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Supporting information for article:

**Structural insight into the rearrangement of the Switch I region in
GTP-bound G12A K-Ras**

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Table S1 Pairwise RMSD values of comparison between K-Ras in complex with different nucleotides, including the SI and SII regions.

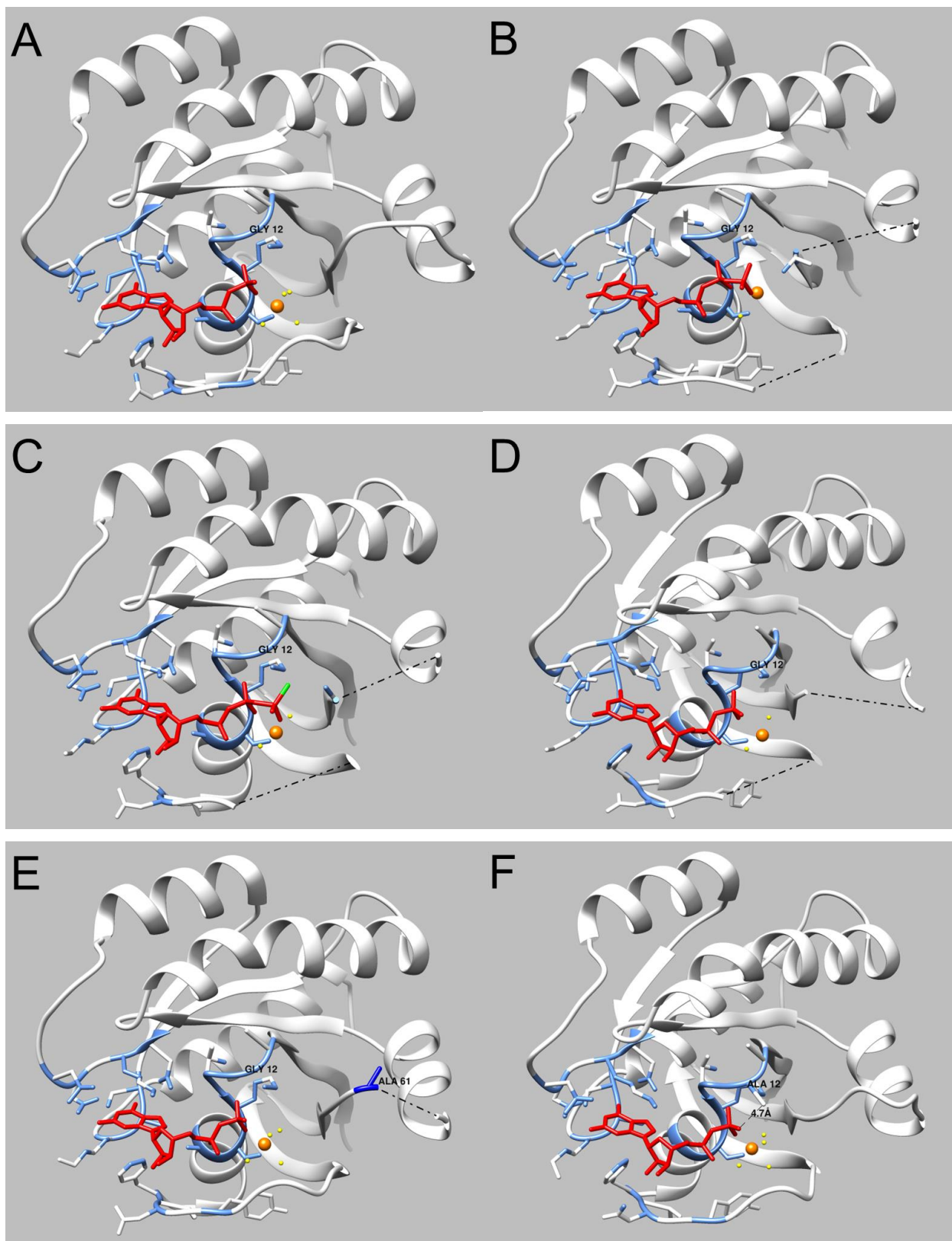
RMSD of the whole structure	WT-K-Ras-GDP (EDTA)	WT-K-Ras-GDP	WT-K-Ras-GTP	WT-K-Ras-GTP γ S	G12A-K-Ras-GDP (EDTA)	G12A-K-Ras-GDP	G12A-K-Ras-GTP	G12A-K-Ras-GTP γ S	G12A-K-Ras-GppNHp	Q61A-K-Ras-GDP
WT-K-Ras-GDP (EDTA)		0.317	0.313	0.275						
WT-K-Ras-GDP	0.317		0.476	0.327		0.307				0.374
WT-K-Ras-GTP	0.313	0.476		0.244			0.852			
WT-K-Ras-GTP γ S	0.275	0.327	0.244							
G12A-K-Ras-GDP (EDTA)						0.185	1.091	0.301	0.307	
G12A-K-Ras-GDP		0.307			0.185		0.654	0.259	0.266	0.350
G12A-K-Ras-GTP			0.852		1.091	0.654		0.619	0.636	
G12A-K-Ras-GTP γ S					0.301	0.259	0.619		0.153	
G12A-K-Ras-GppNHp					0.307	0.266	0.636	0.153		
Q61A-K-Ras-GDP		0.374				0.350				
RMSD of residues in SI region	WT-K-Ras-GDP (EDTA)	WT-K-Ras-GDP	WT-K-Ras-GTP	WT-K-Ras-GTP γ S	G12A-K-Ras-GDP (EDTA)	G12A-K-Ras-GDP	G12A-K-Ras-GTP	G12A-K-Ras-GTP γ S	G12A-K-Ras-GppNHp	Q61A-K-Ras-GDP

