

SUPPORTING MATERIAL

TABLES

System	Number of atoms	Simulation time	Number of copies
Apo TbRET2	63,950	50 ns	2
UTP-bound TbRET2	65,384	50 ns	2
CTP-bound TbRET2	65,385	50 ns	1
ATP-bound TbRET2	65,387	50 ns	1

TABLE S1. The simulated TbRET2 systems.

	Mean volume	Standard deviation
Apo (copy1)	3267.54	257.898
Apo (copy2)	3048.74	204.529
UTP-bound (copy1)	2780.41	154.790
UTP-bound (copy2)	2740.25	183.040
CTP-bound	3049.94	227.703
ATP-bound	2304.80	197.964

TABLE S2. The mean and standard deviation of binding cleft volume (in Å³) during TbRET2 simulations.

	MM-PBSA	MM-GBSA
UTP-bound (copy1)	-143.0902 (0.5917)	-174.5907 (0.6118)
UTP-bound (copy2)	-144.7007 (0.6054)	-178.0872 (0.6181)
CTP-bound	-136.2367 (0.7397)	-153.9985 (0.6823)
ATP-bound (one Mg ⁺²)	-68.6673 (0.6463)	-85.7223 (0.5843)
ATP-bound (two Mg ⁺²)	-173.3133 (0.5087)	-183.2902 (0.4708)

TABLE S3. Mean MM-GB/PBSA binding energies of NTP ligands in kcal/mol. Standard error of the mean for binding affinities are reported in parenthesis.

FIGURE CAPTIONS:

FIGURE S1 Time evolution of the root-mean-square-deviation (in Å) of all C α atoms with respect to the initial structure in the apo and NTP-bound TbRET2 MD simulations.

FIGURE S2 The computed (a) ensemble-averaged and (b) crystal structure electrostatic potential of TbRET2. Negative and positive electrostatic isosurfaces are shown in red and blue, respectively. Isosurfaces are drawn at -9 kT/e and +9 kT/e.

FIGURE S3 Time evolution of heavy-atom RMSD (in Å) of the NTP ligands measured after aligning the trajectories with respect to all C α atoms of TbRET2.

FIGURE S4 Atom name mapping of UTP.

FIGURE S5 Time evolution of the TbRET2 binding pocket volume.

FIGURE S6 Time evolution of the angle and distance between aromatic ring planes of NTP and Tyr319.

FIGURE S7 The final frames of NTP-bound TbRET2 simulations superimposed with respect to all C α atoms. UTP-bound TbRET2 MD copy1: red, UTP-bound TbRET2 MD copy2: silver, CTP-bound TbRET2: blue, ATP-bound TbRET2: green.

