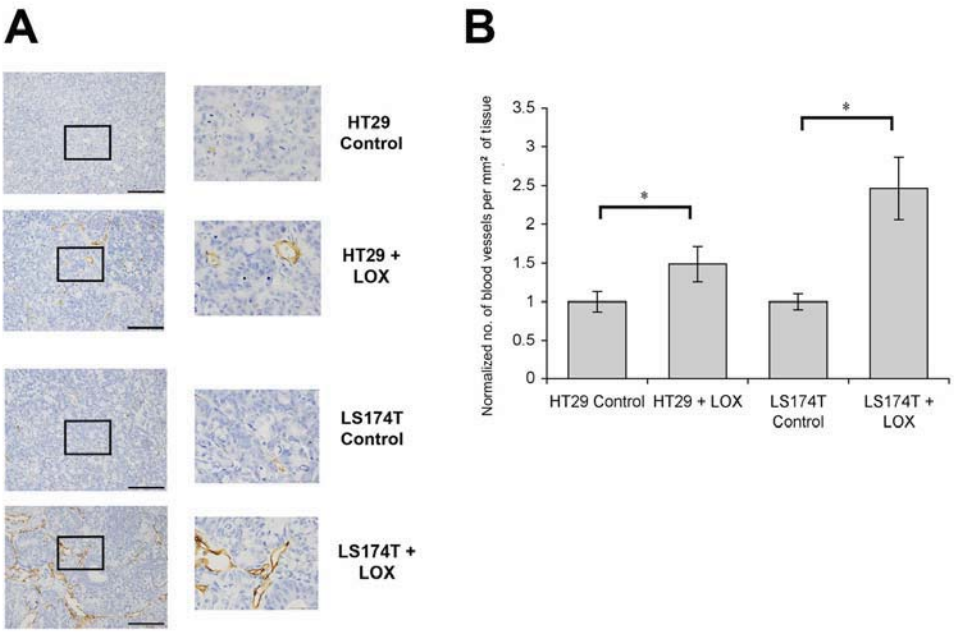
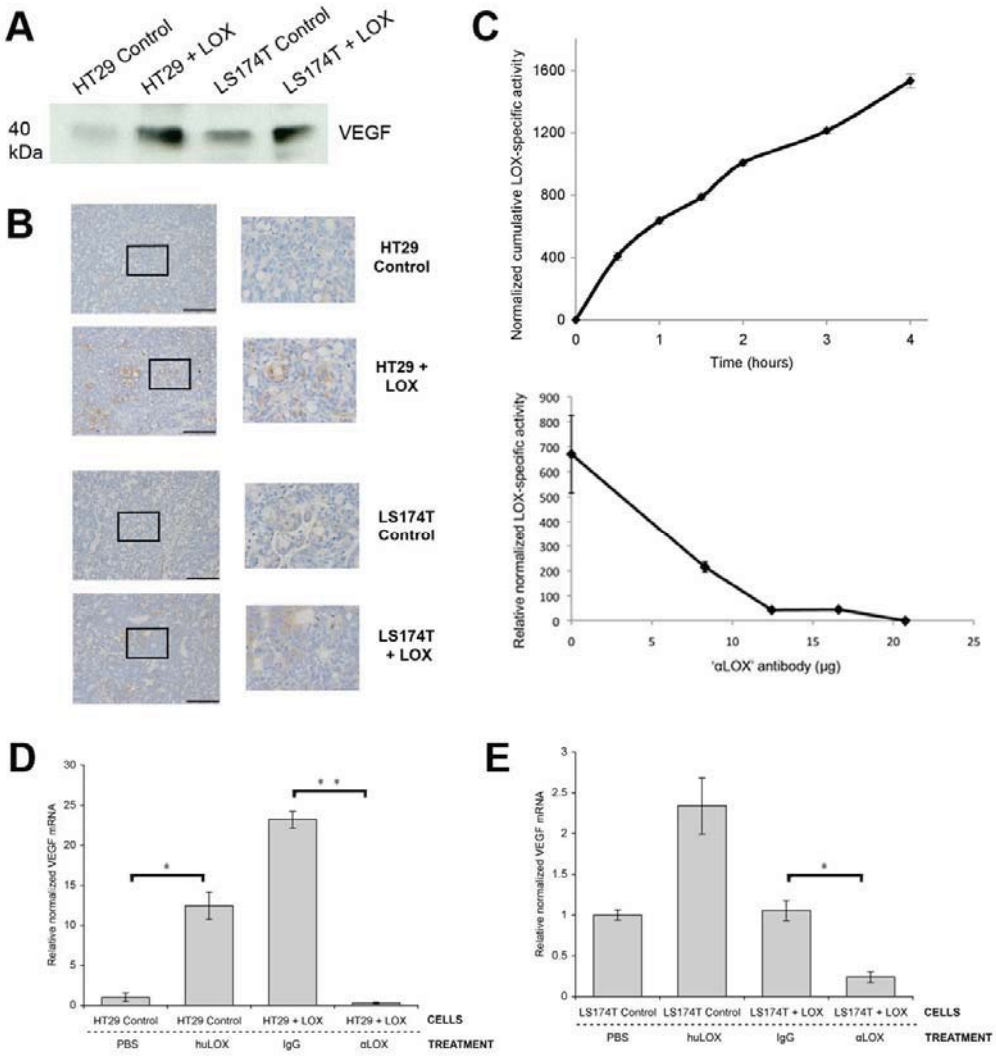
Supplemental Figures



