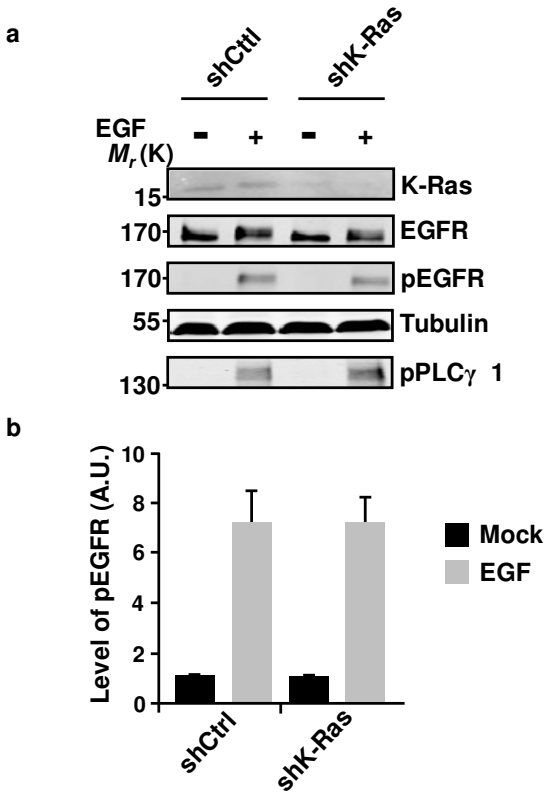
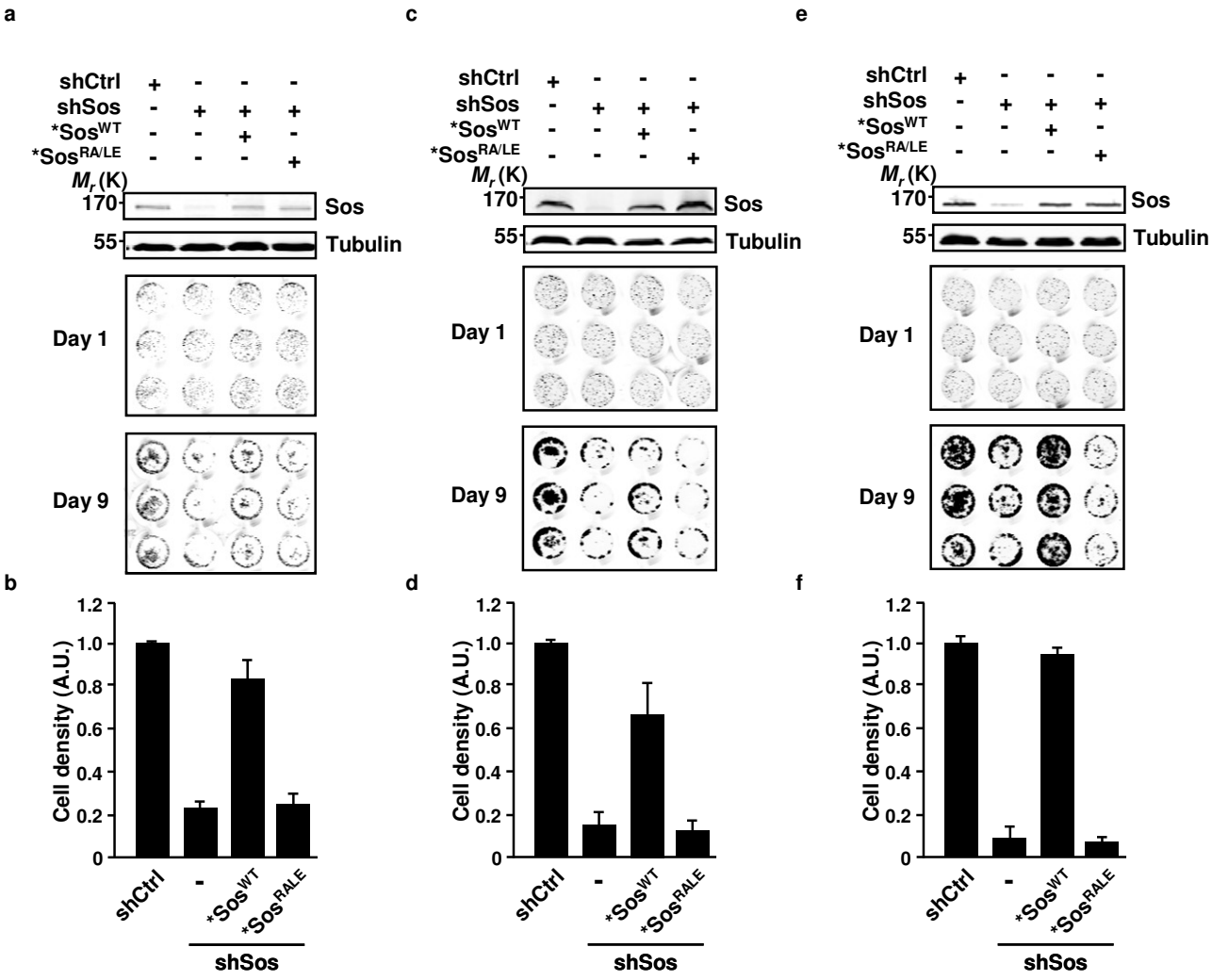
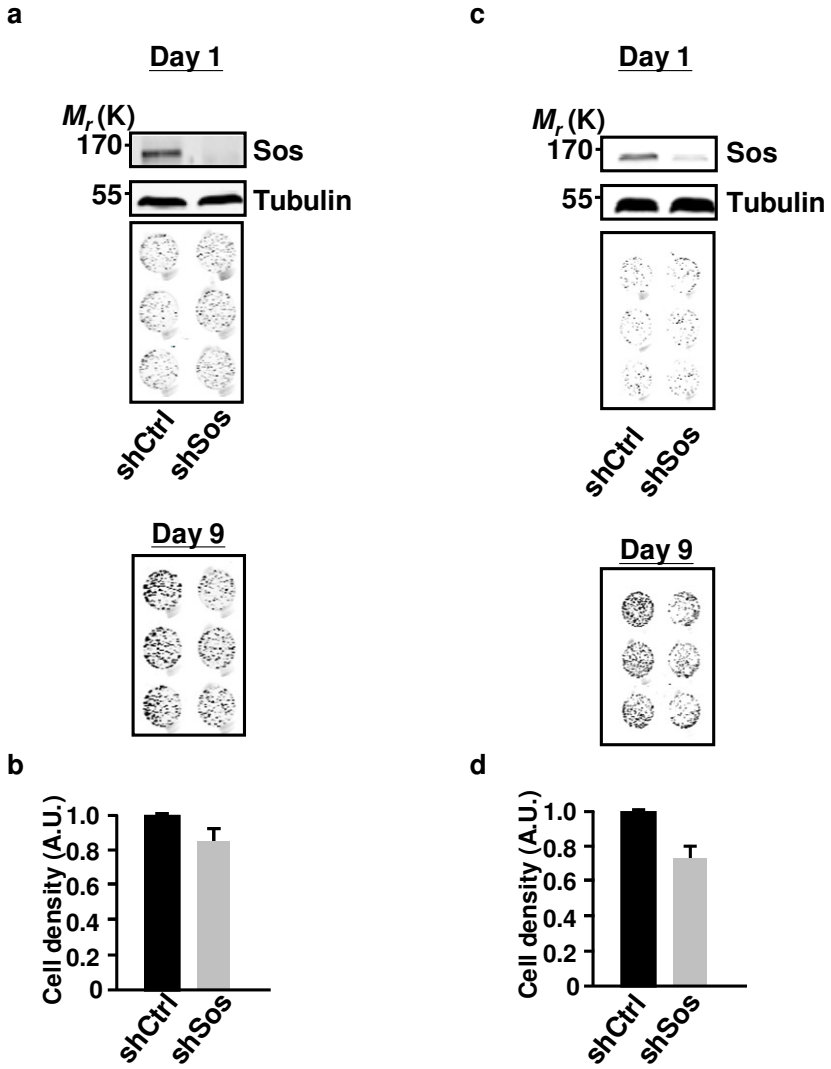


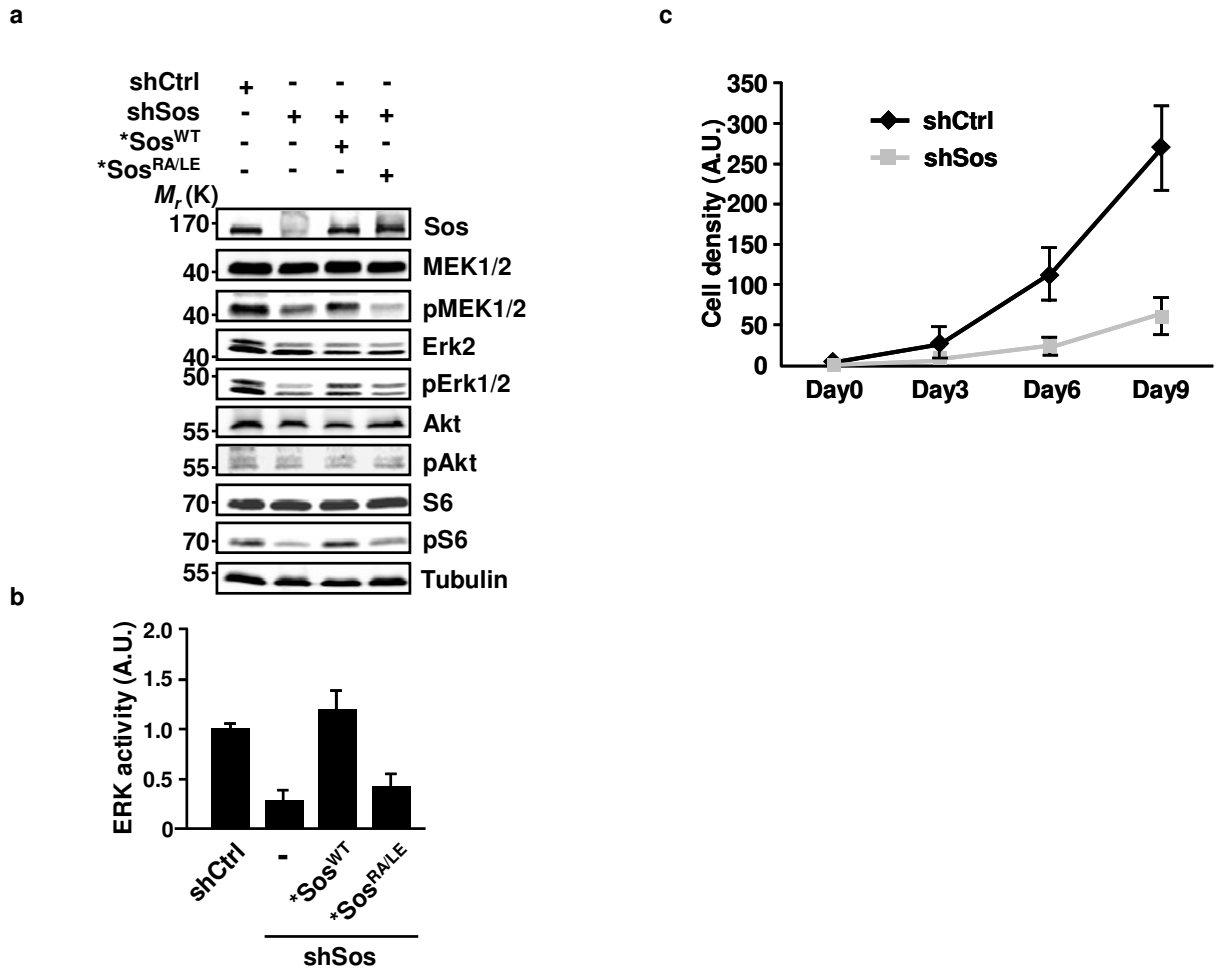
Supplementary Figure S1. K-Ras-deficient pancreatic cancer cells retain normal RTK signalling. (**a**) AsPC-1 cells engineered to express shCtrl or shK-Ras as described in Figure 2a were serum-starved for 20 hr and then stimulated with 50 ng/ml EGF for 10 min at 37^0C. Activation of EGFR signalling pathway was determined by western blotting using anti-phospho-EGFR (Tyr1068) and anti-phospho-PLCγ1 (Tyr783) antibodies. Tubulin was used as a loading control. (**b**) Values are means +/- SD from three independent experiments presented as fold activation compared to shCtrl (mock).



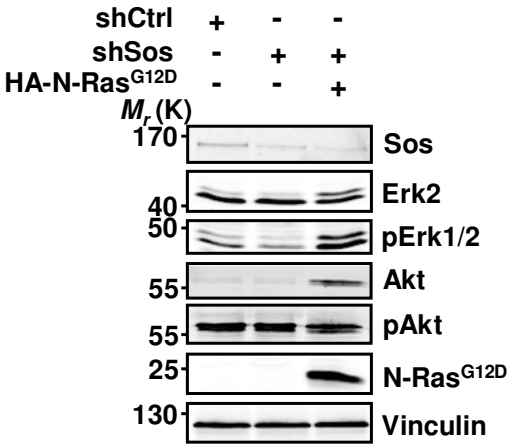
Supplementary Figure S2. Sos-mediated cross activation of WT H-Ras by oncogenic K-Ras is responsible for pancreatic cancer cell growth. (**a-f**) Pancreatic cancer cells [PL45 (**a, b**), CFPAC-1 (**c, d**), and AsPC-1 (**e, f**)] engineered as in Figure 2a to express inducible shCtrl, shSos and shRNA-resistant Sos constructs (*Sos^{WT} or *Sos$^{RA/LE}$) as indicated were cultured in 0.5% serum in the presence of doxycycline for the indicated intervals. Cell density was determined by Syto60 staining and quantified (**b, d, f**) as described in Methods. Values are means +/- SD of technical triplicates presented as fold activation compared to shCtrl. The experiment shown is representative of three independent experiments. Efficiency of knockdown and ectopic expression of Sos were confirmed by western blotting. Tubulin was used as a loading control. A.U., arbitrary units.



