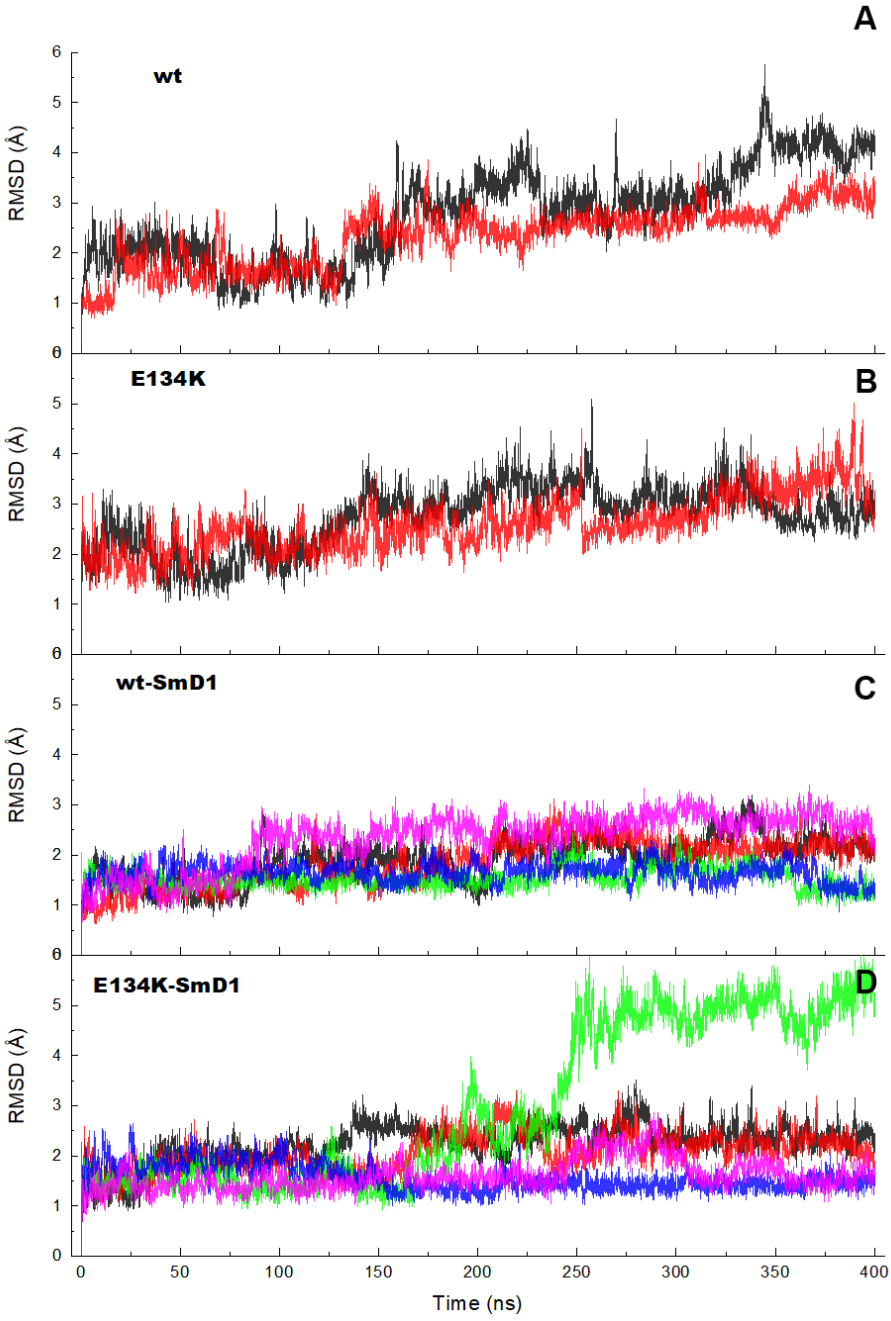

Figure S1. RMSD plots of the core (residues 92 to 139) of Tudor domain. The RMSD was calculated after superimposition of Cα atoms of the protein core of each frame with the initial structure. The terminal regions were exclude due to their very high flexibility, not relevant to monitor the stability of the structured domain. The different kinds of simulations are labeled, following the nomenclature in Table 1: panels A and B correspond to the simulations without the SmD1 tail, panels C and D to the simulations in the presence of the SmD1 tail. The replicas of each simulation are progressively colored (r1 is black, r2 is red, r3 is green, r4 is blue, r5 is purple).