Supplemental Figure S1

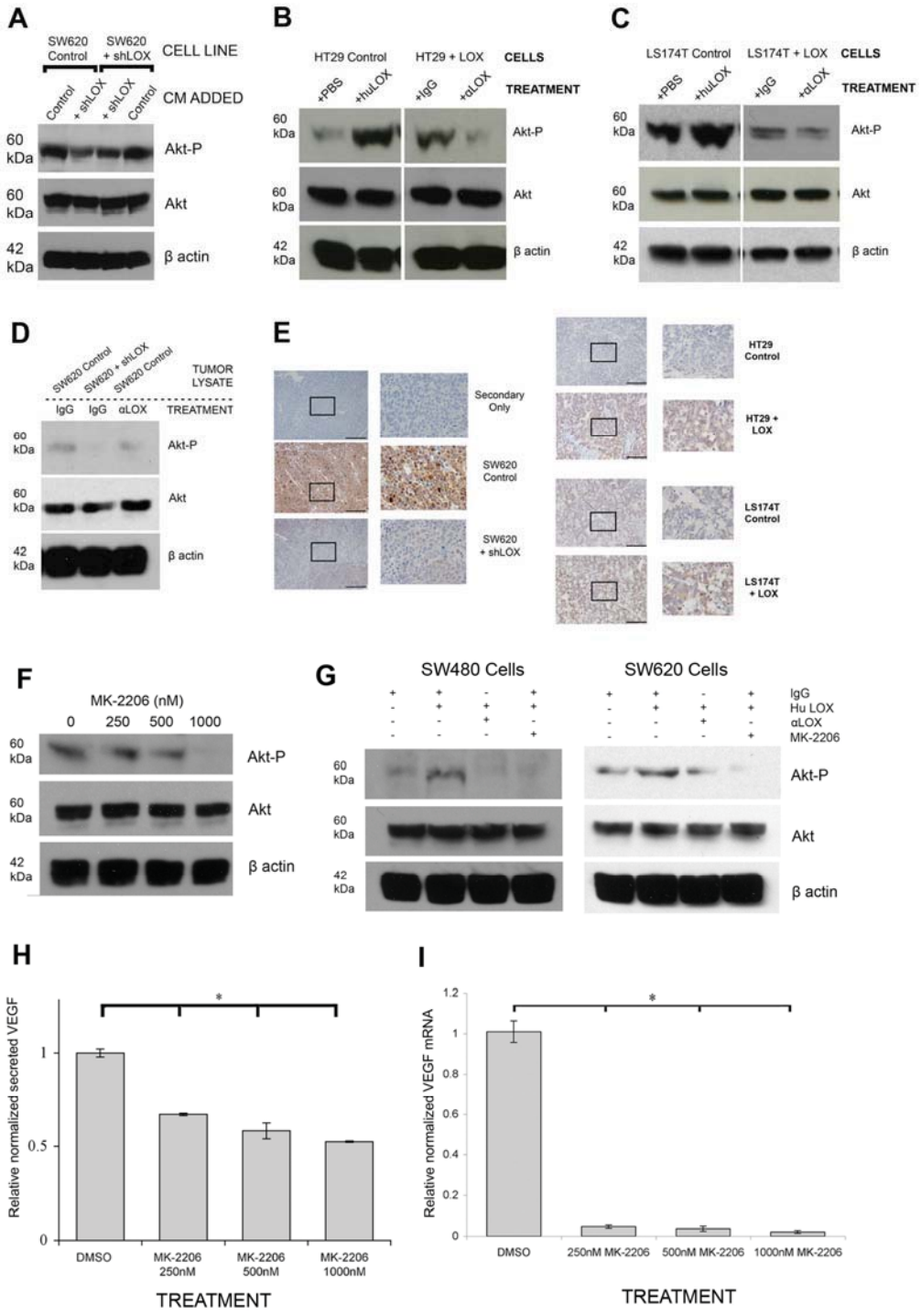
(**A**) Representative immunohistochemical staining of endomucin in sections of HT29 and LS174T tumors grown in nude mice. Endomucin is shown in brown, and cell nuclei in blue. Scale bar represents 200μm. (**B**) Quantification of endomucin positive blood vessel density in HT29 and LS174T subcutaneous tumors grown in nude mice. $n \geq 6$ tumors per condition. Bars represent mean ± SEM. $^{*}p < 0.05$, $^{***}p < 0.001$ using the two sided Student's t test.



