Supplementary Table 1. Antibodies Used in This Study

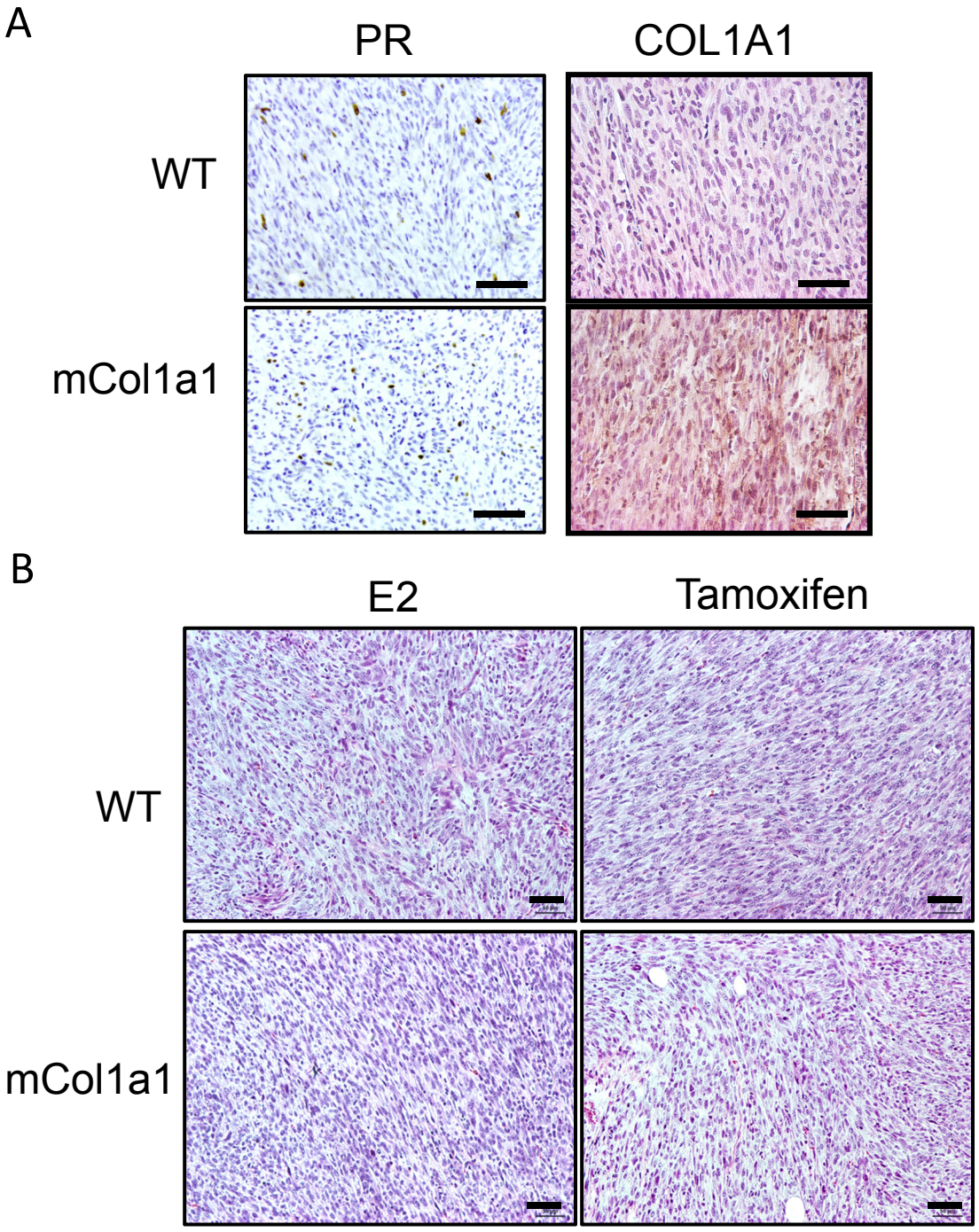
Protein Target	Manufacturer, Catalog No.	Animal Source Mono/ polyclonal	Dilution Used
ERα	Santa Cruz Biotech., sc-542	Rabbit, poly	1:500 (IHC)
PR	Dako, A0098	Rabbit, poly	1:500 (IHC)
Ki-67	Abcam, ab15580	Rabbit, poly	1:750 (IHC)
pS473 AKT	Cell Signaling Tech., 3787	Rabbit, mono	1:50 (IHC)
pS473 AKT	Cell Signaling Tech., 9271	Rabbit, poly	1:1000 (WB)
AKT	Cell Signaling Tech., 9272	Rabbit, poly	1:1000 (WB)
pERK1/2	Cell Signaling Tech., 9101	Rabbit, poly	1:400 (IHC); 1:5000 (WB)
ERK1/2	Cell Signaling Tech., 9102	Rabbit, poly	1:2500 (WB)
PAK1	Cell Signaling Tech., 2602	Rabbit, poly	1:25 (IHC); 1:2000 (WB)
c-JUN	Cell Signaling Tech., 9165	Rabbit, mono	1:400 (IHC)
STAT5A	Santa Cruz Biotech., sc-1081	Rabbit, poly	1:2000 (IHC)
FN1	Abcam, ab23750	Rabbit, poly	1:500 (IF)
POSTN	Abcam, ab14041	Rabbit, poly	1:500 (IF)
COL1A1	Novus, NB600-450	Mouse, mono	1:50 (IHC)

