**Supporting information**

**The RAS-effector interface: Isoform-specific differences in the effector binding regions**

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**S4 Fig. Known structures of the RAS-effector complexes.** Nine structures of RAS-effector domain complexes were found in a PDB search, including HRAS-CRAF-RB (PDB code: 4g0n, 4G3X, 3kud), HRAS-BYR2-RB (PDB code: 1k8r), RAP1A-CRAF-RB (PDB code: 1GUA), KRAS-ARAF-RB (PDB code: 2mse), HRAS-RALGDS (PDB code: 1lfd), HRAS-PI3Kγ (PDB code: 1he8), HRAS-PLCε (PDB code: 2c5l), HRAS-RASSF (PDB code: 3ddc), HRAS-GRAB14 (PDB code: 4k81). An overlaid structure in ribbon presentation (central panel) illustrates the overall contacts of these structures (see also Figure 3). The contact sites (with distances of 4 Å or less) were calculated by Pymol and colored in white. RAS proteins are shown in orchid and the effector domains in olive as indicated.