Supplementary Material

Thr729 in human topoisomerase I modulates anticancer drug resistance by altering protein domain communications as suggested by Molecular Dynamics simulations

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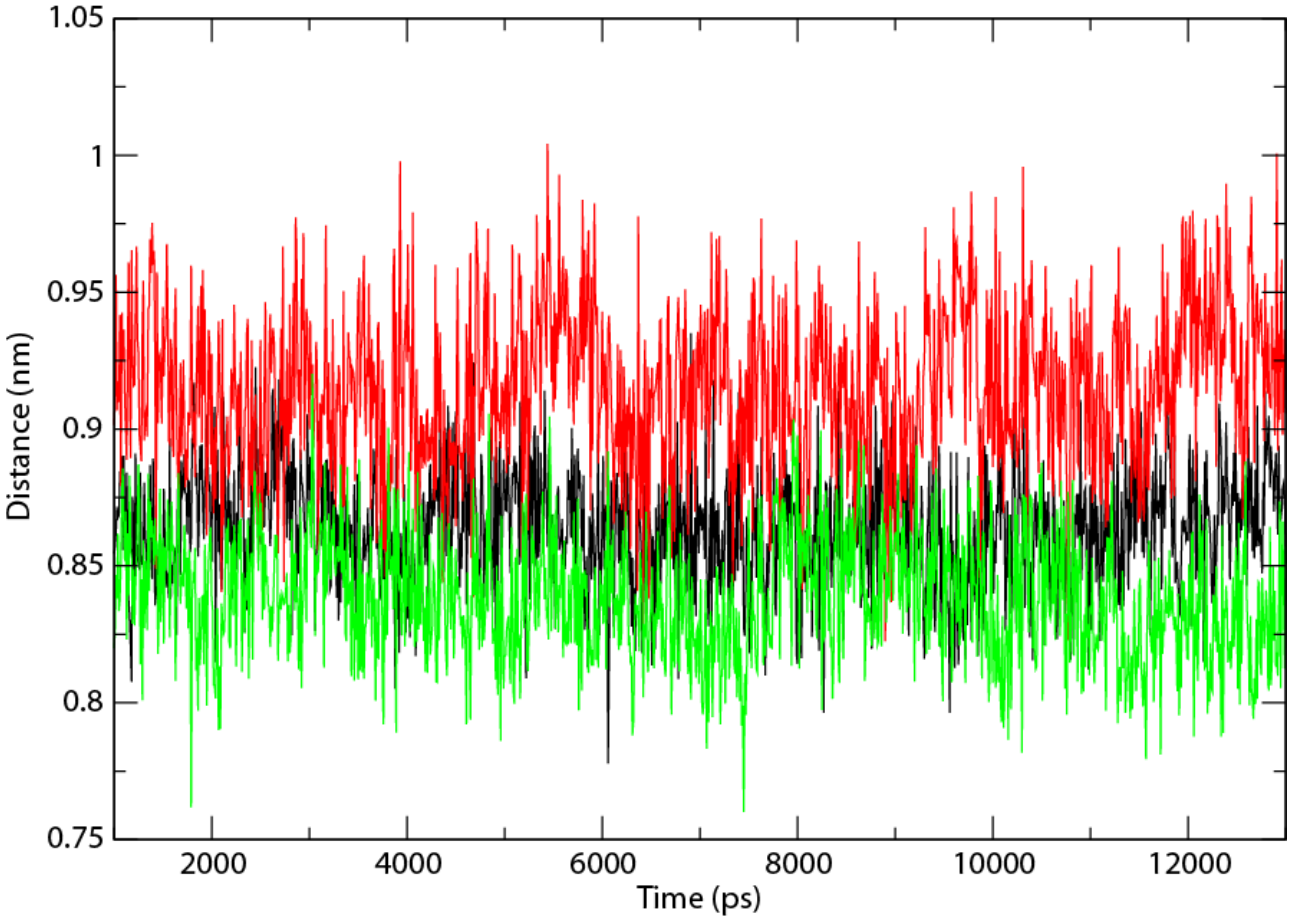

Figure 7. The distance between the c-alpha atoms of Tyr619 and the mutated residue 729 is shown as a function of simulation time for the wild type hTop1p protein (black line), the Tyr729Lys mutant (red line) and the Tyr729Pro mutant (green line).