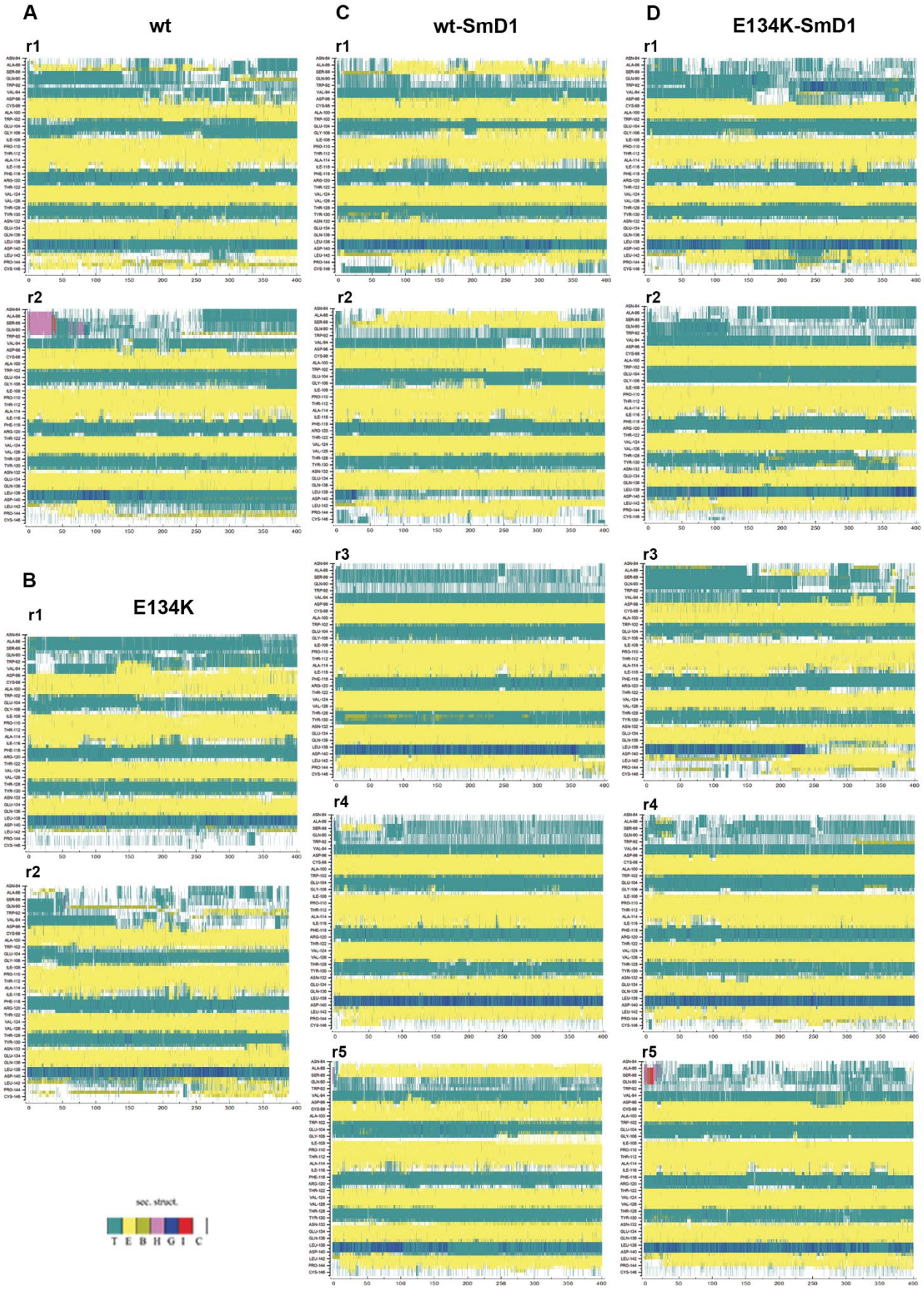

Figure S2. Secondary structure evolution in time. The beta structure of the Tudor domain core is made by the four central strands. The high flexibility of the two long terminal regions is evident. The different kinds of simulations are labeled as previously reported. All the replicas are vertically ordered. Color code for the different secondary structures is reported in the bottom-left part of the figure; namely: turn is green, beta structure is yellow, beta-bridge is tan, α-helix is pink, 3_{10} helix is blue, π-helix is red and coil is white.