FIGURE S1

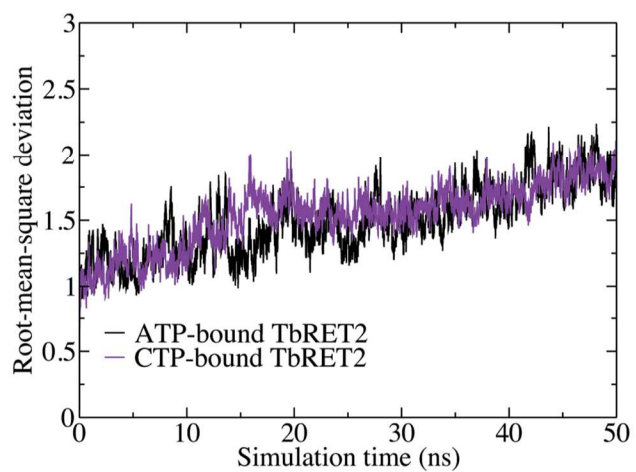
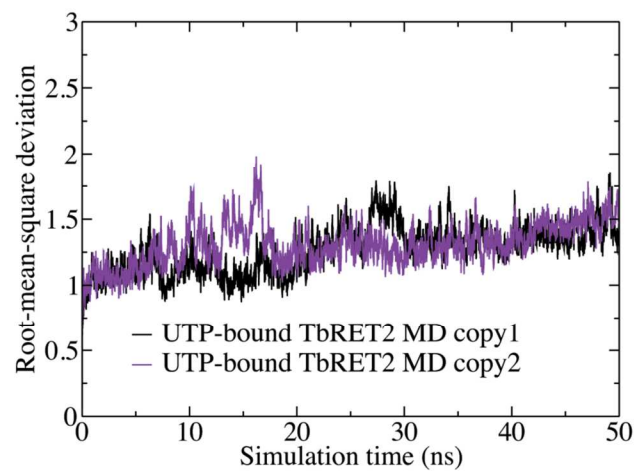
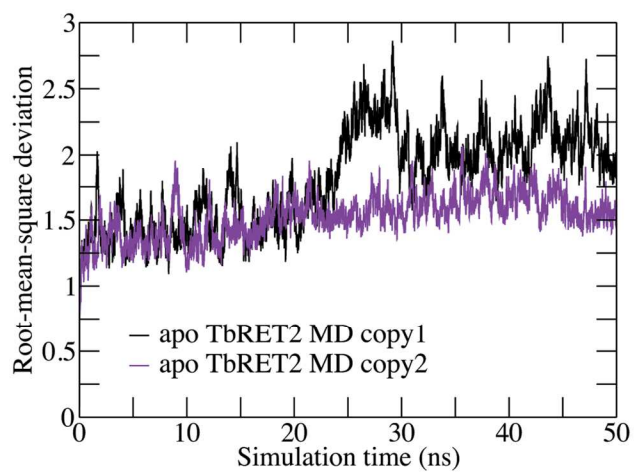
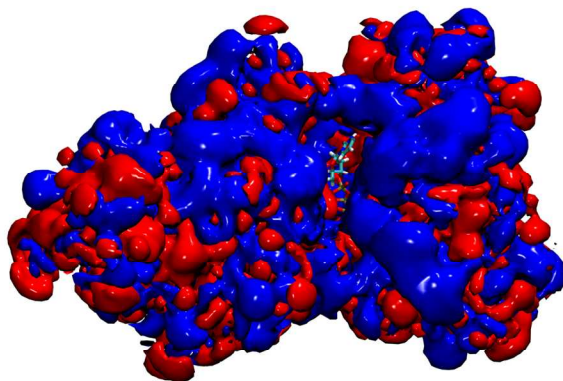


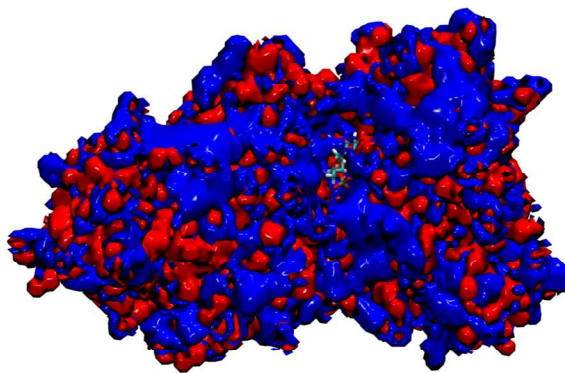
FIGURE S2

a)

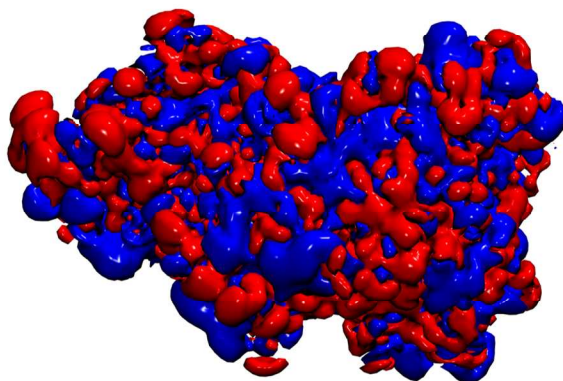


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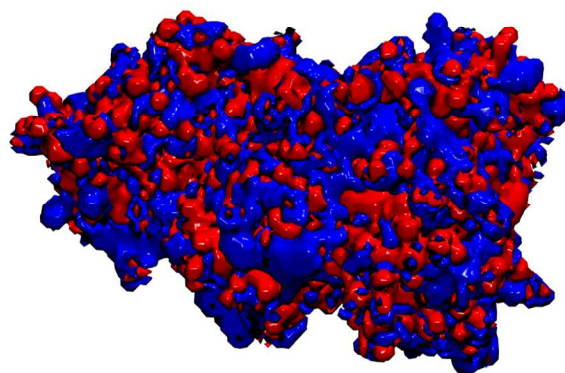
b)