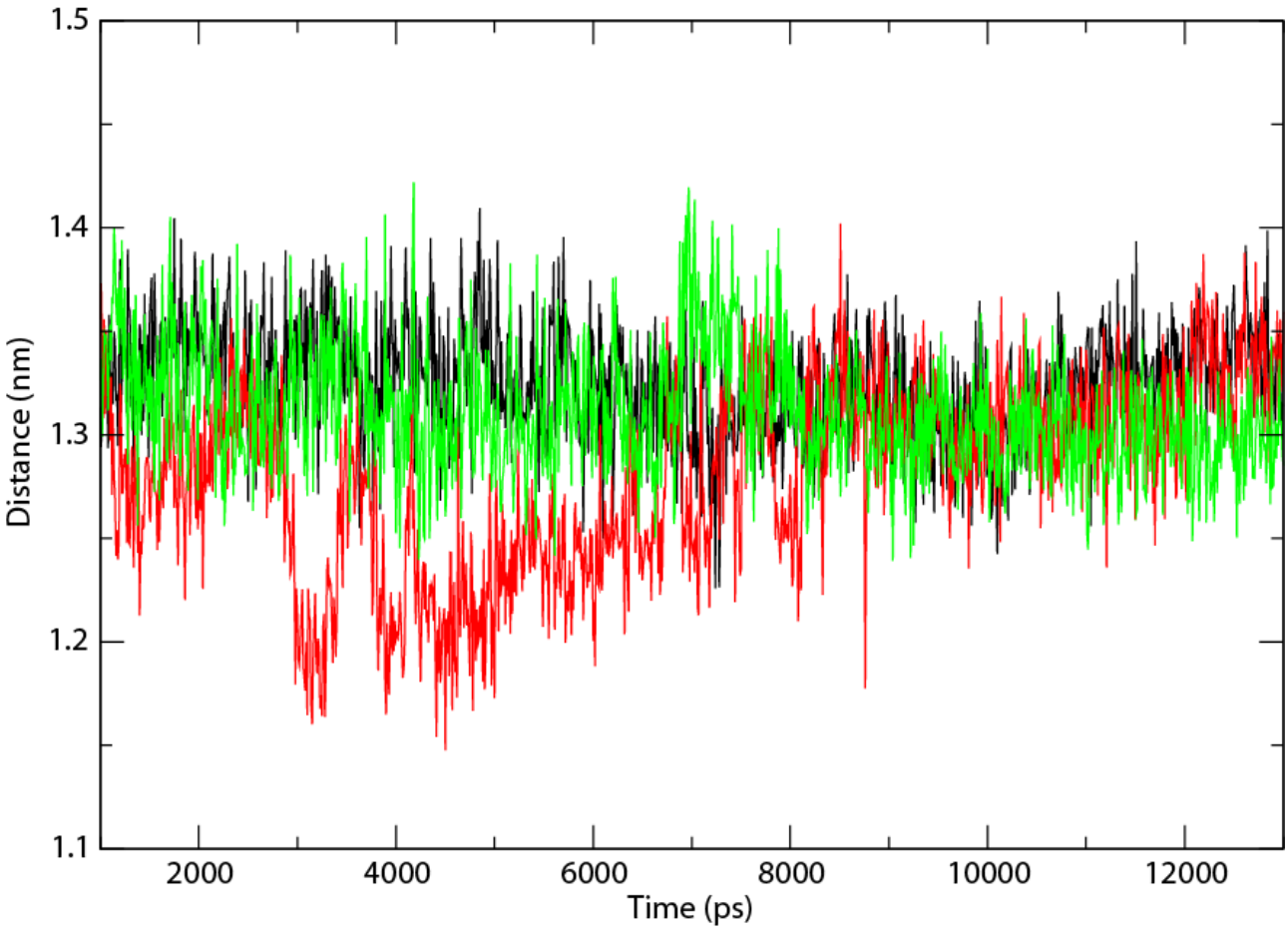

Figure 8. The distance between the c-alpha atoms of Asn722 and the mutated residue 729 is shown as a function of simulation time for the wild type hTop1p protein (black line), Tyr729Lys mutant (red line) and Tyr729Pro mutant (green line).