WT-K-Ras-GDP (EDTA)		0.722	0.775	0.826						
WT-K-Ras-GDP	0.722		1.915	0.746		0.219				0.339
WT-K-Ras-GTP	0.775	1.915		0.244			3.117			
WT-K-Ras-GTP γ S	0.826	0.746	0.244							
G12A-K-Ras-GDP (EDTA)						0.347	2.206	0.869	1.028	
G12A-K-Ras-GDP		0.219			0.347		2.145	0.669	0.868	0.218
G12A-K-Ras-GTP			3.117		2.206	2.145		2.410	2.799	
G12A-K-Ras-GTP γ S					0.869	0.669	2.410		0.477	
G12A-K-Ras-GppNHp					1.028	0.868	2.799	0.477		
Q61A-K-Ras-GDP		0.339				0.218				
RMSD of residues in SI region	WT-K-Ras-GDP (EDTA)	WT-K-Ras-GDP	WT-K-Ras-GTP	WT-K-Ras-GTP γ S	G12A-K-Ras-GDP (EDTA)	G12A-K-Ras-GDP	G12A-K-Ras-GTP	G12A-K-Ras-GTP γ S	G12A-K-Ras-GppNHp	Q61A-K-Ras-GDP
WT-K-Ras-GDP (EDTA)		1.644	0.546	0.418						
WT-K-Ras-GDP	1.644		0.549	0.622		1.514				0.792
WT-K-Ras-GTP	0.546	0.549		0.439			2.403			

WT-K-Ras-GTP γ S	0.418	0.622	0.439							
G12A-K-Ras-GDP (EDTA)						0.280	1.740	0.507	0.533	
G12A-K-Ras-GDP		1.514			0.280		2.077	0.472	0.562	0.798
G12A-K-Ras-GTP			2.403		1.740	2.077		1.885	1.867	
G12A-K-Ras-GTP γ S					0.507	0.472	1.885		0.283	
G12A-K-Ras-GppNHp					0.533	0.562	1.867	0.283		
Q61A-K-Ras-GDP		0.792				0.798				

Table S2 Phi and Psi dihedral angles of residues in the SI and SII regions in K-Ras in complex with different nucleotides.

