



Supplementary Figure S12. FoldX-predicted compensatory mutations in Ras for binding to GEF and GAP. **(A)** Overlay of Ras in complex with a GEF (SOS1) and a GAP (RASA1). **(B)** Structural details for the RasG12R mutation as an example for a non-compensating mutation. Amino acid residues in Ras are shown in blue and neighbouring residues (<3 Å) of RASA1 and SOS1 in green. **(C)** Structural details for the RasP34R mutation as an example for a compensating mutation. Amino acid residues of Ras are shown in blue and neighbouring residues (<3 Å) in RASA1 and SOS1 in green. **(D)** FoldX energies for Ras cancer mutations modelled in complex with GAP (pdb entry: 1WGR) GEF (pdb entry: 1XD2, molecules B and C). **(E)** FoldX energies for Ras RASopathy mutations modelled in complex with GAP (pdb entry: 1WGR) GEF (pdb entry: 1XD2, molecules B and C).