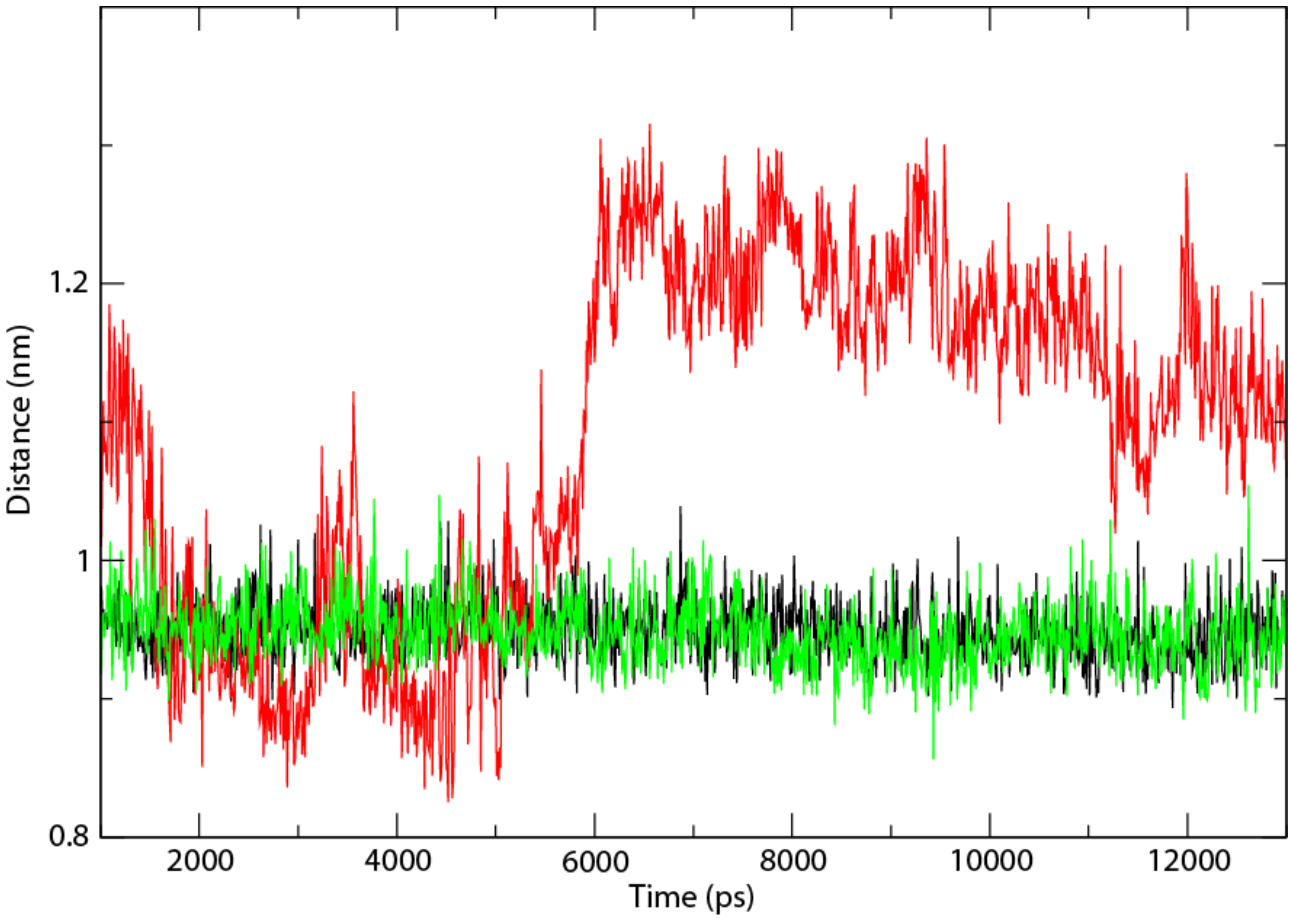

Figure 9. The distance between the c-alpha atoms of Thr606 and Trp732 is shown as a function of simulation time for the wild type hTop1p protein (black line), the Tyr729Lys mutant (red line) and the Tyr729Pro mutant (green line).