(Φ , Ψ) of residues	WT-K- Ras-GDP	WT-K- Ras- GDP (EDTA)	WT-K- Ras-GTP	WT-K- Ras- GTP γ S	G12A-K- Ras-GDP	G12A-K- Ras-GDP (EDTA)	G12A- K-Ras- GTP	G12A-K- Ras- GTP γ S	G12A-K- Ras- GppNHp	Q61A-K- Ras-GDP
Asp30	-79,-23	-93,-20	-70,-39	-69,-41	-69,-27	-76,-27	-60,-36	-77,-33	-70,-32	-52,-46
Glu31	-152,101	-139,126	-132,136	-144,149	-147,81	-149,87	-97,140	-141,107	-139,121	-140,117
Tyr32	-120,143	-170,---	-141,126	-142,---	-106,134	-108,128	-86,108	-107,165	-136,-144	-126,123
Asp33	-53,120	---,---	38,---	---,---	-44,119	-47,111	-115,79	-77,117	41,---	-32,116
Pro34	-67,-11	---,---	---,---	---,---	-69,-13	-58,-13	-64,---	-58,---	---,---	-70,1
Thr35	-103,-12	---,---	---,---	---,---	-95,-19	-91,-18	---,---	---,---	---,---	-102,-20
Ile36	-70,113	---,---	---,---	---,---	-70,107	-69,108	---,---	---,---	---,---	-66,105
Glu37	-108,124	---,---	---,73	---,---	-100,128	-111,123	---,117	---,---	---,---	-99,121
Asp38	-159,172	---,170	-160,-153	---,-164	-169,168	-163,166	-156,177	---,172	---,177	-162,170
Gly60	82,-174	---,---	---,---	---,---	71,59	106,---	---,---	---,---	---,---	85,-163
Gln61	-116,-162	---,---	---,---	---,---	-50,-31	---,---	---,---	---,---	---,---	178,---
Glu62	78,104	---,---	---,---	---,---	-52,-45	---,---	---,---	---,---	---,---	---,---
Glu63	53,77	---,---	---,---	---,---	-106,153	---,---	---,---	---,---	---,---	---,---
Tyr64	-53,127	---,---	---,---	---,---	-64,146	---,---	---,---	---,---	---,---	---,---
Ser65	-59,166	---,---	---,---	---,---	-141,119	---,---	---,---	---,---	---,---	---,128
Ala66	-53,-43	---,---	---,---	---,---	-70,-33	---,---	---,---	---,---	---,---	-73,-34
Met67	-61,-52	---,42	---,---	---,---	-65,-50	---,---	---,---	---,---	---,---	-63,-49
Arg68	-60,-46	-126,48	---,---	---,---	-67,-42	---,---	---,---	---,---	---,---	-63,-46
Asp69	-56,-45	-86,-3	---,-179	---,-24	-52,-47	---,---	---,-36	---,164	---,159	-50,-48
Gln70	-59,-45	-85,-16	-54,-59	-55,-54	-63,-40	---,-41	-59,-58	-49,-62	-81,9	-66,-41
Tyr71	-71,-38	-78,-35	-62,-37	-67,-37	-75,-35	-73,-45	-75,-29	-67,-33	-114,-41	-69,-39
Met72	-61,-43	-61,-46	-63,-38	-57,-36	-64,-45	-58,-51	-69,-30	-65,-41	-56,-40	-60,-47
Arg73	-68,-46	-76,-38	-90,-26	-93,-28	-66,-41	-65,-47	-68,-38	-75,-32	-82,-27	-69,-40
Thr74	-103,-5	-93,-22	-101,-5	-102,-2	-109,-8	-97,-11	-100,-22	-106,-7	-100,-11	-109,-8
Gly75	-56,136	-59,138	-62,141	-59,135	-64,143	-64,136	-58,140	-59,-140	-55,137	-62,144
Glu76	-93,-26	-96,-24	-94,-29	-90,-30	-95,-28	-94,-17	-93,-30	-91,-30	-90,-30	-98,-25



