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Supplemental information

**Mechanisms of isoform-specific residue influence on GTP-bound
HRas, KRas, and NRas**

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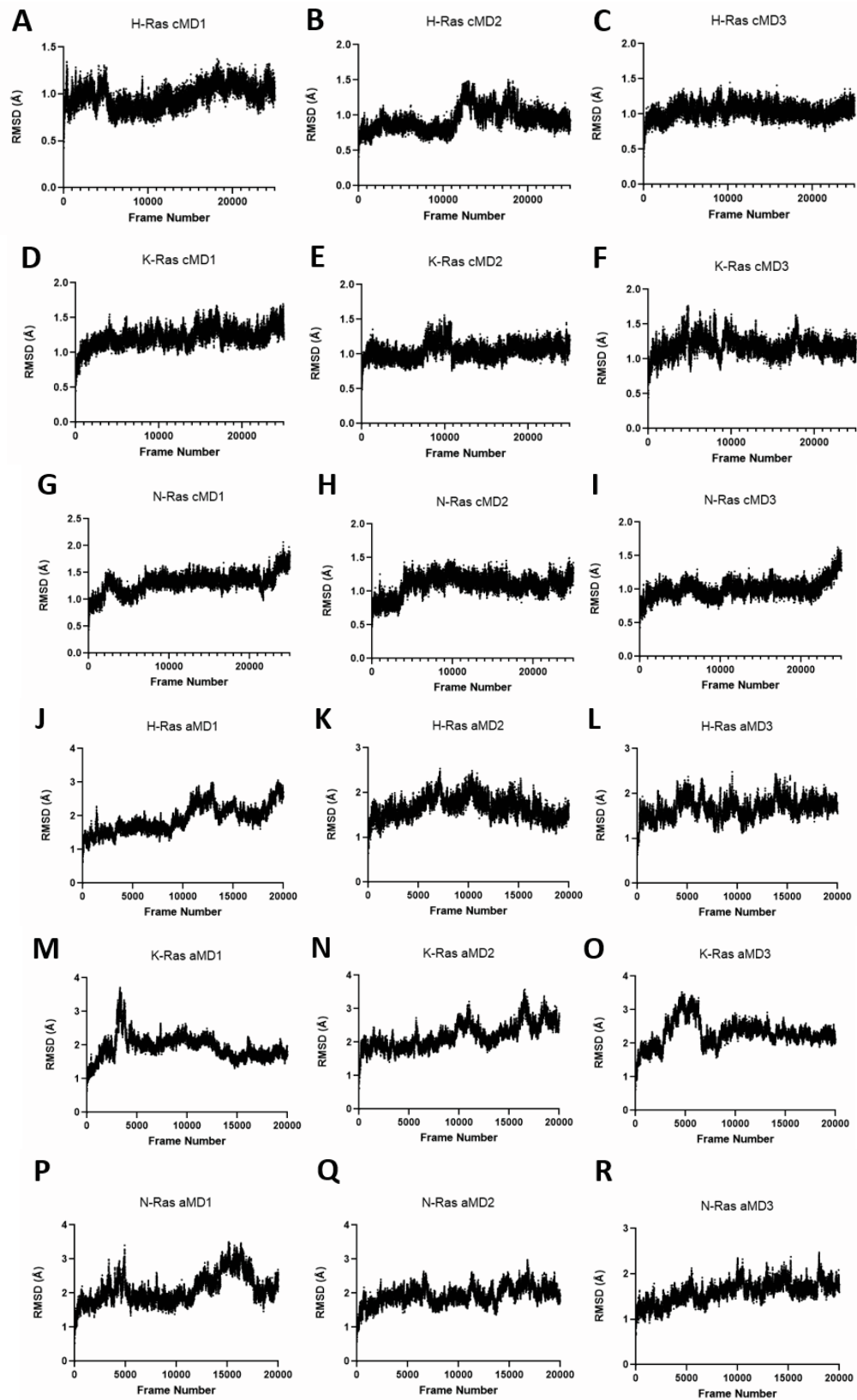


Figure S1. RMSD from starting structure for 18 simulations performed in this study.
A-C: three 200 ns cMD simulations for HRas, starting structure PDB ID 3K8Y.
D-F: three 200 ns cMD simulations for KRas, starting structure PDB ID 5UK9.
G-I: three 200 ns cMD simulations for NRas, starting structure PDB ID 5UHV.
J-L: three 200 ns aMD simulations for HRas, starting structure PDB ID 3K8Y.
M-O: three 200 ns aMD simulations for KRas, starting structure PDB ID 5UK9.
P-R: three 200 ns aMD simulations for NRas, starting structure PDB ID 5UHV.
Each of the triplicate simulations started with randomly generated initial velocities.

