Supplementary Figures and Tables Index:

Figures and Tables are directly related to the paper and mentioned in it. There are included in the supplement because of space issues. Only the most important data/derived results can be down in the paper.

Figure S1. Assigned 1H-15N TROSY HSQC NMR spectra showing chemical shift change upon Eph2A : SHIP2 SAM:SAM complex formation. *This is raw experimental data usually given in this type of study.*

Figures S2. Chemical shift perturbations to 1H and 15N resonances in EphA2 SAM and SHIP2 SAM upon complex formation. *These are results derived from Fig. S1 and are critical input for the structure calculations.*

Figures S3. Superimposed 1H-15N TROSY HSQC spectra for free EphA2 and SHIP2 under various pH conditions. *This is raw data discussed in text on p.5 and esp. p.14*

Figure S4. Superimposed 1H-15N TROSY HSQC spectra for SHIP2-bound EphA2 and EphA2-bound SHIP2 under various pH conditions. *This is raw data discussed in text (p.5/p.14), and are related to Fig. 3 and to Table 3.*

Figure S5. was inserted at the request of the reviewer and shows information from the NOESY spectra. *Referred to on p.5 near top.*

Figure S6. Figure showing location of unambiguous distance restraints and structures calculated without them. This analysis was added at the request of the reviewer. We feel it is important to present it in the paper. *These results are discussed in text (pages p.5 bot. p11 mid , p17/18) and directly relate to Fig. 3.*

Figure S7. Results of RosettaDocking calculations on three HADDOCK clusters. *These computational results are discussed in text (p.6 bot) and is related to Fig.4-6.*

Figure S8. C$_\alpha$ distances between unbound and bound SAM domains for structures from the three clusters. *The result is discussed in the text (p.7 bot.), related to Fig. 3.*

Figure S9. Graphics illustrating models for side-chain contacts between mutant proteins. *Relates to Fig. 4 and Table 3.*

Figure S10. Representative ITC data on WT and mutant SAM domain interactions. *Related to Fig. 4, 7 and Table 3 and text (p.8 top).*

Figure S11. NMR and ITC data on mutant SAM domain interactions. *Related to Fig. 4 and Table 3 and text (p.8 bot).*

Supplementary Tables:

Table S1.Thermodynamic parameters of wild-type EphA2-SHIP2 SAM:SAM complex under various pH conditions measured by ITC. *Discussed in main text (p. 5/14) and relates to Fig. 3, S4 and S8.*

Table S2. Thermodynamic parameters of EphA2 R950E - SHIP2 H1219R SAM:SAM complex under various concentration of NaCl measured by ITC. *Derived data discussed in main text (p.5)*

Table S3. Summary of PALES results of unbound EphA2 and SHIP2 SAM domains. *Is discussed in main text, esp. M&M (p.16/17), Relates to Table 1.*

Table S4. Intermolecular Restraints Used for the HADDOCK Docking Protocol. *Is discussed in main text, esp. M&M (p.16/17), Relates to Table 1.*

Table S5. Structural statistics and ensemble quality of EphA2 – SHIP2 SAM:SAM complex of all three HADDOCK clusters. *Relates to Table 1 and Fig. 3.*

Table S6. This analysis was added at the request of the reviewer. We feel it is important to present it in the paper. *These results are discussed in text (pages p.5 bot. p11 mid , p17/18) and directly relate to Fig. 3 and Fig. S5*

Table S7. This analysis was added at the request of the reviewer. We feel it is important to present it in the paper. *These results are discussed in text (pages p.5 bot. p11 mid , p17/18) and directly relate to Fig. 3 and Fig. S5*