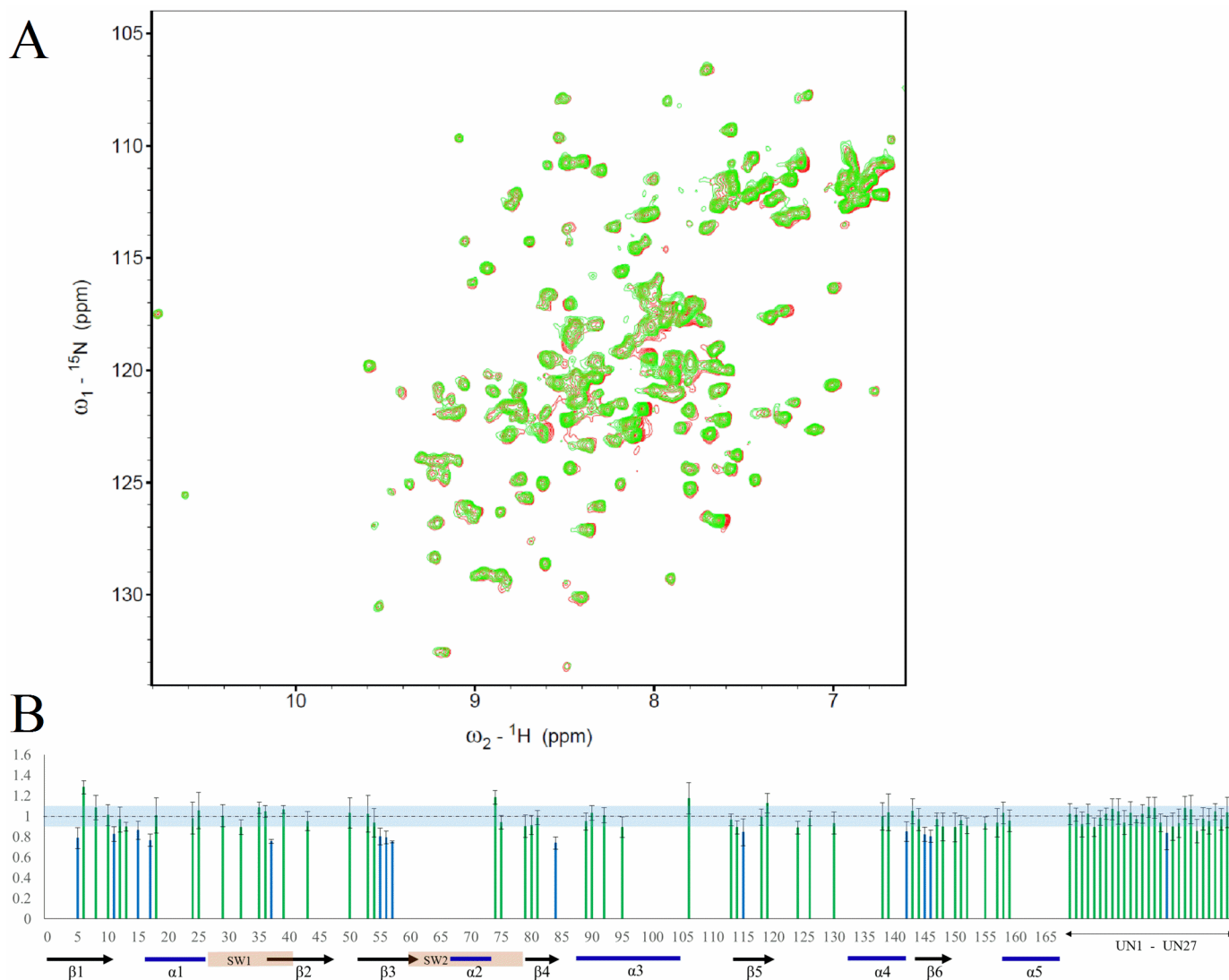
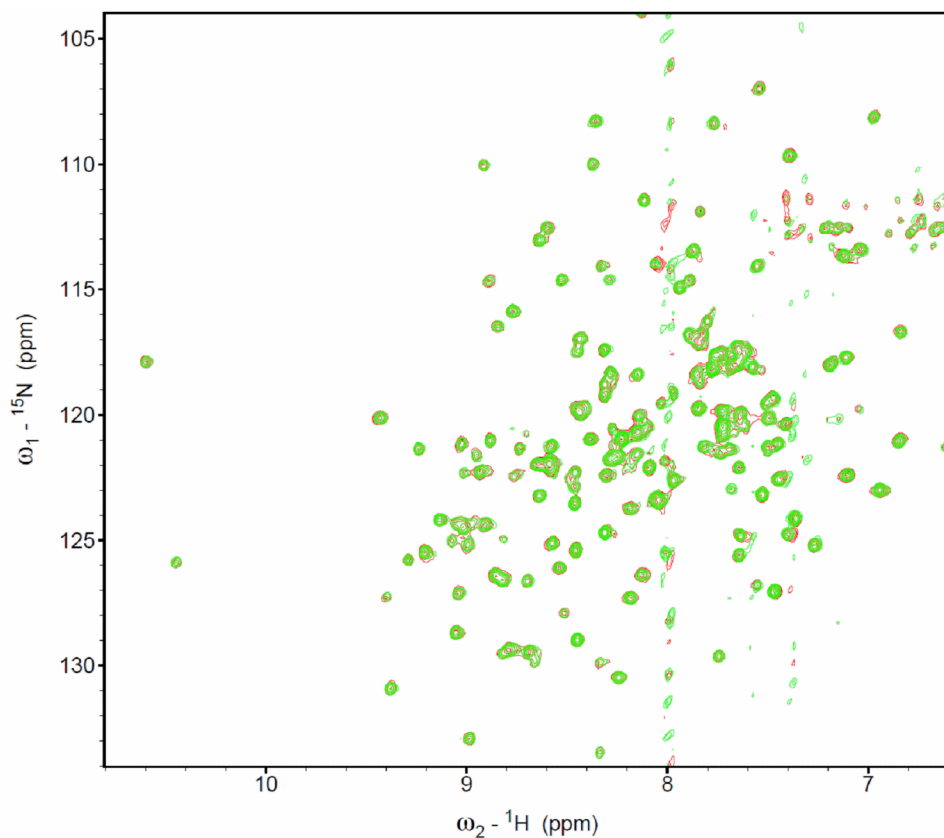


