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Supplemental Information

Dynamic Structural Differences between Human and Mouse STING Lead to Differing Sensitivity to DMXAA

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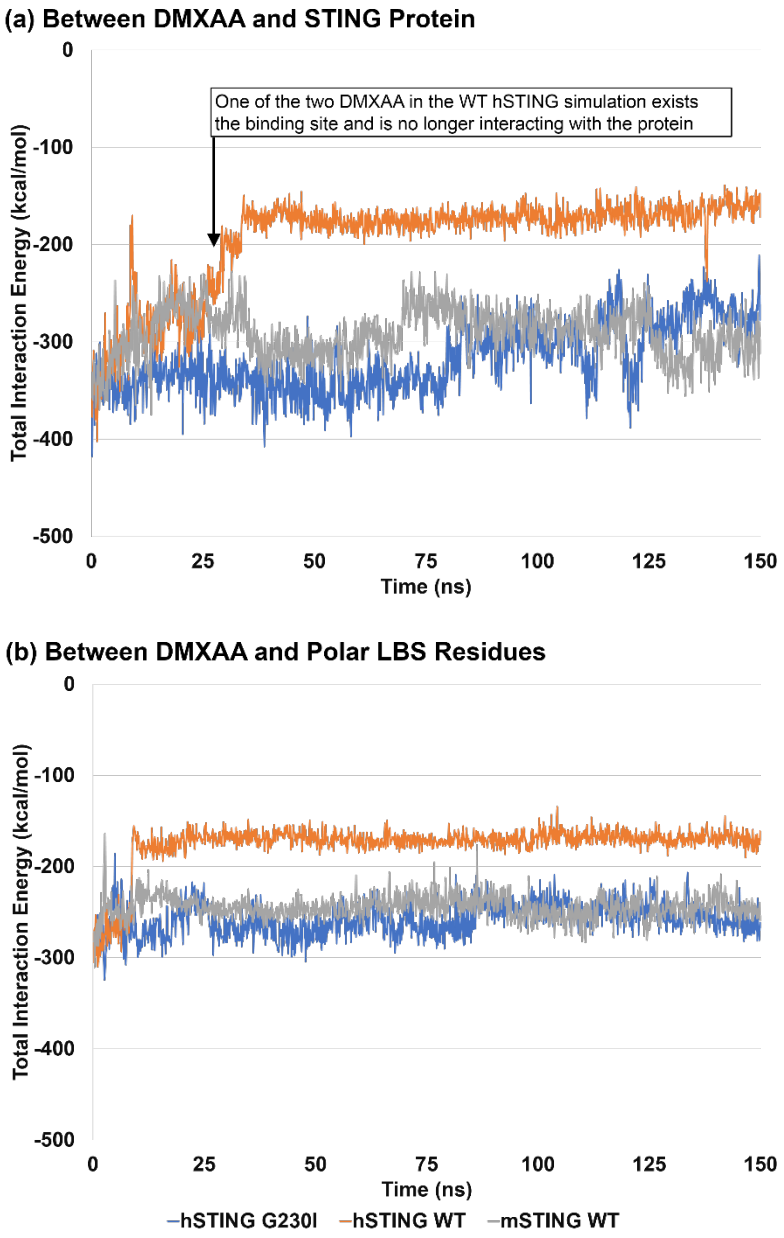

Figure S1. Plot of the (a) total interaction energy between the DMXAA molecules and hSTING G230I (blue), WT hSTING (orange), and WT mSTING (gray) and the (b) total interaction energy between the DMXAA molecules and the polar ligand binding site residues, ARG238, THR263, THR267, and SER162. ARG238 and THR263 form interactions with the carboxylic moiety of DMXAA, while THR267 and SER162 form interactions with the carbonyl group of DMXAA. In the WT hSTING G230I simulation, the decrease in interaction energy between DMXAA and the polar LBS residues results in the eventual exit of the DMXAA.