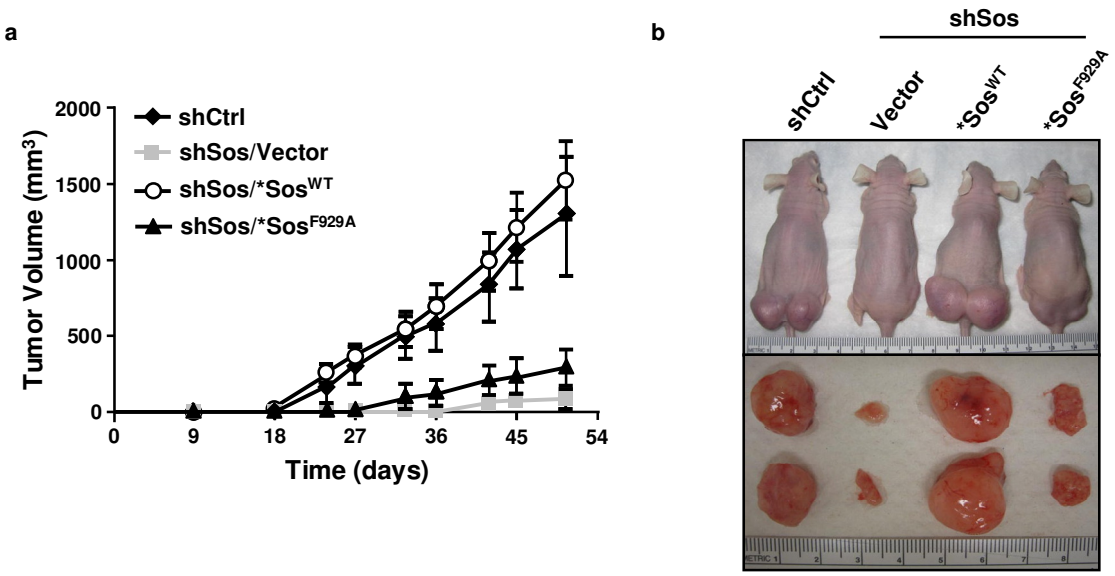
Supplementary Figure S3. Sos is not essential for the growth of pancreatic cancer cells harbouring wild type Ras. (**a-d**) Pancreatic cancer cells [BxPC-3 (**a, b**) and Hs700T (**c, d**)] expressing inducible shCtrl and shSos were cultured in 0.5% serum in the presence of doxycycline for the indicated intervals. Cell density was determined by Syto60 staining and quantified (**b, d**) as described in Methods. Values are means +/- SD of technical triplicates presented as fold activation compared to shCtrl. The experiment shown is representative of three independent experiments. Efficiency of Sos knockdown was confirmed by western blotting. Tubulin was used as a loading control. A.U., arbitrary units.



Supplementary Figure S4. Sos-mediated cross activation of WT H-Ras by oncogenic K-Ras contributes to pancreatic cancer cell growth and signalling. (**a**) PL45 cells engineered as in Figure 2a to express inducible shCtrl, shSos and Sos wobble constructs (*Sos^{WT} or *Sos$^{RA/LE}$) as indicated were cultured in 0.5% serum in the presence of doxycycline for the indicated intervals. Efficiency of knockdown and ectopic expression of Sos were confirmed by western blotting. (**b**) Values of ERK activity are presented as fold activation compared to shCtrl and represent means +/- SD from three independent experiments. (**c**) Effect of suppression of Sos expression on the kinetics of pancreatic cancer cell growth. PL45 cells expressing shCtrl or shSos were maintained in culture for the indicated intervals. Cell density at each time point was analyzed by Syto60 staining. Values are means +/- SD from three independent experiments. A.U., arbitrary units.



Supplementary Figure S5. Sos-mediated cross activation of WT Ras by oncogenic K-Ras contributes to pancreatic cancer cell signalling. MIA PaCa-2 cells engineered as in Figure 2a to express inducible shCtrl or shSos. T7-N-RasG12D was transfected (Lipofectamine 2000, Invitrogen) using standard procedures. Transfection efficiency (>80%) was verified by cotransfecting pEGFP (Clontech). Cells were cultured in 0.5% serum in the presence of doxycycline then lysed, immunoblotted, and probed with the specified antibodies. Data shown is representative of three independent experiments with similar results.



Supplementary Figure S6. Sos GEF catalytic activity is necessary for pancreatic tumour formation. (**a**) MIA PaCa-2 cells harbouring the indicated inducible constructs were injected subcutaneously into mice. Following injections, animals were fed doxycycline-containing diet and tumour growth was measured as described in Methods. Values are means +/- SD (n=3 or 4). (**b**) Representative mice and tumours are shown.