Abbreviations: IF, immunofluorescence; IHC, immunohistochemistry; WB, western blot

Supplementary Table 2. Primer Sequences for RT-PCR

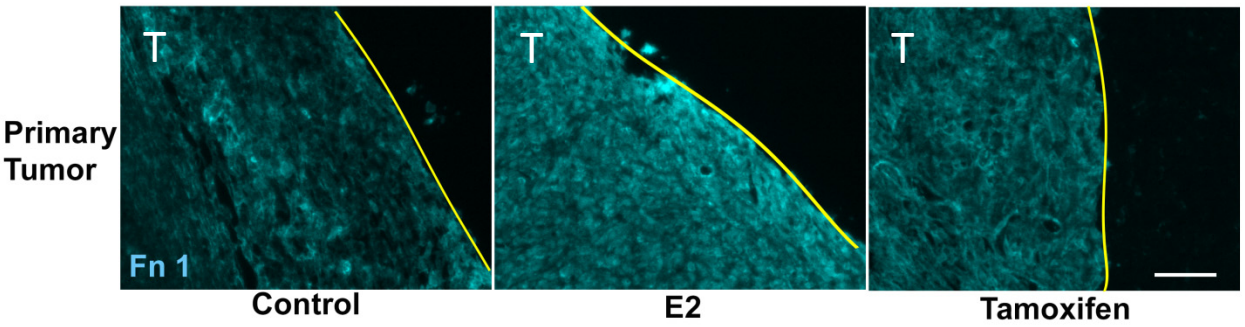
Transcript	Fwd Primer	Rev Primer	Ta (ºC)
18s	5' CGC CGC TAG AGG TGA AAT TCT 3'	5' CGA ACC TCC GAC TTT CGT TCT 3'	60
Col1a1	5' GAC TGG AAG AGC GGA GAG TAC TG 3'	5' CAG GTC TGA CCT GTC TCC ATG TT 3'	60
Cxcl12	5’ CGC GCT CTG CAT CAG TGA C 3’	5’ TCA GAT GCT TGA CGT TGG CT 3’	60
Ccdn1	5’ CAT CAA GTG TGA CCC GGA CTG 3’	5’ CCT CCT CCT CAG TGG CCT TG 3’	65
Fn1	5' CCA GAA CTA CGA TGC CGA TCA 3'	5' TGC GAT ACA TGA CCC CTT CA 3'	60
Fosl1	5’ CGC AAG CTC AGG CAC AGA 3’	5’ AAT GAG GCT GCA CCA TCC A 3’	60
Greb1	5’ CCA CCC CGT GTT GTC TGT AG 3’	5’ CCG CTG AAC ACC ATG TCA GA 3’	60
Lox	5' TGC GCT GCG GAA GAA AAC 3'	5' CGT AGC AGT ACC CTG TGG TCA TAG 3'	62
Ltbp1	5’ CCC TGA CAG CCA CGA ACT TC 3’	5’ AAA TTT GGA GGG CAC TGA CAT T 3’	60
Mmp3	5’ CAG ACT TGT CCC GTT TCC AT 3’	5’ GGT GCT GAC TGC ATC AAA GA 3’	60
Pgr	5’ CAA CCA ACT AGG CGA GAG ACA A 3’	5’ GAA TCA GGG TTA TCT GGT CAT CAA 3’	58
Postn	5’ GGA CCT TGT TTG CAC CAA CC 3’	5’ CGG GTT CGA ATC CCT TTC CA 3’	60
Stat5a	5’ CGA CAG ATG CAA GTG TTG TAT 3’	5’ TCC TGG GGA TTA TCC AAG TCA AT 3’	60
Thbs1	5' CTC AGG CCT GTC TGT AAA GGT 3'	5' ATC TTT CCA GCC GAT GTG GC 3'	60
Thbs2	5' ACC CCA AAA ACA TTG GCT GG 3'	5' ACC AGC GTA GGT TTG GTC AT 3'	60
Tgfb1	5’ ACT GGA GTT GTA CGG CAG TG 3’	5’ GTG AGC GCT GAA TCG AAA GC 3’	60
Tnc	5' GGA TTG GTG TTT CTG CTG TCA A 3'	5' CAG AAA AAC GTC AGA CTG TCT TGT G 3'	58

