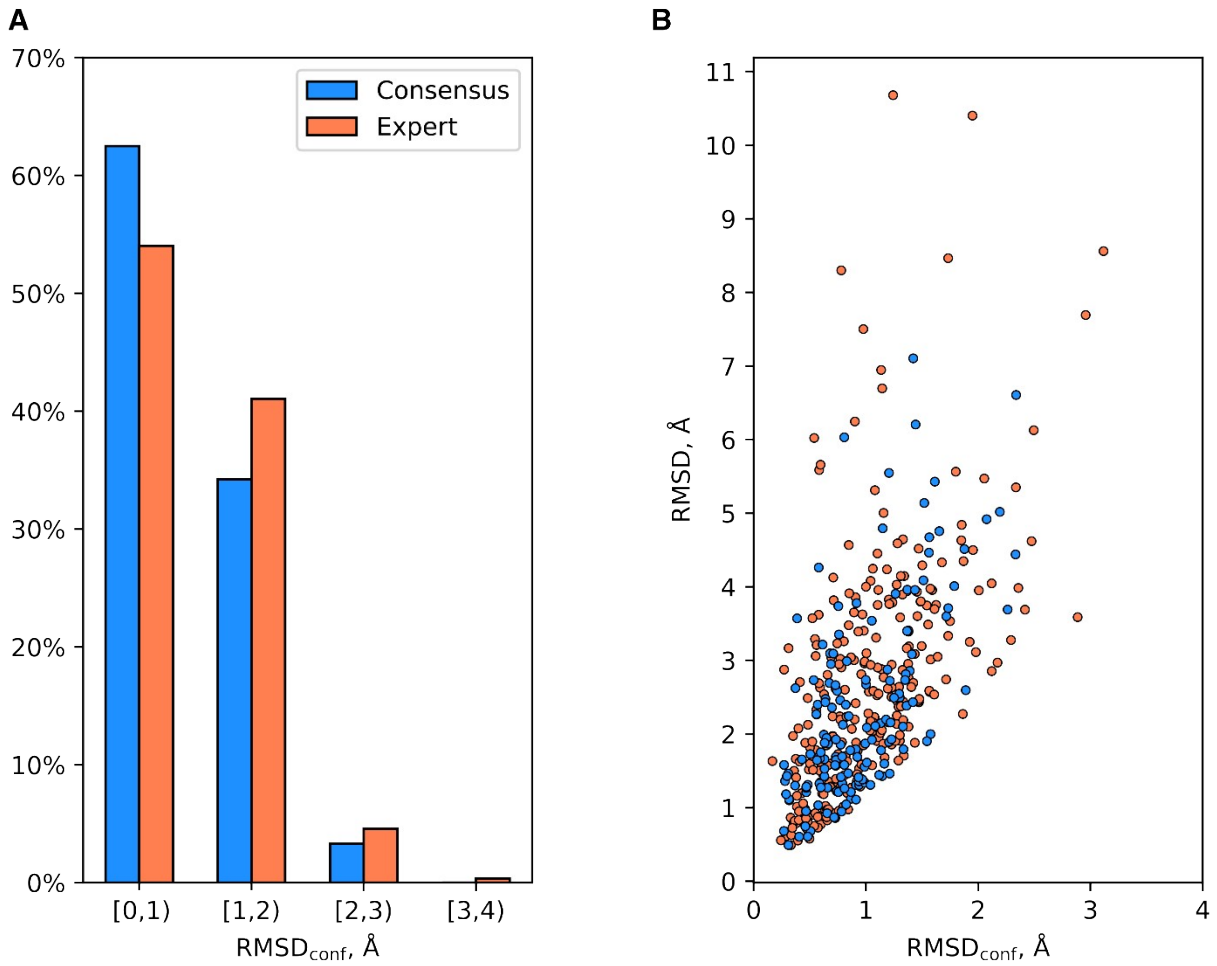

Figure S2. A. The distribution of conformational ligand RMSD of MD representative pose with respect to docked pose. B. Scatter plot of total ligand RMSD versus conformational RMSD of MD representative pose with respect to docked pose.

Conformational ligand RMSD is the RMSD of MD representative structure of ligand aligned to the initial (docked) pose of ligand. Only heavy atoms of ligand are used for both ligand alignment and RMSD calculation.

Total ligand RMSD is obtained by first aligning the MD representative structure of protein-ligand complex to its initial structure on C_α atoms of protein residues forming the binding site of WDR domain, and then calculating the RMSD of MD representative structure of ligand with respect to the initial pose of ligand without additional ligand alignment.

References

1. Boresch S, Tettinger F, Leitgeb M, Karplus M. Absolute binding free energies: A quantitative approach for their calculation. Journal of Physical Chemistry B. 2003;107(35):9535-51.