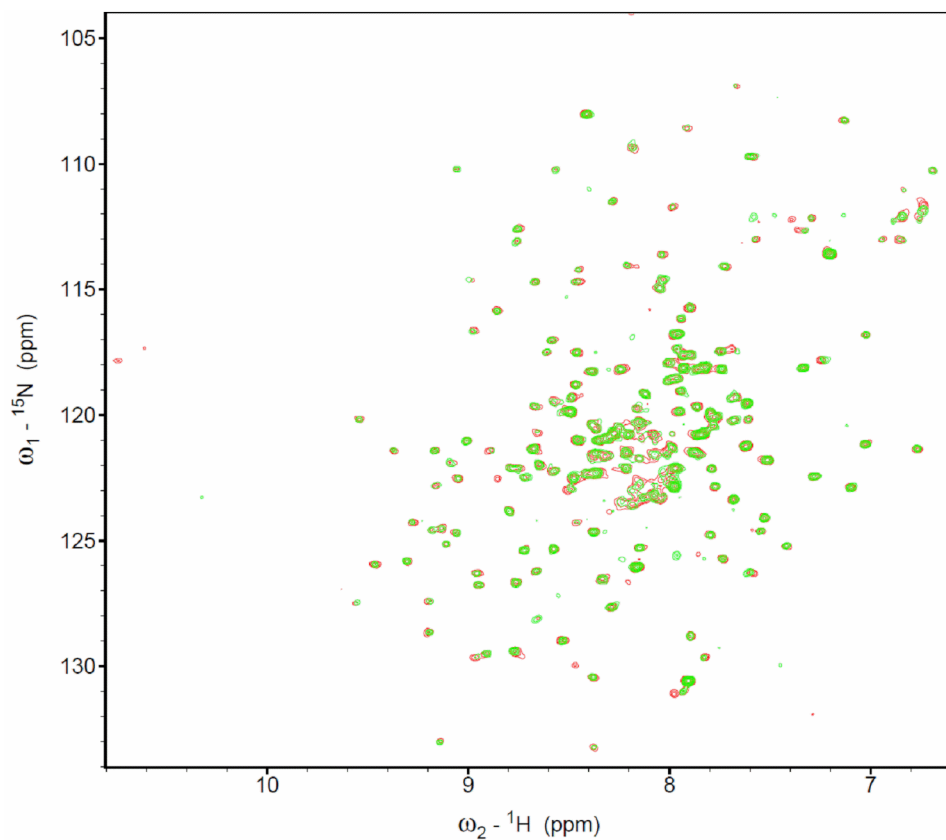
## Supplementary Information



**Fig. S1. K-Ras4B (1-169) interaction with IP3(1,4,5) studied by NMR spectroscopy.** A. Superimposed  $^{15}\text{N}$ - $^1\text{H}$  HSQC spectra of K-Ras4B.G12V.GMPPNP(1-169) recorded at 800 MHz and 25°C, in the absence and in the presence of IP3(1,4,5). B. Peak intensity change as a function of protein sequence. Peak intensity ratio was calculated as  $I^*/I$  from NMR spectrum of full length K-Ras4B (1-169) without IP3(1,4,5) ( $I$ ) and with IP3(1,4,5) ( $I^*$ ). The residues with >10% decrease in peak intensity are shown as blue bars, and the residues whose intensity changed less than 15% are shown as green bars. Residues that could not be assigned in these NMR spectra are left blank, but the data are shown as UN1 to UN27 at the end of the sequence. The K-Ras4B switch regions as well as the secondary structure are indicated at the bottom. For list of intensity perturbed residue, refer to Table S1.



**Figure S2: K-Ras4B (1-169) interaction with DOPC nanodisc containing PIP(4,5)P2 studied by NMR spectroscopy-** Superimposed  ${}^{15}\text{N}$ - ${}^1\text{H}$  HSQC-TROSY spectra of K-Ras4B.G12V.GMPPNP(1-169) recorded at 800 MHz and 25°C, in the presence of DOPC nanodisc containing PIP(4,5)P2 without (red) and with (green)  $\text{Gd}^{3+}$  spin-labeled lipid. The perturbations to intensity are small and thus affected residues are not listed.