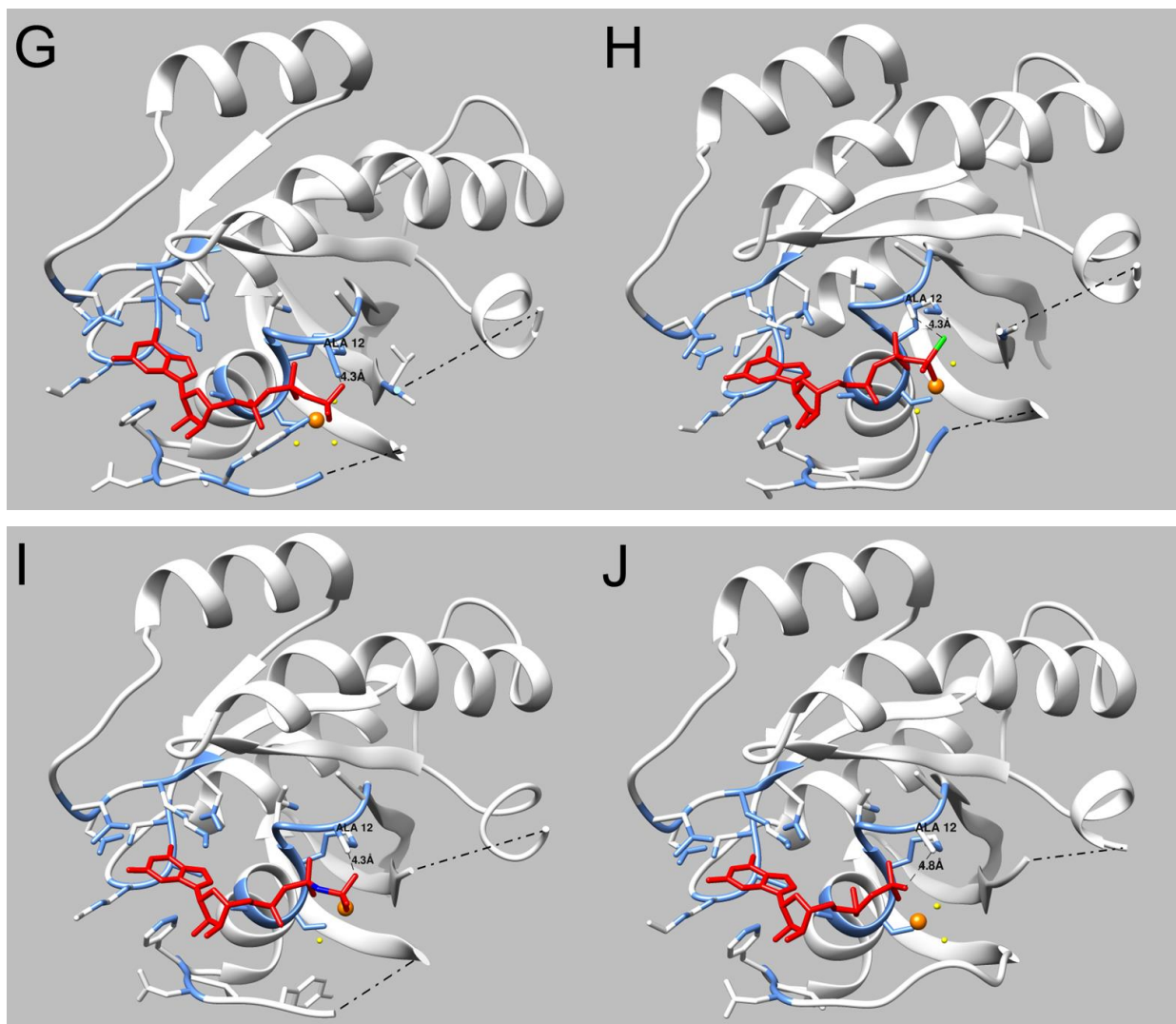


Figure S1 Ribbon diagrams showing nucleotide coordination environments. Ribbon diagram of (A) WT-K-Ras-GDP, (B) WT-K-Ras-GTP, (C) WT-K-Ras-GTPγS, (D) EDTA treated WT-K-Ras-GDP, (E) Q61A-K-Ras-GDP, (F) G12A-K-Ras-GDP, (G) G12A-K-Ras-GTP, (H) G12A-K-Ras-GTPγS, (I) G12A-K-Ras-GppNHp, (J) EDTA treated G12A-K-Ras-GDP. Backbones (white), GDP or GTP (red), Mg²⁺ (orange), water molecules that coordinate with Mg²⁺ (yellow), sulfur atom in GTPγS (green), nitrogen atom in GppNHp (blue), residues within 4 Å of GDP or GTP (cornflower blue).