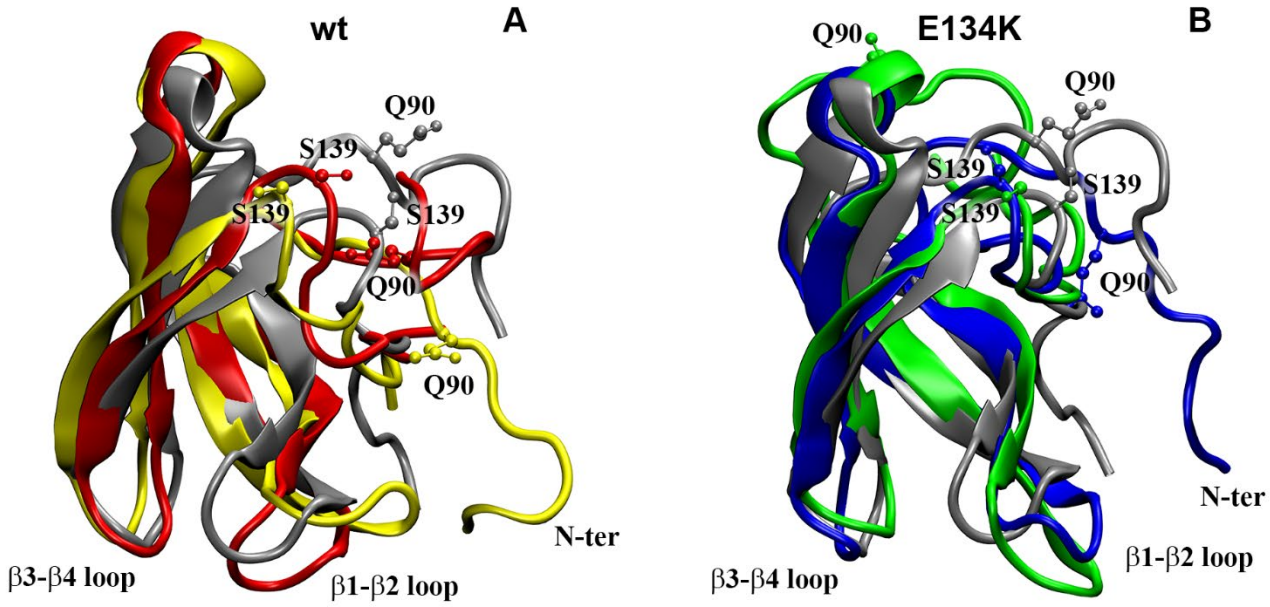

Figure S3. Final conformations of the Tudor domain in the simulations in the absence of the SmD1 tail. Panel A: wt final conformations. In gray is the starting conformation; in yellow the wt_r1 conformation at 330 ns, just before an excessive opening of the cage side of the barrel due to the random interaction with the long and very flexible N-terminus (see also Fig. S2). In red the final (400 ns) wt_r2 conformation. Panel B: E134K final conformations. In gray is again the starting conformation, in green the final E134K_r1, and in blue the final E134K_r2 conformation. In both panels, the superimposition was made on the Cα atoms of the core (residues 92 to 139) of the starting structure. In all structures, residues Gln90 and Ser139 are labelled and represented in ball and sticks, to highlights the breaking of the H-bond between them and the separation of the two long terminal regions. In the absence of the wrapped SmD1 tail, this leads to a destabilization of the barrel, in particular in wt trajectories.