**Figure S3. K-Ras4B (1-188) interaction with DOPC liposome containing PIP(4,5)P2 studied by NMR spectroscopy** - Superimposed  ${}^{15}\text{N}$ - ${}^1\text{H}$  HSQC-TROSY spectra of full length K-Ras4B.G12V.GMPPNP(1-188) recorded at 800 MHz and  $37^\circ\text{C}$ , in the presence of DOPC liposome containing PIP(4,5)P2 without (red) and with (green)  $\text{Gd}^{3+}$  spin-labeled lipid. For list of intensity perturbed residue, refer to Table S1.

<b>K-Ras constructs and lipids</b>	<b>Peak intensity perturbations to residues as seen in NMR spectra</b>
K-Ras (1-169) with IP3(1,4,5) {PIP2 headgroup}	K5, G15, S17, A18, I24, Q25, E37, L53, D54, I55, L56, D57, G75, I84, D92, H95, G115, I142, T144, S145, A146 UN2, UN6, UN7, UN12, UN17, UN27
K-Ras (1-188) with PIP2(4,5) doped DOPC liposome	A11, V12, G13, S17, Y32, I36, S39, D54, D57, G75, D92, H95, D126, I139, E143, T144, G151, Y157 UN1, UN2, UN13, UN15, UN17, UN20, UN27
K-Ras(1-169) with PIP2(4,5) doped DOPC liposome	K5, E37, S39, D54, L56, D57, T148 UN17, UN25

**Table S1. Residue identified to interact with PIP2 headgroup in solution or PIP2 doped liposome by NMR.**

<b>OS1 started:</b> R97(39%), K101(87%), R102(41%), E107(10%), K128(48%), R135(95%), K165 (61%), K169(87%), K176(31%),K177(88%), K178(84%), K179(83%), K180(72%), K182(40%), K184(81%)
<b>OS2 started:</b> M1 (17%), E3 (15%), K5(56%), R41(63%), R73(65%), E76 (15%), K167(69%), K176(40%), K177(36%), K178(49%), K179(86%), K180(94%), K182(36%), K184(82%)

**Table S2. Charged residue identified to interact with PIP2 in the membrane by simulation** (Residues whose atoms are within 3 Å of PIP2 atoms are considered to be interacting, with the % of time in contact given).