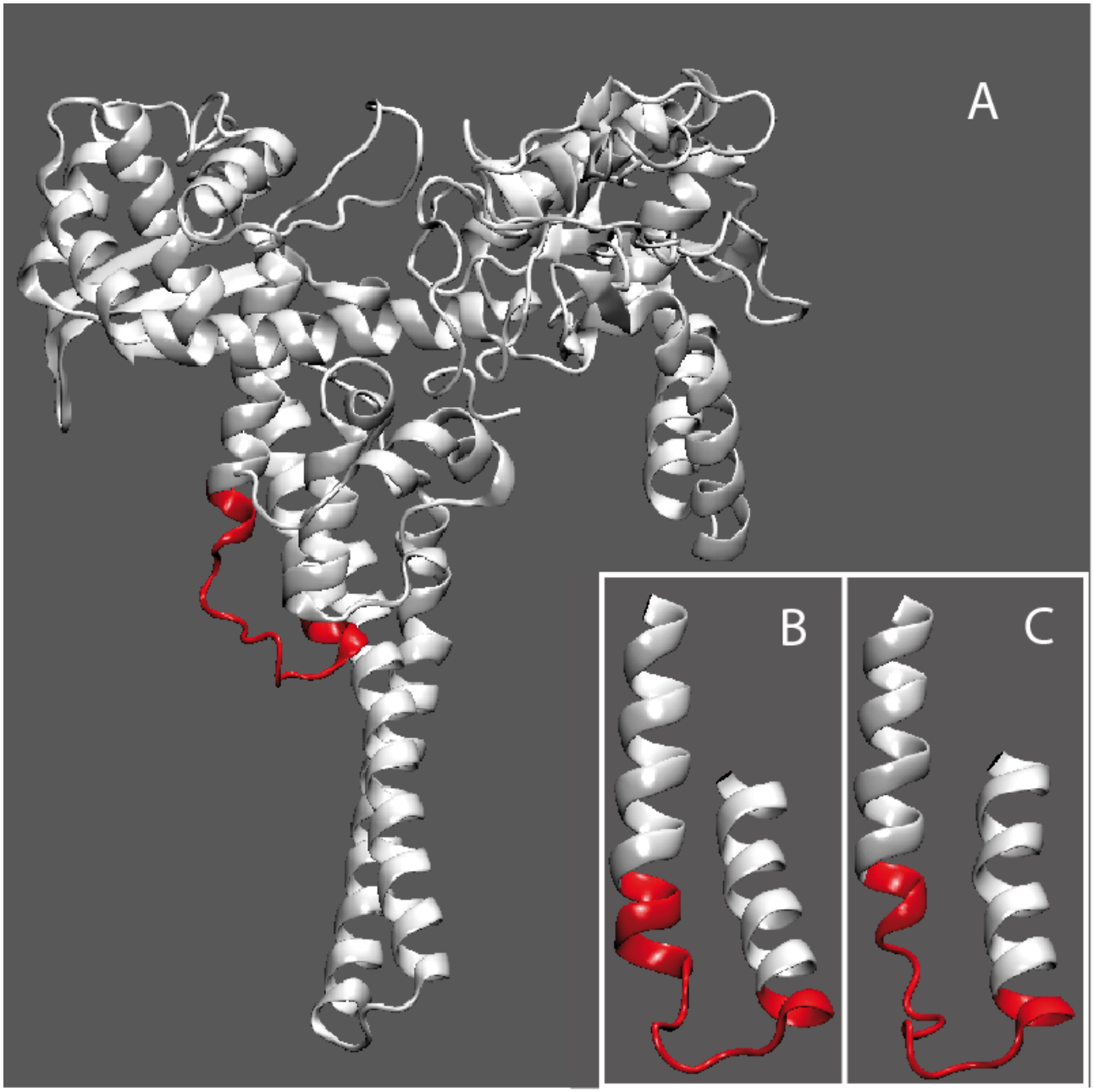

Figure 10. Panel A: Tyr729Lys structure as obtained after 8 ns of simulation time. The region 601-615, having the higher increase in fluctuations with respect to the wild type system, is highlighted in red color. Panels B and C: The region 601-615 is highlighted at the beginning and after 8 ns of simulation time, respectively.