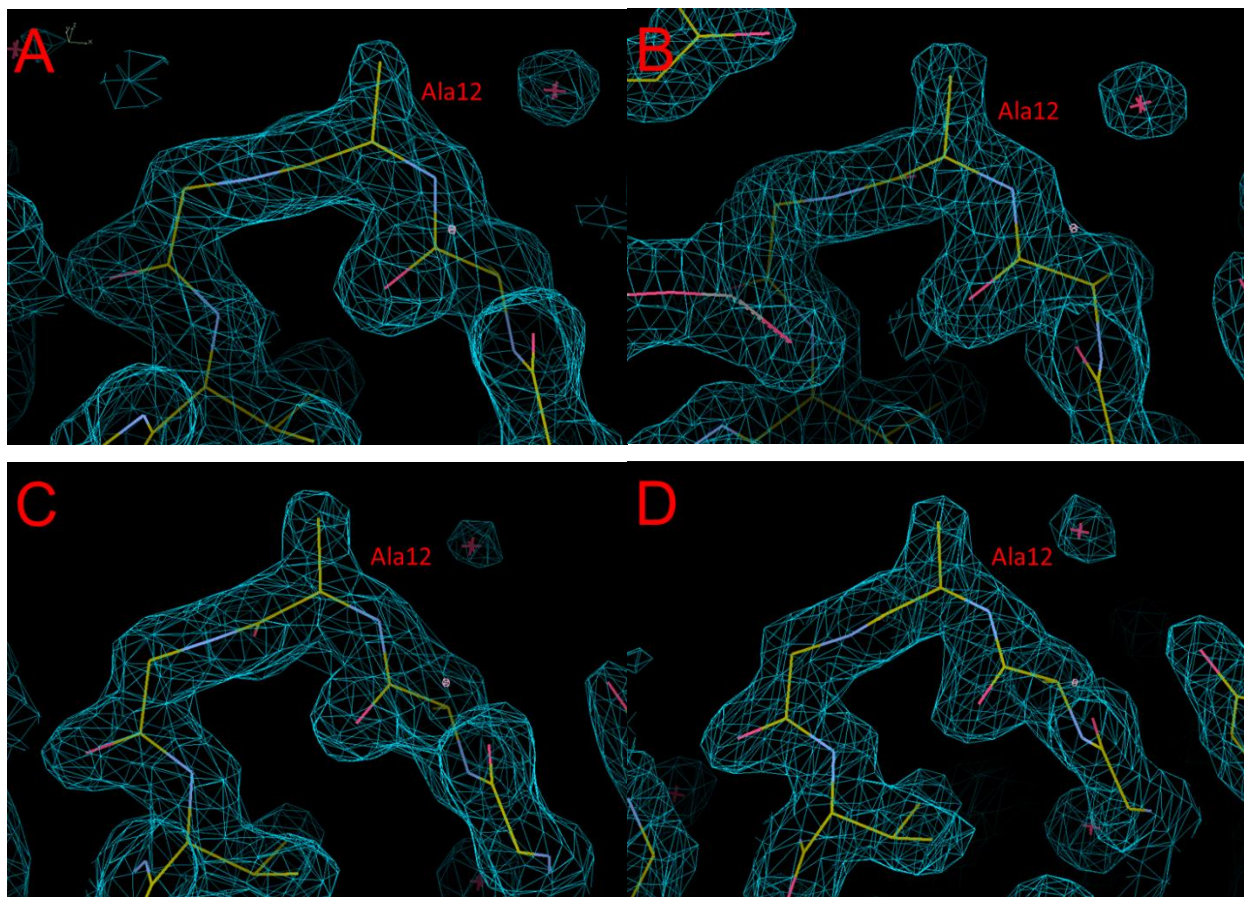


Figure S2 Electron density maps of G12A in various G12A structures. The $2F_o - F_c$ electron density map, contoured at 1σ cut-off highlighting Ala 12 for (A) G12A-K-Ras-GDP, (B) G12A-K-Ras-GTP, (C) G12A-K-Ras-GTP γ S, (D) G12A-K-Ras-GppNHp

