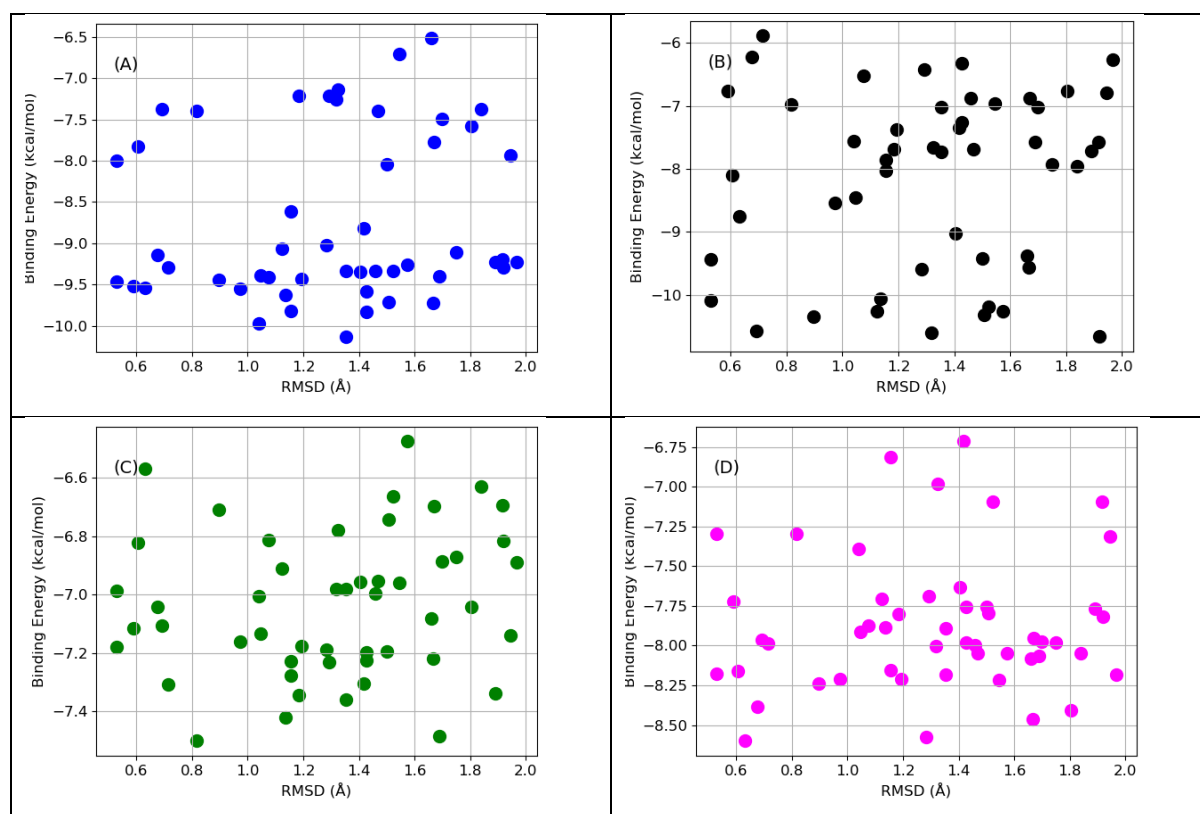


Supplementary Materials

Docking Validation and Benchmarking

To ensure the reliability of our docking simulations, we performed docking validation using well-characterized proteins obtained from their co-crystallized structures alongside their native ligands. The proteins and native ligands were cleaned and prepared following standard docking protocols. Given that all native ligands contained rotatable bonds, fifty distinct conformers were generated for each ligand to account for conformational variability. After re-docking, the native ligand and the best docking pose from the generated conformers (representative) were superimposed using UCS Chimera, and the root mean square deviation (RMSD) was calculated. Notably, the RMSD values were consistently below 2 Å, confirming the reliability of the docking protocol. Figure S2 highlights the RMSD variability among the generated conformers, supporting the robustness of our validation process.