Supplemental Figure S2

(**A**) Representative immunoblot showing VEGF levels in conditioned media collected from the HT29 and LS174T cell lines. kDa = kilodalton. (**B**) Representative immunohistochemical staining of VEGF in sections of HT29 and LS174T tumors grown in nude mice. VEGF is shown in brown, and cell nuclei in blue. Scale bar represents 200μm. (**C**) Activity assay carried out 150ng/ml recombinant human LOX ('huLOX'; top panel), or increasing concentrations of LOX function-inhibiting antibody ('αLOX'; bottom panel) in the presence of 150ng/ml huLOX. (**D**) Effect of

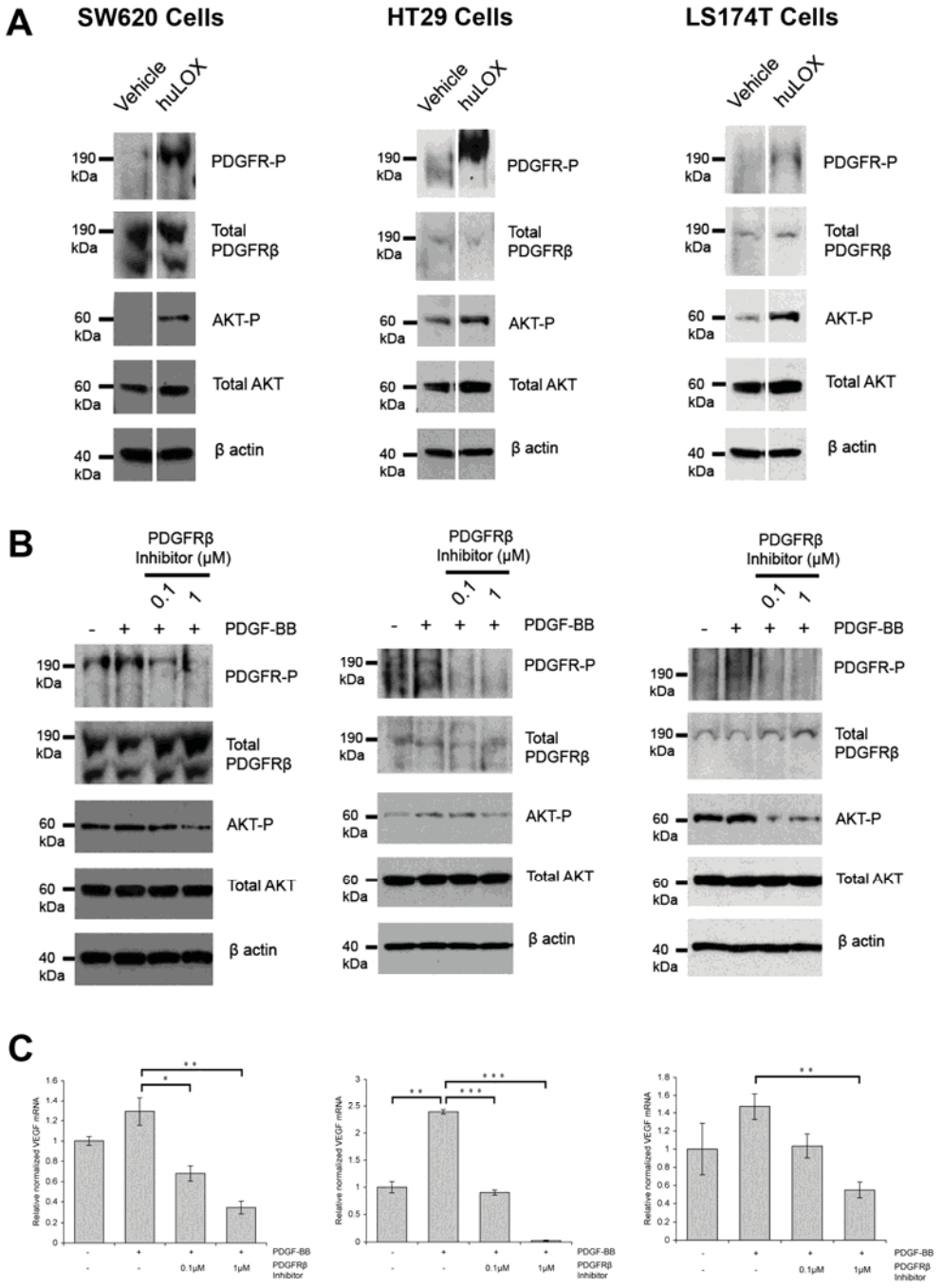
addition of recombinant human LOX ('huLOX') or LOX function-inhibiting antibody ('αLOX') on secretion of VEGF protein in HT29 cells, as determined by qRT-PCR. n = 3 wells per condition. (**E**) Effect of addition of huLOX or αLOX on secretion of VEGF protein in LS174T cells, as determined by qRT-PCR. n = 3 wells per condition. Bars in (**C**), (**D**) and (**E**) represent mean ± SEM. *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$ using the two sided Student's t test.



