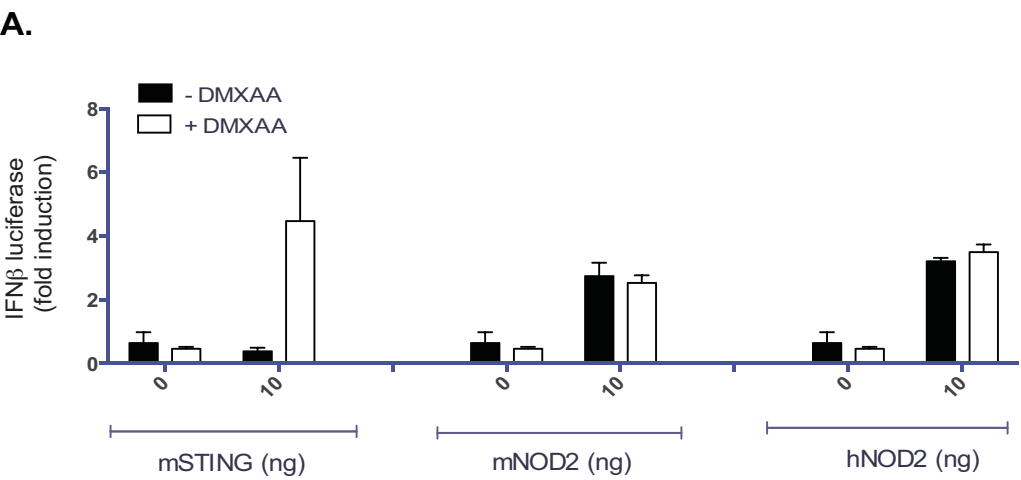
Supplemental Figure Legends.

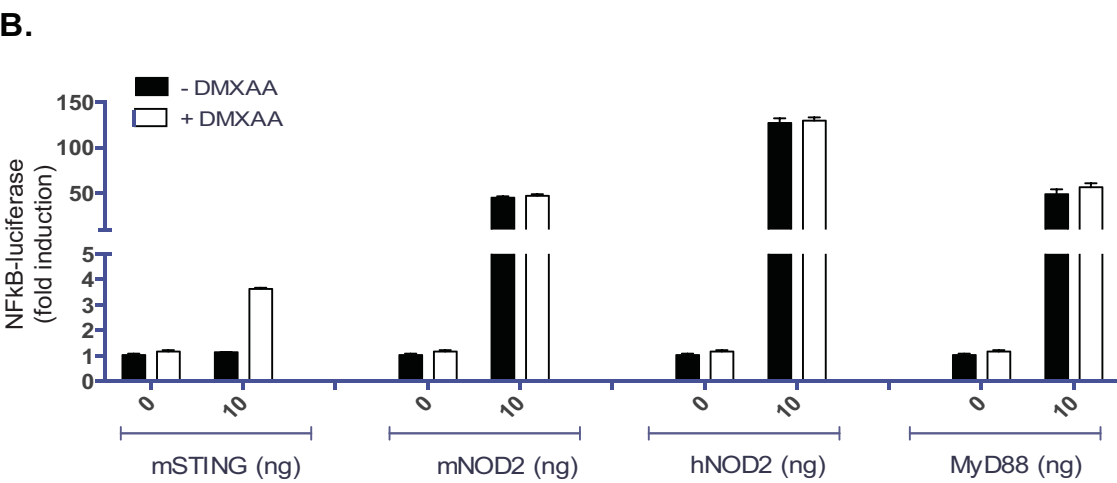
Supplemental Figure 1. STING but neither NOD2 nor DDX41 confers responsiveness of 293T cells to DMXAA. 293T cells were transfected witheither empty vector, mSTING, mNOD2, hNOD2, DDX41 or MyD88 as indicated in the presence of either an IFN-β (A) or NFkB (B) luciferase reporter gene. Transfected cells were stimulated with DMXAA at the doses indicated for 18hours and luciferase activity was measured. Data are presented as the mean ± s.e.m of one experiment representative of three experiments