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FIGURE S3

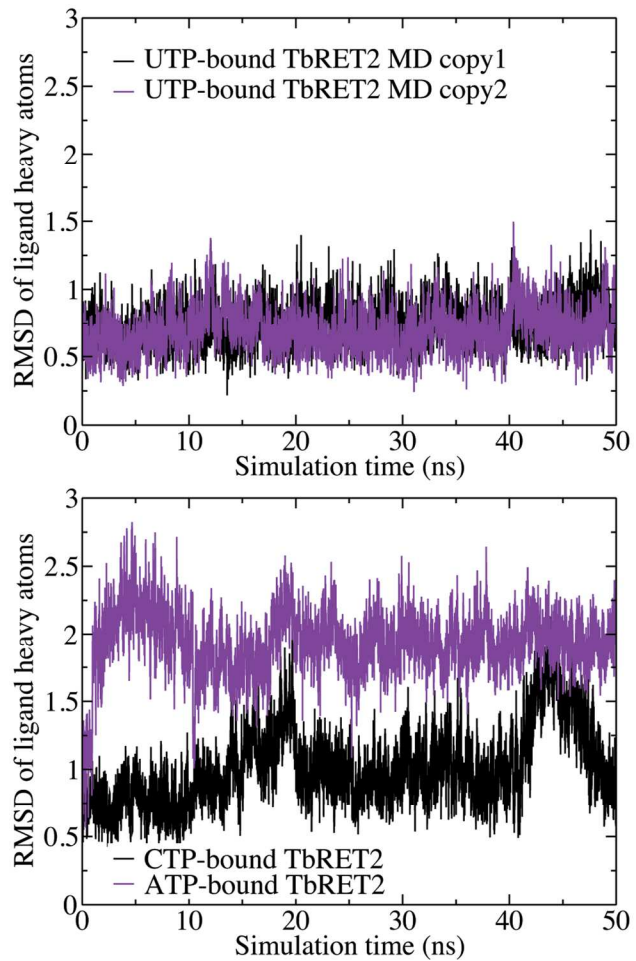


FIGURE S4

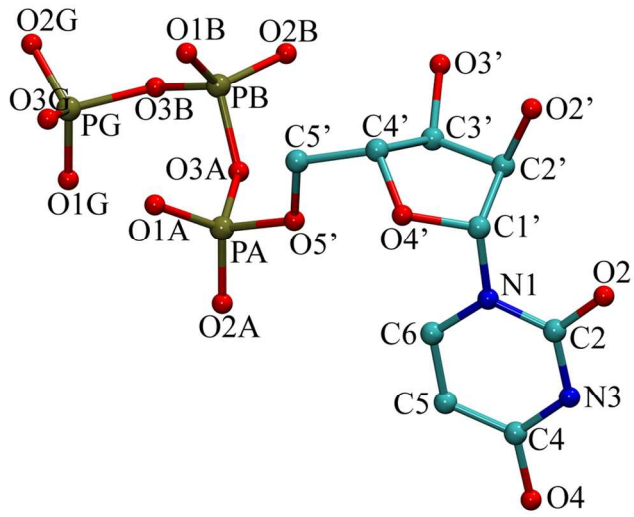