In order to appreciate the substantial statistical convergence of the structural and dynamic results, here we report the average per-residue RMSF and DCC maps analyzed after 8 ns of simulation (i.e. from 1 to 8 ns). Figures 11, 12 and 13 can be compared with Figures 1, 4 and 6, respectively, in which the RMSF and DCC maps are calculated on the whole simulation time (i.e. from 1 to 13 ns).

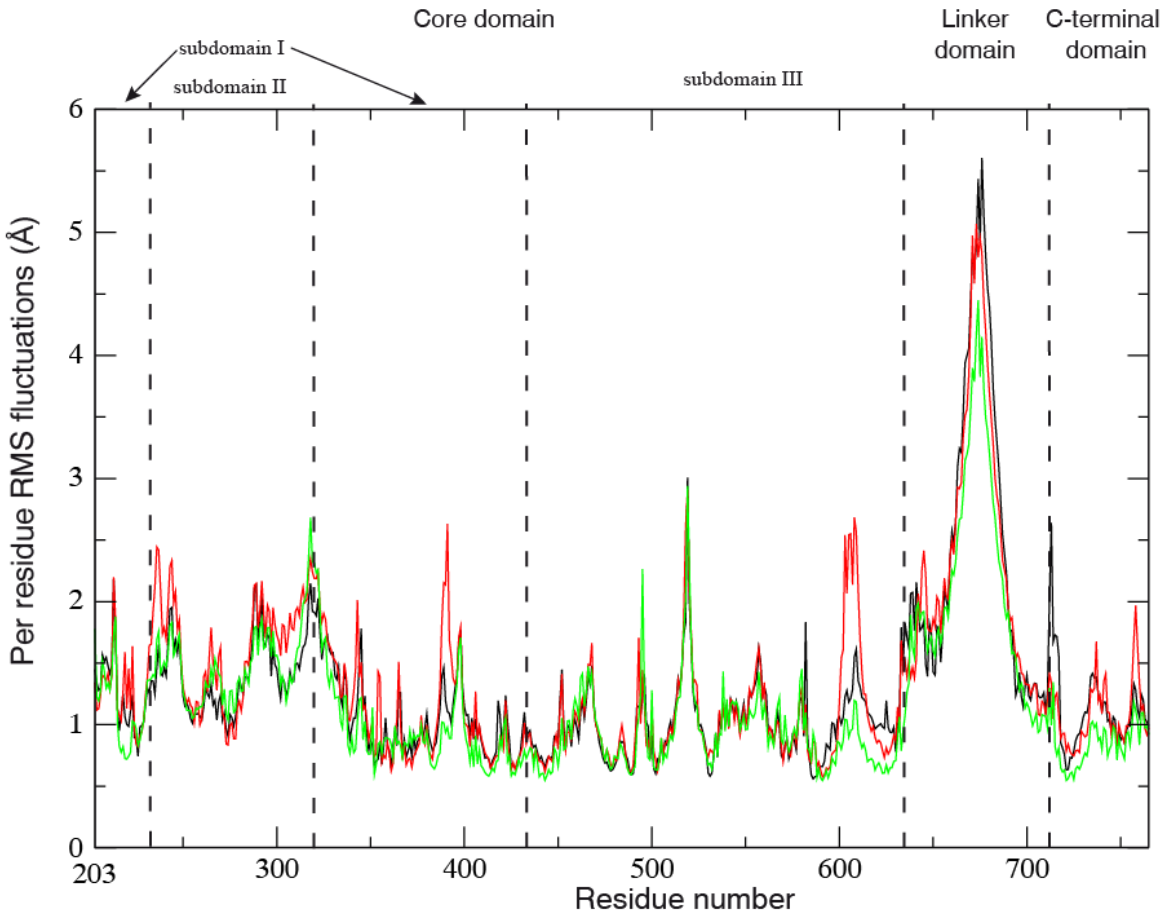

Figure 11. Average per-residue RMSF represented as a function of the residue number for the wild type hTop1p protein (black line), Tyr729Lys mutant (red line) and Tyr729Pro mutant (green line), analyzed on the first 8 ns of simulation time (i.e. from 1 to 8 ns).