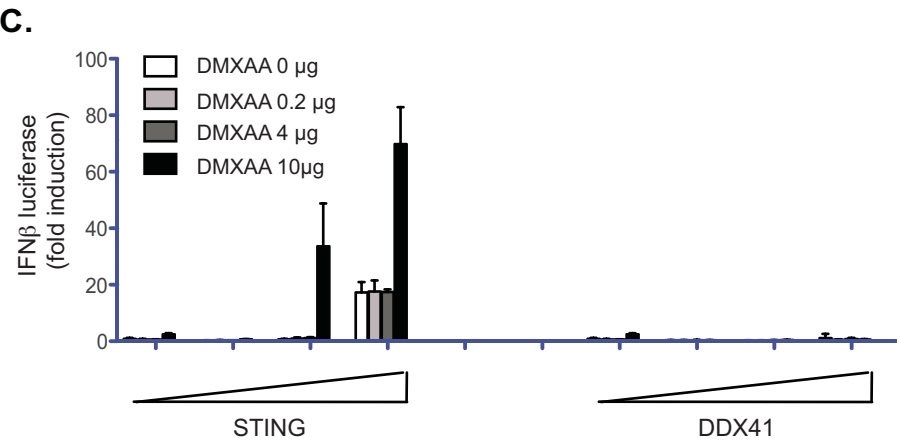
Supplemental Figure 2 Sequence alignment of the human and mouse STING. Identical residues are marked with "*", conserved residues with ":", and partially conserved with ".". Residues involved in c-di-GMP binding in hSTING and their mSTING counterparts are in red, those at the dimerization interface in green, those shown to be essential for signaling but not for c-di-GMP binding in yellow.