FIGURE S5

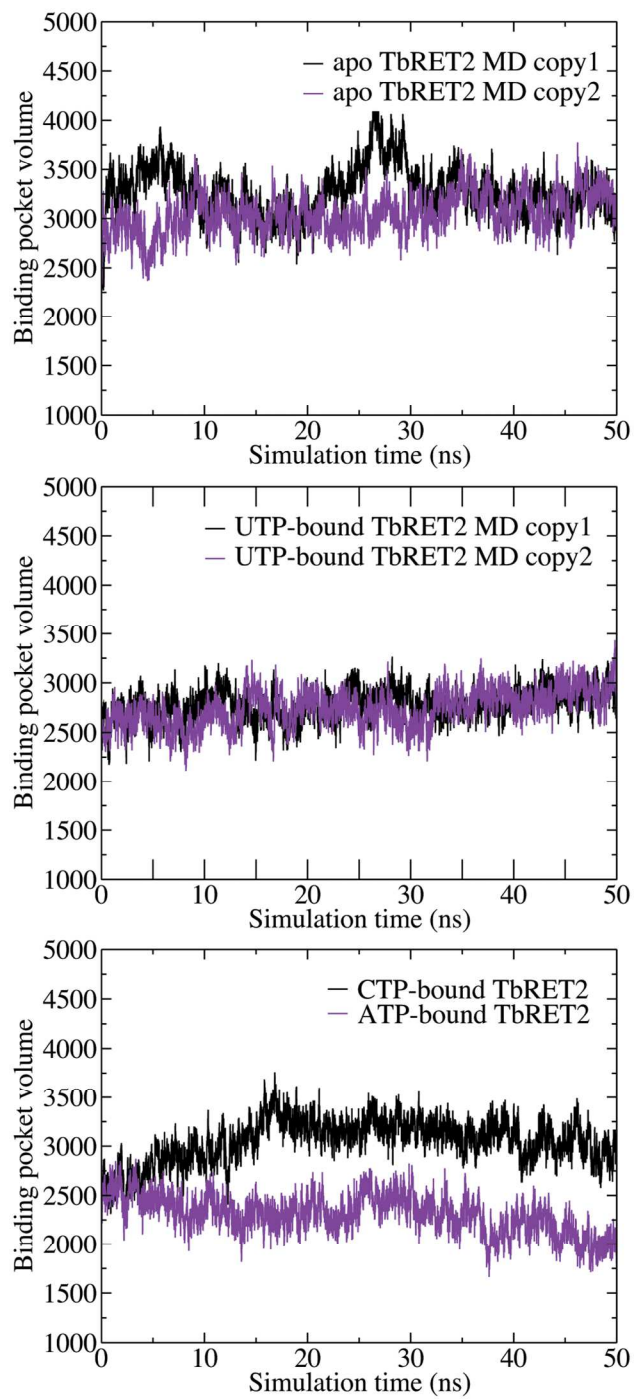


FIGURE S6

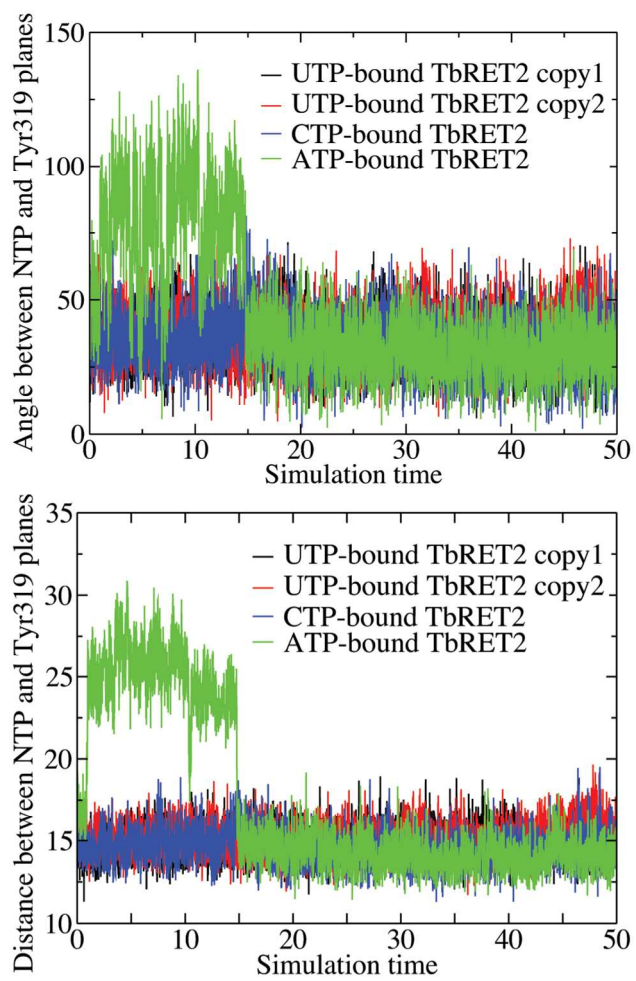


FIGURE S7

