Supporting Information

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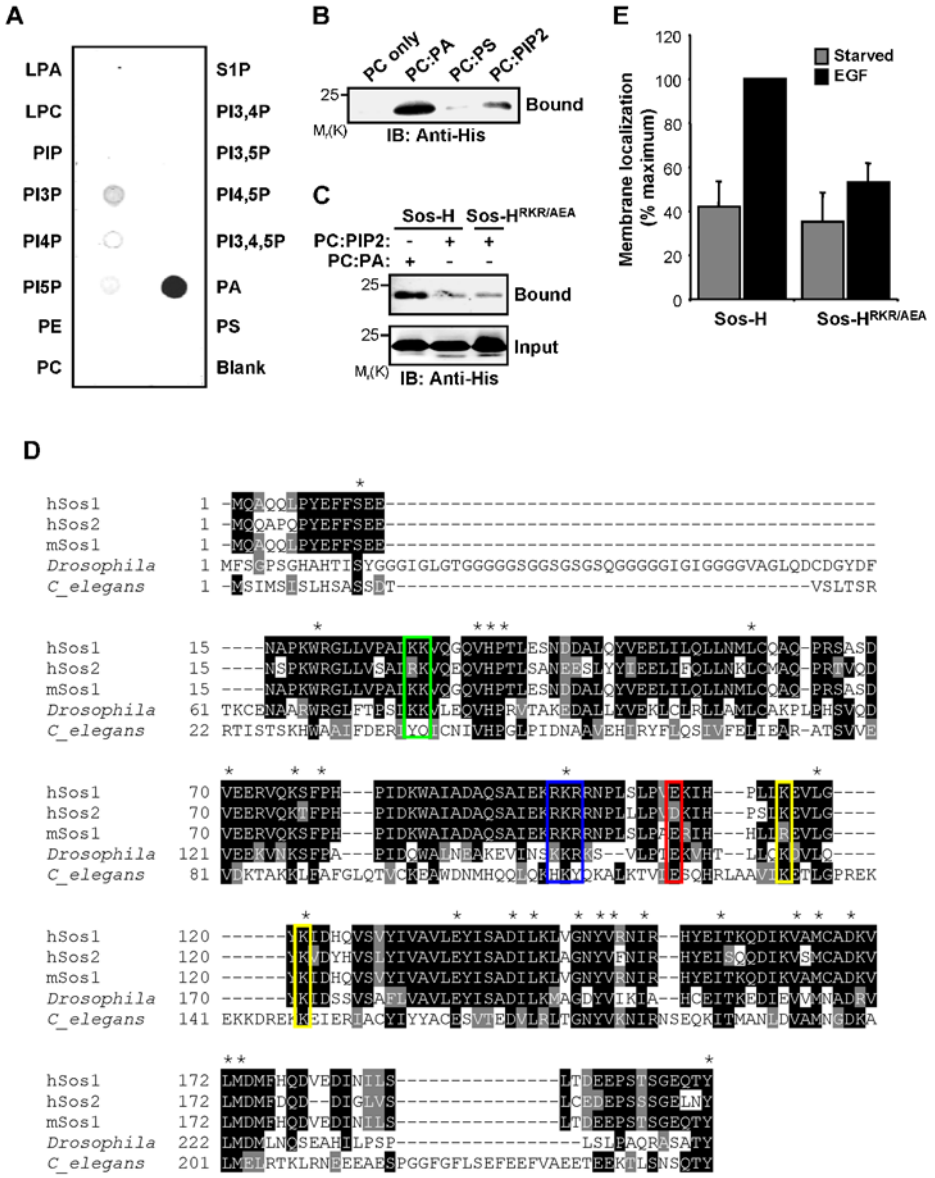

Fig. S1. (*A*) Recombinant Sos-H was incubated on a PIP-strip (Echelon Inc.) and blotted with anti-His antibody. (*B*) His-tagged SOS-H (0.5 μM) was mixed with lipid vesicles comprised of 1 mM of PC only, PC:PA (90:10), PC:PS (80:20) or PC:PIP2 (98:2). Vesicles were pelleted and the amount of Sos-H binding to the vesicles was detected by immunoblotting. (*C*) His-tagged SOS-H or Sos-H$^{RKR/AEA}$ (0.5 μM) was mixed with lipid vesicles comprised of 1 mM of PC:PA (90:10) or PC:PIP2 (98:2) and processed as in *B*. (*D*) Sequence alignment of the Sos-H from *Homo sapiens* (hSos1 and hSos2), *Mus musculus* (mSos1), *Drosophila* and *C. elegans*. Darker shades represent identity and lighter shades indicate similarity. * indicates invariant residue. The green (aa 28, 29), blue (aa 97–99) and yellow boxes (aa 115, 121) represent the regions mutated in this study. The red box indicates the residue mutated in Noonan syndrome, E108K. The alignment was done as described in Materials and Methods. (*E*) GFP-tagged Sos-H or Sos-H$^{RKR/AEA}$ were transfected into COS-1 cells and membrane localization quantified, upon EGF stimulation, as in Fig. 1*E*. Results are mean ± s.d. of three independent experiments.

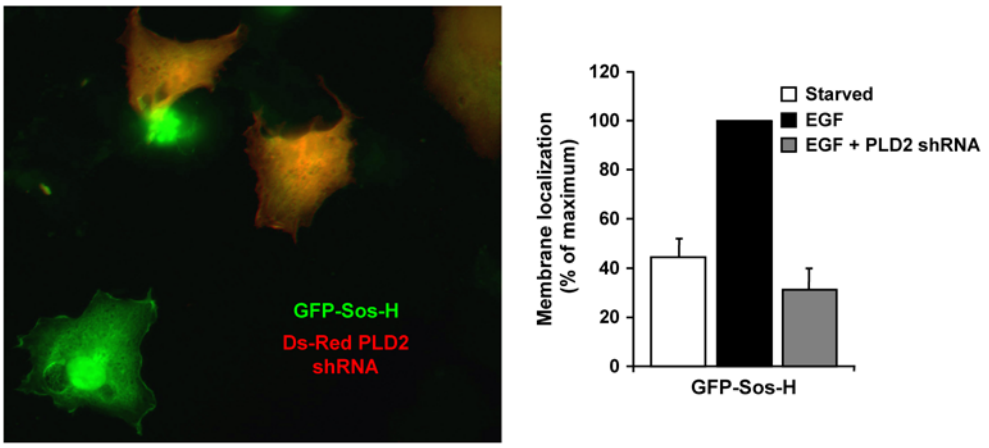

Fig. S2. COS-1 cells were transfected with GFP-Sos-H and Ds-Red shRNA targeting PLD2. Sos-H membrane localization was quantified as in Fig. 1*E*.

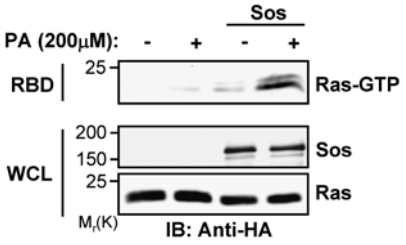

Fig. S3. COS-1 cells were co-transfected with HA-tagged Ras and HA-tagged Sos. Cells were serum starved and then stimulated with 200 μM PA for 15 min and RBD pulldown performed as in Fig. 2.