Supplemental Figure S3

(**A**) Representative immunoblot for phosphorylated Akt(Ser473) ('Akt-P') and total Akt in SW620 cell lysates. CM with low or high LOX levels was added to the cells

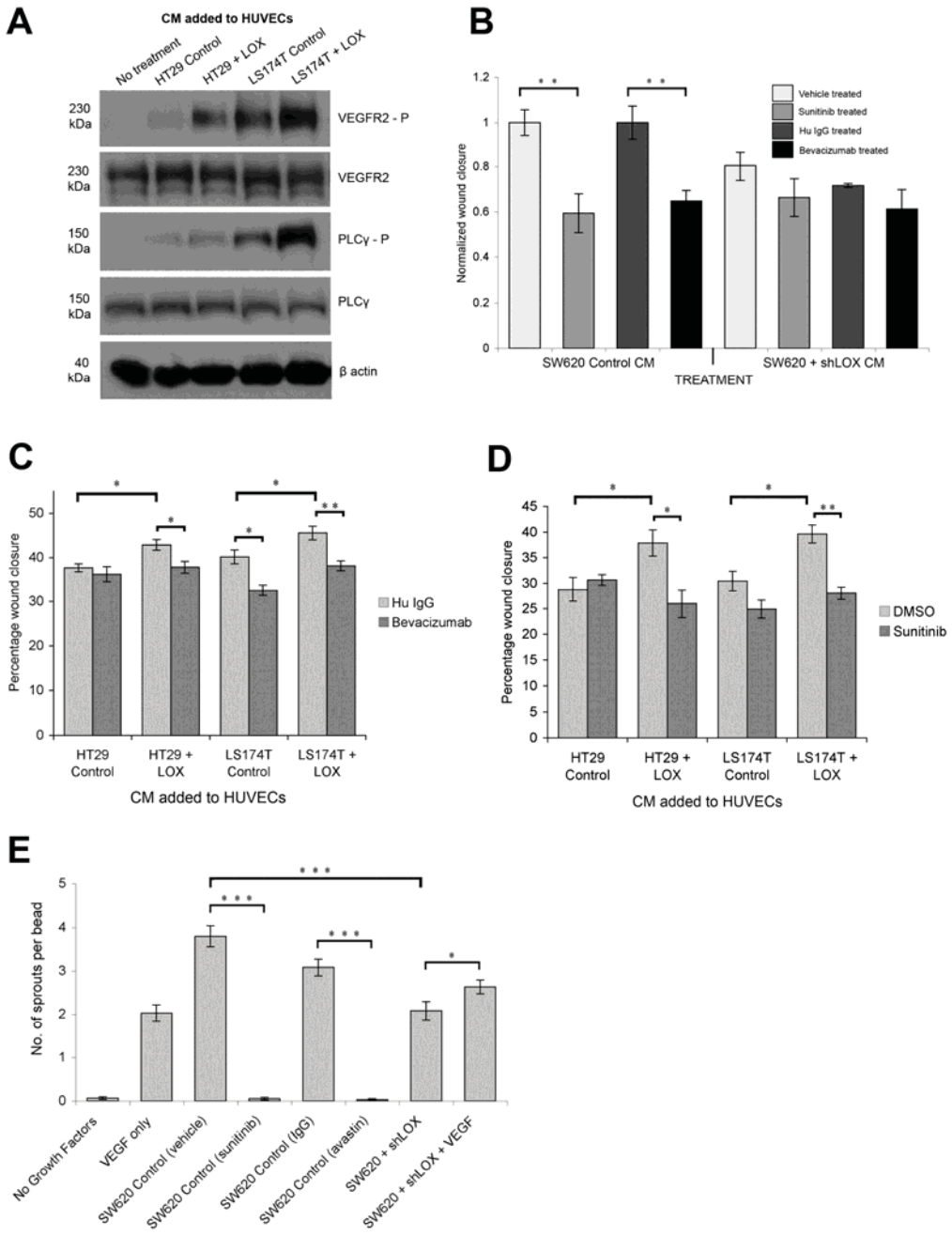
16 hours prior to analysis. β actin was used as a loading control. kDa = kilodalton. (**B**) Representative immunoblot for phosphorylated Akt(Ser473) ('Akt-P') and total Akt in HT29 cell lysates treated with PBS, huLOX, rabbit IgG control ('IgG') or αLOX. β actin was used as a loading control. kDa = kilodalton. (**C**) Representative immunoblot for phosphorylated Akt(Ser473) ('Akt-P') and total Akt in LS174T cell lysates treated with PBS, huLOX, IgG or αLOX. β actin was used as a loading control. kDa = kilodalton. (**D**) Representative immunoblot for phosphorylated Akt(Ser473) ('Akt-P') and total Akt in SW620 tumor lysates treated with IgG or αLOX where indicated. β actin was used as a loading control. kDa = kilodalton. (**E**) Representative immunohistochemical staining of phosphorylated Akt(Ser473) in sections SW620 (left panel), HT29 (centre panel) and LS174T (right panel) subcutaneous tumors grown in nude mice. Phosphorylated Akt(Ser473) is