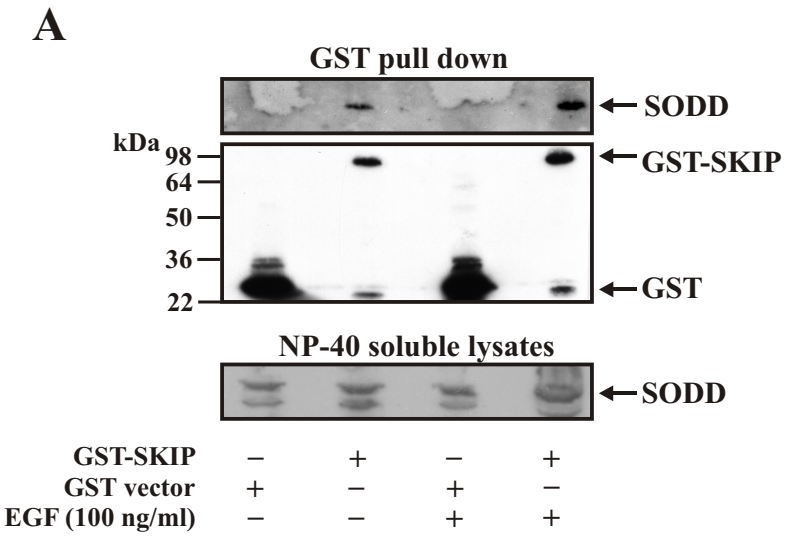
Supplementary Figures.

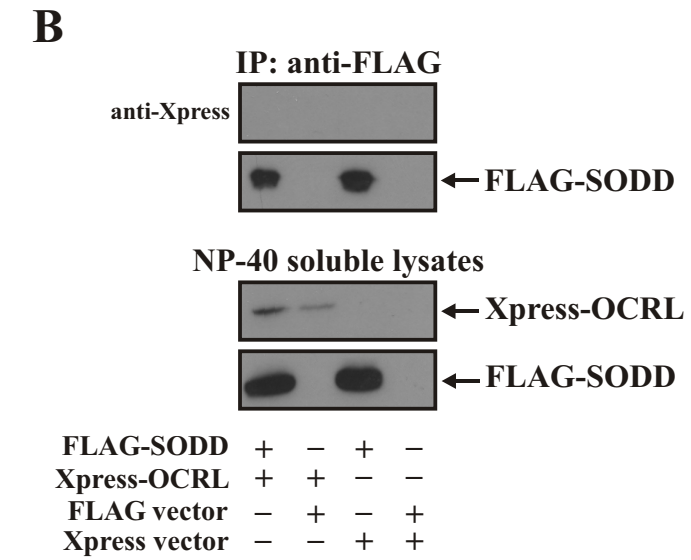
Supplementary Fig. 1. SODD interaction with 5-ptases. *A.* HEK293 cells expressing GST-SKIP or GST were serum-starved or EGF-stimulated (100 ng/mL, 10 min). NP-40-soluble fractions were incubated with glutathione Sepharose and washed extensively. Bound proteins eluted in SDS-PAGE sample buffer (*upper two panels*) or NP-40-soluble input fractions (*lower panel*) were subjected to Western blot analysis with GST or SODD antibodies. *B.* NP-40-soluble fractions derived from COS-7 cells co-expressing FLAG-SODD and Xpress-OCRL (and the vector alone controls as indicated), were immunoprecipitated with FLAG antibodies (*upper two panels*) and immunoblotted with FLAG or Xpress antibodies. Input soluble fractions were also immunoblotted with FLAG or Xpress antibodies (*lower two panels*).

Supplementary Fig. 2. SODD's regulation of SHIP2 PI(3,4,5)P_3 5-ptase activity. COS-7 cells transiently transfected with FLAG-SODD and HA-SHIP2 or vector controls were lysed and immunoprecipitated with HA antibodies and either subjected to PI([^{32}P]3,4,5)P_3 5-ptase assay and the reaction products analysed by TLC (*upper panel*) or immunoblotted with FLAG (*middle panel*) or HA (*lower panel*) antibodies. The migration of PI([^{32}P]3,4,5)P_3 and PI([^{32}P]3,4)P_2 lipids are shown on the right. *B.* The level of PI([^{32}P]3,4)P_2 formed was determined by densitometry, and represented relative to that detected in HA immunoprecipitates derived from HA-SHIP2 and FLAG expressing cells (arbitrarily set as 1). Bars represent the mean ± SEM of three independent experiments.