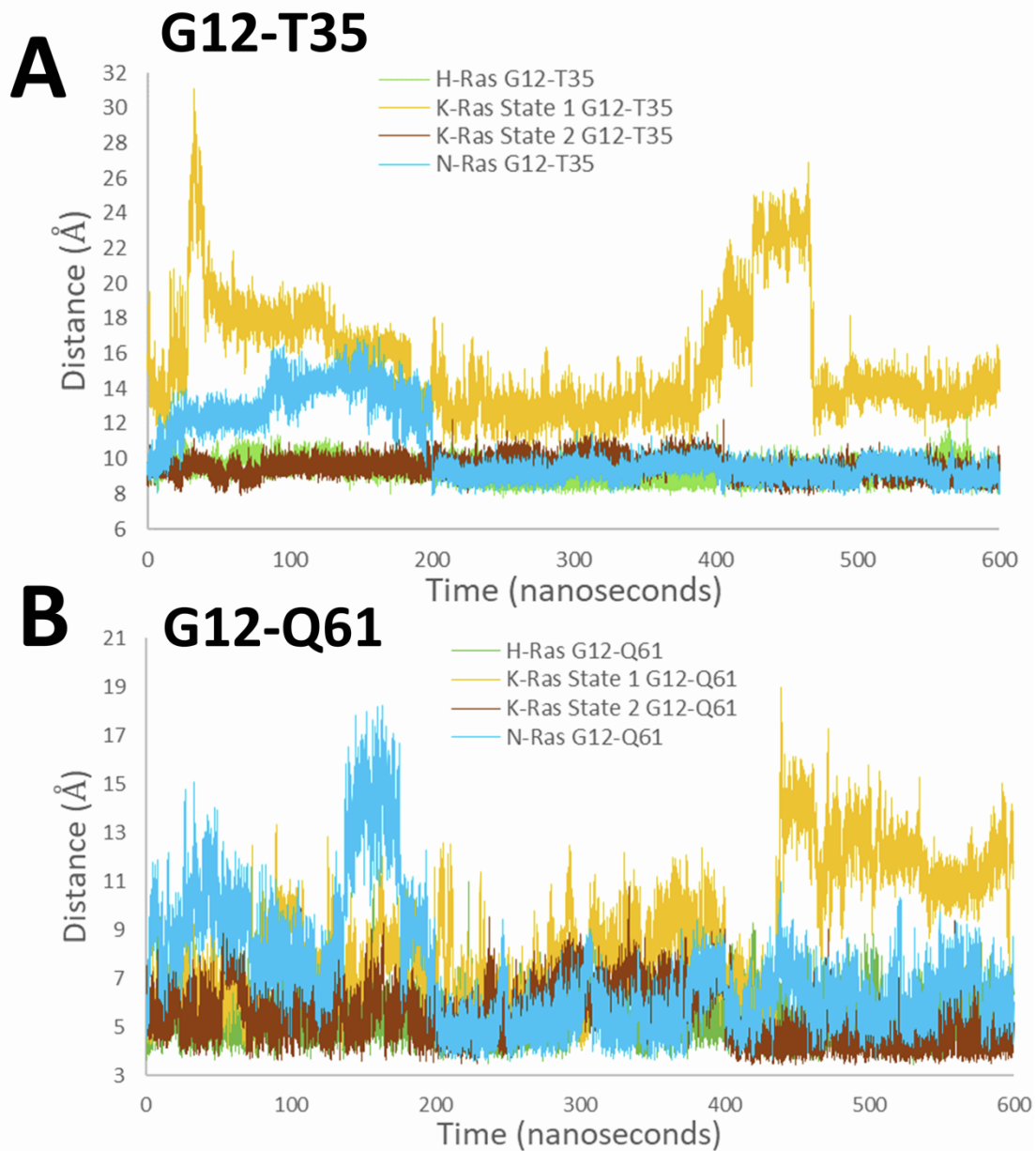


Figure S2. Distance time series for the three aMD simulation replicates for each of the four sets of simulations presented. Replicate 1 is represented as 0-200 ns, replicate 2 200-400 ns and replicate 3 400 – 600 ns for HRas in green, KRas state 1 in yellow, KRas state 2 in maroon and NRas in cyan. The G12-T35 C α distance is indicative of the conformation of switch I. The baseline at around 8-10 Å corresponds to the closed state 2 conformation, while larger distances correspond to various representatives of the open state 1 conformation of the switch. HRas shows one or two transitions to state 1 in the last replicate, while NRas transitions to state 1 early in the first replicate. KRas started in state 2 shows a few transitions to state 1, while KRas started from state 1 mainly samples open conformations of the switch. The G12-Q61 C α distance is a measurement of the openness of switch II, with larger distances associated with a more open switch. HRas remains with a relatively closed switch II throughout the three 200 ns simulation replicates (600 ns), while KRas and NRas significantly sample open conformations of switch II.