shown in brown, and cell nuclei in blue. Scale bar represents 200μm. (**F**) Representative immunoblot for phosphorylated Akt(Ser473) ('Akt-P') and total Akt in SW620 cell lysates treated with the Akt inhibitor MK-2206. β actin was used as a loading control. kDa = kilodalton. (**G**) Representative immunoblot for phosphorylated Akt(Ser473) ('Akt-P') and total Akt in SW480 (left panel) and SW620 (right panel) cell lysates treated with purified human recombinant LOX ('Hu LOX'), αLOX and/or Akt inhibitor MK-2206. β actin was used as a loading control. kDa = kilodalton. (**H**) Effect of MK-2206 treatment on secretion of VEGF protein in SW620 cells, as determined by ELISA. n = 2 wells per condition. (**I**) Effect of MK-2206 treatment on VEGF mRNA in SW620 cells, as determined by qRT-PCR. n = 3 wells per condition. Bars in (**H**) and (**I**) represent mean ± SEM. *$p < 0.05$ using the two sided Student's t test.



Supplemental Figure S4

(**A**) Representative immunoblot for phosphorylated PDGFRβ(Tyr751) ('PDGFR-P'), total PDGFRβ phosphorylated Akt(Ser473) ('Akt-P') and total Akt in SW620 (left panel), HT29 (centre panel) and LS174T (right panel) cell lysates treated with