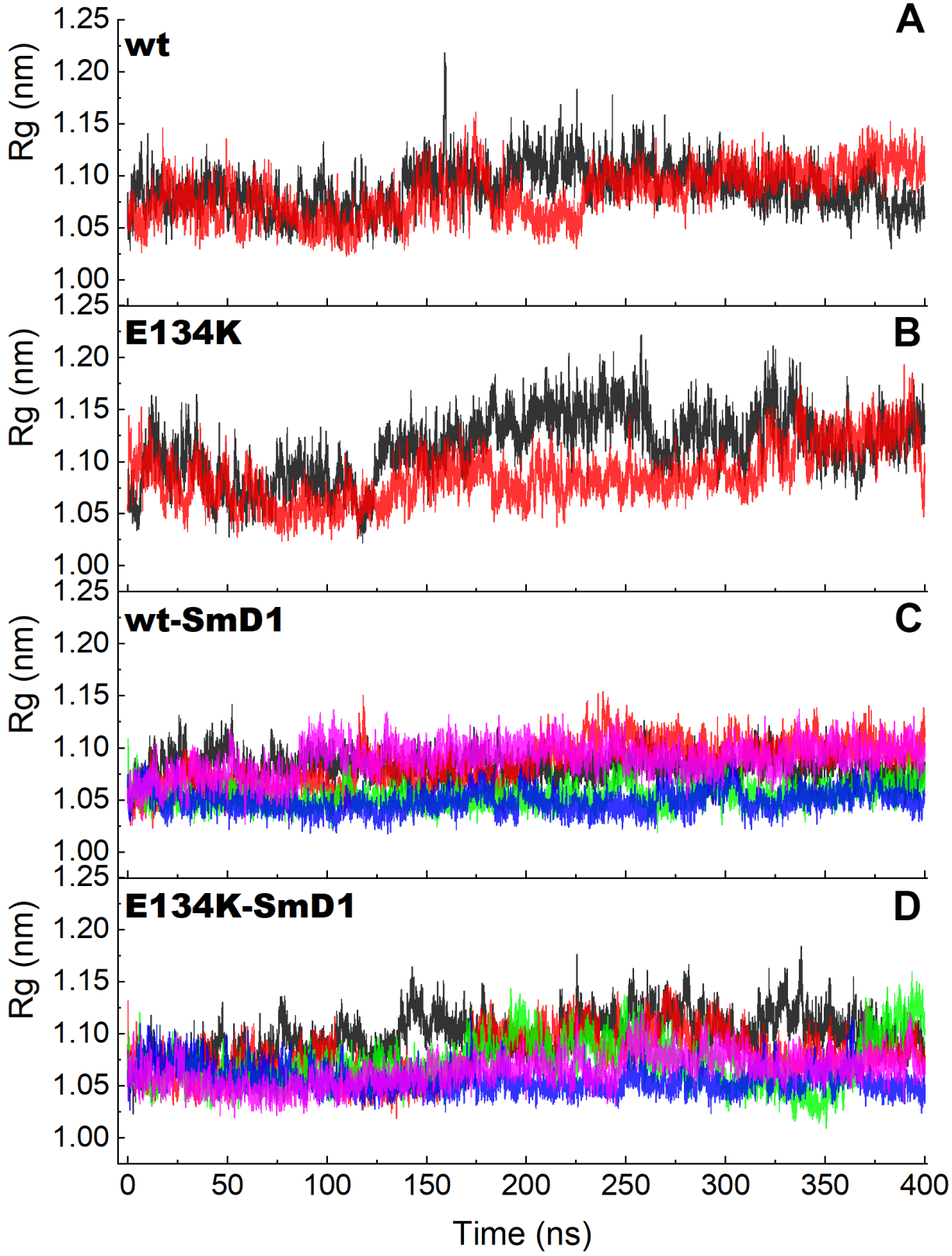

Figure S4. Radius of gyration (Rg) of the Tudor domain core (residue 92 to 139). The Rg was calculated on all the atoms of the protein core. The terminal regions were exclude due to their very high flexibility, not relevant to monitor the stability of the structured domain. The different kinds of simulations are labeled, following the nomenclature in Table 1: panels A and B correspond to the simulations without the SmD1 tail, panels C and D to the simulations in the presence of the SmD1 tail. The replicas of each simulation are progressively colored (r1 is black, r2 is red, r3 is green, r4 is blue, r5 is purple).

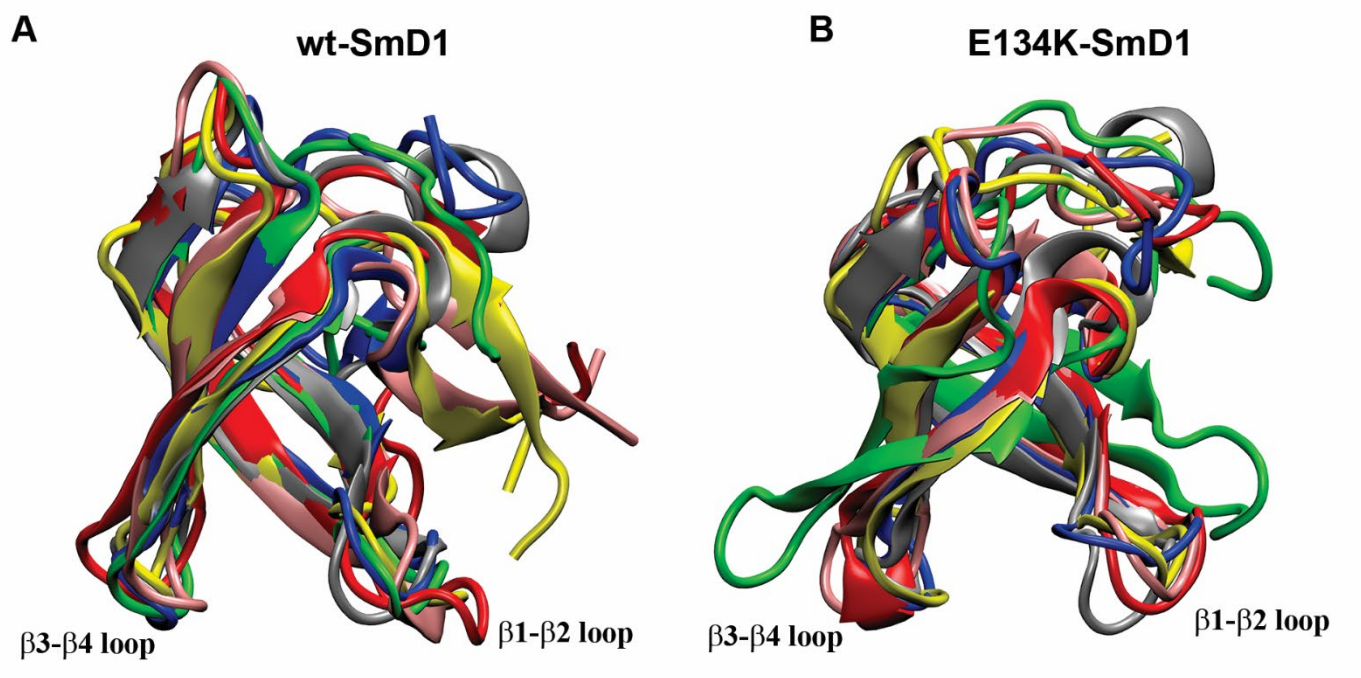

Figure S5. Final conformations (at 400 ns) of the Tudor domain in wt-SmD1 (panel A) and E134K-SmD1 (panel B) simulations. The SmD1 tail is not drawn for clarity. In both panels, the superimposition was made on the Cα atoms of the core (residues 92 to 139) of the starting structure and all replicas are shown and progressively colored (r1 is yellow, r2 is red, r3 is green, r4 is blue, r5 is pink), whereas the starting structure is in gray. β1-β2 and β3-β4 loops are labelled to show the widening of the binding cavity in E134K-SmD1 simulations, in particular in r3 trajectory (in green).