Supplementary Figure 1



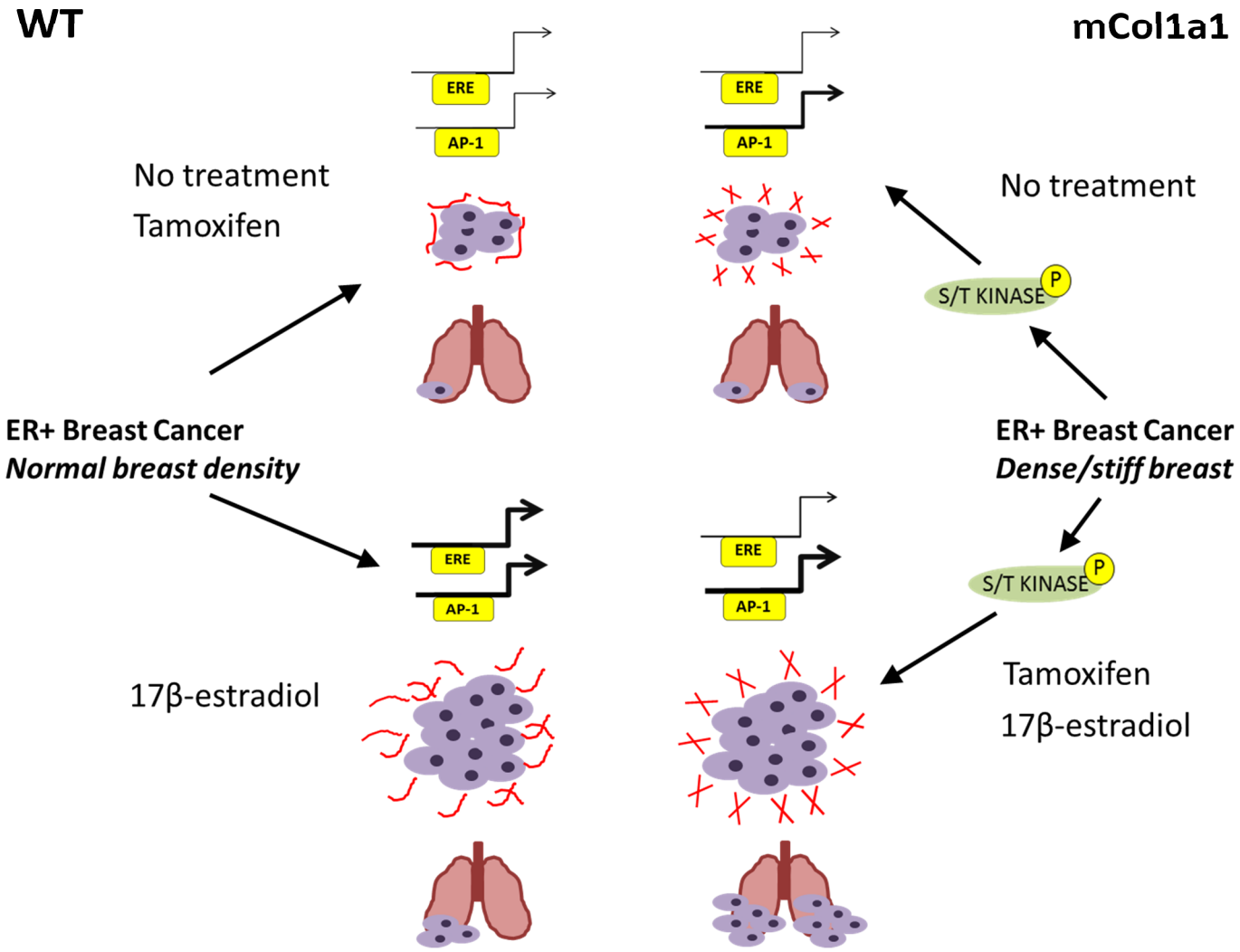
Suppl. Fig. 1. **a** Left**,** Mammary tumors express relatively low levels of progesterone receptor (PR), which is not altered by the mCol1a1 environment. Right, higher levels of COL1A1 protein were observed in the tumors of mCol1a1 mice. **b** Mammary tumor spindle cell morphology is not affected by manipulation of estrogen activity or the mCol1a1 environment. Hematoxylin and eosin (H&E) stained tumors treated with 17β-estradiol (E2) or tamoxifen. **a, b**, Original magnifications, x200; scale bars, 50 μm.

Supplementary Figure 2



Suppl. Fig. 2. Mammary tumors (T) from E2-treated mice express more FN1 (immunofluorescence, pseudo-colored), especially near the tumor boundary (yellow line). Representative images. Original magnifications, x200; scale bars, 50 µm.

Supplementary Figure 3



Suppl. Fig. 3. A dense/stiff ECM enables tamoxifen to drive growth of ER+ primary and metastatic tumors, and enhances 17β-estradiol-driven growth of pulmonary metastases. Diagrammatic summary.
Dense/stiff ECM (↑) increases expression/phosphorylation of kinases upstream of AP-1 factors, which modestly increases AP-1 activity in the absence of supplemental ER ligands (indicated by the weight of the transcriptional arrow). 17β-estradiol drives tumor growth ( ) and both ERE- and AP-1-containing promoters equally, irrespective of the ECM environment. However, dense/ stiff ECM enables tamoxifen to drive tumor proliferation and activate AP-1- but not ERE-regulated target genes. These changes in the primary tumor are associated with significant increases in pulmonary metastatic burden.

Further, E2 modifies the ECM ( ) surrounding primary and metastatic tumors in WT females, underscoring the reciprocity of hormone and ECM interactions in the environments of the primary and secondary lesions in ER+ disease.