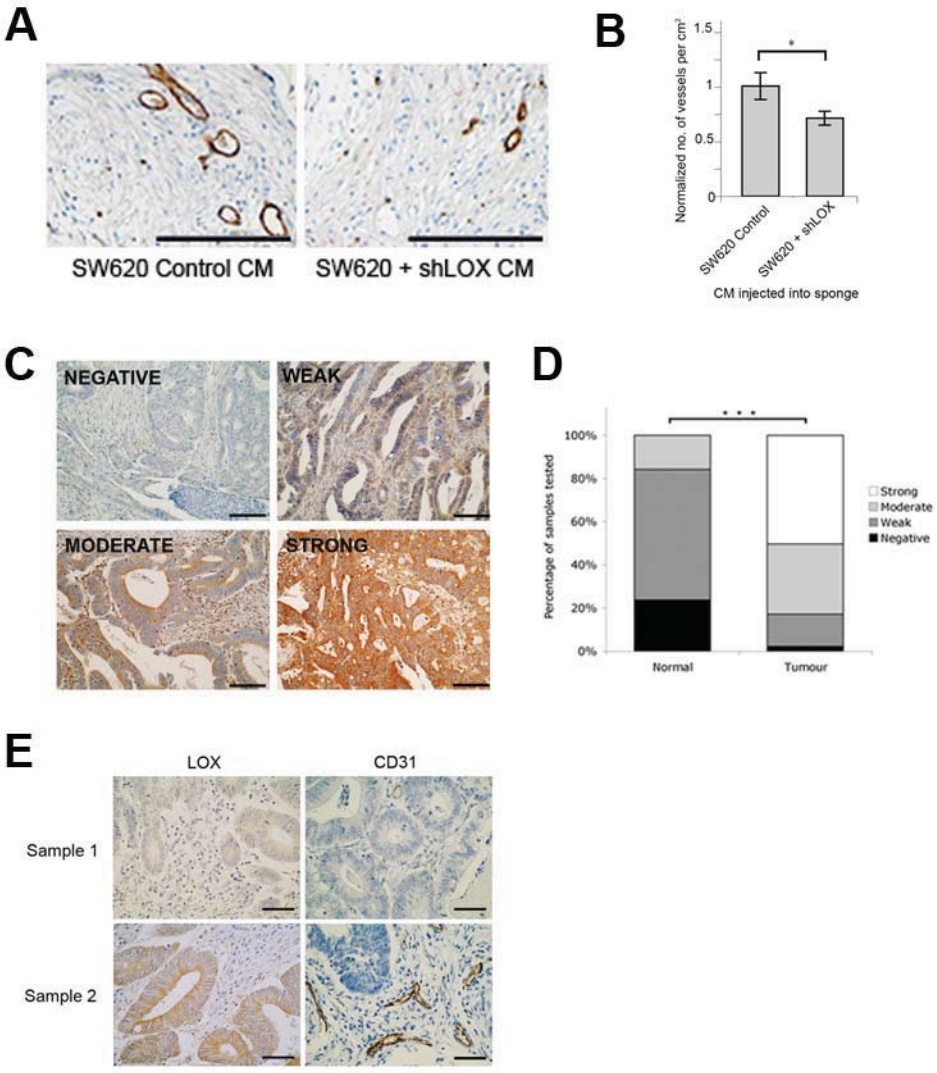
150ng/ml purified human recombinant LOX ('hu LOX') for 10 minutes, 1 hour and 16 hours prior to lysis. β actin was used as a loading control. kDa = kilodalton. (**B**) Representative immunoblot for phosphorylated PDGFRβ(Tyr751) ('PDGFR-P'), total PDGFRβ phosphorylated Akt(Ser473) ('Akt-P') and total Akt in serum-starved SW620 control (left panel), HT29+LOX (centre panel) and LS174T+LOX (right panel) cell lysates pretreated with a PDGFRβ inhibitor for 1 hour then stimulated with 25ng/ml PDGF-BB for 2 minutes. β actin was used as a loading control. kDa = kilodalton. (**C**) Effect of PDGFRβ inhibition on VEGF mRNA in SW620 (left panel), HT29+LOX (centre panel) and LS174T+LOX (right panel) cells, as determined by qRT-PCR. n = 3 wells per condition. Bars represent mean ± SEM. *p < 0.05, **p < 0.01, ***p < 0.001 using the two sided Student's t test.