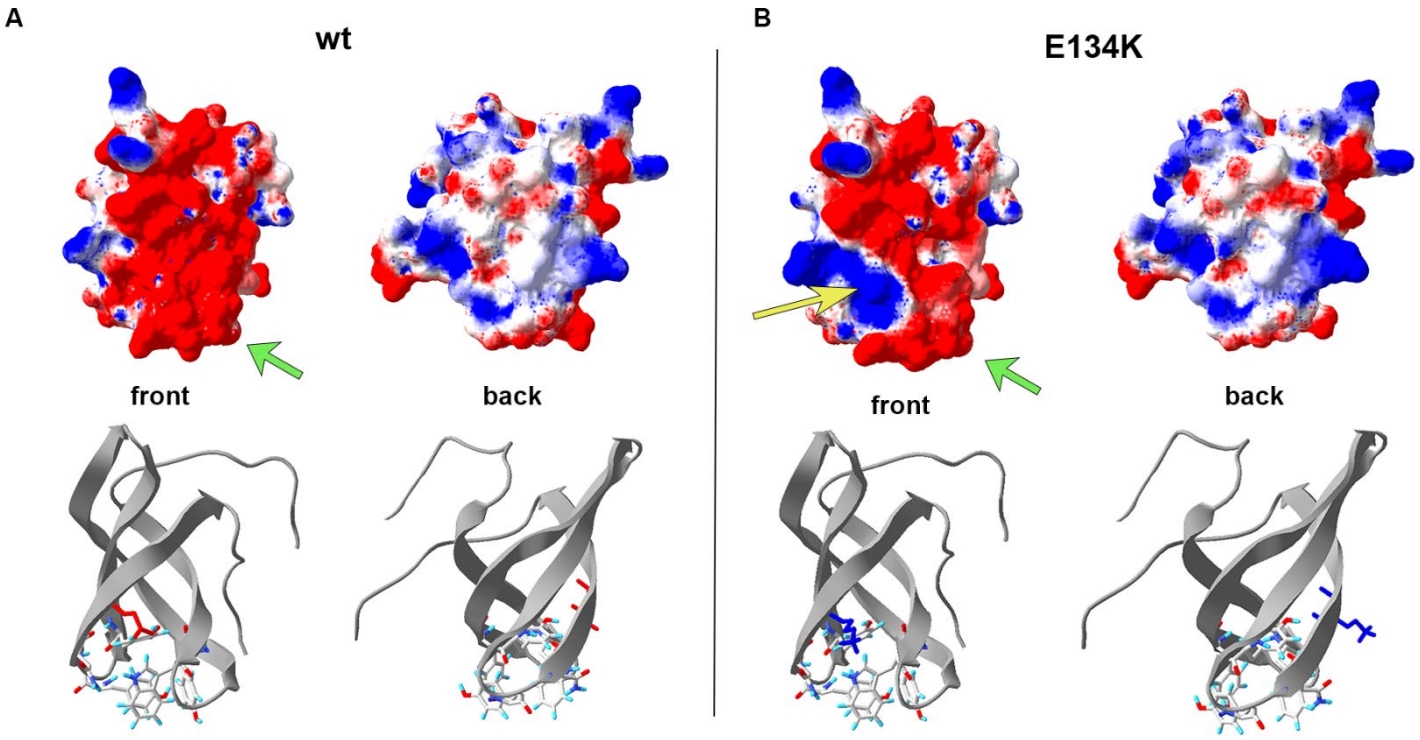

Figure S6. Electrostatic potential surface (top panels) calculated for the Tudor domain in wt (A) and E134K (B) structures. The EP surfaces were calculated with a cutoff of -1.8 k_bT/e for the negative value (in red) and 1.8 K_bT/e for the positive one (in blue), and mapped onto the protein solvent-accessible surface. Both a front and a back view is shown. In the bottom panels the corresponding orientation of the protein is reported in a cartoon representation, with the cage residues highlighted in licorice an colored by atom type. Residue 134 is also in licorice and colored by residue type. The green arrows indicate the negatively charged patches at the surface near the cage; the yellow arrow indicates the increased basicity of the K134 region.