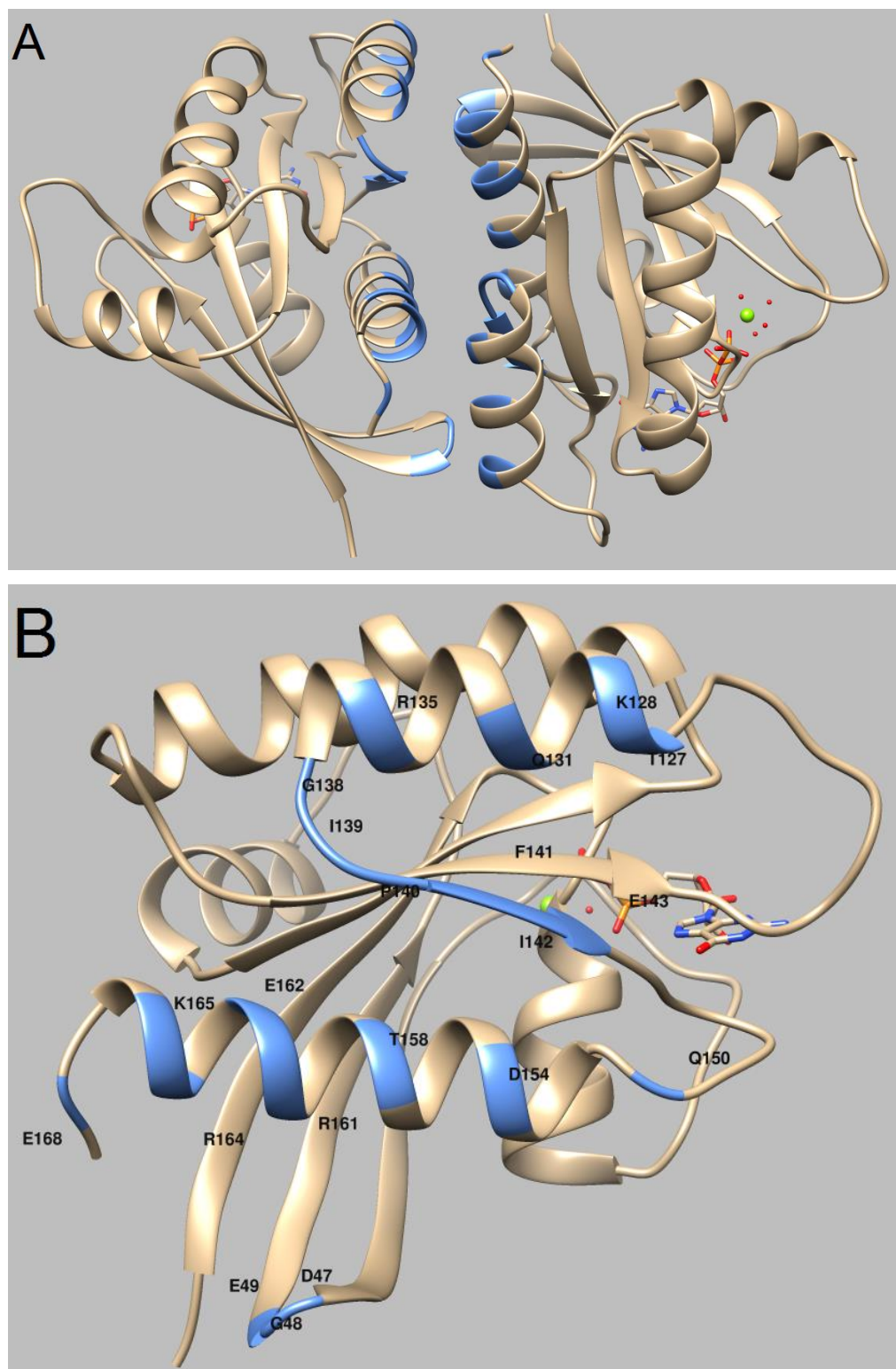


Figure S3 Analysis of G12A-K-Ras-GTP packing interactions in the unit cell. (A) Residues involved in interprotein crystal contacts (cornflower blue). (B) Identification of amino acids involved in the crystal contacts. Residues involved in crystal contacts included residues 47 and 48 in λ 3 loop, residue 49 in β 3

strand, residues 127, 128, 131, 135 in $\alpha 4$ helix, residues 138, 139, 140 in $\lambda 9$ loop, residues 141, 142, 143 in $\beta 6$ strand, residue 150 in $\lambda 10$ loop, residues 154, 158, 161, 162, 164, 165 in $\alpha 5$ helix, and residue 168