Supplemental Fig 3. Ribbon diagram of the human STING CTD structure. The two STING CTDs are colored green and cyan, respectively. The bound c-di-GMP is shown in sticks (orange), and residues different between human and mouse STING are shown in space-filling spheres, which are distal to the c-di-GMP binding pocket.

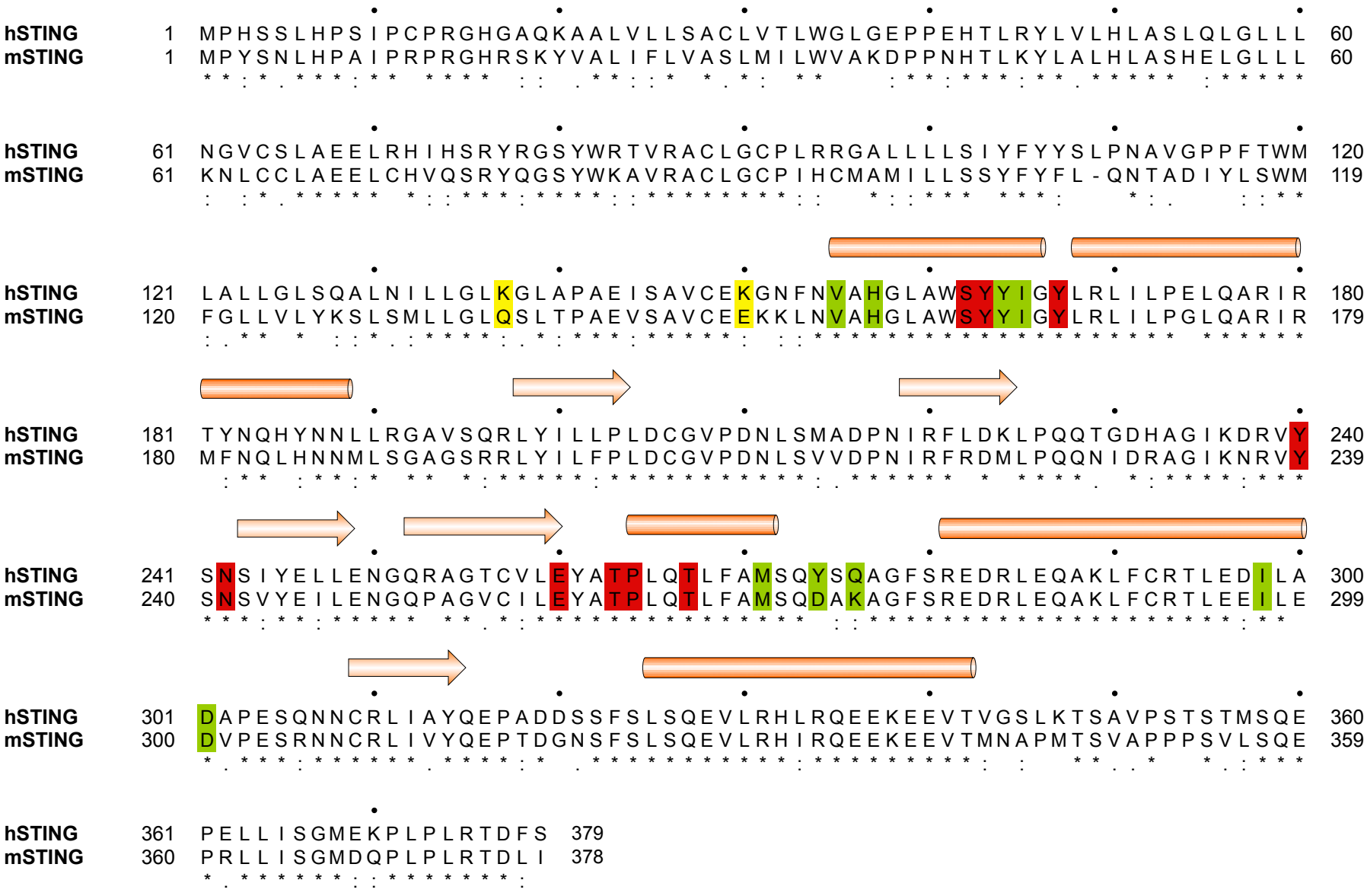
Supplemental Fig 4. Ribbon diagram of a hypothetical model of the STING CTD in complex with DMXAA. The two STING CTDs are colored green and cyan, respectively. The bound DMXAA molecules are shown in sticks (orange).