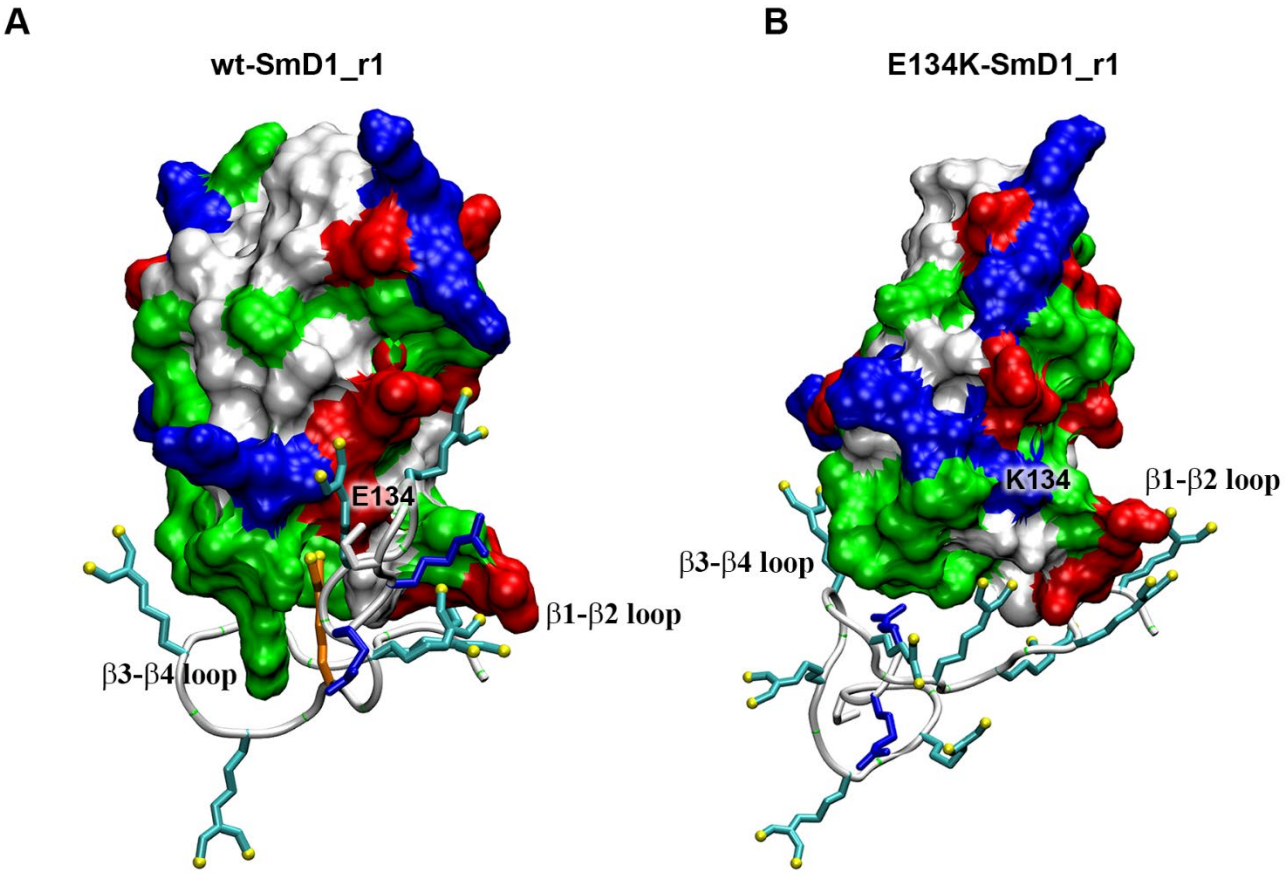

Figure S7. Final conformation of wt-SmD1_r1 and E134K-SmD1_r1 trajectories showing the molecular surface of Tudor domain, colored by residue type. This representation highlights the binding cavity and the contacts of SmD1 tail. Residue 134 is labelled. In the wt structure a DMR is inserted (panel A), whereas in the mutated protein the cavity is open (panel B). The SmD1 tail is represented with a white backbone in cartoon, and DMRs' sidechain in stick and colored in cyan, with the carbons of the symmetrical dimethylation in yellow balls. The DMR the enters the cage is orange, while in blue are colored the two C-terminal arginines that are not methylated.