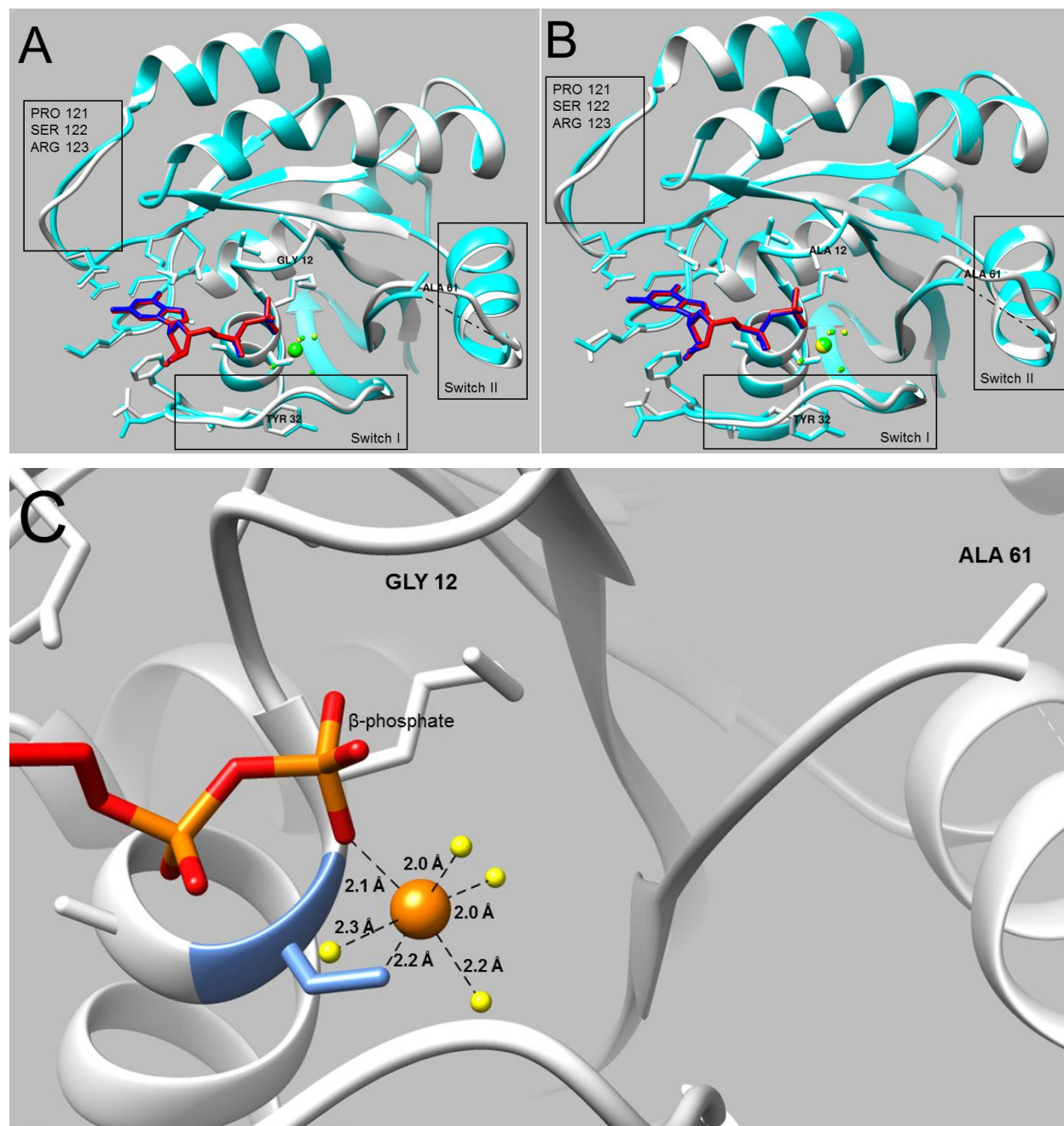


Figure S4 Analysis of the Q61A-K-Ras-GDP structure. A) Overlay of the Q61A-K-Ras-GDP structure (cyan/blue) with the WT-K-Ras-GDP structure (white/red). B) Overlay of the Q61A-K-Ras-GDP structure (cyan/blue) with the untreated G12A-K-Ras-GDP structure (white/red). C) Details of the Mg^{2+} coordination site in the Q61A-K-Ras-GDP structure. The SI and SII loops are highlighted in the boxes.

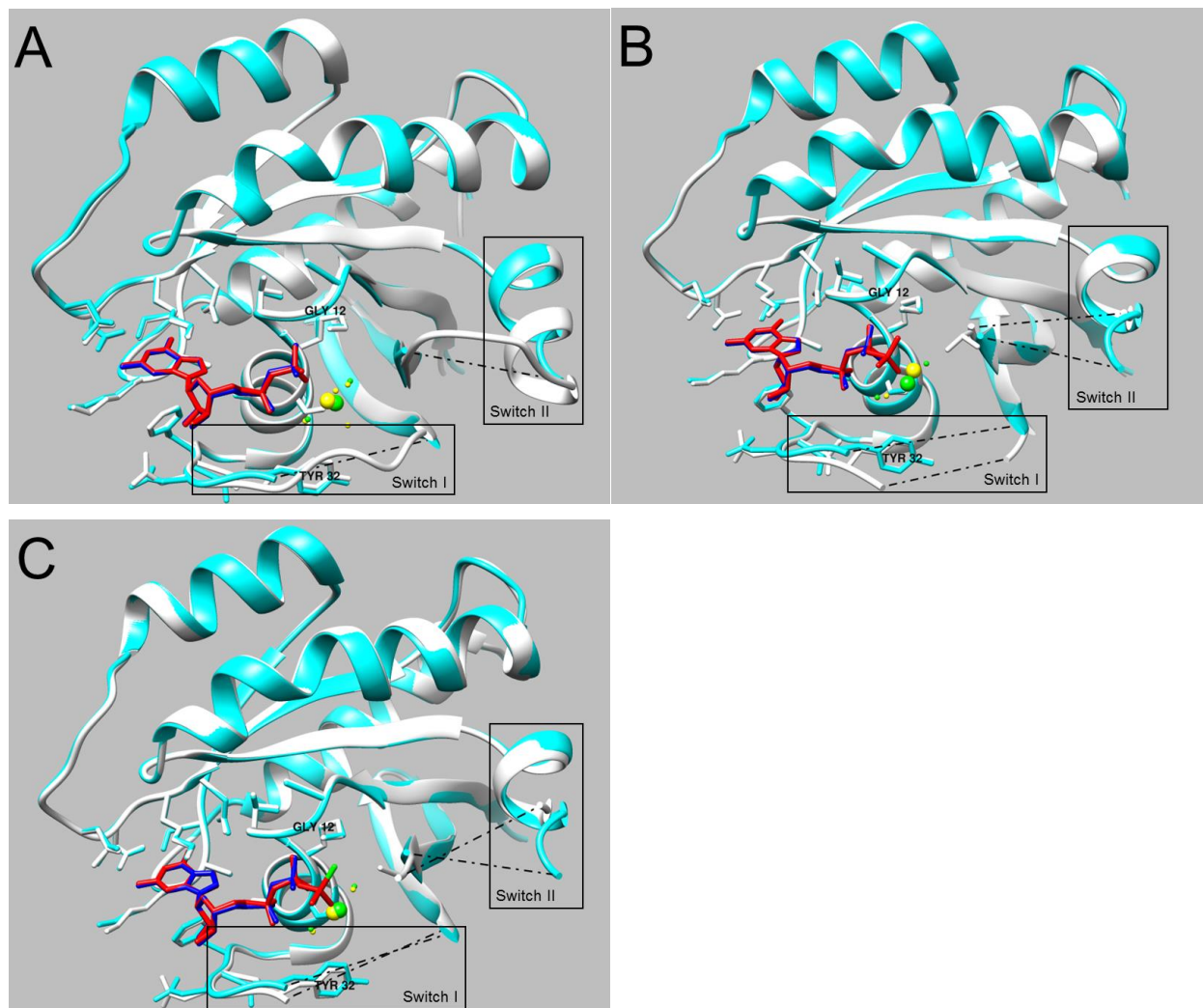


Figure S5 Comparison of WT-K-Ras EDTA treated and untreated structures. Overlays of (A) EDTA-treated K-Ras-GDP (cyan/blue) and untreated WT-K-Ras-GDP (white/red), (B) EDTA-treated WT-K-Ras-GDP (cyan/blue) and WT-K-Ras-GTP (white/red), (C) EDTA-treated WT-K-Ras-GDP (cyan/blue) and WT-K-Ras-GTP γ S (white/red). SI and SII loops are highlighted in the boxes.