Supplemental Figure S5

(**A**) Representative immunoblot showing activity of the VEGFR2 signaling pathway in HUVECs upon stimulation with conditioned media ('CM') collected from HT29 or LS174T CRC cells. Levels of phosphorylated VEGFR2(Tyr1175) ('VEGFR2 - P'), VEGFR2, phosphorylated PLC-γ(Tyr783) ('PLC-γ – P') and PLC-γ are shown. β

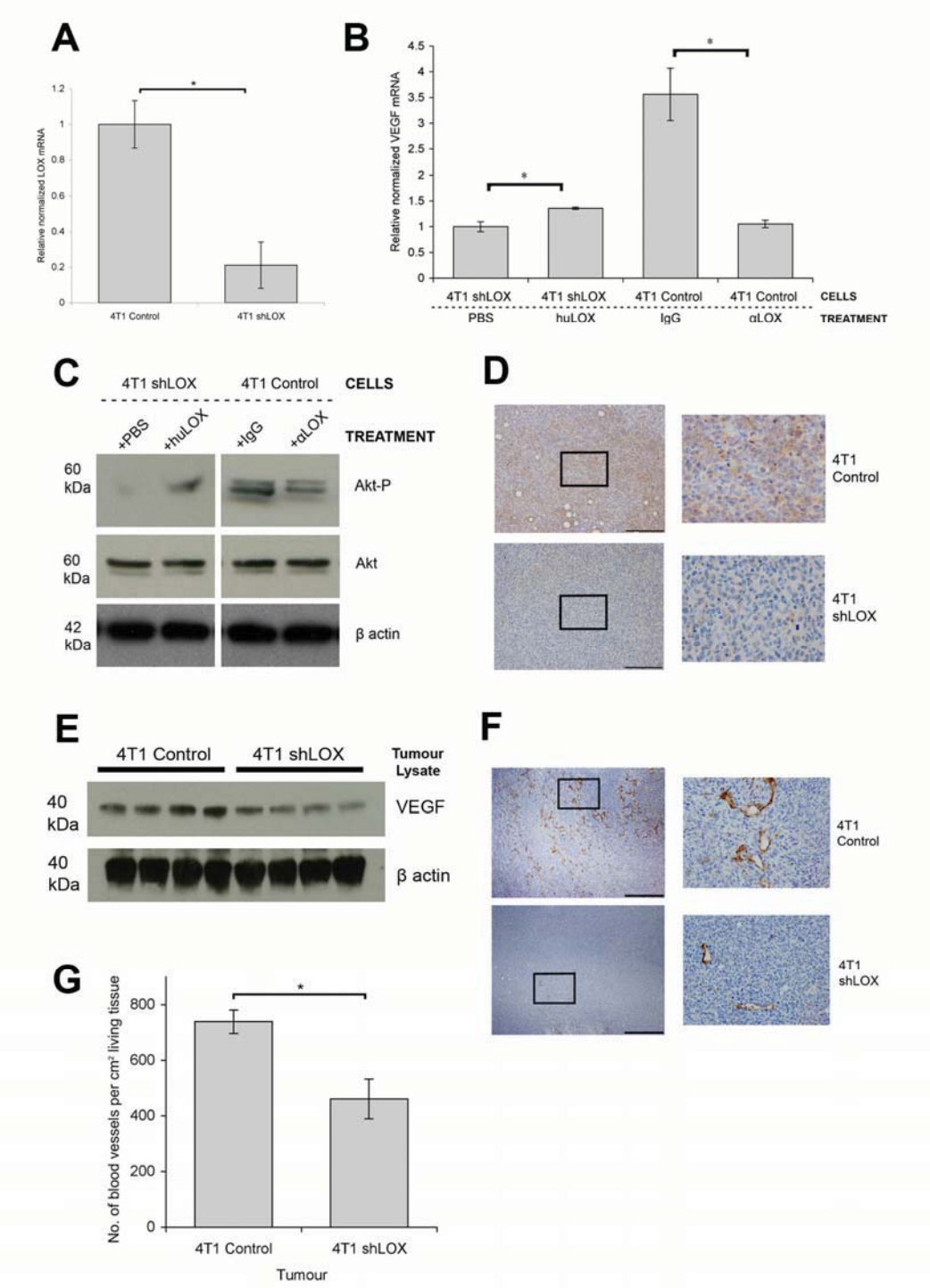
actin was used as a loading control. kDa = kilodalton. (**B**) Quantification of HUVEC migration in the presence of conditioned media ('CM') collected from SW620 CRC cells with manipulated LOX expression. Cells were treated with vehicle, sunitinib (100nM), human IgG control ('IgG', 50μg/ml) or bevacizumab (50μg/ml) where indicated. Measurements of wound area were taken at 0 and 8 hours, and used to calculate percentage wound closure. n = 4 per condition. (**C**) Quantification of HUVEC migration in the presence of conditioned media ('CM') collected from HT29 and LS174T CRC cells with manipulated LOX expression. Cells were treated with human IgG control ('IgG', 50μg/ml) or bevacizumab (50μg/ml) where indicated. Measurements of wound area were taken at 0 and 8 hours, and used to calculate percentage wound closure. n = 4 per condition. (**D**) Quantification of HUVEC migration in the presence of conditioned media ('CM') collected from HT29 and LS174T CRC cells with manipulated LOX expression. Cells were treated with vehicle or sunitinib (100nM) where indicated. Measurements of wound area were taken at 0 and 8 hours, and used to calculate percentage wound closure. n = 4 per condition. (**E**) Quantification of *in vitro* angiogenic sprouting from HUVEC coated beads treated with negative control ('No growth factors'), positive control ('VEGF only') or conditioned media collected from the SW620 cell line. Vehicle, sunitinib (100nM), human IgG control ('IgG', 50μg/ml) or bevacizumab (50μg/ml) were added to the media where indicated. n $\geq$ 2 wells per condition, 15 beads per well. Bars in (**B**), (**C**), (**D**) and (**E**) represent mean ± SEM. *p < 0.05, **p < 0.01, ***p < 0.001 using the two sided Student's t test.