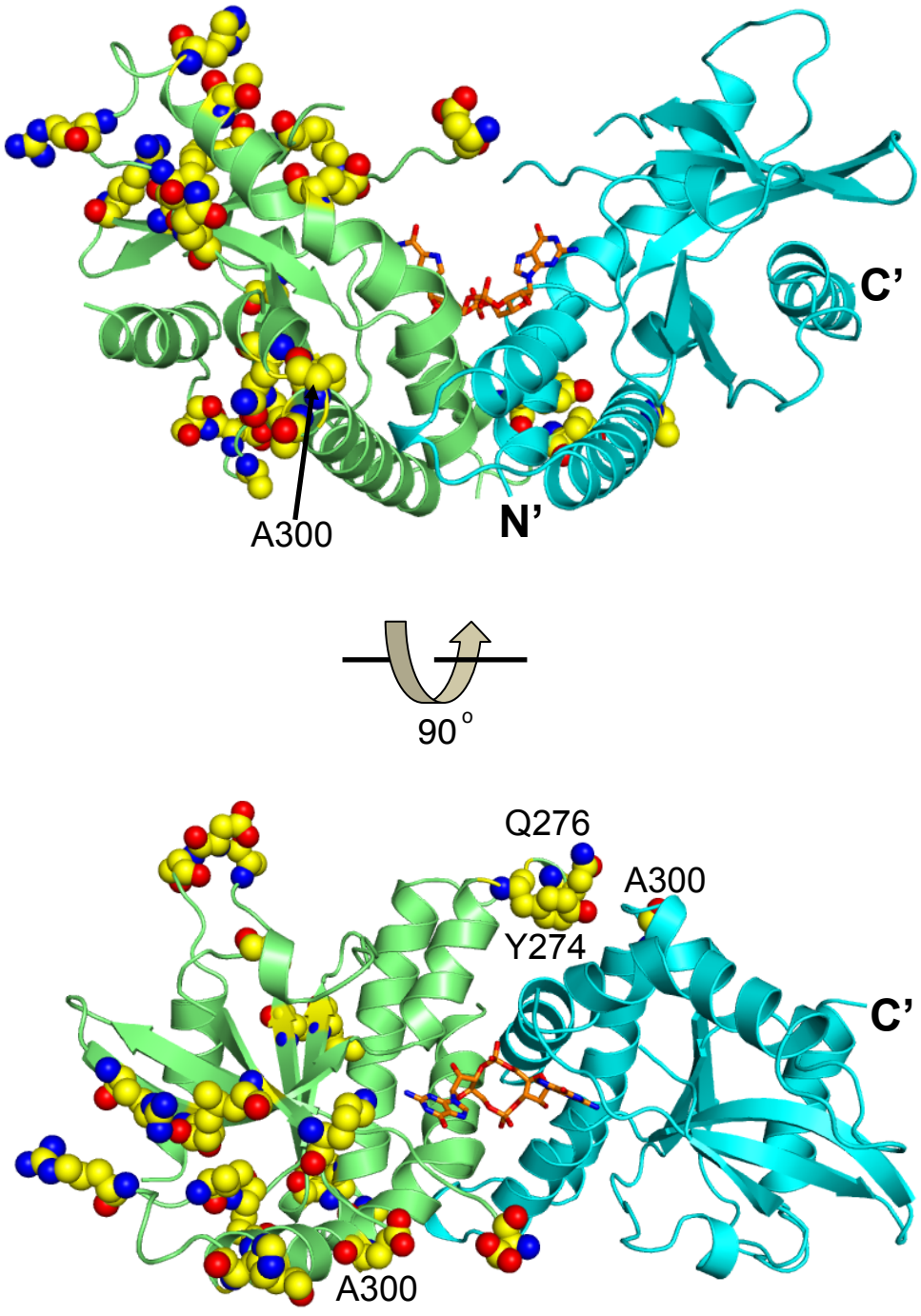




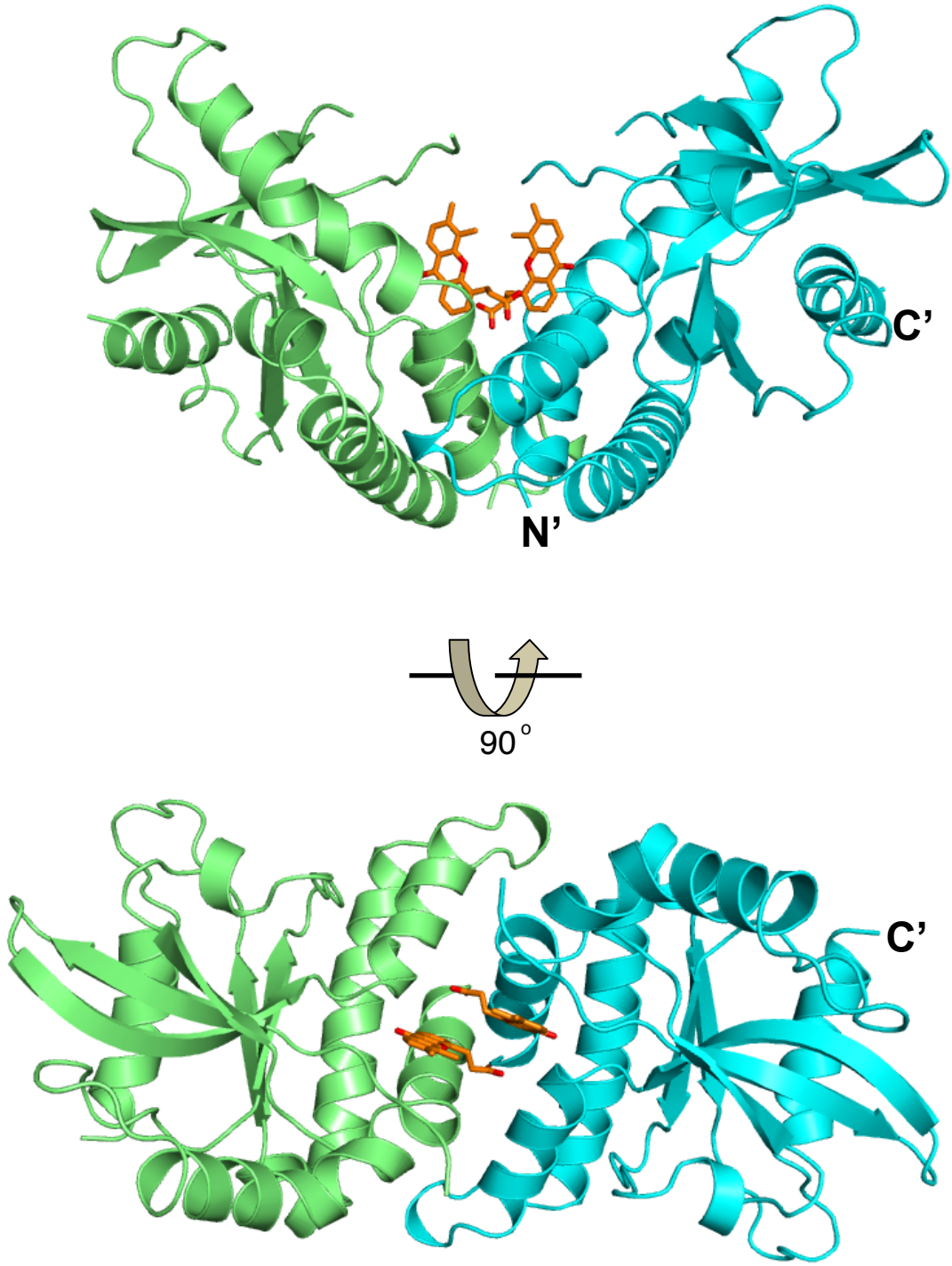
Suppl. Figure 1


hSTING 1 MPHSSLHPSIPCPRGHGAQKAALVLLSACLVTLWGLGEPPEHTLRYLVLHLASLQLGLLL 60
mSTING 1 MPYSNLHPAIPRPRGHRSKYVALIFLVASLMILWVAKDPPNHTLKYLALHLASHELGLLL 60
hSTING 61 NGVCSLAEELRHIHSRYRGSYWRTVRACLGCPLRRGALLLLSIYFYYSLPNAVGPPFTWM 120
mSTING 61 KNLCCLAEELCHVQSRYQGSYWKAVRACLGCPIHCMAMILLSSYFYFL-QNTADIYLSWM 119
hSTING 121 LALLGLSQALNILLGLKGLAPAEISAVCEKGNFNVAHGLAWSYYIGYLRLILPELQARIR 180
mSTING 120 FGLLVLYKSLSMLLGLQSLTPAEVSAVCEEKKLNVAHGLAWSYYIGYLRLILPGLQARIR 179
hSTING 181 TYNQHYNNLLRGAVSQRLYILLPLDCGVPDNLSMADPNIRFLDKLPQQTGDHAGIKDRVY 240
mSTING 180 MFNQLHNNMLSGAGSRRLYILFPLDCGVPDNLSVVDPNIRFRDMLPQQNIDRAGIKNRVY 239
hSTING 241 SNSIYELLENGQRAGTCVLEYATPLQTLFAMSQYSQAGFSREDRLEQAKLFCRTLEDILA 300
mSTING 240 SNSVYEILENGQPAGVCILEYATPLQTLFAMSQDAKAGFSREDRLEQAKLFCRTLEEILE 299
hSTING 301 DAPESQNNCRLIAYQEPADDSSFSLSQEVLRHLRQEEKEEVTVGSLKTSAVPSTSTMSQE 360
mSTING 300 DVPESRNNCRLIVYQEPTDGNSFSLSQEVLRHIRQEEKEEVTMNAPMTSVAPPPSVLSQE 359
hSTING 361 PELLISGMEKPLPLRTDFS 379
mSTING 360 PRLLISGMDQPLPLRTDLI 378

Suppl. Fig 2.



Suppl. Fig. 3



Suppl. Fig. 4.