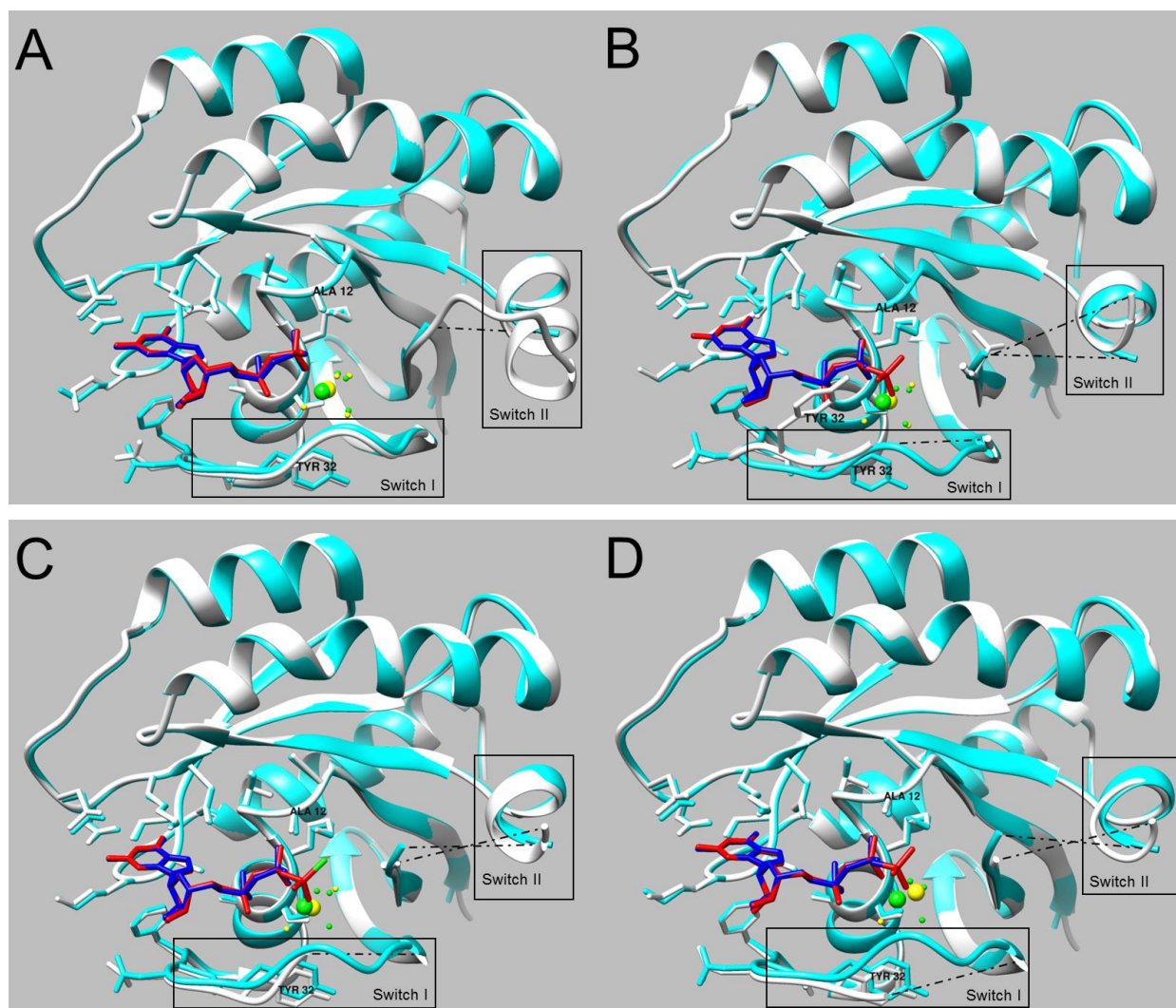


Figure S6 Comparisons of G12A-K-Ras-nucleotide EDTA treated and untreated structures. Overlays of (A) EDTA-treated G12A-K-Ras-GDP (cyan/blue) and untreated G12A-K-Ras-GDP (white/red), (B) EDTA-treated G12A-K-Ras-GDP (cyan/blue) and G12A-K-Ras-GTP (white/red), (C) Overlay of EDTA-treated G12A-K-Ras-GDP (cyan/blue) and G12A-K-Ras-GTP γ S (white/red), (D) EDTA-treated G12A-K-Ras-GDP (cyan/blue) and G12A-K-Ras-GppNHp (white/red). SI and SII loops are highlighted in the boxes.