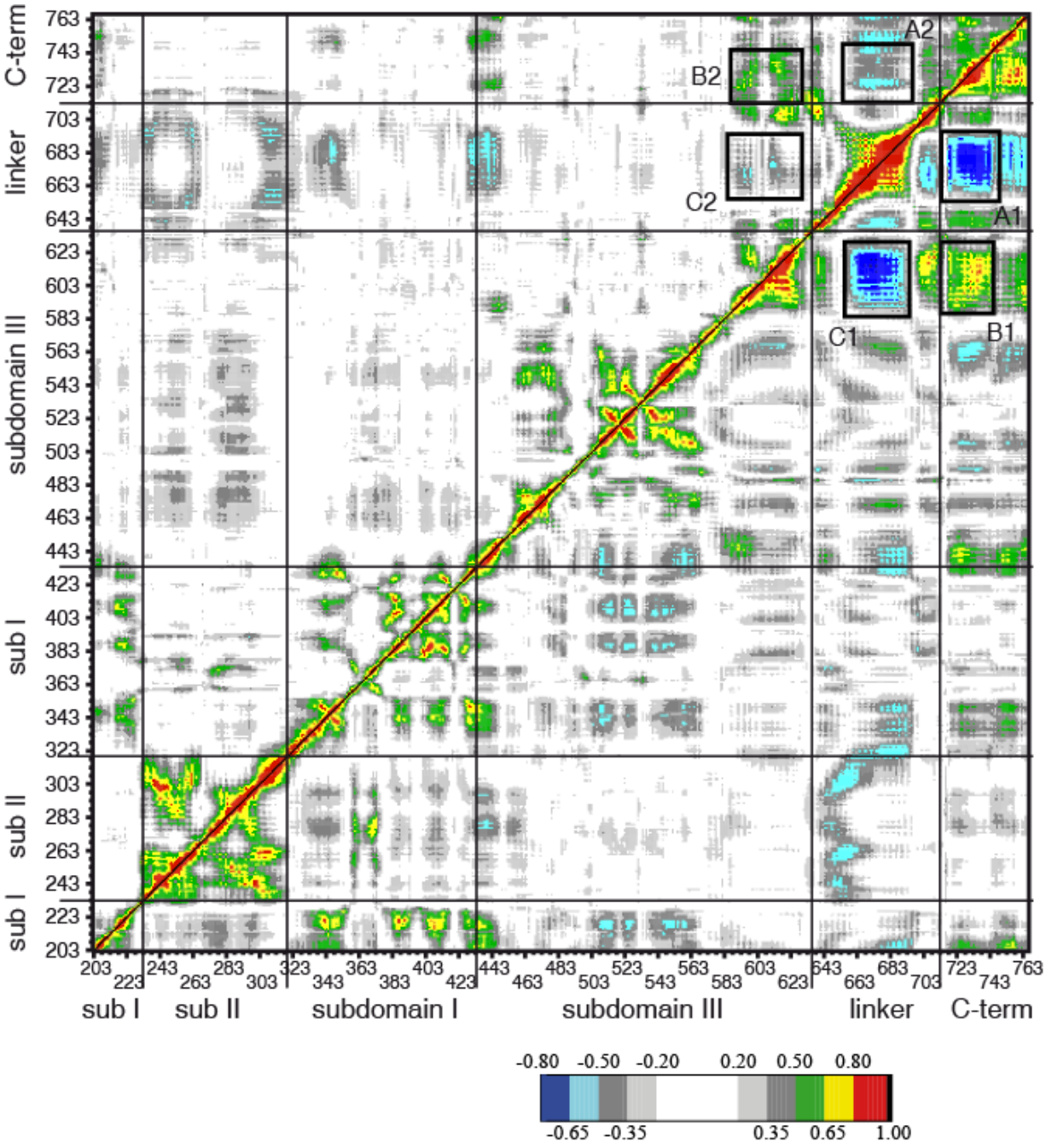

Figure 12. Dynamic cross correlation map for the topo70 (lower right triangle) and T729K mutant (upper left triangle) analyzed on the first 8 ns of simulation time (i.e. from 1 to 8 ns). The color code is as in Figures 4 and 6.