Supplemental Figure S6

(**A**) Representative immunohistochemical staining of endomucin in sections of sponges implanted subcutaneously into mice, and injected three times per week with conditioned media (CM) collected from SW620 control or LOX knockdown ('SW620 + shLOX') cells. Endomucin is shown in brown, and cell nuclei in blue. Scale bar represents 200μm. (**B**) Quantification of blood vessel establishment in sponges implanted subcutaneously into mice, and injected with conditioned media ('CM')

collected from SW620 control or SW620 shLOX cells. Bars represent normalized mean number of blood vessels per cm^2 ± SEM. n = 18 sponges per condition. Data are representative of two independent experimental repeats. *$P < 0.05$ using the two-sided Student's *t* test. (**C**) Representative immunohistochemical staining showing negative, weak, moderate and strong VEGF immunoreactivity. VEGF is shown in brown, and cell nuclei in blue. Scale bar represents 100μm. (**D**) Distribution of VEGF immunoreactivity in a TMA of normal colon tissue (n = 39) and primary CRC tumor samples (n = 497). Samples were scored as 'negative', 'weak', 'moderate' or 'strong', as measured by VEGF immunostaining. ***$P < 0.001$ using the Mann-Whitney U test. (**E**) LOX and CD31 immunohistochemical staining in two representative CRC patient tissues ('Sample 1' and 'Sample 2') taken from the TMA. CD31 and LOX are shown in brown, and cell nuclei in blue. Scale bar represents 50μm. Bars in (**B**) represent mean ± SEM. *$p < 0.05$, ***$p < 0.001$ using the two sided Student's t test.



Supplemental Figure S7

Validation in 4T1 breast cancer model

(**A**) Effect of LOX knockdown on LOX mRNA in 4T1 cells, as determined by qRT-PCR. n = 3 wells per condition. (**B**) Effect of addition of recombinant human LOX

('huLOX') or LOX function inhibiting antibody ('αLOX') on secretion of VEGF protein in 4T1 cells, as determined by qRT-PCR. n = 3 wells per condition. (**C**) Representative immunoblot for phosphorylated Akt(Ser473) ('Akt-P') and total Akt in 4T1 cell lysates treated with the purified huLOX or αLOX. β actin was used as a loading control. kDa = kilodalton. (**D**) Representative immunohistochemical staining of phosphorylated Akt(Ser473) in sections of 4T1 tumors grown in Balb/c mice. Phosphorylated Akt(Ser473) is shown in brown, and cell nuclei in blue. (**E**) Representative immunoblot for VEGF in 4T1 tumor lysates. β actin was used as a loading control. kDa = kilodalton. (**F**) Representative immunohistochemical staining of endomucin in sections of 4T1 tumors grown in Balb/c mice. Endomucin is shown in brown, and cell nuclei in blue. (**G**) Normalized density of endomucin positive blood vessels in 4T1 tumors grown in Balb/c mice. $n \geq 4$ tumors per condition. Bars in (**A**), (**B**) and (**G**) represent mean ± SEM. *$p < 0.05$ using the two sided Student's t test.