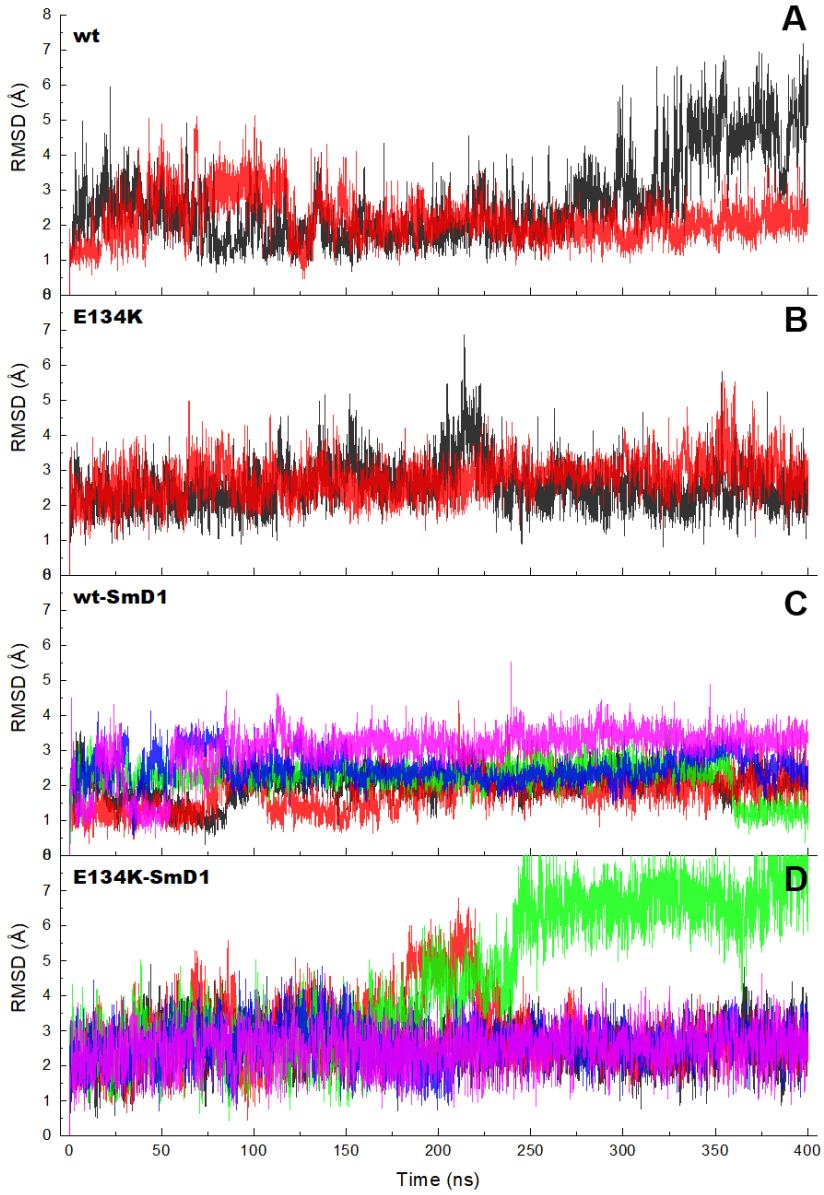

Figure S8. RMSD plots of residue 134 alone, in all the simulations. For each frame, RMSD was calculated on all the atoms of the residue, after superimposition to the starting structure of the Cα atoms of the protein core (residues 92 to 139). The different kinds of simulations are labeled, following the nomenclature in Table 1: panels A and B correspond to the simulations without the SmD1 tail, panels C and D to the simulations in the presence of the SmD1 tail. The replicas of each simulation are progressively colored (r1 is black, r2 is red, r3 is green, r4 is blue, r5 is purple).