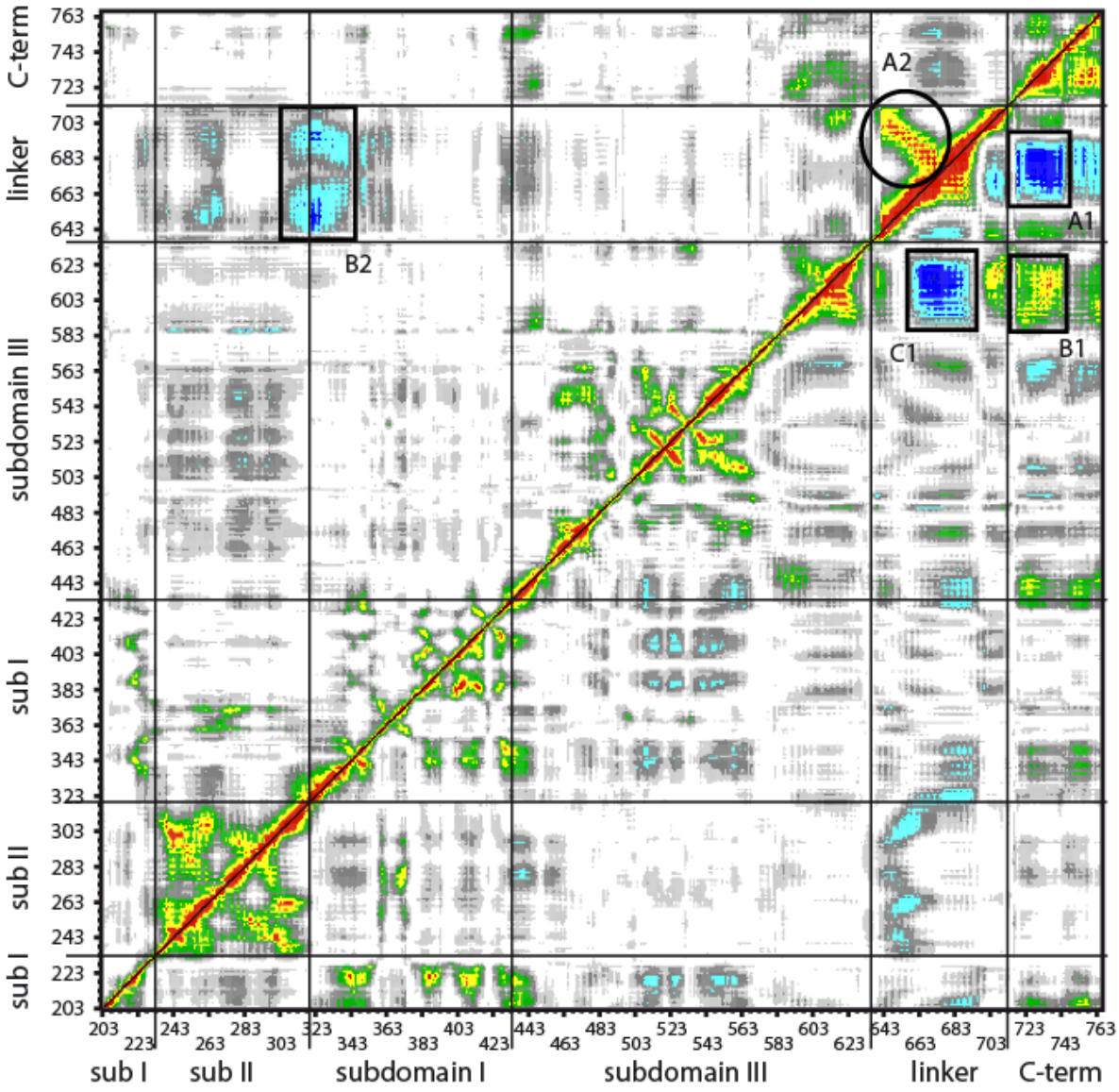

Figure 13. Dynamic cross correlation map for the topo70 (lower right triangle) and T729P mutant (upper left triangle) after 8 ns of simulation time. The color code is as in Figures 4 and 6.