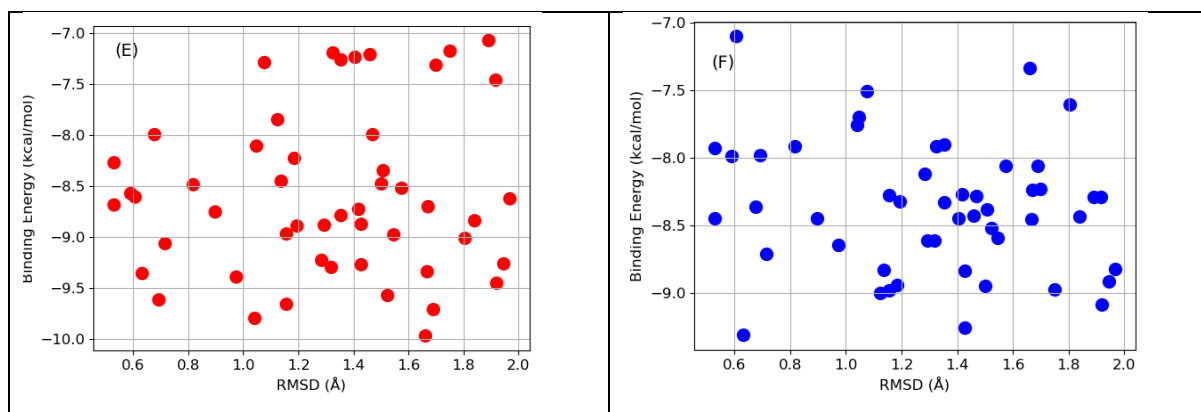


Figure S1: Conformational changes of different conformers indicating their RMSD for (A) 2ZC9 (B) 2ZDA (C) 2ZFP (D) 2ZGB (E) 2ZHQ (F) 2ZIQ

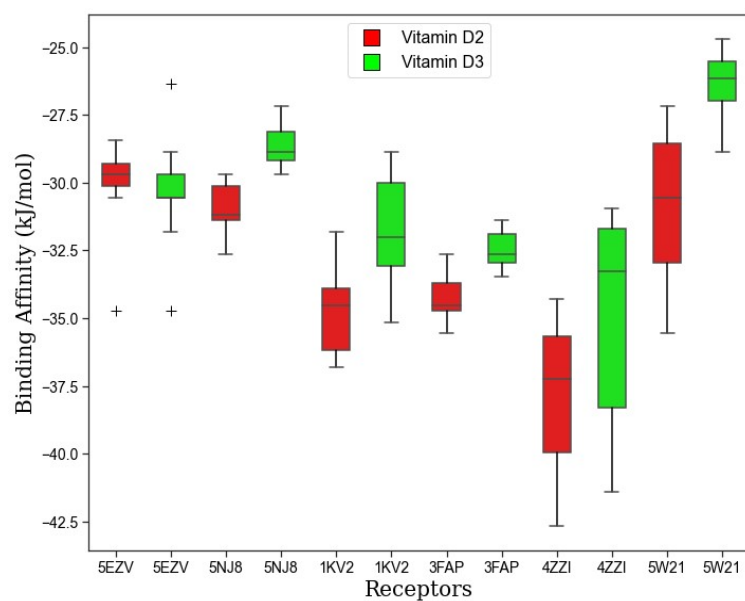


Figure S2: Binding affinity of vitamin D2 and D3 across anti-aging receptors in blind docking.

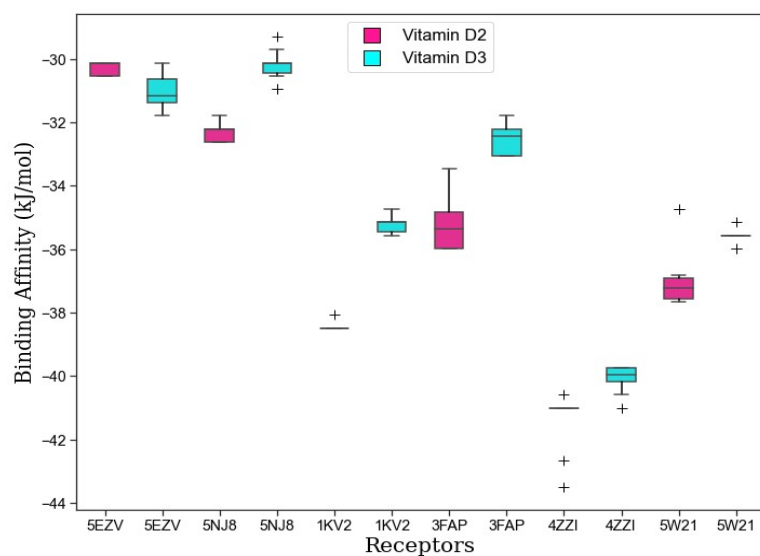


Figure S3: Binding affinity of vitamin D2 and D3 against anti-aging receptors for grid-based docking.