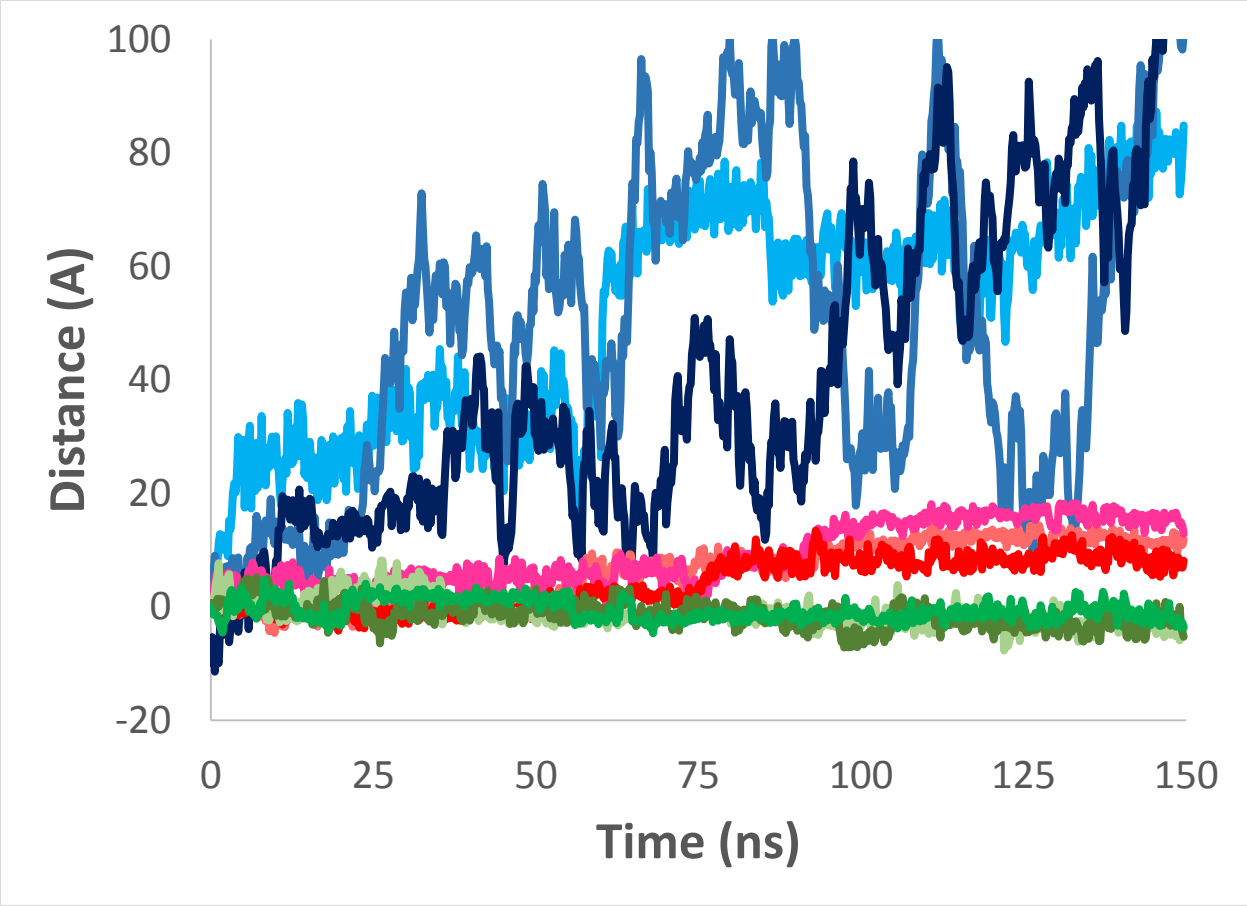

Figure S2. Plot of the distance between Cα atoms of TYR182 on each STING protomer over the course of 150 ns MD simulations. In shades of blue, the three replicates of apo hSTING are shown, in each case the protomers open and separate from each other. In shades of red/pink, the hSTING with cGAMP distances are shown. Although bound to a high affinity native substrate, cGAMP, in each case, the hSTING still moved towards a more open conformation. Lastly, the three replicates of apo mSTING are shown in shades of green. mSTING unlike hSTING, remained in a closed conformation very close to its starting state.