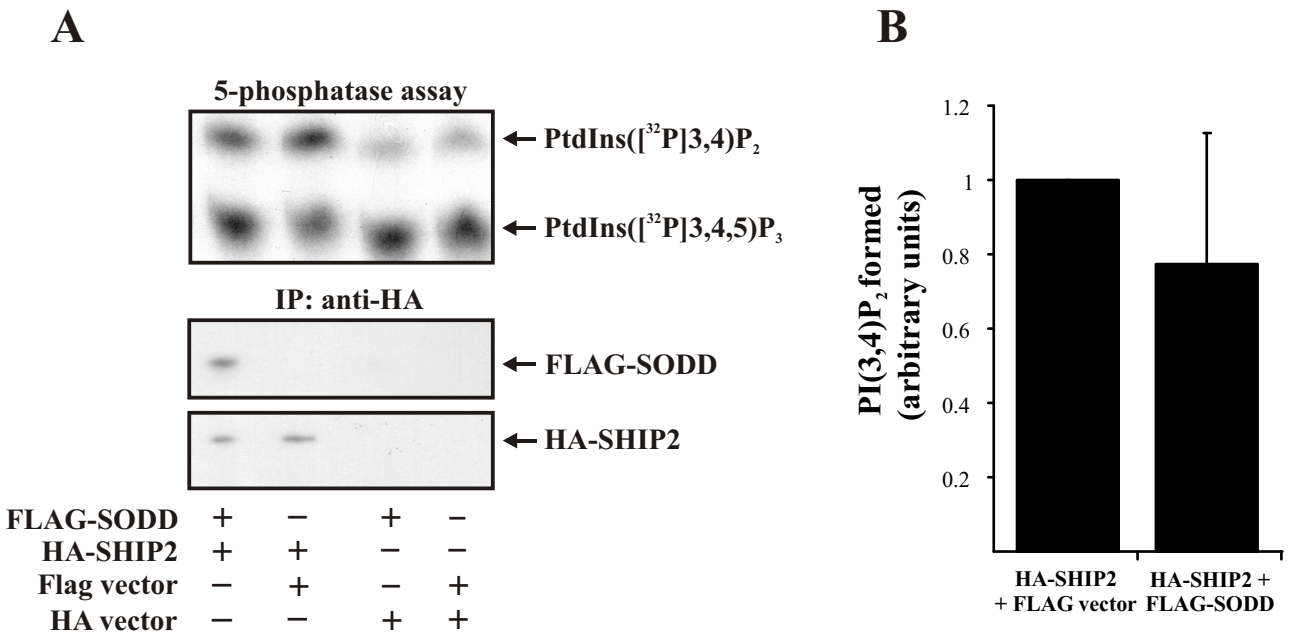
Supplementary Fig. 3. Akt signalling and apoptosis induction in $^{-/-}$SODD MEFs. *A.* RIPA buffer-soluble lysates from spontaneously immortalised $^{+/+}$SODD or $^{-/-}$MEFs were immunoblotted with SODD, SKIP, SHIP2, PTEN, or β-tubulin (total protein loading control) antibodies as indicated. *B.*. Spontaneously immortalised $^{+/+}$SODD or $^{-/-}$MEFs were serum-starved and stimulated with EGF (20 ng/ml). Detergent soluble lysates (50 μg) were immunoblotted with antibodies specific for either phospho-Akt-Ser^{473} (*upper panel*) or β-tubulin (*lower panel*). *C.* Spontaneously immortalised $^{+/+}$SODD or $^{-/-}$MEFs were treated as in (*B*) and the level of phospho-Akt-Ser^{473} was determined by densitometry, standardised to β-tubulin loading control, and represented as a relative value to that detected in $^{+/+}$SODD lysates (arbitrarily set as 1), for each time point. Bars represent the mean ± SEM of three independent experiments (*$p<0.05$). *D.* Spontaneously immortalised $^{+/+}$SODD or $^{-/-}$ MEFs cultured in serum-containing medium were seeded into 8 chamber slides and treated with either agonistic Fas antibody (1 mg/ml) or staurosporine (1 mM) for 8 hours, then subjected to TUNEL assays and examined by confocal microscopy. Quantitative analysis of the level of apoptosis following apoptotic induction was performed by calculating the number of TUNEL-positive nuclei relative to the total number of nuclei in 10 random fields. Bars represent the mean ± SEM of three independent experiments.

SUPPLEMENTARY FIG 1





SUPPLEMENTARY FIG 2



SUPPLEMENTARY FIG 3