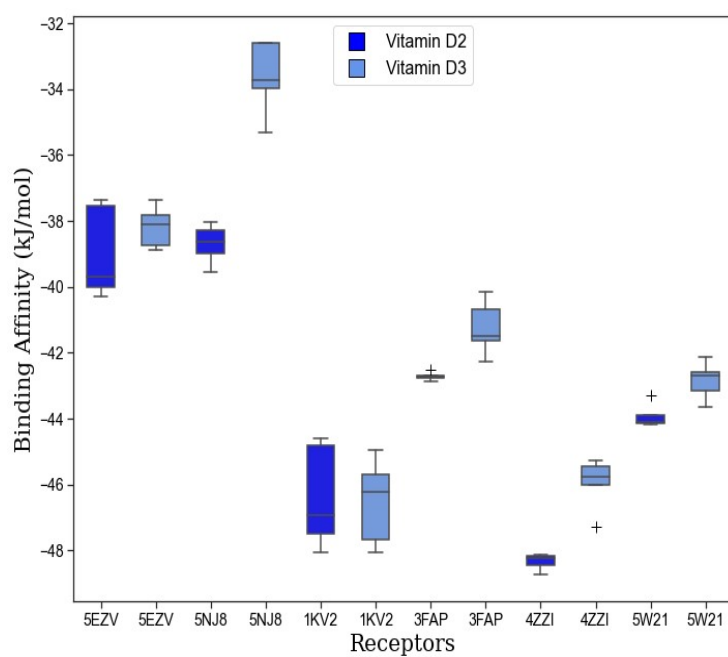


Figure S4: The binding affinity of vitamin D2 and D3 against anti-aging receptors in a hydrated system.

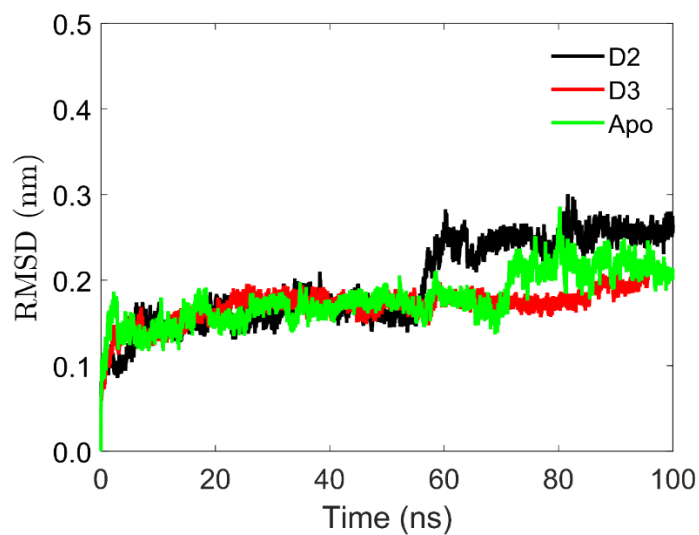


Figure S5: Time-dependent RMSD values for apo and holo of Sirt1 with vitamin D

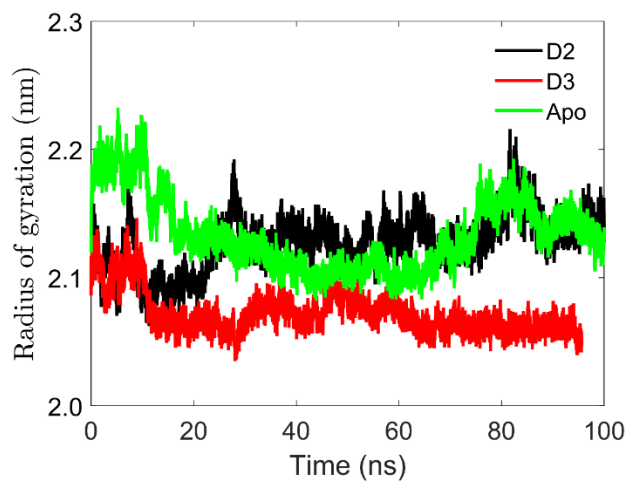


Figure S6: Time-dependent Rg values for apo and holo proteins of Sirt1 with vitamin D

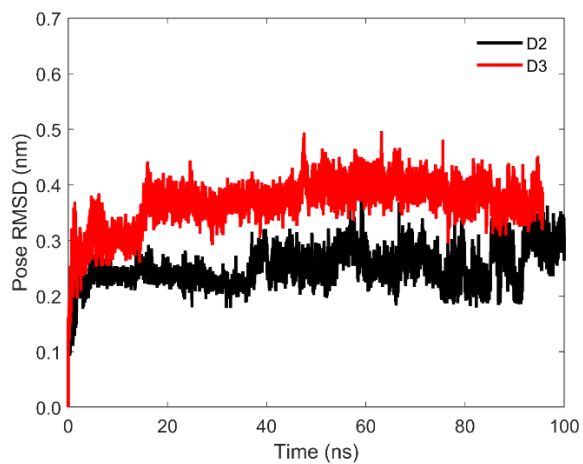


Figure S7: Time-dependent pose RMSD values of vitamin D to the Sirt1 pocket's residues