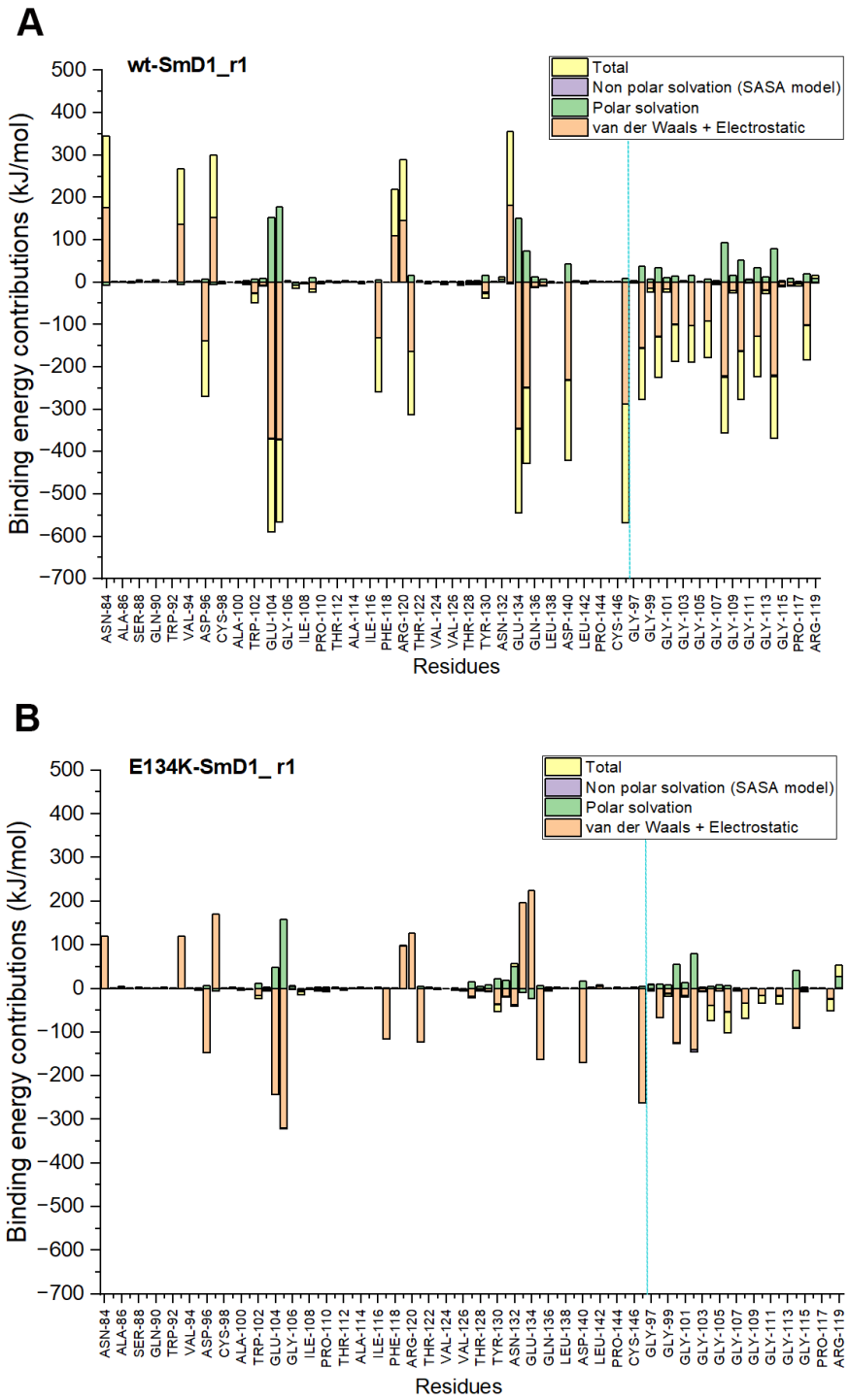

Figure S9. Different energy contributions to the per residue decomposition of average binding energy for wt-SmD1_r1 (A) and E134K-SmD1_r1 (B) trajectories. The cyan dashed line separates the Tudor domain from the SmD1 tail.

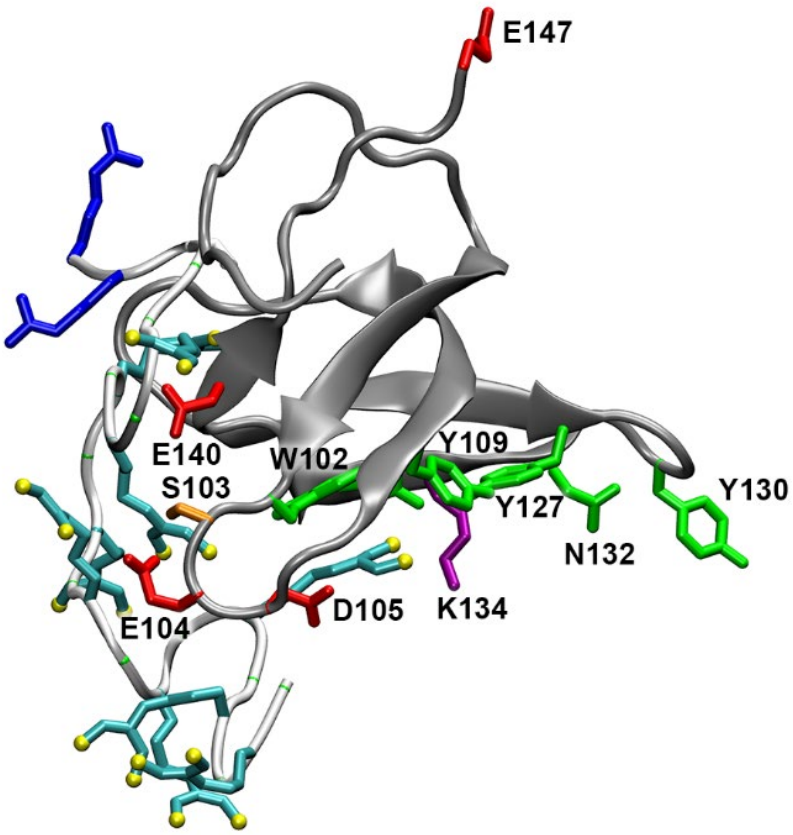

Figure S10. E134K-SmD1_r3 final conformation. In the Tudor structure shown in cartoon (gray), remarkable residues (in licorice) are labeled (in green are the cage residues, in purple Lys134, in red the acidic residues that come in contact with the tail, in orange Ser103). The SmD1 tail is represented with a white backbone in cartoon and the DMRs sidechains in cyan (the yellow balls are the methyl carbons); the not methylated arginines are in blue. The breaking of Lys134-Ser103 H-bond and the abnormal opening of the barrel structure at the cage side is evident.